



# Abstract Book



## 14<sup>th</sup> International Conference on Thalassaemia and Other Haemoglobinopathies & 16<sup>th</sup> TIF Conference for Patients and Parents

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**17-19 November 2017**

Grand Hotel Palace, Thessaloniki, Greece



THALASSAEMIA  
INTERNATIONAL  
FEDERATION



Greek Thalassaemia Association



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# Speaker Abstracts <sup>[1][2]</sup>

**Title:** **Haemoglobinopathies Care & Cure: Have we reached the end?**

**Presenter:** John Porter

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## ABSTRACT

Recent years have seen accelerating advances in the treatment, monitoring and potential cures for haemoglobin disorders, as the interaction between basic science, pharmaceutical research, and practical medicine intensifies. In order to appreciate how close to the end we may have reached, it is helpful to consider the journey thus far.

For thalassaemia syndromes, advances with non-curative treatment began with the establishment of the principles of blood transfusion and their application in the 1950s both to treat anaemia and suppress erythropoietic expansion. The consequences of transfusional iron overload soon became a problem however, with patients dying in their late teens and early 20s, typically with cardiomyopathy. The introduction of desferrioxamine infusions in the 1970s, led to gradual improvement in outcome and the subsequent introduction and licensing of orally active chelation has contributed to improved treatment adherence and improved survival. Morbidity from iron overload, particularly hypogonadotropic hypogonadism remains a serious issue and emergence of new pathologies in older patients, such as in the liver, is a cause for concern. Curative treatment with allogeneic stem cell transplantation was introduced in the 1980s but is only available to a minority of patients and is still associated with significant morbidity and mortality. Novel approaches aimed at decreasing transfusion requirements by improving the efficiency of erythropoiesis, such as with activin receptor traps, may prove useful in both transfusion dependent and non-transfusion dependent thalassaemias. Gene therapy is now a reality for a small number of patients and has the potential for application to many patients in whom allogeneic transplant was precluded by lack of a suitable donors, or was too risky for other reasons such increasing as age.

For sickle cell disorders, advances have included the setting up of specialist clinics, pneumococcal septicaemia prevention programs, the application of blood transfusion for the prevention and treatment of disease complications, the use of hydroxyurea for prevention of painful crises and chest syndrome and allogeneic transplantation for carefully selected patients. New pharmacological agents with novel mechanisms of action are being evaluated at a hitherto unprecedented rate. However thus far, the impact of these advances on survival and quality of life in patients as a whole often lags somewhat behind those of thalassaemia. Disease prevention is a key element to management of both sickle and thalassaemia syndromes but implementation has been highly variable both geographically and even between these conditions at a local level. Prevention of births with sickle cell disorders have been less effective than for thalassaemia, even in countries such as the UK which share the same prevention programs for these conditions. The perceived variability and unpredictability of sickle cell disease is part of the reason for this: if all patients had a uniformly fatal outcome without transfusion, blood transfusion would be more uniformly applied, as with TDT, from an early age with perhaps better overall quality of life and survival.

In order approach "the end," advances in therapy will need to be more affordable and deliverable to populations where the conditions are most prevalent. It is anticipated in the next decade that blood transfusion safety will improve, the cost of chelation will fall, the safety and applicability of allogeneic stem cell transplantation will increase, and with further scientific advances such as CRISPR technology, the cost of gene therapy will fall. In the meantime, to paraphrase a well-known quotation, " *this is not the end, it is not even at the beginning of the end, but it is perhaps the end of the beginning.*"

<sup>[1]</sup> Arranged in order of appearance in Conference Programme

<sup>[2]</sup> Abstracts received by 20 October 2017 have been included

**Title: Migration: The aftershocks to the provision of healthcare****Presenter:** Stephan Lobitz**Affiliation:** Paediatrician, Clinics of the City of Cologne, Pediatric Hospital Amsterdamer, Division of Haematology, Cologne, Germany**Email:** LobitzS@kliniken-koeln.de

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**ABSTRACT**

Migration is the “movement of people to a new area or country in order to find work or better living conditions” (Oxford dictionary). The term “migration” summarizes forced, reluctant and voluntary migration. Voluntary migration is a comparatively constant event. But reluctant and, in particular, forced migration have been subject to substantial change during the last years. At the end of 2016, more than 17.2 million refugees (+ 5.3 million Palestinians) were on the run outside their home countries. 55% of them fled from Syria (5.5 million), Afghanistan (2.5 million) and South Sudan (1.4 million), respectively. The top hosting countries were not, in fact, the Southern and Western European or North American, but some of the poorest countries in the world. With the refugees from countries where disorders of haemoglobin are very prevalent, the number of patients in the host countries significantly increased within a very short period of time. The extraordinary circumstances required rapid rethinking and adaptation and, therefore, did not only pose a big challenge but, in some countries, also a big chance to improve care for patients suffering from hemoglobinopathies.

Although there are certainly several trouble spots in the world, the Middle East crisis was and still is currently the most prominent one. There is a significant prevalence of thalassemia and sickle cell disease among the Syrian and Iraqi population and since the chronically ill were presumably those who left their home countries first, there was a dramatic increase in the prevalence of thalassaemia and sickle cell disease in the host countries. Many patients fled to Western and Northern European countries where hemoglobinopathies were very rare and where the healthcare systems were unable to cope with this sudden increase in patient numbers and complications. For example, disease characteristics were much more pronounced than doctors were used to. Complications occurred that physicians only knew from textbooks. In addition, virtually all families needed significant help in psychosocial matters and many refugees were severely traumatized.

**Methods**

In addition to an extensive review of the literature, international experts for haemoglobin disorders were contacted via email and asked to take part in an online survey. They were asked if and how relevant migration is for their clinical practise, if they did observe changes in the number of patients during the last five years and if and how they responded to these changes.

**Results**

The results of this survey are pending and will be presented and discussed at the TIF conference.



**Title: New Challenges in diagnosis of haemoglobinopathies: Migration of Populations**

**Presenter:** John Old

**Other authors:** Shirley Henderson, Adele Timbs, Janice McCarthy, Alice Gallienne, Melanie Proven, Michelle Rugless, Herminio Lopez, Jennifer Eglinton, Dariusz Dziedzic, Matthew Beardsall, and Mohamed SM Khalila

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## **ABSTRACT**

The current influx of economic migrants and asylum seekers from countries with a high prevalence of haemoglobinopathies creates new challenges for health care systems and diagnostic laboratories. The migration of carriers introduces new and novel haemoglobinopathy mutations to the diagnostic repertoire of a laboratory, often creating new pressures to improve and update the carrier screening technology and diagnostic scope. For antenatal screening programmes, the marriage of partners from different ethnic groups can lead to the risk of compound heterozygote children being born novel mutation combinations, creating problems in the provision of accurate advice regarding the expected phenotype of the thalassaemia or haemoglobinopathy disorder. In the UK, the impact of immigration required the National Haemoglobinopathy Reference laboratory to change the strategy and techniques used for the molecular diagnosis of thalassaemia and the haemoglobinopathies. In 2005, due to the increasingly large range of  $\beta$ -thalassaemia mutations that needed to be diagnosed, the laboratory switched from a three-step screening procedure using ARMS-PCR to a simpler but more expensive one-step strategy of DNA sequencing of the beta and alpha globin genes for all referrals. After ten years of employing this strategy, a further 57 novel thalassaemia and haemoglobinopathy alleles were discovered (11 new  $\beta$ -chain variants, 15  $\alpha$ -chain variants, 19  $\beta$ -thalassaemia mutations and 12  $\alpha^+$ -thalassaemia mutations), increasing further the extremely heterogeneous spectrum of globin gene mutations in the UK population.

**Title: PIGI ZOIS: Pioneering with credibility****Presenter:** Vasilios Perifanis<sup>1</sup>**Other authors:** , Ourania Pantelidou<sup>2</sup>, Nousiou Charikleia<sup>3</sup>, Miranda Athanassiou-Metaxa<sup>4</sup>, Electra Kolokytha-Grammatikopoulou<sup>5</sup>**Affiliation:**<sup>1</sup> Assistant Professor of Hematology, School of Medicine, Faculty of Health Sciences, Aristotle University, Secretary General of PIGI ZOIS,<sup>2</sup> Professor of Endodontology, School of Dentistry, Faculty of Health Sciences, Aristotle University, Vice-president of PIGI ZOIS,<sup>3</sup> Accountant, Treasurer of PIGI ZOIS,<sup>4</sup> Professor Emeritus of Pediatrics, Honorary President of PIGI ZOIS,<sup>5</sup> Dentist, President of PIGI ZOIS, Thessaloniki, Greece.**Email:** bperifanis@yahoo.gr**ABSTRACT**

Annual transfusion requirements in Greece exceed 600000 blood units and nearly 20% of them are used for the transfusion of 3.000 patients with Thalassemia. Thalassemia patients need to be transfused properly at the right time and with safe, fresh blood. PIGI ZOIS is a nonprofit organization that tries to improve the lives of patients through providing proper voluntary blood units to patients and enhancing the Voluntary Blood Donation policy, in Thessaloniki area, which has 350 patients. The mission of PIGI ZOIS is to organize and manage almost 7.000 volunteers to donate their blood for the thalassaemic patients. This is achieved by using a phone call reminder, so that the blood volunteer will donate his/her blood to a compatible young patient. All matches are done by a specialized computer program. PIGI ZOIS has donated 90.000 blood units over a period of twenty years. PIGI ZOIS also aims to raise awareness of Thalassemia through an educational program with children in primary schools, with the ultimate goal of encouraging the children to become donors when they reach adulthood. PIGI ZOIS also runs informative campaigns to the public about disease prevention and the general promotion of voluntary blood donation.



## Title: **International Initiatives in Thalassaemia - Bait-UI-Mal, Pakistan**

**Presenter:** Barrister Abid Waheed Shaikh

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### ABSTRACT

The factors determining the health behaviours may be seen in various contexts: physical, socio-economic, cultural and political. So the utilization of a health care system, public or private, formal or non-formal, may depend on socio-demographic factors, social structures, level of education, cultural beliefs and practices, gender discrimination, status of women, economic and political systems environmental conditions, and the disease pattern and health care system itself. Policy makers need to understand the drivers of health seeking behaviour of the population in an increasingly pluralistic health care system. Also a more concerted effort is required for designing behavioural health promotion campaigns through inter-sectoral collaboration focusing more on disadvantaged segments of the population.

Thalassaemia is the most prevalent genetic blood disorder in Pakistan. It is estimated that there are 8-10 million Thalassaemia Minor cases in the country with a prevalence of 5-6%. It is also estimated that about 100,000 patients suffering from Thalassaemia Major exist in Pakistan and every year this number is increasing by about 6,000. Pakistan is witnessing this large increase in thalassaemic patients due to a lack of proper coordinated, nationwide efforts to contain the inherited form of anaemia, and general public awareness.

Different research studies and diagnosis services are carried out in Pakistan on Thalassaemia prevalence. One such service for prenatal diagnosis of  $\beta$ -thalassaemia was introduced in Pakistan in May 1994. Two renowned Islamic scholars, consulted before the service was introduced, ruled that a pregnancy can be terminated if the fetus is affected by a serious genetic disorder, and if termination is before 120 days (17 weeks) of gestation. During the first 3½ years of the service 300 couples requested the test. Almost all the couples had been informed by their treating doctors. Most diagnoses were made between 10 and 16 weeks of gestation, and only 15 (5%) were reached after the 16th week. DNA analysis was by the amplification refractory mutation system (ARMS). A multiplex ARMS was developed in which three primer combinations identified the mutations in 91.5% of the couples. In 13 couples (4.3%) linkage analysis was required for the fetal diagnosis. In 47/53 (88.7%) women carrying an affected fetus the pregnancy was terminated. In six cases it was declined principally on religious grounds. Postnatal confirmation of the prenatal diagnosis was possible in 117 unaffected children. One year after the start of the service, interviews with 141 couples with an affected child showed that 72% knew of the availability of prenatal diagnosis. Thirty-two of the informed couples had had a pregnancy, but only 18 (56%) used prenatal diagnosis. The main reasons for non-utilization of prenatal diagnosis were the cost of the test and fear of undergoing the test, though some gave no clear explanation. This study demonstrates that prenatal diagnosis is feasible and acceptable in a Muslim country such as Pakistan (Shoaib, Salim 2000).

Another study on Pakistan characterized 1216 beta-thalassaemia alleles from the five major ethnic groups of the country. The complete spectrum comprised 19 different mutations. There are important ethnic and regional differences in the prevalence of mutations. The five most common mutations, IVSI-5 (G-C) (37.3%), Fr 8-9 (+G) (25.9%), del 619 (7.0%), Fr 41-42 (-TTCT) (6.7%) and IVSI-1 (G-T) (5.4%), constitute 82.3% of the total. Fr 8-9 (+G) is the most common mutation in Northern Pakistan (41.3%), whereas IVSI-5 (G-C) is the most frequent mutation in Southern Pakistan (52.2%). Six subjects with transfusion-dependent thalassaemia major showed only a single mutant allele. One subject with transfusion-dependent thalassaemia major showed a novel 17 bp deletion involving Cd126-131. Our findings provide a comprehensive basis for carrying out prenatal diagnosis of thalassaemia in a geographical area where it is found in high frequency (Ahmad, Saleem 1996)

### BRIEF COUNTRY PROFILE OF PAKISTAN

The Indus Valley civilization, one of the oldest in the world and dating back at least 5,000 years, spread over much of what is presently Pakistan. During the second millennium B.C, remnants of this culture fused with the migrating Indo-Aryan peoples. The area underwent successive invasions in subsequent centuries from the Persians, Greeks, Scythians, Arabs (who brought Islam), Afghans, and Turks. The Mughal Empire flourished in the 16th and 17th centuries; the British came to dominate the region in the 18th century.

The separation in 1947 of British India into the Muslim State of Pakistan and largely Hindu India.

**SOUTH ASIA**

Total Area: 796,095 sq km

Land: 770,875 sq km

Water: 25,220 sq km

Population: 208 million (2017)

Country comparison to the world: 36

Land boundaries: Bordering the Arabian Sea, between India on the East and Iran and Afghanistan on the West and China in the North

Total bordering Area: 6,774 km, with Afghanistan 2,430 km, with China 523 km, with India 2,912 km and with Iran 909 km, Coast line 1,046 km

It also controls Khyber Pass and Bolan Pass, traditional invasion routes between Central Asia and the Indian Subcontinent



## Title: **Optimal Blood Transfusion Therapy in Haemoglobinopathies**

**Presenter:** John Porter

**Affiliation:** Professor of Haematology, Head of the Thalassaemia and Sickle Cell Unit, Haematology, Department, University College London, Joint Red Cell Unit, UCLH and Whittington Hospitals, UK

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### ABSTRACT

For reasons of time, this short talk will be confined to the optimal frequency, timing, indications and dosing of blood transfusion. Blood transfusion protocols in thalassaemia syndromes are more widely agreed [1] than for sickle disorders but questions still remain about optimal Hb levels, timing and frequency. In transfusion thalassaemia thalassaemias (TDT), the purpose of blood transfusion is to maximise quality of life by correcting anaemia and suppressing ineffective erythropoiesis, whilst minimising the complications of the transfusion itself. Under-transfusion will limit growth and physical activity while increasing intramedullary and extra-medullary erythroid expansion. Over transfusion may cause unnecessary iron loading and increased risk of extra-hepatic iron deposition however. Although guidelines imply a 'one size fits all' approach to transfusion, in reality this is not the case. Indeed a flexible approach crafted to the patient's individual requirements and to the local availability of safe blood products is needed for optimal outcomes. For example in HbE $\beta$  thalassaemias, the right shifted oxygen dissociation curve tends to lead to better oxygen delivery per gram of Hb than in  $\beta$  thalassaemia intermedia with high Hb F. Patients with E $\beta$ thal therefore tend to tolerate lower Hb values than  $\beta$  thalassaemia intermedia. Guidelines aim to balance the benefits of oxygenation and suppression of extra-medullary expansion with those of excessive iron accumulation from over-transfusion. In an Italian TDT population, this balance was optimised with pre-transfusion values of 9.5-10.5g/dl [2]. However this may not be universally optimal because of different levels of endogenous erythropoiesis with different genotypes in different populations. Recent work by our group [3] suggests that patients with higher levels of endogenous erythropoiesis, marked by higher levels of soluble transferrin receptors, are at significantly lower risk of cardiac iron deposition than in those where endogenous erythropoiesis is less active, as would be the case in transfusion regimes achieving higher levels of pre-transfusion Hb.

In sickle cell disorders, the variability in the phenotype between patients and also within a single patient at any given time means that the need for transfusion also varies. A consideration in sickle disorders, not usually applicable to thalassaemia syndromes, is that of exchange transfusion versus simple top up transfusion. Exchanges have the advantages of lower iron loading rates and more rapid lowering of HbS%. Disadvantages of exchange transfusion are of increased exposure to blood products with inherent increased risk of allo-immunisation or infection, requirement for better venous access for adequate blood flow, and requirements for team of operators capable of performing either manual or automated apheresis, often at short notice. Some indications for transfusion in sickle disorders are backed up by randomised controlled data, such as for primary and secondary stroke prevention, or prophylaxis of sickle related complications for high-risk operations. Others are widely practiced as standard of care without randomised data, such as treatment of acute sickle chest syndrome. Other indications for transfusion, not backed up by randomised studies, but still widely practiced in selected cases, include the management of pregnancy, leg ulceration or priapism and repeated vaso-occlusive crises. Allo-immunisation is more common in sickle patients than in thalassaemia disorders and hyper-haemolysis is a rare but growing serious problem in sickle disorders. It is arguable that increased use of transfusion early in life, is indicated to decrease silent stroke rates and that early exposure to blood will decrease red cell allo-immunisation rates.

- [1] Cappellini, M. D., Cohen, A., Porter, J., Taher, A., Viprakasit, V. TIF Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT) Nicosia (CY) (2014)
- [2] Cazzola M et al. . A moderate transfusion regimen may reduce iron loading in beta- thalassaemia major without producing excessive expansion of erythropoiesis. *Transfusion*;37:135-40 (1997).
- [3] Garbowski et Residual erythropoiesis protects against myocardial hemosiderosis in transfusion-dependent thalassaemia by lowering labile plasma iron via transient generation of apotransferrin *Haematologica* 102(10) 1640-1649 (2017)
- [4] De Baun et al, Controlled trial of transfusions for silent cerebral infarcts in sickle cell anemia *N Engl J Med*; 371:699-710. (2014)

**Title: Endocrine complications****Presenter:** Vincenzo de Sanctis**Affiliation:** Paediatric Endocrinologist, Paediatric & Adolescent Outpatient Clinic, Quisisana Hospital, Ferrara, Italy**Email:** vdesanctis@libero.it**ABSTRACT**

More than five decades ago, thalassemia major (TM) was fatal in the first decade of life. This poor prognosis changed since the survival rates started to increase progressively thanks to the implementation of continuous and significant improvement of diagnostic and therapeutic methods, consisting mainly of an intensive transfusion program combined with chelation therapy and imaging methods. [1-4]

Regular red blood cell (RBC) transfusions eliminate the complications of anemia, compensatory bone marrow expansion, bone changes and splenomegaly, restore the physiological growth throughout childhood and extend survival. The most serious disadvantage of life-saving transfusions is the inexorable accumulation of iron within tissues. Iron is physiologically stored intracellularly in the form of ferritin, a protein whose synthesis is induced upon the influx of iron. When the storage capacity of ferritin is exceeded, pathological quantities of metabolically active iron are released intracellularly in the form of hemosiderin and free iron within an expanded labile pool. This metabolically active iron catalyzes the formation of free radicals, which damage membrane lipids and other macromolecules, leading to cell death and eventually organ failure. Other factors contributing to the variability of cellular iron overload are: a) the cell surface transferrin receptors and the capacity of the cells to deploy defence mechanisms against inorganic iron; b) individual susceptibility to iron toxic effect; c) the development of organ(s) damage secondary to persisting severe iron overload in the years preceding iron chelation therapy; and d) liver disorders, chronic hypoxia and associated endocrine complications. [1-3]

Multi-transfused thalassemia major (TM) patients frequently develop severe endocrine complications mainly due to iron overload, anemia, and chronic liver disease, which require prompt diagnosis, treatment and close follow-up by specialists. [4]

- [1] De Sanctis V, Elsedfy H, Soliman AT, Elhakim IZ, Soliman NA, Elalaily R, Kattamis C. Endocrine profile of  $\beta$ -thalassemia major patients followed from childhood to advanced adulthood in a tertiary care center. *Indian J Endocrinol Metab.* 2016;20:451-459
- [2] De Sanctis V, Elsedfy H, Soliman AT, Elhakim IZ, Kattamis C, Soliman NA, Elalaily R. Clinical and Biochemical Data of Adult Thalassemia Major patients (TM) with Multiple Endocrine Complications (MEC) versus TM Patients with Normal Endocrine Functions: A long-term Retrospective Study (40 years) in a Tertiary Care Center in Italy. *Mediterr J Hematol Infect Dis.* 2016 Apr 12;8(1):e2016022.
- [3] De Sanctis V, Soliman AT, Candini G, Elsedfy H. The recommendation of the International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescent Medicine for the assessment of growth hormone secretion in thalassemia. *Indian J Endocrinol Metab.* 2015;19:306-307.
- [4] Tiosano D, Hochberg Z. Endocrine complications of thalassemia. *J Endocrinol Invest.* 2001;24:716-723.



**Title: National policies in ensuring access to quality & safety of drugs: A challenge or a prerequisite**

**Presenter:** Mahmoud Hadipour Dehshal<sup>1</sup>

**Other authors:** Tabrizi Namini M.<sup>2</sup>

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## **ABSTRACT**

Access to the essential medicines is an important challenge in the developing countries. To have access to the quality and affordable medicines, the pharmaceutical decision makers try different strategies. The production of generic and copy medicines is one of the strategies that if adopted based on the recognized standards and norms can be effective in raising the health status in the developing countries. However, the regulation enfeeblement has somewhat impaired the quality of generic and copy medicines and harmed the health life of consumers. Here we aim to reflect over the role of different beneficiaries including international organizations, governments, pharmaceutical companies, and NGOs in ensuring the feasible and sustainable access of citizens to the essential medicines. We also aim to highlight the importance of the patient status in the enhancement of the medical delivery.

**Title: Adherence to Treatment: Doctor vs Patient Perspective****Presenters:** Farrukh Shah<sup>1</sup>, Georgios Kaltsounis<sup>2</sup>**Affiliation:**<sup>1</sup> Department of Haematology, Whittington Hospital, London<sup>2</sup> Blood Bank Department, AHEPA University Hospital of Thessaloniki**Email:** farrukh.shah@nhs.net; gkaltsoux@yahoo.gr

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**ABSTRACT**

It has been demonstrated over time that patients with haemoglobinopathies who exhibit a high level of compliance to proper therapy benefit not only from higher life expectancy but also from significantly better quality of life. The treatment of thalassaemia consists of blood transfusions and iron chelation therapy. Managing any complications due to iron overload, performing all necessary clinical and laboratory examinations and dealing effectively with psychological issues are also very important. Blood transfusion scheme must be designed by the treating physician according to the patient's clinical needs. Chelation therapy should be aimed at selecting the right medication and the right dose. Examinations should be as organized as possible, and the management of complications depends significantly on cooperation with experienced specialists in each respective field. Ultimately, effectiveness of treatment and patient's psychological well-being (acceptance of the disease and positive attitude) are the most decisive factors, as they seem to be connected to adherence through a mechanism of positive feedback. Hence, professional psychological support should be part of multidisciplinary care. Difference of point of view between doctor and patient can often be the reason behind misinterpretations or misunderstandings.

**Title: Osteoporosis in Thalassaemia****Presenter:** Ersi Voskaridou<sup>1</sup>**Other authors:** Maria Dimopoulou<sup>1</sup>, Evangelos Terpos<sup>2</sup>**Affiliation:**<sup>1</sup> Thalassaemia and Sickle Cell Disease Centre, "Laiko" General Hospital, Athens<sup>2</sup> Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece**Email:** ersi.voskaridou@gmail.com

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**ABSTRACT**

Osteoporosis is a prominent cause of morbidity in patients with thalassaemia major (TM) with a complex pathophysiology. Patients with TM and osteoporosis have elevated markers of bone resorption. This increased osteoclast activity seems to be at least partially due to an imbalance in the receptor–activator of nuclear factor-kappa B ligand (RANKL)/osteoprotegerin (OPG) system, which is of great importance for the regulation of osteoclast differentiation and function. Denosumab is a fully human monoclonal antibody that binds to RANKL and thereby inhibits the activation of osteoclasts by RANKL. By blocking RANKL, denosumab inhibits osteoclast formation, function and survival, thereby decreasing bone resorption and increasing bone mass in postmenopausal women and patients with thalassaemia-induced osteoporosis.



**Title: Quality of Life: Transfusion Dependent Thalassemia vs Non-Transfusion Dependent Thalassemia**

**Presenter:** Mehran Karimi

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**ABSTRACT**

Although the improvements in the treatment and management of thalassemia patients in new years lead to the improved survival and quality of life (QOL) in this group of patients, QOL is still is an important dimension of care in thalassemic patients [1]. WHO defines QOL as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns” [2]. Thalassemia is a chronic disease needs life-long care with multiple physical, mental and social complications that affect QOL in patients. The most important factors which affect QOL in thalassemia are: effects of the disease on family, skeletal and face changes, frequent blood transfusion and drug infusion, sexual impairment and infertility, heart and liver disease as well as endocrine disorders, anxiety and low life expectancy [3].

[1] Gollo G, Savioli G, Balocco M, Venturino C, Boeri E, Costantini M, Forni GL. Changes in the quality of life of people with thalassemia major between 2001 and 2009. *Patient Prefer Adherence*. 2013;7:231-6.

[2] <http://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/>

[3] Telfer P, Constantinidou G, Andreou P, Christou S, Modell B, Angastiniotis M. Quality of life in thalassemia. *Ann NY Acad Sci*. 2005;1054:273-82.

**Title: Let's Talk About Thal: How Communication Can Improve Quality of Life****Presenter:** Laurice M. Levine**Affiliation:** Thalassemia Patient/Patient Advocate, Los Angeles, USA**Email:** LLevine430@aol.com

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**ABSTRACT****Background**

In many parts of the world, research, improved technology, and better medicine have enabled people with thalassemia to live longer. Due to global disparity in healthcare, in areas of the world where thalassemia is most prevalent, the mortality rates are high, and often, patients do not survive past adolescence.

Each stage of life holds different challenges for people with thalassemia, and if patients are fortunate enough to reach adulthood, then they are faced with a new set of challenges uncommon to pediatric patients. Providers, who have dedicated their careers to improving care, now must work toward helping patients achieve a high quality of adult life by addressing such struggles. However, there is one topic that affects patients and providers universally at every stage of life—implementation of the concept can be easy, and it is free: that is COMMUNICATION!

**Method**

I am a 45-year-old thalassemia patient, have 17 years of experience working in thalassemia outreach and advocacy, and follow thalassemia on over 60 social media sites. Consequently, I am aware of patient needs, challenges, and obstacles on a global level. In considering quality of life for patients around the world, I developed a model for communication. I will discuss barriers, considerations, facets of the model, and how patients can collectively use their voice to improve care and implement advocacy.

**Conclusion**

Communication is the key to achieving a high quality of life. It is the foundation for care and can help toward a cure. Providers will learn the benefits of communication; they will have a clearer picture of what patients face. They can compassionately help patients achieve a higher quality of life by overcoming these challenges through using their voices.

There are some challenges that are inherent to thalassemia regardless of what country the patient lives in: blood safety; access to care; expertise; cost of care; social stigma and barriers that patients are working so hard to overcome. A primary way to overcome these challenges is to use our voices.



# Oral Presentation Abstracts

**Title:** **The Strong Link Between Pancreas And Heart In Thalassemia Major.**

**Abstract Category:** Heart and Vascular Abnormalities

**Authors:** Antonella Meloni<sup>1</sup>, Laura Pistoia<sup>1</sup>, Rosamaria Rosso<sup>2</sup>, Francesca Miciotto<sup>3</sup>, Massei Francesco<sup>4</sup>, Tommaso Casini<sup>5</sup>, Giulia Guerrini<sup>6</sup>, Roberto Mattei<sup>7</sup>, Mauro Murgia<sup>8</sup>, Matteo Oliva<sup>9</sup>, Vincenzo Positano<sup>1</sup>, Alessia Pepe<sup>1</sup>.

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**Presentation on 19 November 2017, in Hall "Olympia B", at 08:30**

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## ABSTRACT

### Background

Some preliminary data have postulated a correlation between pancreatic iron overload and heart iron and function in thalassemia major (TM) patients. In the present study we explored systematically in a multicenter study the link heart-pancreas in a large cohort of TM patients .

### Methods

We considered the first 232 TM patients (129 M, mean age 36.95±9.83 years) enrolled in the E-MIOT (Extension-Myocardial Iron Overload in Thalassemia) project. T2\* measurements were performed over pancreatic head, body and tail and global value was the mean. Myocardial iron overload (MIO) was quantified using a T2\* segmental approach. Biventricular function parameters were assessed by cine images. Late gadolinium enhancement (LGE) images were acquired to detect myocardial fibrosis.

### Results

A significant correlation between pancreatic and cardiac iron was reconfirmed in this more numerous population and a normal pancreas T2\* showed negative predictive value of 100% for cardiac iron. Pancreatic iron was correlated to the LV ejection fraction (EF), but not to the right ventricular (RV) EF.

LGE sequences were acquired in 101 TM patients and 43 (42.57%) of them showed macroscopic myocardial fibrosis. Global pancreas T2\* values were significantly lower in patients with fibrosis (6.27±4.12 ms vs 11.15±9.23 ms; P=0.021).

Twenty-two patients showed cardiac complications (11 arrhythmias, 6 heart failure, 2 pulmonary hypertension, 1 vascular disease, and 2 others) and of them 21 had pancreatic iron. Patients with cardiac complications showed a significant lower global pancreas T2\* (7.55±6.11 ms vs 14.31±13.39 ms; P=0.024).

### Conclusion

Pancreatic iron is a strong predictor not only for cardiac iron, but also for cardiac complications supporting a more profound link between pancreatic iron and heart disease in TM. More studies are needed to evaluate the prognostic role of pancreatic iron on cardiac complication.



## **Title: Premature Atherosclerosis in Children with Beta-Thalassemia Major: New Diagnostic Marker**

**Abstract Category:** Heart and Vascular Abnormalities

**Authors:** Laila M Sherief<sup>1</sup>, Osama Dawood<sup>2</sup>, Adel Ali<sup>1</sup>, Hanan Sherbiny<sup>1</sup>, Mohamed Elshanshory<sup>4</sup>, Osama Abd Alazez<sup>3</sup>, Mohamed Abd Alhady<sup>1</sup>, Naglaa M Kamal<sup>5</sup>, Mohamed Nour<sup>1</sup>

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**Presentation on 19 November 2017, in Hall "Olympia B", at 08:35**

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### **ABSTRACT**

#### **Background**

Patients with beta thalassemia major (B-TM) may present with clinical complications due to the oxidative stress induced by iron overload. Early vascular alteration, atherosclerosis and coronary artery disease have emerged as important cardiovascular complications. The aims of the current study were to assess the prevalence of premature atherosclerosis among pediatric B-TM patients and to investigate the diagnostic value of serum osteoprotegerin (s.OPG) assay as an early biomarker for atherosclerosis in thalassemia children.

#### **Methods**

This cross-sectional study included 65 children with B-TM aged 5-18 years, on regular blood transfusion regimen and 50 healthy controls with comparable age and gender. All participants were evaluated for laboratory investigations including, lipid profile, serum ferritin and s.OPG. Carotid artery intima media thickness (CAIMT) was performed by duplex ultrasound for patients and controls.

#### **Results**

The B-TM patients were transfusion-dependent for around  $8.5 \pm 3.8$  years with significantly higher serum ferritin levels, and C-reactive protein when compared to controls. Significantly higher serum triglyceride and atherogenic index of plasma were recorded in patients than comparisons. CAIMT of both side; were significantly increased for patients when compared with controls, and showed positive correlation with body mass index (BMI), serum triglyceride, atherogenic index of plasma, and serum osteoprotegerin levels. Assay of s.OPG revealed significantly higher levels for thalassemia patients than healthy peers. Of particular interest is the positive correlation between OPG levels and CAIMT of both sides and also with serum triglycerides.

#### **Conclusions**

Subclinical atherosclerosis started prematurely in children with B-TM. CAIMT represented a simple, accurate and non-invasive modality for early detection of atherosclerosis. It was correlated well with s.OPG, this finding highlighted the possible validity of s.OPG assay as an early predictor of atherosclerosis in thalassemia children.



## **Title: Hepatocellular carcinoma (HCC) in multitransfused patients with thalassemia (TM) in Greece. Risk factors and therapeutic Approaches**

**Abstract Category:** Hepatological Complications

**Authors:** D.Kountouras, A.Kattamis, F.Petropoulou, A.Kouraklis, K.Maragkos, D.Kyriakopoulou, C.Fragkodimitri, K.Farmaki, M.Drossou, D.Vini, E.Klironomos, A.Vasiliadi, I.Lafatis, E.Vlachaki, B.Toli, I.Koskinas

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**Presentation on 19 November 2017, in Hall "Olympia B", at 08:40**

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### **ABSTRACT**

#### **Introduction**

HCC in patients with TM has been very rare in the past but it has emerged recently as an epidemic.

#### **Aim of the study**

To evaluate survival and risk factors in TM patients with HCC.

#### **Material-Method**

Retrospective study with a long term follow up survival period (2007- 2017). 40 patients with TM and HCC. Diagnosis of HCC was validated using histopathology and/or imaging reports. Cox regression models were used to detect factors independently correlated with survival.

#### **Results**

27M/13F, mean age 45.8 years (SD=5.7 years). Anti-HCV, HCV-RNA and anti-HBc were detected in 80%, 47.5% and 27.5% of patients respectively. Ten patients had previously achieved SVR after anti-viral IFN based treatment. Eight patients (20%) were both anti-HCV and anti-HBc positive while 12.5% were both HCV-RNA(+) and anti-HBc(+). The most common genotype was 1b (42.1%), 3a (21.1%) and 4 (21.1%). Cirrhosis was present in 72.5% of patients. The mean T2\* was 13.8msec (SD=8.2). A single lesion initially was found in 30% of patients while 27.5% had >3 lesions and most of the patients presented a "pop-corn" like multifocal progression pattern (72,5%). In half of them the total diameter at presentation was above 5 cm and 20% of them suffered from an early portal vein thrombosis. Increased levels of aFP (>20ng/ml) detected in 27 patients (67,5%) (Mean 5.172, SD: 1907). Most of the patients (55%) were submitted to locoregional therapy, 17.5% had undergone surgery, 5% transplantation and 22.5% had no treatment. The median survival time was 20 months. The cumulative event free survival rate was 82.2% for the first year, 44.2% for 2 years, 33.2% for 3 years and 20.7% for 5 years. Multiple Cox regression analysis showed that the treatment and the presence of multiple lesions were independently associated with survival (HR=0.11, 95%CI: 0.03-0.40, p=0.001 and HR=6.7, 95%CI: 2.24-20.29, p=0.001, respectively).

#### **Conclusions**

HCC is a rising complication of liver disease in patients with major thalassemia, irrespectively of the presence of cirrhosis or HCV status, with a very aggressive phenotype, multifocal "pop-corn" like progression and early portal vein thrombosis. AFP elevation was absent in one third of patients. A substantial number had advanced HCC at diagnosis therefore no curative treatment could be offered, as a result, a median survival time was 20 months. Effective iron chelation therapy, HCV eradication and better surveillance are mandatory.

**Keywords:** thalassemia,hepatocellular carcinoma,cirrhosis



## **Title: Peripheral Blood Lymphocytes' Sub Populations In Adult Transfusion Dependent Beta Thalassaemia Patients**

**Abstract Category:** Infections

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**Presentation on 19 November 2017, in Hall "Olympia B", at 08:45**

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## **ABSTRACT**

### **Introduction**

Survival of transfusion dependent (TD) beta thalassaemia major (TM) patients has improved significantly over the past few decades as better treatment became available. Consequently, long term and late complications became more common. Susceptibility to infections is one of the causes of morbidity and mortality among TM patients. Pathogenesis is multifactorial. Studies on immune competence in beta-thalassaemia have revealed numerous quantitative and functional defects, including in T and B lymphocyte sub populations.

### **AIMS**

Assessment of peripheral blood lymphocyte sub populations in adult TD TM patients followed and treated in our centre.

### **Patients and Methods**

Peripheral blood T and B lymphocyte sub populations, obtained from TD TM adult (>18 years of age) patients, were assessed by Flow Cytometry and compared to matched healthy controls.

### **Results**

The study included 31 patients, 17 (54.8%) males and 14 (45.2%) females, mean (range) age was 33.1 (22-47) years, 23 (74.2%) were splenectomised (SPX). Thalassaemia patients had significantly higher WBC ( $p=0.001$ ) and absolute lymphocytes counts ( $p=0.006$ ), significantly lower levels of various T lymphocytes' subsets ( $p=0.001$ ), T-LGL ( $p=0.003$ ), T-REG cells ( $p=0.0002$ ) and NK cells ( $p=0.01$ ), and significantly higher B cells ( $p=0.01$ ), compared to controls. In sub group analysis of SPX patients and those with intact spleen, WBC and absolute lymphocytes counts and B cells sub populations were similar in TD TM patients with intact spleen and controls, whereas significantly higher in SPX patients. T-LGL, NK cells and T-REG cells were significantly lower in both sub groups. Differences in CD3+, CD3+4+, CD3+8+, CD3+4+8+ sub populations were insignificant.

### **Conclusion**

TD TM patients have abnormal lymphocyte sub populations, mainly significantly lower T cells and higher B cells. Splenectomy is a major contributor, but other factors may play a role in the aetiology of these alterations which are associated with increased susceptibility to infections among these patients.

## **Title: Long Term Prospective Predictors For Vascular Events And Cardiac Complications In Thalassemia Major Patients**

**Abstract Category:** Heart and Vascular Abnormalities

**Authors:** Antonella Meloni<sup>1</sup>, Laura Pistoia<sup>1</sup>, Pietro Giuliano<sup>2</sup>, Nicola Giunta<sup>2</sup>, Nicola Dello Iacono<sup>3</sup>, Angelica Barone<sup>4</sup>, Maurizio Caniglia<sup>5</sup>, Calogera Gerardi<sup>6</sup>, Maria Grazia Roberti<sup>7</sup>, Ada Riva<sup>8</sup>, Vincenzo Positano<sup>1</sup>, Alessia Pepe<sup>1</sup>.

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**Presentation on 19 November 2017, in Hall "Olympia B", at 08:50**

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## **ABSTRACT**

### **Background**

The aim of this prospective and multicentre study was to assess the predictive value of traditional and non traditional cardiovascular risk factors (CRF) and Cardiovascular Magnetic Resonance (CMR) parameters for vascular events (VE) and cardiac complications (CC) in thalassemia major (TM) patients.

### **Methods**

We considered 957 TM patients (489 F, 30.34±8.23 years) enrolled in the Myocardial Iron Overload in Thalassemia network. Myocardial iron overload was assessed by T2\* technique. Heart function was quantified by cine images. Late gadolinium enhancement (LGE) images were acquired to detect myocardial fibrosis.

### **Results**

One-hundred and six (11.1%) patients were excluded because a CC was present at the baseline CMR. Mean follow-up time was 79.59±28.45 months. We recorded 13 VD (4 peripheral vascular disease, 3 PH, 3 strokes, 1 PE, 1 DVT, 1 angina). No CMR parameters predicted the development of a VD. However, patients older than 40 years showed a significant higher risk of VD than patients younger than 20 years (HR=10.13, 95%CI=1.18-86.74, P=0.035).

Arrhythmias occurred in 43 patients (40 supraventricular, 2 ventricular and 1 AV block) and heart failure in 30 patients, for a total of 86 CC. In the multivariate analysis the independent predictive factors for CC were myocardial fibrosis (HR=5.17, 95%CI=1.85-6.78, P<0.0001), atrial dilation (HR=2.21, 95%CI=1.32-3.70, P=0.003), and ventricular dysfunction (HR=2.15, 95%CI=1.29-3.58, P=0.003).

### **Conclusions**

CMR by a multi-parametric approach provided prognostic information in TM patients. However, when only VE were considered, CMR lose its predicting role, while the importance of the older age emerged as significant risk factors.



## **Title: Study of the Mean Platelet Volume as a Marker of Pulmonary Hypertension in Thalassemic Patients**

**Abstract Category:** Heart and Vascular Abnormalities

**Authors:** Usama R El Safy<sup>1</sup>, Mayy A Mohammed<sup>1</sup>, Manar M Fathy<sup>1</sup>, Deiaa A Abd El Hamid<sup>1</sup>, Ahmed El Hwala<sup>2</sup>, Saad El Esh<sup>3</sup>

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**Presentation on 19 November 2017, in Hall "Olympia B", at 08:55**

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### **ABSTRACT**

#### **Background**

The majority of thalassemic patients on chronic blood transfusion develop pulmonary arterial hypertension (PAH) that is affected with the onset of the disease, duration of treatment and splenectomy. In thalassemic patients with pulmonary hypertension, activation of platelets usually occurs. We focus on our recent study to investigate mean platelet volume (MPV) in thalassemic patients either with or without PAH.

#### **Patients and Methods**

Our study was performed in the paediatric hematology department and outpatient clinic in Zagazig University Hospital –Egypt, during the period from June 2015 to February 2016. The study enrolled 96 thalassemic individual who were divided into 2 groups: Group 1 "pulmonary hypertension group": involved 48 thalassemic individual with PAH and group 2 "control group": involved 48 thalassemic individual without PAH. Thalassemic patients were subjected to full history taking, complete physical examination, recommended laboratory investigations, abdominal ultrasonography and echocardiography.

#### **Results**

In this study, both studied groups revealed a highly significant difference in MPV, but no significant difference in platelet count. They both studied groups hemodynamically showed that there is a highly significant difference in systolic pulmonary artery Pressure (sPAP) and mean pulmonary artery Pressure (mPAP) in thalassemic patients with or without PAH. MPV and clinical characteristics of thalassemic patients showed highly statistically significant association with splenectomy and patient's compliance with medication. The Correlation analysis of all study variables & MPV revealed a highly significant positive correlation with platelet count in both PAH group and control groups; there is also a highly significant negative correlation with sPAP in PAH group, and significant negative correlation with mPAP. The accuracy of MPV as an indicator for platelet activation in thalassemic with pulmonary hypertension is 72.5 which have a highly significant value.

#### **Conclusion**

Our study revealed significantly decrease MPV in thalassemic patients but the decrease was more significant in thalassemic patients with PAH than in those without PAH.

**Title: Pancreatic Iron Loading In Hemoglobinopathies****Abstract Category:** Iron overload and management**Authors:** Antonella Meloni<sup>1</sup>, Laura Pistoia<sup>1</sup>, Alessia Salli<sup>2</sup>, Maria Caterina Putti<sup>3</sup>, Domenico Giuseppe D'Ascola<sup>4</sup>, Crocetta Argento<sup>5</sup>, Carla Pitturru<sup>6</sup>, Lorella Pitrolo<sup>7</sup>, Giuseppe Colaci<sup>8</sup>, Priscilla Fina<sup>9</sup>, Vincenzo Positano<sup>1</sup>, Alessia Pepe<sup>1</sup>**Presenting Author:** Laura Pistoia**Affiliation:**<sup>1</sup> Fondazione G. Monasterio, CNR-Regione Toscana, Pisa, Italy<sup>2</sup> ARNAS Civico Benfratelli-Di Cristina, Palermo, Italy<sup>3</sup> Azienda Ospedaliero-Universitaria di Padova, Padova, Italy<sup>4</sup> Azienda Ospedaliera Bianchi-Melacrino-Morelli, Reggio Calabria, Italy<sup>5</sup> Ospedale San Giovanni Di Dio, Agrigento, Italy<sup>6</sup> P.O. Pediatrico Microcitemico A.CAO, Cagliari, Italy<sup>7</sup> Ospedale V. Cervello, Palermo, Italy<sup>8</sup> Presidio Ospedaliero N°2 "S. Giuseppe da Copertino, Copertino, Italy<sup>9</sup> Ospedale Sandro Pertini, Roma, Italy**Email:** laura.pistoia@ftgm.it**Presentation on 19 November 2017, in Hall "Olympia B", at 09.00****ABSTRACT****Background**

The MIOT (Myocardial Iron Overload in Thalassemia) project is a multicentric study aimed to validate the T2\* Magnetic Resonance Imaging (MRI) technique as non invasive approach for the cardiac and hepatic iron overload assessment in patients with hemoglobinopathies and to correlate the T2\* values with other clinical-instrumental parameters. More recently, the E-MIOT (Extension-MIOT) project has been approved, with the aim of adding the assessment of the pancreatic iron

**Methods**

We report the baseline MRI findings at the end of the first year of recruitment in the E-MIOT study, outlying the differences among different emoglobinopathies.

**Results**

First, we selected all transfusion-dependent (TD) patients: 7 with sickle-cell disease-SCD or thalasso-drepanocytosis (42.9% F, 32.47 ± 17.93 years), 16 with thalassemia intermedia-TI (56.3% F, 36.66 ± 13.72 years), and 232 with thalassemia major-TM (55.6% F, 36.95 ± 9.83 years).

Sex, mean age, serum ferritin levels, MRI liver iron concentration (LIC) values, and global heart T2\* values were comparable among the three groups of patients. Pancreatic T2\* values were significantly lower in TM patients versus both SCD and TI patients (see Figure).

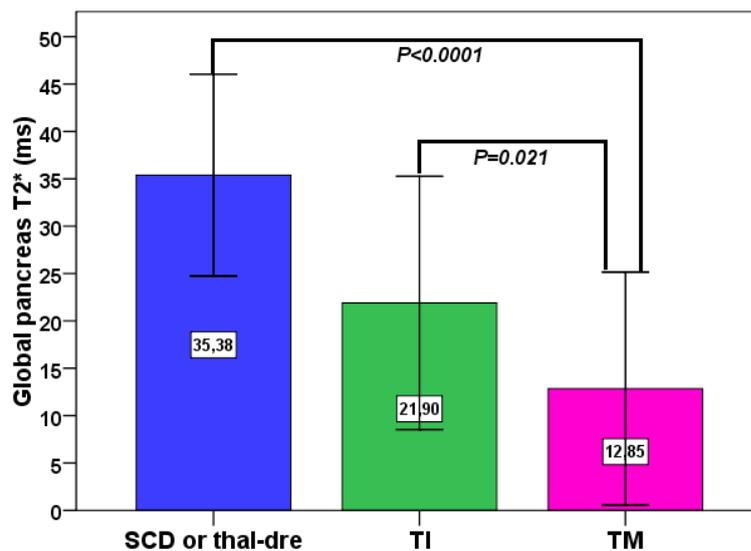
Second, we focused our analysis on all TI patients, divided in two subgroups: transfusion dependent and no-TD. Global pancreas T2\* values and the number of patients with pancreatic iron (T2\* < 26 ms) were comparable between the two groups (see Table).

**Conclusion**

SCD and TI TD patients have lower pancreatic iron loading than chronically-transfused TM patients. Much of this disparity can be explained by the larger transfusional burdens and durations observed in TM patients (years of regular transfusions: 34.18 ± 10.75 in TM, 22.27 ± 18.53 in SCD and 28.33 ± 15.30 in TI, P=0.023). However, TI-TD and TI-noTD patients had comparable pancreatic T2\* values. So, innate differences in iron handling and elimination among different diseases also could contribute to the differences in pancreatic iron loading.



Figure



Table

	TI-noTD (N=16)	TI-TD (N=16)	P
<b>Sex (% of F)</b>	33.3	56.3	0.300
<b>Age (years)</b>	42.78 ± 13.34	36.66 ± 13.72	0.427
<b>Ferritin (ng/ml)</b>	452 ± 251	750 ± 563	0.336
<b>MRI LIC (mg/g dw)</b>	5.37 ± 6.68	5.72 ± 8.58	0.270
<b>MRI LIC &lt; 3 mg/g dw, N (%)</b>	9 (50)	5 (31.3)	0.268
<b>Global heart T2* (ms)</b>	43.94 ± 4.69	36.79 ± 9.58	0.008
<b>Global heart T2* &lt; 20 ms, N (%)</b>	0	1 (6.3)	0.471
<b>Global pancreas T2* (ms)</b>	26.57 ± 10.46	21.89 ± 13.37	0.317
<b>Global pancreas T2* &lt; 26 ms, N (%)</b>	8 (44.4)	9 (56.3)	0.492

**Title: Real Life Experience Of Sitagliptin Use In Patients With Beta-Thalassaemia Major And Diabetes****Abstract Category:** Endocrine Complications**Authors:** Ploutarchos Tzoulis<sup>1</sup>, Shahrzad Zonoozi<sup>1</sup>, Emma Prescott<sup>2</sup>, Romilla Jones<sup>1</sup>, Farrukh T Shah<sup>2</sup>, Maria Barnard<sup>1</sup>**Presenting Author:** Ploutarchos Tzoulis**Affiliation:**<sup>1</sup> Department of Diabetes, Whittington Hospital, Magdala Avenue, London, N19 5NF<sup>2</sup> Department of Haematology, Whittington Hospital, Magdala Avenue, London, N19 5NF**Email:** ptzoulis@yahoo.co.uk**Presentation on 19 November 2017, in Hall "Olympia B", at 09:05****ABSTRACT****Background**

Despite their widespread use in type 2 diabetes, peptidyl peptidase 4 (DPP-4) inhibitors are not routinely prescribed in patients with beta-thalassaemia major ( $\beta$ -TM) and diabetes. This is the first study evaluating the effectiveness and safety of sitagliptin in patients with  $\beta$ -TM and diabetes.

**Methods**

Retrospective case series of five patients at our institution with  $\beta$ -TM and diabetes treated with sitagliptin.

**Results**

Amongst 36 patients with  $\beta$ -TM and diabetes at our institution, five patients (4 females, 1 male), all with strong family history of diabetes and aged between 44 and 50 years, were commenced on sitagliptin at a dose of 100 mg once daily. Sitagliptin was used as 2nd line agent in one patient as add-on to metformin. Among the other 4 patients on metformin and gliclazide combination therapy, sitagliptin was added as 3rd line agent in 2 cases with poor glycaemic control, while it replaced gliclazide in 2 cases with frequent hypoglycaemias. Four out of the five patients responded well to sitagliptin therapy, as evidenced by decrease in fructosamine by 77 and 96 $\mu$ mol/L (equivalent reduction in HbA1c of 1.5% and 1.9%) observed in 2 patients and significant reduction in the frequency of hypoglycaemia without worsening of glycaemic control documented in other 2 individuals. One patient did not respond to sitagliptin therapy and discontinued it after 6 months. No significant side effects such as pancreatitis, arthritis and infections were documented.

**Conclusions**

This is the first study providing evidence that sitagliptin is a safe and effective glucose-lowering agent and is associated with a low rate of hypoglycaemias in patients with  $\beta$ -TM. Sitagliptin could be considered, with caution, for use in patients with  $\beta$ -TM and diabetes, under the supervision and close monitoring of a Diabetologist with expertise in this complex group.

**Title: Isoform-Specific Disruption Of The BCL11A Transcription Factor****Abstract Category:** Gene Regulation and Therapy**Authors:** Constantinos Ch. Loucaria<sup>2</sup>, Thamar B. van Dijk<sup>3</sup>, Petros Patsali<sup>1</sup>, Maria Sitarou<sup>4</sup>, Soteroulla Christou<sup>4</sup>, Sjaak Philipssen<sup>3</sup>, Carsten W. Lederera<sup>2</sup>\*, Marina Kleanthous<sup>1,2</sup>\***Presenting Author:** Carsten W. Lederer**Affiliation:**<sup>1</sup> Molecular Genetics Thalassemia Department, Cyprus Institute of Neurology and Genetics, 1683 Nicosia, Cyprus<sup>2</sup> Erasmus University Medical Center, Rotterdam, The Netherlands<sup>3</sup> Cyprus School of Molecular Medicine, Nicosia, Cyprus<sup>4</sup> Thalassaemia Centre, Ministry of Health, Cyprus

\* Shared last authors.

**Email:** Lederer@cing.ac.cy**Presentation on 19 November 2017, in Hall "Voula Patoulidou" at 08:30****ABSTRACT****Background**

Sickle-cell disease (SCD) and  $\beta$ -thalassemia are common and potentially life-threatening monogenic disorders. Both are caused by defects in  $\beta$ -globin and are suitable targets for gene-therapy approaches. Pathology for both disorders is significantly alleviated by elevated levels of the fetal  $\beta$ -like globin,  $\gamma$ -globin, whose expression is curtailed in most adults by the BCL11A transcription factor. BCL11A is essential for the survival of lymphoid cells, and its extra-long (XL) isoform is particularly abundant in erythroid cells. To date no isoform-specific functional assessment of BCL11A has been undertaken.

**Methods**

CRISPR/Cas9 RNA-guided endonuclease (RGEN) were delivered to HUDEP-2 cells using lentiviral vectors and were utilised to achieve knockout of the  $\gamma$ -globin repressor BCL11A and of its XL isoform. Additionally, bicistronic lentiviral vectors encoding both the RGEN nuclease and sgRNA components were tested in control and patient-derived CD34+ cells.

**Results**

Highly efficient sgRNAs have been identified for different BCL11A target sites, with results in HUDEP-2 cells indicating that BCL11A-XL-specific knockouts give high-level  $\gamma$ -globin expression, albeit with intermittent delay in erythroid differentiation. Likewise,  $\gamma$ -globin induction was achieved in healthy and thalassaemic CD34+ cells with BCL11A knockout controls and XL-specific RGENs, indicating the potential of isoform-specific knockouts for  $\gamma$ -globin induction.

**Conclusions**

Our study investigated the structure-function relationship for the BCL11A transcription factor and its isoforms. BCL11A-XL deactivation allows  $\gamma$ -globin induction and thus possible therapeutic exploitation, whereas potential detrimental effects, in particular in the lymphoid lineage, remain to be investigated.



**Title: Renal iron deposition by magnetic resonance imaging in pediatric  $\beta$ -thalassemia major patients: relation to renal biomarkers, total body iron and chelation therapy**

**Abstract Category:** Diagnostic and Monitoring Techniques

**Authors:** Mohsen Saleh ElAlfy<sup>1</sup>, Nayera Hazaa El-Sherif<sup>1</sup>, Fatma Soliman Ebeid<sup>1</sup>, Eman Abdel Rahman Ismail<sup>2</sup>, Yasser Wagih Darwish<sup>2</sup>, Ahmed Samir Ibrahim<sup>3</sup>, Khalid Abo Elfotoh<sup>3</sup>, Nermeen Adel Shokrey<sup>1</sup>, Dunia Naser Alajeil<sup>1</sup>

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**Presentation on 19 November 2017, in Hall "Voula Patoulidou" at 08:35**

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## ABSTRACT

### Background

Little is known about renal functions in  $\beta$ -thalassemia major ( $\beta$ -TM) in relation to renal iron deposition. Aim: To assess renal iron overload by MRI and its relation to liver and cardiac iron as well type of iron chelator and compliance to chelation on biomarkers of glomerular and tubular functions in children with  $\beta$ -TM.

### Methods

Fifty  $\beta$ -TM patients with no clinical renal impairment were compared with 25 matched healthy controls focusing on transfusion history, chelation therapy, serum ferritin (SF), serum cystatin C, urinary albumin creatinine ratio (UACR) and urinary  $\beta$ 2-microglobulin ( $\beta$ 2M) with calculation of  $\beta$ 2M/albumin ratio. Quantification of liver, heart and kidney iron overload was done by MRI only for  $\beta$ -TM patients.

### Results

Median age; 12 years, 50% females, levels of serum cystatin C, UACR and urinary  $\beta$ 2 microglobulin as well as urinary  $\beta$ 2m/albumin were significantly higher in  $\beta$ -TM patients than the control group. Heavily renal iron loaded patients had significantly higher levels of the studied renal biomarkers. Deferasirox (DFX) therapy n=27 either single (n=8) or combined was associated with higher levels of glomerular and tubular markers compared with the group without deferasirox; whether deferoxamine and or deferiprone therapy. Renal T2\* cutoff <31 msec positively correlated to indirect bilirubin, LDH, cystatin C cardiac iron and LIC and to poor compliance to chelation.

### Conclusion

Asymptomatic alteration in glomerular and tubular functions in pediatric patients with  $\beta$ -TM were related to degree of hemolysis, total body iron, kidney iron deposition, DFX therapy and poor compliance to chelation.



## **Title: Less Means More: Knockdown Of Aberrant HBBIVSI-110(G>A) mRNA restores HBB Expression And Enhances Gene Therapy By Gene Addition In Primary Erythroid Cells**

**Abstract Category:** Gene Regulation and Therapy

**Authors:** Petros Patsali<sup>1,2</sup>, Panayiota Papasavva<sup>1,3</sup>, Coralea Stephanou<sup>1,2</sup>, Soteroulla Christou<sup>4</sup>, Maria Sitarou<sup>4</sup>, Michael N Antoniou<sup>2</sup>, Carsten W. Lederer<sup>1,3</sup>\*, Marina Kleanthous<sup>1,3</sup>\*

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**Presentation on 19 November 2017, in Hall "Voula Patoulidou" at 08:40**

## **ABSTRACT**

### **Background**

Mutations reducing  $\beta$ -globin production and thus causing  $\beta$ -thalassaemia are of global clinical importance.  $\beta$ -Thalassaemia caused by the HBBIVSI-110(G>A) mutation (HGVS name: HBB:c.93-21G>A), which produces an abnormal splice acceptor site, is particularly frequent in many Western countries and usually causes severe thalassaemia major in homozygotes. Cells from patients with HBBIVSI-110(G>A) are difficult to treat with gene therapy by gene addition, suggesting an effect of the mutant locus on normal, endogenous or vector-encoded,  $\beta$ -globin alleles. Towards improved gene-addition treatment of affected patients and supposing that the mutant locus acts in trans by aberrant HBBIVSI-110(G>A)-derived mRNA, we therefore set out to reduce the latter by RNA interference.

### **Methods**

This study employed lentiviral delivery of the shRNAs specific to aberrant RNA, alone or in conjunction with the GLOBE HBB gene addition vector. Substrates were, first, a novel humanised murine erythroleukaemia cell model holding the human HBBIVSI-110(G>A) splice defect and, second, primary CD34+ cells from HBBIVSI-110(G>A)-homozygous patients.

### **Results**

We recognised initially in our humanised murine cell model and then in primary patient-derived haematopoietic stem and progenitor cells, that specific knock-down of the aberrant HBBIVSI-110(G>A) mRNA alone results in extremely significant induction of  $\beta$ -globin production from the mutant locus. In primary cells the resulting  $\beta$ -globin expression and phenotypic correction of erythroid-lineage differentiation is equal to or exceeds that achieved by same-sample control treatment with the clinically successful GLOBE gene-therapy vector. Furthermore, combination of HBBIVSI-110(G>A) knockdown with GLOBE results in significant improvement of both disease parameters compared to either treatment alone.

### **Conclusions**

This study establishes aberrant HBBIVSI-110(G>A) mRNA as the main causative agent of disease severity in HBBIVSI-110(G>A) thalassaemia and as a potent target for mutation-specific gene therapy for  $\beta$ -thalassaemia. It moreover puts forward HBBIVSI-110(G>A) thalassaemia as a paradigm for the importance of allelic heterogeneity when applying gene therapy by gene addition.



**Title: Development of a GalNAc-siRNA Conjugate Targeting a Key Regulator of the BMP/SMAD Signalling Pathway for Treatment of Iron Overload**

**Abstract Category:** Iron overload management

**Authors:** Ute Schaeper, PhD, Manuela Aleku, Sibylle Dames, Steffen Schubert, PhD, and Ulrich Zügel, PhD

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**Presentation on 19 November 2017, in Hall "Voula Patoulidou" at 08:45**

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## ABSTRACT

### Background

In  $\beta$ -thalassemia, a defect in the beta-globin gene causes stressed erythropoiesis, anaemia and gastro-intestinal iron hyperabsorption resulting in iron overload.

Iron overload is a serious complication of  $\beta$ -thalassemia and can lead to organ damage and premature death. The peptide hormone hepcidin is a key regulator and inhibitor of iron absorption and distribution. In patients with iron loading anaemias, hepcidin levels are abnormally low. On the molecular level hepcidin expression can be induced by activation of the BMP/SMAD signalling pathway.

RNA interference is a powerful technology for inhibiting gene expression. Recently our company has developed siRNA conjugate technology for targeting gene expression in the liver. siRNAs conjugated to a GalNAc ligand cluster bind to ASGP receptor predominantly expressed by hepatocytes. A single subcutaneous administration is sufficient to achieve significant and durable reduction of target gene inhibition in mice and in nonhuman primates. The GalNAc-siRNA conjugate SLN124 with specificity for a target in the BMP/SMAD signalling pathway is now in preclinical development for treatment of iron loading anaemias.

### Methods

Lead identification and pharmacological characterization of siRNA conjugates in vitro, in rodent models and in nonhuman primates.

### Results

Identification and pharmacological characterization of the siRNA conjugate SLN124 targeting a key regulator of the BMP/SMAD signalling pathway is reported. Our compound shows dose-dependent and long-lasting target gene inhibition and reduction of serum iron levels in vivo and it is well tolerated in doses up to 30-fold over the effective dose level.

### Conclusions

GalNAc siRNA conjugate SLN124 is a promising candidate for treatment of iron overload in  $\beta$ -thalassemia.



## Title: **The A1 Insulator Reduces The Genotoxicity Of A Beta-Globin Lentiviral Vector**

**Abstract Category:** Gene Regulation and Therapy

**Authors:** Penelope-Georgia Papayanni<sup>1,2</sup>, Panayota Christofi<sup>1,2</sup>, Ioanna Valianou<sup>1</sup>, Evangelia Athanasiou<sup>1</sup>, Garyfalia Karponi<sup>1</sup>, Michalis Gounis<sup>1</sup>, Minas Yiangou<sup>2</sup>, Achilles Anagnostopoulos<sup>1</sup>, Michel Sadelain<sup>3</sup>, George Stamatoyannopoulos<sup>4</sup>, Evangelia Yannaki<sup>1,4</sup>

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**Presentation on 19 November 2017, in Hall "Voula Patoulidou" at 08:50**

## ABSTRACT

### Background

Insertional oncogenesis remains a major limitation for gene therapy. Self-inactivating lentiviral vectors (SIN-LVs), although safer than  $\gamma$ -retroviral vectors, still carry the risk of insertional mutagenesis, especially when, like the globin-vectors, incorporate strong enhancers. The use of chromatin insulators as a means to minimize vector-mediated genotoxicity has been limited majorly by their large size affecting titers. A1 is a recently identified and characterized human, small-sized enhancer-blocking insulator. Aim. We aimed to test whether A1 could reduce vector-mediated genotoxicity in the challenging context of SIN-LVs, using a therapeutic globin-vector and the IL-3-dependent 32D cells, which upon transduction with oncogenic vectors become IL-3-independent, leading to transformation.

### Method

32D cells were transduced with SIN-LVs: the  $\beta$ -globin-TNS9.3.55-, the insulated A1-TNS9.3.55- and the oncogenic SFFV-GFP-vector. Transduced cells were expanded in 10% IL-3 and transduction efficiency was determined by vector copy number (VCN). Transduced 32D cells were seeded in methylcellulose with 10% or 0-1% IL-3 to detect the IL-3-independent and potentially transformed clones. The IL-3-independent clones were i) further expanded in 10% IL-3 and infused in partially myeloablated and IL-3-treated C3H/HeJ mice ii) re-cultured without IL-3. WBC analysis, blood smears, bone marrow (BM) cytospins and tissue histology/immunohistochemistry were performed.

### Results

The A1 insulator did not negatively affect vector titers (TNS9.3.55, A1-TNS9.3.55, SFFV-GFP: 2.8, 1.8, 2.5  $\times 10^8$  IU/ml, respectively). 32D cells were successfully transduced with all vectors (%VCN(+) colonies: 40-100%) and expanded up to 400-fold. A1-insulator decreased the number of IL-3-independent colonies by 78-93% over the uninsulated vectors. The uninsulated vector-transduced, IL-3-independent colonies, were greatly expanded in culture with 10% IL-3 over the A1-transduced colonies (TNS9.3.55, A1-TNS9.3.55, SFFV: 40, 10, 48 fold change, respectively). Most importantly, only the uninsulated vector-transduced colonies were further expanded without IL-3 (TNS9.3.55, A1-TNS9.3.55, SFFV: 25, 0, 35 fold change, respectively), suggesting potential transformation. Indeed, upon transplantation, the uninsulated vector-transduced (TNS9.3.55, SFFV), IL-3-independent and expanded colonies caused overt leukemia (hyperleukocytosis, splenomegaly, bm- and extramedullary site-infiltration).

### Conclusion

Under forced oncogenic conditions, the A1 insulator effectively protected a therapeutic vector from vector-mediated genotoxicity.

**Title: The Role of Polymorphisms in BCL 11A, HBS1L-MYB Intergenic and  $\gamma$  Globin Promoter Region on the HbF Induction and Clinical Severity of  $\beta$ -Thalassaemia**

**Abstract Category:** Non-transfusion dependent thalassaemia

**Authors:** Priya Hariharan, Roshan Colah, K Ghosh, Anita Nadkarni

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**Presentation on 19 November 2017, in Hall "Voula Patoulidou" at 08:55**

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## ABSTRACT

### Background

$\beta$ -thalassaemia a autosomal recessive disorder, displays a wide range of phenotypic heterogeneity from severe transfusion dependent anaemias ( $\beta$ -thalassaemia major) to sporadic blood transfusion dependency ( $\beta$ -thalassaemia intermedia). Recent studies have shown that genetic variants that induce foetal haemoglobin production contribute in ameliorating the clinical severity of the disease. In this study we evaluated the HbF level modulating role of genetic polymorphisms in BCL 11 A, HBS1L-MYB and  $\gamma$  globin promoter region in  $\beta$ -thalassaemia intermedia and  $\beta$ -thalassaemia traits with raised HbF levels.

### Methodology

We studied 100  $\beta$ -thalassaemia homozygous patients (50: Severe cases, 50: Mild cases. 50  $\beta$ -thalassaemia traits with raised HbF (HbF > 2.0) and 50 normal controls. Preliminary screening and  $\beta$ -genotyping was done by CRDB, ARMS or DNA sequencing. 3 SNPs within the BCL11A gene (rs 11886868 C→T, rs 7557939 A→G, rs 4671393 A→G) were detected by real time genotyping, MYB 3 bp deletion(rs 66650371) was determined by ARMS PCR and  $\gamma$  globin promoter was screened by DNA sequencing.

### Results

Nine different  $\beta$ -thalassaemia mutations were detected and 30 % of TI patients showed presence of milder mutations. Among the BCL11A SNPs, only the minor allele C of SNP rs 11886868 C→T was found to be significantly higher in the milder cases [f(C)=0.54 in TI, f(C)=0.38 in TM], however no significant difference was observed in the HbF levels. In both thalassaemia intermedia and thalassaemia trait, the minor allele: 3 bp deletion in the HBS1L- MYB showed significant association with increased the HbF levels (TI : 87.06 %  $\pm$  28.34, p: 0.01,  $\beta$ -thalassaemia traits : 6.9 %  $\pm$  2.1 p=0.04). For  $\gamma$  globin promoter, along with XmN I polymorphism, the minor allele A of +25 G→A (A $\gamma$  globin) was found to be significantly associated with the HbF levels (TI : 81.61%  $\pm$  31.1, p: 0.05 and  $\beta$ -thalassaemia traits : 8.1 %  $\pm$  2.7 p=0.008)

### Conclusion

Identification of genetic polymorphisms that modulate the HbF levels may help in understanding the molecular mechanisms that control HbF expression and the clinical heterogeneity of the disease.



## **Title: Gene Therapy For Beta Thalassemia: Initial Results From The Phase I/II Tiget-Bthal Trial Of Autologous Hematopoietic Stem Cells Genetically Modified With Globe Lentiviral Vector**

**Abstract Category:** Gene Regulation and Therapy

**Authors:** S. Marktel<sup>1,2</sup>, M.P. Cicalese<sup>1,3</sup>, F. Giglio<sup>2</sup>, V. Calbi<sup>1,3</sup>, M. Casiraghi<sup>1,3</sup>, S. Scaramuzza<sup>1</sup>, F. Ciotti<sup>3</sup>, M.R. Lidonnici<sup>1</sup>, C. Rossi<sup>1</sup>, N. Maserà<sup>8</sup>, E. D'Angelo<sup>9</sup>, N. Mirra<sup>9</sup>, R. Origa<sup>10</sup>, G. Mandelli<sup>1</sup>, R. Milani<sup>4</sup>, S. Gattillo<sup>4</sup>, M. Coppola<sup>4</sup>, G. Viarengo<sup>5</sup>, L. Santoleri<sup>4</sup>, A. Calabria<sup>1</sup>, E. Montini<sup>1</sup>, G. Graziadei<sup>6</sup>, L. Naldini<sup>1</sup>, M.D. Cappellini<sup>6</sup>, F. Ciceri<sup>1,2,7</sup>, A. Aiuti<sup>1,3,7</sup>, G. Ferrari<sup>1,7</sup>

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**Presentation on 19 November 2017, in Hall "Voula Patoulidou" at 09:00**

## **ABSTRACT**

### **Background**

Gene therapy for transfusion dependent beta-thalassemia is based on the autologous transplantation of hematopoietic stem cells (HSCs) engineered by lentiviral vectors expressing a transcriptionally regulated human beta-globin gene.

### **Method**

Our contribution to this field was devoted to the clinical development of a gene therapy protocol based on high-titer vector GLOBE, use of lenograstim and plerixafor to obtain mobilized HSCs and a conditioning regimen based on myeloablative treosulfan and thiotepa favoring efficient engraftment of corrected cells with reduced toxicity (TIGET-BTHAL; EudraCT number 2014-004860-39). The route of administration of gene modified HSCs is intraosseous in the posterior-superior iliac crests with the aim of enhancing engraftment and minimizing first-pass intravenous filter.

### **Results**

On the basis of extensive efficacy and safety preclinical studies the clinical trial TIGET-BTHAL was approved and started in 2015 at Scientific Institute San Raffaele, Milan, Italy. The clinical study foresees treatment of 10 patients: 3 adults followed by 7 minors, with a staggered enrolment strategy based on evaluation of safety and preliminary efficacy in adult patients by an independent data safety monitoring board before inclusion of pediatric subjects. As of May 2017, seven patients (3 adults and 4 pediatric patients) with different genotypes ( $\beta^0/\beta^0$ ,  $\beta^+/\beta^+$  and  $\beta^0/\beta^+$ ) have been treated with GLOBE-transduced CD34+ cells at a dose of  $16 \times 10^6$ - $19.5 \times 10^6$  cells/kg and a vector copy number (VCN)/cell ranging from 0.7 to 1.5. The procedure was well tolerated by all patients, with no product-related adverse events. Multilineage engraftment of gene-marked cells was observed in all peripheral blood and bone marrow samples tested. Polyclonal vector integrations profiles have been detected in the first 3 patients tested. So far, the clinical outcome indicates reduction in transfusion requirement in adult patients and greater clinical benefit in younger patients.

### **Conclusion**

Preliminary data suggest that the applied clinical protocol for gene therapy with GLOBE LV is well tolerated and leads to reduced transfusion requirement. Follow up analysis are ongoing and updated clinical outcome will be presented.

**Title: Genome-Editing of BCL11A as Potential Therapy for Beta-Thalassemia and Sickle Cell Disease****Abstract Category:** Gene Regulation and Therapy**Authors:** Michael C. Holmes, Andreas Reik, Edward J Rebar, Jeffrey C. Miller, Yuanyue Zhou, Lei Zhang, Patrick Li, Sagar A Vaidya**Presenting Author:** Michael C. Holmes**Affiliation:****Email:** mholmes@sangamo.com**Presentation on 19 November 2017, in Hall "Voula Patoulidou" at 09.05****ABSTRACT****Background**

Beta-thalassemia and sickle cell disease are genetic disorders caused by mutations in the beta-globin gene which can lead to significant anemia and serious medical complications. Increases in fetal hemoglobin (HbF) have been linked to improved clinical outcomes in patients with beta-thalassemia and sickle cell disease.

**Methods**

We have developed engineered zinc finger nucleases (ZFNs) that precisely cleave and disrupt the erythroid enhancer of the BCL11A gene, which substantially boosts HbF production in erythroid progeny of genome-edited CD34+ hematopoietic stem/progenitor cells (HSPCs). The autologous modified HSPC drug product is named SB-ENH-HSPC.

**Results**

We demonstrate that SB-ENH-HSPC can be manufactured by reproducible, high-level, ZFN-driven modification in peripheral blood mobilized HSPCs at clinical production scale ( $>1e8$  cells). SB-ENH-HSPC is made in a GMP-compliant setting using a clinical-grade electroporation device to deliver the engineered ZFN mRNAs *ex vivo*. Miseq-based analysis of insertions/deletions after treatment of HSPCs with SB-ENH-HSPC demonstrated high levels of on-target modification  $>70\%$ . Using erythroid colony assay genotyping, we found that  $>50\%$  of HSPCs in SB-ENH-HSPC had bi-allelic modification at the BCL11A erythroid enhancer, resulting in significantly higher levels of HbF (gamma globin) mRNA and protein compared to controls. Similarly, we observed comparably high levels of modification in research-scale preparations of HSPCs from patients with beta-thalassemia. We demonstrate that treatment of immune-deficient mice with SB-ENH-HSPC leads to robust long-term (16-24 week) engraftment of donor cells. Targeted gene modification was maintained through multi-lineage differentiation in the bone marrow and peripheral blood, which was otherwise similar to controls.

**Conclusions:**

These results support further clinical development of genome-editing of BCL11A as potential therapy for beta-thalassemia and sickle cell disease.



## **Title: Correlation Between FIBROSCAN and MRI T2\* To Estimate Degree Of Hepatic Iron Overload In Thalassemia Major Patients**

**Abstract Category:** Diagnostic and Monitoring Techniques

**Authors:** Jaswinder Kaur<sup>1</sup>, Anand Gupta<sup>1</sup>, Nishant Wadhwa<sup>1</sup>, V K Khanna<sup>2</sup>, Anamika Baghel<sup>1</sup>

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**Presentation on 19 November 2017, in Hall "Ilida" at 08.30**

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### **ABSTRACT**

#### **Background**

Hepatic iron overload is an important cause of morbidity and mortality in patients with thalassemia major. Current guidelines suggest serum ferritin every three months and annual magnetic resonance imaging transverse relaxation time (MRI T2\*) to monitor hepatic iron load. MRI T2\* is expensive and is not easily available. We investigated the correlation between MRI T2\* and Fibroscan (Transient Elastography) to assess the degree of hepatic iron overload.

#### **Method**

50 patients with thalassemia major >12 years were enrolled into this prospective cross-sectional study. Patients with chronic viral hepatitis were excluded. All patients underwent routine blood investigations, Fibroscan, Liver 1.5 Tesla MRI T2\* and serum ferritin level. Fibroscan was done within 3 months of MRI T2\*. The correlation between fibroscan, MRI T2\* and ferritin levels was determined using spearman correlation test and linear regression analysis.

#### **Results**

27 (54%) patients were male and 23 (46%) were female. Mean age was  $22.7 \pm 6.5$  years and serum ferritin  $2396 \pm 1660$  ng/ml. Median SGPT and SGOT were 32.5 (range:16-120IU/L) and 25(11-224IU/L). Median fibroscan and MRI T2\* readings were 6.35(2.7-36.3 milliseconds) and 4.87(1.7-13.7kPa) respectively. Based on MRI T2\*, 11(22%), 32(64%) and 7(14%) patients had no, mild and moderate iron overload respectively. A moderate inverse correlation was seen between serum ferritin and MRI T2\* readings ( $r=-0.51$ ,  $p<0.001$ ) and a moderate positive correlation between serum ferritin and fibroscan readings ( $r=0.5$ ,  $p<0.001$ ). A weak inverse correlation was seen between MRI T2\* and fibroscan ( $r=-0.27$ ,  $p=0.06$ ). AUC for fibroscan to detect mild and moderate iron overload was 0.60 (CI:0.43-0.78) and 0.71(CI:0.44-0.99) respectively. Fibroscan value  $>6.3$ kPa predicted mild to moderate iron overload with sensitivity and specificity of 56.4 % and 72.7 % respectively.

#### **Conclusion**

Fibroscan and MRI T2\* showed weak correlation. Larger studies are required to validate the use of fibroscan for estimating degree of hepatic iron overload.

**Title: Clinical features and associated genotypes in Iranian H disease****Abstract Category:** Diagnostic and Monitoring Techniques**Authors:** Bagherian H<sup>1</sup>, Abiri M<sup>2,3,1</sup>, Sharifi Z<sup>1</sup>, Shirzad T<sup>1</sup>, Nofereesti H<sup>1</sup>, Amini M<sup>1</sup>, Sarhadi A<sup>1</sup>, Jamali M<sup>1</sup>, Zafarghandi F<sup>1</sup>, Asnavandi S<sup>1</sup>, Masoudifard M<sup>1</sup>, Faeze Rahiminejad<sup>1</sup>, Zeinali S<sup>1,2</sup>**Presenting Author:** Zeinali S**Affiliation:**<sup>1</sup> Dr. Zeinali's Medical Genetics Laboratory, Kawsar Human Genetics Research Center, Tehran, Iran<sup>2</sup> Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran<sup>3</sup> Department of Molecular Medicine, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran**Email:** zeinali@kawsar.ir**Address:**

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**Presentation on 19 November 2017, in Hall "Ilida" at 08.35****ABSTRACT****Background**

Hemoglobin H is one of the most common and heterogeneous form of  $\alpha$ -thalassemia. It results from different types of mutations which lead to imbalance in the formation of  $\alpha$ -globin chains. Clinical heterogeneity can be mostly explained by genetic heterogeneity. There are a few reports from genotype-phenotype correlations in H disease worldwide. Iran is a genetically heterogeneous population, therefore predicting phenotype directly from the genotype is relatively difficult. This study aimed to investigate the genotype-phenotype correlations in 124 patients with H disease and update the molecular spectrum of H disease in Iran. To the best of our knowledge this is first comprehensive study of H disease in Iranian population.

**Method**

The diagnosis of Hb H disease is based on the finding of microcytic, hypochromic anemia in a patient who did not have iron deficiency and whose Hb electrophoresis was not consistent with the  $\beta$ -thal syndrome. DNA was extracted from 124 patients participated in this study. Genetic testing was performed using Multiplex PCR to find common deletions and direct sequencing to find point mutations.

**Results**

The study group consists of 53 deletional, 24 non deletional, 44 two point mutations and 3 were unknown. The most common mutation is -- Med /-  $\alpha$  3.7 (52.8%) which is followed with --20.5/-  $\alpha$  3.7 (28.3 %) of deletional.

**Conclusion**

Our results can provide a basis for predicting the severity of the phenotype based on genotypes and make proper decisions for prenatal diagnosis in H disease.



## Title: **Complications Pattern And Burden Of The Disease In Patients Affected By Beta-Thalassaemia Major**

**Abstract Category:** Iron overload and management

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**Presentation on 19 November 2017, in Hall "Ilida" at 08:40**

## **ABSTRACT**

### **Background**

Despite the correct application of blood transfusions, diagnostic interventions and iron chelation treatments (ICT), beta-thalassaemia (BTM) patients have many complications. Systematic population analyses on types and frequency of these complications are very few. The study aim is to characterize the complications, their risk factors and their clinical and economic impact in a BTM sub-population, part of the Italian Multiregional Thalassaemia Registry (HTA-THAL) collecting almost 2.000 patients. In addition 1 year Adverse Events (AEs) were observed.

### **Method**

Prospective multicentre observational study, consisting of 272 BTM patients from 13 clinical centres aged >12 years. Complications at baseline and AEs were analysed. Risk factors were analysed through chi-squared and unpaired t-tests. Logistic regression was applied to perform the risk factors multivariate analysis.

### **Results**

82.3% of patients were affected by 1 to 6 complications for a total of 554. Cardiac complications were less represented than expected. Musculoskeletal complications have been the mostly represented followed by hepatic, sexual and endocrine diseases. Splenectomised patients, born before 1970, starting ICT when aged >4 years, receiving more than 20 blood transfusions presented a significantly higher complications number.

885 AEs requiring 3125 additional medical services occurred in 1 year. Of these, 34.9% were related to treatments and 65.1% to other causes. AEs, additional medical intervention and costs increase progressively in patients affected by one complication or more respect to not complicated patients.

### **Conclusion**

The complications pattern is changing according to the birth cohort and differentiates the older from the younger patients. The burden of the disease and its costs increase after the onset of the first complication, therefore the prevention is fundamental.

More efforts and more observational studies are necessary to better identify strategies to prevent or reduce complications and their impact. Patients Registries could represent the optimal way to facilitate these studies and provide relevant information.



**Title: Association between serum ferritin reduction and film-coated versus dispersible tablet formulations of deferasirox: A post-hoc analysis of mediation by patient-reported outcomes from the ECLIPSE trial**

**Abstract Category:** Iron overload and management

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## ABSTRACT

### Background

The 24-week ECLIPSE trial demonstrated similar safety of the deferasirox film-coated tablet (FCT) to dispersible tablets (DT), with fewer severe gastrointestinal (GI)-related adverse events (AEs), and more favorable patient-reported outcomes (PROs), including better adherence, satisfaction, palatability, and fewer concerns. FCT patients showed a larger median reduction in serum ferritin (SF) from baseline (−350.0 vs −85.5ng/mL) than DT, despite similar doses (Taher AT et al. Am J Hematol 2017), which may be due to better adherence. This post-hoc analysis estimated to what degree PROs mediated the SF reduction observed with deferasirox FCT versus DT.

### Methods

Transfusion-dependent thalassemia or MDS patients were randomized to receive equivalent deferasirox FCT (N=87) or DT (N=86) doses. PROs were assessed using the Palatability and modified Satisfaction with Iron Chelation Therapy questionnaires, the latter assessing adherence, satisfaction, and concerns. Frequency of GI-related AEs were also assessed. The mediation analysis, used to compute proportion mediated (PM), quantified how much of the association between treatment with deferasirox FCT versus DT and SF reduction was mediated through PRO scores. Subgroup analyses were conducted in: all patients with prior deferasirox DT use (DT non-naïve); all thalassemic patients; DT non-naïve thalassemics.

### Results

Association between deferasirox FCT versus DT treatment and SF reduction was substantially mediated by patient-reported adherence (PM=66.6%, P=0.01). Patient-reported adherence, along with satisfaction, concerns, palatability scores, and frequency of severe GI-related AEs together mediated 90.1% of the association (P=0.01). PM by patient-reported adherence was increased in DT non-naïve patients (PM=80.5%, P=0.01), and in DT non-naïve thalassemia patients compared to all thalassemia patients (PM=68.1%, P=0.03 vs PM=45.0%, P=0.09, respectively).

### Conclusions

Better PROs, particularly patient-reported adherence, are significant mediators of the association between treatment with deferasirox FCT versus DT and SF reduction. PM was increased in patients with prior DT exposure, suggesting their enhanced appreciation for deferasirox FCT over DT.

**Title: Predictors Of Adverse Outcome In Patients With Sickle Cell Disease In SQUH****Abstract Category:** Sickle Cell Disease**Authors:** Alkindi Salam, Al'Adawi Safa, AL-Jadidi Salma, & Pathare Anil**Presenting Author:** Alkindi Salam**Affiliation:** Sultan Qaboos University Hospital, Oman**Email:** sskindi@yahoo.com**Presentation on 19 November 2017, in Hall "Ilida" at 08:50**

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**ABSTRACT****Introduction**

Sickle cell disease (SCD) is an inherited disorder and a major public health problem in Oman with high morbidity and mortality. Therefore, the ability to identify the risk factors that are associated with mortality among SCD patients would permit accurate prognostication and provide an opportunity to decrease the number of death by using effective prophylactic management.

**Methods**

A retrospective cross-sectional study was performed by obtaining clinical and laboratory data from electronic health records of all Omani SCD ( $\geq 11$  years of age) who died at Sultan Qaboos University Hospital. Demographic data, clinical, radiological and laboratory parameters were collected and analyzed.

**Results**

42 SCD patients were identified with 69% being male and 31% female. The age ranged between 11 to 78 years (mean+SD,  $30.9 \pm 14.07$ ). Prior history of Acute chest syndrome (59.52%), stroke (16.67%), hepatic sequestration (11.90%) and dactylitis (4.76%) was observed. These patients in their terminal episode presented with fever (51.22%), cough (28.57%) and crepitation (23.81%). 57.50% had abnormal chest X-ray and 88.46% had abnormal CT chest. There was a significant drop in the Hb and platelet counts from baseline, with a significant rise in the WBC, LDH and CRP levels ( $p < 0.05$ ). Out of 42 patients, 12 got bacterial infection during last episode; two being community acquired whereas, 10 were hospital acquired. Further, six patients got viral infection and 3 got fungal infection. All patients took antibiotics, but 88.1% got blood transfusion, 35.71% had blood exchange and 87.5% required NIV/ventilation. Most of the terminal event were associated with sepsis, sudden death, and respiratory failure.

**Conclusion**

In conclusion, in this cohort of 42 SCD patients, previous history of acute chest syndrome, stroke and sepsis as well as development of acute chest syndrome and infection along with drop in Hemoglobin and leukocytosis were the poor prognostic factors that adversely contributed to mortality.

**Keywords:** Sickle cell disease; mortality; predictors; adverse; outcome



## **Title: Increased Hb F in Beta Thalassaemia Intermedia patients in Sri Lanka associated with Extended Alpha Globin Genes**

**Abstract Category:** Non-transfusion dependent thalassaemia

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**Presentation on 19 November 2017, in Hall "Ilida" at 08:55**

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## **ABSTRACT**

### **Background**

Increase production of HbF in patients with beta thalassaemia compensates the reduce production of adult HbA and thereby reduces the severity of the disease. A previous study in Sri Lanka had shown that beta thalassaemia intermedia (beta TI) patients associated with extended alpha genes had unusually low Hb F levels. In this study we analyzed the Hb F levels in a group of beta TI patients with extended alpha genes and tried to determine how it relate with the beta genotype.

### **Method**

Hb F in all consenting TI patients and their family members were measured by HPLC. Genetic analysis of the globin genes was done by standard methods. Hb F levels of the heterozygous beta TI patients (n=27) with extended alpha genes (Test) were compared with beta heterozygotes (n= 25) with normal alpha gene (Control) and among subsets (subset 1 - RNA processing beta mutations, subset 2 - RNA translational beta mutations) in the test group.

### **Results**

Mean HbF levels in the test and control were 5.23 and 0.87 percent respectively. Seven different beta mutations identified in the test group, IVS I 5 G\_C and IVS I I G\_A being commonest and had five to six alpha globin genes, heterozygous triplicated alpha genes (n=17), homozygous triplicated alpha genes (n=3) and heterozygous quadruplicated alpha genes (n=6). Mean Hb F levels of the test group was significantly high (P 0.0003) from the control group. Further analysis of the Hb F in the test group showed a significant difference in the HbF levels among the two subsets (P 0.0000).

### **Conclusion**

Beta thalassaemia intermedia patients with excess alpha globin gene exhibits High Hb F levels and it is associated with the beta genotype with RNA translational mutations. However, correlation of individual beta mutation with excess alpha for High HbF presentations needs further studies.



**Title: HEMANEXT Novel Blood Storage System Significantly Improves Red Blood Cell Quality And Provides Promise Of Improving Consistency, Safety And Efficacy Of Chronic Transfusions**

**Abstract Category:** Blood transfusion

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**Presentation on 19 November 2017, in Hall "Ilida" at 09.00**

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## ABSTRACT

### Purpose

Develop Hemanext to significantly improve the quality of cold-stored red blood cells by optimizing oxygen during storage.

### Methods

A metabolomics study on the consequences of oxygen content (%SO<sub>2</sub>) in red cell degradation was examined. Leukofiltered RBCs (n=4) from human volunteers were stored in AS-3 under normoxic, hyperoxic, or hypoxic conditions for up to 42 days (%SO<sub>2</sub> ranging from <3 to >95%) prior to UHPLC-MS metabolomics analysis using stable-isotope labeled standards. Additional storage studies were conducted on pool and split units comparing conventionally stored control vs. %SO<sub>2</sub>-reduced.

### Results

Current RBC production processes allow %SO<sub>2</sub> to vary greatly unit-to-unit and to increase throughout storage. RBC hemoglobin was negatively affected by oxygen: i) methemoglobin concentration was positively correlated with %SO<sub>2</sub> throughout storage; ii) the percentage of oxidized proximal histidine (H92) was 30-40% lower in %SO<sub>2</sub>-reduced units; and iii) %SO<sub>2</sub>-reduced units yielded physiologic P50 values through 4 weeks of storage. Additionally, metabolomics workflow revealed that non-enzymatically oxidized lipids were significantly reduced, while GSH/GSSG and NADPH/NADP ratios increased.

### Conclusion

Patients dependent on blood transfusions are dependent on the quality of cold-stored red blood cells. Storage degradation includes: reductions in 2,3-BPG, deformability, energy metabolism and red cell survival. Series of studies clearly shows that Hemanext processing significantly improves these along with many other parameters. There are currently no controls in place to ensure that each red blood cell unit provide consistent content of viable red blood cells or absence of agents associated with adverse events. Hemanext oxygen-management provides a new level of control promising to provide a higher level of quality, consistency and safety for chronic transfusion recipients.



## Title: **ITHANET: The Information And Database Community Portal For Haemoglobinopathies**

**Abstract Category:** Epidemiology

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## **ABSTRACT**

### **Background**

Haemoglobinopathies are the commonest monogenic diseases, with millions of carriers and patients worldwide. Online resources for haemoglobinopathies are largely divided into sites catering for patients, researchers and clinicians separately. However, the severity, ubiquity and surprising genetic complexity of the haemoglobinopathies call for an integrated website as a free and comprehensive repository and tool for patients, scientists and health professionals alike. In response to this unmet need we have developed the ITHANET community portal.

### **Methods**

The ITHANET portal is browser-based and independent of additional plugins; it thus works across all modern browsers and online-enabled devices. It is written in PHP based on the Joomla! content management system, uses the jQuery Javascript library and for enhanced data presentation and visualisation employs the jQuery-UI, DataTables, HighCharts and HighMaps packages.

### **Results**

The ITHANET portal is an expanding resource for clinicians and researchers dealing with haemoglobinopathies. It integrates information on news, events, publications, clinical trials and haemoglobinopathy-related organisations and experts, wiki-based content of protocols, clinical guidelines and educational articles and, most importantly, databases of variations, epidemiology and diagnostic and clinical data. With 2590 fully annotated mutations in over 200 genes, regulatory and intergenic sequences, the ITHANET portal is the largest haemoglobinopathy mutation database. It moreover integrates molecular data with epidemiological and healthcare information for by this time up to 103 different countries. The ITHANET portal is the database partner of choice for the Human Variome Project initiative Global Challenge, accepts, incorporates and credits contributions to its content by local experts from any country in the world, and is freely accessible to the public at <http://www.ithanet.eu>.

### **Conclusions**

Through its comprehensiveness, internal interconnectedness, expandability and the active involvement of global haemoglobinopathy experts in its ongoing development, the ITHANET portal is the future-proof and intuitive port of call for any information relating to haemoglobinopathies.



## **Title: Transition Navigator More Than Just Transfer? Staff Perceptions of a Novel Transition Program and Role**

**Abstract Category:** Miscellaneous

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## **ABSTRACT**

### **Background**

Transition from pediatric to adult health care coincides with various life changes that adolescents and young adults (AYA) face alongside managing a chronic health condition. For AYA with hemoglobinopathies, this transitional period is associated with poor health and social outcomes. In an effort to provide continuous care for these patients as they transition from a pediatric to an adult clinic, a joint transition program was developed.

### **Methods**

A transition program with a dedicated, cross-appointed Transition Navigator (TN) was implemented in 2014 across the hemoglobinopathy clinics at a pediatric and an adult hospital using a quality improvement framework. After two years of operation, a staff evaluation of the program and TN role was conducted. Anonymous surveys were distributed to multidisciplinary hemoglobinopathy staff in the pediatric and adult clinic to obtain their perceptions of the value and impact of the program. Surveys were completed by six pediatric and seven adult care providers. The surveys contained Likert-scale, ranking and open-ended questions.

### **Results**

Response rate was 86% for the pediatric team and 100% for the adult team. Qualitative and quantitative results of the surveys will be presented, including staff perceptions, feedback and suggestions about the program and the TN role.

### **Conclusion**

The transition program was well-received by pediatric and adult care providers. Both teams endorsed the continuation of the program and the TN role. Specific recommendations from the survey will be incorporated into future programming.

**Title: Patients' Satisfaction with the Quality of Nursing Care in Thalassaemia Units****Abstract Category:** Quality of Life**Authors:** Khetam Al-Awamreh**Presenting Author:** Khetam Al-Awamreh**Affiliation:** Maternal & Child Health Nursing Department, Princess Salma Faculty of Nursing,, Al al-Bayt University, Mafrq, Jordan**Email:** al-awamreh.k@aabu.edu.jo**Presentation on 19 November 2017, in Hall "Kallipateira" at 08:35**

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**ABSTRACT****Background**

Patients diagnosed with Beta thalassaemia major (BTM) frequently and regularly visit hospitals for blood transfusion; which is one of the life-saving treatments, companies with the chelating therapy. Patient satisfaction with the quality of nursing care is a strong indicator of the quality of care in hospital (Laschinger et al, 2005). Determinants of quality of nursing care include adequate skills, staff numbers, caring attitudes, effective communication, efficient organizational and management systems, effective community participation, and staffing data (Loan et al., 2003). Alasad and Ahmad (2003) found that Jordanian patients' overall satisfaction were considered relatively low compared to patients in another country.

**Methods**

The purpose of this research is to evaluate patients' satisfaction with the quality of nursing care in thalassaemia units which are located in three Jordanian public hospitals. A descriptive, cross-sectional design used, the data collected from a convenience sample of 400 regular transfused BTM patients. An Arabic translated modify version of patient satisfaction with nursing care quality questionnaire (Laschinger, Hall, Pedersen & Almost, 2005) used to collect the data.

**Results**

A total of 377 completed questionnaires returned with response rate equal (94%). 187 (50.4%) were female and 190 (49.6%) male, most of patients 293 (77.7%) between 15-25 years old, more than half 168 (44.6%) received blood transfusion every 4 weeks, 121 (32.1%) have history of other disorders than BTM, around 307 (81.5%) patients were all over score highly satisfied with the quality of nursing care they received in the units as their rate was excellent and very good. A total of 288 (76.4%) would recommend the units to family and friends.

**Conclusion**

The results show that BTM patients were highly satisfied with the quality of nursing care they received in thalassaemia units' nurses. A total high score was given to the nursing care and concern, information was given to patients, privacy, skill and competence of nurses.



**Title: Twice daily dosing of deferasirox significantly improves clinical efficacy in transfusion dependent thalassemias who were inadequate responders to standard once daily dose**

**Abstract Category:** Iron overload and management

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**Presentation on 19 November 2017, in Hall "Kallipateira" at 08:40**

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## ABSTRACT

### Background

It appears that once daily oral iron chelator, deferasirox, doesn't make up enough bioavailability of the drug for inadequate responder (IR). We hypothesize that adjusting DFX dose from once daily into two dividing dose per day might improve drug exposure and chelating efficacy in such patients.

### Methods

A retrospective cohort of clinical response to twice daily dosing of deferasirox was done in IR Iranian thalassemia patients (having a rising serum ferritin (SF) trend or a reduction of SF less than 30% of baseline levels at least 3 consecutive months, with more than two SF measurements higher than 1500 ng/mL and receiving once daily DFX at an average dosage >35 mg/kg/day for at least 6 months). After switching to twice daily with the same total dose per day, adverse events monitoring were performed every 4 weeks and SF were checked every 3 months. Liver and heart MRIT2\* were performed every 6 months.

### Results

Total 8 patients (3 males) were eligible with a mean age of 18.6 years (range; 10-28 years). There was a statistically significant decrease in serum ferritin levels with twice versus once daily use of deferasirox (2319.00 vs. 1284.19 mg/dl,  $P=0.002$ ). The results of liver ( $p=0.05$ ) and heart ( $p=0.001$ ) MRIT2\* showed improvement. The initial and follow-up ALT and serum creatinine levels did not differ significantly ( $p>0.05$ ). None of the patients required a dose reduction or cessation of the drug related to a toxicity.

### Conclusion

Dividing DFX to twice-daily dose might provide a better bioavailability in selected patients with sustainable therapeutic levels of DFX throughout 24 hr-exposure resulting in a better clinical efficacy. Further pharmacokinetic and pharmacogenetic study in IR patients is warranted and this can provide additional insights on the next level of tailoring iron chelation therapy in patients with transfusional iron overload.

**Keywords:** Deferasirox, Twice-daily dose, Inadequate responders, Thalassemia



**Title: Comprehensive Structured Transition Program With Dedicated Transition Navigator Reduced Lost to Follow-Up And Improved Medication Adherence in Adolescents and Young Adults With Sickle Cell Disease and Thalassemia**

**Abstract Category:** Miscellaneous

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**Presentation on 19 November 2017, in Hall "Kallipateira" at 08:45**

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## ABSTRACT

### Background

Transition from pediatric to adult care is a period of high risk for loss to follow-up, morbidity and mortality in adolescents and young adults (AYA) with hemoglobinopathies. The purpose of this study was to determine whether a transition program with a Transition Navigator (TN) reduced loss to follow-up, and improved medication adherence and appointment attendance compared to an unstructured transfer.

### Methods

A transition program with a TN was deployed across a pediatric and an adult hemoglobinopathy clinic starting August 1, 2014. This observational study compared all AYA with hemoglobinopathies who turned 18 between August 1, 2013 and August 1, 2015. Patients in the cohort prior to the transition program (n=51) were compared to patients who transitioned through the program (n=61). Data from one year prior to last pediatric appointment and one year following first adult appointment were collected.

### Results

The transition program reduced the proportion of patients lost to follow-up from 29% to 7%. In those who were on hydroxyurea or iron chelation, significant increase in the proportion of patients who maintained or improved their medication adherence to  $\geq 4$  days/week was observed in the transition cohort; presence of the program was independently associated with this improvement. A trend towards improvement or maintenance of  $\geq 90\%$  attendance to appointments was observed.

### Conclusion

A transition program with a dedicated TN significantly reduced the number of patients lost to follow-up, and significantly improved and maintained fair to good medication adherence. Further analysis of economic benefit and patient satisfaction will be conducted.



## **Title: Patient Lead Organisations in Successful Policy Advocacy: Lessons From the Maldives**

**Abstract Category:** Quality of Life

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**Presentation on 19 November 2017, in Hall "Kallipateira" at 08:50**

### **ABSTRACT**

#### **Aims and objectives**

Aim of the paper is to validate how patients as advocates can effectively influence policy to improve quality of life for patients especially in an environment where civil society organisations are considered weak with low capacity and in an environment where policy makers are frequently changing.

#### **Background and Introduction**

Maldives has the highest prevalence of beta Thalassaemia in the world with 18% of its population being carriers (SHE 1992). To date over 800 patients have been registered. There are two active NGOs working in this field in the country since 1990s. A nationwide thalassaemia prevention program was initiated by an NGO. To date thalassaemia is not fully mainstreamed in the health system.

Maldivian Thalassaemia Society (MTS) is the only patient parent lead organisation working to safeguard health of patients and ensure they have an equal chance in life. For the past 20 years MTS has been an instrumental NGO in the field, lobbying and helping to set standards for practice, training, and continuing education to define the role of health care providers in thalassaemia program. As an NGO MTS possesses strengths and characteristics that enable it to function as an effective and dynamic agent in this process. One of the strengths is expert patient group to lead the programs. Using their expertise derived from their own life experiences. The emphasis of MTS was on positive advocacy to influence policy changes that impact patients health. Patient advocacy role was crucial with their expertise, and use of precise information without bias.

#### **Method**

This is a case study, triangulated results of the consistent positive advocacy that have resulted in changing policy for the benefit of patients. Advocacy towards a patient centred approach in management and treatment is required to ensure patients an equal chance in life.

#### **Results**

Government authorities and health care providers have made significant efforts in dealing with thalassaemia and sickle cell anaemia compared to the 1990s. MTS have effectively influenced to create policies where it did not exist before, refined ineffective policies. And making sure that only good policies are followed, implemented and enforced. 15 years ago, the average life expectancy of patients was 12 years, it has dramatically improved to 25 years, successful policy advocacy to change policies to benefit patients have played a major role in the changes in patient management and care in Maldives.

Major hall mark of this is the Thalassaemia law enacted in 2012, a patient driven process

Followed by recognition of Thalassaemia as a condition requiring multidisciplinary care, expansion of choice of oral chelators, ferriprox to include in the health budget in 2018, policy changed to include all haemoglobin variants (HbS, HbD, HbE etc) in the National thalassaemia register and eligible for free treatment.

MTS efforts for advocacy with international organisations have provided substantial improvements in the thalassaemia situation in the country, mainly in bringing thalassaemia in the forefront of policy discussions.

#### **Conclusion**

Advocacy for policy changes is a painful, slow and and grueling process, but it is possible. Outcomes so far of MTS work prove that patient lead organisations can successfully influence policies that benefit patients. Strategic planning, working



with the authorities have proved more successful. Educating the health care providers , policy makers and giving factual and precise statistics have proven to work.

Patients are agents of change if they use their life experience and knowledge positively

However, there is still much more work that needs to be done in terms of advocacy, provision of standard services, especially in terms of evidence based research into improving quality of life for patients.

**Keywords:** Advocacy, Policy, Civil Society,Thalassaemia

**Title: Get Connected! Mission #IronCtrl: The Ironchelation Challenge Campaign****Abstract Category:** Quality of Life**Authors:** Aishath Shifneez Shakir**Presenting Author:** Aishath Shifneez Shakir**Affiliation:** Maldivian Thalassaemia Society, Republic of Maldives**Email:** shifneez@gmail.com**Presentation on 19 November 2017, in Hall "Kallipateira" at 08:55**

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**ABSTRACT**

Sickle cell and thalassaemia have long been considered a disease where children are left with severe anaemia, poor growth, huge abdominal organs and childhood death. regular transfusions have alleviated these symptoms and had improved their survival through childhood. However, blood contains large amounts of iron, which the body is incapable of naturally eliminating, and hence many face with severe morbidity and mortality due to complications of iron overload in their early adolescent ages.

Introduction to iron chelators such as Desferoxamine (Desferal), Deferiprone (L1 or Ferriprox), Deferasirox (Asunra or Exjade) have dramatically improved the quality of lives of those who adhere to the iron chelation therapy. T2\* MRI scans can now identify the severity of iron overload in organs such as heart and liver and administration of iron chelation therapy have improved saving many from heart failure and organ complications which has been the number cause of death in thalassaemia at present.

According to the Knowledge, Aptitude, and Perception (KAP) survey done in 2015 by Maldivian Thalassaemia Society, conclusion to the responses among 59 patients were that, there is a heavy focus from clinicians and patients on maintaining optimum Haemoglobin levels through blood transfusion and not so much focus on iron chelation therapy as well as monitoring of the patients on the aspects of growth and development. Although 92% of them wish to reduce excess iron and have a healthy life, only a few have the knowledge and acceptance of the impact of iron overload on their health. However still, many are living with a ferritin level that is life threatening and have not aware of its impact on health as the damages and complications are not readily visible as soon as iron overload begins.

Lack of knowledge of the importance of iron chelation, have lead the sufferers to unintentional discrimination. Unfortunately, it extends from health care practitioners to educations systems and the community. Improved patient knowledge and their positive attitude is very important in shaping up their compliance and healthy progression to adulthood by breaking the stigma towards underestimation of our capabilities, going abroad for higher studies, job opportunities and even choosing a life partner.

Acceptance from community can help patients face the challenge to keep adherence to #ironchelation therapy that will improve the quality of their lives. Change must happen, it is up to us as survivors, to change our lives and lives of others and make it happen.

Get Connected! Mission #IronCtrl - inspired by this year's TIF theme for International Thalassaemia Day #Getconnected, an #ironchelation challenge campaign was initiated by our Maldivian thal/sickle patients to motivate and take active measures to decrease iron overload complications by reducing Serum Ferritin levels to a safe range below 1000ng/mL.

16th TIF International Conference for Patients and Parents sets the right platform to initiate Get Connected! Mission #IronCtrl as a global #Ironchelation Challenge Campaign to inform, community, medical professionals and educators, and other transfusing patients and their families to learn that iron overload is a chronic condition that if not addressed properly can lead to death. lets' all stand with Mission #IronCtrl to tell the community that our condition does not define us. We are not sufferers to be pitied, but survivors.



**Title: Outcome of Home-Based Continuous Deferoxamine Intravenous Infusion via Peripherally Inserted Central Catheter in Thalassemia Major**

**Abstract Category:** Iron overload and management

**Authors:** Khawla Belhouli, Hany Dewedar, Fatheya Alkhaja, Ahmed Farag, Nishi Susan Oommen

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**Presentation on 19 November 2017, in Hall "Kallipateira" at 09:00**

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## ABSTRACT

### Background

Few programs have evaluated the value of deferoxamine intravenous (IVDFO) infusion at home in patients with severe iron overload, although the effectiveness of IVDFO therapy in this group of patients is well established. We describe the safety and efficacy of an outpatient home-based continuous IVDFO therapy to rescue severely iron overloaded thalassemia major (TDT) patients.

### Methods

This was a retrospective cohort study of all adult TDT patients treated with outpatient home-based continuous IVDFO through peripherally inserted central catheter (PICC) from October 2013 - August 2015. These patients were not responding, not tolerating or noncompliant to oral chelation therapy or subcutaneous DFO with cardiac T2\* <8ms or LIC >15mg Fe/g dw or cardiac T2\* 8-15ms associated with compensated or decompensated heart failure, or arrhythmias, or EF < 45% on echo, or two or more endocrinopathies.

### Results

Forty-one patients were enrolled (mean age  $28.4 \pm 5.6$  years). Efficacy was assessed in 25 patients (61.0%) who received therapy for more than 6 months. Concomitant Deferasirox (17, 42%) or Deferiprone 21 (51%) was prescribed. There was significant decrease in mean ferritin ( $p=0.0001$ ) and LIC ( $37.5 \pm 9.9$  to  $12.6 \pm 11.0$ ,  $p=0.001$ ) with a significant increase in cardiac T2\* ( $8.1 \pm 3.5$  msec to  $12.4 \pm 6.3$  msec,  $p=0.002$ ). LVEF improved from a mean of 40% to 60%. Heart failure was reversed in two out three patients. Observed adverse event in all enrolled patients (40) were local skin reaction ( $n=17$ ), renal tubular acidosis ( $n=6$ ), arthritis ( $n=4$ ), line thrombosis ( $n=4$ ), line displacement ( $n=4$ ), local infection ( $n=4$ ), systemic infection ( $n=2$ ), retinopathy ( $n=1$ ) with discontinuation of therapy in (9, 22.0%) and no mortality report.

### Conclusion

Outpatient home-based continuous IVDFO infusion via PICC is safe and highly effective in reducing severe iron overload in TDT patients.



**Title: CRIZANLIZUMAB, A P-Selectin Inhibitor, Increases The Likelihood of Not Experiencing a Sickle Cell-Related Pain Crisis (SCPC) in Patients With Sickle Cell Disease (SCD) While on Treatment**

**Abstract Category:** Sickle Cell Disease

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**Presentation on 19 November 2017, in Hall “Kallipateira” at 09:05**

## ABSTRACT

### Background

Crizanlizumab 5.0 mg/kg significantly reduced the frequency of SCPC events in patients with SCD in the SUSTAIN study. A post-hoc analysis of complete responders (SCPC-free patients) is reported.

### Methods

Patients (16–65 years) with SCD (including HbSS, HbSC, HbSβ<sup>0</sup>– and HbSβ<sup>+</sup>–thalassaemia genotypes) and 2–10 SCPCs in the previous 12 months were randomized 1:1:1 to crizanlizumab 5.0 mg/kg, 2.5 mg/kg or placebo. Hydroxyurea was permitted if received for ≥6 months (stable dose for ≥3 months). Following loading (days 1 and 15), treatment was administered every 4 weeks to week 50; final assessment was at week 52. Frequency of complete responders was summarized for the intent-to-treat (ITT) population and prior SCPC, SCD genotype and hydroxyurea use subgroups.

### Results

198 patients were randomized (ITT population); 62.6% and 37.4% experienced 2–4 and 5–10 SCPCs in the previous year, respectively, and 62.1% were taking hydroxyurea. The most common genotype was HbSS (71.2%). More patients receiving crizanlizumab 5.0 mg/kg (n=24/67; 35.8%) were SCPC-free compared with 2.5 mg/kg (n=12/66; 18.2%) and placebo (n=11/65; 16.9%). In subgroup analyses, crizanlizumab 5.0 mg/kg treatment resulted in a greater proportion of SCPC-free patients compared with 2.5 mg/kg or placebo (prior SCPC: [2–4] 40.5%, 24.4%, 24.4%, [5–10] 28.0%, 8.0%, 4.2%; genotype: [HbSS] 31.9%, 19.1%, 17.0%, [other] 45.0%, 15.8%, 16.7%; hydroxyurea use: [yes] 33.3%, 22.0%, 17.5%, [no] 40.0%, 12.0%, 16.0%, respectively). Among patients with 5–10 SCPCs in the previous 12 months and/or homozygous HbSS, more were SCPC-free when treated with crizanlizumab 5.0 mg/kg compared with placebo. During the study, 33.3% of patients receiving hydroxyurea with crizanlizumab 5.0 mg/kg were SCPC-free (placebo: 17.5%).

### Conclusions

Crizanlizumab 5.0 mg/kg may result in a higher proportion of patients with SCD being SCPC-free compared with placebo, even in potentially higher-risk subpopulations, suggesting that crizanlizumab is an effective disease-modifying agent.



## Poster Abstracts

**Title:** **Providing Thalassaemia Patients with Blood in Azerbaijan**

**Abstract Category:** Blood Transfusion

**Authors:** Parvana Hajiyeva<sup>1</sup>, Jeyhun Mammadov<sup>2</sup>, Chingiz Asadov<sup>1</sup>, Zohra Alimirzoeva<sup>1</sup>

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### ABSTRACT

#### Background

Regular blood transfusions are a crucial aspect of the treatment of thalassaemia. The World Health Organization supports that providing safe and adequate blood should be an integral part of every country's national health care policy and infrastructure. In 2005, the Parliament of the Azerbaijan republic adopted the law "On blood, blood components donation and blood service", and in 2006, the Cabinet of Ministers approved a state program on "Development of blood, blood components donation and blood service". Thus, the state took all responsibility for the development of blood donation and blood service. The purpose of this study was to assess the availability of thalassaemic patients with donor blood.

#### Methods

Based on the study of medical records of the Central Blood Bank of the Institute of Haematology and Transfusiology and the Republican Thalassaemia Centre, the number of thalassaemia patients receiving blood transfusion as well as the number of red cell concentrates (RCC) consumed during the year was calculated. In addition, according to a special formula, the necessary amount of RCC was calculated to treat transfusion-dependent patients during the year and the results obtained were compared.

#### Results

As a result, it was revealed that there are 928 transfusion-dependent patients with thalassaemia in the Republic and 4800 litres of red cell concentrates per year are used for their transfusion therapy. This is the 24% of the total number of the harvested RCC during the year. Calculations carried out using a special formula to carry out transfusion therapy to maintain pre-transfusion haemoglobin at a level of 9.5-10 g/L. These patients require 4454 litres of RCC. When necessary, washed red cells were used (560 litres/year).

#### Conclusion

Thus, the blood service of the Republic of Azerbaijan fully meets the needs of blood and assures donor-recipient compatibility of transfusion-dependent thalassaemia patients.



## **Title: Role of Haemovigilance Acuity for Quality Transfusion: Challenge from the Beginning - an Emergent Country Perception**

**Abstract Category:** Blood Transfusion

**Authors:** Tanzeel Imran, Humera Naz Altaf, Farid Baktiar

**Presenting Author:** Tanzeel Imran

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### **ABSTRACT**

#### **Background**

Haemovigilance is surveillance system that highlights efficiency and adverse events related to transfusion medicine, providing opportunities for institutional improvement by critically evaluating their transfusion sequence. Pakistan as an emergent country is determined to pursue hemovigilance as an necessary tool for quality transfusion and for stipulation of safe blood as evident in developed nations

#### **Objective**

To study the effectiveness of hemovigilance system as essential means for safe blood transfusion practice at our institution.

#### **Material and Methods**

This is a descriptive cross sectional study. Hemovigilance system was introduced and implemented two years ago at Jamila Sultana Foundation (NGO for Thalassemia). During the study period all transfusion events starting from donation to follow up of donor and recipient were recorded from 14 May 2015 till 15 May 2017 with the purpose to improve safety of blood donor and transfusion recipient.

#### **Result**

Total 13400 donors donated blood at our institution. Out of the total donation 12050 red cell, 8023 fresh frozen plasma (FFP), 12050 platelets and 4027 cryoprecipitate components were prepared and subsequently issued. Number of infected bags was 1350 due to various viruses and bacteria. Febrile non-hemolytic transfusion reaction (FNHTR) was most frequent and found in 1.8 % (149/8023), followed by 0.8% (98/12050) allergic reaction from Platelets while 0.7 % (89/12050) from PRBC. Transfusion transmitted infections (TTI) appeared in 0.24% (29/12050) due to various viruses and bacteria. Delayed transfusion reaction noted in 0.17% (21/12050) while 0.047% transfusion-related acute lung injury (TRALI) occurred from PRBC (2/12050) and FFP (3/8023) respectively with 100% mortality. Acute hemolytic transfusion reaction (AChTR) was least frequent at our institution 0.02% (3/12050) and with no mortality.

#### **Conclusion**

Haemovigilance as effective system for strengthening quality blood banking. We highly recommend Haemovigilance development and implementation on national level in emergent countries as an indicator for safe transfusion practice.



**Title: Frequency of clinically significant alloantibodies as a consequence of multiple transfusion in Hemoglobinopathies in different ethnic population of Pakistan**

**Abstract Category:** Blood Transfusion

**Authors:** Tanzeel Imran, Humera Naz Altaf, Farid Baktiar

**Presenting Author:** Tanzeel Imran

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## ABSTRACT

### Background

Thalassemia is the most prevalent genetically transmitted blood disorder in Pakistan. Alloimmunization as a consequence of repeated transfusion is a challenge for developing nation because of diverse inheritance in blood group phenotypes and limited access to latest diagnostic facilities. A region based study has been performed to find prevalence of clinically significant antibodies in different ethnic groups of Pakistan.

### Objective

To determine the prevalence of clinically significant red cell antibodies in multiple transfused patients of hemoglobinopathies in different ethnic population of Pakistan.

### Material & Methods

This is a cross-sectional descriptive study conducted in Jamila Sultana Foundation (NGO for Thalassemia for adult and pediatric patients) January 2016 to March 2017. A total of 356 registered patients on regular transfusion were studied. Among them 339 were thalassemia major, 14 thalassemia intermedia and 3 sickle cell anemia respectively. Alloantibody screening and identification was carried out by column agglutination method (Bio Rad Switzerland).

### Results

From our total registered 356 patients 39% were from Punjab followed by 30% KPK, 17% Sind, 9.9% Baluchistan and 4% Kashmir regions respectively. The prevalence of red cell alloimmunization was 4.5% in KPK, 2.5% in Punjab and 0.2% in Baluchistan region while no patient from Sind and Kashmir developed alloantibodies. The most significant antibody was anti-Kell (K-antigen) both in KPK and Baluchistan whereas anti-Rhesus (E-antigen) was common in Punjab province. This highlighted insight into the difference in inheritance pattern of these blood group antigens in different ethnic population of the country.

### Conclusion

We observed significant alloimmunization in our study population with difference in specificity against red cell antigens in different ethnic population. Thus phenotypic matching for public antigens cannot be overlooked in chronically transfused patients in developing country with limited diagnostic facility.



## Title: **Alloimmunization in Patients with Haemoglobinopathies at the Thalassaemia Unit of the AHEPA University General Hospital of Thessaloniki**

**Abstract Category:** Blood Transfusion

**Authors:** Kaltsounis G.<sup>1</sup>, Chalkia P.<sup>2</sup>, Pantelidou D.<sup>2</sup>, Bakaloudi V.<sup>1</sup>, Pape M.<sup>1</sup>, Girtovitis F.<sup>1</sup>, Ntinopoulou E.<sup>1</sup>, Konstantinidou A.<sup>1</sup>, Chatzikyrkou M.<sup>1</sup>, Perperidou P.<sup>1</sup>, Tzioura A.<sup>1</sup>, Voulgaridou V.<sup>1</sup>, Rapi A.<sup>1</sup>, Floridis K.<sup>1</sup>, Goudias D.<sup>1</sup>, Taliona G.<sup>1</sup>, Kaltsa P.<sup>1</sup>, Papageorgiou V.<sup>1</sup>, Pavlopoulou A.<sup>1</sup>, Poulioudi P.<sup>1</sup>, Georgiadou C.<sup>1</sup>, Papadopoulou A.<sup>1</sup>, Hassapopoulou-Matamis H.<sup>1</sup>

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## ABSTRACT

### Background

Alloimmunization against red blood cell (RBC) antigens is not uncommon in multi-transfused patients. Different rates and types of alloimmunization have been reported depending on the age at first transfusion, the ethnic background, the policy of unit selection (limited or extended matching of blood units in clinically important blood group systems) and other reasons. In this study we analyzed the rate and type of alloimmunization in patients followed at the Thalassaemia and Sickle Unit of the AHEPA University General Hospital.

### Methods

We reviewed records of 388 patients followed at the Thalassaemia and Sickle Unit and transfused either systematically or occasionally. Results were categorized by disease:  $\beta$ -thalassaemia major, sickle cell disease (SCD) and Thalassaemia Intermedia (TI). Screening and identification of antibodies was performed with a 3- and 11-RBC commercial panel (Bio-Rad) at 4°C, at 37 °C by the Indirect Antiglobulin Test, and by the same panels, enzyme -treated. Results were exported from the computer software e-AIMA (Computer Control Systems A.E.) and processed through Microsoft Excel.

### Results

Alloimmunization was detected in 28,7%  $\beta$ -thalassaemia major, 26,1 % in SCD and 23,6% in TI patients. In the majority of  $\beta$ -thalassaemia major patients (66,7%) a single alloantibody specificity was found or two. TI patients tend to form many alloantibodies (70% formed 3 or more). Concerning their specificity, the antibodies with the highest frequency were anti-K in  $\beta$ -thalassaemia major (20,5%), anti-E in SCD (18,2%) and anti-C<sup>w</sup> in Thalassaemia Intermedia (15,7%).

### Summary/Conclusions

In total, 26,3% of the patients exhibit antibodies against RBC antigens. Patients with SCD and TI tend to form more antibodies than patients with  $\beta$ -thalassaemia major. Antibodies against antigens of the Rhesus and Kell systems predominate. Our policy to select units always matched in the Rhesus, and Kell systems for all multi-transfused patients, as well as also matched in the Duffy, Kidd, MNSs, Lewis, Lutheran systems for SCD and TI patients, will certainly reduce the rates observed in the years to come.

## **Title: Transfusion Reactions of Patients Transfused at the Thalassaemia Unit of the AHEPA Hospital of Thessaloniki During the Two-Year Period 2015-2016**

**Abstract Category:** Blood Transfusion

**Authors:** Kaltsounis G.<sup>1</sup>, Ntinopoulou E.<sup>1</sup>, Pape M.<sup>1</sup>, Chalkia P.<sup>2</sup>, Pantelidou D.<sup>2</sup>, Kokkota S.<sup>2</sup>, Zaloufli A.<sup>2</sup>, Diamantopoulou E.<sup>2</sup>, Kourti S.<sup>2</sup>, Spanopoulou D.<sup>2</sup>, Bakaloudi V.<sup>1</sup>, Girtovitis F.<sup>1</sup>, Konstantinidou A.<sup>1</sup>, Chatzikyrkou M.<sup>1</sup>, Perperidou P.<sup>1</sup>, Tzioura A.<sup>1</sup>, Voulgaridou V.<sup>1</sup>, Rapi A.<sup>1</sup>, Floridis K.<sup>1</sup>, & Hassapoulou-Matamis H.<sup>1</sup>

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## **ABSTRACT**

### **Background**

Transfusion reactions are adverse events that may occur during or after transfusion of red blood cells or other blood products. Transfusion reactions in thalassaemic and SCD patients may have severity of varying degree. Methods to prevent their occurrence involve leukodepletion of all RBC unites and administration of washed RBCs to patients who had allergic reactions in the past.

### **Methods**

We reviewed all transfusion reactions observed at the Thalassaemia Unit of our hospital during the two-year period 2015-2016. Results were categorized by type of reaction. The frequency of reactions was calculated based on the total number of transfusions. All RBC units were leukodepleted by laboratory post-storage leukocyte removal filters prior to transfusion, and some were also washed (1-3 times) because of history of allergic reactions.

### **Results**

Twelve transfusion reactions were reported from the Thalassaemia Unit during 2015-2016 (6 each year), while a total of 7229 RBC units were transfused (0,0017%). After clinical and laboratory investigation, 3 (25%) were classified as allergic reactions, 2 (17%) might be attributed to hemolysis in the blood bag that was not recognized prior to transfusion, 1 (8%) was dyspnea related to pre-existing comorbidity (lung cancer) and 6 (50%) were attributed to unrelated reasons that happened to coincide with the transfusion.

### **Summary/conclusions**

Transfusion reactions in patients with hemoglobinopathies are nowadays infrequently observed. The important reduction in the adverse event rate (compared to data from the period of bedside filter use), may relate not only to the superiority of the laboratory filters but also to the implementation of proper blood donor selection and good laboratory practice at the Blood Bank - as well as good clinical practice at the Thalassaemia Unit. Post-storage leukodepletion appears to be an effective method of completely preventing non- febrile haemolytic transfusion reactions.

**Title: Enhanced Transfusion Safety in Thalassemia-Screening for Babesia****Abstract Category:** Blood Transfusion**Authors:** Dorothy Kleinert<sup>1</sup>, Melissa Cushing<sup>2</sup>, Ruchika Goel<sup>2</sup>, Dian Lo<sup>2</sup>, Debra Kessler<sup>3</sup>, Sujit Sheth<sup>1</sup>**Presenting Author:** Dorothy Kleinert**Affiliation:**<sup>1</sup> Division of Pediatric Hematology/Oncology; New York Blood Center, New York<sup>2</sup> Transfusion Medicine; New York Blood Center, New York<sup>3</sup> Weill Cornell Medicine, New York; New York Blood Center, New York**Email:** dok2001@med.cornell.edu**ABSTRACT****Background**

From 2006-2016 there were 9 patients with transfusion dependent Thalassemia diagnosed with transfusion-related babesiosis at our institution. Babesiosis is an intra-erythrocytic infection caused by the tick-borne protozoa, *Babesia microti*. Babesiosis may lead to asymptomatic infection, viral-like syndrome, or severe disease and hemolysis, possibly resulting in death. The disease most severely affects patients who are elderly, immunocompromised, or asplenic; thus placing thalassemia patients at significant risk. In May 2016, our blood supplier began testing red blood cell (RBC) units for babesia antibodies. In this study, we attempt to understand the effect of this testing on our thalassemia patients.

**Method**

In May 2016, our blood supplier began testing all RBC units for antibodies to *B. microti* using an investigational Enzyme Immunoassay (EIA)(Immunitics Babesia microti ELISA). Donors who are repeat-reactive are indefinitely deferred without confirmatory testing.

**Results**

The rate of reactive donations since the onset of screening for antibodies for *B. microti* was 0.6%. It has been found that twenty-one percent of repeat-reactive donations are PCR positive and presumably infectious.<sup>[1]</sup> There were 2,582 RBC units issued to 156 thalassemia patients during the first 12 months of testing. Approximately 15 of the donated RBC units might have been reactive for *B. microti* antibodies if not screened and 3 might have been infectious. No transfusion-transmitted babesiosis was diagnosed in the 1st year since testing began (0/2,582 vs 9/23,000;  $p=0.315$ ), however our study is underpowered to detect a difference after only 1 year.

**Conclusion**

Red cell transfusions are a hallmark of Thalassemia care. These life sustaining treatments are not without risks. The initiation of babesia screening is another step forward in minimizing additional risk of morbidity and potential mortality from red cell transfusions.

**References**

- [1] Levin, A.E., *et al.* Serologic screening of United States blood donors for Babesia microti using an investigational enzyme immunoassay. *Transfusion* (2016).



## Title: **Alloimmunisation and Autoimmunisation in Adult Transfusion Dependent Thalassaemia Patients**

**Abstract Category:** Blood Transfusion

**Authors:** Idit Pazgal<sup>1,3</sup>, Vered Yahalom<sup>2</sup>, Bruria Shalev<sup>2</sup>, Pia Raanani<sup>1,3</sup>, Pinhas Stark<sup>1,3</sup>

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### ABSTRACT

#### Background

Survival of transfusion dependent (TD) beta thalassaemia patients has improved significantly over the past few decades as better treatment became available. Nevertheless, these patients are heavily transfused since early childhood and consequently at risk of developing antibodies against RBC antigens, both alloantibodies and autoantibodies, which in turn have deleterious consequences. We assessed the rate of RBC alloimmunisation and autoimmunisation among TD beta thalassaemia major (TM), beta thalassaemia intermedia (TI) and sickle/beta thalassaemia (ST) adult patients treated in our centre.

#### Patients and Methods

The study included 44 patients, mean (range) age 32.8 (20-54) years, 21 (47.7%) males, 23 (52.3%) females, 32 (72.7%) splenectomised (SPX). Clinical and transfusion records were retrieved from patients' lifelong files.

#### Results

Alloimmunisation was demonstrated in 22 (50.0%) patients, 14 (63.6%) of them had >1 alloantibody. Among males, 13/21 (61.9%) and among females 9/23 (39.1%) had alloantibodies. Among SPX patients 14/32 (43.8%) had alloantibodies, compared to 8/12 (66.7%) with intact spleen. Mean (range) age at first transfusion was 1.7 (0.3-23) years, mean (range) of lifelong cumulative number of blood units transfused was 821 (166-1586).

Anti-Kell antibodies were detected in 12/22 (54.5%) patients having 15 alloantibodies (9 anti-K, 6 anti-Kpa), Rh antibodies in 11/22 (50%) patients having 13 alloantibodies (9 anti-E, 2 anti-D, 1 anti-C and 1 anti-Cw). Autoimmunisation was demonstrated in 2 (4.5%) patients.

Significant inverse correlation was found between lifelong cumulative number of blood units transfused and rate of alloimmunisation ( $p=0.03$  for study cohort,  $p=0.01$  for TM patients).

#### Conclusions

The high rate of alloimmunisation in our TD thalassaemia patients, unexpectedly inversely related to lifelong cumulative number of RBC units transfused, might be attributed to multi transfusions over many years without RBC antigen matching and to relatively high number of SPX patients. Transfusion policies, especially antigen matching for Cc, Ee and K, should be considered in order to reduce alloimmunisation.



## Title: **Different form of clinical presentation of H disease in a family with the same mutation**

**Abstract Category:** Blood Transfusion

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## ABSTRACT

### Background

H disease is one of the subtypes of alpha thalassemia with a range of phenotype from severe anemia to no clinical presentation. Also they differ in transfusion dependency. The disease is mainly caused by the reduced formation of alpha globin chains.

### Method

The diagnosis of the disease is based on finding of microcytic, hypochromic anemia in CBC analysis in a patient who did not have iron deficiency and also Hb electrophoresis was not consistent with the  $\beta$ -thal syndrome. A family suspicious to H disease was referred us for confirmation of clinical diagnosis by genetic testing. DNA was extracted from all members of the family by salting out method. Sanger sequencing of HBB gene and MLPA for a globin gene was done.

### Results

CBC electrophoresis in proband showed reduced A<sub>2</sub> volume. The mother showed near normal A<sub>2</sub>. There was no mutation in  $\beta$  globin gene in proband DNA. Her mother, Proband and her sister showed the same result (heterozygote deletion of 3.7 kb in conjunction with 3.5 kb deletion. The sister had one transfusion in pregnancy and several gall stones.

### Conclusion

There is no definite genotype-phenotype correlation in H disease. This family is a report of H disease in a family with different clinical presentations of the disease that one sister needed transfusion but the other and also mother did not. This is also true about gallstones.

## Title: **Genetic Modifiers of HbF and Phenotypic Severity Among Malaysian $\beta$ -Thalassaemia Patients**

**Abstract Category:** Diagnostic & Monitoring Techniques

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## ABSTRACT

### Background

Clinical manifestations of  $\beta$ -thalassemia is portrayed by the types of  $\beta$ -globin gene mutations, as well as co-inheritance of  $\alpha$ -thalassemia and polymorphisms associated with HbF production. Mutational analysis of  $\beta$  and  $\alpha$  globin genes are routinely analysed; however detection of polymorphisms associated with HbF is limited. Thus, we aimed to identify these polymorphisms and its association with disease severity using a clinical severity score and patients' age of first transfusion.

### Method

DNA samples from 100  $\beta$ -thalassemia patients were genotyped for 34 SNPs in *HBB*, *HBS1L-MYB*, *BCL11A* and *olfactory receptor* gene using the Agena MassARRAY<sup>®</sup>. HBG2:g.

158C>T was genotyped using Restriction Fragment Length Polymorphism PCR (RFLP-PCR).

The genotyping results were analysed using the Hardy Weinberg (HWE) test to ensure that there was no genotyping error. The association between the polymorphisms and clinical severity was analysed using SPSS version 23.

### Results

All 35 types of polymorphism (homozygous wild type, heterozygous or homozygous mutant) were detected. Statistical analysis using the severity score revealed that rs2210366 (*HBS1L-MYB*) and rs2071348 (*HBBP*) were identified as the most highly significant SNP ( $p < 0.05$ ). Whereas, association analysis using age of first transfusion showed that allele G from rs388623 (*olfactory receptor*) and allele C from rs4895441 (*HBS1L-MYB*) are significantly associated with a later age of blood transfusion ( $p < 0.05$ ).

### Conclusion

All 35 type of SNPs identified in our population may either up-regulate or down regulate the phenotypic severity of  $\beta$ -thalassemia patients. These data may be used to further evaluate the severity of our  $\beta$ -thalassemia patients, aiming for a better management of thalassaemia.



## **Title: Phenotype and Genotype Analysis of Alpha Thalassemia Patient with Non-deletional Mutations: Family Study from Medan, North Sumatera**

**Abstract Category:** Diagnostic & Monitoring Techniques

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### **ABSTRACT**

#### **Introduction**

Thalassemia is an inherited hemoglobin disorder due to absent or decrease alpha globin production. One of clinically significant alpha thalassemia type is Hemoglobin H disease (HbH). Non-deletional alpha thalassemia patient is resulted from non-deletional mutation. Patients with non-deletional types of HbH disease are more severe than those with deletional mutations. Recently alpha thalassemia with non-deletional mutations have been increasingly reported in Indonesia. This study aimed to analyze how the non-deletional alpha thalassemia mutation alleles are inherited and how the genotypes correlate with the phenotypes in this family from Medan, North Sumatera province.

#### **Methodology**

Subjects of this study consists of pair of parents and one baby girl with non-dependent blood transfusion. The study includes the hematological and DNA analysis of all members of this family. Hematological profiles consist of complete blood count (CBC), blood smear analysis, and Hb analysis. The DNA was extracted from peripheral blood followed by PCR-RFLP to detect the mutation and to know their haplotypes.

#### **Result and Discussion**

Hematologic phenotype of the father was normal but could not get rid of mild alpha thalassemia trait, whereas hematology profile of the mother was suitable with alpha thalassemia trait. The baby's hematology profile were Hb 9.6 g/dL, MCV 72.1 fl, MCH 24.1 pg, MCHC 33.4 g/dL, RDW 15.6%. Hb anaysis were HbA2 1.7 %, HbF 4.6%, HbCS 1.9, using capillary electrophoresis. This features suitable with HbH disease with thallasemia intermedia non-transfusion dependent thallasemia (NTDT). DNA analysis of the baby were Hb Adana double heterozygote mutation (Codon 59 gene glovin- $\alpha$ 2, GGCglysinàGACaspartate) and Hb Constant Spring (Cd142 globin- $\pm$ 2, TAAstopàCAAglutamic+30aa). Hematology profile of the mother was suitable with alpha thalassemia trait. DNA analysis of the father was Hb Constant Spring or Hb CS (HBA2:c.427T>C) heterozygote, whereas the mother was Hb Adana (HBA2:c.179G>A) heterozygote. The baby girl of this couple had double heterozygous of Hb Adana and Hb CS. The haplotype of the mutation alleles describes how the mutation alleles were inherited.

#### **Conclusion**

We have presented the genotype and phenotype of one family with Hb Adana and Hb Constant Spring. This family is the first case found in Medan, North Sumatera.

**Keywords:** Non-deletional alpha thalassemia mutation, Hb Adana, Hb CS, genotype, phenotype, haplotype.



## **Title: Multidisciplinary care for patients with Thalassemia Major in North-East and East region of Bulgaria**

**Abstract Category:** Diagnostic & Monitoring Techniques

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### **ABSTRACT**

Patients with thalassemia major in North-East and East part of Bulgaria are followed in an outpatient clinic, called Center for coagulopathies and rare anemias which was established in 2013 in the University Hospital St. Marina in Varna. The multidisciplinary team of medical experts gives a full medical, psychological and social support to patients with inborn hematological diseases and rare anemias. The physicians are from different specialties – Hematology, Cardiology, Endocrinology, Gastroenterology, Psychology, Genetic diseases, a Dentist, Obstetrics and Gynecology and Social worker. Patients have a 24-hour opportunity for a telephone contact with a doctor from the center.

There are 38 patients above and 30 patients below 18 years of age. All patients visit the center regularly - every 2 - 5 weeks. They receive regular blood transfusions in order to maintain their hemoglobin level above 95 g/l. Each patient has an individual clinical, laboratory and treatment schedule based on his/her registered or expected complications and results of the chelating therapy.

Thalassemia cardiomyopathy still remains the leading cause of morbidity and mortality among patients with transfusion-dependent Thalassemia Major (TM) despite recent advances in the therapeutic management. Myocardial iron overload together with increased cardiac output are considered the principal causes of cardiac complications especially for the development of heart failure, although patients are regularly transfused and at optimal chelation therapy. This makes the cardiac care of especial importance for the patients with TM.

All patients are seen by a cardiologist at least once per year and whenever there are complaints of dyspnea or palpitations; ECG and Echocardiography is performed each year; Cardiac MRI is performed every two years or more often depending on the result of the T2\*. All patients receive also an annual monitoring for signs and symptoms of endocrine complications.

Patients with TM in North-East part of Bulgaria are all strictly followed by a dedicated Thalassemia team. As per their cardiac care, we have supplied all necessary equipment and we have organized quick and easy approach to a specialist. Thus, there are no patients with overt heart failure, all subtle signs and symptoms of heart complications are recognized and treated as soon as diagnosed.

**Title: Genotyping A Thalassemia Point Mutation by Probe-Gated Silica Nanoparticles****Abstract Category:** Diagnostic & Monitoring Techniques**Authors:** Meltem Ercan<sup>1,2</sup>, Samet Uçak<sup>1</sup>, Bilge Güvenç Tuna<sup>2</sup>, V. Cengiz Özalp<sup>1</sup>**Presenting Author:** Meltem Ercan**Affiliation:**<sup>1</sup> Altınbaş University Tıp Fakültesi Tıbbi Biyoloji Anabilim Dalı, İstanbul<sup>2</sup> Yeditepe Üniversitesi Tıp Fakültesi Biyofizik Bölümü, İstanbul**Email:** meltemkazak@gmail.com**ABSTRACT****Background**

$\beta$ -thalassemia is an inherited blood disorder that can lead to anemia. The causative reason for the disease is known to be mutation(s) in hemoglobin (HBB) gene that produces one of the subunits, called beta hemoglobin. Mutations in the HBB gene can reduce or abolish the production of beta-hemoglobin leading to abnormal hemoglobin protein structure and thus reduced oxygen carrying capacity. Therefore, low number of red blood cells in the blood causes the person's ability to produce hemoglobin and associated anemia complications. The development of simple, reliable, and rapid approaches for molecular detection of common mutations is important for prevention and early diagnosis of genetic diseases, including Thalassemia.

**Methods**

In this study, hybridization trigger was used to detect a single nucleotide mutation of  $\beta$ -Thalassemia, called IVS-110 which was used as a model mutation sequence. Single stranded probe oligonucleotide with perfect matching for IVS-110 mutated sequence were used to cover reporter loaded silica nanoparticles. The principle of the assay uses rigidity changes in DNA structure depending on its flexible single stranded or double stranded helix forms. Genomic DNA were amplified with PCR to obtain single stranded fragment of the mutated region.

**Results**

Samples from IVS-110 mutated  $\beta$ -Thalassemia patients and normal individuals resulted in statistically significant differences when the assay procedure were applied. A ratio of signal from normal complementary sequence (Ncomp) and thalassemia complementary sequence (Tcomp) were used to obtain a homogenous test. In this assay, a ratio value above 1 meant samples with mutated sequence or a ratio value less than 1 meant samples with normal sequence.

**Conclusion**

Oligonucleotide-gated mesoporous nanoparticles-based analysis is a new platform for mutation detection that has the advantages of sensitivity, rapidity, accuracy, and convenience.

**Keywords:**  $\beta$ -Thalassemia, Mutation Detection, Silica Nanoparticles



## **Title: A Novel, Automated, Open-source SNR-based Method to Calculate T2\* Values of the Heart and Liver in Iron Overload Assessment**

**Abstract Category:** Diagnostic & Monitoring Techniques

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### **ABSTRACT**

#### **Background**

Iron overload assessment using T2\* has become the standard tool for measuring iron burden in the heart and liver. More widespread use of this technique is limited by access to dedicated analysis software and difficulty in handling high iron concentrations when the signal drop is significant and corrections are needed. We sought to develop a novel, automated, open-source signal-to-noise (SNR)-based method to analyze heart and liver T2\* images using a HTML5/Javascript platform, comparing the results to a commercial, FDA-approved software.

#### **Methods**

Running the software in a general web-browser, DICOM images were uploaded and region-of-interests drawn. The echo times, pixel intensities and their corresponding standard deviations were automatically passed to the T2\* tool and used to calculate the SNR for each image, automatically truncating the T2\* curve based on SNR cut-off values of 1.5, 2.0 and 2.5 using a linear least-squares method. The results from the developed tool were compared against a commercial software with manual truncation in addition to a previously published method of automated truncation using fitting coefficients.

#### **Results**

Eighty-seven patients underwent T2\* 1.5T MRI of the liver and heart for iron overload assessment (age 31.9±19.8 years; 49% males). Using automated SNR cut-offs, no significant differences in T2\* values were observed compared to the reference manual readings in both organs, except for the 1.5 threshold in the liver. Comparing the three cut-off values, a small but significant overestimation in liver T2\* using the 1.5 cutoff versus 2.0 and 2.5 was observed (mean difference of 0.19 and 0.20ms with P=0.04 and P=0.02 respectively), without any significant differences in heart T2\*. Automated truncation using the fitting coefficients algorithm failed in 21% of the liver cases versus 1.1% using SNR cut-offs (P=0.05).

#### **Conclusions**

The open-source tool with automated truncation using SNR cut-off values provided more robust assessment of T2\* values of the liver and heart compared to previous automated techniques based on fitting coefficients and with comparable accuracy as the manual reference standard. The online tool (<http://www.isodense.com/mcdcm>) might be used as an alternative to standard software packages for analysis of T2\* values while allowing for automated correction of cases with high iron deposits.



## Title: **Contribution of NAT to Blood Safety at a University General Hospital Over One Decade**

**Abstract Category:** Diagnostic & Monitoring Techniques

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## ABSTRACT

### Background

Nucleic Acid Testing (NAT) was implemented for routine blood donor testing on 26/05/2006 in order to enhance blood safety. Due to direct identification of the infectious agents, rather than the immune response to the infection, its main advantage over serology testing is the narrowing of the window period. Detection of occult hepatitis B is also an important gain.

### Methods

Only data from blood donations at the Blood Bank Department of the AHEPA University Hospital of Thessaloniki were analyzed, during the period between 26-05-2006 to 31-12-2016. All donor samples were tested for HBV, HCV and HIV both by serology and by NAT. Procleix Ultrio was used up to 17-3-2014, and then replaced by Procleix Ultrio Plus. Results were exported from the computer software e-AIMA (Computer Control Systems A.E.) and processed through Microsoft Excel. Graphs were created for better visualization of results.

### Results

Out of a total of 258594 blood donations 2 cases in the window period (NAT only) were detected. One out of 107 (0,93%) samples positive for HCV, and 1 out of 26 (3,85%) samples positive for HIV. Moreover 30 cases of occult Hepatitis B and 51 cases of suspected occult Hepatitis B were identified (0,03% of all donations, 18,88% of all samples positive for HBV).

### Summary/conclusions

NAT has contributed in the enhancement of blood safety in our hospital over the last 10 years by preventing at least 1 HCV infection and 1 HIV infection, and possibly many HBV infections transmitted from blood donors suffering from occult Hepatitis B. Given that about 16% of all blood units collected at our hospital are transfused to thalassaemic and SCD patients, this is especially important for this patient population.



## Title: **CMR for Myocardial Iron Overload Assessment: Calibration Curve from the MIOT Project**

**Abstract Category:** Diagnostic & Monitoring Techniques

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## ABSTRACT

### Background

The measurement of myocardial iron by T2\* cardiovascular magnetic resonance (CMR) is fundamental to the best management of thalassemia. However, iron calibration data in humans is limited and CMR calibration varies according to instrumentation and technique. Our aim was to calibrate the T2\*-CMR technique for noninvasive cardiac iron assessment by considering a segmental approach.

### Methods

Four human hearts were studied from transfusion-dependent patients after their death within the MIOT network (Myocardial Iron Overload in Thalassemia). A multislice multiecho T2\* approach was adopted. After CMR, used as guidance, the heart was cut in three short-axis slice and each slice was cut into different equiangular segments, the same ones in which the T2\* was assessed. Tissue iron concentration in the segments was measured with inductively coupled plasma atomic emission spectroscopy.

### Results

T2\* and iron concentration were overall assessed in 36 myocardial segments: 6 in the first heart (year 2004), 6 in the second one (year 2004), 8 in the third one (year 2005), and 16 in the fourth one (year 2010), Figure 1A shows the segmental iron concentration (in milligrams per gram dry weight) plotted versus the correspondent segmental T2\* value (in milliseconds). As expected, the relationship was not linear. In Figure 1B the R2\* values ( $R2^* = 1000/T2^*$ , in s<sup>-1</sup>) were considered. Regression analysis yielded a linear calibration of the following form:  $[Fe]R2^* = 0.0079 \times R2^* - 0.1262$  (R-square=0.999).

### Conclusions

As in the only previously proposed calibration curve by Carpenter et al Circulation 2011, we did not collected hearts with an intermediate iron burden. We found an excellent linear agreement between R2\* and cardiac iron with a model similar to the calibration curve in the gerbil showed by Wood J et al. The results further validate the current clinical practice of monitoring cardiac iron in vivo by CMR.



## **Title: Importance of accessibility to MRI T2\* iron overload imaging technique for thalassemic patients: an experience from Iran**

**Abstract Category:** Diagnostic & Monitoring Techniques

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### **ABSTRACT**

Patients with hemolytic anemia like beta Thalassemia major or sickle cell anemia are characterized by defective biosynthesis of beta globin chains. The most important maintenance treatment in these patients is regular blood transfusion. Thalassemic patients need lifelong transfusions to survive over the second decades of life. The most prevailing consequence of these repeated transfusions is iron deposition in different organs, such as heart, liver, pituitary, pancreas, kidney, etc and causing damage to these organs. An example of such damage is iron overload cardiomyopathy that results from the hemosiderosis in the myocardium, and it often occurs late and can be hard to reverse once established and it is the leading cause of death in patients receiving chronic blood transfusion therapy. In some cases although the iron overload of the liver is low the iron overload cardiomyopathy irreversibly develops.

Single measurements of serum ferritin and biopsy determined liver iron concentrations are inadequate for identifying iron deposition in vital organs in the chronically transfused patients.

Although the liver biopsy and ferritin are conventional gold standard method for iron overload assessment, but they have their drawbacks and cant reflect the iron deposition of internal organs.

A revolutionary technique for iron overload assessment is Magnetic Resonance Imaging (MRI) that provides direct, non-invasive fast and reproducible iron assessments in different tissues. Since its first introduction in early 1980 and matured by 2000, various groups and departments showed interest to apply it for thalassemia fields and developed multiple software for the quantification analysis. The general concept is simple. MRI machines can generate images at various observation or "echo" times to vary the contrast among different organs and the iron acts as small magnets, destroying the homogeneity of the magnetic field in iron-laden tissues. Such a technique needs special requirements of hardware and software which might be available in few or some MRI centers.

Our experience in setting up the first center of MRIT2\* in Tehran, returns to 2008 a collaboration of the Iranian thalassemia society and an interested professor of Radiology. Since then, approximately 18523 thalassemia patients from all parts of Iran have monitored their iron overload to now. Under the supervision of the expert radiologist, the validation and regular calibration of the MRI instruments is done annually in all 3 clinics which are central in Tehran.

For cardiac T2\* data of the monitored population of study the analysis showed ( $25.68177 \pm 112.90158$  ms) while the analysis of the liver T2\* data was ( $6.82727 \pm 7.18163$ ms) and the liver LIC data was ( $4.2547 \pm 3.43764$  mg/g/dry weight). For the cardiac iron overload status 70.08% of thalassemic patients were normal, 11.6% were mild, 9.2 % were moderate and 9.12 were severe. Moreover, for hepatic iron overload status, 34.65% were normal, 26.96% were mild, 31.29% were moderate and 7.1% were severe.

The accessibility of meriting such MRI technique might be preventing irreversible cardiomyopathy or other serious hemosiderosis side effect by early detection of organ iron deposition and optimization in iron chelating regimen. As the pioneer in center , we now have some links through the PACS facilities with other cities to ease the imaging of their patients in their cities while we calculate and deliver their results online.

## **Title: Unusual Fluorescein Angiography and Spectral Domain-Optical Coherence Tomography Findings in Deferoxamine Retinopathy: A Case Report**

**Abstract Category:** Diagnostic & Monitoring Techniques

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### **ABSTRACT**

#### **Background**

Deferoxamine (DFO) use has been associated with numerous adverse events including major organ systems such as the cardiovascular, respiratory, gastrointestinal, nervous, and cutaneous systems, in addition to its side effects on the visual and auditory systems. The ocular toxicity of DFO encompasses a constellation of disease entities, mainly cataract, optic neuropathy, and several patterns of retinopathy.

#### **Methods**

We hereby report a case of irreversible, DFO-induced macular and peripapillary retinopathy at the level of the retinal pigment epithelium (RPE) diagnosed by fluorescein angiography and spectral domain-optical coherence tomography (SD-OCT).

#### **Results**

A 40-year-old woman receiving subcutaneous deferoxamine treatment presented with 2-month history of deteriorating vision in both eyes. Fundoscopy revealed peripapillary “angioid streak”-like lesions, and fluorescein angiography showed bilateral early hyperfluorescence with localized late staining around the optic nerve. Overall, two different types of lesions could be differentiated in the proximity of the optic disk: deep, linear, regular pigmented lesions located in the superonasal quadrant and reminiscent of angioid streaks, and larger irregular pigmented lesions located in the inferior quadrants. Spectral domain-optical coherence tomography demonstrated irregular juxtapapillary reflectivity exclusively limited to the RPE-Bruch’s membrane complex compatible with the angioid streaks demonstrated by fundoscopy, in addition to thickening of the RPE-Bruch’s membrane complex and irregular hyperreflectivity of this layer correlating with focal deposition of material at the level of the RPE. Deferoxamine retinopathy was diagnosed. The aforementioned findings remained unchanged one year later despite discontinuation of treatment with deferoxamine.

#### **Conclusion**

An unusual case of deferoxamine-induced papillomaculopathy was described with emphasis on two types of peripapillary lesions probably denoting acute-on-chronic toxicity, and the use of retinal imaging to study and follow this disease entity was presented. Monitoring the status of the retina in deferoxamine users with a regular screening protocol was strongly defended.

**Title: Iron Overload in Children with Major Thalassemia****Abstract Category:** Diagnostic & Monitoring Techniques**Authors:** Pustika A Wahidiyat, Ellen Wijaya**Presenting Author:** Ellen Wijaya**Affiliation:**Division of Hematology-Oncology, Department of Child Health  
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**ABSTRACT****Background**

Iron overload is important to be evaluated. The current gold standard in evaluating iron overload is MRI T2\* which only available at two centers in Indonesia. Other examination methods are urinary iron excretion level, serum ferritin and transferrin saturation. Assessment of each influencing factors is significant for adequate therapy.

**Objective**

To evaluate iron overload by the value of heart, liver MRI T2\* and pancreas MRI R2\*, urinary iron examination, serum ferritin, transferrin saturation, and to determine factors that are related with iron overload.

**Methods**

A cohort study conducted in children with major thalassemia aged 7-≤18 years old in at Cipto Mangunkusumo Hospital, Jakarta, Indonesia. We performed heart, liver MRI T2\*, pancreas MRI R2\*, 24 hours urinary iron level assessment, serum ferritin and transferrin saturation. Age, amount of transfusion and level of pre-transfusion hemoglobin in 6 months were considered.

**Results**

Heart MRI T2\* showed normal result on 52/55 (94.5%) subjects. Liver MRI T2\* showed normal result on 4 (7.3%) subjects, mild iron overload on 23 (41.8%) subjects, moderate on 17 (30.9%) subjects and severe on 11 (20%) subjects. Pancreas MRI R2\* showed normal result on 11 (20%) subjects, mild iron overload on 31 (56.4%) subjects, moderate on 13 (23.6%) subjects, no subject with severe iron overload. Mean level of urinary iron excretion: 12.828 ug/24 hours, serum ferritin: 3858 ng/mL and transferrin saturation: 82.69%. There was correlation between age to mean serum ferritin ( $r = 0.318$ ,  $p = 0.018$ ). There was no correlation between amount of transfusion and level of pre-transfusion hemoglobin with the value of heart, liver MRI T2\*, pancreas MRI R2\*, urinary iron excretion, ferritin serum and transferrin saturation.

**Conclusions**

Early evaluation of iron overload is important to achieve optimum growth and development in children with thalassemia major. Age has a correlation with the level of serum ferritin.

**Keywords:** major thalassemia, iron overload, early evaluation

**Title: A Unified, One-Step  $\alpha$ - and  $\beta$ -Thalassemia Fast Diagnostic Method****Abstract Category:** Diagnostic & Monitoring Techniques**Authors:** Tom Xu, Chengfeng Jiang, Jinlan Xu**Presenting Author:** Tom Xu**Affiliation:**SenseCare Medicals, Inc., Pleasanton, California, USA  
Urit, Guilin, Guangxi, China**Email:** sensecare@gmail.com**ABSTRACT****Background**

Thalassemia generally is divided into two categories:  $\alpha$ -thalassemia and  $\beta$ -thalassemia. Genetically,  $\alpha$ -Thalassemia is mostly caused by large DNA fragment deletions while common  $\beta$ -thalassemia is from point mutations. Due to their genetic variation difference, it requires different test protocols. Today, most laboratories still use Gap PCR-based electrophoresis for  $\alpha$ - thalassemia and reverse dot-blot hybridization for  $\beta$ -thalassemia. Both methods are tedious and labor intensive with potential for contamination due to requirement for opening the amplified PCR tubes. Combined two tests have more than 10 operation steps and require 2-3 days to finish. Here we present a new fast test method that could accomplish both  $\alpha$ - and  $\beta$ -thalassemia test within 2 hours without causing contamination.

**Method**

Real-time PCR TaqMan assays were designed for HBA1 (FAM probe) and HBA2 (HEX probe) genes for  $\alpha$ -thalassemia detection. For  $\beta$ -thalassemia, allelic discrimination assays were designed with VIC probes for normal genotypes and FAM probes for mutant genotypes. The following 23 types of  $\alpha$ - and  $\beta$ -thalassemia were tested on the same panel: --SEA, - $\alpha$ 3.7, - $\alpha$ 4.2,  $\alpha$ CS $\alpha$ ,  $\alpha$ QS $\alpha$ ,  $\alpha$ WS $\alpha$ , 41-42M, 654M, -28M, 71-72M, 17M,  $\beta$ EM, 43M, -29M, 31M, -32 M, IVS-I-1M, 27/28M, -30M, 14-15M, CAPM, IntM, IVS-I-5 M. Two hundred thirty-nine patient blood DNA samples were used for this study.

**Results**

All tested 239 patient samples were correctly diagnosed for their thalassemia status by the new method. The results were confirmed either by Gap PCR or by reverse dot-blot hybridization.

**Conclusion**

We have developed a fast, unified  $\alpha$ - and  $\beta$ -thalassemia diagnosis method that could be finished within 2 hours, compared to current 2-3 day procedures. Since there is no need to open the amplified PCR tubes, the contamination issue is completely eliminated.



## Title: **Identification of a Denovo Deletion in Alpha Thalassemia; Reporting a Rare Event**

**Abstract Category:** Diagnostic & Monitoring Techniques

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## ABSTRACT

### Background

Alpha thalassemia is one of the most common form of thalassemia which is due to impaired of alpha globin chains. Most cases results from inheritance of the mutated allele from parents to the offspring. Denovo deletion is a very rare event. Here in we report a family with a large denovo deletion which is not hereditary.

### Method

The index case was referred us for genetic testing for investigation of alpha globin genes. DNA was extracted from peripheral blood by salting out and proteinase K. Investigation of common deletions of  $\alpha$  globin (3.7kb, 4.2 kb, Med and 20.5) were performed by multiplex PCR. In addition, point mutations in  $\alpha 1$  and  $\alpha 2$  globin genes were tested by direct sequencing. The deletion discovered with MLPA of alpha globin genes. Paternity testing was also performed.

### Results

The CBC result was compatible with alpha trait. Common deletions of  $\alpha$  globin were negative. Direct sequencing  $\alpha 1$  and  $\alpha 2$  globin genes showed no point mutation. CBC and HB electrophoresis of parents were normal. DNA finger printing confirmed the paternity and maternity. The heterozygote deletion of 3.5 Kb upstream of HBZ discovered with MLPA of alpha globin genes. MIPA results for parents were normal.

### Conclusion

To the best of our Knowledge, this is the first report of a large denovo deletion in Iranian population with alpha thalassemia.

## **Title: Molecular PGD in Iran: Reporting experience on more than 200 blastomeres for diagnosing beta-thalassemia**

**Abstract Category:** Diagnostic & Monitoring Techniques

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## **ABSTRACT**

### **Background**

Preimplantation genetic diagnosis (PGD) has become a useful option for couples with a risk of transmitting a genetic disease, to prevent birth of children affected with monogenic disorders. PGD is a form of very early prenatal diagnosis. In this method, diagnoses performed on blastomeres biopsied from 8-cell stage embryos which are created by in vitro fertilization method (IVF). In this way, one could prevent medical abortion by selecting and transferring unaffected embryos. Other usages of PGD are sex selection and HLA typing. PGD combine with HLA typing is a strategy to select unaffected HLA-matched embryos as a potential donor for stem cell transplantation. Here we present application of molecular PGD to select unaffected embryos for beta-thalassemia carrier couples.

### **Method**

27 beta-thalassemia carrier couples who were candidate for PGD, referred to our laboratory. Peripheral blood samples were collected in tubes containing EDTA and genomic DNA was extracted using salting out method. Mutation detection carried out using direct sequencing. Fragment analysis and haplotype mapping performed to trace defective alleles using multiplex short tandem repeats (STRs). Informative STR markers and selected mutation were checked on each blastomere using nested PCR. Linkage analysis was performed and intended embryos were selected and implanted to mother's uterus.

### **Result**

Since 2009 we have performed PGDs to diagnose beta-thalassemia for 209 blastomeres. 64 of them were just for diagnosing beta-thalassemia, 31 of them were for beta-thalassemia combined with QF, 40 of them were for beta-thalassemia combined with sex selection and 74 of them were for beta-thalassemia combined with HLA typing.

### **Conclusion**

PGD is regarded as a powerful diagnostic tool, for carrier couples who desire a healthy child and wish to avoid medical abortion. Results obtained from linkage analysis and haplotype mapping in parallel with direct mutation detection make this method more accurate and reliable.



**Title: A newly designed panel of 16 STR markers including the best heterozygous markers for detection of  $\beta$ -thalassemia and Aneuploidy screening**

**Abstract Category:** Diagnostic & Monitoring Techniques

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## ABSTRACT

### Background

$\beta$ -thalassemia is the most common hematological disorder worldwide. The carrier frequency of B-thalassemia is high in Iran, therefore prenatal diagnosis (PND) or Pre-implantation Genetic Diagnosis (PGD) could be attractive options to prevent the birth of new Beta-Thalassemia cases. Aneuploidies are the cause of over 50% of all miscarriages. Early aneuploidy screening in conjunction with PND or PGD for thalassemia can decrease the subsequent complication of pregnancy termination.

### Methods

This Study aimed to develop a novel panel for detection of  $\beta$ -thalassemia and aneuploidy screening simultaneously. The panel is based on the study of homozygosity mapping of the 10 (6 novels) STR (Short Tandem Repeat) markers linked to HBB gene. Additionally, quantitative analysis of the critical regions of 21, 18, 13, X and Y-chromosomes was performed using markers of KBC-Aneuquick kit. These markers were amplified in a multiplex PCR reaction which is time-saving and cost-effective technique.

### Results

Allele frequency & heterozygosity assessment of HBB STR markers were studied in 100 unrelated healthy individuals. Totally, 97 alleles were detected. Genotype frequencies of the markers were found to be in agreement with the Hardy-Weinberg equilibrium ( $P \geq 0.1876$ ). Six markers with higher heterozygosity (66.7%-85.2%) were selected. For further confirmation of the homozygosity mapping data, direct mutation analysis was also performed. The results were compatible.

### Conclusion

The panel was used for 14 PGD candidates and the results were successful. We found these markers can be easily applied for PGD, PND of thalassemia and aneuploidy screening or even sex determination. This panel increases the specificity and sensitivity of the diagnosis.

**Keywords:** prenatal diagnosis (PND), Pre-implantation Genetic Diagnosis (PGD), Short Tandem Repeat (STR), Aneuploidy screening

**Title: Endocrinopathies in transfusion dependent thalassemic children: Results from a single center**

**Abstract Category:** Endocrine Complications

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## **ABSTRACT**

### **Introduction**

Endocrine complications in transfusion dependent thalassemia (TDT) patients can present early, initiating in childhood.

### **Aim**

To evaluate the presence of endocrine complications in pediatric TDT patients, followed at a single institution.

### **Patients – Methods**

Medical records were retrospectively reviewed and concerned a 12 month period (January to December 2016). Besides presence of endocrinopathies, data studied included age, gender, iron chelation, pre-transfusion hemoglobin, ferritin level, as well as liver and kidney function.

### **Results**

Thirty two cases with a mean age of 12 years (1.5 – 17 years) were evaluated, out of which 23 (71.8%) were males. Thirty patients were on chelation therapy: 15/32 (46.8%) on deferasirox, 6/32 (18.75%) on desferrioxamine and 9/32 (28.1%) on combination therapy with desferrioxamine and deferiprone. Mean pre-transfusion hemoglobin was 9.3g/dl (8.8-11g/dl) and mean ferritin 1014 ng/mL (359 –2336 ng/mL). Liver and kidney function was normal in all cases. The most frequent complication reported was decreased bone-mineral density, found in 12/32 patients (37.5%) and with a mean Z score of -1.68 measured at L1-L2 lumbar vertebrae. Nine out of 32 patients (28.1%) showed growth retardation, 2 presenting with growth hormone deficiency. Other complications reported were: vitamin D insufficiency in 4/32 patients (12.5%) with a mean 25-OH vitamin D of 15.4 ng/ml, Hashimoto's thyroiditis leading to over hypothyroidism in 2/32 patients (6.25%) and subclinical hypothyroidism in 1/32 patients (3.12%). Hyperparathyroidism, impaired glucose tolerance and pubertal failure were not observed in any patient. Moreover, endocrine complications showed no statistically significant correlation with age, gender, type of iron chelation, hemoglobin or ferritin level ( $P>.05$ ).

### **Conclusions**

Endocrine complication rate was relatively low in the patient group studied compared to other reports. This could be attributed to effective chelation and close monitoring - both necessary in order to prevent endocrinopathies and to avoid further disease burden in thalassemic transfusion dependent children.



## **Title: Evaluation of Pituitary Iron Overload in Patients with Transfusion Dependent Thalassemia**

**Abstract Category:** Endocrine Complications

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### **ABSTRACT**

#### **Aim**

This study aims to evaluate the transfusion-related endocrinologic complications of transfusion dependent patients with thalassemia, quantify the pituitary iron overload, investigate the correlation of hormone insufficiencies with iron overload.

#### **Material and Methods:**

Fifty transfusion-dependent thalassemia patients over the age of 10 that are in regular follow up in Istanbul Faculty of Medicine, Hemoglobinopathy Center were evaluated in the study. Data were collected from patient files and the hospital laboratory results system. Pituitary MRI's were taken to detect pituitary iron overload with a 1.5 Tesla Philips MRI machine with global R2\* in the Department of Radiology between January 2016 and May 2017. Reference data for pituitary R2 were used from 100 normal subjects that have been presented by Wood et al.

#### **Results**

Fourteen patients (28%) had hypogonadotropic hypogonadism, 9 patients (18%) had short stature, 9 patients (18%) had hypothyroidism, 7 patients (14%) had impaired fasting glucose, 4 patients (8%) had amenorrhea, 4 patients (8%) had hypoparathyroidism, 2 patients (4%) had adrenal insufficiency. 44 patients (88%) had pituitary iron overload on MRI. Patients with hypogonadotropic hypogonadism had significantly more severe pituitary iron overload. Patients who have iron accumulation in the pituitary; hypogonadotropic hypogonadism in 14 pts, short stature in 11 pts, diabetes in 9 pts, and amenorrhea in 4 patients. In cases where iron accumulation is not detected in the pituitary; hypogonadotropic hypogonadism and diabetes were not observed except in one case who has short stature.

#### **Discussion**

Regular transfusions and chelation has prolonged survival in patients with thalassemia. Yet, iron overload in a variety of organs continues to decrease the quality of life. It is common practice to keep serum ferritin levels between 500 – 1000 ng/ml to avoid complications associated with iron overload. Some patients have iron overload in the pituitary even with serum ferritin levels below 1000 ng/ml. Therefore, it is not appropriate to dosing of chelation therapy only with serum ferritin levels. In order to detect endocrinologic complications before they are clinically apparent, to evaluate for iron overload and to dosing of chelation more effectively, it would be prudent to routinely obtain pituitary MRI in patients with transfusion dependent thalassemia.

**Keywords:** Transfusion dependent thalassemia, pituitary iron, MRI

## **Title: Pediatric Non-Malignant Blood Disorders Registry: An Epidemiological Tool to Investigate Incidence of Hemoglobinopathies in Saudi Arabia**

**Abstract Category:** Epidemiology

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### **ABSTRACT**

#### **Background**

Several National cancer registries functional worldwide reports incidence of different type of cancers but not a single comprehensive registry reports incidence of Non-malignant Blood Disorders (NMBD). Saudi Arabia is amongst countries reported to have high rates of consanguineous marriages. Prevalence of regional X-linked and autosomal recessive disorders is well documented , of which hemoglobinopathies are widely reported but an exact incidence and its correlation with consanguinity is unknown.

#### **Method**

REDCap (Vanderbilt University) web based data management module was used to develop registry database collecting demographic, consanguinity, diagnostic and survival data after approval by Institutional Review Boards (IRBs) at King Faisal Specialist Hospital and Research Centre (KFSH&RC)- Riyadh and Jeddah.

#### **Result**

Hematology service at KFSH&RC- Riyadh and Jeddah is a tertiary care service accepting pediatric (age below 14yrs) patients with hemoglobinopathies for disease management and possible Bone Marrow Transplant (BMT). Pediatric NMBD registry established in September 2015 with 67(43%) patients registered with Hemoglobinopathies to date, Thalassemia observed in 21%(14) ,Sickle Cell disease, in 72%(48) and Sickle-thalassemia in 7%(5);incidence of consanguinity was 64%(9),58%(28) and 60%(3) respectively, with an overall incidence of 60%(40).Stem Cell Transplant (SCT) performed in 15% patients, another 65% on track to a possible SCT. Important regional epidemiological, clinical, and laboratory data vital for disease prevention and to study effect of consanguinity was obtained.

#### **Conclusion**

Preliminary analysis indicated a need to improve outreach measures in the country for better Thalassemia referrals to tertiary care centers , for SCT and chelation therapy. At this stage of the registry, we would like to invite regional and international hematologists to join or adapt our "one-of-a-kind" cost-effective registry model. We speculate data obtained from this registry will provide strong foundation for a pre-marital screening program aimed at disease prevention. Further, financial estimate on national healthcare system could be estimated for better awareness initiatives.



## Title: **$\beta$ -Thalassaemia Prevalence and Treatment Patterns in Italy: A Survey of Treating Physicians**

**Abstract Category:** Epidemiology

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## ABSTRACT

### Background

Physicians in Italy treating  $\beta$ -thalassaemia were surveyed to evaluate current prevalence and treatment of patients with transfusion-dependent (TD) major (TD-M) or intermedia (TD-I)  $\beta$ -thalassaemia, or non-transfusion-dependent (NTD)  $\beta$ -thalassaemia.

### Method

A preliminary list of 656 possible  $\beta$ -thalassaemia-treating centres covering 85% of Italy's hospital capacity was extracted from the IMS Health list of hospitals and treatment centres; 365 centres providing iron-chelating therapy (ICT) were identified as potential  $\beta$ -thalassaemia-treating hospitals. A haematologist/paediatrician in each ward provided numbers of TD-M, TD-I, and NTD  $\beta$ -thalassaemia patients managed in their ward.

60 geographically-stratified treating physicians received questionnaires about general treatment patterns, focusing on potential drivers of healthcare resource utilization. Physicians each referenced 3–4 anonymized patient records to inform their responses.

### Results

5,748 TD patients receiving regular treatment and 1,296 NTD patients receiving occasional treatment were reported from 114/124 treatment centres. TD patient distribution was heterogeneous; prevalence was highest in Sicily, Sardinia, and Puglia (>500 TD patients each; 3,051 TD patients total). The 7 largest centres managed 1,766 TD patients.

Based on 205 patient records (162 TD; 43 NTD), the most commonly performed tests in the preceding 12 months were complete blood count, ferritin level, echocardiography, and T2\*-weighted MRI. 83/162 TD patients required 1–2 RBC units/month; 78 patients required  $\geq 3$  RBC units/month (data unavailable n=1). Deferasirox was the most commonly administered ICT in TD patients (n=109). 126 TD patients had prior change of ICT; 72 switched from deferoxamine to another agent. In-patient hospitalizations were estimated at 9, 7, and 4 days/year for TD-M, TD-I, and NTD patients, respectively. Endocrine pathologies were the most commonly reported comorbidity in all groups; hepatitis C infection and hepatic and cardiac complications were also reported.

### Conclusions

Prevalence of  $\beta$ -thalassaemia in Italy is regionally focused and likely to consume significant healthcare resources for management of the disease and associated comorbidities.



**Title: The Island Factor in Genetic Responsibility: Social and Environmental Aspects of Thalassaemia in the Maldives**

**Abstract Category:** Epidemiology

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## ABSTRACT

### Background

One of the world's highest prevalences of beta-thalassaemia is challenging the Republic of Maldives. Since 1992 various actors have been involved in activities related to care and prevention. International organizations, local NGOs, public health institutions and their staff, patients and relatives are struggling to implement a genetic screening program and to improve treatment conditions of about 600 patients in the uneven terrain of the 1200 islands comprising archipelago. Despite these comprehensive efforts, and despite the comparatively fortunate standing of the coral island nation as the only upper-middle-income country in South Asia, however, the number of homozygous newborns has remained constant with more than 20 new cases annually, and thalassaemia patients continue to die before their time.

### Method

A medical anthropological approach makes it possible to look beyond the biomedical sphere of thalassaemia. It investigates social and environmental aspects in the performance of 'genetic responsibility' and in the shaping of a 'local thalassaemic biology'.

### Results

An 'island factor' seems to be the stumbling block in thalassaemia-related health equity and genetic responsibility in the Maldives. A much higher share of newborn patients are reported from what is locally known as 'the (outer) islands', and the general health of island patients also falls short when compared with patients from the capital island, Male'.

### Conclusion

Providing and seeking curative and preventive services is challenging in this Small Developing Island State (SIDS) with a population of just about 340,000 living in small population pockets dispersed across a vast more-water-than-land territory. By considering dynamics between genetics, public-health efforts and the unique environment of an archipelago, this presentation scrutinizes the socio-political and spatial foundations of 'the island factor' in 'genetic responsibility'.



## **Title: An Island-wide Hospital Based Epidemiological Survey of Haemoglobinopathies and an Assessment of Standards of Care in 23 Centers**

**Abstract Category:** Epidemiology

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## **ABSTRACT**

### **Introduction and Methods**

There is no data base for haemoglobinopathy patients in Sri Lanka resulting in imprecise knowledge about the distribution and standards of care among patients managed in different centres in the island. The prevention programme commenced in 2007 is not centrally monitored. We carried out a center-wise visitation and data gathering of patients with haemoglobinopathies in 2015. 23 centers were visited by researchers who gathered information from patient records.

### **Results**

Data was obtained of 1768 patients. Three centers had over 200 patients each and another three centers had between 50-100 patients. There were 8 centers with less than 10 patients each. Beta thalassaemia major (BTM) accounted for 1207 (68.2%) patients. There were 363 patients (20.5%) with Haemoglobin E-b thalassaemia. Sickle cell-b thalassaemia accounted for 51 patients (2.85%). The mean age of BTM patients was 13 years range (2-44). Ethnic distribution of the haemoglobinopathies (82.5% Sinhalese, 12% Muslims and 5.2% in Tamils) was discrepant to the national ethnic data. Island wide mean number of new births of all thalassaemics recorded showed a reduction from 66 / year between 2009-2004 to 48/ year between 2010 to 2015. Clinical record keeping was not systematic in most units thus complication rates were hard to obtain. Death data were available only in two units.

### **Conclusions**

This study identified significant inconsistencies in haemoglobinopathy care between centres. Existence of small centres needs to be recognised by the Ministry of Health. A reducing trend of new births over the last decade was observed.

**Title: Incidence of transfusion-dependent thalassemia and their hematologic profile in dr. Cipto mangunkusumo hospital Jakarta, Indonesia**

**Abstract Category:** Epidemiology

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## ABSTRACT

### Introduction

As of October 2016, 9,121 thalassemia patients were identified in Indonesia, among which 2,200 cases were found in Jakarta. Dr. Cipto Mangunkusumo General Hospital (RSCM) in Jakarta alone caters towards 1,637 patients in 2016. The treatment cost for individuals with transfusion-dependent thalassemia in Indonesia reaches Rp 400,000,000 ( $\pm$ \$30,161) per year. Given the increasing epidemiology and high financial costs incurred, it is important to identify the current epidemiology of transfusion-dependent thalassemia. This study aims to evaluate the number of patients with transfusion-dependent thalassemia in RSCM along with their hematological profile.

### Methods

A cross-sectional study was conducted for 6 months (November 2016 – April 2017) in Dr. Cipto Mangunkusumo General Hospital. All thalassemia patients who underwent routine transfusion were interviewed for demographic data and medical information, including type of thalassemia, hematologic profile, and presence of complications.

### Results

At the end of this study, 368 transfusion dependent thalassemia patients were included. Mean age was  $12.3 \pm 7.1$  years. Out of all the samples; 13 (3.6%) were  $\alpha$ -thalassemia, 148 (40.1%) were  $\beta$ -HbE-thalassemia and 207 (56.3%) were  $\beta$ -thalassemia. 314 of the samples was prescribed with daily iron chelation. Mean pre-transfusional Hb value were  $8.0 \pm 1.1$  mg/dL and mean ferritin were  $3669.3 \pm 2724.1$  ng/mL. Available hepatic and cardiac T2\* MRI from 130 samples were gathered; 2 samples with severe cardiac siderosis and 31 patient with severe hepatic siderosis. Thirty-one samples had complications; heart disease (8), diabetes (3), colelithiasis (1), osteoporosis (4) and hepatitis (8).

### Conclusion

Within a time period of 6 months, 368 transfusion-dependent thalassemia patients were treated in RSCM. With pre-transfusional Hb lower than that recommended by TIF (9-10.5 mg/dL) and high serum ferritin, further enhancement in treatment and advocacy are warranted.

**Keywords:** thalassemia major; epidemiology; Indonesia



## **Title: Combined Iron Chelation Therapy in $\beta$ -Thalassaemia Major Patient During Pregnancy: Is it Safe?**

**Abstract Category:** Fertility & Pregnancy

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### **ABSTRACT**

#### **Background**

Management of pregnancy in women with  $\beta$ -Thalassaemia Major ( $\beta$ -TM) who requires transfusion and iron overloaded remains a great challenge. It is considered as high risk for both mother and fetus, and it requires multidisciplinary team approach for favorable outcome. To date, the usage of iron chelation therapy during pregnancy is generally avoided due to its potential teratogenicity. This study evaluates seven pregnancies in four patients with  $\beta$ -Thalassaemia Major who received combined iron chelation therapy during pregnancy.

#### **Methods**

We studied all  $\beta$ -TM female patients who became pregnant while on at least two iron chelation therapy (Desferioxamine, Deferiprone and/or Deferasirox) at Queen Elizabeth Hospital between January 2009 and April 2017. Review of patient's medical records and interview of cases were performed for this study. Data was analysed using descriptive statistics.

#### **Results**

Majority of the pregnancies were unplanned. Iron chelation therapy using Desferioxamine injection and oral Deferiprone were the commonest combination used. One of the patient stopped iron chelation once confirmed to be pregnant, while the others decided to continue their therapy in view of moderate to severe cardiac iron overload. All pregnancies were successful and no fetal toxicity observed. Healthy babies were born with normal growth and development.

#### **Conclusion**

Treatment with combination iron chelation therapy did not prevent delivery of a healthy baby. It should be noted that the usage of iron chelation therapy during pregnancy is not recommended. Further studies are needed to confirm these finding.

**Keywords:**  $\beta$ -Thalassaemia Major, pregnancy, iron chelation therapy

**Title: Gene Therapy of Beta Thalassemia by Lentiviral Transfer of Beta Globin Gene****Abstract Category:** Gene Regulation & Therapy**Authors:** Maryam abbasalipour, Mohammad Ali Khosravi, Morteza karimipour, Kayhan Azadmanesh, Sirous Zeinali**Presenting Author:** Maryam abbasalipour**Affiliation:** Pasteur Institute of Iran, Tehran, Iran**Email:** m.abbasalipour@gmail.com ; stud.m\_abbasalipour@pasteur.ac.ir**ABSTRACT****Background**

Beta thalassemia is a common monogenic disorder caused by partial or complete reduction of beta globin chains synthesis. It is estimated that 1.5% of the global population (80 to 90 million people) are carriers worldwide. Common management consists of regular lifelong blood transfusion plus iron chelation therapy. The transfusion has its complication. Recent years allogenic bone marrow transplantation (BMT) has proved to be the successful cure for over 2000 patients with thalassemia major, however this is restricted due to limited matched-related donor. Therefore, a molecular approach, such as gene therapy for direct healthy beta globin gene transmission, seems quiet promising to cure thalassemia. The goal of beta thalassemia gene therapy is to restore normal RBC production capacity in patients by suitable vector and correct inherited anemia. Autologous Hematopoietic Stem Cells (HSCs), which Self-renew and generate all hematopoietic lineage including the erythroid lineage, are the cellular target of ex-vivo globin gene transfer.

**Methods**

For our purpose, we designed the DEST Lentiviral vector carried normal beta globin gene and it's promoter and packaged lentivirus in LentiX-293 T cell line. Then targeted cells (K562 cells) was transduced by packaged lentivirus containing  $\beta$ -globin cassette. After transduction,  $\beta$ -globin mRNA level was determined by quantitative Real-Time PCR.

**Results**

Our results showed that we have successfully packaged and generated lentivirus in LentiX-293 T cell line and increased expression of beta globin gene in treated cell was confirmed by Real-Time PCR.

**Conclusion**

These data indicated that vector used in this study can be useful in gene therapy in patient's hematopoietic stem cell. The final goal of this study is to examine designed vector in hematopoietic stem cells promising therapeutic strategy for genetic diseases like beta thalassemia.



## **Title: CRISPR/CAS9 Based Genome Editing of Sickle Cell Mutation in Human Hematopoietic Stem/Progenitor Cells**

**Abstract Category:** Gene Regulation & Therapy

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## **ABSTRACT**

### **Background**

Sickle cell disease (SCD) is a common blood disorder caused by a single mutation in human  $\beta$ -globin (HBB) gene that leads to produce red blood cells formed like the crescent-shaped blade of a sickle, which hinders blood flow in the blood vessels and deprives the body's organs of oxygen. Health care and therapeutic approaches constraining suffering and high costs to the governments and patients. CRISPR-Cas9-based genome editing tool enables the rapid genetic manipulation of genomic locus to correct point mutation and small deletions. In this study we planned to utilize the CRISPR/Cas9 system to edit the GTG at codon 6 to GAG in HBB gene in hematopoietic stem cells from SCD patients to evaluate the efficacy of this method and study to use it as a therapeutic approach.

### **Method**

At the first phase we successfully examined CRISPR/cas9 system in HEK293T cell line for converting the Adenine to thymine at codon 6 in HBB gene after survey of off targets and efficiency the best designed guide RNA (gRNA) was selected. At the second phase co-transfection was applied with gRNA-cas9 protein complex and a single stranded DNA oligonucleotide donor (ssODN) on CD34 positive hematopoietic stem/progenitor cells (HSPCs) taken from SCD patients. Editing was measured by direct sequencing and droplet digital PCR (ddPCR).

### **Results**

In HSPCs delivery rate was 65% and up to 5% alleles corrected to wild type. After erythroid expansion, homology direct repair (HDR) rate was increased to 29% at day 4. The rate of off-target was (0.2 %) in HSPCs.

### **Conclusion**

This experiment indicate efficient in vitro editing of codon 6 of HBB gene in CD34+ HSPCs from SCD patients that implies this method can be used as a therapeutic approach for SCD treatment, but complementary in vivo and in vitro experiments and molecular analysis should be considered.

## **Title: Targeted Deletion of BCL11A Gene by CRISPR/CAS9 System for Fetal Hemoglobin Induction in KU812 Cells**

**Abstract Category:** Gene Regulation & Therapy

**Authors:** Mohammad Ali Khosravi<sup>1</sup>, Maryam abbasalipour<sup>1</sup>, Jean-Paul Concordet<sup>2</sup>, Morteza karimipour<sup>1</sup>, Kayhan Azadmanesh<sup>1</sup>, Sirous Zeinali<sup>1</sup>

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### **ABSTRACT**

#### **Background**

The CRISPR/Cas9 genome-editing technology is a versatile and powerful tool to efficiently create genetically engineered living cells and organisms. This system uses a complex of Cas9 endonuclease with a single guide RNA to introduce double-strand DNA breaks at a desired sequence in the genome. DSBs are then repaired by the error-prone Non-Homologous End Joining pathway, resulting in small insertion and/or deletion mutations (indels) which disrupt the targeted genes or it can be repaired by homologous recombination pathway, resulting in introduce very specific mutations into the damaged DNA by using a homologous template targeting vector. B cell lymphoma 11A (BCL11A) is key regulatory component in HbF silencing, so repression of the BCL11A protein could represent a therapeutic target for beta-hemoglobin disorder. KU812 leukemia cells express erythroid markers similar to days 7–14 primary erythroid cells.

#### **Methods**

At the first step, we wanted to test the activity of our constructs on HEK293 cells. We proposed that knockout of BCL11A expression by 200bp erythroid enhancer disruption would result in induction of gamma globin expression. The SpCas9 and a pair of sgRNA expressing vectors were co-transfected into HEK293 cells. Clonal isolation was performed in order to isolate of clonal cells containing bi-allelic deletions through serial dilution. To determine the expression reduction of BCL11A gene, total RNA was isolated from homozygous clones and BCL11A mRNA levels was monitored by RT-qPCR.

#### **Results**

PCR products sequencing results confirmed 200bp targeted deletion in transfected cells and RT-qPCR results showed approximately 5.5-fold reduction in BCL11A expression.

#### **Conclusion**

This study showed that these CRISPR/cas9 constructs bring about targeted deletion and reduction in BCL11A mRNA level. The next step of this study is to examine of these constructs in KU812 cells in order to elimination of inhibitory effect of BCL11A and induction of fetal hemoglobin production.



## Title: **Mutation-Specific Gene Correction at Clinically Relevant Efficiencies by Non-Viral Delivery and Disruption of an Aberrant Regulatory Element**

**Abstract Category:** Gene Regulation & Therapy

**Authors:** Petros Patsalia<sup>2</sup>, Panayiota Papasavva<sup>1</sup>, Claudio Mussolino<sup>3</sup>, Marianna Romito<sup>3</sup>, Giandomenico Turchiano<sup>3</sup>, Soteroulla Christou<sup>4</sup>, Maria Sitarou<sup>4</sup>, Michael N Antoniou<sup>2</sup>, Toni Cathomen<sup>3</sup>, Carsten W. Lederer<sup>1\*</sup>, Marina Kleanthous<sup>1\*</sup>.

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## **ABSTRACT**

### **Background**

Genome editing of primary cells may allow permanent therapy of human disease, but where correction requires homology-directed repair, efficiencies are still too low for most clinical applications. Here we exploit the alternative repair pathway of non-homologous end joining for the disruption of aberrant regulatory elements (DARE) and functional correction of HBBIVSI-110(G>A)  $\beta$ -thalassaemia. At close proximity to coding and regulatory elements, HBBIVSI-110(G>A) is representative of a rapidly increasing number of known disease-causing mutations suitable for correction by DARE, while it nevertheless poses an exceptional challenge through its close proximity to regulatory and coding elements.

### **Methods**

This study employed plasmid-based delivery of TAL effector (TALE) and CRISPR/Cas9-based nucleases in humanised murine HBBIVSI-110(G>A)-encoding cells for initial proof of principle. Subsequent analyses in primary haematopoietic stem and progenitor cells from HBBIVSI-110(G>A)-homozygous patients employed nucleofection of DNA- and virus-free in vitro synthesised (m)RNA instead.

### **Results**

Initial evaluation of DARE in cell lines, including clonal analyses, demonstrated efficient HBB induction and the importance of flanking sequences for recognition of the aberrant splice acceptor site. Through refinement of target sequences and DNA- and virus-free delivery to primary patient-derived cells we established conditions for high-efficiency, low-toxicity nuclease delivery with high on-target and low off-target activity for both nuclease systems. At disruption efficiencies of 60–85% in CD34+ cells, our directly translatable, selection- and transgene-free correction strategy achieved highly significant induction of HBB and highly significant correction of erythroid differentiation as key disease parameters of  $\beta$ -thalassaemia.

### **Conclusion**

Mutation-specific therapy by DARE is highly efficient and suitable for mutations causative of hundreds of inherited diseases. Moreover, our results give clear pointers for efficient on-target design in the presence of highly similar paralogous sequences. In the specific case of HBBIVSI-110(G>A) thalassaemia, efficiency and biosafety of our approach may warrant clinical investigation of mutation-specific rather than generic gene-therapy approaches for haemoglobinopathies.

**Title: Bone marrow transplantation in patients with Thalassemia in Iran****Abstract Category:** Haematopoietic Stem Cell Transplantation (HSCT)**Authors:** Maryam akhavan tavakolli**Presenting Author:** Maryam akhavan tavakolli**Affiliation:** PHD student of anatomy in shahid beheshti university medical science**Email:** mary\_matak@yahoo.com**ABSTRACT****Introduction**

During the last two decades conventional therapy has improved the prognosis of thalassemia .Stem cell transplantation (SCT) remains cure for deferent kind of anemia. mesenchymal-like stem cells have high rate of proliferation and possess multi lineage differentiation potency. Bone marrow transplantation (BMT) remains the only potentially curative treatment for patients with thalassemia major.Bone marrow transplantation (BMT) can prevent or delay progression of the aforementioned complications.

**Method**

The first BM transplantation take place on 1981 in Itly by professor karlly on 14 years old Iranian thalassemy 14 boy.the patients candidates important criteria is:1) age range (median rang between 16\_30) Adult thalassemy patients have more advanced disease, with both disease- and treatment-related organ complications that are mainly due to prolonged exposure to iron overload,2) size of liver and spleen ,liver function test ,complete blood examination and blood iron . However, despite such improvement it still remains a progressive disease with treatment-related complications such as hepatitis, liver fibrosis, and cardiac disease,3) donor, most candidates for BMT do not have a suitable family donor while the most appropriate doner for patients ought to have the same genetical match (an HLA-matched.

**Result**

We conclude that for patients under 16 years of age, transplantation of bone marrow from an HLA-identical donor offers a high probability of complication-free survival, particularly if they do not have hepatomegaly or portal fibrosis. These data show that when donor selection is based on above criteria, the results and survival rate are almost 88% in comparison with European country that have 94% .

**Conclusion**

BMT remains an important treatment option for children with beta-thalassaemia major, particularly when compliance with iron chelation is poor.The main center of Bone marrow transplantation in Iran is SHariati hospital. We have to define that Iran with 299 succeed BMT in thalassemia are the second center in the world, and annually have more than 50 patients treated with some improvement in thalassemia-free survival . Keyword: thalassemia, stem cell, bone marrow ,transplantation



## Title: **Autologous cryopreserved platelets transfusion allowing safe myeloablative allogeneic BMT in a heavily HLA-alloimmunized patient with beta-thalassemia**

**Abstract Category:** Haematopoietic Stem Cell Transplantation (HSCT)

**Authors:** F. Giglio<sup>1</sup>, G. Casirati<sup>1</sup>, M. Zambelli<sup>2</sup>, M. Coppola<sup>2</sup>, R. Milani<sup>2</sup>, C. Parisi<sup>2</sup>, M. Morelli<sup>1</sup>, R. Greco<sup>1</sup>, L. Barzizza<sup>2</sup>, M. Tassara<sup>2</sup>, J. Peccatori<sup>1</sup>, N. Maugeri<sup>3</sup>, L. Santoleri<sup>2</sup>, F. Ciceri<sup>1</sup>, S. Markteli<sup>1</sup>

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## **ABSTRACT**

### **Background**

Patients with transfusion-dependent thalassemias often develop anti-HLA antibodies, associated to platelet-transfusion refractoriness. Thalassemia patients may therefore be refractory to Plt-transfusions necessary during BMT aplasia resulting in increased morbidity and mortality. We describe the use of autologous cryopreserved platelets as the sole support during thrombocytopenia in a beta-thalassemia patient receiving BMT.

### **Method**

A 23-year-old-man with beta-thalassemia major was referred for BMT. Luminex assay documented 28 anti-HLAA antibodies, 49 anti-HLAB, 15 anti-HLAC, 2 anti-HLADQB1 and 1 anti-HLADRB1, resulting in almost certain refractoriness to randomly selected Plt-transfusions. A cryopreservation program of autologous platelets was initiated. Two platelet-pheresis were performed using standard continuous-flow centrifuge technique and citrate (AMICUS). After collection, platelets were irradiated, transferred into CryoMACS freezing bag (target concentration  $1 \times 10^{11}$  platelets/bag) and cryopreserved with 5% DMSO in liquid nitrogen. The patient received myeloablative conditioning with Treosulphan, Thiotepea, Fludarabine followed by  $3.09 \times 10^8/\text{kg}$  mononucleated BM cells from an HLA-identical brother. Plt were transfused in case of  $\text{PLT} < 10 \times 10^9/\text{L}$  or in case of relevant bleeding. Immediately before transfusion, platelet concentrates were thawed in a  $37^\circ\text{C}$  water bath, 10% ACD-A was added, washed to remove DMSO and resuspended in saline. Platelet surface and intracellular antigen expression was assessed before cryopreservation and after thawing. Aliquotes were fixed by Thrombofix<sup>®</sup> and labelled with mAbs against CD61 (glycoprotein-IIIa), GPIIb/IIIa (CD42b) and P-selectin (CD62P) while vonWillebrand factor (vWF) apha granules were analyzed after permeabilization.

### **Results**

Grade IV thrombocytopenia lasted from day +7 to +15. On day +8, three bags containing  $343.8 \times 10^9$  cryopreserved autologous Plts were transfused with no adverse reactions. Pre-transfusion PLT count ( $9 \times 10^9/\text{L}$ ) rose to  $69 \times 10^9/\text{L}$ . On day +12 (PLT  $18 \times 10^9/\text{L}$ ) three autologous cryopreserved PLTs bags ( $347.07 \times 10^9$  PLTs) were transfused resulting in a  $97 \times 10^9/\text{L}$  PLT count. Cryopreservation didn't modify platelet's quality as evidenced by flow cytometric analysis. The patient had an uneventful clinical course except febrile neutropenia and low grade skin GVHD treated with steroids. No minor or major bleeding occurred. PLT count on discharge (Day +27):  $212 \times 10^9/\text{L}$ .

### **Conclusion**

We report safety and efficacy of autologous cryopreserved Plts-transfusion in a thalassemia patient with numerous anti-HLA antibodies undergoing myeloablative BMT. This program will now be implemented for all patients with anti-HLA antibodies receiveing BMT for non-malignant conditions.

## **Title: Secondary Solid Cancer Following Hematopoietic Cell Transplantation in Patients with Thalassemia Major**

**Abstract Category:** Haematopoietic Stem Cell Transplantation (HSCT)

**Authors:** Alessia Pepe<sup>1</sup>, Stella Santarone<sup>2</sup>, Antonella Meloni<sup>1</sup>, Annalisa Natale<sup>2</sup>, Laura Pistoia<sup>1</sup>, Paola Olioso<sup>2</sup>, Gabriele Papalinetti<sup>2</sup>, Liana Cuccia<sup>3</sup>, Anna Spasiano<sup>4</sup>, Roberto Lisi<sup>5</sup>, Mauro Di Ianni<sup>2</sup>, Tiziana Bonfini<sup>2</sup>, Patrizia Accorsi<sup>2</sup>, Stefano Salvadori<sup>6</sup>, Stefano Angelini<sup>2</sup>, Paolo Di Bartolomeo<sup>2</sup>.

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## **ABSTRACT**

### **Background/Methods**

The aim of this retrospective cohort study was to compare the incidence of secondary solid cancers (SSC) in a large monocentric cohort of thalassemia major (TM) patients (n=122; 67 males) who received HCT and survived for at least 3 years versus:

- an hematopoietic cell donors monocentric cohort (n=122);
- a large multicenter cohort of age- and sex-matched TM patients (n=244) treated with conventional therapy and enrolled in the Myocardial Iron Overload in Thalassemia Network.

### **Results**

During a median follow-up of 24 years, 8 transplanted patients were diagnosed with SSC at a median of 18 years after HCT. Three patients died for cancer progression and 5 are living and doing well. Noteworthy, all 3 patients who were diagnosed with oropharyngeal cancer were affected by mild to moderate chronic GvHD. The cumulative incidence of SSC was 0.82% (95% confidence interval [CI]:0.12-5.68%) at 10 years from transplant, 3.86% (95% CI, 1.46-9.99) at 20 years from transplant and 13.24% (95%CI: 6.01-27.81) at 30 years from transplant.

Among the hemopoietic stem cell donors, only one developed a SSC 28 years after donation at age of 38. At 10 and 20 years after hemopoietic stem cell donation, the cumulative incidence of SSC was 0 while at 30 years it was 3.23% (95%CI: 0.46-20.77). Compared to the cumulative incidence of transplanted patient, the difference was statistically significant (P=0.02).

Among the TM patients treated with conventional therapy, 3 cases of SSC were discovered. The cumulative incidence of SSC was 1.32% (95%CI: 0.43-4.04) after 10, 20 and 30 years. Compared to the cumulative incidence of transplanted patient, the difference was statistically significant (P=0.005).

### **Conclusion**

The magnitude of increased risk of SST is fourfold to sixfold for patients treated with HCT as compared with hemopoietic cell donors or with an age- and sex-matched nontransplant well treated TM patients.



**Title: Jervell and Lange–Nielsen syndrome (JLNS) is a rare, autosomal recessive disease associated with congenital sensorineural deafness, and significant QT interval prolongation**

**Abstract Category:** Heart & Vascular Abnormalities

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## **ABSTRACT**

### **Background**

Jervell and Lange–Nielsen syndrome (JLNS) is a rare, autosomal recessive disease associated with congenital sensorineural deafness, and significant QT interval prolongation.

### **Objectives**

Here we examined a 3.5 year-old female patient who had a history of recurrent syncope and congenital sensorineural deafness referred for the LQTS clinical genetic test.

### **Methods**

A consanguineous family with JLNS screened for mutations in KCNQ1 gene using DNA sequencing and haplotype analysis.

### **Results**

Bidirectional Sanger Sequencing revealed a novel homozygous frameshift mutation c.1532\_1534delG (p. A512Pfs\*81) in the KCNQ1 gene. Haplotype analysis with linked STR polymorphic markers, encompassing the KCNQ1 gene, confirmed parental inheritance of the two mutated alleles.

### **Conclusion**

This study revealed the first case of A512Pfs\*81 among Iranian population, that its implication as a diagnostic tool in the clinical setting and in genetic counselling has been discussed. Although control population data suggest this mutation is pathogenic, expert interpretation of genetic test results will remain critical for effective clinical use of LQTS genetic test results.

**Keywords:** Long QT syndrome, Genetic testing, KCNQ1, Jervell and Lange–Nielsen syndrome, Iran

## Title: **NT-pro-BNP Levels in Correlation with Left Atrial Volumes in Beta-Thalassemia Patients for Early Detections of Heart Failure**

**Abstract Category:** Heart & Vascular Abnormalities

**Authors:** Maria Dimova<sup>1</sup>, Branimir Kanazirev<sup>1</sup>, Valeria Kaleva<sup>2</sup>, Svetlana Gercheva<sup>3</sup>, Kristina Petrova<sup>2</sup>, Vesela Zlateva,<sup>1</sup> Yana Bocheva<sup>4</sup>, Silvia Nikolova<sup>5</sup>

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## ABSTRACT

### Aims

To correlate echocardiographic parameters of morphology and function in patients with thalassemia major in comparison to healthy controls with NT-pro-BNP levels to identify subjects with heart failure in order to optimize treatment and to prevent future morbidity.

### Materials and methods

We evaluated 37 consecutive patients with homozygous  $\beta$ -thalassemia and 50 age-matched healthy controls by echocardiography and NT-pro-BNP levels.

### Results

LVMMi (g/m<sup>2</sup>) and relative wall thickness (RWT) were increased compared to controls. Diastolic trans mitral E/A velocities ratio and systolic myocardial velocities-Sm (cm/s) and deformations indices -strain and strain rate (1/sec) were also significantly lower. Left ventricular EF was however normal and E/E' was also not different compared to controls. Left atrial indices showed enlarged LAVi (ml/m<sup>2</sup>) and borderline depression of left atrial ejection fraction (LAEF %). NT-proBNP (pg/ml) levels were significantly higher in TM cohort 80,4 (38,57-189,25) compared to healthy controls -23 (20- 32,80) pg/ml ( $P < 0,0001$ ). There were 11 (29,7%) patients with NT-pro-BNP biomarker above upper reference limit of >125 pg/ml fulfilling criteria for diagnosis of heart failure according to the ESC Guidelines. Patients with TM were then divided into two groups- TM patients with elevated NT-proBNP (TM NT-proBNP+) and TM patients with normal NT-proBNP (TM NT-proBNP-) and the two groups were then compared. The only significant difference between the two groups was left atrial volume index LAVi ( $P = 0,025$ ) and all other indices were no different. There was a moderate yet significant correlation between NT-pro-BNP and LAVi -  $r = 0,44$ ,  $p = 0,009$  and between LVMMi and LAVi-  $r = 0,480$ ,  $p = 0,004$ .

### Conclusions

The only significant difference between the two TM groups - NT-proBNP positive and NT-proBNP negative was left atrial volume index LAVi, which may be used for routine follow-up in these patients.



**Title: Significant improvement of ejection fraction with low-dose beta-blocker in an 18-year old patient with transfusion dependent Thalassaemia**

**Abstract Category:** Heart & Vascular Abnormalities

**Authors:** Maria Dimova<sup>1</sup>, Branimir Kanazirev<sup>1</sup>, Valeria Kaleva<sup>2</sup>, Krasimira Nenova<sup>1</sup>, Kristina Petrova<sup>2</sup>, Vesela Zlateva<sup>1</sup>

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## ABSTRACT

An 18-year old patient with regularly performed hemotransfusions since early childhood and severe myocardial iron overload – T2\* 7,02 since 01.2017 presents for regular check-up with symptoms of weakness and dyspnea. ECG – sinus rhythm, HR 95, after hemotransfusion. Echocardiography- reduced EF- 45,6%, reduced myocardial velocities examined with tissue Doppler imaging.

Treatment: bisoprolol 2,5mg o.d.

Follow-up echocardiography in a month and a half – significant improvement in contractile function, EF -58,5%, HR- 73b.p.m.

Beta-blockers is a standard treatment in patients with heart failure with reduced ejection fraction<sup>1</sup>. However, their apply in patient with thalassemia should be cautious as these patients normally have low blood pressure. In our patient with severe myocardial siderosis and low myocardial contractile function of the left ventricle, we achieved significant improvement after starting treatment with beta-blocker.

## **Title: Lipid Profile Abnormalities in Pediatric Patients with Transfusion Dependent Thalassemia**

**Abstract Category:** Heart & Vascular Abnormalities

**Authors:** Marina Economou, Alkistis Adramerina, Vaia Gourtsa, Aikaterini Teli

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### **ABSTRACT**

#### **Introduction**

Lipid profile abnormalities have been reported in young thalassemia patients and have been considered as a contributing factor to premature atherosclerosis.

#### **Aim:**

To evaluate the lipid profile in transfusion dependent thalassemia (TDT) children followed at a single institution.

#### **Patients – Methods**

Lipid profile assessment was performed in 32 TDT patients. Samples were taken before blood transfusion, following at least 12h overnight fasting. Total cholesterol (TC), triglycerides (TGL), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL -C) were measured, with normal ranges defined as <170-199mg/dl, <75-129mg/dl, <100-129 mg/dl and >45mg/dl, respectively. Additional data studied included age, gender, body weight, iron chelation, mean pre-transfusion hemoglobin level, mean ferritin level, as well as liver and kidney function.

#### **Results**

Mean patient age was 12 years (1.5 – 17 years). Out of 32 patients 23 (71.85%) were males. Body weight was <10th percentile in 9/32 (28.1%) patients and >75th percentile in one. Thirty patients were on chelation therapy: 15/32 (46.8%) on deferasirox, 6/32 (18.75%) on desferrioxamine and 9/32 (28.1%) on combination therapy with desferrioxamine and deferiprone. Mean hemoglobin was 9.3g/dl (8.8-11g/dl) and mean ferritin 1014 ng/mL (359 –2,336 ng/mL). Liver and kidney function was normal in all cases. Mean TC was 95 mg/dl (47-254mg/dl), mean LDL 44mg/dl (7-65 mg/dl), mean HDL 31mg/dl (14-61mg/dl) and mean TGL 80mg/dl (31-241mg/dl). One patient showed increased TC and 2 patients increased TGL. In the majority of patients (29/32, 91%) HDL cholesterol was lower than normal. There was no statistically significant correlation between age, gender, body weight, Hb or ferritin with total cholesterol, TGL, LDL or HDL (P>.05).

#### **Conclusions**

Lipid profile was abnormal in the majority of pediatric patients studied, the most common finding being low HDL level. The role of low HDL in correlation to premature atherosclerosis development needs to be further studied in this patient group.



## **Title: Sofosbuvir-Containing Regimen for the Treatment of Hepatitis C Virus in Patients with Thalassemia major**

**Abstract Category:** Hepatological Complications

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### **ABSTRACT**

#### **Introduction**

Recently introduced Sofosbuvir-containing regimen for the treatment of HCV infection was showing an overall 89% sustained virological response for 12 weeks post treatment (SVR12). However, Sofosbuvir has not been approved for use in patients with hemoglobinopathies. Hence, there is limited experience with this promising regimen effectiveness and side effects in this group of patients. In this study, we aimed to evaluate the efficacy and safety of Sofosbuvir-containing regimen in patients with thalassemia major (TM) and chronic iron overload.

#### **Methods**

Since February 2016, twenty-one adult patients with transfusion dependent TM received 12 weeks treatment with Sofosbuvir-containing regimen; nine patients received Sofosbuvir-ledipasvir, five patients received Sofosbuvir-ledipasvir-ribavirin, five patients received Sofosbuvir-daclatasvir, and two patients received Sofosbuvir-simeprevir. During therapy, all patients had undergone 2 to 3 weekly monitoring of complete blood count, serum creatinine level and liver enzymes. Quantitative HCV RNA levels were obtained at baseline, at 4 weeks after starting therapy, at the end of treatment and at 12 weeks after completing therapy.

#### **Result:**

Among the 21 treated adult ( $32 \pm 8.0$  years) patients, ten (48%) were genotype 1, eight (38%) were genotype 4, two (10%) were genotype 3 and one (5%) was genotype 2. Seven patients (33%) were naïve while 14 patients (67%) were treatment experienced with interferon. SVR12 was achieved in 95% of the treated patients with one relapse in genotype 3 on Sofosbuvir-daclatasvir regimen. Liver enzymes normalized, with significant reduction of ALT ( $p < 0.05$ , pre mean  $55.3 \text{ u/l}$ , post mean  $25.8 \text{ u/l}$ ) and SGOT ( $p < 0.05$ ; pre mean  $48.98 \text{ u/l}$ , post mean  $28.0 \text{ u/l}$ ). There was significantly increased blood transfusion requirements in the ribavirin containing regimen ( $p < 0.016$ ). No severe adverse events were reported.

#### **Conclusion**

Sofosbuvir-containing regimen is safe and highly effective in thalassemia major patient with iron overload

**Title: Safety, efficacy and biochemical response of HCV treatment with Direct Acting Antivirals (DAAs) in 51 multitransfused patients with thalassemia major (TM)**

**Abstract Category:** Hepatological Complications

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## ABSTRACT

### Background

TM patients infected with HCV present very low response to combination treatment with pegylated interferon and ribavirin with a high rate of complications and dropout.

### Aim

Investigating the safety, efficiency and biochemical response of HCV treatment with DAAs in patients with TM.

### Methods

Treatment with DAAs, PCR confirmation of SVR and analysis of variance of biochemical indexes through different time points.

### Results

Sample consisted of 51 patients (24M/27F), mean age 45.5 years (SD=4.9 years). 70.6% of the participants had fibrosis METAVIR stage IV and 29.4% stage III. The most common genotype was 1b (44.0%). INR mean value was 1.42 (SD=0.43), creatinine mean value was 0.77 (SD=0.6) and ferritin mean value was 830.9 (SD=1110.2). 5,9% were treated with Sofosbuvir+Ribavirin, 25.5% with Daclatasvir+Sofosbuvir, 23.5% with Simeprevir+Sofosbuvir, 17,7% with Ledipasvir+Sofosbuvir, 21.6% with Ombitasvir/Paritaprevir/ritonavir+Dasabuvir, and 5,9% with Ombitasvir/Paritaprevir/ritonavir+Ribavirin. Overall SVR was 94,1%, with no drop out or serious adverse events (SAEs). ALT and AST values had a significant decrease from start to the end of therapy ( $p<0.001$ ). Similarly, ALT and AST values had a significant decrease from the end of therapy to three months after the therapy ( $p<0.01$ ). The mean reduction from baseline to three months after the therapy was 56.2 (95% CI: 47.3-65.0) and for ALT 61.1 (95% CI: 53.1-69.1) for AST. The three patients (6.4%) who did not achieve SVR were 2 men (49yrs,Gen4,DAK/SOF and 52yrs,Gen1b,SOF/RIBA) and 1 woman (47yrs,Gen1b, SIM/SOF), all of them with compensated cirrhosis.

### Conclusions

DAAs treatment of HCV in TM patients is safe, highly effective, without SAEs and with a clear biochemical benefit, with significantly lower transaminases after SVR.



## Title: **Correlation between Transient Liver Elastography with Liver Iron Concentration and Serum Ferritin in Adult Thalassemia Intermedia Patients**

**Abstract Category:** Hepatological Complications

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## ABSTRACT

### Background

Iron overload is a common feature of thalassemia intermedia (TI) due to regular blood transfusion and increase gastrointestinal iron absorption. Early detection and adequate iron chelator can significantly decrease related morbidities and mortality due to iron toxicity. Serum ferritin as a simple, rapid and convenient test is widely used to monitor iron overload, but confounded by other conditions such as infection, cancer and severe liver damage. Liver Iron Concentration (LIC) is the best way to measure body iron stores. MRI T2\* as a validated test to identify LIC is expensive and currently not available in all medical services in Indonesia.

### Objective

To identify liver iron overload and correlation between transient liver elastography with serum ferritin, transferrin saturation, LIC and Liver MRI T2\* in adult thalassemia intermedia patients.

### Methods

We conducted a cross sectional study of 45 adult TI patients requiring regular blood transfusion, with and without iron chelator therapy, at Cipto Mangunkusumo Hospital from August 2016 through October 2016. We performed measurements of serum ferritin level, transferrin saturation, transient liver elastography and Liver MRI T2\* (within 1 month from liver elastography analysis). The Pearson and Spearman correlation test were used to evaluate the correlation between transient liver elastography and serum ferritin, transferrin saturation, LIC and Liver MRI T2\*.

### Results

As much as 64,4% of study subject are  $\beta$ -HbE TI with median (IQR) age is 33 (22) years old. As much as 84,4% of study subject have regular blood transfusion. On the basis of liver MRI T2\*, all study subject suffered from liver iron overload, with 48,9% had severe liver iron overload. The median value of Liver MRI T2\* was 1,6 ms. The mean serum ferritin was 2831 (1828) ng/mL, with median value of transferrin saturation was 66%. The mean of LIC corresponding to Liver MRI T2\* and mean liver stiffness measured by transient liver elastography was  $15,36 \pm 7,37$  mg Fe/gr dry weight and  $7,7 \pm 3,8$  Kpa respectively. Liver stiffness correlated with mean serum ferritin ( $r = 0,651$ ;  $p = 0,000$ ), with LIC ( $r = 0,433$ ;  $p = 0,003$ ) and Liver MRI T2\* ( $r = -0,357$ ;  $p = 0,016$ ). No correlation was found between transient liver elastography and transferrin saturation ( $r = 0,204$ ;  $p = 0,178$ ).

### Conclusions

Transient liver elastography correlated with serum ferritin, LIC and Liver MRI T2\*. No correlation was found between transient liver elastography and transferrin saturation.

**Keywords:** Thalassemia Intermedia, serum ferritin, LIC, Liver MRI T2\*, transient liver elastography.



## **Title: Prevalence pattern of Hepatitis viruses among children with $\beta$ -Thalassemia: Two Egyptian Centers Experiences**

**Abstract Category:** Infections

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### **ABSTRACT**

#### **Background**

Blood born hepatitis viruses among children with B-thalassemia become a great problem, although continuous improvements in screening and testing

#### **Objective**

The aim of the study was to estimate prevalence of hepatitis C and B viruses among children with B-thalassemia in 2 Egyptian centers

#### **Patients and methods**

This cross-sectional study was carried on 951 B-thalassemia patients (522 male and 429 female) with mean age  $9.9 \pm 5.1$  years attending Hematology outpatient clinic of Zagazig and Menuofia University Hospitals. All patients were subjected to full history taking, full clinical examination and laboratory investigations including complete blood count, liver function tests, serum ferritin, hepatitis B surface antigen (HBsAg), hepatitis C antibody. The positive HCV antibody results were confirmed by real-time polymerase chain reaction.

#### **Results**

Seroprevalence of HCV was (14.7%) confirmed by PCR. None of the studied cases were HB sAg positive. Seventy four (54.3%) of HCV positive were males and 65 (45.7%) were females. HCV infection are most prevalent among B-thalassemia patients with older age, increased transfusion frequency, total duration of transfusion and higher serum ferritin and liver enzymes.

#### **Conclusion**

Hepatitis C virus infection still a great problem of B thalassemia patients while hepatitis B vaccine success to eliminate hepatitis B virus infection.



## **Title: Genitourinary Tuberculosis: A Case of Persistent Dysuria in Thalassaemia Major Patient**

**Abstract Category:** Infections

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### **ABSTRACT**

#### **Background**

Tuberculosis (TB) remains a major challenge worldwide. In Malaysia, tuberculosis ranked top 5 for communicable diseases; and Sabah has the highest prevalence of TB among other state. Pulmonary tuberculosis is the commonest form of TB in Malaysia. Genitourinary tuberculosis is the second commonest extrapulmonary tuberculosis after TB lymphadenopathy. We report a case of HIV negative genitourinary tuberculosis (GUTB) in a female Thalassaemia Major (TM) who present with persistent dysuria.

#### **Case Report**

36-year-old lady with B-Thalassaemia Major, complicated with iron overload and Hepatitis C liver cirrhosis, presented with 1-month history of dysuria associated with fever and suprapubic pain. On examination, mild tenderness felt over her suprapubic region. Splenectomy scar was noted. Urine microscopy examination was suggestive of urinary tract infection. Her symptoms persisted despite completed a course of antibiotic. In view of persistent symptom and sterile pyuria, early morning urine AFB was sent for 3 consecutive days. Urine AFB was positive at day 3 of urine sampling. Diagnosis of genitourinary TB was further confirmed with urine PCR for TB. CT imaging revealed bilateral mild to moderate hydronephrosis with thickened urothelial lining, with involvement of the left vesicoureteric junction. A repeat HIV serology and induced sputum for AFB were all negative. She was commenced on anti-TB drug and responded well with the treatment.

#### **Discussion**

The diagnosis of GUTB pose a great challenge as it requires high index of suspicion with good laboratory support. Treatment with anti-TB will need modification especially in this patient since she has cirrhotic liver. Close monitoring of her liver and renal function is required during the course of therapy.

**Keywords:** Thalassaemia Major, Tuberculosis, Genitourinary Tuberculosis



## **Title: Similar Trends in Renal Function as Measured by Serum Creatinine During Long-Term Iron Chelation Treatment with or Without Deferasirox in Patients with Transfusional Hemosiderosis**

**Abstract Category:** Iron Overload & Management

**Authors:** Raffaella Origa<sup>1</sup>, Antonio Piga<sup>2</sup>, Immacolata Tartaglione<sup>3</sup>, Giuseppina Della Corte<sup>4</sup>, Andreas Bruederle<sup>5</sup>, Jackie Han<sup>6</sup>, Chiara Castiglioni<sup>7</sup>, Gian Luca Forni for Renal Chart Review Study Investigators<sup>8</sup>

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## **ABSTRACT**

### **Background**

Renal safety data for patients with >5 years of exposure to iron chelation therapy (ICT) is limited. To understand the impact of long term ICT on renal function, Italian patients with transfusional hemosiderosis, included in the deferasirox registration studies were followed through retrospective chart review for ≤13 years.

### **Methods**

Patients with  $\beta$  thalassemia, SCD, MDS or other anemias receiving  $\geq 1$  dose of investigational drug in the deferasirox registration studies, and having  $\geq 1$  post-baseline serum creatinine (SCr) measurement and medical records available were included. Data were collected retrospectively in 3-month intervals from the end of trial registration until the latest patient assessment. Primary endpoint was SCr over time, and patients were evaluated by subgroups. Here we report results for patients receiving only deferasirox or another ICT.

### **Results**

282 patients were included in the retrospective chart review; 98(35%) received only deferasirox and 62(22%) received ICT other than deferasirox. Mean(SD) age at first quarter was 25.9(12.1) and 27.0(10.9) years; the proportion of pediatric patients was 28% and 19%, in deferasirox and other ICT groups, respectively. In deferasirox group, mean(SD) duration of deferasirox exposure was 7.5(1.7) years and mean daily deferasirox dose was 1440.0(423.6)mg. Mean(SD) baseline SCr was  $50.05 \pm 13.69 \mu\text{mol/L}$  in deferasirox group and  $56.44 \pm 10.62 \mu\text{mol/L}$  in other ICT group. Overall SCr values were stable and within the limits of normal throughout the retrospective period for both groups, although in deferasirox group it was 15-20% higher than baseline but showed no increase versus baseline in other ICT group. As expected in growing pediatric patients, mean SCr absolute values increased from baseline proportionally with increase in muscle mass over time.

### **Summary/Conclusion**

The results of this analysis from the retrospective chart review showed no evidence of progressive renal function worsening over time during long-term ICT, with similar trends for patients receiving deferasirox only versus those treated with other ICT.



## **Title: Biodegradable Polyglycerol Based Iron Chelating System for the Treatment of Transfusional Iron Overload**

**Abstract Category:** Iron Overload & Management

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### **ABSTRACT**

#### **Background**

Iron chelation therapy is the most widely used therapeutic approach to improve survival and reduce the iron burden via chelating and excreting the excess iron using Fe (III) specific chelators. However, the current FDA approved iron chelators have limitations such as short vascular residence time, low excretion efficiency, toxicity, and patient non-compliance. Our recently developed hyperbranched polyglycerol based macromolecular iron chelator showed enhanced circulation times and iron sequestration with reduced toxicity compared to gold standard iron chelator, deferoxamine, however, a molecular weight dependent polymer accumulation in organs was noticed. To address this issue, we propose that a pH dependent biodegradable hyperbranched polyglycerols (BHPGs) with optimized degradation profiles conjugated to iron chelator, deferoxamine, would enhance iron sequestration and excretion from the labile plasma iron pool, and will eliminate iron induced toxicity.

#### **Method**

A series of ketal incorporated biodegradable hyperbranched polyglycerols with different molecular weights were designed and synthesized. The optimized BHPGs were conjugated with different densities of desferrioxamine via reductive amine chemistry. Iron binding properties and prevention of iron mediated oxidation of biomolecules were measured through UV-Vis spectroscopy. Molecular properties of the polymeric chelating system were investigated in normal mice, with respect to vascular residence, clearance and biodistribution. Further, iron mobilization and excretion was investigated in iron overloaded mouse model.

#### **Results**

These highly biocompatible BHPGs showed pH and ketal group structure dependent degradation profiles in both in vitro and in vivo studies with minimal tissue accumulation. The optimized biodegradable polymers were conjugated with deferoxamine; these macrochelators showed minimal toxicity and similar iron binding profile as that of non-degradable macromolecular chelator.

#### **Conclusion**

Highly biocompatible Fe+3 specific biodegradable macro chelators have been developed and optimized. These macro chelators are highly compatible in vitro. Extensive in vitro and in vivo characterizations of these novel macrochelators are in progress.

**Title: Iron Chelation: Problems and Solutions from a Nursing Perspective****Abstract Category:** Iron Overload & Management**Authors:** Sarah Al Rahbi**Presenting Author:** Sarah Al Rahbi**Affiliation:** Thalassemia unit, Sultan Qaboos University Hospital, Muscat, Sultanate of Oman**Email:** umrateel29@icloud.com

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**ABSTRACT****Background**

Iron chelation is an essential pillar of management of thalassemia major. All three chelators ( desferroxamine, deferiprone & deferasirox) are provided free of charge to Omani patients. Despite continuous education, compliance remains a problem. This poster discusses specific problems and some solutions.

**Chelators:**

Desferroxamine (DFO): This is the oldest chelator currently available.

Mode: Given parenterally over many hours

Problem: Most patients/parents find it difficult to face the fact that oral chelators are not suitable for them, either due to toxicity or non efficacy.

Intervention: We tried to connect patients of similar ages and gender who were all using DFO so they had a support group.

Deferiprone: Oral 3-4 x/day

Problem: patients were taking their daily tablets either all together or divided into two.

Intervention: We discussed the half-life of all the chelators with each individual patient using graphs.

Deferasirox: Oral 1x/day

Problem: The amount of liquid required to mix all the tablets remains a problem, particularly for the heavier patients. We estimate that sometimes 25% of the medication is left in the glass.

Intervention: This has been difficult to resolve. Currently Jadenu remains unavailable for most of our patients.

IV DFO via Baxter pump:

Problems: The major problems have been logistics. Patients come to our hospital from the peripheries. However, insertion of port-a-cath needle can only be done at the major hospitals, only on working days and only during the normal working day.

Intervention: Currently only used on patients who have their own transport and live near the hospital.

**Conclusion**

Despite the availability of different iron chelators, we continue to face compliance problems. A workshop focused solely on this would be helpful as professionals, in particular nurse practitioners, can share their experiences/solutions



## **Title: Iraqi Experience with Deferasirox in Patients with Sickle Cell/ Beta Thalassemia (HbS/ B-THAL)**

**Abstract Category:** Iron Overload & Management

**Authors:** Hayder Al-Momen

**Presenting Author:** Hayder Al-Momen

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### **ABSTRACT**

#### **Background**

Iron overload plays an important role in increasing morbidity and mortality in patients with sickle cell-beta thalassemia (HbS/ $\beta$ -thalassemia). The anemic state inherent to thalassemia precludes phlebotomies; as such, iron chelation therapy is the only option available to manage iron overload. Deferasirox (DFX) is the most recently developed iron chelator and it has been available in Iraq since 2010, but no local data have been published since that time.

#### **Methods**

The study described is a single-center, prospective, open-labeled study that aims to evaluate the Iraqi experience with the use of Deferasirox to treat HbS/ $\beta$ -thalassemia patients with iron overload, as defined by serum ferritin (SF) levels  $> 1000$  ng/mL. A total of 23 patients with HbS/ $\beta$ -thalassemia were regularly evaluated over a 12-month period at a tertiary care center in Baghdad, Iraq. Of these 23 patients, 11 were chelation naïve (48%) and the remaining 12 patients had been previously chelated with Deferoxamine. This distinction was important in determining starting dose of DFX: chelation naïve patients were started on 20 mg/kg/day of DFX whereas those who had previously received chelation therapy were started at 30 mg/kg/day. Iron overload was assessed through serum ferritin level measurement, at baseline and then every 3 months throughout the study period. Liver alanine aminotransferase (ALT) levels, serum creatinine and platelet counts were regularly monitored at monthly intervals.

#### **Results**

DFX caused significant reduction in SF levels in all patients after one year of chelation therapy. Serum creatinine and ALT remained within normal limits throughout the study for most patients. Patients who experienced significant adverse effects were managed by temporary discontinuation or de-escalation of Deferasirox dose, for up to two weeks, followed by reintroduction of DFX at their initial starting dose and gradual dose escalation.

#### **Conclusion**

DFX has been shown to be a safe and efficacious iron chelator in non-transfusion dependent thalassemias, our study serves to demonstrate that both the safety and efficacy profiles of DFX are applicable in the specific population of HbS/ $\beta$ -thalassemia patients.

**Keywords:** Sickle cell beta thalassemia (HbS/ $\beta$ -Thalassemia), non-transfusion dependent thalassemia, Deferasirox, Iron overload, iron chelation, Iraq.

**Title: Cardiac T2\* MRI Based Management of Iron Overload in Thalassemia****Abstract Category:** Iron Overload & Management**Authors:** Shabneez Hussain<sup>1</sup>, Najveen Alvi<sup>2</sup>, Erum Hassan<sup>3</sup>, Omair Nadeem<sup>4</sup>, Lubaina Ehsan<sup>4</sup>, Khadija Awais<sup>4</sup>, Fatimah Sajjad<sup>4</sup>, Aleezay Asghar<sup>4</sup>, Sadaf Altaf<sup>5</sup>, Asim Qidwai<sup>6</sup>, Salman Kirmani<sup>7</sup>, Babar Hassan<sup>8</sup>**Presenting Author:** Shabneez Hussain**Affiliation:**<sup>1</sup> Presenting and corresponding author, Consultant Haematologist, Fatimid Foundation. Karachi<sup>2</sup> Research Associate, Dept. of Paediatrics. The Aga Khan University & Hospital, Karachi, Pakistan.<sup>3</sup> Medical officer, Kashif Iqbal thalassemia centre, Karachi, Pakistan.<sup>4</sup> Medical students, The Aga Khan University and Hospital, Karachi, Pakistan.<sup>5</sup> Pediatric Haematologist/Oncologist, Department of Paediatrics and Child Health. The Aga Khan University and Hospital, Karachi, Pakistan.<sup>6</sup> C.E.O, Afzal Memorial Thalassemia Foundation, Karachi, Pakistan.<sup>7</sup> Paediatric Endocrinologist, Department of Paediatrics and Child Health. The Aga Khan University and Hospital, Karachi, Pakistan.<sup>8</sup> Pediatric Cardiologist & Associate professor, The Aga Khan University & Hospital, Karachi, Pakistan.**Email:** Pakistan.shabneez.haem@gmail.com ; shabneezhussain@fatimid.org ; najveen.alvi@gmail.com ; erumhasan2012@gmail.com ; sadaf.altaf@aku.edu ; info@afzaalfoundation.org ; salman.kirmani@aku.edu ; babar.hassan@aku.edu**ABSTRACT****Background**

Myocardial siderosis secondary to transfusional iron overload is the most common cause of mortality in thalassemia major (TM). The aim of this study was to establish a T2\* based chelation algorithm in a resource limited setting. We also devised and assessed clinical applicability of chelation adverse events (AE) scoring system.

**Methods**

Patients  $\geq 9$  years of age with TM (n=88) and thalassemia intermedia - TI (n=10) presenting to Fatimid Foundation and Kashif Iqbal thalassemia centre Karachi, Pakistan from November 2014-May 2016 were included. Cardiac T2\* MRI (CMR) results were recorded at baseline and repeated after adequate chelation as clinically indicated. Echocardiography and Holter was also obtained in severe overload or symptomatic cardiac disease. Chelation AEscoring system was devised to ensure safe and compliant drug delivery. Decision to continue, hold or stop the drug indefinitely was determined accordingly.

**Results**

Ninety-eight patients with median age 17(9 – 34) years were included. Median T2\* MRI was 10.4ms (1.7ms-49ms). Repeat T2\* MRI done for 12 patients following targeted chelation therapy demonstrated an increase in median T2\* MRI values from 4.1ms to 5.5ms (p value: 0.07). The median ferritin levels remained unchanged pre-andpost-treatment (5827 and 5677 ng/ml respectively). AEs included nausea, vomiting and cytopenia with Deferriprone; rash with Deferasirox and infusion related local irritation with Deferrioxamine, seen in 54% (n=53) patients. Over 26% (n=25) were Class 1 and 2 (managed by patient counselling). Class 3 and 5 AEs including cytopenia and debilitating arthralgia necessitating drug discontinuation were seen in 29% (n=28%) patients.

**Conclusion**

T2\* CMR directed chelation therapy in TM and TI can help in risk reduction of heart failure and fatal arrhythmias. Over 70% patients may have no or minimal adverse events with chelators manageable by patient counseling. AE reporting system can help improve clinical decision making and result in better drug compliance.

**Keywords:** Cardiac T2\* MRI, Thalassemia Major, Thalassemia Intermedia, Cardiac Iron Overload, Iron Chelation Therapy, Guidelines



**Title: Correlation of serum ferritin levels with hepatic MRI T2 and liver iron concentration in non-transfusion beta thalassemia intermediate patients: A contemporary issue**

**Abstract Category:** Iron Overload & Management

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## ABSTRACT

### Background

Beta-Thalassemia Intermediate (B-TI) is a genetic disease that is milder than beta thalassemia major. The accumulation of iron in different organs causes tissue damage. The T2\* magnetic resonance imaging (MRI) technique is currently the gold standard for iron load detection. However, it is expensive and needs an expert radiologist to report findings. Therefore, we conducted this study to determine an optimal cut-off value of ferritin in proportion to T2 MRI of liver and measurement of liver iron concentration (LIC) for early detection of hepatic iron overload in patients with beta thalassemia intermediate.

### Methods

This cross-sectional study was conducted on 108 patients with B-TI who referred to tertiary hospital, Shiraz University of Medical Sciences, Shiraz, Iran. Serum ferritin, hepatic T2 MRI and liver iron concentration (LIC) were assessed. Receiver operating characteristic curve analysis (ROC) was used to determine the sensitivity and specificity of cut-off value.

### Results

Serum ferritin levels showed a statistically significant negative correlation with T2 hepatic MRI ( $r = -0.290$ ,  $P$  value = 0.003) and positive correlation with LIC ( $r = 0.426$ ,  $P$  value < 0.001) in the patients with B-TI. According to the analysis of ROC curves, the best cut-off value for ferritin to show early diagnosis of liver iron overload was 412 ng/ml.

Calculated sensitivities and specificities were 0.78 and 0.82 for T2 liver MRI and 0.76 and 0.86 for liver iron concentration (LIC) respectively.

### Conclusion

Serum ferritin levels of around 450 ng/ml might be considered as a cut-off point to evaluate hepatic iron overload before using expensive, not readily available T2 MRI. This level of serum ferritin could be considered for starting iron chelation therapy in patients with B-TI in areas where T2 MRI is not available.

**Keywords:** beta thalassemia intermediate, Serum ferritin, liver iron concentration

## Title: **Health Benefits of Green Tea-Curcumin Combination in $\beta$ -Thalassaemia Patients**

**Abstract Category:** Iron Overload & Management

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## ABSTRACT

### Background

Anaemic  $\beta$ -thalassaemias required blood transfusions to maintain normal haemoglobin (Hb) levels and iron chelators to counteract the resulting iron overload. A curcumin (CUR) cocktail potentially ameliorated oxidative stress in transfusion-dependent  $\beta$ -thalassaemia/Hb E (TDT) patients with iron overload. Green tea extract (GTE) rich in epigallocatechin 3-gallate (EGCG) showed potent antioxidant and iron-chelating activity.

### Purpose

We investigated effect of GTE-CUR drink on reducing iron overload and oxidative stress in TDT patients undergoing iron chelation.

### Methods

In randomized study, TDT patients were orally given the GTE-CUR drink (25 and 50 mg EGCG equivalent) for two months and taken blood at 0, 1 and 2 months for analysis of levels of biomarkers.

### Results

When compared to control group, GTE-CUR drinks did not affect white blood cell and platelet levels, Hb and hematocrit; however, red blood cell levels increased following 1 month of treatment. Levels of blood urea, serum alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase activity showed a decreasing trend, but this was not significant and seems to be independent of GTE-CUR dose. Following the 1 and 2 month treatments, there were changes in serum malondialdehyde (-0.07+2.95 and -0.87+1.68  $\mu$ M, respectively) and antioxidant activity (5.08+8.86 and 0.28+13.39 mg trolox equivalent/ml, respectively). There was also a decrease of serum non-transferrin bound iron (-1.20+8.03 and -3.93+3.83  $\mu$ M, respectively) and labile plasma iron (1.91+4.99 and -1.10+2.94  $\mu$ M, respectively).

### Conclusion

Our GTE-CUR drink increases erythropoiesis, improves liver and kidney function, diminishes oxidative stress and iron overload in thalassaemia, and possibly increases patients' length and quality of life.

**Title: Iron Chelators Supply in Brazil****Abstract Category:** Iron Overload & Management**Authors:** Tiago Cepas Lobo, Nina Victória Menezes de Melo, Merula Steagall, Fábio Fedozzi, Sandra Regina Loggetto**Presenting Author:** Sandra Regina Loggetto**Affiliation:** Abrasta (Brazilian Thalassemia Association)**Email:** loggetto.sr@hotmail.com**Address:**

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**ABSTRACT****Objective**

Brazilian Public Health System (SUS) provides the iron chelators (ICs) deferoxamine- DFO, deferiprone-DFP, and deferasirox-DFX. Each Brazilian state buy these drugs and the

Ministry of Health (MoH) reimburses the cost. The objective is to analyse the supply of ICs to better understand the Brazilian current scenario and the drug access in transfusional iron overload (IOL) as thalassemia, sickle cell disease-SCD, myelodysplastic syndrome, bone marrow failure, another transfusional hemossiderosis.

**Methods**

Analytical descriptive study based on secondary data by means of approved governmental documentation (LME) for the dispensation of ICs to people with IOL in SUS from 2010 to 2016. LME is renewed each three months, so one patient needs four LMEs per year to have the complete treatment. Data was obtained through TabWin (data tabulator developed by the MoH). The ethical aspects were respected as the research used anonymized secondary data.

**Results**

The number of LMEs increased by 89.2% (7,213 to 13,651), equivalent to 1,803 patients in 2010 to 3,412 in 2016. DFX had the highest number of LMEs in all years (86.7% in 2016), had the highest growth (122%; LMEs increased from 5,357 to 11,837 or 1,339 patients in 2010 to 2,959 in 2016), being the main drug used by all age groups. DFO decreased 26.4% (1,093 to 804), while DFP increased 32% (763 to 1,010), probably reflecting the lack of the infusion pump in Brazil and consequent migration to DFP in thalassemia patients. In Brazil there are about 550 patients with transfusion dependent thalassemia and 30,000 with SCD, justifying the higher DFX use. The LMEs show that ICs supply by the states increased over the years, but it doesn't allow to analyse individually each pathology, to identify mono or combined therapy and if the supply is regular, and to control treatment adherence.

**Conclusion**

ICs are available in Brazil. We need to develop mechanisms to get the missing data to design public policies for each disease related to IOL.

**Title: A MRI Prospective Survey on Heart and Liver Iron and Cardiac Function in Thalassemia Major Patients Treated with Deferasirox Versus Deferiprone and Desferrioxamine in Monotherapy**

**Abstract Category:** Iron Overload & Management

**Authors:** Antonella Meloni<sup>1</sup>, Laura Pistoia<sup>1</sup>, Rosamaria Rosso<sup>2</sup>, Crocetta Argento<sup>3</sup>, Paolo Ricchi<sup>4</sup>, Sabrina Armari<sup>5</sup>, Saveria Campisi<sup>6</sup>, Antonella Carollo<sup>7</sup>, Mauro Caini<sup>8</sup>, Nicolò Schicchi<sup>9</sup>, Vincenzo Positano<sup>1</sup>, Alessia Pepe<sup>1</sup>.

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## ABSTRACT

### Background

We prospectively assessed the efficacy of deferasirox versus deferiprone and desferrioxamine in monotherapy in a large cohort of thalassemia major (TM) patients by Magnetic Resonance (MR).

### Methods

Among the 2551 TM patients enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) network we selected those with an MR follow up study at 18±3 months who had been received one chelator alone between the 2 MR scans. We identified three groups of patients: 235 treated with DFX, 142 with DFP and 162 with DFO. Iron overload was measured by T2\* multiecho technique.

### Results

Excellent/good levels of compliance were similar in the DFX (98.7%) vs DFP (96.3%) and DFO (97.5%) groups.

Among the patients with myocardial iron overload at baseline, in all three groups there was a significant improvement in global heart T2\* values (DFX:+4.58±5.91ms P<0.0001, DFP:+8.53±6.97ms P<0.0001 and DFO:+3.93±5.21 ms P<0.0001). In DFP and in DFO groups there was a significant improvement in left ventricular ejection function (LVEF) (+4.86±6.99% P=0.044 and +3.87±7.48% P=0.004, respectively). Only in the DFP group there was a significant improvement in right ventricular ejection function (RVEF) (6.69±4.61% P=0.001). The improvement in the global heart T2\* was significantly lower in the DFX versus the DFP group, but it was not significantly different in the DFX versus the DFO group. The improvement in the LVEF was significantly higher in both DFP and DFO groups than in the DFX group while the improvement in the RVEF was significantly higher in the DFP than in DFX group.

Among the patients with hepatic iron at baseline, the changes were not significantly different in DFX versus the other groups.

### Conclusions

DFX monotherapy was significantly less effective than DFP in improving myocardial siderosis and biventricular function and it was significantly less effective than DFO in improving the LVEF.



## Title: **Longitudinal Prospective MRI Study in Pediatric Patients with Thalassemia Major**

**Abstract Category:** Iron Overload & Management

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## ABSTRACT

### Background

We evaluated changes in myocardial and hepatic iron overload, biventricular function, and development of myocardial fibrosis on repeated magnetic resonance (MRI) imaging assessments in pediatric patients with thalassemia major (TM).

### Methods

We considered 68 TM patients enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) project with <18 years at the first MRI scan and who performed a follow-up (FU) study at 18±3 months. Iron burden was quantified by the T2\* technique. Biventricular function was quantified by cine images. Late gadolinium enhancement (LGE) images were acquired to detect myocardial fibrosis.

### Results

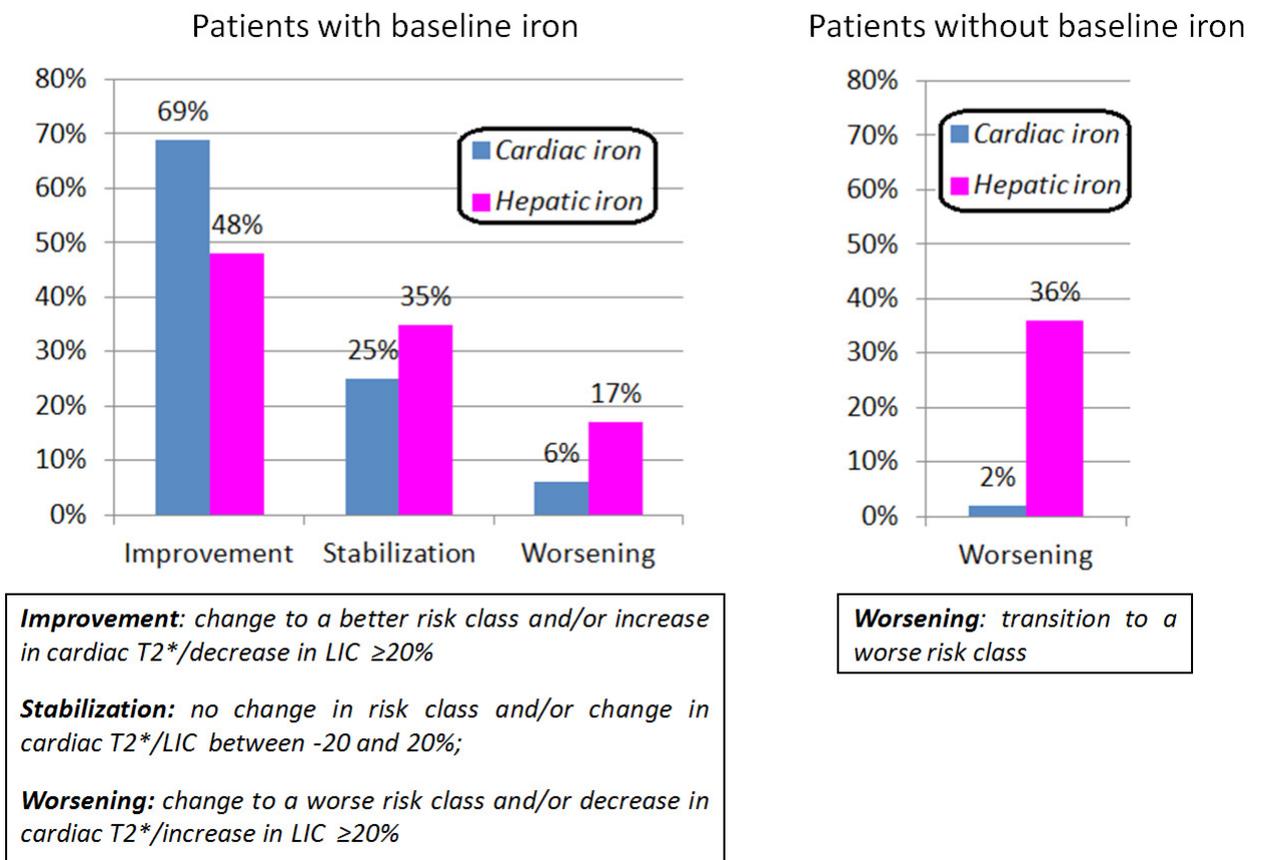
At the baseline MRI, 16(23.5%) patients showed myocardial iron overload (global heart T2\*<20 ms) and 54(79%) patients liver iron overload. Twenty-five patients changed the chelation regimen after the baseline MRI. Globally, a worsening in cardiac iron was found in the 3% of the patients while a worsening in hepatic iron in the 21% of the patients (P=0.003) (Figure 1).

The LV end-diastolic volume index, all RV volumes and the LV mass index were significantly lower at the FU. No significant improvement in global systolic function was found. Six patients had myocardial fibrosis at the baseline MRI and fibrosis was detected for all of them also at the FU. The extent of myocardial fibrosis was comparable between the two scans. At the FU 4 new occurrences of myocardial fibrosis were detected.

### Conclusion

MRI monitoring in children with TM demonstrated a good control of cardiac iron overload in terms of prevention and treatment but the need for further improvement of liver iron overload. Myocardial fibrosis appears mainly multifocal, non progressive and not reversible over a 18-month period. A prompt and aggressive approach to iron overload and a chelation regimen consistent with the high iron intake and the high rate of severe liver iron overload is recommended in children.

Figure 1





## Title: **Significant Improvement of Survival by T2\* Cardiovascular Magnetic Resonance in Thalassemia Major**

**Abstract Category:** Iron Overload & Management

**Authors:** Alessia Pepe<sup>1</sup>, Antonella Meloni<sup>1</sup>, Laura Pistoia<sup>1</sup>, Giovanni Carlo Del Vecchio<sup>2</sup>, Maria Antonietta Romeo<sup>3</sup>, Maria Rita Gamberini<sup>4</sup>, Federico Bonetti<sup>5</sup>, Gennaro Restaino<sup>6</sup>, Vincenzo Positano<sup>1</sup>, Caterina Borgna-Pignatti<sup>8</sup>

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## **ABSTRACT**

### **Background**

In 2004 seven Italian centers showed that heart disease due to myocardial iron overload (MIO) was the main cause of death in thalassemia major (TM). In the same years the noninvasive assessment of MIO was made possible in Italy by the introduction of the T2\* cardiovascular magnetic resonance (CMR). We evaluated if the deployment of T2\* CMR had an impact on the mortality rate.

### **Methods**

Four centers contributed to the present study, updating the data of the enrolled patients until August 31, 2010. For the patients who died, the date of the death represented the end of the study. 577 patients (264 females and 313 males) were included.

### **Results**

One-hundred and fifty-nine (27.6%) patients died, 124 of whom (77.9%) died before the year 2000. Dead patients started chelation therapy significantly later. The following variables were identified as significant univariate prognosticators for the death: male sex (HR=1.87, 95%CI=1.34-2.60, P<0.0001), HIV (HR=2.55, 95%CI=1.25-5.20, P=0.010) and heart failure (HR=8.86, 95%CI=6.37-12.31, P<0.0001).

MRI was not performed in 406 patients (70.4%) and no patient had been scanned before his/her death. Among the survivors, MRI was not performed in the 59% of the cases (P<0.0001). The absence of an MRI scan was a significant univariate prognosticator for death (HR=43.25, 95%CI=11.32-165.33, P<0.0001).

The study was restricted to the patients dead after 2004 (19/159=12%) or followed until August 2010 (N=357). In this subgroup of 376 patients, MRI was not performed in the 52.4% of the survivors and in all dead patients (P<0.0001). The absence of a MRI exam was reconfirmed as a strong predictive factor for death (HR=49.37, 95%CI=1.08-2263.24, P=0.046).

### **Conclusions**

Our data suggests that the use of T2\* CMR, that enables individually tailored chelation regimes reducing the likelihood of developing decompensated cardiac failure, allowed the reduction of cardiac mortality in chronically transfused TM patients.



## Title: **Association Between Cardiac Iron Clearance and Hepatic Siderosis**

**Abstract Category:** Iron Overload & Management

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## ABSTRACT

### Background

This multicenter study aimed to evaluate in thalassemia major (TM) if the cardiac efficacy of the three iron chelators in monotherapy was influenced by hepatic iron levels over a follow up of 18 months.

### Methods

Among the 2551 TM patients enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) network we selected the 98 patients with an MR follow-up at  $18 \pm 3$  months who had been received one chelator alone between the 2 MR scans and who showed evidence of significant cardiac iron (global heart  $T2^* < 20$  ms) at the basal MRI. Iron overload (IO) was measured by  $T2^*$  multiecho technique. We used cardiac  $R2^*$  ( $1000/T2^*$ ) because  $R2^*$  values are linearly proportional to iron. Hepatic  $T2^*$  values were converted into liver iron concentration (LIC) values.

### Results

We identified 3 groups of patients: 47 treated with deferasirox (DFX), 11 treated with deferiprone (DFP) and 40 treated with desferrioxamine (DFO).

Percentage changes in cardiac  $R2^*$  values correlated with changes in LIC in both DFX ( $R=0.469$ ;  $P=0.001$ ) and DFP ( $R=0.775$ ;  $P=0.007$ ) groups. All patients in these 2 groups who lowered their LIC by more than 50% improved their cardiac iron.

Percentage changes in cardiac  $R2^*$  were linearly associated to the log of final LIC values in both DFX ( $R=0.437$ ;  $P=0.002$ ) and DFP groups ( $R=0.909$ ;  $P<0.0001$ ).

Percentage changes in cardiac  $R2^*$  were not predicted by initial cardiac  $R2^*$  and LIC values.

In each chelation group patients were divided in subgroups according to the severity of baseline hepatic iron overload (no, mild, moderate, and severe IO). The changes in cardiac  $R2^*$  were comparable among subgroups.

### Conclusion

In patients treated with DFX and DFP percentage changes in cardiac  $R2^*$  over 18 months were associated with final LIC and percentage LIC changes. The changes in cardiac  $R2^*$  were no influenced by initial LIC or initial cardiac  $R2^*$ .



## Title: **Low Serum Ferritin Levels Do Not Protect from Cardiac and Liver Iron in Patients with Thalassemia Major**

**Abstract Category:** Iron Overload & Management

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## ABSTRACT

### Background

The aim of this multicenter study was to assess the distribution of serum ferritin levels in a cohort of well treated TM patients and the possible protective role of really low levels versus iron accumulation in the heart and in the liver.

### Methods

We considered 1548 TM patients regularly transfused and chelated consecutively enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) Network. Myocardial and hepatic iron burdens were quantified by the T2\* technique. Hepatic T2\* values were converted into liver iron concentration (LIC) values.

### Results

Mean serum ferritin levels < 500 ng/ml were found in 342 (22.1%) patients. Three groups were identified on the basis of mean serum ferritin levels. Both transaminases were significantly lower in patients with serum ferritin < 500 ng/ml and between 500 and 1000 ng/ml versus patients with serum ferritin ≥ 1000 ng/ml.

Among patients with serum ferritin < 500 ng/ml, 9.1% showed significant cardiac iron (global heart T2\* < 20 ms) and 21.6% showed hepatic iron (LIC ≥ 3 mg/g dw). Cardiac and hepatic iron levels were significantly lower in patients with serum ferritin < 500 ng/ml than in the other two groups and in patients with ferritin between 500 and 1000 ng/ml versus patients with serum ferritin ≥ 1000 ng/ml.

Compared to patients with serum ferritin levels < 500 ng/ml, the other two groups showed a significant higher risk of cardiac iron overload (odds ratio-OR=2.03, P=0.002 for patients with ferritin 500-1000 ng/ml and OR=5.96, P<0.0001 for patients with ferritin ≥ 1000 ng/ml) and of hepatic iron overload (OR=3.44, P<0.0001 for patients with ferritin 500-1000 ng/ml and OR=25.43, P<0.0001 for patients with ferritin ≥ 1000 ng/ml).

### Conclusion

Low serum ferritin values, even in the normal range, do not per se exclude cardiac and hepatic iron overload, although decreasing the risk. Before to consider a reduction of the chelator dose in patients whose serum ferritin levels have reached the target, a MRI scan should be performed in order to measure iron levels in the different organs

## Title: **Deferiprone Has a Dose-Dependent Effect on Liver Iron Concentration**

**Abstract Category:** Iron Overload & Management

**Authors:** Antonella Meloni<sup>1</sup>, Laura Pistoia<sup>1</sup>, Domenico Giuseppe D'Ascola<sup>2</sup>, Tommaso Casini<sup>3</sup>, Anna Spasiano<sup>4</sup>, Massimo Allò<sup>5</sup>, Angelo Peluso<sup>6</sup>, Liana Cuccia<sup>7</sup>, Alessandra Quota<sup>8</sup>, Valentina Vinci<sup>9</sup>, Vincenzo Positano<sup>1</sup>, Alessia Pepe<sup>1</sup>

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## ABSTRACT

### Background

Our aim was to assess in thalassemia major (TM) if deferiprone (DFP) had a dose-dependent effect on liver iron concentration (LIC) assessed by quantitative magnetic resonance imaging (MRI).

### Methods

Among the 958 TM patients enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) network, we identified those with an MRI follow-up study at 18±3 months who had been received DFP monotherapy and had no changes in dose of DFP between the 2 MRI scans. Patients were divided into two groups according to the DFP dose: 79 patients with 75 mg/kg/d (group 1) and 39 with >75 mg/kg/d (group 2). Hepatic iron overload was measured by the T2\* multiecho technique and T2\* values were converted into LIC values.

### Results

The two groups had comparable baseline MRI LIC values. The table shows the evolution of different iron overload risk classes between the baseline and the FU MRI. The percentage of patients that worsened their status was significantly higher in group 1 than in group 2 (26.6% vs 7.7%; P=0.016).

Subgroup analysis in patients with hepatic iron overload at baseline (MRI LIC > 3mg/g/dw) was conducted: 48 patients from group 1 (DFP dose: mean 70.6±11.2 mg/kg/d, median 75 mg/kg/d) and 30 from group 2 (DFP dose: mean 85.2±6.6 mg/kg/d, median 84 mg/kg/d). The two subgroups had comparable baseline MRI LIC values (10.2±8.1 mg/g dw vs 11.1±8.7 mg/g dw (P=0.314). While the mean change in subgroup 2 (-1.8±6.3mg/g/dw, P=0.131) was more favourable than in subgroup 1 (+0.1±7.7 mg/g/dw, P=0.903), the change in MRI LIC values did not reach statistical significance between the two subgroups (P=0.579), which may be due to small cohort evaluated.

### Conclusions

In TM patients the worsening in MRI LIC can be prevented by increasing the dose of deferiprone above the widely used regimen of 75 mg/kg body weight.



## **Title: Differential Mobilization of Transferrin and Non-Transferrin Bound Iron Fractions in Thalassaemic Serum by Iron Chelators**

**Abstract Category:** Iron Overload & Management

**Authors:** Sirichai Srichairatanakool<sup>1</sup>, Pimpisid Koonyosying<sup>1</sup>, Suthat Fucharoen<sup>2</sup>, Somdet Srichairatanakool<sup>1</sup>

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### **ABSTRACT**

#### **Background**

Having high transferrin-bound iron (TBI) in plasma of thalassaemia patients, redox non-transferrin bound iron (NTBI) and labile plasma iron (LPI) are detectable and highly taken up into cells by specific mechanisms. Therapeutic iron chelators such as deferoxamine (DFO), deferiprone (DFP) and deferasirox (DFX) along with their combinations are used to remove NTBI and intracellular labile iron pools (LIP) to prevent oxidative cellular damage. The chelators have to remove TBI to make transferrin available to bind the irons released from macrophage and intestinal epithelial cells. We found 1-(N-acetyl-6-aminoethyl)-3-hydroxy-2-methylpyridin-4-one (CM1) and green tea catechins (GTC) lowered levels of NTBI and LPI and tissue iron in iron loaded  $\beta$ -thalassaemic mice.

#### **Purpose**

Our primary objective was to evaluate efficiency of DFO, DFP, DFX, CM1 and GTC chelator, and the couple in removing NTBI and TBI.

#### **Methods**

Serum samples of  $\beta$ -thalassaemia patients after ceasing regular chelation for at least 72 hours were applied to non-denaturing polyacrylamide gel electrophoresis (PAGE) for sieving iron-bound ligand fractions, then being stained with Commassie Brilliant blue and Peril's dyes separately. The treated serum was analyzed with urea PAGE for quantification of diferric-transferrin, C-mono Fe-transferrin, N-mono Fe-transferrin and apo-transferrin forms.

#### **Results**

All tested chelators removed iron from NTBI, preferably albumin-bound iron, with different capabilities. DFP and CM1 were able to remove iron from transferrin with a strong preference for the C- lobe iron-binding site; whereas the combinations (DFO+DFP, DFO+CM1 and DFP+GTE) tend to be better.

#### **Conclusion**

DFP and CM1 working as an iron-shuttling agent may cooperate well with a larger, stronger chelator like DFO to increase chelation efficiency. Identifying actual sites on these toxic irons allows for better chelation treatment and reversal of iron toxicity. Hydroxypyridinones themselves and their shuttling effect have excellent potential for facilitating the redistribution of iron and treatment of  $\beta$ -thalassaemia with iron overload.

**Title: Fermented papaya and antioxidants effects****Abstract Category:** Life Style Issues**Authors:** Hajar Raei Dehaghi**Presenting Author:** Hajar Raei Dehaghi**Affiliation:** MS of Agricultural Engineer, Isfahan Thalassemia Society, Iran**Email:** hajarraie@gmail.com

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**ABSTRACT**

Interaction between antioxidants, free radicals and co-factors is important in preserving health, aging and age-related diseases. Oxidative stress is part of free radicals that is balanced by the body's endogenous antioxidant systems with an input from co-factors, and by the ingestion of exogenous antioxidants. In beta-hemoglobinopathies many aspects of the pathology, are mediated by oxidative stress. Stresses damage organs, reducing their function and eventually leading to the early demise of thalasseemics. Major part of the treatment program for thalasseemics has to be Preventing this damage and this is something patients can take a real role in, as taking natural supplements is fairly easy to do and can have a measured effect on one's own health. Papaya fruit and papaya leaves that are allowed to age slowly over a period of few months yield fermented papaya. Some research indicated that fermented papaya preparation (FPP), a natural health food product obtained by biofermentation of carica papaya, limited oxidative stress on beta-thal, major and intermedia and E-beta-thal.

**Title: Life Test****Abstract Category:** Life Style Issues**Authors:** Tseng Yu-Hsiang**Presenting Author:** Tseng Yu-Hsiang**Affiliation:****Email:** hajarraie@gmail.com

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**ABSTRACT**

I was born in 1982, and diagnosed "Thalassemia" after 8 months of my birth due to my poor mobility, pale and other issues. The doctor told my mom that I had to rely on blood transfusion for whole my life, and this is the prelude of my life.

Since I have memory, when my mom took me to hospital for blood transfusion, I always feel tired and helpless. I feel that time passed so quickly, I remembered I was in hospital just a couple of days ago, and here I am again, needle and pain again.....

Whenever I am in hospital, I do not feel like talking. When doctor or nurse is asking me questions, my mom is always the one who speaks for me. I only nod or shake my head. My mom knows I was unhappy, so she always bought some candy and cookies or Burger king for me on the way back home. By that time, National Health Insurance was not established yet, my mom said, if she does not have 8 thousands or 10 thousands NT dollars, she would not dare to take me to the hospital for the treatment.

Time passed by quickly, now I have grown up and working now. But in Taiwan, the government's regulation of sick leave is only 30 days at most. Although Taiwan's working environment is not kind for disability people. But thanks to National Health Insurance's support, I am able to work normally without affecting my work progress. I can go to hospital and take the treatment on weekends. I can be competent with my job and my illness will not affect me. After all, Taiwan's Thalassemia patients, we are fortunate to be taken care of by the National Health Insurance, which has relieved many families of economic pressure and thanks for the enthusiastic donation of the enthusiastic people. Because of the Blood Foundation, only safe blood will be used on us. Now, I have the ability to take care of myself, but also the ability to economically give my family a better life, so that they can live comfortably happy.



## **Title: The Brazilian Ministry of Health Technical Advisory Committee (Catthalassemia): Acting for the Benefit of People with Thalassemia**

**Abstract Category:** Miscellaneous

**Authors:** Sandra Regina Loggetto<sup>1,2</sup> Mônica Pinheiro de Almeida Veríssimo<sup>1,3</sup>, Silma Maria Alves de Melo (technical manager)<sup>1</sup>

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## **ABSTRACT**

### **Background**

In Brazil, 593 patients with thalassemia are estimated (51.4% beta-major, 43.2% beta-intermedia, 5.4% hemoglobin H-alpha disease), mainly in the Southeast region. Brazilian Ministry of Health (MoH) understands that these people need specific and high cost treatment. Our objective is to report the MoH program developed to thalassemia, guaranteeing access to treatment and increasing survival with quality of life.

### **Method**

The Technical Advisory Committee (CAT-Thalassemia) was created in 2013 by the MoH, under the responsibility of The General Coordination of Blood and Blood Products. The strategic planning was designed to promote and implement actions in partnership with cities and states. CAT-Thalassemia is composed of 16 health professional experts in thalassemia and 2 patients' representatives.

### **Results**

To guarantee the three pillars of treatment (transfusion, iron chelation and adhesion), technical advices, recommendations, manuals, and clinical guidelines were elaborated, giving sustainability, safety and resolution to the development of CAT-Thalassemia actions. Projects have already been carried out ① with focus on guaranteeing and equality of information for hematologists, multiprofessional and multidisciplinary teams, managers and general practitioners (Brazilian Symposium on Thalassemias; the on line, free and continuous TELELAB Course–Thalassemias; Theoretical-Practical Courses for Laboratory Diagnosis; referral protocols to general practitioners, folders), ② to provide an equal treatment for all patients (Guidelines for the Diagnosis and Treatment of Beta-Thalassemias, Center of Reference in Erythrocyte Genotyping, booklet), and ③ to clarify the population (campaigns on thalassemias and blood donation). We are currently ④ conducting technical visits to treatment centers for situational diagnosis and planning of joint actions, ⑤ organizing training in T2\* magnetic resonance, and ⑥ working to maintain educational, equal treatment and information.

### **Conclusions**

Added to transfusional quality assurance, iron overload diagnosis, iron chelators, T2\* technology for the diagnosis and control of chelation, and qualified multiprofessional and multidisciplinary teams, the survival and the quality of life of patients with thalassemia can improve greatly in Brazil. The next step is measure the results in a quantitative basis.



**Title: Disease Knowledge: A Missing Ring in the Chain of Management of Children with Thalassemia Major Management**

**Abstract Category:** Miscellaneous

**Authors:** Khawla Mohd Belhowl, Marya Almansoori, Najm Eddin Babikir, Essam Dohair, Reham Ghanim

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## **ABSTRACT**

### **Background**

Thalassemia major is diagnosed very early in life with most of the education being directed at parents. Unfortunately, a structured educational program (SEP) is not provided thereafter to the child until adolescence. We aimed to assess the disease knowledge in children aged 8-13 years with transfusion dependent thalassemia major at Dubai thalassemia center, before and after the introduction of SEP.

### **Method**

A cross-sectional study was conducted between June to August 2016, and included all children aged 8-13 years with transfusion dependent thalassemia  $\beta$ -TM being treated at the Dubai Thalassemia Centre. Informed consent were obtained from 32 parents (94%) out of 34. We used a questionnaire, developed by our pediatric hematologist that consisted of 16 questions about disease knowledge. The questionnaire was administered pre-and post-provision of two structured educational sessions directed to each child one month apart. For content validity, a pediatric hematologist and a pediatricians have reviewed the questionnaire. The child was helped to complete the questionnaire. External assessor was used to administer post education questionnaire that was done for 29 patients (92%) with three children missing the reassessment (one out of country, one went for bone marrow transplant and one missed appointment).

### **Results**

The assessment showed average pre-educational knowledge level of 24% that improved significantly to 76% ( $P < 0.05$ ) post two structured educational sessions.

### **Conclusion**

Knowledge of pediatric thalassemia patients of their disease was low indicating a defect in the educational program as most of the education is being directed to parents. Introducing a SEP directed to pediatric age group has improved significantly their disease knowledge.

**Title: Preliminary Study: Tuberculosis Infection Among Thalassemia Major Children****Abstract Category:** Miscellaneous**Authors:** Ludi Dhyani Rahmartani, Mikhael Yosia, Nastiti Kaswandani, Pustika Amalia Wahidiyat**Presenting Author:** Ludi Dhyani Rahmartani**Affiliation:** Department of Child Health, Faculty of Medicine, Universtas Indonesia – Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia.**Email:** pa.wahidiyat@gmail.com

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**ABSTRACT****Background**

Thalassemia is an inherited autosomal recessive blood disorder of hemoglobin synthesis. Infection is one of the causes of thalassemia morbidity and mortality. The underlying mechanisms of the increased susceptibility to infections in thalassemia are abnormal immune response due to the disease itself, blood transfusion, iron overload, splenectomy and iron chelation therapy. Indonesia is a country with "high burden country" of tuberculosis; combined with the aforementioned susceptibility to infections, thalassemia patients in Indonesia are very susceptible to acquiring and developing active TB. There is a still limited study about tuberculosis infection in thalassemia patients.

**Purpose**

This study is aims to look upon incidence of tuberculosis infection in thalassemia major patients whilst finding any correlation between tuberculosis manifestation and severity to thalassemia (especially towards iron profile and chronic anemia).

**Methods**

A cross sectional study design was done in patients with thalassemia who undergoes regular blood transfusion. We perform the interferon gamma release assay (IGRA), tuberculin test, chest X-ray and ferritin serum. We also collect clinical data to determine the TB phase in those patients.

**Results**

For this preliminary study, 43 samples were used (25 males and 18 female samples). Mean age for all the samples were  $14.33 \pm 1.78$  years. All of the samples where already treated with iron chelator (1 patient with DFO, 30 with DFP, 2 with DFX, 1 with DFP DFX and 2 with DFO DFP). Mean ferritin value for all 11 samples with positive Interferon-Gamma Release Assay (IGRA) were  $4247.27 \pm 2471.68$  ng/mL, while their mean transferrin saturation were  $83.18 \pm 17.59\%$ . All 11 patients with positive IGRA had no complaints of any symptoms (in relation with those included in TB scores).

**Conclusion**

Through this preliminary study, 25.6% of all the samples had positive IGRA results whilst having no complaints of symptoms associated with tuberculosis. Further study with larger sample is needed in order to see any correlation present between iron profiles and manifestation of tuberculosis in thalassemia major patients.

**Keywords:** thalassemia major; tuberculosis; ferritin; transferrin saturation; indonesia



## **Title: Effect of breastfeeding versus infant formula on iron status of infants with beta thalassemia major**

**Abstract Category:** Miscellaneous

**Authors:** Usama Roshdy El Safy<sup>1</sup>, Manar Mohamed Fathy<sup>1</sup>, Tamer Hasan Hassan<sup>1</sup>, Marwa Zakaria<sup>1</sup>, Mohamed Abdel Kader Al Malky<sup>1</sup>, Mohamed Arafa<sup>1</sup>, Hany El Sayed<sup>1</sup>, Ashgan Al Ghobashy<sup>1</sup>, Boshra Zaho<sup>1</sup>, Attia Abdel Wahab<sup>1</sup>, Mohamed Hosam Mourad<sup>2</sup>

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### **ABSTRACT**

#### **Background**

Thalassemia major or Cooley's anemia is the most severe form of beta thalassemia in which the complete lack of beta protein in the hemoglobin causes a life-threatening anemia requiring regular blood transfusions and extensive ongoing medical care. These extensive, lifelong blood transfusions lead to iron-overload that must be treated with chelation therapy to prevent early death from organ failure. We compared serum iron and ferritin levels amongst infants aged up to one year with beta thalassemia major according to their feeding types, including exclusively breastfed, exclusively formula fed and combined (both breast and formula) fed types.

#### **Methods**

Sixty out of 176 screened infants with transfusion dependant beta thalassemia major were recruited from the outpatient clinic of thalassemia at Zagazig University Hospital in Egypt, between 2007 and 2014. Patients were classified into three groups (20 patients per group) according to type of feeding. Group 1: exclusive breastfeeding, around 6–8 feeds per day; group 2: exclusive infant formula feeding, 120–150 ml of formula per kilogram of body weight per day divided into 6–8 feeds and group 3: combined breastfeeding and formula per day.

#### **Results**

Serum iron and ferritin levels were lower in group 1 compared to groups 2 and 3. The mean serum iron for group 1 was 73, 87 and 96 ug/dl at 6, 9 and 12 months respectively, while that for group 2 was 85, 99 and 112 ug/dl at 6, 9 and 12 months respectively and for group 3 was 78, 92 and 99 ug/dl at 6, 9 and 12 months respectively. The mean serum ferritin for group 1 was 283, 327 and 497 ng/ml at 6, 9 and 12 months respectively, while that for group 2 was 310, 389 and 591 ng/ml at 6, 9 and 12 months respectively and for group 3 was 291, 345 and 515 ng/ml at 6, 9 and 12 months respectively. The differences were not statistically significant.

#### **Conclusions**

Breastfed infants with beta thalassemia major may accumulate less iron than infants fed iron fortified formula anticipating later onset of iron overload in the breastfed infants. Larger studies are needed to support these findings.

## **Title: Bone Disease in Pediatric Patients with B-Thalassemia Major: Experience in a Tertiary Care Hospital in Upper Egypt**

**Abstract Category:** Miscellaneous

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### **ABSTRACT**

#### **Background**

Improved survival in patients with  $\beta$  thalassemia major (TM) allowed for several complications of the disease and its treatment to manifest, one of which is bone disease. Objectives: This study was conducted to determine the prevalence of bone-related abnormalities within this population.

#### **Methods**

Forty two children and adolescents aged 5 -19 years, with transfusion-dependent TM in Assiut, Egypt, participated in this cross-sectional study. Medical history by interview and review of medical records as well as physical examination including anthropometric measures were done. CBC& serum ferritin were assayed. Bone densitometry using DEXA was performed and Height for age Z- score (HAZ) adjusted BMD Z-scores were calculated.

#### **Results**

underweight and short stature were observed in 73.8% and 69 % of the patients, respectively. Delayed Puberty was noted in 71.4% of the patients who reached pubertal age. These may be indicators of ? pituitary defect and malnutrition among thalassemic subjects in this study. Osteoporosis (BMD Z-scores  $\leq$  -2 with a clinically significant fracture history) was detected in the lumbar spine and femoral neck in 28.5% and 47.6 % of subjects, respectively. After height adjustment these figures were 2.3% and 33.3%, respectively. Forty-seven percent of patients had a history of fractures and the cumulative risk for which increased with age. Seventy-eight percent of patients reported bone pain, whilst back/hip pain was present in 69 % of thalassemic children and adolescents. Genu valgus deformity and scoliosis were seen in 40.5% and 11.9 % of patients.

#### **Conclusion**

High prevalence of low bone density and deficit in other aspects of bone health among thalassemia patients make routine bone health assessment necessary for this vulnerable group. Considering influencing factors, dietary counseling and preventive supplementation therapy for this high risk group of children and adolescents may be necessary. This should be assessed by future intervention studies.



**Title: Australia is a country built on immigration and consequently our Haematology laboratories see a diverse range of Haemoglobinopathies**

**Abstract Category:** Miscellaneous

**Authors:** Anne Gilbert

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## **ABSTRACT**

Australia is a country built on immigration and consequently our Haematology laboratories see a diverse range of Haemoglobinopathies. The Royal College of Pathologists Australia Quality Assurance Programme (RCPA-QAP) has a comprehensive programme for Haemoglobinopathies. It includes analysis of Hb A2, Hb F and Hb variant (where present). There is also an educational component for each survey. Four surveys are distributed per year. This presentation will discuss a selection of recent surveys, ranging from heterozygous beta thalassaemia to common and rare Hb variants.



**Title: Case report Co-occurrence of Hereditary elliptocytosis and Heterozygous  $\beta$ -Thalassemia**

**Abstract Category:** Miscellaneous

**Authors:** Hadeel Ibrahim

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## ABSTRACT

An 18-year-old-female was referred to undergo hemoglobinopathy investigation for chronic anemia.

Physical examination was normal videlicet no jaundice nor organomegaly The peripheral blood film smear showed a striking anisopoikilocytosis encompassing ovalocytes, elliptocytes, rod elliptocytes but no nucleated RBC, additive to the hypochromia and microcytosis as the MCH and MCV were 19.2 pg and 56.5 fl respectively, her hemoglobin level was 94 g/L.

Hb HPLC yielded a chromatogram with and Hb A2 of 5%.

Thus the incidental discovery of co-existent Hereditary elliptocytosis and Heterozygous  $\beta$ -Thalassemia was made overt.

Iron status assessment, G6PD enzyme assay, and the reticulocyte count were all normal.

Parents were related, however, they deny any history of receiving blood transfusion or splenectomy in the family. Worthy to mention that her sister had been diagnosed as a  $\beta$ -thalassemia carrier.

Due to the genetic constraint interfered with identifying the exact molecular abnormality underlying this cytoskeletal red cell abnormality.

Reviewing the literature in this regard, Two types of hemoglobinopathies had been suggested by Aksoy and Erdem in 1968; one type where the combined HE and BTT produces no mutual enhancement of the involved genes and the other type in which the combined genes for HE and BTT causes either a summation of their clinical effects or mutual enhancement of the expressivity of either of the involved genes in the form of uncompensated hemolysis. B-globin gene is located on the short arm of chromosome 11.

HE is usually inherited in an autosomal dominant mode, with a variety of possible molecular defects responsible for HE are those attributed to deficiency of the spectrins (80% of cases of HE), protein 4.1, or Glycophorin C protein.

Worthy to mention that the genes for  $\beta$ -thalassemia and elliptocytosis are not allelic



## **Title: Frequency of silent Brain lesions and aspirin protection evaluation over three years follow up in thalassemia patients**

**Abstract Category:** Miscellaneous

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## **ABSTRACT**

### **Background**

Silent brain ischemia and white matter lesions might be associated with overt cerebrovascular accident (CVA) over time in beta thalassemia major (TM) and intermediate (TI). Aspirin may be protective in these patients so that we evaluated brain MRI in thalassemia patients to see whether aspirin is protective or not.

### **Methods**

A cross sectional study was conducted on 15 B-TI and 5 B-TM patients at Shiraz Hematology research Center. These patients were randomly selected from 90 TM and TI patients who had performed brain MRI (diffusion weighted imaging method) before and underwent second MRI after three years follow up. All of them had no overt neurological defects. The patients divided into two groups based upon taking aspirin or not.

### **Results**

Median age of the patients was 32 years, ranged from 8 to 42 years. Sixteen patients were females. The median platelet count was 415500/microliter (range: 80000-1030000/microliter). Eight patients were on regularly Aspirin. From those, three patients had normal MRI and developed no lesions within three years. Previously, white matter lesions (WMLs) were determined in 10 patients and in new MRI it has been detected in 12 patients. From those, 9 patients (81.8%) underwent splenectomy. From two patients with normal previous MRI and WMLs in new MRI, one patient was not using Aspirin. Three patients had WMLs both in previous studies and current study but findings in new MRI were reported as more than before. From those, 1 patient was using Aspirin regularly, 1 patient irregularly and other patient was not using Aspirin.

### **Conclusion**

Our study showed close follow up is needed for patients at high risk of silent brain lesion. Aspirin could be protective against new or progressive brain lesions or ischemia so that low dose aspirin (80-100 mg per day) is recommended in high risk thalassemia patients.



**Title: Anthropometric Status of Thalassemia Major Patients in Dr. Cipto Mangunkusumo Hospital, Jakarta**

**Abstract Category:** Miscellaneous

**Authors:** Afiffa Mardhotillah, Mikhael Yosia, Teny Tjitra Sari

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## ABSTRACT

### Background

The effect of chronic anemia and hemosiderosis is appalling towards growth of thalassemia major patients. Those with low adherence and access towards continuous transfusion and chelation therapy are at risk of short stature and malnutrition. With clinical concerns usually falls heavier upon the main disease (thalassemia) itself, patient and doctors usually lacks attention towards patient's nutritional status.

### Objective

The aim of this study is to report anthropometric status (weight, height, MUAC) of adolescence and adult patients in Dr. Cipto Mangunkusumo Hospital (RSCM).

### Method

This is a cross-sectional study conducted in Dr. Cipto Mangunkusumo Hospital (RSCM). Sample included are thalassemia major patients who undergoes transfusion in RSCM without any special diet (vegetarian, low gluten, etc). Those with comorbidities other than thalassemia are excluded. Anthropometric status was measured by trained clinician. Nutritional status was categorized by using MUAC for age. Iron profile and significant haematology examination values were gathered from the sample's medical record. Statistical analysis was done using SPSS.

### Result

A total of 139 samples were included in this study, mean age was  $26.28 \pm 6.32$  years. Mean pre-transfusion hemoglobin was  $7.36 \pm 0.85$ , and mean ferritin value was  $6021.66 \pm 3586.74$ . All of the patients were administered with iron chelator; 21 with DFO, 80 with DFP, 25 with DFX, 11 with DFP DFO, and 2 with DFP DFX. From anthropometric data obtained, mean height was  $150,7 \pm 10$ , mean weight was  $41,9 \pm 8,7$ , and the average of mid upper arm circumference (MUAC) was  $20,0 \pm 2,9$  cm for male and  $21,2 \pm 2,8$  cm for female. We found 43% were severely undernourished, 45% were undernourished, only 12% were well-nourished.

### Conclusion

Based on the study alone, more than half of the sample where undernourished. Extra attention and care towards nutritional status of thalassemia patient is needed.

**Keywords:** thalassemia major; anthropometric; indonesia; MUAC; nutrition



## Title: **MRI for the Diagnosis of Cardiac and Liver Iron Overload in Patients with Transfusion-Dependent Thalassaemia: An Algorithm to Guide Clinical Use When Availability Is Limited**

**Abstract Category:** Miscellaneous

**Authors:** Ali Taher<sup>1</sup>, Amr Ajlan<sup>2</sup>, Basim A.A. Al Ebadi<sup>3</sup>, Hany Dewedar<sup>4</sup>, Ahmed S. Ibrahim<sup>5</sup>, Lamis Ragab<sup>6</sup>, Omar Trad<sup>7</sup>, Ahmed S. Wataify<sup>8</sup>, Lily L.L. Wong<sup>9</sup>, and Vip Viprakasit<sup>10</sup>

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## ABSTRACT

### Background

Patients with transfusion-dependent thalassaemia (TDT) develop iron overload (IOL) secondary to repeated transfusions and remain at risk of increased morbidity and mortality. Magnetic resonance imaging (MRI) is a validated and internationally reproducible modality for iron assessment in the liver and heart of TDT patients, allowing better tailoring of iron-chelation therapy. However, despite its established utility and widespread use, MRI is not always available or affordable, especially in resource-poor regions where TDT prevalence is highest. Moreover, in healthcare centres with large patient volumes, assessment for all patients at regular intervals is not always feasible. Also, recent international guidelines on MRI in thalassaemia do not always provide sufficient guidance on when or whom to assess with MRI.

### Methods

To address these gaps in TDT management, a consensus panel of thalassaemia experts from the Middle East, North Africa and Asia Pacific proposed a simple and practical algorithm to guide the use of MRI for the detection and monitoring of IOL in TDT, while considering its availability and accessibility for TDT patients.

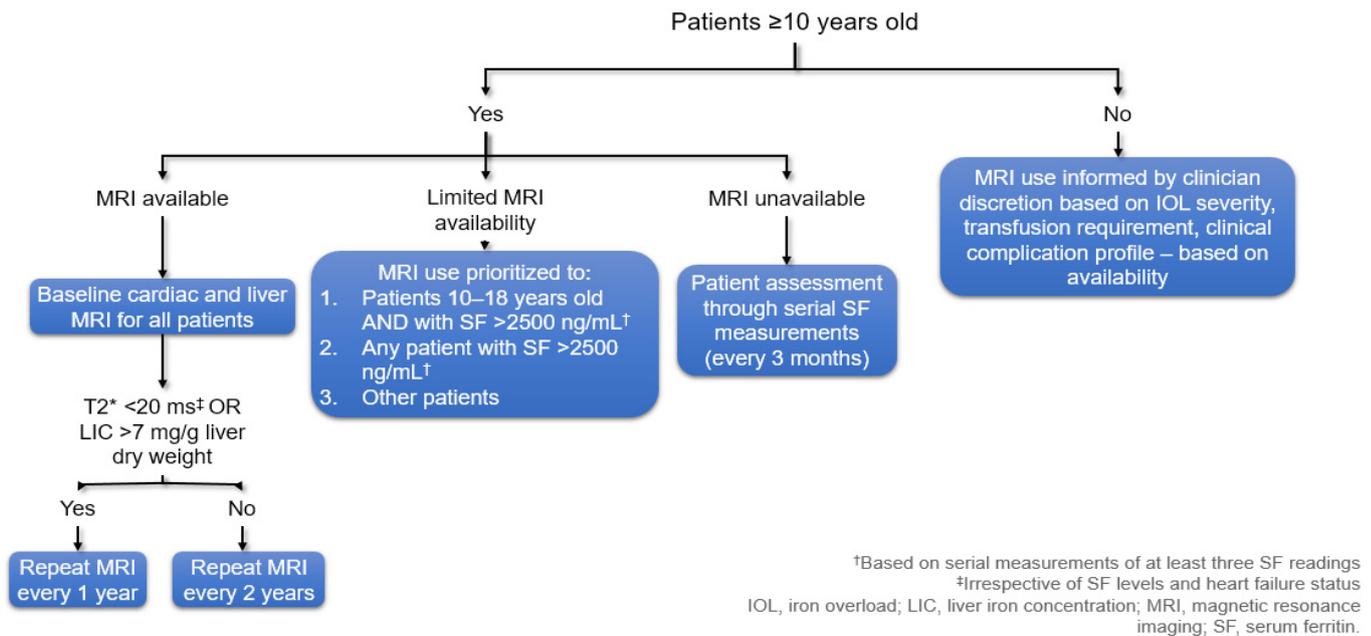
### Results

Age is the main determinant for initial MRI measurement. Consequently, in an ideal situation whereby MRI is easily accessible, all TDT patients aged  $\geq 10$  years, regardless of all other characteristics, would be candidates for baseline IOL screening by MRI. MRI could still be requested in patients  $< 10$  years old with severe IOL or suspected heart or endocrine complications, or based on the physician's judgement. Where MRI is not accessible for all patients, those aged 10–18 years with serum ferritin (SF)  $> 2500$   $\mu\text{g/L}$  should be prioritized, followed by any patient with SF  $> 2500$   $\mu\text{g/L}$  to optimize chelation therapy and prevent complications. Liver and heart examination should be performed simultaneously. Follow-up testing frequency depends on baseline reading: repeat MRI annually when myocardial T2\*  $< 20$  ms or liver iron concentration (LIC)  $> 7$  mg/g liver dry weight (based on validated methods and standard calibration between MRI and tissue LIC); otherwise, repeat every 2 years. The proposed thresholds and frequency should be considered irrespective of SF levels and heart-failure status. Patients with heart failure, however, would need to be monitored and managed according to standard of care for heart disease. Finally, where MRI is unavailable, serial SF values obtained every 3 months should be used to monitor IOL (Figure 1).

### Conclusion

In the absence of practical guidelines for assessing and monitoring IOL in TDT patients, and with persistence of challenges in availability and access to MRI in resource-poor countries with high patient volumes, the development of an algorithm for MRI in IOL assessment herein is a first step towards improving the management of these patients. The consolidation of this algorithm in the clinical setting is essential to optimize the use of MRI and, consequently, clinical outcomes among this population.

Figure 1. Algorithm to guide MRI use in transfusion-dependent thalassaemia across countries with limited resources





## **Title: Causes of Hospital Admission in $\beta$ -Thalassemia (CHAT) in Lebanon from 1995 to 2015: a pilot retrospective study from a tertiary care center**

**Abstract Category:** Miscellaneous

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## **ABSTRACT**

### **Background**

Causes of hospital admission have been studied in sickle cell disease. However, only two reports, limited to patients with thalassemia major (TM), have been published to date on the causes of hospital admission in thalassemia patients. This is a pilot study investigating the causes of hospitalization of both TM and thalassemia intermedia (TI) patients during the period from 1995 to 2015 in a tertiary care center in Beirut, Lebanon.

### **Methods**

Our retrospective, cross-sectional study recruited 33 adult TM and TI patients admitted to the American University of Beirut Medical Center (AUBMC) during the 20-year period from 1995 to 2015, with in-hospital stays exceeding 24 hours in duration.  $p$ -values  $< 0.05$  in logistic regression analysis using STATA Data Analysis and Statistical Software 13 were considered statistically significant.

### **Results**

Our search yielded a total of 205 admissions corresponding to 33 adult patients (mean age  $32.6 \pm 15.6$  years [25.6 years in TM versus 41.0 years in TI,  $p = 0.003$ ]). 15 patients (45.5%) had TM and 18 (54.5%) had TI. 125 admissions (61.0%) were in TM patients, while 80 (39.0%) were in TI patients. Patients with TM were more likely to have a longer hospital stay per admission than patients with TI (6.3 days versus 3.6 days, respectively;  $p = 0.034$ ). Overall, the three most common causes of hospitalization were transfusion therapy (54.6%), infection (12.2%), and chemotherapy (7.3%). In TM, the most common causes of hospital admission were transfusion therapy (66.4%), infection (9.6%), and bone marrow transplantation (7.2%), whereas in TI, these were transfusion therapy (36.3%), chemotherapy (18.8%), and infection (16.3%).

### **Conclusion**

This study is the first to examine the causes of hospital admission among patients with  $\beta$ -thalassemia in Lebanon, and it is the first in the literature to explore such causes in patients belonging to the TI subset.

**Title: Selenium level of patient with thalassemia major in dr. Cipto Mangunkusumo hospital Abstract Category: Miscellaneous**

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## ABSTRACT

### Background

As increase of labile iron is highly correlated with oxidative stress (which in time would result in complications in vital organs), there are trepidation over antioxidant hyper-consumption in patient with iron overload. One of the effected antioxidant is selenium, which is a major contributor to glutathione peroxidase. Data or reports regarding selenium status in thalassemia major patient are still very limited. This study aims to evaluate and report level of selenium status of thalassemia major patient in Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

### Methods

In this cross-sectional study, patients with thalassemia major from Dr. Cipto Mangunkusumo Hospital (RSCM) were included. Serum selenium level where measured in all samples in Jakarta. Patient with special diet and comorbidities other than thalassemia were excluded. Significant medical data of all the patients were gathered from their medical record. Data analysis was done using SPSS.

### Results

A total of 122 patients (62 females and 60 males) were included with mean age of  $26.07 \pm 6.66$  years. All of the patients included were already prescribed with iron chelation (5.8% with DFO, 76.4% with DFP, and 17.6% with DFX). Mean pre-transfusion hemoglobin were  $7.82 \pm 1.18$  g/dL, mean ferritin value were  $6048.44 \pm 3589.39$  ng/mL while mean transferrin saturation were  $90.26 \pm 18.71\%$ . Mean value of selenium were  $51.93 \pm 8.8$  ng/mL (normal range of 70-150 ng/mL). From all the samples included, 95.9% had selenium deficiency. No significant relationships were found between pre-transfusion hemoglobin, ferritin value and transferrin saturation towards selenium level.

### Conclusion

Selenium deficiency are observed nearly of the samples; extra care and further studies is necessary in order to further analysis selenium status in thalassemia patient and its relationship towards oxidative stress, organ damage and further complications.

**Keywords:** combination therapy; iron chelator; thalassemia major

**Title: Quality of Life in Thalassemia Patients: A Multicenter Study****Abstract Category:** Miscellaneous**Authors:** Anisa Setiorini, Teny Tjitra Sari, Rini Sekartini, Nia Kurniati**Presenting Author:** Teny Tjitra Sari**Affiliation:** Hematology-Oncology Division, Department of Child Health, Faculty of Medicine, Universitas Indonesia – Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia.**Email:** pa.wahidiyat@gmail.com**Address:**

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**ABSTRACT****Background**

Thalassemia is a chronic condition and this condition affect patient's quality of life, because of the disease and the effect of treatment itself. Blood transfusion and chelating agent given for thalassemia children in a lifetime could give a good quality of life compared to healthy children. Assesment is needed to determine and to improve the quality of life in thalassemic patient.

**Methods**

We performed a cross-sectional study from January – March 2017 in Cipto Mangunkusumo Hospital, Harapan Kita Hospital, and Tangerang Public Hospital. Thalassemia children aged 2-18 years were involved, the assesment used PedsQL™ 4.0 generic scale score parent-proxy report.

**Results**

From the 387 children, the assesment showed: physical fuction 81,89 (15,59), social fuction 88,87 (16,34), emotional function 75,48 (17,14), and school function 61,49 (18,98). The school fuction has lowest score affected parameter studied. Mean scores for quality of life in children with thalassemia were 76,88 (12,92).

**Conclusion**

Thalassemic children have a good quality of life in general (72,8%) but the school and emotional functions still have a low score.

**Keywords:** thalassemia, children, quality of life, PedsQL



**Title: Modified Alternating Combination Iron Chelation Therapy in Thalassemia Major Patients Abstract Category: Miscellaneous**

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## ABSTRACT

### Background

With increased life expectancy of thalassemia major patients following improved treatment regimens, minimizing iron overload and its associated side effects becomes a pertinent issue. Due to limited resource and budgeting, there are instances when usual continuous or alternating therapy cannot be commenced. This study aims to identify the effectiveness of using a modified alternating combination therapy in thalassemia major patients with hemosiderosis.

### Methods

This is a retrospective study evaluating patients with modified alternating combination therapy done in thalassemia major patients treated at Dr. Cipto Mangunkusumo Hospital, Jakarta. The data for iron chelation treatment doses, iron profile, and MRI examinations were collected from patient medical records and interviews.

### Results

Nine subjects with mean age of 15 (range 8 to 33) years were included in this study, 2 of which were treated with DFP+DFO (7 days of DFP with 2-3 days of DFO infusion), 2 with DFX+DFO (7 days of DFX with 2-3 days DFO infusion) and 5 with DFP+DFX (7 days of DFP and 3 days of DFX) combination. All included patients have received combination iron chelation therapy for at least 1 year. Serum ferritin results showed better iron control in those receiving DFP+DFO and DFX+DFO combination therapy, while transferrin saturation results were generally raised in all groups. Most of the subjects receiving DFP+DFX combination showed improvements in myocardial T2\* MRI results, while hepatic T2\* MRI results showed no difference between the two groups.

### Conclusion

Promising results can be seen in the group receiving DFP+DFX combination therapy, partly due to the fact that both drugs are available in oral form, which may promote patient compliance. However, due to the limited number of patients and length of observation, further studies are warranted to evaluate modified alternating combination therapy in a larger sample population for a longer period of time.

**Keywords:** combination



**Title: Assessment Towards Health Related Quality of Life in Indonesian Children with Thalassemia Major**

**Abstract Category:** Miscellaneous

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## ABSTRACT

### Background

Research and studies that looked upon Health Related Quality of Life (HRQoL) in Indonesia are still limited, even more in children with chronic disease such as thalassemia. This study aims to investigate whether lower quality of life is present in children with thalassemia major, who would need to consider blood transfusion as part of their daily life. HRQoL are assessed using PedsQL 4.0 to look upon: physical, emotional, social, school functioning compared to their healthy siblings.

### Methods

A cross-sectional study was done for one month in Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia (RSCM). Children with thalassemia age 5-18 years who undergoes routine blood transfusion was administered with a validated Indonesian version of the PedsQL 4.0. At the same time, patient's healthy siblings where also given the same questionnaires. Children with thalassemia and their siblings were age and gender adjusted and put into 2 different groups. Additional information such as level of education and socio-demographic data were collected from both patients and healthy sibling.

### Results

Thirty thalassemia major patients and their respective siblings agreed and gave informed consent to be interviewed. Median age for the subjects is 11.9 (ranging from 5 to 18) years and sibling is 13.2 (ranging from 7 to 18) Years. After calculating result in all four respective fields and comparing them between the two groups, thalassemia group reported having significantly lower quality of life compared to their healthy sibling.

### Conclusion

This study found that thalassemia does have negative impact on patient's perceived physical, emotional, social and school functioning compared to their healthy siblings. With finding of significant difference in HRQoL based on PedsQL 4.0, continuous support and understanding from government, health care providers, school and family is vital in maintaining and improving good quality of life in children with thalassemia.

**Keywords:** thalassemia major; quality of life; pedsq



**Title: Case Series of Joint Effusion, Purpura and Gum Bleeding in beta-thalassemia Major Patient: Overlooked Effect of Scurvy?**

**Abstract Category:** Miscellaneous

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## ABSTRACT

### Background

Iron overload increases oxidative stress and in turn causes hyperconsumption of antioxidant. One of the affected substance being ascorbic acid (Vitamin C). Even though theory had suggested hyperconsumption of Vitamin C is present; its relationship with iron inside the human body causes complexity in administering supplementation. This study will present two case of bleeding in beta-thalassemia major patient related to deficiency of Vitamin C (scurvy).

### Case 1

10-year-old boy with beta-thalassemia major came with gum bleeding and severe pain followed by swelling on his left knee joint. Blood examination had continuously shown moderate thrombocytopenia between 33000/ $\mu$ L to 126000/ $\mu$ L, pre-transfusion haemoglobin level ranging from 5.3 to 10.9 mg/dL, serum ferritin between 2800 ng/mL to 3614 ng/mL, normal PT/APTT results and MRI T2\* showing mild siderosis in the pancreas and heavy siderosis in the liver. X-ray genu dextra/sinistra shows osteoporotic bones with periosteal reactions. Lab test shows low serum Vitamin C, subsequent treatment with 100 mg of Vitamin C supplementation resulted in patient's clinical improvement.

### Case 2

11-year-old girl with beta-E-thalassemia was admitted to RSCM due to worsening episode of gum bleeding. She was diagnosed with suspected gingival enlargement and oral cavity infection. Oral examination detected radix gangrene (16,36,44), pulp gangrene (26,35,46), gingival hypertrophy at the maxilla and mandible regions, and dental caries (37,47). Biopsy of the mass showed gingival ulcer, chronic inflammatory granulomatosis without signs of malignancy. She also complains of joint swelling and pain on her left knee. Lab test shows low serum Vitamin C, subsequent dental treatment and 100 mg of Vitamin C supplementation resulted in patient's clinical improvement.

### Conclusion

Scurvy (Vitamin C deficiency) is an often forgotten and overlooked condition in thalassemia major patients.

**Keywords:** thalassemia major; scurvy; vitamin c; bleeding; joint effusion



## **Title: An Open-Label Randomized Clinical Trial with Multiple Doses of Pegylated Bovine Carboxyhemoglobin (Sanguinatetm) in Thalassemia Patients**

**Abstract Category:** New Advances in Treatment

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## **ABSTRACT**

### **Background**

Conventional treatment for thalassemia is based on regular blood transfusion which could posed further problems including increase risk of infection, iron overload and alloimmunization to the patients. Newly developed SANGUINATETM, is a dual oxygen and carbon monoxide transfer agent that has received orphan drug status from the US FDA for the treatment of anemic and ischemic hypoxia such as sickle cell anemia. This study presents results from Phase IIa trial of SANGUINATETM in low and high dose cohorts in 32  $\beta$ -thalassemia patients with non-transfusion dependent thalassemia ( $\beta$ -NTDT).

### **Methods**

An open-label randomized Phase IIa study enrolled 32  $\beta$ -NTDT patients aged 18-55 year old. 24 subjects received either a low dose (160 mg/kg) of SANGUINATETM or SOC. Another 8 subjects received either a high dose (320 mg/kg) of SANGUINATETM or SOC. Patient's safety, pharmacokinetics, erythropoiesis, iron status and cardiac functions were evaluated.

### **Results**

No serious adverse events that related to SANGUINATETM were found in multiple both dose levels. One subject exhibited urticarial rash after infusion with SANGUINATETM for 2-24 hours probably due to allergy to SANGUINATETM components and was recovered by intravenous injection with dexamethasone and anti-histamine. There were no increase in hemoglobin and hematocrit level. Transient increase in systolic and diastolic pressure was seen in some patients but returned to baseline within 24-72 hours. Three patients had an increase in right ventricular systolic pressure after infusion without any cardiac symptoms and returned to normal within 72 hours. Iron contents remained constant throughout the study.

### **Conclusions**

This trial established the safety and tolerability of SANGUINATETM at both dose levels in thalassemia patients. SANGUINATETM will be a good option for thalassemia patients who developed alloantibodies to blood transfusions. This study permitted its advancement to study other thalassemia clinical trial related to hypoxia such as pulmonary hypertension and chronic leg ulcers.

## Title: **Production and Transduction of Human Recombinant Tat-B-Globin Chain into K562 Model Cell System for Thalassemias**

**Abstract Category:** New Advances in Treatment

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## ABSTRACT

### Background

Protein Transduction Domain (PTD) technology has been emerged as a promising therapeutic approach for genetic/metabolic diseases. Previously, we applied this technology to deliver successfully the mitochondrial protein Sco2 into a cytochrome c oxidase deficient cell culture model. Considering that  $\beta$ -thalassemias are severe congenital hemoglobinopathies, characterized by reduced or absent production of adult  $\beta$ -globin chain and thus imbalanced globin chain synthesis, we decided to apply PTD technology as a protein therapy approach.

### Method and Results

We designed and produced recombinant fusion of the human  $\beta$ -globin chain, linked to the TAT peptide (the most widely used PTD) after transformation of bacterial *E. coli* cells. Produced 10xHis-XaSITE-TAT- $\beta$ -globin-HA was harvested from IPTG-induced bacteria in the form of inclusion bodies (IBs) and solubilized in 1 M L-Arginine solution. Solubilized IBs, enriched in 10xHis-XaSITE-TAT- $\beta$ -globin-HA were characterized by western blotting with anti-hemoglobin beta.IgG and anti-HA.IgG antibodies as well as LC-MS/MS analytical technology. IBs were also subjected to 10xHis-XaSITE-TAT- $\beta$ -globin-HA's stability testing, prior to transduction experiments into K-562 cells, lacking the human  $\beta$ -globin chain. The produced human recombinant TAT- $\beta$ -globin has been stable for long time in storage conditions. The transduction was studied in a time- and concentration- dependent manner. Analysis of the extracted lysates derived from transduced K-562 cells confirmed the transduction of recombinant stable fused human TAT- $\beta$ -globin chain. Bioinformatic analysis of possible complexation of human recombinant TAT- $\beta$ -globin with human  $\alpha$ -globin chain suggested that this possibility can occur in silico via best fit. Therefore, additional experiments are underway to demonstrate whether the transduced fused human TAT- $\beta$ -globin forms stable  $\alpha_2$ (TAT- $\beta$ -globin) $_2$ -like tetramer in control and hemin-treated K-562 cells.

### Conclusion

These findings indicate for the first time that fused human recombinant TAT- $\beta$ -globin can be transduced successfully into proerythroid cells, unable to synthesize  $\beta$ -globin chain, suggesting that such a protein approach can be applicable in erythroid related disorders, like human  $\beta$ -thalassemias.



## **Title: The use of mobile applications for distance learning in patients with Beta Thalassemia**

**Abstract Category:** New Advances in Treatment

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### **ABSTRACT**

#### **Objective**

Thalassemia is an inherited hemoglobin disorder that involve patients permanently. Education has a great impact on patients' self-management. The purpose of this study was assessment of effect of distance learning on increasing beta thalassemia patients' knowledge.

#### **Methods**

A before-after cross-sectional study with a simple randomized Sampling has been conducted on 166 thalassemia patients, 125 transfusion dependent (TDT) and 41 non-transfusion dependent (NTDT). Pre-test was done through sending e-questionnaire (included demographic information and 20 basic questions about thalassemia) by social networking applications such as "Telegram" and "WhatsApp". Then, the brief educational texts about thalassemia were sent through the same way and after 10 days post-test was conducted. Data were analyzed using independent samples t-test, spearman's correlation and paired samples t-test.

#### **Results**

Among 166 thalassemia patients who had received the questionnaire, 68 patients (%40.96) answered both pre-test and post-test (NTDT: 19 and TDT: 49) and 105 patients (%63.25) just answered the pre-test (NTDT: 23 and TDT: 82). Patients had a mean age of  $30.2 \pm 5.9$  years totally, (NTDT:  $32.7 \pm 7.7$  and TDT:  $29.6 \pm 5.5$ ), 61.2% were college educated (NTDT: 57.1% and TDT: 63.4%). serum ferritin was 1680 in average (NTDT: 1338 and TDT: 1864). Average of pre-test scores was significantly higher than post-test scores. Although younger (under 30 years old) and TDT patients had better knowledge totally, average of scores in both age and thalassemia type groups were similarly 2 score higher in post-test. The patients who use Deferoxamine and deferasirox had significant higher post-test scores (P. value<0.05). Despite college educated had better knowledge at the beginning of the study, statistical significant knowledge increasing in low educated patients were more remarkable. There was no remarkable correlation between serum ferritin level and level of education in patients. (P. value>0.05). Finally, the highest increase in patient's knowledge was related to information about the amount of iron in each blood bag (44% raise) and extramedullary hematopoietic masses (37% raise).

#### **Conclusion**

Using distance education in all subgroups of beta thalassemia patients had fairly benefits. Since nowadays such educational methods are chipper and more available than traditional methods, it is highly recommended to use them with wider spread.

**Keywords:** distance learning, Beta-thalassemia, applications



**Title: Effect of Hydroxyurea on Spermatogenesis in Egyptian Patients with Thalassemia Intermedia**

**Abstract Category:** Non-transfusion Dependent Thalassemia

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## ABSTRACT

### Background

Hydroxyurea frequently used in thalassemia intermedia patients might have effect on spermatogenesis. Aim of the Work: Assessment of the effect of hydroxyurea treatment in patients with thalassemia intermedia on sperm parameters and its reversibility on discontinuation of HU.

### Patients and Methods

Twenty fully pubertal patients with thalassemia intermedia regularly followed at Ain Shams University Thalassemia center; willing to join the study and after informed consent had been taken were recruited. They were two groups [1:1] as regard receiving HU for more than one year or not and they subjected to full clinical assessment. Sperm parameters (number, abnormal forms, motility and forward progression), were performed at enrollment and reassessment after six months after stopping HU treatment.

### Results

Eleven patients receiving HU had statistically significant lower parameters of sperm count in comparison to those not receiving HU. Six months off HU therapy, there was statistically significant improvement in all sperm parameters. There were statistically significant relations between total sperm count and HU dose, compliance and duration of therapy.

### Conclusion

HU was hazardous as regards all sperm parameters in the studied B-thalassemia intermedia; this effect was reversible and counselling should be taken with pubertal male patients on the hazards of HU on fertility with close follow-up.



## Title: **Clinical Features and Morbidities of Hb H disease in Taiwan**

**Abstract Category:** Non-transfusion Dependent Thalassaemia

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## ABSTRACT

Patients with non-transfusion-dependent thalassemia experience a wide array of clinical complications despite their independence from frequent, regular red blood cell transfusions. They have the higher incidence of osteoporosis, extramedullary hematopoiesis (EMH), hypogonadism, cholelithiasis, thromboembolic disease, pulmonary hypertension, silent cerebral ischemia, and leg ulcers. Thalassemia is highly prevalent in Taiwan and Hb H disease is predominant. But limited data are available about clinical features and morbidities. Here, we studied clinical features and morbidities in Taiwanese patients with Hb H disease.

We collected 90 patients with Hb H disease in three hospitals since 2014 Nov till 2016 July. Male to female were 43/59. The mean age was 33.1 years ( from 0.5 to 92.3 years). Two cases died of pulmonary hypertension and old age at 31 years old and 87 years old. Alfa-globin gene genotype studies were done in 44 cases. The (--(SEA)) type of  $\alpha(0)$ -thalassemia mutation was detected in all patients. Twenty- four (57.1%) cases were deletional ( $\alpha(3.7)/\alpha(4.2)$ /unknown 19/4/1) and 20 (42.9%) were nondeletional (CS/RS 18/2) type. The mean of Hemoglobin (Hb) and serum ferritin level were 8.7 g/dL and 730 ng/mL. We also revealed the positive correlation between age and serum ferritin level. The liver iron concentration (LIC) were 6.694 mg Fe/g dw (n=35). The Hb, ferritin and LIC level were not different between deletional and non- deletional groups. They received the transfusion management : 1 with regular transfusion  $\leq$  6 weeks interval, 5 with irregular transfusion  $\geq$  6 weeks interval, 27 with occasional transfusion and 57 without transfusion. Fifteen cases received splenectomy. There were significantly higher prevalence for transfusion frequency and splenectomy in non-deletional group. The prevalence of morbidities were 16/79 for cholelithiasis, 12/90 for thromboembolic event, 4/90 for heart failure symptoms ( 2 for pulmonary hypertension), 5/90 for arrhythmia, 3/90 for bone fracture, 5/20 for osteoporosis and 0 for renal stone. There were non-significantly higher prevalence for morbidities in non-deletional group.

The study provides the clinical features and the prevalence of morbidities in Hb H disease in Taiwan. Surprisingly, the prevalence of thromboembolic event and pulmonary hypertension are overlooked in our routine Hb H disease care. We need to schedule close and careful clinical follow up of Hb H patients as they get older, they get some morbidities or they are non-deletional genotype.

## **Title: The Impact of Liver Steatosis on the Ability of Serum Ferritin Levels to Predict Liver Iron Concentration Among Non-Transfusion-Dependent Thalassaemia Patients: A Cross-Sectional Evaluation**

**Abstract Category:** Non-transfusion Dependent Thalassaemia

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## **ABSTRACT**

### **Background**

Fatty liver is a common abnormality encountered in western countries among patients undergoing imaging of the abdomen and is associated to systemic inflammation and to increased ferritin levels, frequently unrelated to iron overload. We analyzed the impact of the presence of fatty liver in the parameters of iron overload among our patients with Non Transfusion dependent Thalassaemia (NTDT).

### **Methods**

111 patients with NTDT were cross-sectionally evaluated; the diagnosis of liver steatosis was ultrasound-based (US). Liver iron concentration (LIC) measurements were available for 64 patients who underwent a magnetic resonance Imaging (MRI) scan within the Myocardial Iron Overload in Thalassaemia (MIOT) network.

### **Results**

Liver steatosis was frequently (35.5%) encountered among our patients with NTDT and was significantly more prevalent in males with respect to females (49.0% vs 24.6%,  $p=0.008$ ). Patients with liver steatosis had significantly higher levels of alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), ALT/AST ratio, and ferritin than those without, but LIC values were comparable.

At ROC curve analysis, a ALT/AST ratio  $>0.89$  predicted the presence of liver steatosis with a sensitivity=0.872 and a specificity=0.901 ( $P<0.0001$ ).

Overall, ferritin levels positively correlated with LIC values ( $R=0.558$ ,  $P<0.0001$ ) but in patients without steatosis there was a strong relationship between ferritin and LIC values ( $R=0.656$ ,  $P<0.0001$ ) while in patients with steatosis the correlation was moderate ( $R=0.426$ ,  $P=0.05$ ).

### **Conclusion**

Our data show that liver steatosis affected also patients with NTDT and should be suspected in presence of a ALT/AST ratio  $>0.89$ . Recently, serum ferritin thresholds to predict clinically relevant liver iron concentrations for guiding chelation therapy when MRI is unavailable in patients with NTDT have been provided. The presence of liver steatosis may lead to overestimate the magnitude of iron burden and may be responsible for anticipating or exceeding chelation treatment in patients with NTDT in absence of a LIC evaluation.



## **Title: MRI Prospective Survey on Cardiac Iron and Function and on Hepatic Iron in Non Transfusion-Dependent Thalassemia Intermedia Patients Treated with Desferrioxamine or Non Chelated**

**Abstract Category:** Non-transfusion Dependent Thalassaemia

**Authors:** Antonella Meloni<sup>1</sup>, Maria Rita Gamberini<sup>2</sup>, Laura Pistoia<sup>1</sup>, Maria Grazia Bisconte<sup>3</sup>, Teodosio Grippo<sup>4</sup>, Giovanni Palazzi<sup>5</sup>, Nicola Romano<sup>6</sup>, Anna Pietrapertosa<sup>7</sup>, Leonardo Sardella<sup>8</sup>, Paolo Preziosi<sup>9</sup>, Vincenzo Positano<sup>1</sup>, Alessia Pepe<sup>1</sup>

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## **ABSTRACT**

### **Background**

Our study aimed to prospectively assess by quantitative Magnetic Resonance imaging (MRI) the efficacy of Desferrioxamine (DFO) and its advantages with respect to the absence of chelation therapy in non transfusion-dependent (NTD) thalassemia intermedia (TI) patients.

### **Methods**

Among the 185 TI patients enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) network and with a MRI follow-up study at 18±3 months, we selected 65 NTD patients. Iron overload was assessed by the multiecho T2\* technique. Biventricular function parameters were quantified by cine sequences. Liver T2\* values were converted into liver iron concentration (LIC) values.

### **Results**

We considered 18 patients who have not received any chelation therapy (50% males; 37.83±14.29 years) and 33 patients who had received DFO alone between the two MRI scans (51.5% males; 38.85±7.83 years). The two groups were comparable for age, sex and baseline MRI data.

No patient treated with DFO had cardiac iron. At baseline only one non-chelated patient showed a pathological global heart T2\* value (<20 ms) and he recovered at the FU. The percentage of patients who maintained a normal global heart T2\* value was 100% in both groups. A significant increase in the right ventricular ejection fraction was detected in DFO patients (-3.48±7.22%; P=0.024). The changes in cardiac T2\* values and in the global systolic biventricular function were not significantly different between the two groups.

In patients with hepatic iron at baseline (MRI LIC ≥3 mg/g/dw), the reduction in MRI LIC values was significant only in the DFO group (-2.20±4.84 mg/g/dw; P=0.050). The decrease in MRI LIC values was comparable between the groups (P=0.155).

### **Conclusions**

In this small population of sporadically or non transfused TI patients, DFO therapy showed no advantage in terms of cardiac iron but its administration allowed and improvement in right ventricular function and hepatic iron overload.

## Title: **Psychometric Properties of a Patient-Reported Outcomes Symptom Measure for Patients with Non-Transfusion-Dependent Thassaemia (NTDT-PRO<sup>©</sup>)**

**Abstract Category:** Non-transfusion Dependent Thassaemia

**Authors:** Ali Taher<sup>1</sup>, M. Domenica Cappellini<sup>2</sup>, Vip Viprakasit<sup>3</sup>, Pranee Sutcharitchan<sup>4</sup>, Dalia Mahmoud<sup>5</sup>, Abderrahmane Laadem<sup>5</sup>, Anzalee Khan<sup>6</sup>, Chad Gwaltney<sup>7</sup>, Gale Harding<sup>8</sup>, Kenneth Attie<sup>9</sup>, Xiaosha Zhang<sup>9</sup>, Jun Zou<sup>5</sup>, Joseph Pariseau<sup>5</sup>, X. Henry Hu<sup>5</sup>, Antonis Kattamis<sup>10</sup>

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## **ABSTRACT**

### **Background**

NTDT-PRO<sup>©</sup> is a disease-specific patient-reported outcomes (PRO) instrument to assess symptoms experienced by non-transfusion-dependent thalassaemia (NTDT) patients; it was developed in accordance with US FDA PRO development guidelines. It measures presence and severity of tiredness (T), weakness (W), and shortness of breath (SoB) both during physical activity and at rest. The items are grouped into two domains: T/W and SoB. We report its measurement properties regarding symptom distribution characteristics, reliability, and validity.

### **Method**

NTDT patients were enrolled in a prospective observational study. All patients completed NTDT-PRO<sup>©</sup> daily and the SF-36v2 and FACT-An questionnaires at baseline and every 3 weeks. Data from the first 12-weeks were included in this analysis. Cronbach's alpha statistics were analysed for internal consistency. Test-retest reliability was assessed by intraclass correlation coefficient (ICC) in patients who reported "no change" on their overall  $\beta$ -thalassaemia symptoms at 3-week follow-up. Convergent validity was evaluated by Pearson correlation coefficient of the NTDT-PRO<sup>©</sup> domain scores with SF-36v2 and the fatigue subscale (FACIT-F) of FACT-An.

### **Results**

Fifty NTDT patients were enrolled; mean age 32.9 years and 36 patients were female. At baseline, positive correlations ( $\geq 0.41$ ) for all paired symptoms were observed. The correlation coefficients between symptoms and domains ranged from 0.62 to 0.85. Cronbach's alpha statistics were 0.91 and 0.73, and ICCs were 0.90 and 0.92 for T/W and SoB domains, respectively. As expected, all SF-36v2 subscales had negative correlations with T/W and SoB at both 3-week and 12-week follow-ups, and the vitality subscale showed the highest corrections ( $-0.72$  and  $-0.56$ ;  $-0.77$  and  $-0.66$ , respectively). Similarly, FACIT-F had negative correlations with T/W and SoB domain scores at both follow-ups ( $-0.74$  and  $-0.61$ ;  $-0.80$  and  $-0.55$ ).

### **Conclusion**

NTDT-PRO<sup>©</sup> is a reliable and valid instrument. Additional validation on sensitivity to change and assessment of what constitutes meaningful change in clinical trial setting is ongoing.

**Title: Thalassaemia Prevention Program in Azerbaijan (Preliminary Report)****Abstract Category:** Prevention**Authors:** Chingiz Asadov, Zohra Alimirzoeva, Tahira Mammadova, Eldar Abdulalimov, Gunay Aliyeva, Aysel Mikayilzadeh**Presenting Author:** Gunay Aliyeva**Affiliation:** Institute of Haematology and Transfusiology, Baku, Azerbaijan**Email:** asadovchingiz@gmail.com

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**ABSTRACT****Background**

Azerbaijan is an endemic region for thalassaemias and it has been a serious public health problem for a long time. After approval of the regulations "On public care for patients suffering from hereditary blood diseases with haemophilia and thalassaemia" in 2006, the state program on the treatment and prevention of thalassaemia provided adequate provision of these patients with safe blood products and iron chelators, and haemopoietic stem cell transplantation was introduced as the only available curative option. In June 2015, the Cabinet of Ministers of the Republic of Azerbaijan decided the approval of the national thalassaemia prevention program, which includes the initiation of a mandatory premarital screening across the whole country alongside with the implication of public awareness campaign, genetic counselling and prenatal diagnosis.

**Methods**

The mandatory premarital screening for  $\beta$ -thalassaemia was carried out by generally accepted methods including the determination of erythrocyte indices via automated analysers, and haemoglobin fractions by capillary electrophoresis. Prenatal diagnosis was implemented through amniocentesis or chorionic villus sampling followed by molecular analysis via ARMS or RDB hybridisation techniques.

**Results**

By the date of April 2017, 11215 of 258521 individuals applying for a marriage certificate have been identified as carriers of  $\beta$ -thalassaemia. In 95 couples, both partners were identified as carriers and all were directed to the genetic counselling. 5 couples decided the cancellation of marriage. Pregnancy occurred in 44 couples; prenatal diagnosis was cancelled in 8 of them due to the rejection or the gynaecological contraindication of the procedure. 5 fetuses were identified as homozygous/compound-heterozygous, 18 as heterozygous and 4 as healthy. All homozygous/compound-heterozygous pregnancies were terminated. The rest of the couples with ongoing pregnancies are at the initial gestational stage and currently waiting for the appropriate week.

**Conclusion**

The national thalassaemia prevention program is currently being successfully implemented in Azerbaijan.



**Title: Role Of Prenatal Diagnosis in Thalassemia Prevention-an Experience at Punjab Thalassemia Prevention Program (PTPP), Pakistan**

**Abstract Category:** Prevention

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## **ABSTRACT**

### **Aims**

To study the experience of providing facility of Prenatal Diagnosis (PND )and termination of pregnancy (TOP) to at risk couples through PTPP.

### **Background**

Pakistan has 5 % carrier frequency of beta thalassemia and about 6000 children are born annually with thalassemia major. Huge and increasing disease prevalence poses an immense burden on health care services of Pakistan .Programs offering population screening, both prospective and retrospective, and prenatal diagnosis of at risk couples are considered a viable options for disease reduction.

### **Material and Methods**

The retrospective study was carried out to find the outcome of 1869 prenatal diagnosis that were performed from 2012-2016 at PTPP. After genetic counseling, ultrasound guided trans-abdominal chorionic villus sampling was done at 11-15 weeks of gestation. Mutation analysis was carried out by ARMS PCR method.

### **Results**

Maternal age ranged from 17-43 years. 12 CVS done in first pregnancy because of known family history and both were carrier. Rest opted for CVS, had one or more children with beta thalassemia major .Consanguinity accounts for 86 % . DNA analysis revealed 456 fetuses unaffected, 899 heterozygous and 514 thalassemia major.16 mutations were most frequent. The 6 most common mutations found were Fr 8-9, IVS 1-5, Fr 41-42, Cd 5, Cd 30 and Cd 15(90 % of total). The less common mutations were IVS I-I, Del 619, Fr 16, Cap 1+, IVS II-I and 2 rare mutations(Cd 48,-527-T+ATA).The miscarriage rate was 0.75 % due to the procedure. TOP done in 498 affected pregnancies. Refusal in 16 due to family pressures, pregnancy beyond 120 days, and 2 due to twin pregnancy in which other fetus was unaffected.

### **Conclusion**

The study has found acceptability for prenatal diagnosis in families at risk for beta thalassemia major children. TOP is generally carried out in most of the cases.



**Title: The Prevalence of Thalassemia and Inherited hemoglobin disorders in Albania (Tirana area 2015-2017)**

**Abstract Category:** Prevention

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## ABSTRACT

Thalassemia and Hemoglobin disorders are recognized as one of the most common inherited diseases worldwide. Detecting and characterizing variant hemoglobins and thalassemias depends primarily on clinical laboratory methods, but also in patients information about this examination. The aim of this study is to determine the prevalence of thalassemia and hemoglobin disorders in Tirana's population 2015-2017, to start up a prevention mandatory program. CE electrophoresis (acetat cellulose Mini Lite) were used for the detection and confirmation of thalassemia and hemoglobin variant. We include in the study 1383 patients males and females tested occasionally in Genius diagnostics laboratory medicine in Tirana in the last two years. 152 cases were diagnosed with thalassemia or hemoglobin disorders. What we notice most is that the origin of the patients was from different part of Albania because of the migration. We found (5.78%) cases from Tirana, (26.3%) from Fieri, (29.60%) from Lushnja, (15.3%) from Kavaja, (3.28%) from Berat, (3.28%) from Vlora, (3.94%) from Elbasan and (2.63%) from Durrës. 103 were females (67.73%) and 49 (32.23%) were males 0-38 years old. We have found a considerable % of thalassemia minor which is more frequently, 112 patients (73.68%), 4 patients with thalassemia major (2.63%), 26 patients with heterozygous drepanocytosis (17.0%), 3 patients with thalasso - drepanocytosis (1.97%), 3 patients with Hgb Lepore (1.97%), 4 patients with delta - beta thalassemia (2.63%). In total the % of sickle cell disease was (9.07%), so 29 patients. The outcomes let us understand the importance and necessity of Pre-Conception Screening and including hemoglobin electrophoresis as a mandatory screening in new couples (premarital group) to prevent, establishing equal access to quality health.

**Keywords:** hemoglobin; hemoglobinopathies, prevention, thalassemia

**Title: A Study of Knowledge, Attitudes and Practices Related to Thalassemia among the Palestinian University Students**

**Abstract Category:** Prevention

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## ABSTRACT

The study aimed to identify the degree of knowledge, attitudes and practices related to thalassemia among Palestinian university students in the northern governorates of Palestine. 520 students randomly selected to respond to a questionnaire consisting of (24) items, which was verified for its validity and stability. In addition, a focus group discussion with 20 students was conducted to identify their scientific competencies in the targeted questions.

The results showed that the degree of knowledge, attitudes and practices related to thalassemia among Palestinian university students was with a medium degree. There are significant differences in the degree of knowledge of thalassemia according to gender and specialization.

There are differences between the averages for the degree of students' attitudes and practices related to thalassemia according to gender variable and for males, while there are no differences between the averages according to the specialization variable, the school year and the place of residence.

Based on the findings we can conclude health education targeting university students did not give the issues of interaction between science, technology and society appropriate consideration that might enable students to acquire the needed competencies for life.

The study recommended increasing awareness of Thalassemia and promoting the positive attitudes towards Thalassemia patients and genetic trait holders through interactive educational programs in context.

**Keywords:** Thalassemia, Knowledge, Attitudes and Practices, University Students, Palestine

**Title: Punjab Thalassaemia Prevention Programme****Abstract Category:** Prevention**Authors:** Hussain Jafri**Presenting Author:** Hussain Jafri**Affiliation:** Punjab Thalassaemia Prevention Programme**Email:** hussain1@hotmail.com**Address:**

Hussain Jafri

2<sup>nd</sup> Floor, New Emergency Building, Sir Ganga Ram Hospital, Lahore, Pakistan.**ABSTRACT****Background**

Beta-thalassaemia is the most common, inherited disorder in Pakistan with a carrier prevalence rate of around 5.3%. There is a cultural tradition of consanguineous marriages and there are more than 6000 affected births annually, meaning 17 affected births per day. The majority of Thalassaemics do not get optimal treatment facilities; therefore, the only hope lies in adopting a preventive program on the lines pursued by countries like Cyprus, Turkey and Iran. Punjab is the largest province of Pakistan with a population of around 110 million people. Punjab Thalassaemia Prevention Program (PTPP) was initiated by the Government of the Punjab in 2010 that is working towards providing comprehensive Thalassaemia prevention services in the province.

**Method** The PTPP is operational in all 36 districts of Punjab and is providing comprehensive prevention services that include awareness, extended family screening, pre-marital screening, genetic counseling, pre-natal diagnosis, trainings and research. The first DNA lab in public sector providing free prenatal diagnoses of thalassaemia has also been established.

**Results** The PTPP has created mass awareness through electronic and print media. Furthermore, 2356 small scale events and 74 major seminars have also been organized all over the province. The project's main focus has been on the extended family screening and so far more than 100,000 people have been screened and results show a carrier frequency of 33% in such families. Moreover, more than 20,000 premarital screenings of young prospective couples have also been conducted. A total of 2,094 prenatal diagnosis tests have been performed, out of which 576 Thalassaemia Major fetuses identified and terminated.

**Conclusion** The PTPP has been extremely successful programme due to which the Government has decided to convert this project into a permanent service through the establishment of Punjab Thalassaemia Prevention Authority. Moreover, the Government has also decided to enact a law on mandatory premarital Thalassaemia screening in Punjab.



**Title: Estimating Prevalence of Thalassemia Trait in Himachal Pradesh, India through PPS sampling of marriageable age college students**

**Abstract Category:** Prevention

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## **ABSTRACT**

### **Background**

Thalassemia has never been a priority with the state government of Himachal Pradesh due to popular belief that it runs along "Lahore- Gujarat-Punjab" belt in India. Therefore no thalassemia testing facility is currently available even in medical colleges of the state. No study has ever been done to assess the magnitude of genetic disorders in the state.

### **Methods**

The authors realized the need for sensitizing the Himachal Government over the issue and formulated a project proposal that was sanctioned from the National Rural Health Mission (NRHM). All the colleges including private ones were line listed and a random number was selected and a list of colleges that fall in 20 clusters was selected. In each college selected students having an age of 18-25 were asked to pick slips for inclusion or exclusion and those included were tested for HPLC. No one was denied the right for test even if our sample size increase and only first 111 sample were included as per sample size.

### **Results**

A total of 2469 students volunteered against the requirement for 2220 students. Since a student having HPLC value of HBA2 as 3.7 was found to have a mutation G>C and was include and was made as cut off as against the accepted norm of 3.5, the overall prevalence rate was found to be 1.76 % that translates to a whopping 1,23,000 for population of 70, 00000.

### **Conclusion**

There has been a spillover of genetic disorders from the Punjab belt to neighbouring areas and we need to check this by having facility of HPLC machines in at least medical colleges and need massive awareness campaigns to make aware general population to the threat of thalassemias.



**Title: Attitudes towards non-invasive prenatal diagnosis among obstetricians in Pakistan, a developing, Islamic country**

**Abstract Category:** Prevention

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## ABSTRACT

### Background

Non-invasive prenatal testing (NIPT) utilising cell-free fetal DNA (cfDNA) in maternal plasma can be used to test for fetal trisomies and some other conditions. Advances in NIPT technologies result in a rapidly expanding range of testable conditions and it is anticipated that NIPT for Thalassaemia shall also be available in the future. The simplicity, safety, accuracy and availability of NIPT early in pregnancy raise a number of ethical and social concerns. Doctors are now introducing NIPT into private prenatal health care in Pakistan, where there is a lack of research on ethical and social concerns of NIPT to inform implementation. Stakeholders views are essential for informing implementation strategies for NIPT. We explored attitudes towards NIPT among obstetricians in Pakistan.

### Method

A 35-item questionnaire was distributed and collected at eight events (a national conference and seven workshops in five cities) for obstetric professionals on advances in fetal medicine.

### Result

Responses from 113 obstetrician show positive attitudes towards implementation of NIPT: 95% agreed prevention of genetic conditions was a necessity, and 97% agreed public hospitals should provide prenatal screening tests. However, participants also agreed the availability of NIPT would increase social pressure on women to have prenatal screening tests and to terminate an affected pregnancy (53% and 63%, respectively). Most participants would not offer NIPT for sex determination (55%), although 31% would. The most valued aspects of NIPT were its safety, followed by its utility and then accuracy.

### Conclusion

Participants generally supported the implementation of NIPT but raised concerns about social implications. Therefore, national policy is needed to regulate the implementation of NIPT, and pretest information and post-test genetic counselling are needed to mitigate social pressure and support parents to make informed decisions.

**Title: Red blood cell indices and HbA2 level evaluation in parents of patients suffered from Thalassemia Major**

**Abstract Category:** Prevention

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## **ABSTRACT**

### **Background and objectives**

Thalassemia is one of the most common and challenging disease in our country, especially in north of Iran. For preventing birth of major betha-thalassemia patients in our country, the before birth screening design is performed by hygiene systems but in some cases the couples have normal RBC indexes and HbA2 is observed but the result of this marriage is to give birth to a child affecting major-thalassemia.

This study is performed to find the frequency of natural RBC indexes and/or HbA2 in parents of thalassemic patients referring to Amirkola Thalassemia center.

### **Materials and methods**

Parents of 300 patients undertaking treatment of blood transfusion from Amirkola Thalassemia center were studied and MCV, MCH and HbA2 were measured. For those who had normal HbA2, serum Ferritin level was checked to distinguish from those who had combination of minor Thalassemia with iron deficiency.

The serum Ferritin level was checked and in case of low Ferritin, the iron combination was prescribed. After the end of treatment, HbA2 was checked again and the results were collected and after entering the computer, were analyzed.

### **Discussion**

In this study 7 cases [3 men and 4 women] had normal HbA2 and 5 ones (1.7%) [1 man and 4 women] had normal MCV and 4 cases (1.3%) [1 man and 3 women] had normal MCH while a woman (0.3%) had normal MCV, MCH and HbA2.

### **Results**

The result of this studied showed that 7 cases of major Thalassemia children's parents didn't have diagnostic indexes according to hygiene systems and it shows that screening tests before marriage does not role out minor Thalassemia (Heterozygote) and further studies in this field is recommended to find the real frequency of those Thalassemia gene carriers with normal laboratory tests presentation (including RBC indexes and/or HbA2) and also it is necessary to determine the type of mutation of these patients with genetic studies.

**Keywords:** MCV, MCH, HbA2, Thalassemia screening before marriag



## **Title: Efficacy of Thalassemia and Sickle Cell Disease Prevention in Northern Greece: 15 Year Experience, Practice and Policy Gaps for Natives and Migrants**

**Abstract Category:** Prevention

**Authors:** S.Theodoridou, A.Ballasopoulou, A.Teli, M.Economou, D.Adamidou, E.Vlachaki, T-A.Vyzantiadis, D-A. Giannakopoulou, O.Karakasidou, E.Skatharoudi, E.Voskaridou.

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### **ABSTRACT**

Haemoglobinopathies, constitute the most frequent monogenic disorders worldwide and in Greece. The spectrum of mutations is influenced by the number of immigrants who have settled down in Greece the last two decades.

We report the results of the implementation of the prevention program in Northern Greece, over a 15-year period (2001-2015).

The first line screening methodology tests of identifying the carriers of the abnormal genes and the couples at risk are simple and similar all over the prevention units of the country. Couples identified as being at risk, are also given genetic counseling and prenatal diagnosis is offered. Both DNA analysis and in selected cases haemoglobin biosynthesis is performed in the National Thalassemia Centre. 33.837 subjects were screened individually or as couples in our Thalassemia Prevention Unit. 3659 were couples that both partners carried the abnormal genes. 91% of those were natives, while 9% were immigrants.

We had 1598 pregnancies among these couples. In 371 couples, both partners carried an abnormal haemoglobin gene and genetic counselling was offered. The remaining 42 pregnancies involved couples who were doubly heterozygous for mutations that do not cause severe clinical disease and were exempted from prenatal diagnosis.

In 13 pregnancies there was a positive family history and the prevention was retrospective. The retrospective prevention represents the 2.95% of the total native couples at risk and the 18.5% of the total immigrant couples. All the rest pregnancies at risk were identified through pre-conceptual screening.

Except the Greek couples that had the prenatal diagnosis, there were 3 couples of Muslim Minority of west Thrace, 1 Gypsy couple permanently situated in our region, and 14 immigrant couples that had had 27 prenatal diagnosis. The immigrants used efficiently the public health sector even though most of them did not speak the Greek language and no translated leaflets are available



**Title: New Challenges in the Prevention of Haemoglobinopathies Due to the Impact of Foreign-Born Residents in Cyprus**

**Abstract Category:** Prevention

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## ABSTRACT

Haemoglobinopathies are the most common monogenic diseases in the world. The impact of immigration has resulted in an increase in the incidence of thalassaemia in Europe. The Community Screening Laboratory for Thalassaemia and other Haemoglobinopathies in Cyprus has completed 40 years of preventive services to the Cyprus population. Over the last 7 years we have been faced with new challenges due to the increase of foreign-born residents and marriages among Cypriots and foreign-born and marriages among foreign-born couples. From 2010 to 2016 a total of 53,637 persons were examined. We identified 347 couples with the risk of  $\beta$ -thalassaemia. 327 couples were of Cypriot origin and 15 couples were of mixed marriage i.e Cypriot origin with foreign born persons mainly from both endemic and non-endemic countries like Syria, Jordan, Italy, Roumania, Bulgaria, Pakistan, Albania, France, Greece, Congo, and Thailand. Five foreign-born couples had the risk of having babies with  $\beta$ -thalassaemia. Seven couples had the risk of Haemoglobin S and  $\beta$ -thalassaemia.

This is a new development and the share of mixed marriage couples and exclusively foreigners' marriage couples accounts for 5,74%, or 1-5 cases per year of the total couples at risk. We present two case studies in order to demonstrate the current challenges with these new increasing type of couples. It seems that most of these couples are uninformed about the need for population screening and they simply come during pregnancy.

The major challenges for these couples at risk are:

- They are ignorant for the need of Thalassaemia screening
- There are difficulties in communication because of language barrier
- Religious and cultural barriers, and
- Inability to perform comprehensive family studies since parents live usually abroad.

Revising the national prevention program strategies to reduce such cases should be considered.



**Title: The Psychosocial Burden of Patients with Transfusion-dependent Beta-thalassaemia in Azerbaijan**

**Abstract Category:** Psycho-social Support

**Authors:** Chingiz Asadov<sup>1</sup>, Jeyhun Mammadov<sup>2</sup>

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## ABSTRACT

### Background

The objective of this study was to identify the psychosocial burden of children with transfusion-dependent beta-thalassaemia in Azerbaijan.

### Methods

Parents of 200 transfusion-dependent patients with beta-thalassaemia aged 5-16 years who were on treatment at the Republican Thalassaemia Centre in Baku were interviewed. The parents answered a structured questionnaire (developed by Ratip & Modell) on behalf of their children.

### Results

As a result of the survey, it was found that the psychosocial burden affected many aspects of life, such as education, leisure time, sports opportunities, difference from friends / siblings, social interactions, family adaptation, anxiety, isolation and stigmatization. The analysis of the results showed a significant relationship between socio-demographic characteristics, such as age, sex, school class, current education, work, family income and the occurrence of complications with variables of psychosocial load, including education, leisure time, sports opportunities and differences from friends, social interactions and stigmatization.

### Conclusion

The findings suggest the need for psychological support as well as medical help for thalassaemic families. Health professionals need to assess the psychological status of children with thalassaemia and that of their families in order to minimize these burdens.

**Title: An Insight Into Psychological Disorders Related To Thalassemia: A Foresee into Future****Abstract Category:** Psycho-social Support**Authors:** Tanzeel Imran, Humera Naz Altaf, Farid Baktiar.Rohina**Presenting Author:** Tanzeel Imran**Affiliation:** Pathologist, Jamila Sultana Foundation, Pakistan**Email:** dr\_tanzeel@yahoo.co.uk

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**ABSTRACT****Background**

Thalassemia is genetic disorder affecting all organs with tremendous impact on patient physical and psychological life. These psychosocial issues if not acknowledge and approached timely will have severe consequence not only on patient health but will effect family financial resources and national health budget allied for thalassemia wellbeing.

**Objectives**

To determine common physiological problems and help patients to adopt optimally to minimize their impact for improved quality of life .

**Material and Methods**

This case-control study was carried out in Jamila Sultana Foundation from January 2016 to February 2017 (NGO for thalassemia) studied 356 registered patients .Informed consent taken from minor parents and adult patients.Periodically all patients under went psychological review at different stages of disease starting from initial diagnosis to the transition period of adulthood including growing body growth, schooling experience and marriage affairs.

**Results**

We found serious mental health difficulties including depression, anxiety, panic attack, denial and social phobia the most frequent disorders with significant impact on patient behavior in all ages .Age allocation in our study population comprises 25% children, 33% in transition phase and 42% adults patients with females predominance 62%.Depression was the main psychological issue found in 100% of adult and transition age group patients while in children parents and psychiatrist identify anxiety 39% and panic attack 51%. However due to periodic sessions both with parents and patients themselves over 13 months these issues were minimized and improvement in psychological approach was appreciated by standard health questionnaire.

**Conclusions**

We found that by introducing counseling session for patients and there families as an integral part of treatment plan had great impact on patients well being. So it is highly recommended to establish protocols for developing countries to incorporate psychiatric consultation as an essential part of therapeutic modalities.

**Title: Transition Readiness in Thalassemia****Abstract Category:** Psycho-social Support**Authors:** Michelle Lahat**Presenting Author:** Michelle Lahat**Affiliation:** MSW, LCSW, Children's Hospital Los Angeles, USA**Email:** mlahat@chla.usc.edu

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**ABSTRACT****Background**

Due to advances in research and clinical care, life expectancy for Thalassemia patients has improved and patients are thriving into adulthood (Levine and Levine, 2010). In response to new challenges of transition from pediatric to adult medical care, the Thalassemia team at Children's Hospital Los Angeles has developed PASSAGES: A transition program serving as a bridge between pediatric and adult medical care. The program consists of a process to vet community adult providers, a nurse navigator to support patients through the process, and an education program (transition clinic) which is guided by a Transition Questionnaire (TQ) needs assessment survey.

**Methods**

Prior to the initial transition clinic visit, a 38-question survey is administered to each patient to determine knowledge of their disease, genetics, past medical history, and transition readiness. The survey is intended to guide the transition education provided by the interdisciplinary team. After the patient has attended three transition clinic appointments, the same survey will be administered again to determine efficacy of these educational interventions.

**Results**

Fourteen patients ranging in age from 17 to 21 years of age have completed the initial TQ to date. Initial TQ responses and face-to-face interactions with patients demonstrated that patients did not have sufficient understanding of insurance and very few had the knowledge to advocate for themselves in the adult medical system. Some patients also lacked understanding regarding their specific diagnosis and the reasons for the medications they are prescribed.

**Conclusion**

The PASSAGES transition program is designed to guide Thalassemia patients from pediatric to adult care. The education component addresses insurance, self-advocacy, and individualized transition preparation to address the gaps in knowledge demonstrated by the TQ responses. A standardized program combined with a focus on individual needs will provide Thalassemia patients the ability to successfully transition to adult care.

**Title: Ad hoc informative strategies as a crucial tool to empower children affected by haemoglobinopathies involved in a multinational clinical study**

**Abstract Category:** Psycho-social Support

**Authors:** Lucia Ruggieri<sup>1</sup>, Maria Cavallo<sup>2</sup>, Mariangela Lupo<sup>2</sup>, Ludovica Frizziero<sup>3</sup>, Maria Caterina Putti<sup>3</sup>, Lorella Pitrolo<sup>4</sup>, Floreta Kurti<sup>5</sup>, Eleni Nastas<sup>5</sup>, Manika Kreka<sup>5</sup>, Jorida Zogaj<sup>6</sup>, Ariana Zaka<sup>6</sup>, Donato Bonifazi<sup>2</sup>, Adriana Ceci<sup>1,2</sup> on behalf of the DEEP consortium.

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## ABSTRACT

### Background

The need to actively involve children in the decision-making process related to a clinical trial is part of the updating guideline 'Ethical considerations for clinical trials on medicinal products conducted with minors' prepared by the European Commission and the Paediatric Committee within the Regulation EU 536/2014. Unfortunately, available data and publications show that ad hoc strategies to inform minors to be enrolled in clinical trials are rarely produced. To empower minors in DEEP-2 Study (an efficacy and safety trial to compare deferiprone versus deferasirox in 388 paediatric patients aged 1 month- <18 years from Mediterranean area countries) age-tailored information booklets and assent forms have been prepared. Moreover, a study to investigate the quality, the comprehensibility and the likeability of the informative booklets for patients involved in the DEEP-2 trial has been performed (QuBo).

### Methods

3 informative booklets and 2 ad hoc assent forms were prepared for different ages in six languages thanks to a collaborative effort involving pharmacologists, paediatricians, child psychologists and illustrators, in an easy-to-manage format, a charming graphic including picture, a simple vocabulary and sentences structures. In the QuBo pilot study, two age-tailored questionnaires were distributed.

### Results

QuBo pilot study has been completed in Albania (at the UHCT and Lushnja centers, on 4 and 9 patients aged 6-10 and 11-18 yrs respectively) and in Italy with 5 patients in Padua centre (3 aged 6-10 and 2 aged 11-18 years) and 3 patients in Palermo centre (aged 11-18 years).

### Conclusion

The QuBo pilot study has demonstrated that the use of informative booklets in DEEP-2 trial has been appreciated by children and adolescents and has favoured the understanding and participation of children in the clinical trial. As general recommendation, it has highlighted the need to consider children and families' active participation as a fundamental step to reach consensus and compliance to treatments.

### Acknowledgements

The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7) under grant agreement no 261483 (DEferiprone Evaluation in Paediatrics, DEEP).



**Title: The Academic and Social Experiences of Students with Thalassemia in Mainstream School: A Narrative Study**

**Abstract Category:** Psycho-social Support

**Authors:** Natasha, Caecillia M.

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## **ABSTRACT**

### **Background**

Growing up with thalassemia makes many children with it do not be able to do their activities normally. One of the activities that will be affected very much is activity in school. Students with thalassemia tend to find many difficulties in school, especially in academic and social aspects. This study examined the experiences of Indonesian students with thalassemia in school related to academic and social in narrative way. The researcher of this study is a thalassemia survivor too.

### **Methods**

This study uses narrative research as the research approach to discover the challenges, strategies, and supports experienced by 4 students and former students with thalassemia during their school lives. The data was gotten within several steps, interviews, transcribing, and coding process.

### **Results**

The result shows that there are some challenges that faced by the students and former students with thalassemia which are managing time, maintaining academic performances, maintaining body conditions, maintaining activities, and bullying, however, they are already have and applied different kinds of strategies in order to meet the school requirements. The participants also get some supports from the school, teachers, and peers.

### **Conclusions**

Students and former students have different kinds of academic and social experiences during their school lives. They faced some challenges, but they already have their own strategies in order to meet the school requirements. They also get some supports from their school surroundings which are teachers and peers. There are some students and former students with thalassemia that has been successful too, socially and academically.

**Keywords:** thalassemia, academic, social, experiences, school, narrative.

**Title: Psychological Support in Thalassaemia****Abstract Category:** Psycho-social Support**Authors:** Chen Ting-Yu**Presenting Author:** Chen Ting-Yu**Affiliation:** Taiwan Thalassaemia Association**Email:** qgirl4858@gmail.com**ABSTRACT****Objectives**

Family members are the best support to patient with Thalassaemia physically and psychologically. To achieve it, the professionals from Taiwan Thalassaemia Association will help family members to understand symptoms and signs by observing and communicating with patient. Professionals will also provide the best way that the family members could provide psychological treatments.

Our patient: High and med risk Thalassaemia patient.

**Process**

1. Helped family members to understand Thalassaemia symptoms and ways to improve them. Improved communications between patients and families by understanding patient behaviors.
2. Improved family relationship by holding events letting patients and family members to share individual experiences. Provided success stories that could create positive psychological impacts to patients.
3. Enhanced self-confidence and teamwork by interacting more frequently and closely with other people.
4. Provide individual counseling in medical treatment, psychological health, socialization, financial aids, and government resources.
5. Provided self-management plans to improve treatment compliance and lower blood iron level.

**Results**

1. Held four 3-hour workshops with total of 72 patients attending.
2. Held four forums with total of 85 patients attending. Patients were highly involved and satisfied.
3. Created Thalassaemia club. Yoga professionals help patients to relax muscles and relieve stress with total of 18 hours.
4. Counseling services of 51 individual counseling and 399 psychological sessions. This service has successfully helps patients in career development and job search.
5. Self-management result. A total of 59 patients involved in the plan and 48 of them have controlled their Blood ferritin number and 2 of them even drop the Blood ferritin for more than 2,000ng/ml.

**Conclusion**

Our plan has help high-risk patients to improve their family relationship and their family members to enhance communication. The self-management tool helped patients to control the blood iron and decrease the impact of the symptoms. Counseling services helped patients to improve self-confidence, be more connected to the sociality, and leverage more resources. All these results show the success of the plan.



## Title: **Quality of Life Assessment in Thalassemia Patients and their Families Using DASS-42**

**Abstract Category:** Quality of Life

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## **ABSTRACT**

### **Background**

This study aimed at assessing quality of life issues in thalassemia patients and their families in Lahore, Pakistan.

### **Methods**

A cross-sectional survey was conducted in different transfusion centers in Lahore. The proforma comprised of questions on demographic/clinical characteristics and the DASS-42 scale. Informed consent was obtained from all respondents; for patients under 14 years of age, their relatives' responses were recorded instead.

### **Results**

Of a total 41 respondents, 16 (39%) were from Amina Bashir Memorial Trust, 13 (31.7%) from Sir Ganga Ram Hospital and 12 (29.3%) from Sundas Foundation. 22 (53.7%) were females. 25 (61%) respondents were patients whilst 16 (39%) were relatives (defined as 'respondent status').

Amongst patients, 21 (84%) had thalassemia major whilst 4 (16%) had thalassemia intermedia or NTDT. Cardiovascular morbidities were present in 3 (12%), diabetes mellitus in 2 (8%) and hepatitis in 11 (44.0%) of these patients. Of 22 patients who underwent iron chelation therapy, 8 (36.4%) used oral, 4 (18.2%) intravenous/subcutaneous and 10 (45.5%) both of aforementioned methods. Majority patients (90.9%) had good chelation therapy compliance, defined as adherence to doctor's recommended guidelines.

DASS-42 scores were transformed into ordinal categories based on the DASS manual (Normal = 'N', Mild = 'ML', Moderate = 'MD', Severe = 'S' and Very Severe = 'VS'). Females had higher average anxiety (S vs MD) and stress (MD vs ML) levels compared to males. Relatives had higher average anxiety (S vs MD) level compared to patients. With respect to transfusion centers, average scores ranged from N to ML for depression, MD to S for anxiety and were MD for stress.

### **Conclusion**

DASS-42 scores indicate considerable emotional distress amongst thalassemia patients and their families. Introduction of psychological counselling in tandem with conventional treatment would greatly help patients and families better cope with the intensive treatment schedules.

**Title: My Tears and Laughs Life with Thalassemia****Abstract Category:** Quality of Life**Authors:** Ming-Yuan Chang**Presenting Author:** Ming-Yuan Chang**Affiliation:****Email:** 104352019@nccu.edu.tw**Address:**

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**ABSTRACT**

I am Ming-Yuan, Chang coming from Taiwan. As a  $\beta$ -thalassemia patient since I was born, there have been so many daunting hurdles in my life path. In this submission I want to share my unique life experience different from others with people around the world. I have never ever done this before. To open my heart and talk to myself so closely, find who I am and recognize who I am, are so much important issues for all the thalassemia patient. Due to the reason that there might be bright side and dark side existing in the bottom of our deeply heart since we have fought for life and breathing for so many years.

The methods which I share my story would be divided into two parts. One is days of tears and the other one would be days of laughs. In days of tears I would talk and share the obstacles I met for approximately twenty-five years including the life with countless injections and drugs, my heart failure experience, and the pressure under thalassemia, even the student life whenever I must live a life with thalassemia. Conquering over the thalassemia has been the most important issue for so many years, and ever for the coming future of searching a job in our society. While in days of laughs, I would talk about some of my achievements. Here I was lucky that I met music when I was young. I then convinced my mom to let me learn how to play the flute and the piano. For the reason why my mom said yes was that she always hope me to forget my pain by the enjoyment of music. I have also been so thankful to the accompany of music.

Hope that each thalassemia patient has a super cool life.



## **Title: Subjective Well-Being; Life Satisfaction, Happiness and Optimism of People with Thalassemia in Aceh, Indonesia**

**Abstract Category:** Quality of Life

**Authors:** Farah Diba<sup>1</sup>, Ida Fitria<sup>2</sup>, Nurjannah Husien<sup>3</sup>

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### **ABSTRACT**

#### **Background**

According to World Health Organization, Indonesia has 6-10% carrier for thalassemia trait. Aceh, one of the provinces in Indonesia has 1,34% prevalence of people with thalassemia above the national number (0.1%). Thalassemia case in Aceh is considered new to the community, especially in rural areas. Like the iceberg phenomenon, there are approximately 350 regular registered people with thalassemia performing blood transfusions monthly to Zainoel Abidin Hospital, the only provincial reference General Hospital in Aceh, but many more undiagnosed patients out there. Thalassemia is a chronic disease that lasts a lifetime, so it is important to conduct this study aiming to measure how the Subjective Well-Being (SWB) of people with thalassemia in Aceh, focusing on 3 aspects: life satisfaction, happiness and optimism. This study will look at the Subjective Well-Being variations in three demographic aspects such as origin, family economic status and gender.

#### **Methods**

This study will describe how the Subjective Well-Being of people with Thalassemia using quantitative descriptive approach by giving SWB scale for thalassemia patients who are staying at the center of thalassemia, Zainoel Abidin Hospital within a period of one month. The respondent's criteria is adolescent age ranging 13-20 years old. In addition, this study will also conduct in-dept interviews for 6 people with thalassemia who are also in the same place.

#### **Expected Result**

The result is to describe on the three aspects of the Subjective Well-Being and describes the meaning of SWB qualitatively perceived by the person with thalassemia.

#### **Conclusion**

This research will contribute information about how people with thalassemia interpret happiness, satisfaction and life optimism. The study will also be a reference for the foundations and hospitals to provide the best services to thalassemia patients from all over Aceh. This research is a baseline research for further research on the topic of thalassemia in Aceh.

**Keywords:** Self Well-Being, Health, Thalassemia in Aceh



## **Title: Questionnaire Survey on the Opinions in Marriage and Reproductive Choices of People with Transfusion Dependent Thalassemia**

**Abstract Category:** Quality of Life

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### **ABSTRACT**

#### **Background**

In Iran, the largest population age of the people with transfusion dependent Thalassemia (PTDT) are in their reproductive age. Therefore, it is an urgent task to create a better support program for PTDT's marriage / reproductive life, and a basic study on their opinions in marriage and reproductive choices is needed.

#### **Methods**

Questionnaire survey of 113 married / single PTDT, who came to the Thalassemia Center in Seyed-al-Shoahad hospital in Isfahan, was conducted in 2016 and 2017.

#### **Results**

Among the 113 PTDT (mean age was 28 years old, 52 male and 61 female PTDT), 35 were married, 68 were single, 6 were engaged, and 4 were divorced or widowed. 31% of them had ever received hormone replacement therapy. 55.8% of them thought marriage is very important, while 38.9% of them answered that marriage is not very important or not important at all. 61.9% had ever fell in love with somebody. To the question 'which has a negative impact on your marriage choice?', 41.6% of them answered 'the symptoms and complications of Thalassemia', while 48.7% of them chose 'negative image of Thalassemia in the society'. 24.8% of them thought appearances of PTDT had a negative impact, and 24.8% chose employment discrimination. 37.2% of them had thought of getting married with PTDT partner, because they could understand each other's pain and situation better. At the same time, 60.2% of them had never thought of getting married with PTDT partner, because they did not want to add another PTDT to their family or they preferred having children with a healthy partner. 56.6% of them would like to receive treatments for infertility if they needed, but 22.1% of them would not.

#### **Conclusion**

Pre / post-marital educational programs should be created to let PTDT have various marriage and reproductive choices.



## **Title: The Effects of Thalassaemia Patients' Self-Monitoring and Management of Health**

**Abstract Category:** Quality of Life

**Authors:** Hsiu Min Huang, Ting Yu Chen, Kai Hsin Lin

**Presenting Author:** Hsiu Min Huang

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### **ABSTRACT**

#### **Background**

Thalassaemia major(TM) requires regular blood transfusions in a lifetime. Sufferers who are unable to comply with transfusions once every 2-4 weeks with daily iron chelating therapy easy risk of complications, such as heart failure, diabetes, osteoporosis etc. A tracking study of 88 TM patients who age more than ten shows 38.5% (33) patients, serum ferritin > 2,500 ng / ml; 38.6% (34) patients, cardiac T2 \*value <20 ms, showing that more than one third of patients' iron chelation therapy need to be strengthened (Lu et al., 2013). The aim of this study is to monitor the compliance rate of TM patients' blood transfusion and iron chelation therapy and follow-up data, such as hemoglobin and serum ferritin. Conduct a self-monitoring and management of health campaign activities. By encouraging, assisting and tracking to raise the compliance rate of their daily iron chelation therapy, urge the reduce of serum ferritin and the decrease of disease complications.

#### **Methods**

1. Design patients' health passports, including a disease overview, medical treatment, such as blood transfusion, examination data, such as ferritin, liver and kidney function, and records of daily iron chelation therapy. 2. Promote and encourage patients to record on the health passport. 3. The patients should fill in their passports. Also, they should bring the passports whenever they seek medical services. In order to keep the latest examination data and give a stamp of approval by the attending physicians. 4. Evaluate record of health passport and following criteria as below: (1) Take iron chelation therapy more than 90% in whole year. (2) Keep the hemoglobin level > 9.0gm%. (3) Maintain serum ferritin less than 2,000 ng / ml.

#### **Results**

1. There were 78, 56, 60 patients participating in this study from 2014-2016 respectively. 2. The hemoglobin level maintained an average of 8.0-11.8gm% per person. 3. Serum ferritin <1000ng / mL accounted for 43.3-55.4%, 1000-2000ng / mL for 35.7-39.8%; and >2000ng / mL for 7.8-20%. 4. There are a few, about 2-3 patients, serum ferritin up to 6000-8000ng / mL, even a patient whose serum ferritin up to 13000ng / mL in 2016 dropped to 8574ng / mL at the end of the year.

#### **Discussion**

High risk thalassaemia major patients need to have a continuous care of medical team. Provide them with physical, psychological and social assistance according to their individual needs. The Self-monitoring and Management of Health campaign activities showed good results which can serve as a reference for the medical team.



## **Title: Comparison of Quality of Life in Patients With $\beta$ -Thalassemia Intermedia And $\beta$ -Thalassemia Major In Southern Iran**

**Abstract Category:** Quality of Life

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### **ABSTRACT**

#### **Background**

Increased life expectancy in patients with  $\beta$ -thalassemia ( $\beta$ -thal) requires healthcare professionals to give greater attention to improving their quality of life (QoL). We aimed to evaluate health-related QoL (HRQoL) and its determinants in patients with  $\beta$ -thal intermedia ( $\beta$ -TI) compared with  $\beta$ -thal major ( $\beta$ -TM).

#### **Methods**

In this cross sectional study, 118 patients with  $\beta$ -TI, referred to the Thalassemia Clinic of Shiraz University of Medical Sciences, Shiraz, Iran, were investigated from January to June 2014 in southern Iran. A Short Form-36 (SF36) questionnaire was used. We had previously conducted a similar study in 101 patients with  $\beta$ -TM (12 to 38 years). Compared data of the two studies were analyzed.

#### **Results**

Mean age was  $26.5 \pm 6.5$  (12 to 48) years in  $\beta$ -TI and  $19.5 \pm 4.4$  (12-38) years in the  $\beta$ -TM group. The best scales of HRQoL were physical functioning (PF) ( $76.8 \pm 26.6$ ) and bodily pain (BP) ( $70.1 \pm 24.8$ ) in the  $\beta$ -TI group. Males had significantly better score only in vitality dimension compared to females ( $p = 0.020$ ). Higher education ( $p = 0.023$ ) in univariate analysis and age  $\leq 20$  years (B coefficient = 13,  $p = 0.008$ ) in multivariate analysis showed significant relationships with higher total HRQoL score in  $\beta$ -TI. Comparison of  $\beta$ -TI and  $\beta$ -TM, after adjusting for covariates, total HRQoL was similar between the two groups. In evaluating the subscales, only PF showed a better condition in patients with  $\beta$ -TM [adjusted mean difference = 12.5, 95% confidence interval (95% CI): 5.6-19.3,  $p < 0.0001$ ].

#### **Conclusion**

Contrary to our expectations, QoL in patients with  $\beta$ -TI were not better than  $\beta$ -TM. Training programs and psychosocial support of all patients with  $\beta$ -TI and  $\beta$ -TM as well as their care providers with more focus on older patients, females and the patients with lower educational degree should be taken into account.

**Keywords:** Beta-thalassemia, Health, Quality of life, SF36



**Title: Necessity of Introducing a Thalassemia Team for Better Treatment of Thalassemia Major Patients in Emergency Unit**

**Abstract Category:** Quality of Life

**Authors:** Shayan Taherizadeh, Seyed Masoud Marandi

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Iran, Isfahan, khiyaban-e panj ramazan, khiyaban-e jami sharqi, plak-e 122, tabaq-e 1

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## ABSTRACT

### Background

Thalassemia major patients sometimes need to visit the emergency unit in local hospitals due to some situations particularly seen among Thalassemia major patients, such as cardiac / respiratory problems, hypoglycemia, hypocalcemia, and thrombosis.

### Methods

I will introduce case studies of 10 Thalassemia major patients who presented to emergency units in 2 hospitals in Isfahan city.

### Results

In 5 cases, the physicians, who did not know Thalassemia Major treatments or their possible complications well enough, took the responsibility of the Thalassemia major patients medical treatment. Therefore, due to the inaccurate diagnosis or inappropriate treatment by the physicians on site, one patient died and other patients had to suffer from unnecessary hardships, losing 3 to 6 months time for their recovery.

### Conclusion

There is an urgent necessity to create and introduce a thalassemia team, which consists of the physicians with expertise in Thalassemia treatment so that any hospital workers can refer to their expert viewpoints and protocols for Thalassemia treatment.



**Title: Efficacy of Sports Therapy for Improving Thalassemia Major Patients' Quality of Life**

**Abstract Category:** Quality of Life

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Iran, Isfahan, khiyaban-e panj ramazan, khiyaban-e jami sharqi, plak-e 122, tabaq-e 1

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## **ABSTRACT**

### **Background**

Most Thalassemia Major patients are young and we love sports. There are many sports activities available in Iran, and the Thalassemia Society supports the patients to join and enjoy football, badminton, shooting, and cycling.

### **Methods**

I will introduce two case studies based on the sports activities seen in Isfahan, Iran. One example is a male futsal team and the other example is a male bicycle team in Isfahan.

### **Results**

- 1) Isfahan male futsal team: Futsal team members gather weekly and practice. Once or twice a year, we have tournament matches among teams from different provinces.
- 2) Isfahan male bicycle team: Bicycle team members go for a practice ride weekly or monthly together. In 2013, 4 team members traveled 1,700 kilometers by bicycle from Isfahan to Mashad, with the message "Illness is not the end of life: Patients with special diseases need special attention".

I understood 4 improvements in the members' life after they joined the sports activities; (1) Better self-care management, (2) better social relationships, (3) better psychological status, (4) less feeling of fatigue. Also sports activities are one of the best ways to show the ability of the patients, and to bring our message to more people in the Iranian society. This improves the members' self-confidence.

### **Conclusion**

Sports should be understood as therapeutic activities for Thalassemia Major patients, because sports can improve the quality of life and self esteem of Thalassemia Major patients.



**Title: OUR CURE HOME!**

**Abstract Category:** Quality of Life

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## ABSTRACT

*Louis Kahn (famous architect): the things that an architect makes, prior to be changed to a mason, should be a response to human nature!*

The architect knows that ; What kind of spatial impression is built by this body!

And what is the impact of this spatial impression on human life?!

Studying all activities undertaken for good spirits condition, in order to enhance the quality of life. And the fact that how much does this matter has to do with our life space, even health care space in which we spend a main part of our lifetime. Further studies are about opinion poll and experience, and the process of question and answer is performed. Whether as an element of this society, having the experiences of a thalassemia, Or as an architect, for designing Health Care Centers, we want know how can help us this information for having perfect cure center with good feeling ..

I have faced with a question...

And that is why one must spend a routine of treatment for a lifetime, step on hard and solid space of the hospital, where there are always surgeries, hospitalized patients, and emergency ward. How much these things affect his spirit. This space and this image, and the fact of being always patient remind us the dependence to others.

From the generalities of the first section, I imagined a house with yard and open space, for my design

In order to provide the requirements such as enough light, appropriate view, fresh air... and comfort.

And since the desire of human to the nature is undeniable rule of the universe, and the main reason of his comfort. I have made a detached structural suggestion for invitation of the nature to the deep inside of the body.

In other part, I faced with another question...

Why the patients feel obliged to secretiveness, in their social activities, due to inappropriate conduct of the society. Where is that unpleasant image that we are, now, the witness of the gap between patients and the society? Isn't that the patient is aware of his condition, from the very beginning of his life, and accepts his special condition, after years, and tries always to be like a normal person, and just like all people tries to study, work, earn his life, and get married, because he has accepted his interior land of being! Suggestion of clear access, and without complexities, to open and half-open ... The opportunity to face with and knowing is given to the society.... Only with an image! Full of dynamism, brightness, satisfaction, desire of living, and even a bilateral portal can be created, by establishing and designing joint cultural spaces. Because, unfortunately, we found the patients with low self-esteem and a tendency to solitary lifestyle.

By continuing the studies, some part of which is expressed here, and understanding the spatial impression, the maximum comfort and satisfaction can be created, by the help of architecture. So we reach to the proven fact... that...The course of life is alive in architecture. The name of raw material is space. And its importance lies in its impact on life, to the point in which it gives us the motivation, courage and belief...

**Title: Quality of Life (QoL) Survey- United Kingdom Thalassaemia Society****Abstract Category:** Quality of Life**Authors:** Mary Petrou<sup>1</sup>, Elaine Miller<sup>2</sup>, Iliya Constantinou<sup>2</sup>, Matthew Darlison<sup>3</sup>, Bernadette Modell<sup>3</sup>**Presenting Author:** Mary Petrou**Affiliation:**<sup>1</sup> Institute of Women's Health, University College London<sup>2</sup> United Kingdom Thalassaemia Society<sup>3</sup> CHIME, University College London**Email:** M.Petrou@ucl.ac.uk**Address:**

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**ABSTRACT**

Quality of life (QoL) measures are used to evaluate the effectiveness of services. For adult-onset diseases, research on meeting patients' needs in a more holistic way has focused on predictors of health-related quality of life (HRQL). However existing questionnaires do not fully apply for life-long disorders such as thalassaemia.

**Aims**

To obtain the views of thalassaemia patients, on the effect of thalassaemia and its treatment on their QoL.

**Methods**

We developed a patient-specific survey to investigate variables affecting QoL in thalassaemia (service provision, emotional health, forming relationships, social relationships, employment, education, building a family, having friends, other demographic variables). Questionnaires were sent to 516 patients age 15 and above. 137 (26.5%) responded.

**Results**

76% of respondents were still transfused during the day. Transfusion was available out of hours in only 51% of centres. Only 30% of respondents were offered clinic times outside the work/ education day: a third of respondents missed 16 days or more from work/education.

Society's attitude to thalassaemia still impacts on patient's wellbeing: 67% of respondents experienced problems arising from social attitudes; half were not fulfilling their hopes in relation to building a family, and 33% said that thalassaemia interfered with forming and maintaining a relationship. 46% considered that their emotional health (with their physical health) affected their education/work and social activities.

**Conclusions**

This survey has highlighted important factors affecting patient's wellbeing. With modern treatment including the ability to become parents, to have a career and a family life, new social concerns have arisen - peer concerns for growth and maturity, socio-cultural problems such as being regarded as sick and therefore 'unmarriageable', and social exclusion because of being regarded as sick. Patients want to live normal lives like their peers and find it hard to accept any unnecessary restrictions due to their condition. These considerations need to be addressed to improve the holistic outcome of treatment for each patient.



## **Title: Role of Natural Killer Cells and Interferon-Gamma in Children and Adolescents with Sickle Cell Disease**

**Abstract Category:** Sickle Cell Disease

**Authors:** Mohsen ElAlfy<sup>1</sup>, Amira Abdel Moneam Adly<sup>1</sup>, Fatma Ebeid<sup>1</sup>, Deena Samir Eissa<sup>2</sup>, Eman Abdel Rahman Ismail<sup>2</sup>, Yasser Hassan Mohammed<sup>3</sup>, Aya Saad<sup>1</sup>, Manar Ahmed<sup>1</sup>

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## **ABSTRACT**

### **Background**

Patients with sickle cell disease (SCD), particularly children, have an increased susceptibility to infection. Natural killer (NK) cells are a type of cytotoxic lymphocyte critical to the innate immune system. Infection of a dendritic cell or macrophage by intracellular bacteria or viruses can stimulate the cell to produce interleukin-12 which triggers NK cells to produce interferon (IFN)-gamma which in turn stimulates CD4+ T-cells to differentiate into T-helper-1 (TH1) effector cells and exhibit their cytolytic activity. Aim: To evaluate the role of NK cells as well as IFN-gamma levels in children and adolescents with SCD.

### **Methods**

Forty SCD patients in steady state were studied focusing on history of frequent vaso-occlusive crisis, transfusion history, hydroxyurea therapy, hematological profile and serum ferritin. Liver and cardiac iron overload was assessed by magnetic resonance imaging. Analysis of NK cells (CD3-/CD16+/CD56+) was done by flow cytometry. Serum levels of interferon-gamma were assessed by enzyme linked immunosorbent assay (ELISA). Patients were compared with 40 age- and sex-matched healthy controls.

### **Results**

NK cells ( $20.31 \pm 11.45\%$ ) and IFN-gamma levels (median, 200 pg/mL) were significantly higher in patients than in controls (NK cells,  $6.56 \pm 1.44\%$  and IFN-gamma, 25 pg/mL, respectively;  $p < 0.001$  for both). Patients with history of frequent sickling crisis ( $> 3$  attacks / year) had higher levels of IFN-gamma than those without. NK cells were positively correlated to HbS ( $r = 0.826$ ,  $p < 0.001$ ) and indirect bilirubin ( $r = 0.676$ ,  $p < 0.001$ ). A significant negative correlation was found between IFN-gamma and cardiac T2\* ( $r = -0.346$ ,  $p = 0.039$ ) as well as duration of hydroxyurea ( $r = -0.906$ ,  $p < 0.001$ ).

### **Conclusions**

Increased NK cells in SCD with increased production IFN-gamma suggests that these cells are functionally activated which may reflect a host's immunological mechanism in an attempt to modulate persistent antigen-antibody response among those patients.

**Keywords:** Sickle cell disease, natural killer cells, interferon-gamma, vasocclusive crisis.

**Title: CD4+CD28null T Lymphocytes in Paediatric Patients with Sickle Cell Disease****Abstract Category:** Sickle Cell Disease**Authors:** Mohsen ElAlfy<sup>1</sup>, Amira Abdel Moneam Adly<sup>1</sup>, Fatma Ebeid<sup>1</sup>, Deena Samir Eissa<sup>2</sup>, Eman Abdel Rahman Ismail<sup>2</sup>, Yasser Mohammed<sup>3</sup>, Aya Saad<sup>1</sup>, Manar Ahmed<sup>1</sup>**Presenting Author:** Amira Abdel Moneam Adly**Affiliation:**<sup>1</sup> Pediatrics Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt<sup>2</sup> Clinical Pathology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt<sup>3</sup> Pediatrics Department, Faculty of Medicine, M.U.S.T. University, Cairo, Egypt**Email:** amiradiabetes@yahoo.com**ABSTRACT****Background**

Sickle cell disease (SCD) is increasingly appreciated as an inflammatory condition associated with alterations in immune phenotype and function. CD4+CD28null T lymphocytes are a subset of long-lived directly cytotoxic CD4+ T lymphocytes that have pro-inflammatory functions. Aim: To assess the percentage of CD4+CD28null T lymphocytes in 40 children and adolescents with SCD compared with 40 age- and sex-matched healthy controls and evaluate their relation to hemolysis, iron overload, vaso-occlusive crisis and response to therapy.

**Methods**

SCD patients in steady state were studied focusing on history of frequent vaso-occlusive crisis, transfusion history, hydroxyurea therapy, hematological profile and serum ferritin. Analysis of T cells was done by flow cytometry for assessment of CD4+ T lymphocytes and CD4+CD28null T lymphocytes.

**Results**

Patients with SCD had higher WBCs and lower hemoglobin level compared with controls. CD4+ T lymphocytes and CD4+CD28null T lymphocytes were significantly higher in patients than in controls ( $p=0.001$  and  $p=0.039$ , respectively). Patients with history of frequent sickling crisis ( $>3$  attacks/year) had higher percentage of CD4+CD28null T lymphocytes than those without (median [IQR], 5.29 [3.0 – 11.0] versus 2.37 [1.94– 2.99] %;  $p=0.008$ ). The levels of these cells were significantly lower among hydroxyurea-treated patients ( $p=0.045$ ) as well as those on combined chelation and hydroxyurea therapy ( $p=0.009$ ). There were significant positive correlations between CD4+CD28null T lymphocytes and transfusion index ( $r=0.537$ ,  $p<0.001$ ) and transfusional iron loading rate ( $r=0.324$ ,  $p=0.042$ ). CD4+CD28null T lymphocytes were negatively correlated to cardiac T2\* ( $r=-0.692$ ,  $p<0.001$ ) and duration of hydroxyurea therapy ( $r=-0.62$ ,  $p<0.001$ ).

**Conclusions**

Increased expression of CD4+CD28null T lymphocytes highlights the role of immune dysfunction in pediatric patients with SCD. Alteration of this subset of T lymphocytes is related to iron overload and higher incidence of vaso-occlusive crisis. Hydroxyurea and/or iron chelation therapy significantly contributes to lowering cytotoxic lymphocytes and attenuates immune dysfunction.

**Keywords:** Sickle cell disease, CD4+CD28null T lymphocytes, vasocclusive crisis, iron overload, hydroxyurea.



## **Title: Spectrum of Clinical and Radiological Features in Sickle Cell Disease Patients with Acute Chest Syndrome**

**Abstract Category:** Sickle Cell Disease

**Authors:** Alkindi Salam, Al-Busaidi Ikhlas, Raniga Sameer, Pathare Anil

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### **ABSTRACT**

#### **Background**

Acute Chest Syndrome (ACS) is the most important cause of death and the second most common cause of hospitalization in SCD patients. This aim of this study was to ascertain the spectrum of clinical, radiological and laboratory findings in these patients.

#### **Methods**

A retrospective cross-sectional case control study was performed at the Sultan Qaboos University Hospital by obtaining information from the hospital patient medical records. 100 episodes of SCD patients with ACS and 20 episodes of patients without ACS were included in this comparative study. Demographic data, clinical, radiological and laboratory parameters were collected and analyzed.

#### **Results**

The mean age of the cases and controls was 27.62 and 25.75 years respectively. In the cases group, males (63%) predominated and also developed ACS earlier (27yrs.) than the female patients (31yrs.). Fever, tachypnea, reduced saturation, bilateral crepitation and NIV were significantly different between the cases and controls ( $p < 0.05$ ). Among the laboratory parameters, Hb levels were found to drop significantly in the cases, whereas, WBC baseline and the highest level of WBC recorded were significantly higher in the cases ( $p < 0.05$ ). Further, the only significantly abnormal biochemical parameter was S.LDH at presentation ( $p < 0.05$ ). 4% of ACS patients had bacteremia, compared to none in patients without ACS. Most SCD patients with ACS needed antibiotics and blood transfusion/exchange (65%) as the major treatment modality.

#### **Conclusion**

The major risk factors predisposing to ACS were fever, tachypnea, dropping saturation, bilateral crepitation, drop in the Hb and rise in the WBC counts along with high LDH at presentation. Bacterial infection contribute to 4% of ACS episodes. The most important markers that signify severity were NIV and multi-lobar atelectasis/consolidation.

**Keywords:** sickle cell disease; acute chest syndrome; ACS; infections



## **Title: Clinical and Laboratory Features of Respiratory Viral Infections in Sickle Cell Disease Patients, with Particular Emphasis on H1N1**

**Abstract Category:** Sickle Cell Disease

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### **ABSTRACT**

#### **Background**

Patients with sickle cell disease (SCD) are immunocompromised and are at an increased risk of developing infections. Further, respiratory infections are a risk factor for triggering acute chest syndrome (ACS), which is the leading cause of mortality. Therefore, this study aimed to investigate the clinical, laboratory and radiological manifestations of respiratory viral infections in SCD patients.

#### **Methods**

A retrospective cross-sectional study was conducted in adult SCD patients attending the Sultan Qaboos University Hospital (SQUH) with viral infections between June 2013 and July 2016. Demographic data, clinical, radiological and laboratory parameters were collected and analyzed.

#### **Results**

In 76 SCD patients with confirmed viral infections, totaling 100 episodes, rhinovirus was the most prevalent viral infection (36%) followed by adenovirus (16%). H1N1 virus was seen in only 9% of cases. 93% of the patients were on penicillin prophylaxis, while 57% were on hydroxyurea therapy. 39% patients were splenectomized (surgically and autosplenectomy). 41 (54%) had previous history of ACS. 88% presented with pain, followed by fever (57%) with a mean duration of 6 days; and cough (51%). Other symptoms included throat congestion (25%), chest pain (22%), crepitation (22%) and runny nose (12%). Laboratory investigations revealed a significant fall in the mean Hb, WBC count and Platelet count from baseline, whereas there was a significant rise in the mean lymphocyte and retic count, LDH and CRP levels during infective episodes ( $p < 0.05$ ). Pleural effusion was seen in 22%, whereas, 14% developed lung changes of atelectasis or consolidation. Interventions included blood transfusions (45%), ventilation (11%), central venous catheter (8%) and urinary catheter (3%). In the 100 episodes, 32% developed ACS, with two deaths associated with Parainfluenza 3 virus.

#### **Conclusion**

Rhinovirus was the commonest virus in SCD patients, whereas, parainfluenza 3 was associated with significant adverse outcome. H1N1 was associated with a mild course and acute chest syndrome was the commonest complication.

**Keywords:** sickle cell disease; viruses; respiratory; H1N1; spectrum



## **Title: Impact of Hydroxyurea on Splenic Function in Young Patients with Sickle Cell Disease**

**Abstract Category:** Sickle Cell Disease

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### **ABSTRACT**

#### **Background**

Patients with sickle cell disease (SCD) can develop functional asplenia, even from a young age, as a result of sickle-induced infarcts. Hydroxyurea (HU) is a cytotoxic drug that ameliorates hemoglobin S polymerization mainly by increasing hemoglobin F (HbF). Despite documented benefits of HU on laboratory and clinical parameters in children with SCD, its role on splenic function remains unclear.

#### **Aim**

To prospectively evaluate the impact of HU on splenic function, as estimated by percentage of Howell Jolly bodies and liver/spleen scintigraphy in young patients with sickle cell disease.

#### **Patients-Methods**

Twelve young patients with SCD (11 with sickle/beta-thalassemia and one with sickle cell anemia), aged 3.5-18 years, participated in the study. HU was given at a mean daily dose of 14 mg/kg (10- 20mg/kg) for a 4 year period. Nine patients were non-splenectomized at entry study, while one underwent splenectomy during the treatment period. Splenectomized patients had the same evaluation as non-splenectomized, so as to detect possible ectopic splenic presence and/or splenic remains. Splenic function was assessed at baseline and after 4 years of therapy through <sup>99m</sup>Tc sulfur-colloid uptake measurement using visual inspection, and through quantitative analyses using spleen/liver ratios, as well as Howell-Jolly (HJ) bodies' assessment by flow cytometry.

#### **Results**

At baseline study 2 of 8 (25%) non-splenectomized patients had functional asplenia as assessed by liver/spleen scintigraphy, while 6 (75%) had impaired splenic function. No splenectomized patient had splenic remains or ectopic spleen. At study exit there was a mild improvement on splenic function in only one non-splenectomized patient, with no scintigraphic change in the rest of patients. With regards to Howell Jolly bodies' percentage, no significant difference was detected in any patient after 4 years of therapy.

#### **Conclusions**

HU therapy's effect on spleen function warrants further studying, involving larger number of patients.

## **Title: Effect of Hydroxyurea on Coagulation Parameters in Young Patients with Sickle Cell Disease**

**Abstract Category:** Sickle Cell Disease

**Authors:** Eleni Papadopoulou<sup>1</sup>, Aikaterini Teli<sup>1</sup>, Evaggelia Farmaki<sup>1</sup>, Anna Taparkou<sup>1</sup>, Sophia Vakalopoulou<sup>2</sup>, Vassilia Garipidou<sup>2</sup>, Marina Economou<sup>1</sup>

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## **ABSTRACT**

### **Background**

Sickle cell disease (SCD) is characterized by a hypercoagulable state. SCD patients have shown high levels of thrombin, abnormal activation of fibrinolysis, decreased levels of anticoagulant proteins, activation of platelets and increased circulating levels of soluble tissue factor. Hydroxyurea (HU) is a cytotoxic drug that is used in patients with SCD, ameliorating disease severity by HbF induction. However, other mechanisms may also be involved - including alterations in the coagulation system.

### **Aim**

To evaluate the effect of HU on coagulation system parameters in young patients with SCD.

### **Patients-Methods**

Eleven young patients with SCD (10 with sickle/beta-thalassemia and one with sickle cell anemia), aged 3.5-18years, participated in the study. HU was given at a mean daily dose of 16.3mg/kg (14.5-19mg/kg) for a 3year period. Prothrombin time, activated partial thromboplastine time, D-dimers, fibrinogen and levels of coagulation factors VIII, XII, von Willebrand, as well as levels of protein C, protein S and antithrombin III were measured before and 3 years after HU therapy – during a steady-state condition.

### **Results**

At baseline study all patients had increased levels of D-Dimers. At study exit there was a statistical trend concerning D-dimers' levels ( $1380 \pm 707$  vs  $968 \pm 535$   $\mu\text{g/l}$ ,  $p=0.091$ ). Moreover, there was a significant decrease in prothrombin time ( $14.05 \pm 1.38$  vs  $12.87 \pm 0.65$ ,  $p=0.027$ ) and antithrombin III levels ( $98.7 \pm 11.3$  vs  $89.4 \pm 16.2$ ,  $p=0.044$ ). The remaining parameters studied did not show significant change during treatment period.

### **Conclusions**

The study indicates that HU therapy may have substantial effects on coagulation activation and natural inhibitory systems in young SCD patients.

**Title: The bamboozling HbS ... a case of transfusion-acquired hemoglobinopathy****Abstract Category:** Sickle Cell Disease**Authors:** Hadeel Ibrahim**Presenting Author:** Hadeel Ibrahim**Affiliation:** Hereditary Blood Diseases Center, AL-Karama Teaching Hospital, Baghdad, Iraq**Email:** hadeelhematology@yahoo.com

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**ABSTRACT**

Case Report ....

A 4-year-old child presented with long standing history of hepatosplenomegaly and pallor that necessitated frequent blood transfusion.

The CBC showed the following; RBC  $2.75 \times 10^{12}/L$ , Hb 60 g/L, HCT 18%, MCV 65.4 fL, MCH 21.8 pg, MCHC 333 g/L, RDW 42.3%, PLT  $355 \times 10^9/L$ , WBC  $6.4 \times 10^9/L$ , Lymphocytes  $3.5 \times 10^9/L$ , and granulocytes  $2.2 \times 10^9/L$ .

Addressing the likelihood of thalassemia major without an on file Hb HPLC report, Hb HPLC (BioRad Variant II,  $\beta$ -thalassemia Short Program) was performed in our specialized center. Interestingly the chromatogram obtained was a bit odd since it showed a small peak of HbS constituting no more than 7.2% of the total hemoglobin percentage despite being relatively small to be considered as significant (as patients with sickle cell trait HbAS, HbS is expected to be around 40%) yet could not be ignored as the same result appeared on repeating the test trice, the possibility of carryover was ruled out

On the other hand, the suspicion of  $\delta$ -chain variant, Hemoglobin A2' (A2 prime) which does elute in the sickle(S)-window, was defeated as parents hemoglobin analysis yielded no such variant.

family study was considered altogether, both parents proved to be carriers for  $\beta$ -thalassemia with HbA2 results of 5.2, and 5.4 respectively, with no peaks at all in the S-window.

Digging down in the patient's history, he turned out to have received blood recently no more than 14 days, the unit transfused most probably was from a sickled-trait donor, a piece of information that was not spelled out earlier which drove us into the dilemma of repeated testing and confusion with respect to the result interpretation

This case shades a light on the importance of careful history taking in patients required to undergo hemoglobin analysis with respect to the last transfusion received

Transfusion-acquired or apparent hemoglobinopathy is a recognized phenomenon with the widely available HPLC technique

**Title: Catalonia Newborn Screening Program. Prevalence of Sickle Cell Disease****Abstract Category:** Sickle Cell Disease**Authors:** Marín JL<sup>1</sup>, Pajares S<sup>1</sup>, López RM<sup>1</sup>, Argudo A<sup>1</sup>, Mañu MM<sup>2</sup>, Gutiérrez V<sup>3</sup>, Beneitez D<sup>3</sup>, Blanco A<sup>3</sup>, Fernández RM<sup>4</sup>**Presenting Author:** Marín JL**Affiliation:**<sup>1</sup> Catalonia Newborn Screening Laboratory. Hospital Clínic<sup>2</sup> Erythro-pathology Laboratory. Hospital Clínic<sup>3</sup> Reference and Diagnostic Clinical Unit. Hospital Vall d'Hebron<sup>4</sup> Public Health Agency of Catalonia. Departament de Salut. Generalitat de Catalunya.**Email:** jlmarin@clinic.cat

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**ABSTRACT****Background**

Catalonia is the Autonomous Community in Spain (CCAA) with the largest population from Africa and the highest number of newborns with African parents. Newborn screening (NBS) for sickle cell disease allows the early detection of the disease, take prophylactic measures and a decrease in its morbidity and mortality. In January of 2015 we started the NBS for sickle cell disease (SCD) in Catalonia.

**Aims**

To know the prevalence in both, SCD and carriers of HbS; as well as to compare these prevalences with the other diseases included in the NBS Program and with those of other Spanish CCAA.

**Material and Methods**

Paper blood samples from all newborns from 2015 and 2016 were prospectively analyzed by capillary electrophoresis (CapillaryS2Neofast, Sebia). Phoresis (Sebia) and Nadons (Limit4) softwares were used for the validation of results.

**Results**

The total number of newborns studied was 140,519. The prevalences for the FS, FSβTAL and FSC phenotypes were 1/4,258 (n=33), 1/70,259 (n=2) and 1/23,419 (n=6), respectively. The prevalence for SCD was 1/3,427 (n=41) and for HbS carriers of 1/156 (n=898). The most prevalent disease in our NBS Program is Congenital hypothyroidism (1/1,979), followed by SCD (1/3,427); Cystic fibrosis (1/6,518); Hyperphenylalaninemias (1/8,742); Diseases of mitochondrial beta-oxidation of fatty acids (1/6,368); Organic acidurias (1/8,860) and aminoacidopathies (1/12,416). The prevalence of SCD in other Spanish CCAA was the following: Catalonia (1/3,427); Basque Country (1/4,416); Madrid (1/4,964); Valencia (1/6,700) and Balearic Islands (1/6,756).

**Conclusions**

1. The prevalence of SCD in Catalonia is 1/3,427 and the HbS carriers is 1/156.
2. SCD is the second most prevalent disease in our NBS program.
3. The prevalence of SCD in Catalonia is the highest of all known prevalences in the different Spanish CCAA.
4. These results confirm and justify the necessity of include this disease in the Catalonia NBS Program.

**Title: Sickle Cell Disease in the Danish Immigrant Population: a Prevalence Study****Abstract Category:** Sickle Cell Disease**Authors:** Amina Nardo-Marino, Andreas Glenthøj, Jesper Petersen, and Henrik Birgens.**Presenting Author:** Amina Nardo-Marino**Affiliation:** Department of Haematology, Herlev and Gentofte Hospital, Copenhagen University Hospital, Denmark.**Email:** amina.nielsen.nardo-marino@regionh.dk**Address:**

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**ABSTRACT****Background**

Due to population migration, sickle cell disease (SCD) is becoming an increasing health concern in Northern Europe. No previous studies have attempted to assess the disease burden in Denmark. However, accurate data on the prevalence of SCD is needed in order for health care professionals to ensure optimum clinical care for all patients.

**Methods**

In Denmark, the vast majority of tests for hereditary haemoglobin disorders are performed at the Centre for Haemoglobinopathies at the Department of Haematology, Herlev and Gentofte Hospital. As SCD is associated with severe clinical manifestations, we assumed that most patients with SCD living in Denmark had been in contact with a Danish health care facility and, thus, had been diagnosed at the Centre for Haemoglobinopathies. Through a local database, it was possible to identify all patients diagnosed with SCD from 1995-2016. Furthermore, we contacted consultant physicians in charge of treating SCD at all haematological and paediatric departments in Denmark, in order to identify any additional patients.

**Results**

We identified 106 patients with SCD living in Denmark. The prevalence of SCD in Denmark was found to be 1.9 per 100,000, with a prevalence of 22.4 per 100,000 in the immigrant population. Fifty-five patients were female (51.9%) and ages ranged from 0-63 years, with a mean age of 20.2 years. Most patients originated from West Africa (37.7%) and the Middle East (34%). Seven different genotypes were present (HbSS, HbS/ $\beta$ 0-thalassaemia, HbS/ $\beta$ +thalassaemia, HbSC, HbSD, HbS/HbLepore, and HbS/HbHope), with HbSS being the predominant variant (50.9%).

**Conclusions**

SCD is a rare condition in Denmark, although patient numbers are likely to be increasing. Data from our study will help promote awareness and encourage appropriate clinical management of all children and adults living with SCD in Denmark, as well as other Scandinavian countries.

**Title: Milestones Along My Personal Journey with Hydroxyurea****Abstract Category:** Sickle Cell Disease**Authors:** Aishath Shifneez Shakir**Presenting Author:** Aishath Shifneez Shakir**Affiliation:** Patient Advocate & Executive Committee Member, Maldivian Thalassaemia Society, Maldives**Email:** shifneez@gmail.com

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**ABSTRACT**

For long sickle cell and thalassaemia were thought to be childhood diseases. It was believed that there was no future for these kids but to suffer the consequences of inheriting the genes and so their future was unplanned.

I am Shifneez, 34 years old sickle beta-thalassaemic from Maldives. My parents were told I will not live up to be 14. I grew up as a very active student in school, graduated in teaching and worked at the very school I studied at. I had my first sickle crisis at the age of 14. After about 5 years of not knowing what sickle cell can do, I was introduced to this drug called Hydroxyurea (HU) in 2003. After I got married and was ready to have a family, I was advised by my physicians to avoid becoming pregnant while taking HU. understandably, they told me about the potential harm to the fetus. I was left with a real dilemma: Take a drug with unknown effects on fetal development or give up a helpful, necessary medication that has kept me healthy since I started it.

Many SCD patients are not willing to take a chance and go through pregnancy, let alone take the risk of continuing pregnancy with HU. hence, there is not a lot of clinical evidence with pregnancy while taking HU. My determination to start a family, despite being aware of the risks associated, past 12 years, I have had 3 pregnancies each experience different with regard to HU therapy. Today, I am a mother of 2. I had my last pregnancy and lactation while taking HU. HU, the only disease-modifying therapy approved for SCD, has continuously shown to improve the quality of life of adults and children with sickle cell. I hope the story of my personal journey can break the barrier and open the possibility for others like me to reach their milestones and dreams.

**Title: Sickle Cell and Exchange Blood Transfusions in the Paediatric Realm****Abstract Category:** Sickle Cell Disease**Authors:** Adrienne Woods**Presenting Author:** Adrienne Woods**Affiliation:** Children's Hospital, Westmead, Sydney, NSW, Australia**Email:** adrienne.woods@health.nsw.gov.au

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**ABSTRACT**

Packed Red Blood Cell Transfusions and Red Blood Exchange Transfusions (RBCX) have been used to successfully treat patients with Sickle Cell Disease. RBCX can be performed manually or using an automated process with an apheresis machine. The apheresis technology has the benefits of better control of blood fluid balance, decrease in allo-immunisation, iron neutral or negative procedure and an overall safer treatment for the patient.

In 2015, The Children's Hospital at Westmead, Sydney transitioned from a manual RBCX to an Automated RBCX program. We have performed RBCX on 13 patients, aged from 4 years to 19 years, with the number of procedures exceeding 230. The development of the service has met with a series of challenges including vascular access, management of side effects, individualisation of patient RBCX programs and logistics of service provision.

Two case studies will be presented illustrating the concepts briefly outlined below:

1. Vascular access necessary for a RBCX requires 2 separate intravenous sites, ideally peripheral cannula's. However if peripheral access is problematic, due to poor patient veins and/or child trauma, we are then reliant on Intravenous Port-a-caths, which come with their own unique set of issues. Concepts and ideas for the practical management of IV insertion and management to aid flow rates for the successful RBCX in our paediatric service are discussed.
2. Each RBCX program is tailored to the patient, with considerations of their pre-existing iron status and chronic health issues. If the patient is iron loaded then typically a Depletion RBCX is performed until the serum ferritin meets the target range. This marked decline in iron significantly reduces complications relating to iron loading and removes the necessity for iron chelators with their inherent side effects and costs.

**Title: Hb Aghia Sophia in Northern Greece****Abstract Category:**  $\alpha$ -thalassaemia syndromes**Authors:** D-A. Giannakopoulou, E.Yfanti, O.Karakasidou, E.Skatharoudi, D.Adamidou, T-A.Vyzantiadis, S.Theodoridou**Presenting Author:** D-A. Giannakopoulou**Affiliation:** Hippokraton Thalassaemia Unit & National Thalassaemia Centre**Email:** hmesogiaki@ippokratio.gr

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**ABSTRACT**

Alpha-thalassaemia is inherited as an autosomal recessive disorder characterised by a microcytic hypochromic anaemia, and a clinical phenotype varying from almost asymptomatic to a lethal haemolytic anaemia. It is probably the most common monogenic gene disorder in the world and is especially frequent in Mediterranean countries, South-East Asia, Africa, the Middle East and in the Indian subcontinent. Several mutations have been described. Those mutations can affect globin gene expression in any step and many of those mutations are rare causes of alpha thalassaemia. We report the case of a Greek couple who was counseled preconception ally in our Thalassaemia Prevention Unit, because the female was known as heterozygous carrier of  $\beta$  thalassaemia (IVSI-110G>A/NI. Her partner was screened and showed an hemoglobin (Hb) of 13.8g/dl, Red blood cells (RBC)  $5.16 \times 10^9/L$ , Mean corpuscular volume (MCV) 78.0 fl, Mean corpuscular haemoglobin (MCH) 26.4pg, HbA2 2.6%, with inclusion bodies found in his blood smear, while his ferritin levels were 72. Peripheral blood smear also showed anisocytosis and microcytosis. They both came from a village near Thessaloniki in Northern Greece. Genetic analysis revealed that the male carried the rare Haemoglobin Aghia Sophia found for the first time in Northern Greece. Hb Aghia Sophia HbA1: c.187\_189delGTG is a deletion of codon 62 of the alpha -1 gene leading to  $\alpha^+$  thalassaemia. Genetic counseling was offered for a future pregnancy. Occasionally, especially in countries where thalassaemia is uncommon,  $\alpha$ -thalassaemia trait may be confused with iron deficiency anaemia, especially when the iron status is not carefully assessed. Haematological parameters for thalassaemia and iron deficiency are quite similar therefore ferritin levels should be measured. If the microcytic hypochromic parameters persist in a patient with normal levels of ferritin elevated RBC and normal (or low) HbA2, (especially in patients originating from areas where haemoglobinopathies are common) there is a good chance that the individual is a carrier of  $\alpha$ -thalassaemia. Molecular analysis is usually required, especially in silent  $\alpha$ -thalassaemia and  $\alpha$ -thalassaemia trait to confirm the haematological observations.



## Title: **Management of Haemoglobin Barts Hydrops Fetalis Syndrome with Exchange Transfusions**

**Abstract Category:**  $\alpha$ -thalassaemia syndromes

**Authors:** Jeremy Ong, Carolyn Greely, Don Bowden, Zane Kaplan

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### ABSTRACT

Haemoglobin (Hb) Bart's hydrops fetalis syndrome results from deletion of all four  $\alpha$ -globin genes. Whilst generally considered fatal in the antenatal period, with improved perinatal care, rare patients are surviving into adulthood. Here we present the case of a 24-year-old female with Hb Bart's hydrops fetalis syndrome managed with regular exchange transfusions.

#### Case Report

The patient was born at 35 weeks' gestation with no hydropic features. She was homozygous for the South-East Asian two-gene  $\alpha$ -deletions. Her initial haemoglobin was 7g/dL, with 86% Hb Bart's. She received three-weekly blood transfusions and iron chelation with deferoxamine. Her care was transferred to Texas, USA at age 8.

She underwent splenectomy age 14. This was complicated by recurrent post-splenectomy venous thromboembolisms. Due to concerns of hyperviscosity precipitating further thrombosis, she only received transfusions every eight weeks to maintain a haemoglobin between 10-12g/dL. Her iron chelation was changed to deferasirox. She returned to Australia age 23.

On her return, her haemoglobin was 10g/dL, with 51% HbH. Her functional haemoglobin was 4.9g/dL, and she suffered severe lethargy and dyspnoea. Her plasma free haemoglobin was 3000mg/L, indicating significant haemolysis, erythropoietin 1255U/L and ferritin 1956 $\mu$ g/L. She commenced fortnightly partial exchange with one unit of packed red cells, with reduction in HbH to 38%. Four months later, she started automated red cell exchange transfusion by apheresis with 6 units of red cells. Within three months, her pre-transfusion HbH dropped to 27% with haemoglobin 12g/dL, giving a trough functional haemoglobin of 8.7g/dL. Her symptoms significantly improved, erythropoietin normalised to 33U/L and plasma free haemoglobin reduced to 83mg/L. Her ferritin was 1468 $\mu$ g/L.

Discussion Hb Bart's hydrops fetalis syndrome is characterised by profound haemolysis. Excess endogenous production of HbH reduces functional haemoglobin, impairs oxygen delivery and promotes haemolysis. A transfusion program similar to that used to treat patients with transfusion dependent  $\beta$ -thalassaemia does not adequately address these issues. Regular exchange transfusions can suppress erythropoiesis, and improve functional haemoglobin and tissue oxygenation to a significantly greater degree than regular transfusions. It can also ameliorate the risk of siderosis. Splenectomy should be avoided in these patients given the high risk of thrombosis. Whilst previous experience employing aggressive hypertransfusion regimens have proved effective at reducing HbH levels, this is at the cost of severe iron overload. This case demonstrates the successful utilisation of regular exchange transfusions in the management of Hb Bart's hydrops fetalis syndrome.



## A few words about Thalassaemia International Federation (TIF):

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**TIF** Thalassaemia International Federation is an NGO founded in 1986 by a small number of patients and families representing National Thalassaemia Associations in Cyprus, Greece, UK, USA, and Italy, countries in which these diseases have been recognised as an important matter for public health and where the first programmes for prevention and management have been implemented.

**MISSION** To improve the survival and quality of life of patients with thalassaemia through the promotion and support of: education, advocacy and capacity building of patients' and their families' awareness and education programmes for the community collaboration with national, regional and international health authorities aiming to (a) prioritise thalassaemia on national, regional and International health agendas; (b) develop and implement national disease specific programmes for its effective control, prevention and holistic care, and research programmes and studies focused on the final, total cure (c) Establish equal access of every patient with thalassaemia to high quality health and social care services provided through truly patient-centred healthcare systems.

**VISION** Establishment of equal access of every patient with thalassaemia to high quality health and social care services provided through truly patient-centred healthcare systems.

## BECOME MEMBERS OF THE THALASSAEMIA COMMUNITY

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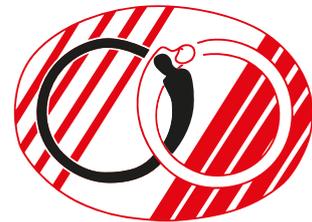
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