12. DISEASE BURDEN OF TRANSFUSION-DEPENDENT THALASSAEMIA
TIF'S PERSPECTIVE

AUTHORS: Amid A., Angastiniotis M., & Eleftheriou A.

INTRODUCTION

As defined by most relevant bodies, "disease burden" is the impact of a health problem as measured by financial cost, mortality, morbidity, or other indicators. It is commonly measured by calculating the years of life lost due to premature mortality plus the equivalent "healthy" years of life lost due to disability. In general, it is the impact of living with illness and injury and dying prematurely.

This implies a systematic collection, analysis and interpretation of population health data, which in many situations is just not done and accurate data are not available. Rather, patchy information is derived from publications on small aliquots of patients, usually from academic centres. This is particularly true if the disease is relatively rare. The requirements for data collection include accurate diagnosis, classification of subgroups of disease, patient numbers, complication rates, and especially mortality figures. In addition, the impact on quality of life and family economics must be considered.

Disease entities that are present from birth require lifelong treatment and collect multi-organ complications as the patient grows in years, often resulting in premature death. They are particularly difficult to report with accurate information. Another factor which complicates data collection and comparison between countries and regions is the significant differences in quality of care and availability of adequate treatment modalities to manage all patients with equity. WHO defines quality of care (QoC) as the provision of healthcare services that improve desired health outcomes for individuals and populations through effective, efficient, and safe means [1].

It may be asked further who carries this "burden". It can be the patient, the family, society, the health service, or the ministries of finance, but in fact all are affected. These concerns are addressed by the Global Burden of Disease Study, which is important to know and understand since, at the central-provider level, many decisions are based on its results and it remains the guide for health policymakers in all countries.

THE GLOBAL BURDEN OF DISEASE STUDY (OR GBD PROJECT)

This study was initiated in the early 1990s by the World Bank because of concerns that health services around the world were not effectively dealing with health challenges. Major issues causing premature mortality and disability, consequent to disease, were not being addressed because of inappropriate resource allocation, especially in the developing world. Planning should be based on both the prevalence of a given disease or risk factor and the relative harm it causes. In the World Development Report 1993 by the World Bank [2] the following issues were raised concerning health systems (see box below):

- **Misallocation of Funds: investing in health interventions of low cost-effectiveness. The example given is surgery for most cancers, as compared to the treatment of common diseases such as tuberculosis.**
- **Inequity: spending disproportionately on the affluent, so the poor lack quality care.**
- **Inefficiency: wasting money, for example on brand names as opposed to generic drugs, poor supervision of staff and underutilisation of hospital beds.**
- **Exploding costs: for example, a rapidly growing demand for costly tests and procedures.**
- **Governments are urged to pursue economic growth policies that will benefit the poor.**
- **Finance and implement a package of public health interventions to deal with the substantial externalities surrounding infectious disease control, prevention of AIDS, environmental pollution, and behaviours (such as drink driving) that put others at risk.**

However, in this report we see no reference to congenital or hereditary diseases, which require lifelong investment and affect poor and rich alike. Even the The World Summit for Children did not mention these conditions. This has led policymakers to not include them in their priorities.

These sensible housekeeping concerns were then given practical measures by the Global Burden of Disease project (GBD) and supported by the WHO. Indicators were developed quantifying the contribution of disease and public health concerns. Indicators include disability-adjusted life years (DALY), which is the number of years of healthy life lost due to death and illness. These indicators aid health services to prioritise by identifying disadvantaged groups and targeting health interventions [3]. They are all valid points for good health planning, but they are based on economy and "appropriate" use of funds, aiming to reduce waste. These are important considerations, especially when resources are limited, and they support the maximum benefit at a population level. When it comes to the needs of the individual with a rare disease, the ethics of this approach become debatable. Should the rights of the individual be sacrificed to the benefit of the total or should the system consider how best to serve all members of society? A cancer patient who needs surgery in this model would be deprived because it is not a cost-effective intervention. But if such a person can afford private care, then surgery can be made available even if this increases inequality. Health as a human right of all cannot be satisfied and inequalities will continue because the limited resources must be allocated to benefit the majority.

The issue that we at TIF raise is not that we believe the World Bank or the WHO or the GBD project are wrong approaches, but that in their effort to get the best out of limited resources, they have reduced health to a series of indices that are used by administrations to prioritise health but often forget the person. In addition, the indices used are based on inadequate information and they can often be misleading. The objective is to find solutions for congenital and chronic conditions which may be rare and so not given priority in service provision. Experience, even with the inaccuracies and approximations available to this global review, is that resources to adequately address the needs of such patients are not allocated, leading to suffering and early death, when in fact treatment can lead to the growth of productive citizens. In this respect resources, including economic resources are wasted more so than if adequate investment was offered to raise tax-paying citizens as encountered in some countries.

The GBD continues as an independent project with the support of the WHO and funds from the Gates Foundation. It has adopted measures quantified in terms of quality-adjusted life years (QALYs) or disability-

adjusted life years (DALYs) [4]. Both of these metrics quantify the number of years lost due to disability (YLDs), sometimes also known as years lost due to disease or years lived with disability/disease. One DALY can be thought of as one year of healthy life lost, and the overall disease burden can be thought of as a measure of the gap between current health status and the ideal health status (where the individual lives to old age free from disease and disability). A cost-effective policy or intervention is measured by the ratio of cost to health benefits or DALYs gained.

Cost effectiveness, according to the 1993 report, is difficult to estimate, since costs vary between countries and outcome measures are difficult to estimate in complex multi-organ diseases in which morbidity is often difficult to monitor, and survival is variable.

THE BURDEN OF β-THALASSAEMIA

Morbidity in β-thalassaemia is due to the effects of the primary condition anaemia, ineffective erythropoiesis with expansion of haemopoietic tissue, organomegaly, poor growth, and fragile bones. These are partially, rarely totally, corrected by blood transfusion. Then, from childhood, tissue damage starts due to the toxicity of unbound iron. This tissue damage increases with age, leading to organ dysfunction mainly in the heart, endocrine system, and liver. The degree to which these effects are present in individual patients will depend on availability, individual tailoring, and adherence to iron chelation, so that in a population of patients, a spectrum of morbidity is encountered. The level of morbidity will also determine the quality of life but also the mortality rate in a given population.

The extent of morbidity or the complication rates, measured by various parameters, is a reflection of the quality of clinical management as well as patient adherence. Patient adherence is often episodic, as periods of tissue damage alternate with periods of intensified iron chelation that partially rescues the vital organs. Over time there is a cumulative effect, with increasing organ dysfunction and so disability becomes established to varying degrees. Effective management by the conventional clinical tools available today will minimise these catastrophic effects. The clinical interventions required to prevent and manage these complications are complex and expensive, requiring clinical expertise and organisation, which in turn mean adequate investment at central government level. Many countries are reluctant to invest to the extent required, deciding that there are other priorities for the limited resources available. The result is that the majority of the global thalassaemia patient population is treated sub-optimally. Sub-optimal treatment is self-defeating since it allows complications to increase and premature death to be the final outcome, increasing instead of decreasing the burden of thalassaemia.

All the measures proposed, whether years of potential life lost (YPLL) or DALYs, must rely on data very difficult to come by [5]. As recorded in this Global Review of Thalassaemia Services, very few centres treating patients keep registries and very few countries keep a national registry of patients even to know patient numbers, let alone to record morbidity and mortality data. Classifying haemoglobin disorders according to these measures and comparing their public health importance to other diseases is, therefore, largely based on estimations or even guesswork. Better data collection should become a goal and should be promoted in all countries. At the same time, there is a need to better understand how the term "burden" is applied to conditions that manifest at birth, progress throughout life with increasing organ involvement, but, with an appropriate therapeutic approach such as applying conventional treatment, can result in long survival with a good quality of life. The number of data items that need to be collected and appropriately recorded to add up to a meaningful concept

of the term "burden" in thalassaemia is demonstrated in a series of recent published attempts to estimate burden [6, 7].

Disease burden in β-thalassaemia is a complex concept which needs several parameters to adequately define:

1. The total number of patients, including the total needing treatment and those needing partial treatment.
2. The age distribution of these patients, since the needs of each age group are different. This demonstrates both the effectiveness of preventing affected births and the effectiveness of clinical services provided that contribute to a reduction in mortality.
3. Complication rates: These vary from population to population according to timely interventions and quality of care.
4. The needs in the treatment modalities: Blood transfusion, iron chelation, and monitoring and treating complications (mainly but not confined to allo-immunisation, heart disorders, liver disease, endocrine conditions, renal complications etc.)
5. Loss of productivity: Can this be expressed in terms of DALYs? DALYs is a summary measure that combines mortality and morbidity measures, assessing non-fatal outcomes.
6. The degree of social support in place, including the degree that financial costs for treatment and other out-of-pocket expenses are reduced and, if possible, eliminated.
7. The cost of all these parameters is essential to assess, since economic burden will indeed determine resource allocation. However, costs alone are an incomplete measure, since they fail to capture pain and suffering that impact on the quality of life of the patients themselves and importantly their families.
8. Quality of life elements (pain, discomfort, anxiety/depression, effect on daily activities).

Quality of life and functionality status, mental and emotional effects of patients, and the repercussions on the family and social environment have to be incorporated into the equation.

Measures that only consider one or two of these aspects will not portray the whole spectrum or describe the real burden. Reliance on a single measure can be very misleading where any chronic disease is concerned and can effect public health and individual wellbeing.

There is no challenge to the philosophy of a disease classification which utilises the prevalence of a disease along with both morbidity and mortality outcomes.

TIF, as a humanitarian organisation, cannot adopt an isolated economic model. A more analytical and critical look at the impact of thalassaemia on patients and on society is required to demonstrate the obvious inequalities across the world and use any proposed tools to promote health policies which reduce inequalities. We need to use our burden of disease measures to show what can be done wich quality care and to provide policymakers with tools to measure their own achievements or deficiencies. Monitoring progress cannot rely on costs alone, which may lead health authorities to only adopt prevention measures without increasing support to patients.

An issue that makes comprehensive assessments even more important is the advent of newly approved treatments which may also be curative. Affordability is a major obstacle increasing the inequalities, allowing the wealthy to become transfusion-free while the majority continue to receive inadequate conventional therapy, thereby increasing disease burden.

The parameters of disease burden, described above, are developed separately in each chapter of this Review. The classification of anaemias in the GBD report (2019), which mentioned that haemoglobinopathies are in the 17th position of the 0-9 age group in terms of DALYs but not in any other age group [8]. Indeed, thalassaemia is a lethal disease of childhood in most parts of the world, even though the privileged now survive to the sixth decade or more. This "positioning" is based on disability weights, which for thalassaemia were found to be 0.501 (0.403–0.600) in 2016 and 0.485 (0.425–0.545) in 2019, the difference presumably being due to reduced mortality [9]. It is recognised that haemoglobinopathies are a significant source of death and disability. (Disability weights represent the magnitude of health loss associated with specific health outcomes and are used to calculate years lived with disability (YLD) for these outcomes in a given population. The weights are measured on a scale from 0 to 1, where 0 equals a state of full health and 1 equals death.)

MORTALITY AND MORBIDITY OF β-THALASSAEMIA

From the incomplete data in TIF's possession, there is a global population of over 800,000 patients with β-thalassaemia and almost 60,000 new cases are being added each year. The global prevalence could be significantly higher, acknowledging the absence of effective prevention in most countries. However, one may understand that an almost equal number to those born annually dies at an early age due to suboptimal care. Non-transfusion-dependent thalassaemia patients may have a better life expectancy [10, 11]. Both morbidity and mortality in β-thalassaemia depends on optimal control of the anaemia (maintaining the level of haemoglobin above 9-10g/dl) and iron control (maintaining serum ferritin below 1000ng/dl) throughout life [12]. The burden of disease increases as morbidity increases, over and above all the financial and social issues. Premature, avoidable mortality is a burden to family and society, and it is difficult to reduce it to a single measure.

RESULTS CONCERNING THE BURDEN OF DISEASE ACCORDING TO WHO REGIONS

East Mediterranean Region Haemoglobinopathy Status

Introduction

The East Mediterranean region of WHO includes all Arab-speaking nations, except for Algeria, and Iran, Pakistan, and Afghanistan. The total population is over 740 million inhabitants. This large group of countries has great diversity in economic and social development, which is reflected also in the quality and availability of services for haemoglobin disorders. One unifying element is that in all countries of the region, Islam is the prominent religion, which is accompanied by similar cultural attitudes that may affect issues like prevention. Another common practice in all these states is the high rate of cousin marriage, which has an effect on the birth incidence of inherited disorders such as thalassaemia.

Another characteristic of the Arab nations is the high prevalence of both thalassaemia and sickle cell genes. This results in increased incidence of beta thalassaemia, homozygous sickle cell anaemia, and HbS/beta thalassaemia patients, increasing the burden of these disorders on patients, families, and the health system.

In this report we attempt to describe the current situation of haemoglobinopathy services in the region in relation to the health systems and quality of services as affected by economic and political factors. The huge

diversity concerning economic development, the high level of displaced populations and the armed conflicts which affect many areas of the region make haemoglobin disorders a public health issue of great concern. In the midst of pressing problems, patients who need lifelong complex services are often forgotten or sacrificed to other priorities, resulting in poor outcomes.

Socio-economic development

- In 5 countries more than 25% of the population is living below the international poverty line, i.e. USD 1.90/person/day, as defined by the World Bank (current IPL is USD 2.15/person/day, affecting 9.2% of the world's population)
- There is generally a low investment in health

Table 1. Socioeconomic and health investment indicators in the EMR

Country	HDI rank	WB rank	HE/cap WHO data in USD	HE/%GDP WHO data	UHC index
Afghanistan	0.478 low	LIC	81	15.5	41/100
Bahrain	0.875 VH	HIC	1,110	4.72	76/100
Djibouti	0.509 low	LMIC	63	2.01	44/100
Egypt	0.731 high	LMIC	151	4.36	70/100
Iran	0.774 high	UMIC	573	5.34	74/100
Iraq	0.686 med	UMIC	202	5.08	59/100
Jordan	0.72 high	LMIC	299	7.5	65/100
Kuwait	0.831VH	HIC	1,533	6.31	78/100
Lebanon	0.706 high	LMIC	994	7.95	73/100
Libya	0.718 high	UMIC	381	3.89	62/100
Morocco	0.683 med	LMIC	187	5.99	69/100
Oman	0.816VH	HIC	845	5.33	70/100
Pakistan	0.544 low	LMIC	36	2.95	45/100
Palestine	0.715 high	UMIC		•	•
Qatar	0.855 VH	HIC	2,188	4.18	76/100
Saudi Arabia	0.875 VH	HIC	1,211	5.54	74/100
Somalia	Not rated	LIC	•	•	27/100
Sudan	0.508 low	LIC	23	3.02	44/100
Syria	0.577 med	LIC	89	3.05	64/100
Tunisia	0.731 high	LMIC	223	6.34	67/100
UAE	0.911 VH	HIC	2,192	5.67	82/100
Yemen	0.455 low	LIC	64	4.25	42/100

- Pure economic criteria do not always reflect service development. For example, Iraq and Palestine are classified as upper middle-income countries, but political and social disturbances over the years have not allowed them to fulfil their potential despite having given priority to services for haemoglobin disorders.
- The Human Development Index (HDI) is a statistical composite index of life expectancy, education (expected years of schooling of children at school-entry age and mean years of schooling of the adult population), and per capita income indicators. It expresses human development beyond purely

economic criteria and is a better reflection of the ability of countries to deal with health issues especially where complex services are required. The under-5 mortality rate, in the absence of thalassaemia mortality data and since untreated patients will contribute to this indicator, reflects the HDI index: those countries with a low HDI score are exactly those with an under-5 mortality rate of more than 30/1,000 livebirths. On the other hand, those with an under-5 mortality of <10/1,000 are those with a very high HDI score. There is a very obvious difference between the very high HDI countries of the Arab peninsula and the rest of the countries of the region. Iran stands out in that it has developed advanced services for thalassaemia despite politico-economic difficulties

- UHC service coverage index combines 14 tracer indicators of service coverage into a single summary measure, as a measure of SDG Indicator 3.8.1. Coverage of essential health services is defined as the average coverage of essential services based on tracer interventions. The indicator is an index reported on a unitless scale of 0 to 100, which is computed as the geometric mean of 14 tracer indicators of health service coverage. The tracer indicators are organised by four components of service coverage: 1. Reproductive, maternal, newborn and child health; 2. Infectious diseases; 3. Noncommunicable diseases; 4. Service capacity and access. Examples of a satisfactory UHC index are 81/100 for Cyprus, 85/100 for France, 77/100 for Greece, and 88/100 for the UK. Concerning the services to thalassaemia patients, it seems that countries with UCH index >71 provide free and good quality services (Bahrain, Iran, Kuwait, Lebanon, Qatar and UAE), those with an index between 60-70 seem to have developing services (Egypt, Oman, Jordan, Morocco, Syria and Tunisia), and those whose index is 40-50 have poor services, and patients have to rely on family resources to obtain the needful (Afghanistan, Iraq, Pakistan, Sudan and Yemen representing 51.4% of the region's population). Djibouti, Somalia and Libya are relatively low incidence areas and are left out of this equation. The correlation of services and family spending for services with the UHC index needs further investigation.

- The EMR is a populous region with over 740 million inhabitants. Yet health spending is restricted. Taking the health expenditure per capita as an indicator, only 5/21 countries actually spend more than USD 1,000/capita (serving 7.3% of the region's population); another 7/21 countries spend USD 200–1,999/cap (22.5% of the region's population; 9/21 countries spend ISD 199/cap and these host 70.2% of the region's population.

- Currently many thalassaemia patients are hoping to survive amid protracted emergencies in Syria, Afghanistan, Yemen, and Palestine (Gaza mainly). This includes natural disasters such as earthquakes affecting NW Syria and floods in Libya.

- According to a UNICEF report (2020) 22.5% of children in the general population under 5 years of age were stunted, 9.2% wasted, and 9.9% were overweight. The Arab region also ranked second for adult obesity in the world in 2019, with 27% of the adult population obese. https://www.unicef.org/mena/reports/enhancing-resilience-food-systems-arab-states. Basic health and nutrition issues are of general concern but also reflect on the health of haemoglobinopathy patients, which is why BMI can be regarded as a measure of quality of service as well as of the socio-economic status of a community.

- Migrations and refugees:

Jordan: Four out of 10 people living in Jordan are migrants (https://www.iom.int/countries/jordan). Only 658,000 Syrians are registered in the country, but a total of 1.3 million are estimated to be living outside the camps (UNHCR https://www.unicef.org/jordan). Most (85%) live below the poverty line. Possibly, 185 thalassaemia patients are among them. In addition, there are 2 million registered Palestinian refugees. Of these, 370,000 (18%) are hosted in 10 recognised camps. Also 67,000 Iraqis, 15,000 Yemenis, and 6,000 Sudanese are in Jordan. There are a possible 450 thalassaemia patients from these groups [13].

Lebanon: Lebanon hosts 1.6 million refugees mostly from Syria. Almost 90% are in extreme poverty.

Internally displaced persons: There are 12.6 million internally displaced people (IDPs) in the MENA countries.

Yemen: In this country of prolonged civil conflict, 78% of the population is living below the poverty line, making life even more precarious for the 90,700 refugees and asylum-seekers and 4.5 million displaced Yemenis.

North-west Syria: In north-west Syria, 2.7 million people are already displaced, and 4.1 million people are reliant on humanitarian aid.

Table 2. Overall health status in the region

Country	IMR/1000 livebirths Unicef 2020	Under 5 mortality/1,000 livebirths	Life expectancy	Healthy life expectancy at birth HALE
Afghanistan	42.3	55.5	66.5	53.9
Bahrain	7	8.6	81.6	65.9
Djibouti	44	50.4	66	57
Egypt	12.47	17.5	72.85	60.4
Iran	9.81	11.8	78	66.3
Iraq	20.2	22.6	72.05	62.7
Jordan	12.2	13.2	78.13	65.1
Kuwait	5.86	8.8	80.45	67.8
Lebanon	8.65	18.3	78	66.0
Libya	8.5	30.8	73.25	65.2
Morocco	14.9	16.6	75.20	63.7
Oman	5.8	10.4	80.45	64.7
Pakistan	53.5	58.5	67.34	56.9
Palestine	14.2		73	
Qatar	5.3	6.0	81.73	67.1
Saudi Arabia	5.0	6.4	79.19	65.6
Somalia	60.7	104	59	49.7
Sudan	36.34	50	66.10	59.9
Syria	14.3	20.6	73	62.9
Tunisia	9.89	12.9	76.94	66.9
UAE	4.58	5.0	83.23	67.3
Yemen	40.38	39.3	69.58	57.5

Table 3. Available services

Country	Doctors /1,000 pop	Density of nurses per 1,000 people	MRI density per million population	VNRD as % of total donations	National haemovigilance programme
Afghanistan	0.254	0.4	0.1	40.5	no
Bahrain	0.92	2.5	2.3	99.5	No
Djibouti	0.2	0.7	No data	No data	No data
Egypt	0.45	1.9	No data	14.3	no
Iran	1.58	2.1	3.8	100	yes
Iraq	0.71	2.4	1.63	No data	No
Jordan	2.56	3.3	3.92	50	Yes
Kuwait,	2.29	7.4	5.3	70	no
Lebanon,	3.2	1.7	8.3	No data	no
Libya	1.9	6.5	7.0	No data	No
Morocco,	0.73	1.4	0.7	75	yes
Oman,	1.99	3.9	4.4	100	no
Pakistan,	0.98	0.5	0.22	10.5	yes
Palestine,	No data	No data	5.5	No data	No data
Qatar,	2.49	7.2	11.2	100	No data
Saudi Arabia	2.76	5.8	3.0	40	yes
Somalia,	0.02	0.1	No data	35	No
Sudan,	0.28	0.8	0.32	17	no
Syria	1.46	1.5	No data	No data	No data
Tunisia	1.22	2.5	0.54	34	Yes
U A E	2.88	5.7	10.6	93.5	Yes
Yemen.	0.2	0.8	1.15	41	No

- Data on blood transfusion is from the WHO *Global Status Report on Blood Safety and Availability 2016* (most data from 2013 reports). These figures may have improved since then; but for patients who have all their lives dependency on transfusions the indication is of long-term deficiencies in quantity and quality of blood.
- MRI density / million inhabitants: 1 magnet/million is regarded as the minimum adequacy. This means that Afghanistan, Morocco, Pakistan, Sudan, and Tunisia have no possibility to serve thalassaemia iron measurements, while Iraq and Yemen will also have difficulties to provide machine time.
- Whole blood processed into components in this region is 65% of donated blood, compared to 99% in Europe.

Table 4. Epidemiology of haemoglobin disorders

Country	β-thal carriers	HbS carriers	Expected β-thal patient births/1,000	Expected SCD births/1,000	Known β-thal patients	Known SCD patients
Afghanistan	3.8 (Delacour 2013)	0	0.361	0	5,372	0
Bahrain	2.9	13.8	0.210	6.7	21	600
Djibouti	0	?				
Egypt	1.8	0.35	0.09	0.33	9,258	1,166
Iran	4	1	0.4	0.225	20,777	2,000
Iraq	3.5	0.7	0.313	0.135	17,624	7,804
Jordan[13]	3.5	1.5	0.306	0.319	1,450	216
Kuwait	2.12	1.81	0.112	0.274	475	600
Lebanon	2.3	1.8	0.132	0.288	375	387
Libya	1.5	2	0.056	0.250	?	?
Morocco	1.67	1.76	0.07	0.224	1,100	5,000
Oman (Al Riyami 2001)	2.2	5.8	0.121	1.479	591	8,000
Pakistan	6	0.25	0.900	0.077	50,000	?
Palestine	4	1.25	0.401	0.288	864	131
Qatar	3	5	0.225	1.375	163	354
Saudi Arabia	2.37	4.24	0.14	0.951	8,919	26,000
Somalia	0	rare				
Sudan	3.9	2.4	0.380	0.612	665	?
Syria	5	0.5	0.625	0.131	7,700	1,200
Tunisia	2.21	1.9	0.122	0.3	742	1,526
UAE	3	1.5	0.225	0.281	2,000	?
Yemen	4.4	2.2	0.484	0.605	800	11,000

Because of the scarcity of national registers and the often-small sample surveys, epidemiological data for the region is incomplete. However, even inaccurate data on carrier frequency still indicate that the region is rich in the prevalence of both thalassaemia and SCD. TIF contacts in each country have reported the numbers of patients, and the number with β-thalassaemia exceeds 130,000, while sickle cell patients are at least 60,000, but with data missing for several populations of the region. The numbers alone are indicative of a high burden of disease, which is increased by inadequate case management in many locations, leading to an increase in complications and premature death.

In the EMR, Iran has one of the best records of thalassaemia management, and this is reflected in the age distribution of patients. In an analysis of 1,831 patients in Northern Iran [14] (about 10% of the Iranian thalassaemia population), the mean age of patients was 30 ± 9.7 years (76% TDT). This can be compared to a report from neighbouring Iraq where 65% of patients were <18 years and 35% > 18–35 years (in contrast, in Italy 68% were aged ≥35 years and 11% were aged ≤18 years).

One factor increasing the prevalence of haemoglobin and other hereditary conditions in the EMR is the customary practice of cousin marriage in all countries of the region. This is expressed as the inbreeding coefficient >0·0156 (this coefficient measures the proportion of loci, where the offspring of consanguineous marriage is predicted to receive identical gene copies from both parents).

Country notes indicating latest burden of disease and outcomes:

Afghanistan: The political upheavals have not allowed investment and policies to address the needs of TDT patients. There is lack of information and epidemiological data crucial to policy, services, and interventions. Because of low UHC index, patients of low economic status cannot afford basic treatment, and they often neglect seeking treatment. Children Afghanistan Charity Organisation (CACO) funds the only free thalassaemia paediatric clinic in Afghanistan, which treats more than 300 patients who need blood transfusions and other treatments. The clinic is part of Mazar-e Sharif Hospital. Most of thalassaemia patients have limited access to regular and safe blood transfusions (Qaderi et al 2021) [15]. Around 300 new affected births per year are expected and the figure of 16,500 existing patients was quoted by NGO LSOA (Life Saving Organisation of Afghanistan), which was active in the care of thalassaemia patients in 2012 (new information suggests only 5300 known patients). There is no prevention programme. The burden of disease on both family and patients is highest, but health authorities so far provide very little to relieve this effort.

Bahrain: Sickle cell is mainly prevalent in this country with a haemoglobinopathy programme going back to 1984. This includes a prevention programme based on obligatory premarital screening. In a recent analysis (Bahram, 2023) [16], 67% of at-risk couples decided to proceed with their marriage, and 60% of at-risk couples have a positive attitude toward IVF with PGD. Concerning patient care, a recent survey of caregivers noted that 14.8% reported catastrophic health expenditure and other practical difficulties in providing care for sickle cell patients, including dissatisfaction with hospital facilities and insufficient healthcare services. This is despite the country having high HDI and long-term service development (Al Saif, 2022) [17]. These are suggestive that quality of care and patient satisfaction are not simply a matter of economics. Patient centred care requires staff education as well as organisation of the patient journey.

Egypt: From a sample of 200 patients with beta-thalassemia major (mean age 24.6840± 5.30761) attending one clinic, 48% had a ferritin level >3500 ng/mL with a total of 72.5% above 2500 ng/Ml. According to BMI measurements, 23.5% were underweight and 9.5% overweight. There is need to pay attention to iron overload in Egypt reference centres (Ibrahim, 2023) [18] as the effect will be an increasing complication rate and a threat to life. In another study involving 30 young thalassaemia patients (ages 14.77±2.45), LIC was 13.40 (8.86–25.00) mg Fe/g dw, while the median (IQR) cardiac T2* was 18.7 (2.1–17.1) ms. The β-TM patients in this small study had no clinical heart disease with a mean EF% and FS% of 65.7 ± 8.41 and 36.63 ± 6.47, respectively, yet the longitudinal systolic strain values by STE were significantly lower compared to standard control values, which might reflect an early LV dysfunction. In this study also iron overload is evident (Tantawy et al, 2022)19.

Less than 1% of the Egyptian population donates blood, according to the World Health Organization (WHO). In 2018, 28% of units were from family replacement [15]. This inevitably results in low pretransfusion haemoglobin in TDT patients.

In a survey of thalassaemia patients aged from 2–12 years (mean 11.34), 9.17% already had hypothyroidism, 7.5% had disturbances of glucose homeostasis (not diabetes), 6.66% had hypoparathyroidism, and 66.7% were regarded as malnourished based on Z-scores of BMI. These results may seem similar to those of other countries, but the age group of patients is much younger; this indicates poor management, which is confirmed by a very low pretransfusion haemoglobin (6.82g/dl mean, 7.5 median) and a high serum ferritin (mean 3631) [16]. Similarly analysing the result of heart and liver iron in children (10.8 ± 2.4 years) by MRI measurements, heart was relatively free of iron, but 80% had moderate to severe hepatic iron load [17]. Age distribution of patients is relatively nonhomogeneous, with 39% of patients between 10 and 20 years of age and 16% younger than 5 [18].

These reports from reference centres in the country, are indicative of a yet inadequate patient care system with an increasing disease burden as patients survive to adulthood. Furthermore, economic difficulties on a national

level did not allow the purchase of chelating agents during several months of 2024; this is bound to increase the disease burden of the 10,000 or so thalassaemia patients living in Egypt, and results will become obvious during the coming years, even if the deficit is corrected. Indeed, patient reports to TIF confirm frequent interruptions in the supply of chelating agents. This can explain the early onset of iron overload.

A premarital screening programme was initiated this year and has already reached almost one million individuals (Dr Mona Hamdy, personal communication). From the first 3,513,642 cases screened, 1.77% are β-thalassaemia carriers and 0.35% are sickle cell carriers, which are much lower results than those reported from surveys over past years. Raising public awareness for a prevention programme in a country of over 100 million population, an adult literacy rate of around 75%, and where almost 60% live in rural areas is indeed a challenge. There is a marked cultural preference for consanguineous marriage (30–40% of all marriages), as well as a high rate (59.5%) of a positive family history of β-TM [18]. This provides an additional target for screening to hopefully yield many more carriers at preconception level. The Ministry of Health has identified 302 medical centres nationwide to conduct analyses, and in each there is a counselling office

Egypt has for decades required a high share of out-of-pocket (OOP) health spending as well as a fragmented health system with inefficient resource allocation, and low-quality and low utilisation of public health sector services. A universal health coverage (UHC) policy and a universal health insurance (UHI) law were implemented in 2019, with a phased implementation plan across six different geographic regions in Egypt, with the aim to cover the entire country by the end of 2032. This partial implementation has not yet reached many thalassaemia patients, and it is difficult to assess its effect.

Iran (Islamic Rep. of): Iran is also a country with a high burden of β-thalassaemia. Over the years services have developed and experienced has been gained in both disease prevention and management. Centres of expertise have developed in main urban centres where the condition is most prevalent.

Survival and other outcome indicators reflect the quality of care in this country. However, published figures may not represent the total thalassaemia population in a country. In an analysis of 1,831 patients in Northern Iran (about 10% of the Iranian thalassaemia population), the mean age of patients was 30 ± 9.7 years (76% TDT) [14]:

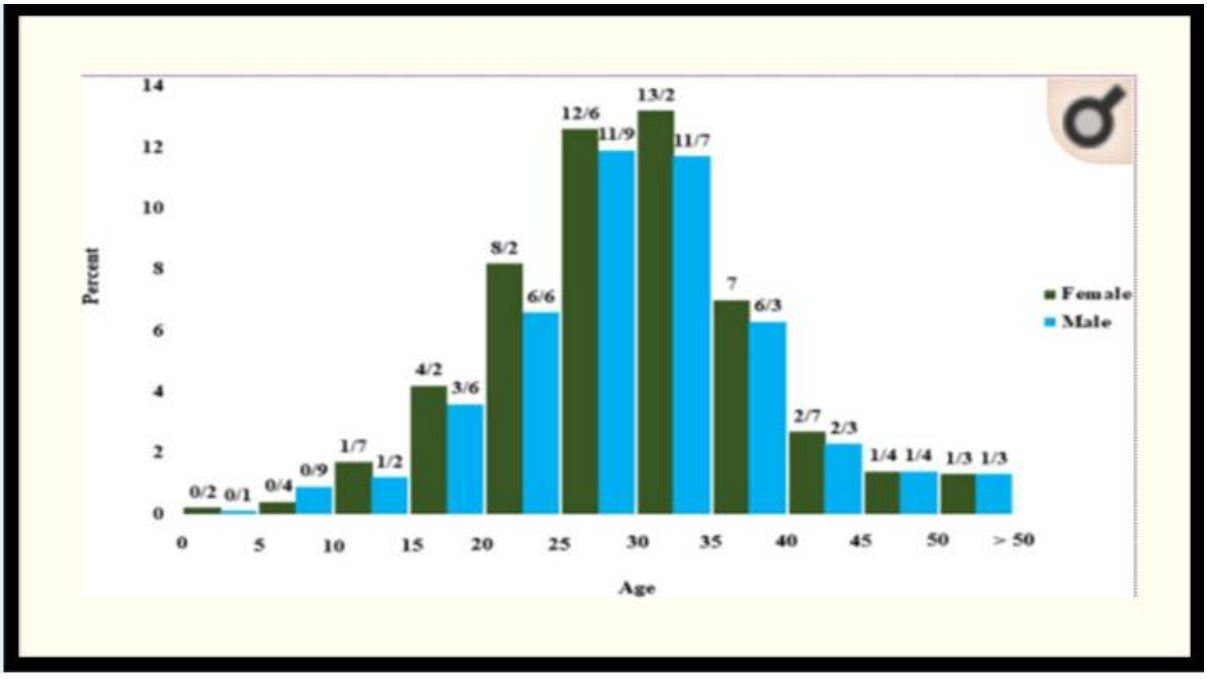

Figure 1. Distribution of 1,385 transfusion-dependent patients by age and gender, Mazandaran Province, 2016

In this group cardiac iron was measured by MRI was similar to that found in reference countries. However, liver iron was much higher in that only 14.6% had an LIC <3. In another major centre, a review of endocrine complications in 2019 [19], found much higher incidences of hypogonadism and bone disease than in reference countries, while diabetes and hypothyroidism were much the same.

A report from Tehran said that all Thalassemia Clinic patients undergo annual examination for cardiac and liver iron load by liver and heart T2* MRI. Whether this practice is followed by all treatment centres is not reported.

In a much larger cohort [20] of 5,491 patients from various parts of the country, the mean age was only 23.8 ± 11.3 years (71.7% TDT).

Concerning clinical outcomes

In a Tehran centre, of 90 patients with the mean age of 20.5 ± 7.6 years, 56.7% had a serum ferritin in the low to normal range, 25.6% had normal LIC (>above 6.3 ms), and 40% had mild (2.8-6.3 ms); myocardial iron was normal (>20 ms) in 61% [21]. These results are better than many other high HDI countries and approach achievements in the very high western group of nations. These good results are confirmed in the reduction of age standardised deaths between 2010 and 2019 (0.17 to 0.1). Services are uneven, however, and the Sistan Baluchistan province seems to present the lowest performance [22].

In another study from Iran, features of QoL correlated to the patients' laboratory findings, such as liver function and fasting blood sugar, as well as education, indicating that quality of care and outcomes of treatment play a significant role in estimating the quality of life and the burden of disease [23].

In 2016 [24], the annual cost to treat each patient with major thalassaemia was estimated to be USD 8,321.8, according to World Bank data. GDP/capita in 2017 was USD 5,520.3. Average family income would be less, and so universal health coverage supports patients, even though access to some services (such as MRI) is limited. The cost of preventing the birth of a major thalassaemia patient through screening was calculated to be USD 32,624. In comparison, the cost of managing a patient with thalassemia major is about USD 136 532 per year [24]. Iran has attempted to reduce birth incidence while upgrading patient care despite an economic embargo which is limiting its ability to import medications.

Iraq: The total number of patients in Iraq, according to reports communicated by the national Thalassaemia Committee, based on reports from the various treatment centres in the country, there are around 17,624 thalassaemia patients, of which 8611 are thalassaemia major. In addition, 7,800 patients suffer from sickle cell syndromes. Programming at central level for thalassaemia services is under way and patients receive support for their treatment.

A cohort of 150 patients from Dohuk was studied [25]. This is a young cohort representing about half of the attendees, so they present with low ratios for organic complications like heart disease and diabetes. The high mean levels of ferritin and the high positivity rate for HCV (35.3%) are danger signals for this group if management is not upgraded soon. These results are representative of many patient outcomes in which services meet with obstacles in their development, either economic or political. A study published in 2020 had the following findings:

- The median age of the enrolled patients was 13 years (range: 1–35 years), and only 2.0% were 30 years or older. In Iraq the bulk of β-TM patients are children or adolescents. This confirms an older report from a peripheral unit where the higher percentage of patients were at age < 10 y. (47.2%) [26]
- The mean pre-transfusion haemoglobin was 8.6±1.0 g/dL, and it was maintained at ≥ 9.0 g/dL in 38.7% of patients.
- Thalassaemic faces were noticeable in around half of the patients (50.7%).

- The median serum ferritin was 2762 µg/L, with 53.3% of the patients having serum ferritin in excess or equal to 2500 µg/L.

This is evidence of suboptimal management, which may be worse in other parts of the country, confirming other studies which point to an uneven level of care.

In a survey of 242 TDT patients, from Sulaymaniyah (northeastern Iraq) [27], 83 patients were TDT, and the rest 159 NTDT. The mean age was 17 ± 10.2 years, with a range of (1.4–54 years). Of the TDT patients, 65% were <18 years and 35% > 18–35 years, and the following complications were listed:

- Bone disease 75.9%, growth retardation 44.4% (in those <18years), hypothyroidism 13.4% (in those >18years), diabetes 6% (in those >18 years), pulmonary hypertension 7.2% (in those >18 years).
- In the same study, 159 cases of NDTD patients were studied with reduced incidence of bone deformities, osteoporosis, growth retardation, and diabetes.
- There was an increased incidence of hypothyroidism (16.8%) and pulmonary hypertension (11.3%) including isolated cases of thrombosis, leg ulcers, and extra-medullary haemopoiesis.
- Serum ferritin was <1000µ/l in 31.3% of the TDT group and in 76.6% of the NTDT (32% of these were regularly transfused). These results indicate a good level of care in this region of Iraq.

A more recent unpublished report of the **TIF Arab Thalassaemia Associations Forum (TATAF)** noted:

- Pre-transfusion haemoglobin is <7g/dl in 35% of patients, 7–9g/dl in 50%, and only in 15% of patients is it kept over 10g/dl.
- 47% of patients experience various transfusion reactions.
- 1% are infected by transfusion transmitted infections (TTI).
- MRI for iron measurements is not available.
- Complications recorded are in the heart (30%), hypoparathyroidism (13%), and osteoporosis (14%).
- Poor compliance to iron chelation is witnessed generally.
- Peak age of patients is between 16–25 years.
- Secondary education in patients over the age of 16 years is completed by 6.6% and university by 2.8%.
- Causes of death are due to infections (38%), cardiac complications (74.5%), and severe anaemia (4.2%).

In a recent study of the cost of thalassaemia management, Lafta et al. assessed a cohort of 214 TDT patients in Baghdad, and they estimated direct medical costs at USD 6,815/year and indirect costs at USD 3,995, adding up to USD 10,810/patient/year [28]. This study noted that most of the healthcare services for thalassemia in Iraq are almost free, which means that the main burden will be on the governmental health expenditure. However, more than a quarter of the sampled families reported that, in addition to the physical and social burden, they are suffering a significant economic burden due to the frequent shortages of medicines [28].

The impression is of a country that has central planning for thalassaemia services, including prevention, with financial patient support and progress towards UHC. However, services have not reached an equitable level either in patient care or disease prevention (without prevention, 1,132 new affected patients are calculated to be born annually). The country is paying the price of successive conflicts and political turmoil. Nevertheless, the existence of national planning and an expert national advisory committee encourages progress in Iraq so disease burden should reduce in the coming years.

Jordan: Despite governmental attentional to thalassaemia over many years, caregivers in Jordan experience financial burden associated with regular hospitalisation and unpaid leave for employed mothers [29] and the need for psychosocial support is emphasised. These remarks are in keeping with the country's UHC index and other indicators. Furthermore, 4/10 people living in Jordan are migrants [30], 1.3 million are refugees from Syria, while 2 million are registered Palestinian refugees, and others from Iraq, Yemen and the Sudan. Some 81% live in urban areas outside of refugee camps, and 85% of these live below the poverty line. Of these refugees, 82% were able to access health services while the rest were unable to afford fees and increasing health costs. This is bound to affect thalassaemia patients [31].

According to the National registry, in 2017 there were 1,450 thalassaemia patients in the kingdom [32]. According to the estimated carrier rate (2–4%, mean 3.5%), there may be 76 new affected births each year if no prevention. So, a further 500 new cases may have been added in the last seven years, even though ongoing premarital counselling may have reduced this (no reports on the effectiveness of prevention have been recently published).

Effectiveness of clinical care is still to be improved. For example, in the Alabbadi report [33], the pre-transfusion haemoglobin averages at 7.75g/dl and the serum ferritin is still above 2500 ng/l.

The average annual cost was estimated to be JOD 2,674 (USD 3773.7) for a single thalassaemia Jordanian insured patient and JOD 4,627 (USD 6,529.8) for an uninsured patient. The annual cost for a non-Jordanian patient was estimated at JOD 4,751 (USD 6,704.8) if insured and JOD 6,651 (USD 9,386.2) if uninsured [33]. The Jordanian Ministry of Health (MOH) is solely responsible for treating these patients from the pre-marital programme until required medications, regardless of their nationality. This imposes an extra burden to the Jordanian health budget, as the inflow of refugees from Syria and Palestine continues. Such population movements make prevention also difficult to implement efficiently. A mandatory National Premarital Thalassemia Screening Program was implemented in Jordan in 2004, however, results in terms of affected births prevented are not known.

Kuwait: This is a high-income country with well organised health services, which are reflected in all indices such as life expectancy of all age groups. The healthcare system is state-funded, with free care for citizens via the Ministry of Health (MOH). Expatriates (approximately 70% of the population) pay an annual fee for a mandatory public health insurance card, accessing care through public and private facilities. In this way all haemoglobinopathy patients are covered with no out-of-pocket expenses.

The carrier rate is 1.2% for β-thalassaemia, and 1.99% for sickle cell disease, including another 0.5% for other variants, according to the premarital screening programme. The ongoing premarital screening programme aims to reduce at-risk marriages.

There is a National Thalassaemia Committee supported by the Ministry and Parliament, and it is responsible for the development of policies and services for these disorders. Currently there are around 500 thalassaemia patients and 600 with SCD. The blood supply is adequate and safe; the Central Blood Bank is AABB accredited for many years and is state-of-art. All three chelating agents are provided. Multidisciplinary care is not well organised. Patients will be seen by a specialist when necessary (i.e., after a complication arises), MRI for iron measurements is available but whether all patients are covered is not clear. HSCT is available in the country and thalassaemia, as well as SCD, have been transplanted.

One challenge is engaging patients and involving them in thalassaemia-related activities.

Lebanon: Lebanon is another Middle East country with a long history of thalassaemia control. The average age of a cohort of 228 thalassaemia patients treated at the Chronic Care Centre in Beirut is 32.1 years [34]. This alone is indicative of improved patient care in this country. 54.4% were employed and university level was reached by 26.3% subjects, 7.9% reached high school level, and 32.5% have a level less than high school. The existence of

a national reference centre in the country contributes to better outcomes despite political and economic difficulties.

Despite this effort, Lebanon is also host to 1.5 million refugees from Syria, most of whom have to rely on out-of-pocket spending even for primary care services. Medicine and health are amongst the top five reasons for a family to resort to debt, according to a UNHCR report [35]. The fate of most patients with chronic disorders like haemoglobin disorders is not known. A minority of thalassaemia patients, 138, were cared for by a clinic in the Bekaa Valley created by the Medicines sans Frontier, which catered for children up to the age of 14 years. This charity service followed a treatment protocol, maintaining a pre-transfusion haemoglobin of 9.24g/dl on average and an average serum ferritin level of 2659ng/dl (range 424–6020ng/dl). Over a period of 5 years and having access to the three chelating agents, the clinic was able to maintain monitoring parameters to safe levels. MRI T2* was also possible for 19 patients. This outcome in a relatively resource poor setting is a blessing for this minority of patients (Issa L et al. Abstract, 2023 TIF International Conference). The plight of the migrant and refugee populations in the Middle East is a major concern.

As in Jordan, the ongoing prevention programme is likely to be hampered by the influx of refugees and the disease burden is likely to increase.

Morocco: Local experts suggest that that there are 1,100 thalassaemia patients with a mean age of 16 years, and up to 5,000 SCD patients, but there is no national registry to confirm these figures. Concerning patient care, 95% are treated in six referral centres located in public university-run hospitals, making up a total of 17 thalassaemia treatment centres. Each of these centres reports yearly to the Health Ministry, which regards patient numbers as accurate. Treatment is free. However, access to chelating agents is very difficult and TIF receives complaints from patients. The Ministry of Health has discussed a poor supply of infusion pumps but claims no shortages, rather poor prescribing by the doctors.

A virtual meeting between the National Ministry of Health, local experts, TIF, and representatives of the Arab Forum took place 22 September 2022. The result of the meeting was recorded in a Memorandum of Understanding between TIF and the Ministry of Health, which expressed their joint desire to collaborate in the areas of prevention and control of haemoglobin disorders, through strengthening the professional capacities of medical and paramedical personnel from the Ministry of Health in this area. The MoU recommended the creation of a joint multidisciplinary expert advisory committee to make suggestions on prevention, public awareness, preparation of national treatment guidelines, and the organisation of various activities, including conferences, workshops, forums, etc.. The lack of prevention is likely to continue increasing disease burden along with the increasing complication rates in the affected patient population.

Further meetings with the Ministry representative and the main clinicians in charge of thalassaemia in Rabat have continued (latest in November 2025), and concerns were discussed as well as plans to collaborate with TIF for solutions. One main issue arises from the fact that there is now a growing adult population of patients. Until now all thalassaemia patients were treated in paediatric units. According to Moroccan regulations, these departments should treat up to the age of 18 years. Both patients and paediatricians report concerns since adult haematology departments are not ready to offer services. Proposed strategies include the training of adult haematologists and adult patients in self-management. The aim is to achieve smooth transitioning to adult centres.

There are 16 small support associations without a strong voice, so one objective is to encourage unity. A survey has been organised by the Ministry concerning services and patient adherence. Results will be shared.

It has been decided to organise a national workshop in late March 2026.

Oman: A recent analysis of liver function and iron load parameters is revealing of current trends in patient care in Oman. In this study of 91 patients, the median age (IQR) of the subjects was 33 (9) years, and BMI was 23.8

(6.1) kg/m2. Despite regular chelation and blood transfusions, there was a significant iron overload with rising SF levels and LIC measurements by MRI. The median SF levels rose from 1309 at the start of chelation to 1881 ng/mL, which was statistically significant. There was also a comparable and statistically significant rise in the LIC from a median level of 10.2 to 14.2 g/dry wt. of liver. However, with sustained patient education and compliance monitoring, it was encouraging to see the results of sustained chelation efforts, with the median LIC decreasing significantly to 7 g/dry wt. at the last follow-up [36]. These results do not differ significantly from those of advanced centres of Europe and so there is an accepted good level of care at least in one University reference centre in the country. In another recent study of 187 patients with β-TM with a median follow-up of 24.9 years, those born after 1980 had a lower risk of death (P = 0.005), hypogonadism (P = < 0.0001), and cardiac complications (P = 0.004), while overall complication rates were similar to advanced centres [37]. State support and universal coverage help in achieving these good results. Family support has also contributed greatly to the quality of life of thalassaemia patients [38].

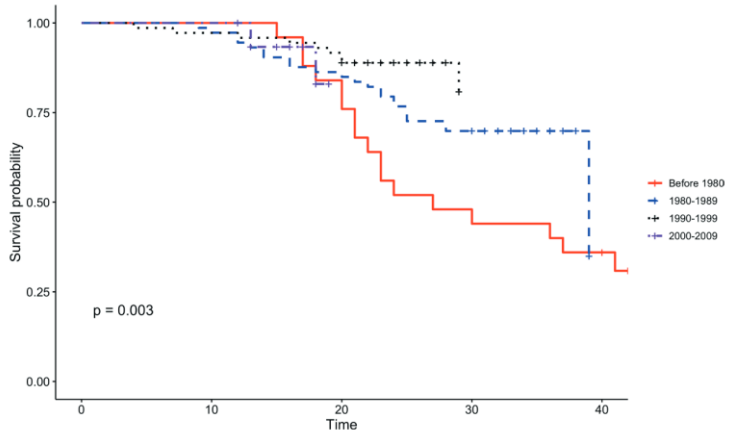

Figure 2. Overall survival according to the birth cohort

These are acceptable results, and coupled with the fact that there is ongoing prevention, the disease burden is likely to improve over the years. In one report 71.5% took a premarital screening test before marriage, even though the test is not compulsory and is offered on a voluntary basis [39]. In this same study, 23.3% cancelled engagement upon receiving positive screening results, while 13% of participants continued with marriage for either emotional or family reasons.

Pakistan: This is a low HDI country with a high burden of thalassaemia, and a challenge to access services. A study of 21 parents of children with thalassaemia found there was a low level of education and knowledge. Only three (14.28%) parents declared that they knew that they carried a genetic trait, indicating also poor counselling. Challenges that were physical, socio-emotional, financial, and familial were detected in this small group [40]. Despite poor resources, the country has done significant work to improve its thalassaemia status. This includes establishing reforms of private philanthropic organisations which offer services to the majority of patients [41]. However, there are no standard management protocols, although prevention programmes have been initiated in most provinces [42].

Patients and families are not adequately supported by the healthcare system. In a recent study of 100 thalassaemia patients and their families, the total expense incurred on treatment by the end of the month was PKR 5000–10,000 (USD 31-62) in a government run hospital, while in the private sector the total expense incurred on treatment by the end of the month was around PKR 80,000 (USD 500). Around 37% of families have an average monthly income of PKR 525,000 (USD 150) only, and as a result they spend their income to satisfy medical expenses, while 31% compromised on their children's education expenses, and 23% curtailed the health expenses of their other children [43]. Apart from the out-of-pocket expenses which often exceed income, caregivers' lack of knowledge leads to delayed diagnosis and poor outcomes. To further add to the burden,

there is social stigma to deal with and poor response to prevention because of ignorance and high consanguinity rate, which maintains the birth of around 5,000–6,000 new cases each year [44].

Such a system of poor support is coupled with poor clinical service, and so increasing complication rates and early mortality. In this setting charity organisations have been formed to support patients by developing their own clinical services, which include blood banking, transfusion units, and free or subsidised chelation. The quality of these independent services is variable, but may also be of good standard. The result is an uneven level of patient care and outcomes. A saving grace comes from a prevention programme, which was initiated in the Punjab and is currently expanding in the other provinces. However, national figures on prevention are not yet available and despite efforts the bulk of the population is not reached [45]. This lack of adequate investment means the burden of thalassaemia is likely to increase in the coming years.

In recent years there has been increasing use of thalidomide to either reduce or even eliminate transfusion requirements in both TDT and NTDT patients. This is meant to support the lack of adequate and safe blood. Reports from this country and other Asian settings indicate that the treatment is effective (in around 60% of patients) and with a good safety profile. Recently, there was a National Dialogue on repurposing this drug in the management of transfusion-dependent thalassaemia (Islamabad, 22 October 2025). Haematologists from India and Bangladesh shared experiences with colleagues from Pakistan. Decisions include conducting long-term trials to assess efficacy and safety, and also exploring combinational therapies with other HbF inducers or gene-based strategies.

The Central Government has drafted "The National Thalassemia and Other Genetic Disorders Prevention and Genomic Health Policy Pakistan 2025–2035". This document has comprehensive suggestions for a nationally coordinated prevention programme. Improvements in patient management are mentioned but given less emphasis and many aspects are not discussed. Prof Hassan Zaheer, a close collaborator of TIF, has made extensive comments on the document and has requested TIF to also assess and offer additional suggestions. TIF has reviewed the document and added a few comments concerning the need for better coordination of patient care. TIF feels that a nationally coordinated policy for thalassaemia is a major step forward for Pakistan and has the potential to improve the fate of thousands of patients.

Palestine: These are self-governing territories under constant political and economic pressure and the danger of armed conflict (which materialised in 2023–2024). A recent quality of life study indicated poor scores in all domains in 104 patients in the West Bank and Gaza [46]. This is a reflection of both social conditions and clinical services in a country offering the best possible services under the circumstances, having given priority to haemoglobin disorders. In a 2021 study of 309 patients with b-thalassemia, the average age was 23.4 ± 10.4 years, which is comparable to many countries outside the developed world. However, the pre-transfusion Hb level was 8.4 ± 1.4 g/dl, and 73.1% had iron overload with serum ferritin (SF) levels ≥ 1,000 µg/L (mean ± SD = 3,175.8 ± 3,378.8µg/L, ranging 75.5–17,450.0). MRI was not available to measure iron in heart and liver [47]. These are incomplete data, yet they reflect a population of patients who will have increased complications in later life and confirms the findings of poor quality of life referred to in the first study. In the 2nd quarter of 2023, Gaza became a war zone, and the fate of the over 300 thalassaemia patients is yet to be known since communication was lost. TIF is aware that medications have reached the patient population only sporadically, blood transfusion is a problem for many since the needs of casualties are given priority. In addition to deteriorating patient care, war casualties have been reported. At least 27 patients have reached Egypt, but their fate is also in doubt. Both blood supply and iron chelation are in doubt in this war zone which is currently expanding. At the time of writing (December 2025), despite a shaky truce, the situation of thalassaemia patients along with all the Gaza population is unchanged and there is a constant treat to life.

TIF has been asking for help from WHO (EMRO) and many involved NGOs with little influence on any substantial help reaching our patients. This is a sad and frustrating situation which we believe can only be resolved by

international intervention at the highest governmental level. However, compassion takes second place to the need for political victory in such conflicts.

Qatar: This is a high-income country, and if income was the only factor, it would be expected that patient care was of high quality. Thalassaemia patients are estimated at 163, and SCD patients are around 550 in a population of over 3 million. Comprehensive services are offered for both paediatric and adult patients. In a study of 2018, LIC was assessed by hepatic R2 MRI, an indication of the availability of this technology. However, 35% of patients (young patients' age mean: 21.7 years; range 9–35 years) were found to have an LIC ≥ 15 mg/g/dw and high serum ferritin (4,488 ± 2,779µg/L); this is a reflection of unmet needs even in a high-income setting [48].

In Qatar, premarital screening was initiated in 2009 for thalassaemia, sickle cell disease, classical homocystinuria, cystic fibrosis, as well as STDs, including hepatitis B, hepatitis C, rubella, and HIV/AIDS, while optional screening is provided for spinal muscular atrophy (SMA). Births with β-thalassaemia are expected to be reduced based on a predisposition to cancel marriage in the case of incompatible screening results [49, 50].

Saudi Arabia: This is a high-income country with a high burden of haemoglobin disorders, especially SCD. The most recent estimates are of about 9,000 β-thalassaemia patients and up to 26,000 SCD patients in the country. Saudi Arabia provides free access to healthcare services to both Saudis and non-Saudis working in government sectors. In addition, the Saudi Ministry of Health (MOH) has requested the private sector to contribute more to health spending through alternative financing and delivery systems, specifically health insurance. To reduce the financial burden, the government has implemented Compulsory Employment-Based Health Insurance (CEBHI), for major enterprises employing more than 500 employees. This type of insurance is paid by employers for health-related costs and covers all private-sector employees. The National Health Insurance System (NHIS) is a programme designed by the government so a country can achieve UHC. The NHIS is used as a tool for basic health needs for everyone who has paid premiums, independently or collectively [51].

The importance of the insurance coverage is that an estimated 44% of the population are non-Saudis. All non-Saudi employees in the private sector are now required to get health insurance under the Cooperative Health Insurance (CHI), which includes their dependents. Most of these employees originate from other Arab countries or the Indian sub-continent, with a high prevalence of haemoglobinopathy genes. These need to be treated and costs are high. A recent study estimated the direct cost of TDT at USD 28,097.24 per patient-year, a significant cost burden [52].

Issues concerning the adequacy of clinical services can be identified reflecting quality of care and impacting disease burden to patients, but reports are few:

Underweight (BMI) ranges for 20–40% of the patient population (mainly <20 years of age) [53, 54]. This is a better performance than many countries outside the west.

Blood supply depends to a great extent on public awareness as well as on organised blood drives; it is an issue of community involvement. A 2021 study from the eastern provinces indicated that for 158 patients over a three-year period, 14,508 units of packed red cell units were ordered, and 9,530 units were received, that is, 34% of demanded units were not supplied [55]. This inevitably will impact Hb levels in patients and thus long-term outcomes, and patients have reported to TIF pre-transfusion Hb that is usually 6-7g/dl. In addition RBC alloimmunisation rate among SCD patients was 18.6%, and the rate among thalassaemia patients stood at 19.5% in a recent publication [56]. This seems average for Middle East countries, where rates ranged from 2.87 to 30% among transfused-dependent patients and comparable to Iran where 24.7% of TDT patients were positive for alloantibodies [57, 58]. Italy reports alloimmunisation around 3.1% to 5.2%, and up to 11.4% [59].

Despite issues like these, the Kingdom is adopting policies for "Health Sector transformation through Model of Care strategies", which include the development and implementation of dedicated blood disorder programmes (Dr Hatoon Ezzat, personal communication).

The premarital screening programme, established in 2004, has now screened over 5.5 million partners. This programme was supported by an educational programme for counsellors. The screening revealed that 1.38% are β-thalassaemia carriers and 4.25% are sickle cell carriers. The at-risk marriages have reduced from 3% in 2004 to 85% in 2020. The programme includes a newborn screening programme (mainly for SCD and other variants, including alpha thalassaemia).

A registry of inherited blood disorders (IHBD) has been created, and has comprehensive data on 23,481 (mainly SCD) patients and aimed to reach 65,000 by the end of 2024. This is a model programme, which can be imitated by other countries of the region.

Syria: This country has been subject to prolonged conflict, which has disrupted services and prevented development, severely affecting the prognosis of thalassaemia patients. The prevalence of the condition is significant. with approximately 5% of the population carrying the beta thalassaemia gene. The National Thalassaemia Programme in Syria was established in 1997, aiming to optimise both patient care and prevention. The Syrian conflict, since its eruption in 2011, had particularly detrimental effects on thalassaemia patients, especially those who were displaced. From March 2019, a total of 4,677 patients have been registered to receive chronic blood transfusions in the areas under Syrian government control. However, all services have suffered, and this includes the loss of trained medical and nursing staff. In the city of Homs, before the conflict the median age of patients was 14 years, whereas in recent years during the conflict the median age is 10 years; economic sanctions imposed during the conflict disrupted the supply of medications, and a significant percentage (15.1%) of the patients had not received any chelation for six years, spanning from 2012 to 2018, due to their being trapped in the armed conflict areas. The median SF concentrations of the patients significantly increased from 3274 ng/ml in 2009 to 4672 ng/ml in 2019 (P < 0 0001). Iron overload and poor outcomes are to be expected in this country [60]. A new government was established in March 2025. One effect is that sanctions have been lifted and so it is hoped that despite many health problems awaiting solution, at least the supply of medications may soon become uninterrupted. Although there is hope for the future the latest report from Latakia up to April 2025 indicated that thalassaemia patients exhibit high rates of iron overload and under-vaccination, reflecting challenges in disease monitoring and preventive care [61].

Patients are currently recruiting especially in cities like Hama and Homs under a group called "The Syrian Thalassaemia Youth Team". They have gathered information and located 4,451 patients in various cities. They have requested TIF assistance and TIF is investigating avenues to offer assistance and promote care.

Tunisia: The most recent estimates are of almost 800 thalassaemia patients and 1,500 SCD in Tunisia. Blood transfusion is adequate and all three iron chelating agents are available. Despite this, a study carried out on affected patients affected shows that for them, this chronic haemoglobinopathy is a disability hampering their physical activities, their social integration, their academic results, and their emotional life [62]. This is an indication that quality of care is still lacking. In one study, published in 2017, of 100 transfused thalassaemia patients older than 10 years (16.1 ± 5.2), the cardiac T2* was under 20 ms in 30% of patients and under 10 ms in 21% of patients. Abnormal liver iron concentration (LIC >3 mg/g dw) was found in 95% of patients. LIC was over 15 mg/g dw in 25% of patients [63].Information following this publication has been patchy but currently patient outcomes seem to be similar. *Guidelines on Management of Thalassemia Syndromes* were published by Prof Mohamad Bejaoui in 2014 and a second edition in 2019-2020 based on international guidelines.

The healthcare system in Tunisia includes universal coverage via the CNAM for most citizens through a tax-funded system. However, a conference report on 121 patients with beta Thal, in five centres, with an average age of 27 years (17–66years) found that less than half had social security - medical coverage (Dr M Achour, Dr S Mahjoub 2022). Average ferritin was 3889.3 ng/l (96–21325) and 83% of patients have ferritin level > 1000ng/l.

The average age in 2022 was 20.5 years, with only 5% above 25 years. These are indications of unmet needs in thalassaemia care in this country.

Premarital screening has been mandatory since 1994. Prenatal diagnosis has been available since 1991, but uptake is poor.

United Arab Emirates: The UAE is a high HDI country with long standing services aiming to serve thalassaemia patients and to prevent disease. The latest estimate is of 2,000 thalassaemia patients of which half are expatriates who make up around 90% of the population. The majority come from the Indian subcontinent and fewer from the Far East and Egypt. These are ethnic groups rich in thalassaemia genes. In a recent study [64] of 255 thalassaemia patients, 65.5% were non-UAE nationals; 73.3% were in the > 18 years age group, while 90.6% had thalassaemia major. The UAE has a mandatory health insurance system ensuring all citizens and residents have coverage. Nationals enjoy free public care, and expats require employer-sponsored plans or purchase private plans, which is mandatory since 2025.

Clinical services are well organised.

In a study of 137 TDT (median age of 12 years (range 2–49 yrs), severe iron load in the liver (LIC) was noted in 16.1% (≥15 mg/g dw) and normal/mild LIC in 62% (<2-7 mg/g dw). T2* of the heart was normal in 83.9% (>20ms) and sever in 6.9% [65]. These results are improved compared to other countries of the region, especially compared to the results of Qatar with a similar age range of patients.

The mean total annual direct medical cost per patient was AED 131,156 (95% CI: 124,735–137,578) = USD 307,963.89, of which ICT was the most expensive component, followed by blood transfusions. The median (IQR) household annual income was AED 96,000 (USD 26,136.57). These high costs reflect the wealth of the country.

There is an ongoing premarital screening programme. In one report, 0.31% of couples screened were declared high-risk, but all of them had married each other, despite the known "incompatibility status" [66].

Yemen: Yemen, a nation of approximately 42 million, is an impoverished country due prolonged civil war. Haemoglobinopathies pose a significant health concern. β-thalassaemia trait is estimated at 4.4%, with around 800 thalassaemia patients and about 11,000 SCD. In a study of almost 500 patients, 50.4% were younger than 10 years [67] This in itself is an indication of the effects of armed conflict on chronic conditions such as thalassaemia. Yemen is classified with a HDI index of 0.470 (low). Yemen needs much support and a permanent peace.

Conclusions

The countries of the region have considerable variability in economic and social development. However, as far as services for haemoglobin disorders are concerned, even high HDI countries are reporting results which need improvement, based on indicators such as iron overload. The large refugee population in the region further complicates the prioritisation of haemoglobin disorders. Despite some countries being in the high resource group, the overall picture of the region requires attention and policies which may favour these chronic patients. In the high resource states mainly of the Arab peninsular, there is compulsory health insurance for the large migrant population.

WHO South-East Asia Region (SEAR)

Introduction

The WHO South-East Asia Region is home to over 2 billion people, a quarter of the world's population. There are 11 states: Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste. WHO has country offices in all of them. The WHO South-East Asia Regional office is based in New Delhi, India.

With the region prone to natural disasters, disease outbreaks, and health risks from climate change, one of WHO's key priority is to strengthen emergency risk management for sustainable development. Promoting universal health coverage – health for all – and building robust health systems are key priorities. The Region has eight flagship priority programmes aligned to WHO's global triple billion goals and the UN Sustainable Development Goals:

1. Maternal and Child Health: to accelerate the reduction of maternal, neonatal, and under-five mortalities.
2. Eliminate Measles and Rubella by 2023.
3. Universal Health Coverage: Continue progressing towards UHC with focus on human resources for health and essential medicines.
4. Neglected Tropical Diseases
5. Noncommunicable Diseases: Prevent and control noncommunicable diseases through multisectoral policies and plans, with focus on "best buys".
6. Antimicrobial Resistance: Further strengthen national capacity building for preventing and combating Antimicrobial Resistance.
7. Health Emergencies: Scale-up capacity development in emergency risk management in countries.
8. End Tuberculosis: Accelerate efforts to end TB by 2030.

WHO Collaborating centres: As of January 31, 2022, there are 105 active WHO Collaborating Centres across eight member states of WHO South-East Asia Region. These include:

- Two for blood safety and blood transfusion services: The National Blood Transfusion Service Sri Lanka, in Colombo, and the Thai Red Cross Society, Bangkok.
- One for Strengthening Ethics in Biomedical and Health Research at the Indian Council of Medical Research, Bangaluru.
- Two for reproductive health, including birth defect and stillbirth surveillance and newborn-birth defects database (NBBD): Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, and the Indian Council of Medical Research (ICMR), Mumbai. Siriraj Reproductive Health Research Centre, Bangkok and Chulalongkorn University, Bangkok.
- One for community-based activities in the area of maternal, newborn, child and adolescent health at the Mahatma Gandhi Institute of Medical Sciences, Sewagram, Wardha.
- One for NCD prevention and control, through the identification and collation of policies, tools, and best practices and research studies on NCDs, enhancing the skills and competencies of doctors, nurses and health workers. At the All-India Institute of Medical Sciences (AIIMS), New Delhi.

Policies promoted by the Regional Office:

Blood donation (based on World Blood Donor Day 2023 speech by RD): In the South-East Asia (SEA) Region, around 19.4 million units of blood are collected, which constitute around 0.94% of the region's population donating blood. Ideally, any country's requirement for safe blood can be met easily if 1 to 3% of the total population donates regularly. Of the 11 member states, only three have achieved 100% voluntary non remunerated donations (VNRDs) while the rest of the member states are striving to achieve 100% VNRDs (average of 82% VNRDs in SEA Region). 100% of donated blood is tested for transfusion-transmitted diseases.

Universal coverage: Between 2010 and 2019, the region increased its UHC service coverage index from 47 to 61. Between 2000 and 2017, the region reduced the number of households impoverished or further impoverished from out-of-pocket spending on health from 30% to 6%. In 2017, around 299 million people in the region faced catastrophic health spending, and an estimated 117 million people in the region were pushed or further pushed below the purchasing power parity poverty line of USD 1.90 a day. An estimated 40% of health budgets in low- and middle-income countries are spent on medicines, with much of the cost borne out-of-pocket by patients.

Manpower development: Since 2014, the density of doctors, nurses, and midwives in the region has improved by over 30% – a tremendous achievement.

World Birth Defects Day: Globally, an estimated 8 million newborns are born with a birth defect every year. Nine out of every ten children born with a serious birth defect are in low- and middle-income countries. The most common severe birth defects are heart defects, neural tube defects, and Down syndrome. In the WHO South-East Asia Region, birth defects are the third most common cause of child mortality, and the fourth most common cause of neonatal mortality, accounting for 12% of all neonatal deaths. Between 2010 and 2019, birth defects increased as a proportion of child mortality in the region, from 6.2% to 9.2%, and in four countries, birth defects now contribute to more than 20% of under-five mortality. In 2019, birth defects contributed to at least 117 000 deaths in the region, equal to around 22% of the global total. All Member States have initiated hospital-based birth defect surveillance and are implementing national action plans to prevent and manage birth defects. Six Member States – Bangladesh, Bhutan, India, Maldives, Myanmar, and Nepal – continue to support a WHO-developed online database to better track birth defects. To date, the database has recorded more than 4.7 million births in the region, including about 51 000 infants born with birth defects. The region has several priorities:

- First, improving the coverage and quality of preventive interventions such as rubella immunisation, quality antenatal care.
- Second, enhancing health system capacities to detect, treat, and care for birth defects, with a focus on adapting new WHO guidance on universal screening of newborns for hearing impairment and eye abnormalities.
- Third, sustaining and expanding surveillance and improving data systems, with a focus on strengthening not just coverage and quality, but analysis and application.
- Fourth, increasing support for parents and caregivers for early childhood development and improving disability care.

"Every child has the right to survive and thrive, with full access to quality and comprehensive health and social services. On World Birth Defects Day, WHO reaffirms its commitment to support all countries of the Region to urgently strengthen health systems to prevent, detect, manage and care for birth defects, for every child, everywhere." RD speech

Patient safety: Since 2015 the WHO South-East Asia Region has made targeted efforts to reduce unsafe medication practices and errors, with a focus on addressing counterfeit and substandard products, and enhancing patient safety and reporting systems. This is in line with the Region's Strategy on Patient Safety 2016–2025. Most countries of the region now have in place national patient safety and/or quality strategies that are aligned with the new Global Patient Safety Action Plan 2021–2030. The Plan aims to advance policies, strategies, and actions to eliminate all sources of avoidable risk and harm to patients and health workers.

Child health in the South-East Asia Region: Member States in the region have demonstrated significant progress in reducing newborn and child mortality over the last two decades, and the region achieved the MDG4 target of two-third reduction in under-five mortality in 2016. The progress has continued during the SDG phase, and by 2019 five countries in the region achieved the 2030 target of under-five and newborn mortality and the Region as a whole is likely to reach the 2030 target for under-five mortality but may narrowly miss the newborn mortality target. In the South-East Asia Region, around 52% of under-five mortality is contributed by deaths during the neonatal period. The most common causes of under-five mortality in the region is the complications of prematurity followed by pneumonia and diarrhoea. Commonest causes of neonatal mortality are prematurity, birth asphyxia, and neonatal infections. However, the coverage of evidence-based interventions remains low and uneven in several Member States. There is a large disparity in child health by wealth status, residence (rural vs. urban), mother's education level and social status, not only in mortality but also in the coverage of interventions.

Noncommunicable diseases in the South-East Asia: Noncommunicable diseases (NCDs), principally cardiovascular diseases, cancer, diabetes, and chronic respiratory diseases, impose a major and growing burden on health and development in the South-East Asia Region. In the region, 62% of all deaths are due to NCDs, accounting for 9 million persons. Of particular concern is the high proportion of premature mortality from NCDs (deaths before 70 years of age).

Research is indispensable for resolving public health challenges. Research for health spans five generic areas of activity:

- Measuring the magnitude and distribution of the health problem.
- Understanding the diverse causes or the determinants of the problem, whether they are due to biological, behavioural, social or environmental factors.
- Developing solutions or interventions that will help to prevent or mitigate the problem.
- Implementing or delivering solutions through policies and programmes.
- Evaluating the impact of these solutions on the level and distribution of the problem.

A new "Research and Innovation Unit" was established in January 2022 within the Healthier Population and Non-Communicable Diseases (HPN) Department.

The vision is to achieve the best possible public health outcomes and health equity in the South-East Asia Region powered by the latest in science, innovation and evidence [Regional strategy on research for health 2018–2022].

Table 5. Socio-economic development

Country	HDI rank	World Bank rank	HE/cap in USD WB data	HE as % GDP WB data	UHC index WB data
Bangladesh	0.685 med	LMI	16	2.39	52
Bhutan	0.698 med	LMI	307	4.39	60
India	0.685 med	LMI	79.52	3.31	63
Indonesia	0.728 high	UMI	127.5	2.69	55
Maldives	0.766 high	UMI	1150.7	9.65	61
Myanmar	0.609 low	LMI	58	5.2	52
Nepal	0.622 low	LMI	88.27	6.66	54
Sri Lanka	0.776 high	LMI	145.5	4.36	67
Thailand	0.798 v high	UMI	369.98	5.35	80
Timor Leste	0.634 med	LMI	174.9	4.32	62

Comments

This group of countries are generally in the "developing" category, with only Thailand, Maldives, and Indonesia gaining the upper middle-income category. This difference is less obvious when the Human Development Index is considered, since Thailand and the Maldives reflect better social development, Indonesia lags with the other members of the group, and Sri Lanka ranks higher. Overall, as far as health service support is concerned the table provides evidence that the Maldives and Timor Leste are spending more on health. In general, however, with the exception of Thailand, no country in the region offers secure UHC to all its citizens as reflected in the UHC index (defined in the section for EMR countries). The level of coverage and healthcare development that is derived from the table suggests that thalassaemia patients and their complex demands on the health system may not be adequately supported in the countries of the region, while Thailand and the Maldives are more likely to offer the necessary services.

The Democratic People's Republic of North Korea is not included in this discussion both because thalassaemia is very rare in the Korean peninsula but also because economic and other data are not available.

This generally poor health development is reflected in the overall health indicators of the populations of these counties:

Table 6. Health indicators and healthcare support in selected South and Southeast Asian countries

Country	IMR/1000 livebirths	Under-5 mortality/1,000 livebirths	Life expectancy	Healthy life expectancy at birth HALE
Bangladesh	24	29.1	74.67	63.1
Bhutan	19	23	72.97	64.8
India	25	28	72.03	58.1
Indonesia	17	21	71.15	60.7

Maldives	5	6	81.07	66.7
Myanmar	34	39	67.46	59.8
Nepal	23	27	70.78	60.2
Sri Lanka	5	6	77.48	67.0
Thailand	8	8.7	76.03	65.8
Timor Leste	36	42.3	67.69	59.5

In this respect, the Maldives, Sri Lanka, and Thailand also stand out with indices which approach those of developed and resource rich nations. They indicate more organised and effective health services and stand out as being categorised as high HDI countries. In contrast the rest indicate a poor performance even they are though improving compared to past years. It is also a reflection of the large populations with often diverse cultures and tribal divisions. This picture is reflected in the achievements concerning thalassaemia.

Table 7. Available services

Country	Doctors/1000 population	Density of nurses/1000 population	MRI density/ million population	VNRD as % of total donations*	National haemovigilance program
Bangladesh	0.7	0.5	0.49	22%	YES est 2018
Bhutan	0.5	2.1	1.33	80%	Yes 2016-7
India	0.7	1.7	0.21	76%	Yes 2012
Indonesia	0.6	4.0	NA	91%	Yes
Maldives	2.1	4.7	2.9	36%	No
Myanmar	0.7	1.1	0.24	99%	Not only in central est
Nepal	0.9	3.3	NA	83%	Yes
Sri Lanka	1.2	2.5	0.42	100%	Yes 2009
Thailand	0.9	3.2	NA	100%	Yes 2001
Timor Leste	0.8	1.7	NA	18-20%	No

** Voluntary non-remunerated blood donations to ensure blood safety in the WHO South-East Asia Region to support universal health coverage* ISBN Number: 978-92-9021-044-3 © World Health Organization 2023

The indicators used are derived from the needs of thalassaemia patients. Adequate overall manpower is inadequate in all of the countries; in contrast, the UK and Cyprus have 3.2 doctors/1000. Only the Maldives approaches this figure, and so the possibility of devoted doctors for haemoglobin disorders is limited in all the region. Likewise, the possibility for MRI monitoring of iron load is limited (compare with Cyprus MRI density of 14/million and Greece of 29/million).

Blood safety is improving in the region with the exception of Bangladesh, the Maldives, and Timor Leste. For the rest, there remains the question of whether good practices are found throughout the country – especially in India.

Table 8. Prevalence and burden of thalassaemia and HbE disorders in selected South and Southeast Asian countries

Country	β- thal carriers	HbS carriers	HbE carriers	Expected β-thal births/1,000	Expected HbE/β- thal births/1,000	Estimated β- thal patients	Estimated NTDT patients

Bangladesh	2.12%	0.1%	8.59%	0.11	0.91	1,2000	30,000–40,000
Bhutan	0.7%	0	4%	0	0.01	NA	NA
India	3.9%	3%	1%	0.38	0.2	150,000	NA
Indonesia	5%	0	6%	0.63	1.5	13,612	NA
Maldives	18%	0.13%	0.9%	8.16	0.81	666	NA
Myanmar	0.5%	0	26%	0.1	0.65	NA	4,079
Nepal	4%	5%	4.4%	0.4	0.88	730	NA
Sri Lanka	2.2%	0.15%	0.5%	0.12	0.06	2,000	NA
Thailand	2.9%	0	24.6%	0.21	3.57	2,070	9,6390
Timor Leste	5%	0	6%	0.63	1.5%	NA	NA

Four countries of the region have a significant number of sickle cell carriers:

- India has 3% AS carriers, which leads to 0.82/1,000 births of SCD syndromes with over 125,000 patients
- Maldives has AS 0.13%, which leads to 0.12/1,000 births and 14 known patients
- Sri Lanka has 0.15% AS, which leads to 0.12/1,000 births and 51 known patients
- In Nepal, AS is said to be 5%, but this is confined to one geographical area, and could lead to 1.63/1,000 affected births. Total patients are not known.
- In Bangladesh AS is estimated at 0.08%

The whole region has a major prevalence of haemoglobin disorders, and yet, because of poor resources and uneven development of services, thalassaemia services are not given priority in health planning. This is reflected in the policies of the regional WHO office which hardly mentions haemoglobin disorders (see the outline of polices in the introduction to this section). However, much progress in specific issues such as increasing health coverage, blood adequacy and safety, and creating reference centres in certain locations are examples of more development. Patient support groups are gaining ground, but prevention programmes are very limited in the region.

Bangladesh: In Bangladesh, the population is over 160 million people, and many health issues must be considered, including water-borne diseases, essential nutrition, and improved water sanitation and hygiene. There is no national registry, but the carrier rate indicates a high prevalence, and the estimate is of over 50,000 affected patients. According to a study by Khan et al., most of the patients suffer from Hb E/b-thal and many are NTDT [68]. In a recently developed dataset of 617 (465 excluding 152 carriers) patients, thalassaemia intermedia (NTDT) was the most common type (65%), followed by major (35%) [69].

To quote a recent description of the situation, "Facilities for blood transfusion are not present in all the district hospitals. Furthermore, blood transfusion is also a costly procedure for the patients to afford, frequently due to the lack availability. Chelating agents are also very expensive due to low supply" [70]. Treatment is not free and so the patients from economically weaker families are undertreated. Health services are a mix of public (government), private, and NGO providers. The system is underfunded, with a shortage of skilled workers and high out-of-pocket spending.

The burden of disease in this country is huge, and families are not supported adequately to deal effectively with the children's medical needs. Families affected by beta-thalassaemia encounter significant financial burden due to the high cost of treatment [71]. In a recent review, it was estimated that most patients bear 74% of treatment

costs out-of-pocket, leaving many deprived of adequate care [72]; the authors of this review extrapolated that "nearly 70,000 patients are suffering from various thalassaemia syndromes in Bangladesh".

Currently, most infants are neither diagnosed nor treated and probably die in early infancy from the consequences of anaemia. Organised treatment is only available at the thalassaemia clinics in Dhaka and in Chittagong. There have been national guidelines since 2019 but the majority of treating physicians do not implement them. Blood is not filtered and often whole blood is given. Voluntary donation is inadequate. All three iron chelators are available but not free of charge; indeed, patients pay for many services including laboratory tests and MRI. Alternative medications aiming to reduce transfusion burden are often used, including thalidomide and hydroxyurea. The result is that iron load is high and co-morbidities increase. Indeed, blood transfusion is also a costly procedure for the patients to afford. Moreover, the costs of treatment, even when discounted, are beyond the means of the large majority of families, so that only 1% of the thalassaemia population benefit from reasonable management [70].

These findings are similar to a report from a TIF delegation visit in 2019 [73]. The team also emphasised the wide variation in prevalence across the country:

Table 9. Regional variation in thalassaemia and HbE carrier frequencies in Bangladesh

Division	Number tested	Het b-thal	AE	EE	% het b thal	% AE	% EE
Barisal	77	2	4	2	2.6	5.2	2.6
Chittagong	260	17	20	1	6.5	7.7	0.4
Dhaka	475	12	39	4	2.5	8.2	0.8
Khulna	159	2	8	0	1.3	5.0	0.0
Rajshahi	338	14	44	0	4.1	13.0	0.0
Rangpur	116	5	31	7	4.3	26.7	6.0
Sylhet	14	1	1	0	7.1	7.1	0.0
% of Total Tested	1,439	53	147	14	3.7	10.2	1.0

These carrier frequencies are challenged by a recent survey of 1,000 university student from three districts, using capillary electrophoresis and molecular studies; the findings were 1.7% for β-thalassaemia carriers and 5.8% of HbE carriers [74]. Tribal groups have higher carrier rates for both β-thalassaemia (4.8%) and HbE (about 35%)

The TIF delegation also confirmed that all of the patients were inadequately chelated, transfusions for those with thalassaemia major are generally insufficient, and pre-transfusion Hb is generally 6-8 g/dl. These basic findings indicate that there is need for more effort from the health authorities, despite other pressing health issues, to improve quality of care. The needs were also demonstrated by a study on the Health-Related Quality of life which concluded that "This study found an association between lower income, blood transfusion, disease severity, comorbidities, and medical expenses and the deterioration of HRQoL among the patients". The conclusion is that "National action plans are required to guarantee the holistic welfare of thalassemia patients" [75].

Bhutan: A small mountain country, with a population less than 800,000 people, Bhutan has a low prevalence of β-thalassaemia genes and HbE. On the other hand, α-thalassaemia is more common. However, clinically important mutations are rare, and little is known about services.

India: Because of its large population (now over 1.4 billion) and high prevalence of thalassaemia and sickle cell genes, India bears a large burden of the global haemoglobinopathy population. The estimate is of 100,000–150,000 thalassaemia patients [76]. There are an estimated 125,000 SCD patients. Every year 0.5/1,000 live births will be added suffering from beta thalassaemia and HbE/ beta thalassaemia (around 15,000 new affected births/ year).

The distribution of these genes is heterogeneous both geographically and among tribal and linguistic groups. In a recent review of the literature the β-thalassaemia carrier rate in the general population amounted to 3.74% (95% CI 2.52-4.97), but it was higher in the tribal groups [77].

Universal health coverage is not yet fully implemented in India even though the government introduced the Ayushman Bharat Yojana scheme to bring the healthcare services within the reach of the community. Healthcare out-of-pocket expenditure was estimated at around 62.6%, but it is estimated to have fallen to about 40% of total health expenditure, so haemoglobinopathy cannot be free of health-related expenses. If the entire present cohort of 150,000 thalassaemia patients was receiving adequate care, the annual cost would be USD 448 million. And with an added cohort of 125,000 cases over a decade by 2026, the annual cost of care is predicted to escalate to USD 820 million [78]. The government provides blood transfusion and iron chelators free of cost through civil hospitals. Patients must register with a thalassaemia society or care programme to access these free treatments.

Even though government hospitals cover the cost of treatment of thalassaemia, this does not satisfy all needs and patients supplement by out-of-pocket expenses. There is support from NGOs, but again not all needs are satisfied. In a recent estimate of cost for treating children younger than 12 years in Mumbai, the cost was found to be USD 981 per patient per year. A recent publication found that the annual cost of treatment and management of a thalassaemia major patient amounts to USD 32 (INR 2,681) in government hospitals and USD 3,840 (INR 3,14,906) in private hospitals; this can reach up to USD 292 (INR 24,006) in government and USD 34,391 (INR 28,19,764) in private over 24 years (mean life expectancy of thalassemia patients). The cost to the family is around USD 5,389-13,474 per year, according to age and complications [79]. Direct costs contributed to 94% of the cost of illness with chelation therapy (23%) and blood investigations (21%) being major contributors. Even at subsidised rates, the financial burden to the families from lower socioeconomic strata is considerable [80]. Such financial issues result in undertreatment but also in psychological stress in both patients and families [81]. Overall, the quality of life (QoL) of patients (children in a current study) significantly correlates with their carers' CarerQoL, mother's educational level, parent's working status, as well as quality of care [82]. The social support to patients through the Disability Act of 2016 is an important development, since it includes thalassaemia and sickle cell disease. It covers support for education, employment, accessibility, social security, and community living, and it mandates 4% reservation in government jobs which helps the increasing adult population of patients.

Quality of care is variable across India, with some mainly academic centres offering near optimal care, even though at a cost, while the majority of patients receive substandard treatment. This is reflected in outcomes. One example is the rate of transfusion-transmitted infections, which reflects the quality of blood banking: 39.9% of regularly transfused children were found to have TTIs, with hepatitis C being the most common (34.5%), followed by hepatitis B (4.5%) and human immunodeficiency virus (1.8%); this was found to be related to the per capita monthly family income, as well as the blood transfusion frequency [83]. In another study of 328 β-TM children attending the thalassaemia day care unit of a medical college, 48.2% were malnourished with a mean body mass index of 13.9 kg/m2; this was related to socio-economic factors such as caste and mothers' education (compare with 7.8 % of children in the USA (Fung et al. 2010)) [84]. It is noteworthy that most reported results involve children with thalassaemia, indicating the overall age distribution of patients in

India. In contrast a report to TIF from expert patients in India (Varesh and Anubha, March 2021) involving 740 patients across several states, this indicates an improving survival:

Table 10. Age distribution of thalassaemia patients in India (Report from Expert Patients, 2021)

Age group	% of patients
<10 years	25%
10-20	30%
20-30	25%
30-40	15%
>50 years	4%

This indicates that 44% are young adults (20–40 years old), even though in this cohort there may be a selection of treating centres from academic units. The overall picture of undertreatment of the majority is not negated, hope however for improvement of patient care is present. According to a recent report, a National Policy has been proposed for the management and prevention of haemoglobinopathies that will embark on a comprehensive programme, providing adequate care and augmenting the existing public healthcare services. It will also include training, genetic counselling, and easier access to preventive options, as well as a National Registry.

The overall picture of clinical services for thalassaemia patients in India is one of gradual improvement, but the journey has not yet reached its goal. In a recent presentation by the Haemoglobinopathies subcommittee of the Indian Paediatric Haematology Group [85], it was stated that 68 centres across India participated in the survey with 11,660 patients, and the findings in summary are that MRI T2* is offered to half of these; leukodepleted packed red cells are offered to 84%, but filters are purchased by the patient in 41% of centres. In addition, one-third reported difficulty in "arranging blood donors". Concerning patient outcomes, they reported growth retardation in 60% of patients, 75% have iron overload, 37% have psychosocial issues, and multidisciplinary care was available in 62% of centres.

In a review of the literature concerning quality of life in thalassaemia patients of india it was clear that children experience a low QoL, and it was concluded that there is need to increase parental and family awareness, to promote the use of support groups, psychosocial counselling, and emotional support [86]. However, improving the level of medical care and offering comprehensive financial coverage will go a long way to reducing the burden of both the patient, the family and the state. Another suggestion is establishing a robust public-private partnership, along with training healthcare providers, private and government doctors in urban and rural areas, strengthening the blood bank, and supporting the management of b-TM [87].

Indonesia: Indonesia has a relatively high incidence of thalassemia, with approximately 3–10% people being carriers. According to national data, there are over 13,000 patients under treatment. With a population of 280 million, the prevalence is expected to be much higher if the carrier rates are accurate.

The country introduced a universal health coverage scheme in 2014, and these patients are included to benefit from free treatment of both blood transfusion and iron chelation. However, adjuvants necessary for quality care, such as MRI and multidisciplinary care, are not available across this large territory to all patients. The age distribution of patients in this country is not known. In fact, the vast geographical area over which patients are scattered and the variable quality of services in each region make it impossible to generalise. Reference centres for thalassaemia management are mainly in Jakarta, and so it may be expected that these centres represent the best possible care that is offered in the country. One state-of-the-art centre is located in the Cipto Mangunkusumo Hospital [88]. In this unit both children and adults are treated, and all treatment has in recent years been fully supported by national health coverage. Patients are regularly monitored, and MRI is available. In a 2018 report from this hospital of MRI results on liver and heart iron, the measurements on 546 patients were analysed, 56.4% were under the age of 18 years and 43.6% were over 18 years. For the purpose of this report and for comparison with other adult populations, the findings of the over-18-year population are

reproduced. Heart iron deposition was found within the normal range (>20ms) in 82.7% of adults, which is comparable to countries like Italy, Cyprus, and Greece, while liver iron concentration was within normal rage in only 13.4% of the patients. Despite these results, the key message here is that patient care can achieve good results in any country, provided that the services are supported by universal coverage.

In a cohort of 240 adolescents with TDT, all (100%) had a pretransfusion haemoglobin below 8g/dl [89]. In a group of young adults from a unit in Java (mean age, 21.5 ± 7.2 years), 15–53 years, the mean haemoglobin before blood transfusion was 7.2 ± 1.7 g/dL, and mean serum ferritin was 4414.5± 3165.2 ng/mL [90]. These results are evidence of undertreatment, and organ complications are expected. Similar results were reported from a reference centre in Jakarta on a group of 30 patients with ages ranging from 13–41 years. The mean serum ferritin was 9,019.3ng/ml (SD3,889.4) in patients with a cardiac T2* <20ms and 4,118.4 (SD2,373.6) in those with a T2* >20ms [91]. Similar findings are still being reported from Indonesian hospitals [92, 93]. The reasons given include the uncertain availability of iron chelators in some rural areas, poor adherence to iron chelation therapy, and maintaining pretransfusion haemoglobin to acceptable levels [94]. These findings confirm that quality improvement is needed, and international guidelines adopted.

Deferiprone had a lower mean annual cost of USD 3,581 than deferasirox, which had a cost of USD 6,004. This has been considered, and deferiprone was the most common iron chelator used (86.7%). Detailed medical and non-medical costs have yet to be calculated, so the national health insurance is unable budget adequately for all patients in the country [95].

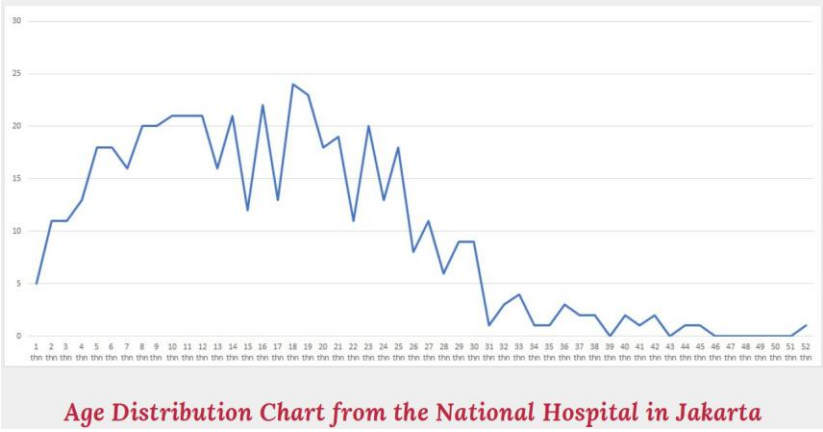

Figure 3. *Age distribution chart from the National Hospital in Jakarta*

The burden of disease in Indonesia remains high and is probably underestimated. More diligent estimates of patient numbers is needed as well as age distribution data, which cover the whole country.

The Maldives: The Maldives is an island nation in the Indian Ocean, with a population currently estimated at over 500,000 people. It consists of 1,900 islands, of which 200 are inhabited. It has the world's highest concentration of carriers at 16–18% of the population [96, 97]. Screening over the years of 110,504 individuals indicated a β-thalassemia carrier frequency of 16.2% [98].

The latest report is of 666 registered patients, which amounts to around 1 for every 800 inhabitants. This is a considerable burden of disease, and has led the Ministry of Health to recognise thalassaemia as a major public health issue. This has led to long standing programmes of raising awareness, screening, and patient care. There is one reference centre where the majority of patients receive routine treatment freely provided by the state. Despite this, optimum care is still to be achieved. In a recent survey, about 46% of patients have a serum ferritin below 2500ng/ml, while the rest are above that level (the mean ferritin was 3,339.6 µg/l). The mean haemoglobin level was 8.35 (SD 0.95) while 42% of subjects had a haemoglobin level of 9 gm%. 55.7%) and

claimed they were always compliant to chelation, while the rest claimed to be compliant sometimes [99]. MRI assessment of iron overload is still unavailable despite efforts. There is increasing economic development, which hopefully will assist in offering optimal care in the coming years. All treatment is offered free of charge since universal coverage is available.

Despite these service deficits, there is a growing population of patients. In a TIF survey, 63.9% of adults were employed fully and 69.4% were married. These are indications of good social integration.

Ongoing prevention for many years has been partially successful in reducing birth incidence, but it is hindered partly because of the difficulty of raising awareness and reaching remote islands.

A "10 Year Master Plan for Thalassemia Control and Prevention 2024–2034" has been drawn by the MBS (Maldivian Blood Services) and signed by Aminath Shirna, Minister of State for Health. The results of this national policy is expected to bring results in the coming years.

Myanmar: This is a country with a very low prevalence of β-thalassaemia, the overall carrier rate being only 0.5%, while HbE is 26%. Only one province, Kayin, reports a high β-thalassaemia carrier rate of 8.9% but the population is only 1.5 million compared to the 54 million of the whole country. The reported 4,000 patients are mostly NTDT. According to a report from the Yangon Children Hospital, the levels of haemoglobin (Hb) appear to be very low and patient management poor [100]. Blood transfusion has been provided free of charge since 2014. Since most (70%) of patients are NTDT, only 18% of patients in Yangon have a serum ferritin level >2000ng/dl. HCV positivity is 12.6%. However, universal coverage has not yet been applied, and so family contribution is necessary. The health system is a mix of private and public, but it lacks adequate funds and patients have high out-of-pocket costs, making thalassaemia care very basic. In addition, we are not aware of any government policy regarding prevention.

Nepal: In Nepal, both sickle cell genes and thalassaemia genes are frequent. Sickle cell is more concentrated towards western parts of Nepal and especially in the Tharu ethnic population. In contrast, the distribution of β-thalassaemia is found throughout the country and among all ethnic groups [101]. Most known β-thalassaemia patients are treated at the Children's Hospital in Kathmandu. The challenges in managing chronic conditions like beta-thalassaemia in remote rural areas, where healthcare access and awareness are limited, mean that many patients are left untreated or seriously undertreated [102]. The Nepal Thalassaemia Society reported an estimated total of 730 thalassaemia patients in the whole country, 140 of these in Kathmandu.

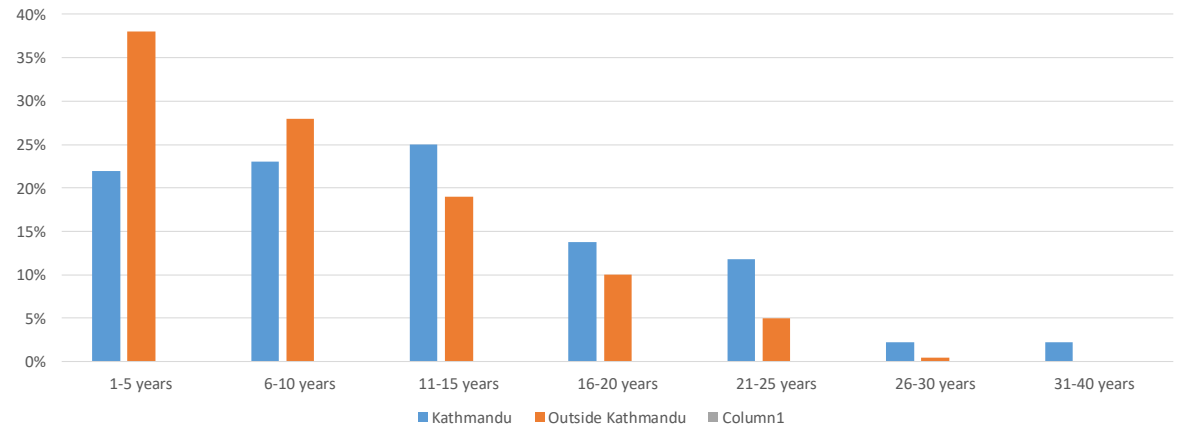

Figure 4. *Nepal age distribution of 730 patients in Kathmandu and outside of the capital.*

All basic treatment is paid by government funds. In a recent publication, the medical charts of 54 thalassaemia major patients, registered at the Civil Service Hospital, were retrospectively analysed: The median age of the patients was 17 years (3–34 years); 71% of patients failed to maintain haemoglobin above 9.5 gm% primarily because of the unavailability of red blood cells; the mean serum ferritin was 4486.12 ng/mL (range 469–9585 ng/mL). In a recent 2025 report from a paediatric population (Kanti Children's Hospital in Kathmandu), the mean age was 7.5±3.7 years, the pre-transfusion Hb was 8.86g/dL while 49% had a serum ferritin >2500ng/ml with 22tp % being >5000ng/ml. This is an indication of poor chelation attributed to poor compliance in 31.5%, and it is reflected in some degree of organ damage in 55.6% even at this young age [103]. Overall, 80% [104] of patients reported interrupted use of iron-chelating agents because of frequent shortages of medicines; 93% of patients were found to have stunted growth; overall, 7.6% had cardiac complications, and 5.5% had hypothyroidism; 54.1% of females of reproductive age had primary amenorrhea. The average cost of thalassaemia care was NRS 70,000 (~USD 533) in paediatric patients and NRS 250,000 (~USD 1,906) in adult patients per annum. This includes the cost of blood transfusion, commutes to the transfusion centre, and iron-chelating agents [104]. There is no prevention programme, and the fate of patients outside Katmandu is unknown. Much work has yet to be done in Nepal to improve the services, but at least government interest has been aroused. Similar results are reported in a survey from a peripheral hospital [105]. Nepal's healthcare services, as well as the medical community, have increased their interest in thalassaemia in recent years, and if this continues, progress towards reducing disease burden will also increase, even though prevention is still at limited.

Sri Lanka: The majority of patients in Sri Lanka have β-thalassaemia and a minority (16%) have HbE/ β-thalassaemia. In one review 61% of patients had low pretransfusion haemoglobin levels (< 9.0 g/dL) despite receiving high transfusion volumes (> 200 mL/kg/year) [106]. In a more recent report from two tertiary centres, low pre-transfusion Hb was confirmed in 58.3%, while iron chelation seems to be much improved compared to countries of this region, since 40.3% of patients had a serum ferritin < 1000ng/ml and only 9.7% had >2500ng/ml [107].

Sri Lanka does not have a regular national registry, but a recent report collected data from most if not all treatment centres [108]. Data on 1,774 patients from 23 centres were collected and found that 1,219 patients (68.7%) had homozygous β-thalassaemia, 360 patients (20.3%) had haemoglobin E β-thalassaemia, and 50 patients (2%) had sickle β-thalassaemia. Patients with thalassaemia major, with a mean age of 13.2 (SD 7.6) years (range 5 months—44years), and they were significantly younger than those with HbE β-thalassaemia [mean age 21.5 (SD 12.9) years, range 6 months to 60 years; p<0.0001]. This is a typically young, undertreated population of patients with a mean serum ferritin level of 2383.

According to a report from the patient support association in 2019, the government spends over Rs. 800,000/- (about USD 2,400) per child annually, "who will invariably die at a young age".

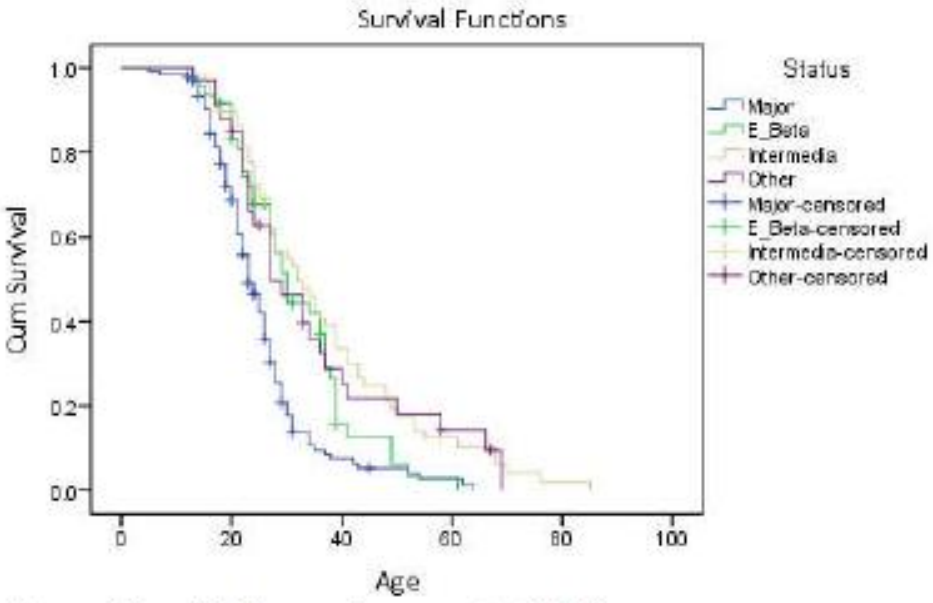

Figure 3. Survival functions of thalassaemia patients in Sri Lanka by disease subtype (Hemals Thalassaemia Care Centre, 2017)

A sharp decline in survival after the age of 30 years is seen especially in β-thalassaemia major [109]. The overall survival of patients of β-TM is still not on a par with that of the Mediterranean countries [110]. In contrast, median survival of HbE/ β-thalassaemia patients was 49 years [111].

In Sri Lanka, the Ministry of Health started a thalassaemia screening programme for school children and young adults in 2005. The programme is voluntary and based on the "Safe Marriages" concept, so community awareness is of vital importance if birth incidence is also affected. One of the most fundamental issues with the thalassaemia screening programme is that it has operated without central control: individual hospitals conduct their own screening programmes, which are not collated by the Ministry of Health, and annual births showed no clear reduction until 2012 [108, 109]. Limited prenatal diagnosis service is available at academic centres [112].

A cost of illness study was published in 2020, which discussed the cost of treating children (< 18 years) in 2017. The total annual direct hospital cost was USD 2,092 per patient year. Added household costs were USD 206 (total societal burden of USD 2,807 per patient year). Despite support, relatively low household income resulted in about 1 in 4 households experiencing catastrophic costs (> 10% of total income) [113]. According to a recent case study conducted in the Kurunegala district among 75 thalassaemia major patients registered at the National Thalassaemia Centre, 47% of their parents were in debt due to overwhelming expenses for their children [114]. In addition, most of the adult thalassaemia patients in Sri Lanka are unemployed.

Sri Lanka has a medical community and an infrastructure of services that could result in excellent outcomes. Poor central support to service development and quality, as well as family support, does not help the country to achieve the standards that it is capable of. A holistic approach that addresses educational, economic, and psychosocial is now needed to supplement the medical services provided and the increasing age of patients.

Thailand: Thailand is a country with constant development, and has recently moved to the high HDI category. It is characterised by a large, affected population of haemoglobinopathy patients, with a very large majority having HbE/ β-thalassaemia. In addition, there is a high prevalence of alpha-thalassaemia (20–30%) and

variants like Hb Constant Spring (1–8%). The burden of disease in terms of patient numbers was summarised by Prof Suthat Fucharoen in 2019 during a SEATHAF conference:

Table 11. Estimated burden of haemoglobinopathy in Thailand: At-risk couples, Affected births, and Living patients (Prof. Suthat Fucharoen, SEATAF Conference, 2019)

Conditions	Couples at risk/year	Affected births/year	Living patients
Homozygous β-thal	828	207	2,070
HbE/ β-thal	12,852	3,213	96,390
Hb Bart's hydrops fetalis	3,332	833	0
HbH disease	22,400	5,600	336,000
Total	**39,412**	**9,853**	**434,460**

There is a long tradition of research and service development which has made Thailand a reference country for the whole SE Asia. Despite this, case management is uneven across the country, and so patient data are variable. In a multi-centre study, including peripheral centres, conducted between 2015 and 2017, the mean haemoglobin level was 7.1 ± 1.3 g/dl in patients with TDT and 7.7 ± 1.2 g/dl in patients with NTDT. The mean serum ferritin was 2,250 ± 2,313 ng/ml in patients with TDT, and 1,483 ± 1,530 ng/ml in patients with NTDT (Overall in Thailand, over 50% of patients have NTDT). The patients who were over 18 years were selected, and the mean ages were similar between the TDT and NTDT groups, 27.8 years vs. 29 years. Examples of complications in this group include extramedullary haematopoiesis, detected in 12.5% of TDT patients and only 4.9% of NTDT patients, indicating possible under-transfusion [115]. In a more recent cohort from Chiang Mai, including 209 TM and 279 HbE/ β-thal patients, predominant causes of mortality were infection-related (36.9%) and cardiac complications (27.7%). The mean age of these patients was 13 years, and a main predictor of poor outcome was iron overload, identified as serum ferritin >3000ng/ml, affecting 16.4% of this cohort [11]. Hospital admissions were also mainly due to iron overload with infections being the second cause [116].

It is important to remember that, in Thailand, non-deletional haemoglobin H (Hb H) disease presents an additional burden due to the need for blood transfusions by many of the affected patients; the most common non-deletional mutations are haemoglobin Constant Spring (Hb CS) and haemoglobin Pakse (Hb Pakse). In a study of 208 paediatric patients with alpha-thalassaemia, 32.0% had non-deletional Hb H; lower haemoglobin levels, hepatosplenomegaly, gallstones, facial changes, and retarded growth were found to be more common compared to those with the deletional types. Non-deletional HbH patients had higher liver iron concentration and serum ferritin levels, which correlated with transfusion frequency [117]

For patient care national guidelines have been prepared based on TIF's *Guidelines for the Clinical Management of Thalassaemia*, but modified to be a realistic reflection of local circumstances.

The cost of treatment as estimated in 2010 [118] is as follows:

- for ages 1-10 years – EUR 2,900 /year
- for ages 11-20 years – EUR 5,000 /year
- for ages 21-30 years – EUR 7,230 /year

The health system of Thailand is divided into three schemes, reaching all of the 68.4 million population (2018):

- The Universal Coverage Scheme (USC), this is the largest scheme covering 48.8 million people.
- Civil Servant Medical Benefit Scheme (CSMBS) covering 4.97 million people.
- The Social Security Scheme (SSS) covering 14.47 million people.

Under these schemes all thalassaemia patients are supported for full treatment. Haematopoietic Stem Cell Transplantation (HSCT) is still out-of-pocket, with a projection for full support by 2020.

The cost to manage patients with TDT and living 10 to 30 years is approximately USD 39,393 to USD 20,000/patient covering regular blood transfusions and iron chelation [119]. A cost-benefit analysis of an 8-year prevention programme in Chiang Mai province (north Thailand), involving 21,975 pregnant women and their husbands and which resulted in the prevention of 80 affected births, cost USD 93,667. This included screening and prenatal diagnosis. For the same period the cost of treatment was USD 6,756,401. This means that the benefit vs. cost is 72:1.

Both treatment and prevention are reimbursed under the universal coverage insurance scheme. Since 2002, Thailand's entire population of 63 million has been entitled to a comprehensive health benefit package [120].

A national prevention programme was initiated in 1997. This includes antenatal screening in the first trimester of pregnancy and the availability of prenatal diagnosis all free of charge [121]. Aborting the foetus with thalasseemia diseases was not well-accepted. Other challenges affecting prevention include the fact that medical personnel do not inform patients about PND availability, laboratory errors are another preventable issue, and approximately 50% of pregnant women attend antenatal clinics late in pregnancy. However, this is a well-studied population with sensitised authorities, and a reduced burden is expected.

Timor Leste: little is known about thalassaemia in this country. It is assumed that it has the same pattern of disease as Indonesia, of which it was once a province. A 2007 WHO epidemiological study on Hb disorders in countries of the SEA Region estimated 25 births every year with β-thalassaemia major and HbEβ-thalassaemia However, there is no published information on services and TIF has no member associations in the country.

Comments:

This WHO region hosts one of the largest thalassaemia populations in the world. It consists mainly of LMIC countries, with large geographical areas and complex population structures with tribal groups, linguistic subgroups, and a variety of religions and cultures. National programmes are scarce and quality of care varies, ranging from a few centres of excellence to many centres unable to meet the real needs of patients. Much work has to be done at the national levels, which depends on raising awareness and advocacy both by professionals and support associations. This is an area where TIF activities should be constant and almost daily.

WHO West Pacific Region (WPR)

Introduction

The Western Pacific Region is home to almost 1.9 billion people across 37 countries and areas. Headquartered in Manila, Philippines, it includes countries such as China, with 1.4 billion people, and Niue, home to just 1,000 people.

There are 15 country offices across the region: 11 WHO representative offices and four country liaison offices. Together with the Regional Office, the 15 country offices support 37 countries and areas. Of interest to TIF, because of significant presence of thalassaemia are Australia, Brunei Darussalam, Cambodia, China, Hong Kong, Laos, Macao, Malaysia, Papua New Guinea, Philippines, Singapore, and Vietnam. However, there are other member states with reported thalassaemia syndromes but no real data. The TIF database records that there are around 4,000 new births per year affected by beta thalassaemia syndromes and a minimum of 40,000 living patients (excluding China)

The region is characterised by unprecedented economic growth, while migration and urbanisation in the region have created opportunities for better lives.

Developing health training programmes and supporting the building of comprehensive local health services have been the main policies. While recognising that communicable diseases remain a significant public health issue, the increased prevalence of noncommunicable diseases, coupled with ageing populations throughout the region, means there needs to be a greater emphasis on preventive and health promotion activities, even as communicable diseases continue to require considerable resources.

Three main priorities have emerged for the regional office that reflect the Western Pacific's unique economic, social, and environmental context:

1. Health security, including antimicrobial resistance.
2. NCDs and ageing (mainly heart disease, stroke, cancer, diabetes, and chronic respiratory diseases are responsible for 86% of deaths in the Western Pacific Region).
3. Climate change and the environment.

Projects and services promoted to address these issues:

1. Communications for Health (C4H): On 20–21 April 2023, the World Health Organization (WHO) Regional Office for the Western Pacific convened the Member States Consultation on the Draft Regional Action Framework on Communication for Health (C4H). C4H is a tool for health to help individuals, health workers, policymakers, and government leaders make decisions every day that affect people's health. At the consultation, attendees discussed evidence-based, strategic communications, that is, using communication principles and processes to target a particular audience for a specific purpose, based on known audience needs and preferences for tackling complex health challenges. Whether it be promoting health-protective behaviours, increasing vaccination rates, reducing stigma around mental health, or advocating for inclusive health policies, strategic communication can play an important role. Communication is, in itself, a public health intervention: it is a technical field backed by theory and evidence.

2. Behavioural and social sciences for better health: Investigate the cognitive, social, and environmental drivers and barriers that influence health-related behaviours. Applying behavioural and social sciences requires a multidisciplinary approach and the adoption of theory, methods, research, practical tools, and techniques drawn from psychology, sociology, anthropology, communications, marketing, economics, systems thinking, and design thinking, among others. Behavioural and social sciences evidence can contribute to and complement other public health efforts that focus on the non-medical factors that influence health outcomes. WHO includes behavioural and social sciences in its work in different ways and across a variety of issues.

3. Essential Medicines and Health Technologies: The Essential Medicines and Health Technologies (EMT) unit supports Member States to improve access to essential, high-quality, safe, effective, and affordable medicines and health products.

4. Health Policy and Financing: The Health Policy and Financing (HPF) unit provides technical assistance to Member States to develop robust health financing systems across the core functions of revenue collection, pooling, and purchasing. HPF also supports countries to develop coherent and realistic health legislation, policies, strategies, and plans, with strong links between national and operational levels, and to monitor their implementation.

5. Equity and Social Determinants: The Equity and Social Determinants (ESD) unit collaborates with Member States and other stakeholder groups to advance the SDGs by addressing the underlying social determinants of health. ESD supports countries to develop and implement health policies and programmes that enhance health equity and integrate approaches that are pro-poor, gender-

responsive, and human rights-based. WHO Western Pacific Regional Office supports Member States in developing and implementing their national health policies, strategies and plans by:

i. Engaging in technical collaboration to build national capacity for equity-focused policy and programme design, data collection, and analysis, and multisectoral and multistakeholder collaboration.
ii. Fostering country-led regional peer learning and cooperation.

6. Noncommunicable Diseases: Noncommunicable diseases (NCDs), principally cardiovascular diseases, cancer, diabetes, and chronic respiratory diseases, are the leading causes of death and disability in the Western Pacific Region. The WHO Western Pacific Region NCD and Health Promotion Programme supports Member States to implement global and regional action plans to prevent and control NCDs by:

i. Raising the priority accorded to NCDs through international cooperation and advocacy;
ii. Strengthening national capacity to accelerate country responses;
iii. Reducing modifiable risk factors through the creation of health-promoting environments;
iv. Strengthening health systems to address prevention and control of NCDs through people-centred primary health care and universal health coverage;
v. Promoting national capacity for high-quality research and development;
vi. Monitoring trends, determinants and progress to achieve global, regional and national targets through evidence-based interventions.

7. The Health Information and Intelligence (HII) unit supports Member States to strengthen health information systems, promote the adoption and scaling up of digital health and the utilisation of integrated health information for decision-making.

8. The Innovation and Research (INR) unit aims to define WHO's meaningful contribution to better leverage innovation for health. This is accomplished by taking the process of iterative development from the stimulation and identification of innovation to its adaptation and scale-up, including financial, systems, technological, and social innovation. Public health innovation refers to the development of a new process, policy, product, or programme that increases quality, impact, and efficiency. It goes beyond mere ideation and piloting, to implementation at the national level.

9. The Universal Health Coverage (UHC) unit supports Member States' efforts to transform health systems on their UHC journey with tailored strategies informed by new ways of working, best practices, tools, and strategic direction. This is accomplished by:

i. Convening the Technical Advisory Group on Universal Health Coverage in the Western Pacific Region (UHC TAG) and providing technical support;
ii. Identifying areas of synergies with UHC for possible collaborative efforts through the Technical Advisory Group Alliance, a coordination mechanism engaging all TAGs in the Western Pacific Region to collectively work towards achieving the For the Future vision;
iii. Sharing best practices and knowledge to advance UHC with health system transformation in countries;
iv. Promoting these policies and strategies by the regional office as tools for the development of thalassaemia services, since the burden of thalassaemia is high in this region.

Table 12. Socio-economic development

Country	HDI rank	WB rank	HE/cap WB data in USD	HE/%GDP WB data	UHC index
Australia	0.951	High	6,731	9.93	87
Brunei	0.829	High	665.87	1.82	78
Cambodia	0.593	LMIC	109.53	4.71	58
China	0.768	UMIC	672.45	5.37	81
Hong Kong	0.952	High	NA	NA	NA
Laos	0.607	LMIC	41.35	2.02	52
Malaysia	0.803	UMIC	458.22	3.91	76
Papua New Guinea	0.558	LMIC	81.11	2.62	30
Philippines	0.699	LMIC	194.06	5.11	58
Singapore	0.939	High	4,320.5	4.9	89
Vietnam	0.703	LMIC	188.9	4.59	68

The countries of this region vary from very rich to very poor. This is reflected in the health expenditure which varies from USD 6,000 to USD 40. Some countries, even those in the LMIC category, are making an effort to improve health by devoting a higher percentage of their GDP to health services, while a few countries do not seem to be addressing the health needs of their population. Universal health coverage seems to be characteristic of the wealthy countries, demonstrated by the fact that low HDI countries also have the lowest UHC Index. It can be predicted that quality of services will suffer in these same settings.

Hong Kong is a special administrative region in China with a much higher HDI level than mainland China. We will deal with it as a separate entity even though politically it is part of the PRC. The population of 7.4 million benefits from a more advance healthcare system with different outcomes. Likewise, Taiwan, a country of 23 million, is not recognised as an independent country and so it is not listed in any WHO region. However, it has high economic development and the HDI was estimated at 0.93 in 2023. A mandatory, national health insurance system was introduced in Taiwan in 1995 to all citizens. Health expenditures is 6.4% of GDP. As with Hong Kong, we will refer to Taiwan separately since both are high prevalence countries which have developed services for thalassaemia.

Table 13. Overall health status in the region

Country	IMR/1,000 livebirths	Under 5 mortality/1,000 livebirths	Life expectancy	Healthy life expectancy at birth
Australia	3.1	4	83.73	70.19
Brunei	8.2	9	74.54	65.6
Cambodia	20.3	23	71.46	61.5
China	4.5	6	78.79	68.5
Hong Kong	1.17	1.97	85.83	NA
Laos	35.2	39	69.27	60.5
Malaysia	6.8	8.0	76.42	65.7
Papua New Guinea	32.0	40	66.12	57.1
Philippines	22.14	27	72.3	62.0
Singapore	1.54	2.0	84.27	73.6
Vietnam	14.0	20.0	74.74	65.3
Taiwan	3.9	4.1	79.84	NA

These basic health indicators are related to HDI and wealth of the countries. The same is true of the various services.

Table 14. Available services

Country	Doctors/1,000 population	Nurses/1,000 population	MRI density per million	VNRD as % of total donations	National haemovigilance programme
Australia	4.1	13.7	14.71	100	Yes
Brunei	1.61	6.7	2.39	100	No
Cambodia	0.2	1.0	0.07	100	No
China	2.5	3.5	NA	Almost 100	No
Hong Kong	1.3	8.2	NA	100 shortages	Yes
Laos	0.4	1.2	0	70	No
Malaysia	2.3	3.5	2.89	99.9	
Papua New Guinea	0.1	0.5	0	NA	No
Philippines	0.8	4.8	0.3	41	No
Singapore	2.6	6.2	7.76	100	Yes
Vietnam	0.8	1.5	NA	40% of needs	No
Taiwan	1.6	4.6	NA	100	Yes

- Manpower is an important contributor to quality of health services. If the number of doctors and nurses is insufficient for the whole service, then it is probable that thalassaemia clinics will not have adequate staffing. In this region, Cambodia, Laos, Papua New Guinea, the Philippines, and Vietnam have less than one doctor per 1,000 of the population. The same countries, with the exception of the Philippines, are lacking in nurses.

- The possibility of using MRI to measure iron in the heart and liver seems possible only in Australia, Brunei, Malaysia, and Singapore. Very large patient populations of this region cannot benefit.

- Adequacy and safety of blood is also deficient, except for four countries with the least number of patients (Australia, Hong Kong, Singapore, and Taiwan). To make matters worse, many patients have to pay for blood since many countries do support all patients with universal coverage. In a report from southern China, patients need to pay USD 260.6/ month for blood while the monthly family income is USD 198.5 (1.3 times more than the monthly income), to which serious shortages in donated blood must also be added. This adds to the burden of disease and takes away one's wellbeing, quality of life, and survival [122].

Country	β-thal carriers	HbE carriers	Expected β-thal patient births/1,000	Expected HbE/β-thal births/1,000	Known β-thal patients	Known HbE/ β-thal patients
Australia	0.4	0.4	0.004	0.008	332	•
Brunei	2	3.7	0.1	0.37	179	•
Cambodia	0.2	34.4	0.001	3.44		•
China	0.66%	•	0.334	•	•	•
Hong Kong	3.05	0.33	0.233	0.05	382	•
Laos	2.6	30	0.169	3.9	275	•
Malaysia	2.9	2.6	0.21	0.377	4,906	3861
Papua New Guinea	5	NA	0.625	NA	•	•
Philippines	1.2	0.4	0.036	0.024	600	•
Singapore	1.6	1.7	0.064	0.136	258	•
Vietnam	1.63	3.5	0.066	0.285	20,000	•
Taiwan	1.1	•	•	•	454	•

Table 15 Epidemiology of the thalassaemias in the West Pacific

- In Table 15, the number of patients represents only the last numbers reported to TIF by local collaborators and it can only be an approximation. Apart from Vietnam and Malaysia, most countries of the region report small numbers. However China is expected to have a large affected population, but because of a lack of registry and each region having a separate policy, even an approximation is not possible. Based on carrier frequency of β-thalassaemia in the southern provinces, the expected affected births are around 2,000 (1,966). This could mean almost 30,000 patient living up to the age of 15 years, without considering HbE (low frequency) and alpha thalassaemia (high frequency).
- In the reported patient numbers, the total given does not differentiate TDT and NTDT, except in Malaysia, which maintains a national registry.
- It is important to mention that there may be other countries with which TIF has little contact and data. The Vanuatu archipelago, for example, is said to have a 5.7% carrier rate of β-thalassaemia, which would provide 0.8 affected births per 1,000 livebirths. The α-thalassaemia rate is even higher. In particular, in one small island, Maewo, the carrier rate for beta thalassaemia exceeds 20% [123]. This is a small population of over 300,000 people, but more detailed information is needed, and the fate of patients needs to be investigated.
- In New Zealand, a recently created patient support group has identified 61 thalassaemia patients in the country. These haemoglobin disorders predominantly affect ethnic minorities from Africa, South Asia, Southeast Asia, and the Mediterranean, who are recent immigrants to this country, while the Maori and older European populations have a negligible prevalence of these genes.

Country summaries

Australia: Australia is a country of immigrants in which about 12% of the population has ancestors from thalassaemia-prevalent countries. The number of known thalassaemia patients is over 300, but since there is no national registry this may be a minimal number. Some estimate the prevalence to be 600 with thalassaemia and a small number (80+) with sickle cell syndromes. Australia is a high-ranking economy, and its medical services are characterised by a very strong infrastructure and an active contribution to medical research. In this research thalassaemia is well represented. The level of clinical care for thalassaemia may be regarded as on par with European reference centres and so outcomes can be a measure of comparison with those other countries. In one study of iron loading and its control, it was found that mean serum ferritin in TDT patients was 1686ng/ml and 1,230 in NTDT patients, with only 10% exhibiting cardiac sideroris by MRI T2* measurements; on the other hand, hepatic iron load was high (LIC by R2 Ferriscan) in 48% of all thalassaemia patients and 33% of TDT patients [124]. In a more recent survey of adult women with TDT and age range from 18 years to over 50 years, 63.3% had a serum ferritin of <1,000 ng/ml and the complication rate was similar to that of western countries' reference centres; 33.3% had hypogonadism, 15.0% had diabetes mellitus, and 21.7% had hypothyroidism 21.7% [125]. These outcomes are comparable to those reported by European reference centres. For prevention, carrier screening tests are available and free with a referral from many GP clinics. Screening is voluntary, but it is not certain that community understanding is enough to bring most couples to the counselling clinic. Prenatal diagnosis and preimplantation genetic testing are available.

In summary the burden of disease is reduced by good clinical services, but there is a question whether birth incidence is affected by the current level of preventive services.

Brunei Darussalam: Brunei Darussalam is a Sultanate of 452,524 (2023 est) people that is located on the island of Borneo. Most of the population is of Malay origin, with some indigenous people and a Chinese minority. It is an oil rich country with a booming economy. Thalassaemia and HbE are carried by about 5–6% of the population, and 200 patients are reported to be under treatment [126]. Of these patients, 55 are on regular

transfusions according to a newspaper report from the main treatment hospital (Women and Children Centre of Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital). Concerning the level of care and the outcomes of patients, little is known because of no published data and also there is no patient association linked to TIF. Voluntary screening is available and awareness promoting events organised by the Women and Children services take place annually.

Cambodia: In Cambodia, β-thalassaemia is carried by only 0.2% of the population; however, HbE is carried by 34.4%, so that thalassaemia syndromes are frequent, with about 130 new cases per year. There are large regional differences in the frequency of thalassaemia genes; for example, in one region (Preah Vihear) the carrier rate of HbE is 55.9%. In addition, there is a prevalence of non-deletional as well as deletional alpha thalassaemia [127]. HbE/ β-thalassaemia is the most common form requiring treatment along with non-deletional α-thalassaemia, however, numbers are not known. A large proportion of these patients are likely to have NTDT, but severity is expected to be variable and morbidity to increase with age. Packed red cells (PRCs) are available at most referral hospitals (provincial hospitals). Oral iron chelators [deferiprone (DFP) and deferasirox (DFX)] are only available from a private pharmaceutical company [128]. In the National Pediatric Hospital, Phnom Penh, there are about 450 children registered as haemoglobinopathy (2018) of which 150 are severe cases (115 β- Thal, 45 α- Thal/HbH disease). In 2011, the Ministry of Health developed and published the *National Guideline for the Clinical Management of Patients with Thalassemia in Cambodia*. The guideline is not generally known or practised outside the National Pediatric Hospital. Oral deferiprone (GPO-L1, product of Thailand) is available in private pharmacies, but it is not on the list of essential medicines of the Ministry of Health, so it is not often used. The other chelating agents are not available in the country (information from Dr Try Lytheang, Department of Paediatric Hemato-Immunology, National Paediatric Hospital, Phnom Penh 2019). These facts and the absence of health insurance coverage means that the majority of patients do not benefit from adequate medical care and so disease burden is expected to increase with age and early death is a common outcome.

China: China is a country with a huge population (estimated in 2023 to be 1,425,671,352 people) and a large geographical territory. Thalassaemia and other haemoglobin disorders are highly prevalent only in the territories south of the Yangtze River. Migration flows are expected to carry the genes to the northern territories, but there are currently no data on the extent of epidemiological change. The nationwide prevalence of β-thalassaemia is 0.66% in mainland China [129]. Current knowledge of epidemiology is summarised in Table 16.

Table 16. Epidemiology of thalassaemia and haemoglobin disorders in Southern China

	Fujian	Guangxi	Guangdong	Guizhou	Hainan	Hong Kong	Sichuan	Yunnan
α thal carriers	3.17%	14.95%	8.53%	9.76%	12.69%	5%	1.66%	?
β thal carriers	1.32%	6.78%	4.53%	4.9%	2.09%	3.05%	3.2%	3.7%
HbE carriers	0	0.42%	0.1%	0	0	0.33%	0	1.6
Expected β thal/1,000	0.044	1.15	0.513	0.03	0.109	0.233	0.256	0.342
Expected β /HbE/1,000	0	0.142	0.023	0	0	0.05	0	0.296
Total β thal births	18	803	552	17	132	16	202	224

Total β /HbE births	0	99	24	0	0	3	0	194
Total α thal hydrops	18–20	902	182	17	13	19	1-2	94

In these eight provinces, almost 2,000 new patients are added every year who are homozygote β-thalassaemia to which 320 with HbE/ β-thalassaemia are added. The births of significant syndromes of α-thalassaemia are not known, but since non-deletional forms exist the burden of disease increases even more. In addition, several thousand cases of hydrops fetalis are expected in these provinces (3,325 were reported as the annual incidence in Guangxi). To this burden the relatively rare cases of thalassaemia found in the northern provinces must also be added. The contribution of northern Chinese populations may be greater than expected, since a recent study of 974 pregnant women in the north found that around 3% were diagnosed as β-thalassaemia carriers [130]. The total number of living patients across China is not known, but a recent publication estimates that about 300,000 people in China have thalassaemia major or intermedia requiring medical intervention, even though 15,000 are currently being treated [131].

The level of care is variable. There are centres of excellence mainly in university hospitals, but poor care is witnessed (from TIF visits) in rural and small urban settings. A 2011 report to TIF from the China Thalassemia Association stated that thalassaemia patients face poverty, discrimination, and employment and insurance problems. Inequalities were found to be associated with low education and place of residence. Progress is, of course, ongoing and there is now nation-wide availability of partial or full insurance for prenatal genetic testing, RBC-transfusions, iron-chelating drugs, and haematopoietic cell transplants, even though regional differences remain. Even so, more than half of patients do not receive needed transfusions because of supply shortages [131]. There is also need improve prevention practices. Nevertheless, over the years there is an increasing trend in healthcare institutions, medical personnel, and healthcare expenditures in the country, which is expected to also benefit thalassaemia patients [132].

The clinical burden still remains high in Southern provinces, as indicated in a recent report on 190 patients. Of these patients, most (61%) had a β^0/β^0 genotype, and so the majority were transfusion dependent and 86.6% were over 20 years old; median pre-transfusion Hb was 8.6mg/dl and only 20% maintained a level >9mg/ml; median serum ferritin was 3080ng/ml and was <1000 in only 10%. This is below internationally accepted standards [133]. In another study of 145 young patients (10–12 years) ,there was iron deposition in the heart of 49%, with serum ferritin levels of >2500ng/ml [134]. Because of these discrepancies, national guidelines and standards are now being developed [135].

The undiscounted lifetime direct medical cost for a patient with β-thalassaemia major was estimated to be USD 518,871 (95% CI: USD 293,524–USD 744,217), 75.6% of which was due to the cost of iron chelation therapy; the annual direct medical cost, direct non-medical cost, and indirect cost per adult patient with β-thalassaemia major at 56 kg were USD 13,478, USD 2,542, and USD 4,000, respectively [136]. The gross national income per capita in China is forecast to amount to EUR 11.87k in 2023.

These facts indicate that the burden of disease is still high both in economic terms and in medical outcomes. Hong Kong is a special case with a highly developed economy (the GDP per capita in Hong Kong is expected to reach USD 44,931.00 by the end of 2023) and more organised and uniform health services (e.g. IMR <2/1000). The 350–400 patients under treatment are expected to have better outcomes even though recent data are not available.

Prevention programmes exist now in all the high prevalence provinces, but they are most organised in Guangxi and Guangdong. Premarital screening and prenatal diagnosis (PND) for the prevention of thalassaemic foetuses are available [137]. In these provinces significant reduction of birth incidence has been achieved.

Laos: Laos is a country of 7.5 million in which HbE is the predominant variant with much less β-thalassaemia. The predominant clinical syndrome is expected to be NTDT. Health services are generally "poor" in this low resource country, as evidenced by a high IMR and under-5 mortality. This is reflected in thalassaemia services in which patient care is indeed limited, and treatment is only available in the capital city of Vientiane. The level of blood transfusion seems adequate and bedside filtration of packed red cells is offered. However, for iron chelation, only deferiprone is offered. Patient care is suboptimal on this evidence. Prevention has started and there is a screening service in Laos which consists of premarital screening (voluntary), preconception screening (voluntary) and antenatal screening (mandatory). According to the National Strategy of Maternal and Child Health, screening for thalassaemia, along with anaemia in general, is a required obstetric service. The intention is to reach ANC attendance of 100% by 2025 (at present 60% coverage only). There is a laboratory screening algorithm for antenatal clinic screening. Amniocentesis is available in the capital Vientiane, along with a guideline for the safe termination of pregnancy. Molecular diagnosis is available in the capital. In the provinces, however, there are limited human resources [unpublished information from Dr. Alongkone Phengsavanh, Dept of OBGYN, and Dr. Sourideth Sengchanh, Dept of Paediatrics, University of Health Sciences 2019] [138].

Malaysia: Malaysia has maintained a thalassaemia patient register for many years. The most recent report was published in 2025 on 8,681 patients [139], which rose to 9,342 in 2025. Of these, 5,442 are graded as TDT and 3,900 as NTDT [140]. The majority of the patients were in the group of 5.0–24.9 years of age (5,146–7.984 patients, 64.45%), and the largest number of patients were between 10.0 and 14.9 years (1.394, 17.46%). However, this large cohort includes a spectrum of severity, including HbE/β-thalassaemia, thalassaemia major, intermedia, and HbH disease. For those with thalassaemia major, the peak age group is 10.0–14.9 years. For HbE/β-thalassaemia, the peak age group iwas 15-20 years. As seen in the age distribution curve, this is a young patient population (Figure 4). This is an indication that much improvement is required across the treatment centres in Malaysia to improve outcomes by conventional treatment, which is also evidenced by the distribution of patients according to the level of ferritin.

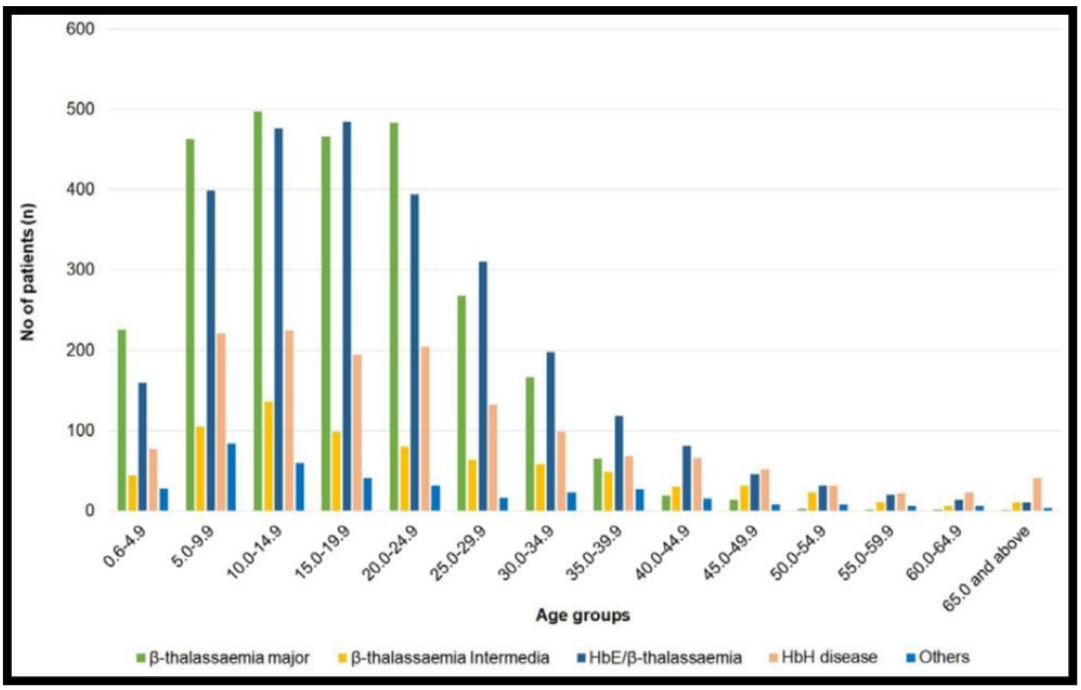

Figure 4. Age distribution of thalassaemia patients in Malaysia

In economic terms, the lifetime cost for a TDT patient has been calculated to be USD 561,208, with chelation cost accounting for 56.9% of the total, followed by blood transfusion costs at 13.1% of the total. Including the family healthcare expenditure, then lifetime cost is estimated to be USD 606,665 [141]. The survival probability of 45 years of age has risen from 65% in 2007 to 85% in 2017. Government-funded, public universal healthcare is accessible to all legal residents of Malaysia and provides low-cost universal and comprehensive services.

In assessing the burden of thalassaemia, it essential to review results from provinces where many patients are treated. In a 2024 report from Sarawak on patients aged 10 years and above (median 21 years), 34.8% had mean serum ferritin 2500ng/ml and above, and 66.6% had liver iron concentration (LIC) ≥7mg/g. These are indications that burden of disease will increase rather than decrease over time [142]. In another report on the clinical findings of 200 TDT patients (aged 24–36 years), 65.5% maintained a pre-transfusion Hb <9g/dl, a serum ferritin of >2500ng/ml in 55.5%, a cardiac MRI measurement of >20ms in 75.7%, and a severe LIC in 66.3% [143]. These are indications that progress in case management is still needed in Malaysia, despite its high rank in HDI and its upper-middle-income status. Also, blood supplies are adequate and include NAT testing and leukodepletion in all centres. However, adherence (i.e., actually taking the medications reliably) remains at low levels (21–40%) [140].

As in many countries, issues such as adherence and psychosocial support must also be considered to improve outcomes and reduce the morbidity burden. In a recent study amongst adolescents with TDT, only 51.4% had good adherence [144].

In a 2023 TIF patient survey on service quality, 10 responses received were in the Malay language, representing 0.125% of the total Malay patient population. The average age of this group was 31.7 years (range 21–48), which may indicate an adult population or at least one that is growing past childhood. Only three patients were employed full time, while five were looking for work. This may reflect employer prejudice towards chronic disease. Five patients had less than a high school education, with three having completed secondary and two with tertiary education. Seven patients were single and three married. Pre-transfusion Hb was below 9mg/dl in 9/10 patients, a fact which must be confirmed since this is below guidelines. Chelating agents are available, with no interruptions in supply. Ferritin levels are measured every three months in only half of the respondents, while the other half are tested every 6 months. Two patients did not know their ferritin level, while three were below 1000ng/ml, and 3 had >4000ng/ml. Cardiac T2* is measured annually in 9/10 patients, but measurements are far below the performance experienced in reference countries; only 2/10 have T2* >20ms, while three patients did not answer (presumably they were not aware of their result). Liver iron is measured by MRI in 9/10 patients, while one did not respond. Two patients reported LIC <7 mg/kg dw, while three did not know their result. Despite universal health coverage, three patients stated that they pay for blood transfusion! Concerning the availability of multidisciplinary care, none of the patients responded to the question. This was a very small sample of the total patient population, but the indications are that service, knowledge, and community awareness still need improvement.

In November 2016 the prevention policy (initiated in 2004) was reviewed by launching a nationwide screening of 16-year-old students, and complemented by a cascade screening of high-risk families. The reduction in birth incidence has not been significant so far partly because only about 28% of at-risk couples accept both prenatal testing and pregnancy termination (information from Dr Mohammed Hishamshah 2018). Also, knowledge of thalassaemia among unmarried individuals is found to be low [145]. There seems to be poor understanding of the meaning of being a carrier and the need for prevention [146].

Papua New Guinea: Little is known about thalassaemia cases in Papua New Guinea, and TIF has only been able to communicate with one doctor and one parent. The north coastal region of the country is where malaria is hyperendemic and where most thalassaemia genes are found. A2006 study found that the frequency of the alpha thalassaemia genotype in pregnant mothers was 0.61 [147].

A study of 21 patients and their families in 2021 found they were transfused at very low Hb levels, and "no child was receiving chelating agents, and most had clinical evidence of iron overload. There were important impacts of thalassemia on quality of life, including very poor school attendance and some aspects of children's self-perception. Families faced significant burdens and made genuine sacrifices to care for their children" [148]. In fact, this report referred to just blood transfusion and no attempt to treat iron overload. This is a situation reminiscent of the 1960s in most countries. If an old study is found to be true, then 5% of the population of this country could be carriers of beta thalassaemia, and almost 100 new affected children can be expected to be born every year. If this is also true, then most will die without a diagnosis during childhood.

Philippines: Limited population studies of Filipinos in Hawaii and Taiwan found gene carrier frequencies of 9.1% and 6.8%, respectively [149, 150]. Another study in Taiwan showed a β-thalassaemia carrier frequency of 0.9% in Filipinos [150]. This confirms Mutolsky's findings of the 1960s [151].

Haemoglobin disorders are now included in the national newborn screening programme [152]. The alpha thalassaemia syndromes, especially HbH disease, are predominant, while β-thalassaemia is rare.

Being a rare disease in a low resource country means that it has not been given priority in health policy. Inclusion in the NBS programme is one step taken, as is the creation of a national registry, which however has never been completed: in 2019, there were 60 β-thalassaemia cases and 15 HbE/beta thalassaemia cases. Knowledge concerning thalassaemia is very limited among health professionals, according to a report from Dr Maria Liza T. Naranjo, M.D, National Children's Hospital, Manila, in 2019 (SEATHAF meeting). There is a health insurance system (PHILHEALTH) that covers blood transfusion (USD 52.33 per day) as outpatient care for a maximum of 22 days/ year and hospital admissions (USD 133.00) a maximum of 44 days/ year. Iron chelation is not supported but this is in the pipeline. Blood donation is 41% from volunteers, 44% from replacement donations (usually by family members, and 15% from paid donors. Pre-transfusion Hb can fall to 3–4g/dl (at a cost of USD 28–105) in many parts of the country. Leukodepleted, packed red cells are not always available, and the cost rises to USD 34–166. There is no NAT testing. Monitoring of iron overload is by serum ferritin and MRI T2* (private) at a cost of USD 285.71. All three iron chelating agents are available in the country, but only at the patient's expense (Dr Marites B. Estrella, 2019). Many patients still die between 9–15 years, although many survive up to around 30 years. With these facts, disease burden is high due to the lack of support to families, increasing complications, and premature death [153]. A recent analysis of 116 patients with all types of thalassaemia found that 82% were under the age of 12 years and only 8% were above 16 years (information from Dr Maria Liza T. Naranjo, October 2025). Currently, 62.5% of the patients have to pay for iron chelation, while 37.5% are government-assisted.

Singapore: In contrast to its neighbours, Singapore is a very high-income country with developed health services and adequate insurance coverage for its citizens. The population (6 million est. for 2025) is multi-ethnic, but Chinese are predominant (76%), with Malays at 15.4% and Indians at 7.4%. In a molecular study of cord blood specimens, the carrier frequency for alpha-thalassaemia mutations was about 6.4% in the Chinese, 4.8% in Malays, and 5.2% in Indians. Only alpha deletions were observed in the Chinese. The carrier frequency for beta-thalassemia mutations was 2.7% in the Chinese, 6.3% in Malays, and 0.7% in Indians [154].

The National Thalassaemia Registry (NTR) in Singapore was established in 1992. This is a genetic registry linked to the prevention programme, and it provides a record of thalassaemia's prevalence has evolved over the years. 105 cases of thalassaemia major were registered between 1992 and 2019: 2.91% are α-thalassaemia, 0.93% are β-thalassaemia, and 0.64% are HbE carriers

There is a significant patient population which is offered treatment according to guidelines. However, results according to a recent report indicate that iron chelation could be better: liver iron loading was the most common transfusion-related complication and occurred in 79% of patients. Cardiac iron loading (T2* technology is available at a cost of USD 270) was noted in 28.3%, and endocrine complications were present in 34.2%. Liver iron loading was significantly associated with higher mean ferritin levels. The cohort of older

thalassaemia patients aged 31–50 experienced significantly higher rates of cardiac iron loading, endocrine complications, and lower TranQOL scores compared to younger age cohorts [155].

A National Programme for Thalassaemia Screening was initiated in 1992 at the KK Women's and Children's Hospital. This programme registers all thalassaemia carriers, provides free counselling, and subsidised screening for USD 15 (spouse and first-degree relatives).. Genetic counselling is provided to at-risk couples with informed choice for prenatal diagnosis (unpublished informationfrom Law Hai Yang, Deputy Director, National Thalassaemia Registry, KK Women's and Children's Hospital, 2018).

Patient numbers are as follows: beta thalassaemia major 102 (64 Chinese), intermedia 17 (14 Chinese), HbE/beta thalassaemia 139 (98 Malays), HbH disease 699 (582 Chinese), other haemoglobinopathies 477 (272 Chinese).

Vietnam: α-Thalassemia is particularly prevalent in Vietnam, with a reported prevalence rate of 51.5%. Carriers of β-thalassaemia are overall only 1.63% and HbE 3.5%. A newer study of 10,112 first-time pregnant women and their husbands indicates alpha thalassemia is 10.73%, the carrier rate of beta thalassemia is 2.24%, and 0.29% (29 patients) of patients carry both alpha thalassemia and beta-thalassemia gene mutations [156]. The different findings may be due to regional differences. In a similar study from south Vietnam (Ho Chi Minh City), 7.82% were carriers of α-thalassemia (α-thal), 5.31% were carriers of β-thalassemia (β-thal), and 0.63% were concurrent α-/β-thal carriers, and the differences again may be regional [157]. Also, from South Vietnam, 6.2% of women were found to be carriers of β-thalassaemia [158].

Patient numbers are not known (because of the lack of a national registry), but local experts estimate about 20,000 with clinically significant syndromes (information comes from discussions with doctors at the National Institute of Haematology and Blood Transfusion NIHBT, Hanoi). These patients are from different ethnic communities and geographical regions of the country; the majority are those of the Kinh ethnicity, but there are also 54 other ethnic or tribal groups [159]. The disease is present in all regions of Vietnam, but it is more prevalent among mountainous ethnic minorities. The level of care varies considerably, but it is regarded as improved in the main urban centres of Hanoi and Ho Chi Minh City. Low pre-transfusion haemoglobin level (62.1 ± 1.7 g/dl) has been reported in the past and is still the reality in some regions, with some patients not chelated [160]. A study of 288 health-insured paediatric patients (mean age of 10.4 (±11.3) years) found that the average annual economic burden of thalassemia treatment was approximately USD 426.7 (±294.0), in a region in which the average income was USD 158.7 /month. The treatment was costly for low-income patients, as it cost nearly a quarter of an adult's annual income in the region. Health coverage is not complete (UHC index 68) and so out-of-pocket expenses are required. This considerably reduces the possibility of optimal care and increases the burden of disease in terms of increased morbidity and mortality [161].

Of the patients treated at the NIHBT, 16.6% are under the age of 6 years, 27.4% are 6–15 years, 27.7% are 16-30 years, and 28.3% are over the age of 30 years. Also, 49.1% have HbE/thalassaemia, 27.7% have beta thalassaemia, 16.1% have HbH disease, and 7.2% have HbH Hb Constant Spring. Health insurance reimburses 100%, 95%, or 80% of the diagnosis and treatment costs, while the country is moving toward the implementation of universal health coverage. Blood donation is voluntary unpaid (100%). DFO is provided only for in-patients and DFP and DFX for outpatients. (presented by Dr Ha Nguyen Thi Thu, NIHBT Thalassaemia Clinic SEATHAF, 2018).

According to a 2025 report from ViTA (the national thalassaemia association), 91% of the blood supply is in major hospitals, and so there is unequal access, with insufficient blood in high-prevalence provinces. Concerning quality, there is limited leukocyte-filtered and phenotype-matched blood outside large hospitals. Voluntary donations account for 98% of blood in Vietnam.

All three iron chelating agents are available and mainly produced in Vietnam. Despite this, cost is high and there is limited access in remote areas. With an incomplete UHC system, many patients cannot afford lifelong therapy and they fail to achieve optimal adherence.

To prevent thalassaemia, in 2021, the Prime Minister approved the National Target Programme, part of which is the prevention of thalassaemia in ethnic minorities and in mountainous areas. The objective is to reduce the number of children born with thalassaemia and gradually improve the quality of life of children born with thalassaemia. This is achieved through screening and counselling as part of the pre-marital health check but also through screening women in pregnancy [162]. Prenatal diagnoses (PND) and (PGD) are offered in collaboration with the obstetric hospitals in Hanoi. These programmes are small-scale and fragmented, but there is an effort to raise community awareness and promote genetic counselling. Another limiting factor is the cost of thalassaemia screening tests, which is entirely borne by the individuals themselves.

The picture is of fairly rapid development in this large country and hope for the coming years.

Taiwan: Taiwan is a high income, high HDI country with a high prevalence of thalassaemia syndromes. It has had a single-payer, national health insurance programme since 1995. There is a registry database for catastrophic illness, which includes patients who suffer from major diseases and are granted exemption from co-payment.

In Taiwan, patients with TM primarily are treated with RBC transfusion and iron chelation, including leukocyte-depleted RBCs, to maintain pretransfusion haemoglobin levels greater than 10 g/dl. Iron chelation therapy includes DFO, oral deferiprone, and oral deferasirox, tailored to individual needs. In a study of 2011, the median age of TDT patients was 17.2 years (range, 0.1–48.0 years), with 58.1% of patients being younger than 20 years and 41.9% older than 20 years. The mortality rate fell from 2.9% in 2007 to 0.7% in 2011. The complication rates have patterns similar to those of reference countries [163]. In a more recent study of 2,984 patients with beta-thalassaemia, the mean (SD) age was 37.8 (23.7) years, which again is indicative of a survival rate analogous to that of reference countries [164].

A National Thalassemia Major Prevention Programme has been in place since 1993. A study conducted in 2012 indicated a 91% reduction in the incidence of thalassaemia major compared to the period between 1986 and 1995 in Southern Taiwan. Consideration must be given to the impact of interracial marriage, since global migration and international marriage has affected the distribution of haemoglobinopathies in Taiwan. A more comprehensive prenatal screening for new immigrants with a longer follow-up is warranted [165].

As far as disease burden goes, Taiwan appears to report results analogous to reference countries such as Italy.

Comments

As in other WHO regions, the thalassaemias take second place in the interest expressed by governments and even the regional office. Quality of service still remains a function of a healthy economy and prevalence rate. Middle level economies with high prevalence, including Malaysia and China, are promoting policies that are expected to give results in the near future, while other countries have yet to adopt such policies or offer needed support to families and patients.

WHO European region (EUR)

The European region, as all the others, has a wide variation in the effectiveness of health systems.

Table 17

Country	HDI rank	WB rank	HE/cap WB data in USD	HE/%GDP WB data	UHC index
Albania	0.810	UMIC	414.35	6.19	64
Armenia	0.811	UMIC	674.79	9.96	68
Austria	0.940	High	6,208.64	10.88	80
Azerbaijan	0.789	UMIC	304.20	3.98	66
Belgium	0.951	High	5,404.62	10.76	80
Bosnia	0.804	MIC	667.3	8.72	66
Bulgaria	0.845	High	1,011.09	7.66	73
Croatia	0.889	High	1,344.19	7.22	80
Cyprus	0.913	High	2,864.16	8.87	80
Denmark	0.962	High	6,432.37	9.42	80
Finland	0.948	High	4,902.04	9.66	80
France	0.920	High	4,865.18	11.88	80
Germany	0.959	High	6,232.59	11.80	80
Georgia	0.844	UMIC	477.71	7.26	68
Greece	0.908	High	1,768.11	8.5	77
Ireland	0.949	High	6,448.02	6.12	80
Israel	0.919	High	4,223.87	7.34	80
Italy	0.915	High	3,228.44	8.52	80
Kazakhstan	0.837	UMIC	420.98	3.74	80
Kyrgystan	0.720	LMIC	85.88	4.92	69
Malta	0.924	High	3,352.77	9.52	80
Montenegro	0.862	UMIC	1,107.06	10.92	72
Netherlands	0.955	High	5,796.03	10.10	80
North Macedonia	0.815	UMIC	561.69	7.62	74
Norway	0.970	High	8,692.58	7.95	80
Poland	0.906	High	1,543.71	7.00	80
Portugal	0.89	High	2,743.58	10.00	80
Romania	0.845	High	902.27	5.75	78
Russian Federation	0.832	High	1,078.23	6.92	79
Serbia	0.833	UMIC	903.12	9.66	72
Spain	0.918	High	2,910.84	9.74	80
Sweden	0.959	High	6,152.33	10.89	80
Switzerland	0.970	High	10,963.43	11.71	80
Tajikistan	0.691	LMIC	78.61	7.63	67
Turkiye	0.853	UMIC	358.88	3.70	76
Turkmenistan	0.764	UMIC	579.15	5.37	75
UK	0.946	High	5,366.78	10.87	80
Uzbekistan	0.740	LMIC	169.43	7.36	75
Ukraine	0.779	UMIC	369.90	8.20	76

The countries of this region can be divided into those in which the haemoglobinopathy genes are prevalent in the indigenous populations (mainly along the Mediterranean coast) and those where these genes are rare but are being introduced by migration flows in recent decades.

- Countries with a carrier rate for β-thalassaemia >2%: Albania, Azerbaijan, Bulgaria, Cyprus, North Macedonia, Greece, Italy, Malta, Tajikistan, Turkey, Uzbekistan.
- Countries with a carrier rate for β-thalassaemia 1–1.99%: Armenia, Bosnia, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, Portugal, Romania, Serbia, Spain, Turkmenistan.

- Countries with a carrier rate for β-thalassaemia <1% in the indigenous population: Austria, Belgium, Croatia, Denmark, France, Germany, Ireland, Netherlands, Russian Federation, Sweden, Switzerland, United Kingdom.

Table 18. High prevalence countries

Country	% β-thal carriers	% HbS carriers	Expected β-thal patient births/1,000	Expected SCD births/1,000	Known/est β-thal patients	Known/est SCD patients
Albania	5.0	1.4	0.625	0.399	356	174
Azerbaijan	3.71	0.8	0.344	0.164	1,350	200
Bulgaria	2.5	0	0.156	0	270	0
Cyprus	14	0.27	4.9	0.191	659	56
North Macedonia	2.6	0	0.169	0	25	0
Greece	8.1	0.6	1.64	0.252	3,241	1,080
Italy	4.3	2.1	0.462	0.562	7,102	2,280
Malta	3.0	0	0.255	0	21	0
Tajikistan	5.0	0	0.625	0	NA	NA
Turkey	2.2	0.44	0.121	0.053	5,500	4,300
Uzbekistan	3.0	0	0.225	0	250	0
Total					18,774	8,090

- High-prevalence countries, like other European countries, have also been accepting immigrants from the Middle East and Africa. The effect of these migrations is not documented in Table 18, since it is a changing picture each year. The table reflects only the indigenous population. In general, migrations have introducing more SCD than β-thalassaemia.
- The estimate of affected births is not calculated, since the countries with the highest carrier prevalence have developed effective prevention programmes, which have been running for several decades and have significantly affected birth incidence.
- Cyprus, Greece, Italy, and Turkey have developed services for both prevention and patient care that include socio-economic coverage; this means catering for both financial and psychosocial needs of patients. Turkey, being a large country with areas that are less developed and with major migration/refugee issues, has regional deficiencies in patient care, which authorities are trying to address.
- In the rest of this group of countries, services provided do not satisfy all needs to the same extent. This increases the burden of disease and results in poor outcomes for patients.

Albania: Albania has just under 3 million people. Both β-thalassaemia and SCD are prevalent, and treatment centres are at two locations, the Mother Tereza Hospital in Tirana and the General Hospital of Lushnjë. Published literature is scarce, but according to the latest report (2022) from collaborators in the country, the following information is provided:

- Patients: There are 291 thalassaemia major patients (180 Tirana, 110 Lushnje, 1 Fier) and 290 patients with sickle cell syndromes (190 Lushnje, 5 Fier, 95 Tirana). There have been 7 new births in Tirana in three years. There are no known HbH cases, according to the report.

- Blood transfusion: Shortages are seasonal in July and August. However, there is also a chronic shortage. since donations in Albania are 12/1,000 inhabitants. Safety is now assured since the national transfusion service is well equipped and has been centralised since 2010.
- Iron chelation: All three chelators are available and free of charge.
- MRI is still not available.
- Multidisciplinary care: MDC works well in the hospital service in Lushnje. In Tirana, family physicians have to refer patients to specialists; this is usually not proactive monitoring but only once a complication is suspected.
- Prevention: There is no national programme for prevention. If premarital couples are informed by their GP, they go to private lab. The prevention of having a 2nd affected child is practised

These practices are not conducive to optimal care and good outcomes.

Azerbaijan: Azerbaijan is a country of high prevalence of beta thalassaemia. With the carrier rate of 4–8.6%, β-thalassaemia is one of the most prevalent hereditary disorders in the country {129}. There are almost 2,000 patients with haemoglobin disorders under treatment in the country, or around 1 per 5,000 of the population, amounting to a significant public health burden. All patients in the country are treated in one centre in Baku, the Republican Thalassaemia Centre, and they are investigated and provided with blood for transfusion again by one centre, the Institute of Haematology and Transfusion Medicine. This means that clinical and scientific expertise are concentrated and provided for the benefit of patients.

- There is considerable support for this centre from the Heydar Aliyev Foundation, making the services sustainable and allowing development. There is also support from the Azerbaijan Thalassaemia Association, headed by a group of well-informed patients.
- There has been universal health coverage under a compulsory health insurance system since 2021, and patients pay no out of pocket expenses.

With these advantages there has been progress over several years. A prevention programme of premarital screening has been mandated by law since 2015; there is also genetic counselling of at-risk couples and the offer of prenatal diagnosis. Since 2015 over 500,000 people have been tested, of which 3.7% have been found to be carriers of beta thalassaemia.

Patients express deficiencies in the quality of care, which must be given consideration.

- Reactions to blood transfusion are frequent. There is no haemovigilance programme and so these reactions may not be reported. It was confirmed, for example that 20–25% of the patients have been infected by HCV (in the Azeri population of blood donors, around 5% are carriers of this virus).
- There are periodic interruptions in supplies of chelating agents, especially of desferrioxamine. Measurement of cardiac and liver iron by MRI is still not available, and so those that can afford it travel to other countries, mainly Turkey, for their annual tests.
- Vaccinations and post-splenectomy prophylaxis do not seem to be offered.
- The element of multidisciplinary care, with monitoring by cardiologists or endocrinologists at least, is not offered.

It is clear that despite progress, there are still gaps in the provision of optimal care in this country in which resources are limited (GDP/cap = USD 7,736.7 and 5.9% of the population were living below the national poverty line in 2021).

Bulgaria: Bulgaria has a carrier frequency of 2.4% overall, but carriers are mostly in specific regions, along the Black Sea coast and the south. New affected births each year are estimated at 11 while the latest estimate for the prevalence is around 300 patients. If however, we consider an average of 6% carriers in the coasted areas, where the population is around 1 million, then the homozygote's birth rate in these regions goes up to 0.9/1,000, which means that 9 babies may be born is these regions alone. There is need to create a national patient registry for thalassaemia, which will help greatly in describing the true picture and identifing patients living in low prevalence areas of the country. Bulgaria's health system is based on a compulsory social health insurance scheme, with a single purchaser – the National Health Insurance Fund (NHIF). Despite this, some are uninsured and so out-of-pocket health spending is often necessary. To what extent this affects thalassaemia patients is uncertain. In general, all basic treatment is offered free of charge, including monitoring with MRI techniques for all patients, according to guidelines. There is a growing adult patient population, whose iron status is improving over the years [166].

Prevention is not centrally organised and there is limited or no recorded effect on birth incidence, and there is limited use of prenatal diagnosis.

Cyprus: Cyprus was one of the first countries to respond to the high burden of β-thalassaemia, dating from the early 1970s. Carrier rates were estimated at 15–17% in the 1960s, even though over the years the rate seems to have fallen to 12–14% [167, 168]. The approach to thalassaemia control in Cyprus was comprehensive from the beginning, combining prevention, based mainly on premarital screening, and improving patient management according to the evolution of evidence based clinical guidelines.

From a recent analysis of the Cyprus Thalassaemia Registry (care of Dr S. Christou, 2020) the following age distribution was obtained for patients with β-thalassaemia major: The mean age of patients is 42.3 years, (median 44 years), with a gradual reduction due to patient loss in the 6th decade.

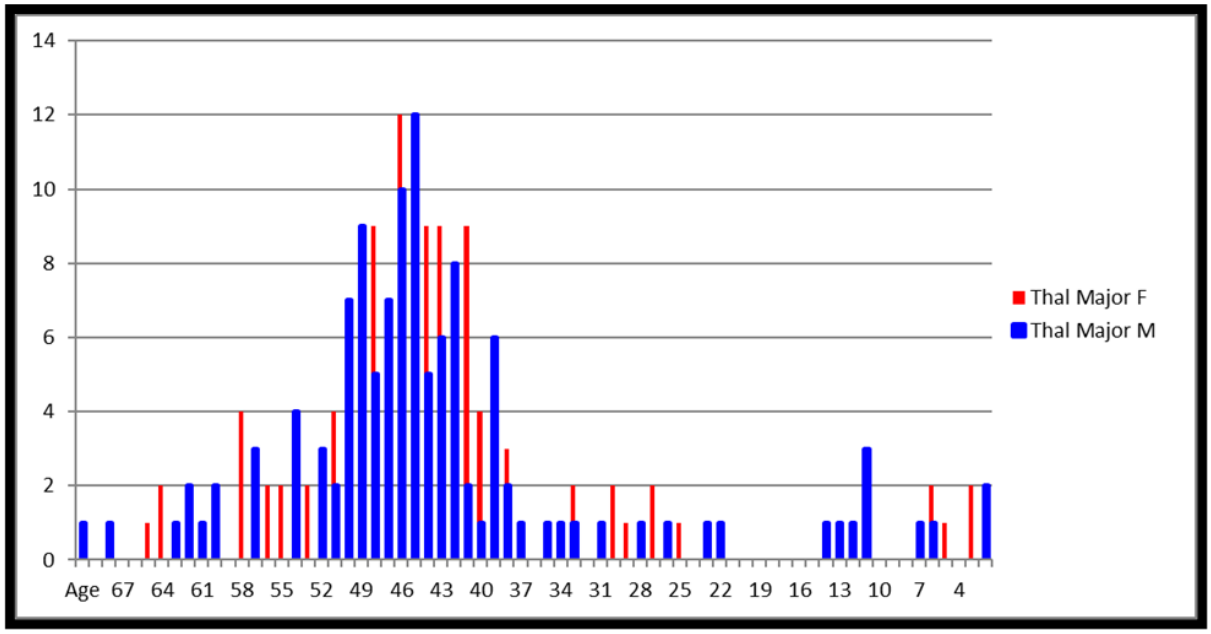

Figure 5. Age distribution of β-thalassaemia major patients in Cyprus

In the recently published data, 538 TDT patients were studied over a total of 19,083 patient years. Median age at 30 December 2018 was 40.9 yrs, IQR 38.0–47.6 [10]. Overall, the mortality was 5.0 per 1,000 patient years in the follow up. The causes of death are shown to be shifting away from cardiac deaths to liver, infectious causes,

and malignancy deaths. In a more detailed analysis of the same cohort, which includes almost all of the TDT patients in Cyprus, 80.4% of individuals survive up to 50 years of age. The effect of genotype on survival and complication rates is analysed in ref. 132, indicating that delays in transfusion and iron chelation due to milder genotype has resulted in more severe long-term outcomes.

Concerning the complications of TDT, the figures reported by the treatment centres of Cyprus, are comparable to the reported results from Greece and Italy, and seem, at the national level, to be the best at this time. The report shows that 48.9% have a serum ferritin level <1000ng/ml, 85.4% have a cardiac T2* >20ms, and 51% an LIC <3 mg/g dw (73.5%< 7 mg/g dw). Also, almost 30% have completed tertiary education and 74% are working full time, while around 50% are married or cohabiting [169]. These results are indicative of strong support from the health authorities and the community.

The adult population of thalassaemia patients are active in various professions and the reduction in new births, demonstrate the reduction in "burden" that conventional therapy allows. The need to limit new births in the 1970s became imperative as resources such as donated blood and iron chelating agents were increasingly introduced for patient survival, but the addition of new affected births each year made it impossible to maintain supplies; the result was that early death was unavoidable. Saving resources has allowed for optimal care to be offered with good outcomes. However, since the 1970s when the prevention programme was initiated much has changed: the condition is now a chronic disease of adults, and the prospect of novel therapies, including curative approaches is now a reality. This influenced the attitude of at-risk couples who are more optimistic about the future, and some accept the birth of an affected child much more than in the past. The premarital screening mandated by the Orthodox Church is now less relevant since civil weddings are increasing. In fact, social changes allow couples to create families without marriage, and prejudice or social isolation of carriers or affected patients is no longer an issue. Such changes have resulted in the birth of new patients to couples who know their carrier status and have been counselled. According to the national registry, there have been 31 β-thalassaemia homozygote births from 2020 to 2024, and 10 SCD births. In addition, migrations from the Middle East and Africa are recording an increase in SCD (clinics on the island are now following 31 SCD immigrant patients).

North Macedonia: From past surveys, the average incidence of the beta-thalassaemia (thal) trait in North Macedonia is 2.6% [170]. This is a small country of 2 million people, with few reported patients – only 25 were last reported to TIF.

The HDI is currently 0.784, which is high ranking but still below its neighbours. There is a compulsory insurance-based health system, with near universal coverage. There have been reports from patients of low pre-transfusion Hb, but detailed information on patient outcomes is not available. No prevention programme is active.

Greece: The National Registry for Haemoglobinopathies in Greece (NRHG) was established in 2009. In 2012 the first review of the registry was published, and in 2019 the analysis of the period 2010 to 2015 was published [171]. The total number of registered patients in this report is 4,032; 2,099 (52.06%), of these are categorised as TDT; 873 (21.65%) are NTDT patients; 1,032 (25.6%) patients have sickle cell anaemia (SCA) or S/β-thalassaemia. The total number of alive patients per age group during this period is provided in Figure 6 below:

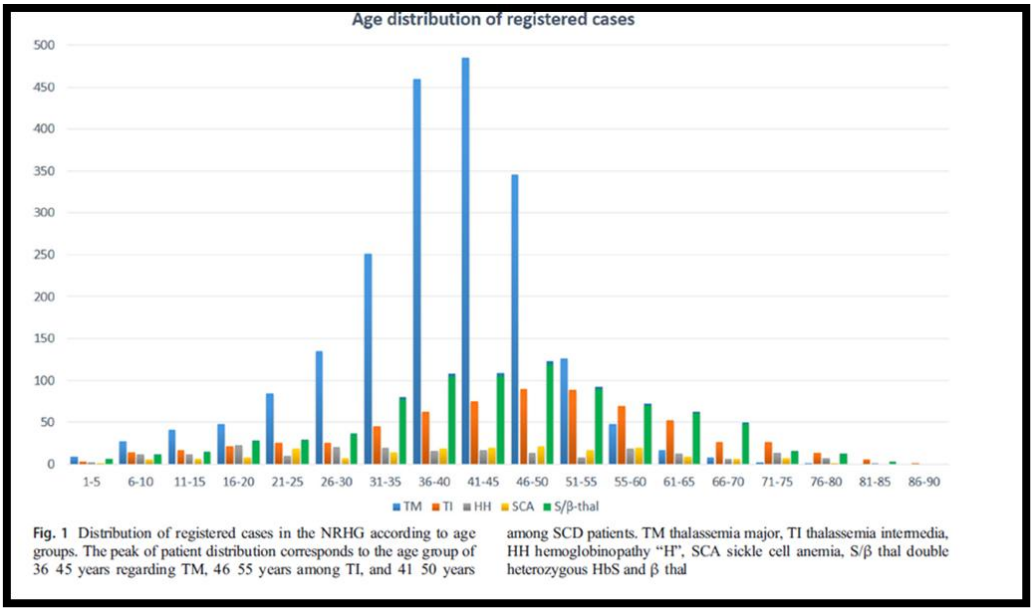

Fig. 1 Distribution of registered cases in the NRHG according to age groups. The peak of patient distribution corresponds to the age group of 36 45 years regarding TM, 46 55 years among TI, and 41 50 years among SCD patients. TM thalassemia major, TI thalassemia intermedia, HH hemoglobinopathy "H", SCA sickle cell anemia, S/β thal double heterozygous HbS and β thal

Figure 6. Age distribution of registered cases

The peak of patient distribution corresponds to the age group of 36–45 years among TM patients, 46–55 years among TI cases, and 41–50 years among sickle cell disease (SCD) patients. These results are comparable to those of Italy, UK, and Cyprus. In a study of 201 eligible adult patients, the median (interquartile range, IQR) age was 45.7 (40.2–50.5) years; 75.6% > 40 years old; the average pre-transfusion haemoglobin, median (IQR) was 9.9 (9.4–10.3) g/dL; the average serum ferritin, median (IQR) was 549.3 (287.2–1034.8) µg/L, with 70% having ferritin <1000 µg/L; MRI LIC, median (IQR) was 2.2 (1.3–4.8) mg Fe/g dw; myocardial T2* was Normal (>20 ms) in 90.5% of patients and mild (≥14 to ≤20 ms) in2.5% of patients [172].

Despite good outcomes, barriers to access healthcare among beta-thalassaemia patients receiving transfusions still persist, especially for those who live far from transfusion centres and have lower incomes [173].

In a multicentric study of TDT patients in Greece, the participants' mean age was 39 ± 9 years (range:18–68). Almost half of the study population were married (46%) and had offspring (42%). Most participants had a higher educational level (77%), and 59% were employed. Only 7% of the participants had an abnormal heart MRI T2*, whereas 39% of the participants had an abnormal liver MRI T2*. Health-related quality of life was assessed, and it was noted that despite good medical care, adult TDT patients exhibit significantly lower HRQoL compared to the general Greek population. Employed TDT patients exhibited both significantly and clinically higher quality of life scores. The relevance to burden of disease is that employment, allowed by good clinical care, enhances quality of life and wellbeing [174].

Patient mean annual cost per patient was estimated to be €32,064 in 2014 [175].

Prevention in Greece has been a weapon to reduce burden of disease since the 1970s. In a recent report from Northern Greece, through the implementation of the haemoglobinopathy screening programme in this region during the last 20 years (2001–2020), the decrease in affected births is 95% and a constant number of 0–4 sick newborns are recorded annually [176].

Italy: According to a 2025 report, the national density of patients with haemoglobinopathies in Italy was 16.0 patients/100,000 inhabitants: 8.7 patients/100,000 inhabitants for TDT, 3.3 patients/100,000 inhabitants for NTDT, and 3.9 patients/100,000 inhabitants for SCD [177].

Italian health services have a long tradition in both prevention and patient management, with good survival and morbidity outcomes, according to a series of publications by Borgna-Pignatti over the years [178]. Here we refer to the latest presentation, which is based on the WebThal database [179]. The cohort in this study represents 3,986 thalassaemia patients treated at 36 centres in Italy, which treat over 50% of the total number of patients in the country. Of the patients with thalassaemia major, 68% were aged ≥35 years and 11% were aged ≤18 years. Patients with thalassaemia intermedia were slightly older:

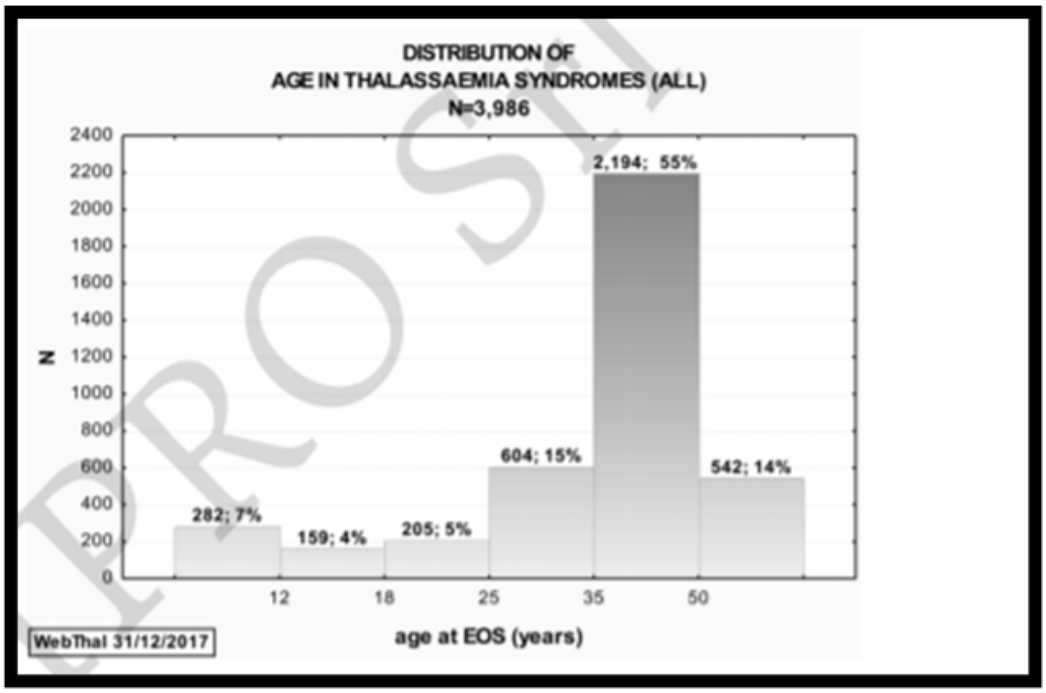

Figure 7. Age distribution of patients with thalassaemia syndromes at 36 treatment centres in Italy

This age distribution bears witness to the successful provision of conventional treatment in Italy and compares well with Cyprus and Greece. This also holds true where the complication rates are concerned. It also demonstrates the limitations of conventional treatment in allowing all patients to have a "normal" lifespan, even under the best conditions.

A second registry exists covering 182 centres and 1,873 TDT patients [180]. An interesting observation from this registry was that centres which treated 30–80 patients show a higher percentage of appropriately monitored patients, compared to centres with fewer patients, supporting the need for reference centres.

A recent study of a longitudinal cohort of 709 transfusion-dependent β-thalassaemia major patients (51.1% males), born between 1970 and 1997, and followed through 2020 at seven major centres in Italy, showed an overall survival probability at 30 years being 93.3% (95%CI: 88.6–98.3) in the youngest birth cohort (1985–1997). The study concluded that survival in patients with β-thalassaemia major continues to improve with adequate access to care, best practice sharing, continued research, and collaboration between centres [181]. Older patients are more likely to develop multiple disease-related morbidities, including osteoporosis, endocrine disorders, liver disease, renal dysfunction, and cancer. Research into clinical outcomes of the older generation of thalassaemia patients, which is increasing in numbers, is needed [182]. In an analysis of 214 TDT patients from Italy, the mean was 46.7 years. Compared to most of the patients of the world, this is a very satisfying record and evidence of the good application of conventional therapy. Yet, the mortality rate is still much higher than matched controls; this same group of patients utilize healthcare resources as their ages increase (e.g. out-

patient service rates). So the burden of TDT must be seen in this light as demanding more and more services, and not simply as an improving outcome [183].

Italy is one of the few countries in which near optimal care is offered free to patients and, through good clinical care and the reduction of new affected births, the burden of disease is reduced. However, immigration of both refugees and economic migrants is altering the epidemiology of haemoglobin disorders and especially increasing sickle cell disease prevalence [184].

Malta: Malta is a small but developed country with a very high HDI (0.918). Only 29 patients are followed with the predominance of a mild β++ mutation (IVS1-6). There is no published data on patient outcomes and no prevention programme.

Turkey: Turkey is a large Mediterranean country with a variable gene frequency of β-thalassaemia across its territory. It is reported that there are 5,500 known patients. However, considering one study of treatment centres with missing data, infrequent care for NTD β-thalassaemia patients, and other errors, there may be as many as 8,000 patients of both TDT and NTDT [185]. This same study estimated that the total annual direct medical care cost in Turkey was approximately USD 95,491,900, with TD β-thalassemia patients accounting for USD 58,347,900 (61.1%), and it concludes that the costs reported were likely underestimated. This is a considerable burden for this upper-middle-income country, which also has a large refugee population from neighbouring Syria, which also has a high frequency of thalassaemia. Services to thalassaemia patients, including refugees, is under Universal Healthcare Insurance. However, there is a parallel private healthcare option and some out-of-pocket expenses are required.

In 2012, the Turkish Society of Pediatric Hematology set up a National Registry for Haemoglobinopathies. A recent review of the registry produced an age distribution, presented in Figure 8.

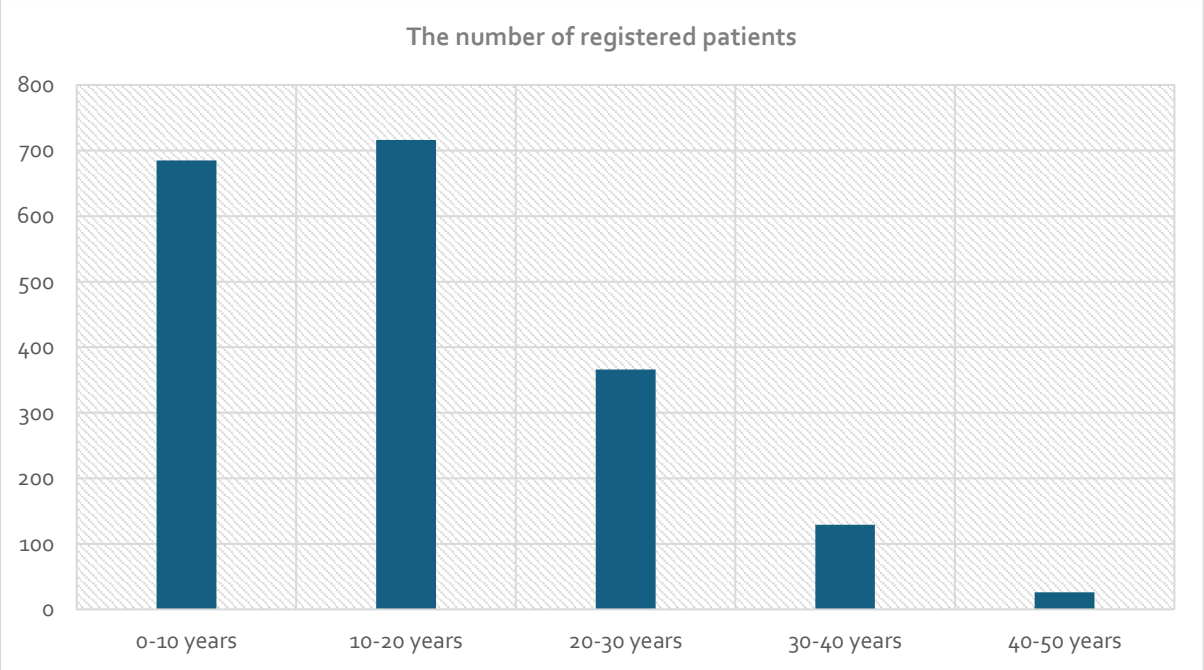

Figure 8. Age distribution of β-thalassaemia patients in Turkey

This is a relatively young patient population, which is due to the variable quality of services in a large country and to a large refugee population [186].

A haemoglobinopathy control programme has been implemented since 2003 and has reduced the annual affected births in recent years.

There is a national scientific committee for thalassaemia, which has an advisory role with the Ministry of health. Doctors and patient groups have limited influence beyond their centres.

Countries with a carrier rate for β-thalassaemia <2%

Of countries with a carrier rate of beta thalassaemia that is less than 2%, Romania, Spain, and Portugal have patient populations which have drawn attention of health authorities, while little is known about the countries of central Asia (the "-stans").

Romania: β-Thalassaemia is uncommon in the Romanian population, with an uneven distribution across the country. The carrier rate is estimated at 1% and there are 200–300 affected patients. Most patients are treated at the National Institute of Transfusion Hematology every 2-6 weeks, and every 3 months biochemical values and virus infection markers are monitored. However, there is no proactive multidisciplinary follow up and no MRI assessment of iron overload. Most of the patients attend this centre even though they may live up to 300–400 kms from the city. They are transported by ambulance to and from the centre.

Only five new cases are expected every year in a country with a population 20 million. This makes this condition a rare disease in this country. There is no screening programme, but prenatal diagnosis is possible [187].

Spain: Thalassaemia is a rare disease in Spain. An update of the Spanish registry of haemoglobinopathies (REHem-AR), published in 2024, recorded 187 cases of β-rhalassaemia, 115 (54%) with TDT, 72 with NTDT, and 27 withHbH disease. This is a significant increase on the recorded cases in the 2020 report [188]. There are also 1,317 SCD patients on the registry. The geographical distribution across the country is very heterogeneous with a prevalence ranging from 0.1% to 5% [189]. The sickle cell genes are much more common and increasing because of migrations mainly from Africa.

The Spanish healthcare system currently offers specialised resources for the diagnosis and management of haemoglobinopathies, supported by expert centres and trained healthcare professionals. Spain introduced neonatal screening programmes in 2003 and fully implemented universal screening to all the regions in 2021. Results have shown that the incidence of SCD varies regionally, influenced by local demographic patterns, from 1 in 3,000 in Catalonia to 1 in 10,000 in Murcia. An increasing number of cases have been registered to allow increase in survival by more than 95.5% at 20 years of age in SCD, and 96.7% in thalassaemia major [190].

Portugal: Like Spain, Portugal has very few β-thalassaemia patients (around 40), but almost 1,000 SCD patients, also because of migrations. The National Newborn Screening Programme is the main source of data concerning SCD. Screening in the Lisbon and Setubal districts revealed sickle cell disease in 1:928 newborns (2.2% carriers); when this was extended to the whole country the birth incidence fell to 1:2,449 (1.4% carriers), indicating a higher concentration in the south [191]. The predominance of HbS is related to the migration flows from Africa in the post-colonial period, as well as immigrants from Brazil.

Thalassaemia is rare in Portugal. A recent small survey found 1.12% were carriers of α-thalassaemia and 0.45% carried β-thalassaemia [192].

Low prevalence European countries

This group are mainly Northern European countries in which migrations have introduced haemoglobinopathy genes, mostly in the 20th and 21st centuries. The main host countries are UK, France, the Netherlands, Germany, and the Nordic countries. No country is exempt from these migrations, and Italy, Greece, Cyprus, Turkey are also adding to their disease burden, especially of the sickle cell syndromes [193].

Of the host countries, the UK and France, due to their colonial history, have historically the oldest permanent populations that originated from high prevalence areas. For this reason, policies to address the haemoglobinopathy burden were developed.

Table 19. Prevalence of β-thalassaemia and sickle cell disease in low prevalence European eountries

Country	Known β-Thalassaemia patients	β-Thalassaemia patients/100,000	Known SCD patients	SCD patients/ 100,000
United Kingdom	2,310	3.3	15,039	21.6
Netherlands	350	1.94	2,000	11.1
Germany	600	0.71	5,000	5.9
France	800	1.2	32,400	48.6
Denmark	83	1.4	236	3.93
Sweden	700	6.6	670	6.2
Switzerland	22	0.25	500	5.5
Austria	60	0.65	Na	na
Belgium	62	0.52	358	3.0
Croatia	16	0.41	5	0.13
Ireland	22	0.40	500	9.1

In considering the data in Table 19, it is noted that, apart from the UK and France, other countries do not have a registry (under development in Germany), so the data are estimates from local experts. In addition, data may be changing from year to year because migrations continue, and also new affected births are not controlled. In the UK a programme of antenatal clinic screening has been ongoing for many years; this is supported by counselling and prenatal diagnosis services.

United Kingdom: The UK Haemoglobinopathy Registry [194] provided the data for the numbers of patients and for the age distribution of thalassaemia patients. According to the patient support organisation (UKTS), in 2025 there were 2,310 thalassaemia patients living in the UK, all with an immigrant background. The younger patients are due to the difficulty of reaching all affected families in a multicultural society as well as new migrations. The older age groups are the result of optimal clinical management in reference centres even though many immigrant families reside in areas where clinics may see less than 5 patients.

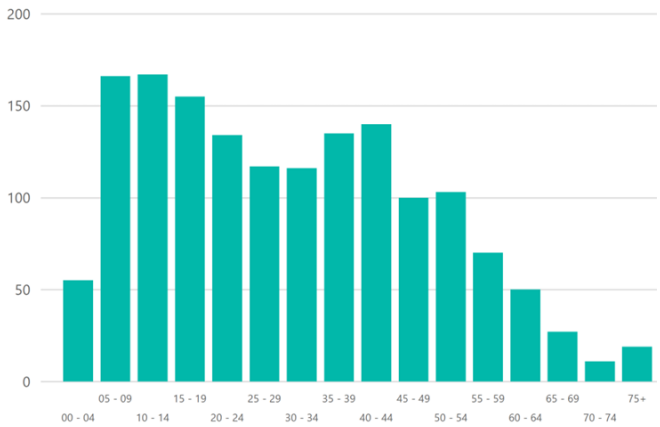

Figure 9. Thalassaemia patients in the UK by age group (copied from the Annual data Report 2020–2021).

The 10-year crude mortality rate is 6.2% for the UK thalassaemia patients. If compared to the age/sex adjusted death rate in the general population, which is 1.2%, this suggests that even in a country offering optimum conventional care, a "normal" life span is not supported. Similar conclusions arise from a 2024 study of 237 TDT patients with a mortality of 1.19 per 100 person years, compared to 0.2/100 in control groups. Like the Italian patient population, morbidity and service usage increases with age [195].

Programs in Europe include newborn screening that are designed to identify sickle cell patients.

France: A national thalassaemia registry is ongoing in **France** with similar results [196]. As in the UK, the strong health service infrastructure allows for optimal care in reference centres, but in regions of the country where patient density is particularly low the lack of clinical experience leads to a reduction in service quality. For example, the result of the national registry presented in 2019 indicated of the 666 patients (441 with TM), the median age was 23 years. Only 50–60% of patients had had an MRI iron measurement [197]. These reports are confirmed by a 2024 report, which indicates that patients with TDT in France experience significant clinical complications, elevated mortality, and substantially utilise healthcare resources [198].

As in other European countries, SCD is increasing more than thalassaemia. It is estimated that there are 32,400 patients with sickle cell syndromes. SCD was acknowledged as a national health priority under the French Public Health Act of 2004. [199].

In Germany an SCD registry has been established with an estimated number of at least 2000 patients [154]. Also, newborn screening is ongoing [200]. Migration patterns have resulted in a higher national prevalence and increased healthcare burden in Germany for both thalassaemia and SCD. There is limited real-world evidence on the clinical burden and healthcare system impact associated with managing sickle cell disease and transfusion-dependent β-thalassaemia in Germany. As a rare disease requiring complex clinical protocols, the level of patient care is heterogeneous, and patient reports indicate that many are undertransfused (Hb 7–8g/dl). This indicates a major need in the Northern European setting where a rare disease policy is yet to be applied and there is no hub and spoke arrangement of reference centres to support patients.

Similarly, Sweden, Switzerland, Austria, Belgium, Croatia, and Denmark have very robust healthcare infrastructure, but thalassaemia is rare. Quality improvement programmes are ongoing through professional groups such as the Nordic Forum for Haemoglobin Disorders.

The general agreement is that the burden of these diseases is increasing in Europe because of migration, and so policymakers and professionals are alerted to plan for services which will favour the best patient outcomes.

WHO American Region (PAH)

Epidemiology

In the American continent, thalassaemia is a rare condition while sickle cell disease is much more common. TIF has active members in five countries with a thalassaemia prevalence: Argentina, Brazil, Canada, Trinidad and Tobago, and the USA. There are contacts with individual patients from Mexico, Cuba, Venezuela, and Suriname.

Table 20. Estimated prevalence of β-thalassaemia and sickle cell disease in select countries of the Americas and health Indicators

Country	β-thalassaemia carrier rate	Estimated number of patients b-thal	Sickle cell disease carrier rate	Estimated SCD patients
Argentina	1.35% 0.8% in 4000 donors [201]	No data	0.7%	No data
Uruguay	0.41% [202]	No data	0.76% (2.22% in Afro descendants)	No data
Jamaica	1% [159]	No data	9.8% (neonatal screening) [158]	No data
Brazil	0.25%-3% maximum in Sao Paolo [203] Overall about 1%	473TM+ 338 TI= 811	2% (neonatal screening) [160, 161] 1.1% to 9.8% in various regions [162]	98000
Canada	0.5% +0.25% E [204]	1200 est	0.76% [163, 165]	6000 [8]
USA	0.4%–1.55% [205]	3665 (CAF est)	0.75%	100000 [166]
Trinidad &Tobago	3.5%-6.7% [206]	100	9.9% (9.32% by NBS)	No data
Colombia	No data	409 ?1189	7.9% [207] 5-12% in coastal areas [208]	No data
Cuba	0.45%	No data	3% [209]	4000 [172]
Peru	2.05%	130	3.3%	
Suriname	1%	No data	7% (11.4% in Creoles [210]	No data
Venezuela	1.48%	141	1.96	3200
Country	**IMR/1,000 livebirths**	**Under 5 mortality/1,000**	**Life expectancy**	**Healthy life expectancy at birth HALE**
Argentina	8	10	77.98	64.8
Uruguay	5	7	78.16	65
Jamaica	10.9	12.4	72.37	61.7
Brazil	12.9	14.4	76.57	61.8
Canada	4	5	83	69.8
USA	5.1	7	79.61	63.9
Trinidad &Tobago	15	16.3	74	61.9
Colombia	11	12	78.09	65
Cuba	4.1	8	78.33	64.6
Suriname	15	16	73.9	60.3
Peru	14	16	78.12	63
Venezuela	22	24	72.84	62

Table 15. Health expenditure and performance in the Americas: HDI Rank, World Bank Data, and UHC Index

Country	HDI rank	WB rank	HE/cap WB data USD	HE/%GDP WB data	UHC index
Argentina	0.865	UMIC	1,730.88	9.86	79
Uruguay	0.862	High	1,850.81	8.59	82
Jamaica	0.720	UMIC	468.35	7.78	74
Brazil	0.786	UMIC	848.57	10.31	80
Canada	0.939	High	6,112.02	11.22	91
USA	0.938	High	12,434.43	16.50	86
Trinidad & Tobago	0.807	High	1,292.02	6.43	75
Colombia	0.788	UMIC	534.44	7.69	80
Cuba	0.762	UMIC	1,199.35	11.79	83
Suriname	0.722	UMIC	343.85	5.92	63
Peru	0.794	UMIC	445.86	6.09	71
Chile	0.878	High	1,714.89	10.10	80
Venezuela	0.709	Low	208.57	4.55	75.1

Affected countries of the Americas are all either upper middle income or high-income countries, according to World Bank rankings. However, health expenditure varies considerably, and this is reflected in health performance; those with a low expenditure per capita (Jamaica, Brazil, Colombia, and Suriname) having the highest IMR, under 5 mortality, and the lowest life expectancy, including healthy life expectancy at birth (HALE).

Beta thalassaemia is indeed a rare condition in the Americas, but as a multi-organ disorder it requires daily treatment and constant multidisciplinary monitoring and care. Treatment is shared in the same clinical settings as SCD

- TIF data suggest that there are about 200–300 affected births annually in the Americas. The patient population is unknown since there are no patient registries and national reports are rare. From TIF Member Association reports, from some but not all counties of the region, we estimate 6,500–7,000 patients with beta thalassaemia syndromes across the continent.
- Estimated costs along with other epidemiological information are scarce in the region. A recent USA 2019 study indicated an average total healthcare cost per patient per year (PPPY) for regularly transfused patients at USD 128,062 [211]. These costs are much lower in other countries (for example in the UAE the mean annual direct cost was found to be USD 35,713 [64], which is likely to be nearer to the cost in counties like Brazil provided that optimum care is available.
- Prevention programmes: There are no nationally organised prevention programmes for haemoglobin disorders in the American continent with the only exception being a screening programme applied in Canada in the 1980s. Neonatal screening for sickle cell disease is now common practice in many countries of the region.
- Blood Transfusion: It has been estimated that the Latin countries of the whole region require around 10 million units per year; in 2018, 6.33 million units were collected, of which 2.32 million were from voluntary non-remunerated donations. Even though there are no direct reports on the supply to haemoglobinopathy patients. with these figures there is likely to be a shortage. This was confirmed in a report from the Society of Inherited and Severe Blood Disorders Trinidad and Tobago (SISBDTT), where they state that no extensive cross matching is done at this time and filters for filtering blood are not available in some instances. Mainly thalassaemia patients reported blood shortages and under-

transfusion in 2025 (donated blood amounts to about 21,000 units, whereas about 60,000 units are needed). One patient reported pretransfusion haemoglobin of 5.9g/dl. These examples are confirmed by WHO data of blood donations rates of 15.6/1,000 pop in 2017 [212]. The level of care and patient outcomes are known to be of a high level in reference centres, especially in North America. Little is known concerning patient care in the rest of the continent, with the exception of **Brazil**, where an active patient driven organisation (ABRASTA, a member of TIF) has promoted service development and guideline development [213]. In an evaluation of iron overload of 136 patients, 92% TDT, with a median age of 18 years, and median baseline ferritin was 2.033ng/ml (range: 59-14,123) and LIC was 8.4(1.0–51.0/9.4) mg/g dw. [214]. These results are indicative of a fair level of care in the major reference centres of Brazil.

This level of service development has not reached all patients across **Brazil**. In many Brazilian states access to health services is difficult because of the long distances, but also because of the rarity of thalassaemia. In such a setting prevention programmes such as screening are difficult to implement. Newborn screening is practised and in one report β-thalassaemia was found in 1.96% of the samples tested [203]. In another report on 8,952 people, sickle cell trait was detected in 2.49% (2.10–2.97%) and minor thalassemia in 1.1% (0 0.84–1.43%).

Likewise in **Argentina,** a 0.8% incidence of thalassaemic carriers among 4,000 blood donors was diagnosed [215]. Optimal treatment for b-thalassaemia has been established in reference centres in Buenos Aires (Aurora Feliu Torres / Gabriela Sciuccati communication to TIF) but not necessarily in all peripheral centres.

Trinidad &Tobago: The Caribbean islands of Trinidad & Tobago have the highest prevalence of β-thalassaemia genes in the Americas. This is mainly among the 35.4% who are of Indian origin and were brought in the 19th century as plantation workers of which 3.5% carry β-thalassaemia. Only 63 patients are identified as being under treatment and the level of care has not reached optimal levels even though blood transfusion and chelation are provided free. Multidisciplinary monitoring is still to be upgraded. In a recent poster describing the state of beta-thalassaemia major patients, 90% had a pre-transfusion Hb of <8g/dl (ave 7.16g/dl) and significantly elevated serum ferritin levels [216].

USA: In the USA, a national surveillance registry exists for SCD and includes all thalassaemia syndromes but does not cover the whole country. Like the European countries, thalassaemia syndromes are increasing in the USA due to migrations, mainly from Asia, and they are found more on the west coast. The latest figures for β-thalassaemia and E/β-thalassaemia are 1,379 cases. SCD is much more common, with around 70,000–100,000 cases.

The US a Thalassaemia Clinical Research Network is a collaboration of the major reference centres in the country, but does not cover all patients with thalassaemia, since many live in areas where each medical unit serves a very small number of patients. In this respect the USA also resembles Northern Europe. The quality of care in refence centres and the Clinical Research Network is of a high level and innovative, and conventional treatments are in trial phases.

A study of adult thalassaemia patients compared two groups, those 18 to 39 years and those older than 40 years. The younger group were mostly of Asian descent and included thalassaemia syndromes such as haemoglobin E/b-thalassaemia, HbH Constant Spring, and HbH disease. The older group were mostly of Greek or Italian ancestry and had predominantly β-thalassaemia (TDT & NTDT). The achievements in education and employment are similar to those of the European reference centres, as is the control of iron overload (serum ferritin in the last 12 months had a mean 2434ng/ml in the younger group and 1251ng/ml in the older group; LIC

(by MRI) was 10.6mg/g dw SD10.5 in the younger group and 4.5mg/g dw in the older group). Complication rates are also similar to European reference centres [217]. These outcomes reflect the achievements of current evidence-based protocols in large countries where the majority of patients benefit from experienced medical care, while some are treated in peripheral centres. Very few patients are not covered by health insurance.

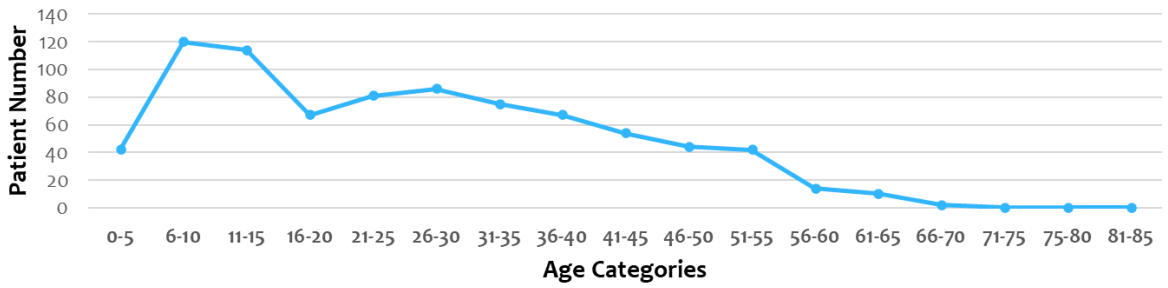

Figure 10. Age distribution of patients from the Cooley's Anemia Foundation Database, 2021

This indicates a younger age group compared to refence countries in Europe, but the effect of recent migrations must be considered.

Carrier screening is limited and voluntary with no national policy. Newborn screening is, however, almost universal [218].

Projected lifetime healthcare costs were estimated to be USD 7.1 million for patients with TDT at age 50 compared to USD 235,000 for matched controls. After age 36, each additional year of life added USD 152,482 to the total lifetime costs for patients with TDT and USD 7,258 to those for matched controls [219]. This study used administrative claims data to evaluate real-world clinical complications, treatments, HCRU, and healthcare costs in patients with TDT in the United States. However, indirect healthcare costs (e.g., absenteeism, presenteeism) were not included, so total costs may be even higher.

A recent study of thalassaemia-related deaths in the USA, from 1999 to 2020, found 2,797 deaths; 74% had beta thalassaemia and 18% had alpha thalassaemia. Most deaths were still cardiovascular-related but 18% were from malignancies. Infection, which is so common in many thalassaemia populations, was the cause of death in only 3% of cases. Overall, there is a decreasing trend in thalassaemia-related mortality over the years. Weaknesses in this study include the lack of information on the comorbidity burden and on prior interventions [220].

Canada: Canada has almost as many thalassaemia patients as the USA, around 1,200, and about 5,000 SCD patients

Chile: A study from southern Chile found a carrier rate for β-thalassaemia of 0.24%. In addition, even though SCD was regarded as rare, it is becoming more recognised due to increased immigration, particularly from Haiti, Colombia, and Venezuela, but exact prevalence is not yet known.

Colombia: Colombia appears to have a significant carrier rate for β-thalassaemia and SCD, however published studies are on cases referred for suspected diagnosis so they are not unbiased.

Suriname: The population of Surinam includes diverse subgroups such as Creole (African descent), Hindustani (Indian descent), and Javanese (Indonesian descent). This implies that both β-thalassaemia and SCD are expected to be prevalent. No population-based survey was found.

Peru: The highest prevalence of β-thalassaemia in South America was reported in Peru, where among 5206 outpatients, 2.05% carried β-thalassaemia and 3.3% carried the sickle cell gene [221]. This should signify a considerable burden of disease. No reports have been produced from this country concerning patient care, outcomes or prevention.

WHO African Region (AFR)

Only two countries in this WHO region have a significant thalassaemia problem.-These are Algeria, which has an Arab and Berber population similar to its Maghreb neighbours, and Mauritius, which has a large proportion of people of Asian origin.

Algeria: Despite the absence of a national registry, a multicentre, retrospective, cross-sectional, descriptive study, conducted in 2017, indicated an increasing adult population.

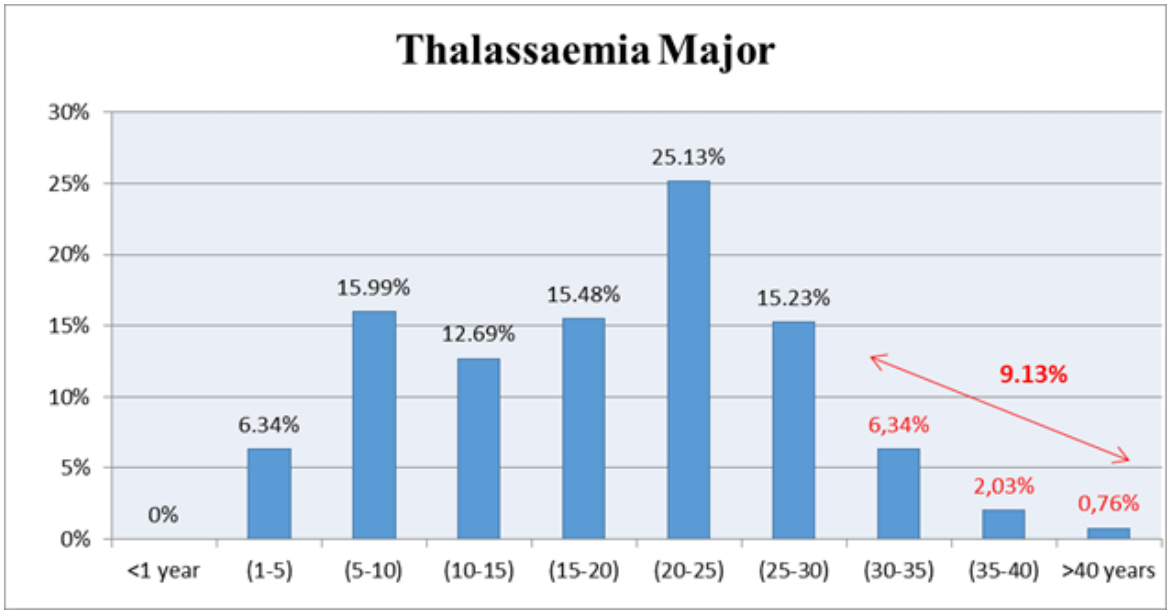

Figure 11. Age distribution of thalassaemia major patients in Algeria

Age distribution of Algerian thalassaemia patients [222]: The average age is 18,21 +/- 9 years. Average pre-transfusion haemoglobin is 8,05 g/dl (7-10,5 g/dl) and average serum ferritin is 3281ng/ml; cardiac arrhythmias are in 48.72%, hepatic fibrosis is in 47.61%, hypogonadism is in 60.7%, hypothyroidism is in 21,67%, hypoparathyroidism is in 14,31%, and diabetes is in 25,49%. A newer report by Dr Djenouni (Conference Report, 2024) made the following comments on the current situation in 2024: The transfusion programme for major thalassaemia is inadequate, due to insufficient blood donation. Only two chelators are available in Algeria: deferoxamine and deferasirox. There is also a lack of infusion pumps for deferoxamine use. Even so, there is a reduction in the frequency of complications and an improvement in median survival.

β-thalassaemia ranks second after sickle cell disorders in Algeria, with 0.1/1,000 annual expected β-thalassaemia births compared to 0.17/1,000 with SCD. The estimated number of thalassaemia patients is 1,500–3,000 compared to almost 5,000 with SCD.

The average age of major thalassaemia TDT is 17.90 years [range 1-44 years], while that of the intermediate form (NTDT) is 23 years old with extreme range of 1–61 years [223]. Monitoring of iron overload is based mainly

on serum ferritin while only 8.8% of patients received cardiac and hepatic MRI, which is limited to the capital Algiers.

At a virtual meeting with TIF in September 2022, local experts informed TIF that two only iron chelation agents are available, but they are provided free of charge. The conclusion is that the burden of disease is high in Algeria with much effort to improve services outside the capital being required.

In a 2024 report from the Hereditary Anaemia Associations to TIF, the number of patients is increasing at an alarming rate because of no prevention programme. However, no figures were provided.

Mauritius: Mauritius is a small island in the Indian Ocean, with a population of approximately 1.25 million. 68% of the population are of Indian origin and thalassaemia is prevalent in this community. 3.85% carry β thalassemia. In a TIF delegation visit in 2019, there were 110 known thalassaemia patients and around the same number of SCD patients. By 2022 the local services reported an estimate of 250 patients. There was no clinical service specifically devoted to thalassaemia, and patients were transfused in various hospitals. However, the national Thalassaemia Society of Mauritius (TSM) was created in 2009, which has promoted service development and the training of both medical and nursing staff. The Ministry of Health has supported their effort, and free care is offered in public hospitals for all patients, with no out-of-pocket expenses. A "Standard protocols & guidelines for management of patients with thalassemia" was launched in 2022 with the collaboration of TIF and the Ministry of Health. This development effort is ongoing and outcomes for patients are expected to improve in the coming years.

SURVIVAL DATA

In the European countries (WHO region), where around 1,025 new annual affected births may be expected, there are 25,200 recorded patients (in hospital, clinic, regional, or national registries). This is probably the most accurate record of patient numbers, compared to other regions of the world. In 20 years, there would be 45,700 if there is no effective prevention programme. This gives a ratio of births to patients of 0.04. In the Arab World, 8,240 new cases are expected with currently 91,400 recorded patients and a ratio 0.09. In the WHO Southeast Asia region plus Pakistan, the estimate is of 257,000 patients with 42,000 expected annually. The ratio in this region is 0.163, indicating a much higher death rate in childhood. There is a gradation of survival across regions of the world reflecting a different burden of premature mortality.

Survival of patients in all countries depends on the birth cohort, since older patients suffered from treatment in their early years, which is suboptimal by today's standards. Iron toxicity damage was therefore inevitable even though chelation and monitoring improved over the years. An example is the Kaplan- Meyer chart from Cyprus.

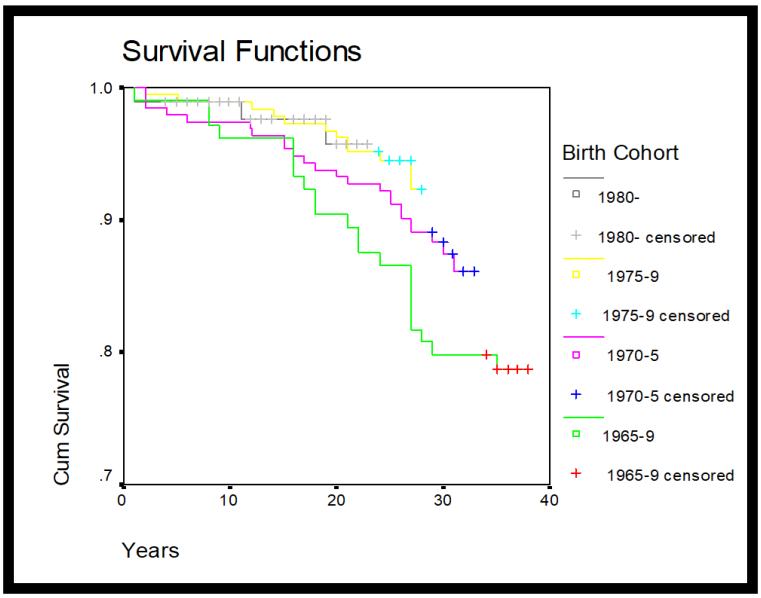

Figure 12. Survival functions - Cyprus

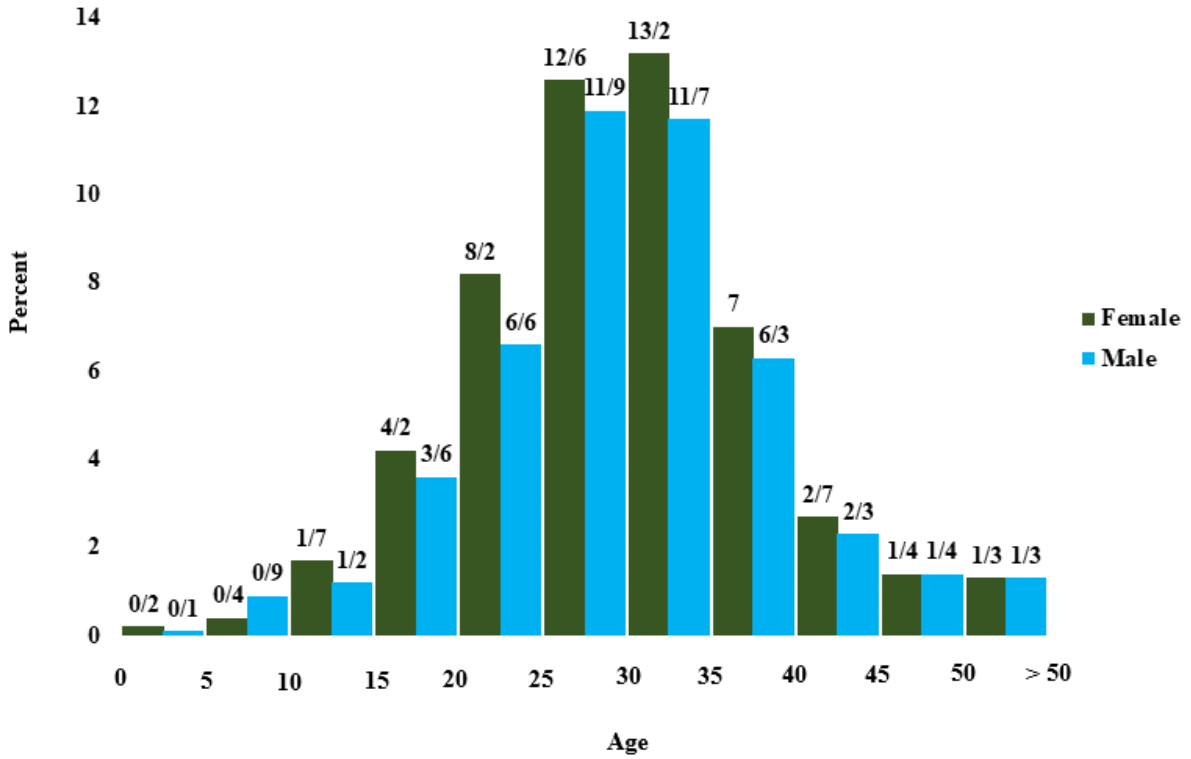

Figure 13. Distribution of 1,385 transfusion-dependent patients by age and gender, Mazandaran Province, 2016

This current survival data bear witness to the successful provision of conventional treatment in Italy, Cyprus, and Greece. This also holds true where the complication rates are concerned (see Table 1). It also demonstrates the limitations of conventional treatment in allowing all patients to have a "normal" lifespan, even under the best conditions.

Another example is that of Taiwan (China): The analysis of patient survival data is based on a nationwide population-based cohort study [224] analysed between 2007–2011; the data were obtained from the Taiwanese National Health Insurance Research Database. After excluding those patients receiving haematopoietic stem cell transplantation, 454 patients were included. The median age was 17.2 years (range, 0.1–48.0 years), indicating a young population receiving less than optimum management, despite good health infrastructure and universal coverage (99%). The NHI programme in Taiwan has covered all treatment expenses since 1995. In addition, 58.1% patients being younger than 20 years is probably an indication of a poor prevention effort. However, survival probability was calculated to be satisfactory. This is a young population of patients with a need to upgrade monitoring and treatment:

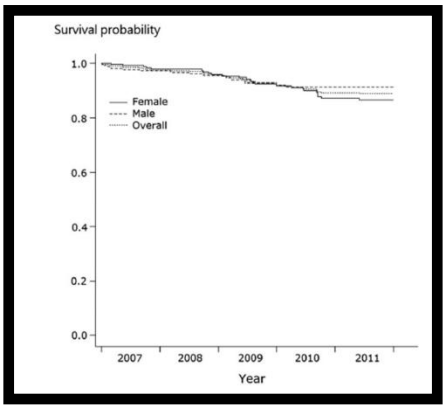

Figure 14. Survival probability of patients with thalassaemia major in Taiwan, 2007–2011. 44 (9.7%) of the 454 patients died. There was no significant difference in the survival probability between female and male patients. (log-rank test, P = 0.57)

Table 16. Reference countries

Country	Cyprus	Greece	Greece	Italy	Italy
Centre	2 centres (50%)	1 centre (Aghia Sophia)	National	MIOT centres	WEBTHAL 36 centres
Year	2020	2019	2015	2019	2020
Number of patients		435	2,099		3,149
Median age	44	33.3	36-45	31.17	37 (4-78)
Heart disease	8.8%	8.6%	28.14%	4.4%	30.2%
Hypogonadism	28.4%	21.6%			
Bone disease	33.7%				
Hypothyroidism	13%	20.7%			9.5%
Diabetes	14.7%	7.3%			8.3%
Malignancies		6.1%	6%		
HCV +					
Ferritin <1000	48.9%		56%		
Ferritin 1-2500	25.9%		30%		
Ferritin >2500	25.2%		14%		
Mean Ferritin					
Cardiac T2* >20	85.4%	86.5%	86.49%	88%	85%
Cardiac T2* 10-19	10.1%	7.4%	7.43%		12%
CardiacT2* <9	4.5%	6.1%	6.07%		3%
LIC <3	51%	52.1%	51.84%		45%
LIC 3-7	22.5%	18.5%	18.38%		29%
LIC 7-15	13%	14.6%	15.07%		16%
LIC >15	13.5%	13.5%	14.71%		10%

Table 17. Countries of Europe and Asia where programmes for TDT exist

Country	United Kingdom	Australia	Indonesia	Iran (Islamic Rep. of)	Iran (Islamic Rep. of)	France	Thailand	Malaysia	Sri Lanka	Egypt	Iraq	Maldives
Centre	National	National	Cipto centre	Shiraz	Mazandaran	National	Multicentre	National	National		Dohuk	National
Year	2019	2019	2018	2019	2019	2019	2017	2019	2019	2019	2019	2018
Number of patients	612		238	713		666	127	2,676	1,688		150	81
Median age	Adults	>18	>18	10-62	30± 9.7	23	27.8±11.4	10-14.9	13.2±7.6	13	13 (1-35)	
Heart disease	18%			72.6%		18.6%	4%HF				2.7%	
Hypogonadism			51%(2024)	10.7%		47%	11%	22%			52.8%	
Bone disease	40%		68% (2021)	15.9%								
Hypothyroidism						9.6%	7.1%				7.3%	
Diabetes	34%					7.8%	7.9%				3.3%	
Malignancies												
HCV +						20.6%					35.3%	
Ferritin <1000		62.3%				11.3%		18.18%		0%		11.8%
Ferritin 1-2500						24.9%		35.17%		47.5%		34.2%
Ferritin >2500						4.8%		46.65%		52.5%		53.9%
Ferritin mean					3300	1104 (120-8553)	2250±2313		2383			3339
Cardiac T2*>20		77.7%	82.7%		70.5%							
Cardiac T2*10-19		11.8%	11.4%		23.5%							
Cardiac T2* <9			5.9%		5%	8.5%						
LIC <3			13.4%		32%							
LIC 3-7			20.6%		14.6%							
LIC 7-15		32.9%	29%		10.1%	25.8%						
LIC >15			37%		2.9%	38.2%						

Comments on the burden of disease

Even in high resource countries that traditionally offer optimal care, such as Italy, a recent report found that 85% of patients suffer from one or more comorbidities; the most frequently reported comorbidities are osteoporosis (74.28%), and endocrine problems (54.28%), fertility issues (40.95%), and dental problems (27.62%). Also, there are significantly reduced levels of HRQoL compared with the general population, influencing physical and social activities. Patients perceived a high burden of disease, with fear of adverse events from treatment as well as the disease [225]. Very similar findings are reported from other clinical and social settings; one example being a study of patients from Malaysia [226].

Patients' quality of life can be severely affected by issues such as bone pain and leg ulcers, which may not be life threatening. This is particularly true of the "milder" thalassaemia syndromes. In a report from Sri Lanka, a new leg ulcer was recorded in 45 (22.2%) of 196 patients with HbE thalassaemia who were most irregularly transfused and had a steady state haemoglobin of 6.4 ± 0.2 g/dL [227]. In Thailand from a total of 459 NTDT (87.6%) and 65 TDT (12.4%) adult patients, osteopenia/osteoporosis was detected in 69.8%, gallstones in 67.6%, and abnormal vitamin D levels in 67.6%. These predispose patients to pain and effect their quality of life [228].

CONCLUSION

There is a considerable gap in published information on patient numbers, nationwide survival, morbidity, and mortality rates that would support the better assessment of the level of contribution of thalassaemia to the national disease burden.

Such an assessment would help in decision-making and appropriate budget allocations. It would support disease prioritisation and the development and/or strengthening of disease-specific policies at the national level. Our findings, albeit incomplete and on occasions roughly estimated, suggest that these disorders contribute significantly to countries' disease burden and that many and multiple efforts are needed by competent authorities to alleviate the pain and suffering and the premature death of patients with these disorders.

REFERENCES

[1] World Health Organization, 'Quality of care'. Accessed: Jan. 16, 2026. [Online]. Available: https://www.who.int/health-topics/quality-of-care

[2] J. H. Bryant, P. F. Harrison, and I. of M. (US) B. on I. Health, 'World Development Report 1993: Investing in Health', in *Global Health in Transition: A Synthesis: Perspectives from International Organizations*, National Academies Press (US), 1996. Accessed: Jan. 19, 2026. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK209090/

[3] C. J. Murray, 'Quantifying the burden of disease: the technical basis for disability-adjusted life years.', *Bull. World Health Organ.*, vol. 72, no. 3, pp. 429–445, 1994.

[4] S. B. Thacker, D. F. Stroup, V. Carande-Kulis, J. S. Marks, K. Roy, and J. L. Gerberding, 'Measuring the Public's Health', *Public Health Reports®*, vol. 121, no. 1, pp. 14–22, Jan. 2006, doi: 10.1177/003335490612100107.

[5] S. Soteriades, M. Angastiniotis, D. Farmakis, A. Eleftheriou, and A. Maggio, 'The Need for Translational Epidemiology in Beta Thalassemia Syndromes: A Thalassemia International Federation Perspective', *Hematol. Oncol. Clin. North Am.*, vol. 37, no. 2, pp. 261–272, Apr. 2023, doi: 10.1016/j.hoc.2022.12.011.

[6] C. Paramore, L. Levine, E. Bagshaw, C. Ouyang, A. Kudlac, and M. Larkin, 'Patient- and Caregiver-Reported Burden of Transfusion-Dependent β-Thalassemia Measured Using a Digital Application', *Patient - Patient-Centered Outcomes Res.*, vol. 14, no. 2, pp. 197–208, Oct. 2020, doi: 10.1007/s40271-020-00473-0.

[7] M. Betts, P. A. Flight, L. C. Paramore, L. Tian, D. Milenković, and S. Sheth, 'Systematic Literature Review of the Burden of Disease and Treatment for Transfusion-dependent β-Thalassemia', *Clin. Ther.*, vol. 42, no. 2, pp. 322-337.e2, Feb. 2020, doi: 10.1016/j.clinthera.2019.12.003.

[8] T. Vos *et al.*, 'Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019', Oct. 2020, Accessed: Jan. 16, 2026. [Online]. Available: https://hdl.handle.net/20.500.11815/2547

[9] N. J. Kassebaum, D. Weatherall, M. Naghavi, and C. J. Murray, 'A systematic global analysis of death and disability due to haemoglobinopathies and haemolytic anaemias between 1990 and 2010', *The Lancet*, vol. 381, p. S73, Jun. 2013, doi: 10.1016/S0140-6736(13)61327-6.

[10] P. Kountouris *et al.*, 'Effect of HBB genotype on survival in a cohort of transfusion-dependent thalassemia patients in Cyprus', *Haematologica*, vol. 106, no. 9, pp. 2458–2468, Jul. 2020, doi: 10.3324/haematol.2020.260224.

[11] A. Tantiworawit *et al.*, 'Survival and causes of death in patients with alpha and beta-thalassemia in Northern Thailand', *Ann. Med.*, vol. 56, no. 1, p. 2338246, Apr. 2024, doi: 10.1080/07853890.2024.2338246.

[12] K. M. Musallam *et al.*, 'Impact of lifetime anaemia and iron control on outcomes in β-thalassaemia: Data from the longitudinal de-LIGHT study', *Br. J. Haematol.*, vol. 207, no. 4, pp. 1578–1588, 2025, doi: 10.1111/bjh.70047.

[13] S. Bellizzi, C. Aidyralieva, L. Alsawhala, A. Al-Shaikh, A. Santoro, and M. C. Profili, 'Vaccination for SARS-CoV-2 of migrants and refugees, Jordan', *Bull. World Health Organ.*, vol. 99, no. 9, p. 611, Sep. 2021, doi: 10.2471/BLT.21.285591.

[14] M. Kosaryan, H. Karami, H. Darvishi-Khezri, R. Akbarzadeh, A. Aliasgharian, and K. Bromand, 'Treatment Status of Patients with B-Thalassemia Major in Northern Iran: Thalassemia Registry System', *Iran. J. Public Health*, vol. 48, no. 7, pp. 1335–1345, Jul. 2019.

[15] *Global Status Report on Blood Safety and Availability 2021*, 1st ed. Geneva: World Health Organization, 2022.

[16] R. A. Mahmoud, A. Khodeary, and M. S. Farhan, 'Detection of endocrine disorders

in young children with multi-transfused thalassemia major', *Ital. J. Pediatr.*, vol. 47, p. 165, Jul. 2021, doi: 10.1186/s13052-021-01116-2.

[17] M. S. Elfeshawy *et al.*, 'Non-invasive depiction of hepatic and myocardial iron overload using MRI: doi: 10.7417/CT.2025.5274', *Clin. Ter.*, vol. 176, no. 5, Sep. 2025, Accessed: Jan. 19, 2026. [Online]. Available: https://clinicaterapeutica.it/ojs/index.php/1/article/view/1362

[18] A. A. M. Adly and F. S. E. S. Ebeid, 'Cultural Preferences and Limited Public Resources Influence the Spectrum of Thalassemia in Egypt', *J. Pediatr. Hematol. Oncol.*, vol. 37, no. 4, p. 281, May 2015, doi: 10.1097/MPH.0000000000000327.

[19] M. Bordbar *et al.*, 'Prevalence of endocrine disorders and their associated factors in transfusion-dependent thalassemia patients: a historical cohort study in Southern Iran', *J. Endocrinol. Invest.*, vol. 42, no. 12, pp. 1467–1476, Dec. 2019, doi: 10.1007/s40618-019-01072-z.

[20] A. Ansari-Moghaddam, H. A. Adineh, I. Zareban, M. Mohammadi, and M. Maghsoodlu, 'The survival rate of patients with beta-thalassemia major and intermedia and its trends in recent years in Iran', *Epidemiol. Health*, vol. 40, p. e2018048, 2018, doi: 10.4178/epih.e2018048.

[21] S. Sobhani, F. Rahmani, M. Rahmani, M. Askari, and F. Kompani, 'Serum ferritin levels and irregular use of iron chelators predict liver iron load in patients with major beta thalassemia: a cross-sectional study.', *Croat. Med. J.*, vol. 60, no. 5, pp. 405–414, Oct. 2019.

[22] K. Sheikhi *et al.*, 'Epidemiology of the Incidence, Prevalence, and Mortality of Thalassemia in Iran: A Secondary Analysis of Global Burden of Disease 2019', *Health Sci. Rep.*, vol. 8, no. 8, p. e71129, Jul. 2025, doi: 10.1002/hsr2.71129.

[23] M. Khodashenas, P. Mardi, N. Taherzadeh-Ghahfarokhi, B. Tavakoli-Far, M. Jamee, and N. Ghodrati, 'Quality of Life and Related Paraclinical Factors in Iranian Patients with Transfusion-Dependent Thalassemia', *J. Environ. Public Health*, vol. 2021, no. 1, p. 2849163, 2021, doi: 10.1155/2021/2849163.

[24] F. Esmaeilzadeh, B. Ahmadi, S. Vahedi, S. Barzegari, and A. Rajabi, 'Major Thalassemia, Screening or Treatment: An Economic Evaluation Study in Iran', *Int. J. Health Policy Manag.*, vol. 11, no. 7, pp. 1112–1119, Feb. 2021, doi: 10.34172/ijhpm.2021.04.

[25] R. K. Sadullah, S. D. Atroshi, and N. A. Al-Allawi, 'Complications and Challenges in the Management of Iraqi Patients with β-Thalassemia Major: A Single-center Experience', *Oman Med. J.*, vol. 35, no. 4, p. e152, Jul. 2020, doi: 10.5001/omj.2020.72.

[26] A. A. Alkinani, 'An epidemiological study of thalassaemia patients attending thalassaemic center in Wassit governorate', *World J. Pharm. Res.*, pp. 1–12, Oct. 2017, doi: 10.20959/wjpr201710-8949.

[27] S. Amin *et al.*, 'Molecular Characterization and Disease-Related Morbidities of β-Thalassemia Patients from the Northeastern Part of Iraq', *Int. J. Gen. Med.*, vol. 13, pp. 1453–1467, Dec. 2020, doi: 10.2147/IJGM.S277947.

[28] R. K. Lafta, 'Burden of Thalassemia in Iraq', *Public Health Open Access*, vol. 7, no. 1, pp. 1–7, 2023, doi: 10.23880/phoa-16000242.

[29] G. M. Abu Shosha, M. Al-Kalaldeh, and N. Shoqirat, 'Nurses' experiences of psychosocial care needs of children with thalassaemia and their families in Jordan: A phenomenological study', *Nurs. Open*, vol. 9, no. 6, pp. 2858–2866, Jul. 2021, doi: 10.1002/nop2.992.

[30] 'IOM Jordan | International Organization for Migration'. Accessed: Jan. 19, 2026. [Online]. Available: https://jordan.iom.int/

[31] UNHCR, 'UNHCR Socio-economic situation of refugees in Jordan Q2 2023', Jordan, Aug. 2023. Accessed: Jan. 19, 2026. [Online]. Available: https://data.unhcr.org/en/documents/details/103118

[32] D. Hasan, A. Al Tibi, G. Burghel, and A. Abdelnour, 'Determining the current prevalence of β-thalassemia variants in Jordan', *Arch. Med. Sci. AMS*, vol. 19, no. 2, pp. 523–527, Mar. 2023, doi: 10.5114/aoms/161096.

[33] I. Alabbadi *et al.*, 'Exploring the Economic Aspects of β-Thalassemia in Jordan in 2019', *Jordan J. Pharm. Sci.*, vol. 15, no. 3, Art. no. 3, Sep. 2022, doi: 10.35516/jjps.v15i3.412.

[34] R. Bou-Fakhredin *et al.*, 'A Report on the Education, Employment and Marital Status of Thalassemia Patients from a Tertiary Care Center in the Middle East', *Hemoglobin*, vol. 44, no. 4, pp. 278–283, Jul. 2020, doi: 10.1080/03630269.2020.1797776.

[35] UNHCR, 'Lebanon: Health Access & Utilization Survey among Refugees in Lebanon - 2022', Lebanon, Survey, Jun. 2023. Accessed: Jan. 19, 2026. [Online]. Available: https://data.unhcr.org/fr/documents/download/103183

[36] H. Khan *et al.*, 'Correlation of Transient Elastography with Liver Iron Concentration and Serum Ferritin Levels in Patients with Transfusion-Dependent Thalassemia Major from Oman', *Mediterr. J. Hematol. Infect. Dis.*, vol. 15, no. 1, p. e2023048, Sep. 2023, doi: 10.4084/MJHID.2023.048.

[37] S. Daar *et al.*, 'Mortality and complications in Omani patients with beta-thalassemia major: a long-term follow-up study', *Acta Bio Medica Atenei Parm.*, vol. 94, no. 4, p. e2023191, 2023, doi: 10.23750/abm.v94i4.14856.

[38] A. Al-Rushaidi, S. Al-Hinai, and H. Al-Sumri, 'Health-related Quality of Life of Omani Adult Patients with β-Thalassemia Major at Sultan Qaboos University Hospital', *Oman Med. J.*, vol. 39, no. 2, p. e613, Mar. 2024, doi: 10.5001/omj.2024.62.

[39] M. A. S. A. Al Zeedi and Z. G. Al Abri, 'Attitudes and impact among people with abnormal premarital screening test results in Muscat governorate's primary healthcare centers in 2018', *J. Community Genet.*, vol. 12, no. 1, pp. 163–169, Jan. 2021, doi: 10.1007/s12687-020-00493-1.

[40] I. U. Rehman *et al.*, 'Challenges of having a child with thalassemia in Pakistan: A phenomenological study', *J. Pediatr. Nurs.*, vol. 72, pp. e179–e186, Sep. 2023, doi: 10.1016/j.pedn.2023.06.026.

[41] S. Waseem, S. H. Ahmed, T. G. Shaikh, and M. Mehedi Hassan, 'The battle against Thalassemia in Pakistan: Way to move forward', *Transfus. Clin. Biol.*, vol. 30, no. 2, pp. 177–178, May 2023, doi: 10.1016/j.tracli.2022.11.003.

[42] S. Khaliq, 'Thalassemia in Pakistan', *Hemoglobin*, vol. 46, no. 1, pp. 12–14, Jan. 2022, doi: 10.1080/03630269.2022.2059670.

[43] M. Qamar and B. T. Shaikh, 'Out of pocket expenditure on thalassemia major and its implications on the household economics', vol. 34, no. 1, pp. 91–94, Jan. 2022.

[44] M. Baqar, J. M. Ahmed, M. Asim, N. Pradhan, and S. Altaf, 'Experiences of family caregivers of children living with thalassaemia-major in Karachi: a phenomenological study', *BMJ Public Health*, vol. 2, no. 2, Nov. 2024, doi: 10.1136/bmjph-2024-001359.

[45] S. A. Bakar Bhura and W. B. Khan, 'Addressing the Thalassemia Burden in Pakistan: The urgent need for a mandate on premarital screening', *JPMA J. Pak. Med. Assoc.*, vol. 74, no. 8, p. 1578, Aug. 2024, doi: 10.47391/JPMA.11100.

[46] P. Kohlbry, B. Al-Karmi, and R. Yamashita, 'Quality-of-life of patients living with thalassaemia in the West Bank and Gaza', *East. Mediterr. Health J. Rev. Sante Mediterr. Orient. Al-Majallah Al-Sihhiyah Li-Sharq Al-Mutawassit*, vol. 29, no. 6, pp. 425–435, Jun. 2023, doi: 10.26719/emhj.23.045.

[47] R. Aldwaik *et al.*, 'Health Status of Patients With β-Thalassemia in the West Bank: A Retrospective-Cohort Study', *Front. Med.*, vol. 8, p. 788758, Dec. 2021, doi: 10.3389/fmed.2021.788758.

[48] I. Kanbour *et al.*, 'Severe Liver Iron Concentrations (LIC) in 24 Patients with β-Thalassemia Major: Correlations with Serum Ferritin, Liver Enzymes and Endocrine Complications', *Mediterr. J.*

Hematol. Infect. Dis., vol. 10, no. 1, p. e2018062, Nov. 2018, doi: 10.4084/MJHID.2018.062.

[49] M. Al-Shafai, A. Al-Romaihi, N. Al-Hajri, N. Islam, and K. Adawi, 'Knowledge and Perception of and Attitude toward a Premarital Screening Program in Qatar: A Cross-Sectional Study', *Int. J. Environ. Res. Public. Health*, vol. 19, no. 7, p. 4418, Apr. 2022, doi: 10.3390/ijerph19074418.

[50] A. Bener, M. Al-Mulla, and A. Clarke, 'Premarital Screening and Genetic Counseling Program: Studies from an Endogamous Population', *Int. J. Appl. Basic Med. Res.*, vol. 9, no. 1, p. 20, Mar. 2019, doi: 10.4103/ijabmr.IJABMR_42_18.

[51] B. A. AlJohani and B. A. Bugis, 'Advantages and Challenges of Implementation and Strategies for Health Insurance in Saudi Arabia: A Systemic Review', *Inq. J. Health Care Organ. Provis. Financ.*, vol. 61, p. 00469580241233447, Sep. 2024, doi: 10.1177/00469580241233447.

[52] O. O. Radhwi, A. Alshehri, B. Alajlani, and E. M. Mansory, 'The direct costs of transfusion-dependent beta-thalassemia in Saudi Arabia: A cost of illness analysis study', *Medicine (Baltimore)*, vol. 104, no. 27, p. e43238, Jul. 2025, doi: 10.1097/MD.0000000000043238.

[53] A. M. Habeb *et al.*, 'Endocrinopathies in beta-thalassemia major. Prevalence, risk factors, and age at diagnosis in Northwest Saudi Arabia', *Saudi Med. J.*, vol. 34, no. 1, pp. 67–73, Jan. 2013.

[54] F. Habbash *et al.*, 'Endocrine Complications and the Effect of Compliance with Chelation Therapy in Patients with Beta Thalassemia Major in Eastern Province of Saudi Arabia', *J. Blood Med.*, vol. 13, pp. 763–774, Jan. 2022, doi: 10.2147/JBM.S386594.

[55] M. H. Albagshi *et al.*, 'Blood Demand and Challenges for Patients With Beta-Thalassemia Major in Eastern Saudi Arabia', *Cureus*, Aug. 2021, doi: 10.7759/cureus.17470.

[56] W. Bawazir, 'A Meta Analysis of RBC Alloimmunization in Transfused Sickle Cell and Thalassemia Patients in Saudi Arabia', *Clin. Lab.*, vol. 71, no. 03/2025, 2025, doi: 10.7754/Clin.Lab.2024.240827.

[57] A. Z. Al-Riyami and S. Daar, 'Red cell alloimmunization in transfusion-dependent and transfusion-independent beta thalassemia: A review from the Eastern Mediterranean Region (EMRO)', *Transfus. Apher. Sci.*, vol. 58, no. 6, p. 102678, Dec. 2019, doi: 10.1016/j.transci.2019.102678.

[58] A. Davoudi-Kiakalayeh, R. Mohammadi, A. A. Pourfathollah, Z. Siery, and S. Davoudi-Kiakalayeh, 'Alloimmunization in Thalassemia Patients: New Insight for Healthcare', *Int. J. Prev. Med.*, vol. 8, p. 101, 2017, doi: 10.4103/ijpvm.IJPVM_246_16.

[59] M. Franchini *et al.*, 'Red blood cell alloimmunisation in transfusion-dependent thalassaemia: a systematic review', *Blood Transfus.*, vol. 17, no. 1, pp. 4–15, Jan. 2019, doi: 10.2450/2019.0229-18.

[60] H. Touma, L. A. Youssef, L. Al-Salhi, W. Ismail Al-khalil, and K. AlKeba, 'Prevalence and Management of Transfusional Iron Overload in Syrian Beta Thalassemia Major Patients Pre and during the Syrian Conflict', *BioMed Res. Int.*, vol. 2023, p. 8911518, Sep. 2023, doi: 10.1155/2023/8911518.

[61] S. M. Jatal, S. J. Harfouch, and R. M. Harfouch, 'Insights into the Clinical Features of Thalassemia Patients from Latakia, Syria', Jun. 02, 2025, *Research Square*. doi: 10.21203/rs.3.rs-6735385/v1.

[62] M. Barouni, S. Aroua, F. Mellouli, M. Bejaoui, and S. Abbes, '[Psychosocial and academic consequences of beta-thalassemia major in Tunisia]', *Soins. Pediatr. Pueric.*, vol. 40, no. 308, pp. 38–42, 2019, doi: 10.1016/j.spp.2019.03.008.

[63] M. Ouederni *et al.*, 'Myocardial and liver iron overload, assessed using T2* magnetic resonance imaging with an excel spreadsheet for post processing in Tunisian thalassemia major patients', *Ann. Hematol.*, vol. 96, no. 1, pp. 133–139, Jan. 2017, doi: 10.1007/s00277-016-2841-5.

[64] S. Alshamsi, S. Hamidi, and H. O. Narci, 'Healthcare resource utilization and direct

costs of transfusion-dependent thalassemia patients in Dubai, United Arab Emirates: a retrospective cost-of-illness study', *BMC Health Serv. Res.*, vol. 22, no. 1, p. 304, Dec. 2022, doi: 10.1186/s12913-022-07663-6.

[65] L. A. Kurban *et al.*, 'Optimized serum ferritin prediction of iron overload in transfusion-dependent thalassemia: likelihood ratio and age-adjustment approach', *Ann. Saudi Med.*, vol. 43, no. 2, pp. 90–96, Mar. 2023, doi: 10.5144/0256-4947.2023.90.

[66] R.-A.-A. Salama and A.-K. Saleh, 'Effectiveness of premarital screening program for thalassemia and sickle cell disorders in Ras Al Khaimah, United Arab Emirates', *J. Genet. Med.*, pp. 26–30, 2016.

[67] T. A. A. Abdulrahman, A. Alhaj, and M. E. M. Saif, 'Thalassemia Phenotypes and Associated Mortality among Yemeni Patients: A Single-Center Retrospective Analysis', *Yemeni J. Med. Sci.*, vol. 14, no. 1, pp. 7–12, Mar. 2021, doi: 10.20428/yjms.v14i1.1703.

[68] W. A. Khan, B. Banu, S. Sadiya, and G. Sarwardi, 'Spectrum of Types of Thalassemias and Hemoglobinopathies: Study in a Tertiary Level Children Hospital in Bangladesh', *Thalass. Rep.*, vol. 7, no. 1, p. 6354, May 2017, doi: 10.4081/thal.2017.6354.

[69] S. S. Ayon, Md. E. Hossain, Md. S. U. Miah, B. M. M. Arafin, A. Chowdhury, and N. N. I. Prova, 'Thalassemia dataset covering clinical, socioeconomic, and mental health aspects', *Data Brief*, vol. 63, p. 112082, Dec. 2025, doi: 10.1016/j.dib.2025.112082.

[70] M. A. Chowdhury, R. Sultana, and D. Das, 'Thalassemia in Asia 2021 Overview of Thalassemia and Hemoglobinopathies in Bangladesh', *Hemoglobin*, vol. 46, no. 1, pp. 7–9, Jan. 2022, doi: 10.1080/03630269.2021.2008957.

[71] A. Mitro *et al.*, 'β-Thalassemia in Bangladesh: Current Status and Future Perspectives', *Thalass. Rep.*, vol. 14, no. 3, pp. 49–59, Jul. 2024, doi: 10.3390/thalassrep14030007.

[72] M. S. Hossain, F. Islam, S. Akhter, and A. Al Mossabbir, 'Thalassemia in Bangladesh: progress, challenges, and a strategic blueprint for prevention.', *Orphanet J. Rare Dis.*, vol. 20, no. 1, p. 1, Jul. 2025, doi: 10.1186/s13023-025-03744-x.

[73] P. Telfer, M. Petrou, M. Bhattacharyya, A. Islam, and A. Dalton, 'Delegation Visit to Bangladesh', Feb. 2019.

[74] A. Khan Mohiuddin *et al.*, 'A pilot study-thalassemia screening program in Bangladesh', presented at the TIF International Conference on Thalassaemia & Other Haemoglobinopathies, Malaysia: Thalassaemia International Federation, Nov. 2023.

[75] M. J. Hossain *et al.*, 'Health-related quality of life among thalassemia patients in Bangladesh using the SF-36 questionnaire', *Sci. Rep.*, vol. 13, no. 1, p. 7734, May 2023, doi: 10.1038/s41598-023-34205-9.

[76] P. Singh, S. Shaikh, S. Parmar, and R. Gupta, 'Current Status of β-Thalassemic Burden in India', *Hemoglobin*, vol. 47, no. 5, pp. 181–190, Sep. 2023, doi: 10.1080/03630269.2023.2269837.

[77] D. Sumedha and K. Anita, 'Prevalence of beta thalassemia carriers in India: a systematic review and meta-analysis', *J. Community Genet.*, vol. 14, no. 6, pp. 527–541, Dec. 2023, doi: 10.1007/s12687-023-00683-7.

[78] S. Sinha, T. Seth, R. B. Colah, and A. H. Bittles, 'Haemoglobinopathies in India: estimates of blood requirements and treatment costs for the decade 2017–2026', *J. Community Genet.*, vol. 11, no. 1, pp. 39–45, Jan. 2020, doi: 10.1007/s12687-019-00410-1.

[79] R. Gupta, N. Radhakrishnan, R. Shankar, and S. Ray, 'Comparative Analysis of the Cost of Thalassemia Screening VS Treatment in Different Healthcare Sectors in Delhi National Capital Region.', *Indian J. Public Health Res. Dev.*, vol. 16, no. 2, p. 254, Apr. 2025, doi: 10.37506/beprt342.

[80] A. Uchil, M. Muranjan, and N. J. Gogtay, 'Economic burden of beta-thalassaemia major receiving hypertransfusion therapy

at a public hospital in Mumbai', *Natl. Med. J. India*, vol. 36, pp. 11–16, Jul. 2023, doi: 10.25259/NMJI_580_20.

[81] S. Sahu, A. Agrawal, J. Shrivastava, and S. Tonk, 'Psychiatric disorders and caregiver burden in children with transfusion dependent β-thalassaemia and their caregivers', *World J. Clin. Pediatr.*, vol. 12, no. 3, pp. 125–132, Jun. 2023, doi: 10.5409/wjcp.v12.i3.125.

[82] B. Biswas, N. N. Naskar, K. Basu, A. Dasgupta, R. Basu, and B. Paul, 'An Epidemiological Study of the Quality of Life of Children With Beta-Thalassemia Major (β-TM) and Its Correlates in Kolkata, West Bengal, India', *Cureus*, Mar. 2023, doi: 10.7759/cureus.36888.

[83] B. Biswas, N. N. Naskar, K. Basu, A. Dasgupta, R. Basu, and B. Paul, 'Transfusion-transmitted infections, its risk factors and impact on quality of life: An epidemiological study among β-thalassemia major children', *Asian J. Transfus. Sci.*, vol. 16, no. 1, p. 99, Jun. 2022, doi: 10.4103/ajts.AJTS_74_18.

[84] B. Biswas, N. N. Naskar, K. Basu, A. Dasgupta, R. Basu, and B. Paul, 'Malnutrition, Its Attributes, and Impact on Quality of Life: An Epidemiological Study among β-Thalassemia Major Children', *Korean J. Fam. Med.*, vol. 42, no. 1, pp. 66–72, Jan. 2021, doi: 10.4082/kjfm.19.0066.

[85] N. Radhakrishnan *et al.*, 'Survey to assess the quality of services available for thalassemia diagnosis and management in India', presented at the 2023 TIF International Conference on Thalassaemia & Other Haemoglobinopathies, Kuala Lumpur, Malaysia: Thalassaemia International Federation, Nov. 2023, p. 137. Accessed: Jan. 16, 2026. [Online]. Available: https://thalassaemia.org.cy/wp-content/uploads/2024/01/ABSTRACT-BOOK-e_version-1.pdf

[86] S. Chinnaiyan, J. Sylvia, S. Kothandaraman, and B. Palanisamy, 'Quality of life and thalassemia in India: A scoping review', *J. Fam. Med. Prim. Care*, vol. 13, no. 4, p. 1183, Apr. 2024, doi: 10.4103/jfmpc.jfmpc_1787_23.

[87] S. S. Yadav, P. Panchal, and K. C. Menon, 'Prevalence and Management of β-Thalassemia in India', *Hemoglobin*, vol. 46, no. 1, pp. 27–32, Jan. 2022, doi: 10.1080/03630269.2021.2001346.

[88] P. A. Wahidiyat, S. D. Iskandar, and D. Sekarsari, 'Evaluation of Iron Overload Between Age Groups Using Magnetic Resonance Imaging and Its Correlation with Iron', vol. 50, no. 3, 2018.

[89] A. Mardhiyah, S. L. Panduragan, H. S. Mediani, and I. Yosep, 'Factors Associated With Quality of Life Among Adolescent With Beta Thalassemia in Indonesia: A Cross-Sectional Study', *Sage Open Nurs.*, vol. 10, p. 23779608241255638, Apr. 2024, doi: 10.1177/23779608241255638.

[90] P. I. Fianza *et al.*, 'Iron Overload in Transfusion-Dependent Indonesian Thalassemic Patients', *Anemia*, vol. 2021, no. 1, p. 5581831, 2021, doi: 10.1155/2021/5581831.

[91] M. M. Djer, S. L. Anggriawan, D. Gatot, P. Amalia, S. Sastroasmoro, and P. Widjaja, 'Correlation Between T2* Cardiovascular Magnetic Resonance with Left Ventricular Function and Mass in Adolescent and Adult Major Thalassemia Patients with Iron Overload', *Cardiovasc. Magn. Reson.*, vol. 45, no. 4, 2013.

[92] W. Marhaeni, F. V. Felicia, A. L. Sumadi Jap, E. Hartoyo, and P. Andayani, 'Comparing serum ferritin levels during COVID-19 infection and recovery period in pediatric patients with transfusion-dependent thalassemia, a single-center study', *Front. Med.*, vol. 10, Feb. 2023, doi: 10.3389/fmed.2023.1056599.

[93] T. D. Atmakusuma, R. Kalwani, S. A. Nasution, and C. M. Rumende, 'Correlation of Serum Ferritin and Cardiac Iron Toxicity with Cardiac Function in Transfusion Dependent Beta-Thalassemia Major Patients', *Acta Medica Indones.*, vol. 53, no. 3, pp. 291–298, Jul. 2021.

[94] P. A. Wahidiyat *et al.*, 'Thalassemia in Indonesia', *Hemoglobin*, vol. 46, no. 1, pp. 39–44, Jan. 2022, doi: 10.1080/03630269.2021.2023565.

[95] T. T. Sari, P. A. Wahidiyat, L. D. Rahmartani, S. D. Iskandar, and I. A. Putri, 'Comparison of Yearly Cost Related to Complications Between Deferasirox and Deferiprone Monotherapy in Thalassemia', *J. Pediatr. Hematol. Oncol.*, vol. 46, no. 6, p. e402, Aug. 2024, doi: 10.1097/MPH.0000000000002894.

[96] N. Firdous, S. Gibbons, and B. Modell, 'Falling prevalence of beta-thalassaemia and eradication of malaria in the Maldives', *J. Community Genet.*, vol. 2, no. 3, pp. 173–189, Sep. 2011, doi: 10.1007/s12687-011-0054-0.

[97] M. Angastiniotis, 'The Maldives: WHO Mission', Thalassaemia International Federation, Nicosia, 2014.

[98] I. Mustafa *et al.*, 'Genetic epidemiology of beta-thalassemia in the Maldives: 23 years of a beta-thalassemia screening program', *Gene*, vol. 741, p. 144544, May 2020, doi: 10.1016/j.gene.2020.144544.

[99] S. Mansoor, Z. Othman, A. Othman, and M. Husain, 'A Descriptive Study on Quality of Life among Adolescents with Beta-Thalassemia Major in the Maldives.', *Int. Med. J.*, vol. 25, no. 4, p. 211, Aug. 2018.

[100] A. A. Khaing, P. P. Myint, K. Paiboonsukwong, N. Win, S. Fucharoen, and O. Sripichai, 'Clinical Severity of β-Thalassemia Pediatric Patients in Myanmar', *Hemoglobin*, vol. 46, no. 1, pp. 66–70, Jan. 2022, doi: 10.1080/03630269.2022.2025825.

[101] R. M. Shrestha, R. Pandit, U. K. Yadav, R. Das, B. K. Yadav, and H. C. Upreti, 'Distribution of Hemoglobinopathy in Nepalese Population', *J. Nepal Health Res. Counc.*, vol. 18, no. 01, pp. 52–58, Apr. 2020, doi: 10.33314/jnhrc.v18i1.2303.

[102] P. Adhikari, 'Addressing complexities in β-thalassemia care: a case series from a resource-limited setting', *Ann. Med. Surg.*, vol. 86, no. 9, pp. 4979–4983, Aug. 2024, doi: 10.1097/MS9.0000000000002471.

[103] B. N. Adhikari *et al.*, 'Clinico-epidemiological Profile of Transfusion-dependent Thalassemia Patients in a Tertiary Care Children's Hospital in Nepal: An Observational Study.', *J. Nepal Med. Assoc.*, vol. 63, no. 290, p. 754, Oct. 2025, doi: 10.31729/jnma.v63i290.9213.

[104] B. Sharma Poudyal, A. Devkota, and P. Kouides, 'Thalassemia care in Nepal: In dire need of improvement', *EJHaem*, vol. 4, no. 2, pp. 548–550, Mar. 2023, doi: 10.1002/jha2.681.

[105] D. Tiwari, S. K. Gupta, N. B. Thapa, and K. Devkota, 'High Serum Ferritin Levels among Blood Transfused Thalassemic Patients Admitted to the Department of Paediatrics in a Tertiary Care Centre: A Descriptive Cross-Sectional Study', *JNMA J. Nepal Med. Assoc.*, vol. 61, no. 262, pp. 543–545, Jun. 2023, doi: 10.31729/jnma.8195.

[106] S. Mettananda *et al.*, 'Blood transfusion therapy for β-thalassemia major and hemoglobin E β-thalassemia: Adequacy, trends, and determinants in Sri Lanka', *Pediatr. Blood Cancer*, vol. 66, no. 5, p. e27643, 2019, doi: 10.1002/pbc.27643.

[107] W. Wijenayake *et al.*, 'Hepatic and renal functions of paediatric patients with thalassaemia: a cross-sectional study from two large thalassaemia centres in Sri Lanka', *BMJ Open*, vol. 15, no. 2, p. e089784, Feb. 2025, doi: 10.1136/bmjopen-2024-089784.

[108] A. P. Premawardhana *et al.*, 'A nationwide survey of hospital-based thalassemia patients and standards of care and a preliminary assessment of the national prevention program in Sri Lanka', *PloS One*, vol. 14, no. 8, p. e0220852, 2019, doi: 10.1371/journal.pone.0220852.

[109] A. Menike, 'Survival of medically treated beta thalassaemia patients in Sri Lanka (2000 – 2017)', *Int. J. Dev. Res.*, vol. 08, no. 04, pp. 19963–19967, Apr. 2018.

[110] A. P. Premawardhena and H. D. P. Madushanka, 'Thalassemia in Sri Lanka', *Hemoglobin*, vol. 46, no. 1, pp. 71–73, Jan. 2022, doi: 10.1080/03630269.2022.2025826.

[111] A. P. Premawardhena *et al.*, 'Survival and complications in patients with haemoglobin E thalassaemia in Sri Lanka: a prospective, longitudinal cohort study',

Lancet Glob. Health, vol. 10, no. 1, pp. e134–e141, Jan. 2022, doi: 10.1016/S2214-109X(21)00446-0.

[112] K. K. Nanayakkara, U. G. Rodrigo, K. L. N. Perera, and C. D. Nanayakkara, 'Pre-natal diagnosis of thalassaemia in Sri Lanka: A ten year review', *J. Obstet. Gynaecol.*, vol. 37, no. 7, pp. 861–863, Oct. 2017, doi: 10.1080/01443615.2017.1306841.

[113] H. Reed-Embleton *et al.*, 'A cost-of-illness analysis of β-Thalassaemia major in children in Sri Lanka – experience from a tertiary level teaching hospital', *BMC Pediatr.*, vol. 20, no. 1, p. 257, Dec. 2020, doi: 10.1186/s12887-020-02160-3.

[114] L. H. M. R. L. Ambillapitiya *et al.*, 'Bridging the Gaps in Thalassemia Care in Sri Lanka: Challenges and Way Forward', *Public Health Chall.*, vol. 4, no. 4, p. e70122, 2025, doi: 10.1002/puh2.70122.

[115] S. Chuncharunee, N. Teawtrakul, N. Siritanaratkul, and N. Chueamuangphan, 'Review of disease-related complications and management in adult patients with thalassemia: A multi-center study in Thailand', *PLOS ONE*, vol. 14, no. 3, p. e0214148, Mar. 2019, doi: 10.1371/journal.pone.0214148.

[116] P. Charoenkwan *et al.*, 'Causes of Hospitalizations in Pediatric Patients with Thalassemia under the National Health Coverage Scheme in Thailand', *Thalass. Rep.*, vol. 14, no. 1, pp. 10–17, Mar. 2024, doi: 10.3390/thalassrep14010002.

[117] N. Sangkha *et al.*, 'Clinical Spectrum and Genotypes of Children with Hemoglobin H in Northeastern Thailand', *Mediterr. J. Hematol. Infect. Dis.*, vol. 17, no. 1, p. e2025081, Nov. 2025, doi: 10.4084/MJHID.2025.081.

[118] A. Riewpaiboon, I. Nuchprayoon, K. Torcharus, K. Indaratna, M. Thavorncharoensap, and B. Ubol, 'Economic burden of beta-thalassemia/Hb E and beta-thalassemia major in Thai children', *BMC Res. Notes*, vol. 3, no. 1, p. 29, Jan. 2010, doi: 10.1186/1756-0500-3-29.

[119] P. Leelahavarong, U. Chaikledkaew, S. Hongeng, V. Kasemsup, Y. Lubell, and Y. Teerawattananon, 'A cost-utility and budget impact analysis of allogeneic hematopoietic stem cell transplantation for severe thalassemic patients in Thailand', *BMC Health Serv. Res.*, vol. 10, p. 209, Jul. 2010, doi: 10.1186/1472-6963-10-209.

[120] K. Kantamaturapoj *et al.*, 'Legislating for public accountability in universal health coverage, Thailand', *Bull. World Health Organ.*, vol. 98, no. 2, pp. 117–125, Feb. 2020, doi: 10.2471/BLT.19.239335.

[121] C. Rerkswattavorn, N. Sirachainan, D. Songdej, P. Kadegasem, and A. Chuansumrit, 'Preventable Severe Thalassemia among Children', *Hemoglobin*, vol. 42, no. 3, pp. 148–153, May 2018, doi: 10.1080/03630269.2018.1502196.

[122] S. Chen *et al.*, 'Transfusion burden and willingness to pay for temporary alleviation of anemia status in transfusion-dependent beta-thalassemia patients in China', *BMC Health Serv. Res.*, vol. 24, no. 1, p. 1215, Oct. 2024, doi: 10.1186/s12913-024-11547-2.

[123] M. Ganczakowski *et al.*, 'Thalassaemia in Vanuatu, South-West Pacific: frequency and haematological phenotypes of young children', *Br. J. Haematol.*, vol. 89, no. 3, pp. 485–495, 1995, doi: 10.1111/j.1365-2141.1995.tb08353.x.

[124] P. J. Ho *et al.*, 'Cardiac and hepatic siderosis in myelodysplastic syndrome, thalassemia and diverse causes of transfusion-dependent anemia: the TIMES study', *HemaSphere*, vol. 3, no. 3, p. e224, Jun. 2019, doi: 10.1097/HS9.0000000000000224.

[125] H. K. Matthiesson, V. Berdoukas, and E. M. Briganti, 'Experiences, Knowledge Gaps and Information Needs of Women in Australia with Transfusion Dependent Thalassaemia in Regard to Fertility and Pregnancy', *Matern. Child Health J.*, vol. 27, no. 11, pp. 1961–1967, Nov. 2023, doi: 10.1007/s10995-023-03683-8.

[126] S.-C. Chong *et al.*, 'Thalassemia in Asia 2021 Thalassemia in Brunei Darussalam', *Hemoglobin*, vol. 46, no. 1, pp. 15–19, Jan. 2022, doi: 10.1080/03630269.2021.2008959.

[127] T. Munkongdee *et al.*, 'Molecular Epidemiology of Hemoglobinopathies in Cambodia', *Hemoglobin*, vol. 40, no. 3, pp. 163–167, May 2016, doi: 10.3109/03630269.2016.1158723.

[128] C. Sophâl, 'Thalassemia Status in Cambodia', *Hemoglobin*, vol. 46, no. 1, pp. 10–11, Jan. 2022, doi: 10.1080/03630269.2021.2008956.

[129] K. Lai, G. Huang, L. Su, and Y. He, 'The prevalence of thalassemia in mainland China: evidence from epidemiological surveys', *Sci. Rep.*, vol. 7, no. 1, p. 920, Apr. 2017, doi: 10.1038/s41598-017-00967-2.

[130] M. Lin *et al.*, 'Early screening of thalassemia in pregnant women in northern China by capillary electrophoresis for the determination of hemoglobin electrophoresis', *Cell. Mol. Biol. Noisy--Gd. Fr.*, vol. 69, no. 10, pp. 174–178, Oct. 2023, doi: 10.14715/cmb/2023.69.10.25.

[131] W. Wang *et al.*, 'Thalassaemia in China', *Blood Rev.*, vol. 60, p. 101074, Jul. 2023, doi: 10.1016/j.blre.2023.101074.

[132] Z. Liang, D. Wu, C. Guo, and J. Gu, 'Temporal trend of population structure, burden of diseases, healthcare resources and expenditure in China, 2000-2019', *BMJ Open*, vol. 13, no. 1, p. e062091, Jan. 2023, doi: 10.1136/bmjopen-2022-062091.

[133] Z. Tang *et al.*, 'A Retrospective Study of Unmet Blood Transfusion Needs and Status of Iron Overload in 190 Transfusion-Dependent Thalassemia Patients from Southern China', *Hemoglobin*, vol. 49, no. 4, pp. 281–285, Jul. 2025, doi: 10.1080/03630269.2025.2517134.

[134] S. Zhang, W. Zhao, L. Sun, G. Liang, X. Wang, and H. Zeng, 'Assessment of cardiac iron deposition and genotypic classification in pediatric beta-thalassemia major: the role of cardiac MRI', *BMC Med. Imaging*, vol. 25, no. 1, p. 31, Jan. 2025, doi: 10.1186/s12880-025-01567-7.

[135] Committee of Thalassemia Prevention and Treatment, China Maternal and Child Health Association, Subspecialty Group of Hematology, Society of Pediatrics, Chinese Medical Association, China Thalassemia Prevention and Control Collaboration Network, and Editorial Board of Chinese Journal of Contemporary Pediatrics, '[Guidelines for iron chelation therapy in thalassemia in China (2025)]', *Zhongguo Dang Dai Er Ke Za Zhi Chin. J. Contemp. Pediatr.*, vol. 27, no. 4, pp. 377–388, Apr. 2025, doi: 10.7499/j.issn.1008-8830.2411001.

[136] X. Zhen *et al.*, 'Economic burden of adult patients with β-thalassaemia major in mainland China', *Orphanet J. Rare Dis.*, vol. 18, no. 1, p. 252, Aug. 2023, doi: 10.1186/s13023-023-02858-4.

[137] P. Chen, W.-X. Lin, and S.-Q. Li, 'THALASSEMIA in ASIA 2021: Thalassemia in Guangxi Province, People's Republic of China', *Hemoglobin*, vol. 46, no. 1, pp. 33–35, Jan. 2022, doi: 10.1080/03630269.2021.2008960.

[138] A. Phengsavanh, S. Sengchanh, C. Souksakhone, B. Souvanlasy, and V. Sychareun, 'Current Status of Thalassemia in Lao People's Democratic Republic', *Hemoglobin*, vol. 46, no. 1, pp. 58–61, Jan. 2022, doi: 10.1080/03630269.2022.2069034.

[139] H. M. Ibrahim *et al.*, 'Observational study on the current status of thalassaemia in Malaysia: a report from the Malaysian Thalassaemia Registry', *BMJ Open*, vol. 10, no. 6, p. e037974, Jun. 2020, doi: 10.1136/bmjopen-2020-037974.

[140] L. Yusof, 'Thalassemia Care in Malaysia', Malaysia, 2025.

[141] A. A. Shafie, J. H. Y. Wong, H. M. Ibrahim, N. S. Mohammed, and I. K. Chhabra, 'Economic burden in the management of transfusion-dependent thalassaemia patients in Malaysia from a societal perspective', *Orphanet J. Rare Dis.*, vol. 16, no. 1, p. 157, Dec. 2021, doi: 10.1186/s13023-021-01791-8.

[142] L. C. Chow, 'Iron burden and endocrine complications in transfusion-dependent thalassemia patients In Sarawak, Malaysia: a retrospective study'.

[143] G. Y. Chun, N. A. Mohd Tahir, F. Islahudin, V. Selvaratnam, and S. C. Li, 'Drug-related

problems among transfusion-dependent thalassemia patients: A real-world evidence study', *Front. Pharmacol.*, vol. 14, Apr. 2023, doi: 10.3389/fphar.2023.1128887.

[144] R. Mohamed, A. H. Abdul Rahman, F. Masra, and Z. Abdul Latiff, 'Barriers to adherence to iron chelation therapy among adolescent with transfusion dependent thalassemia', *Front. Pediatr.*, vol. 10, p. 951947, Oct. 2022, doi: 10.3389/fped.2022.951947.

[145] M. A. Mohd Nor, N. S. Idris, M. Mohd Zulkifli, R. Abu Bakar, and I. Ahmad, 'Thalassemia screening: Low level of knowledge among unmarried youths in Kota Bharu, Kelantan, Malaysia', *Malays. Fam. Physician Off. J. Acad. Fam. Physicians Malays.*, vol. 17, no. 1, pp. 57–65, Mar. 2022, doi: 10.51866/oa.31.

[146] N. Hussein *et al.*, 'Experiences and insights of thalassaemia carriers from an indigenous community in Sabah, Malaysia', *J. Community Genet.*, vol. 16, no. 5, pp. 557–567, Oct. 2025, doi: 10.1007/s12687-025-00800-8.

[147] A. O'Donnell, A. Raiko, J. b. Clegg, D. j. Weatherall, and S. j. Allen, 'α+-Thalassaemia and pregnancy in a malaria endemic region of Papua New Guinea', *Br. J. Haematol.*, vol. 135, no. 2, pp. 235–241, 2006, doi: 10.1111/j.1365-2141.2006.06274.x.

[148] V. R. Nagiria, J. D. Vince, and T. Duke, 'Living with thalassaemia in Papua New Guinea, the experience of children, adolescents and their families', *J. Paediatr. Child Health*, vol. 57, no. 10, pp. 1589–1593, 2021, doi: 10.1111/jpc.15538.

[149] J. Hall, J. Yuen, J. Hunt, B. M. Chu, and Y. E. Hsia, 'The thalassemias among Laotians, Chinese and Filipinos in Hawaii: prevalences, gene frequencies, geographic distributions, screening strategy', vol. 49, no. 4, pp. 470–470, 1991.

[150] T.-M. Ko, H.-L. Hwa, C.-W. Liu, S.-F. Li, J.-Y. Chu, and Y.-P. Cheung, 'Prevalence study and molecular characterization of α-thalassemia in Filipinos', *Ann. Hematol.*, vol. 78, no. 8, pp. 355–357, Aug. 1999, doi: 10.1007/s002770050528.

[151] A. G. Motulsky, E. Stransky, and G. R. Fraser, 'Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency, Thalassaemia, and Abnormal Haemoglobins in the Philippines', *J. Med. Genet.*, vol. 1, no. 2, pp. 102–106, Dec. 1964, doi: 10.1136/jmg.1.2.102.

[152] C. D. Padilla *et al.*, 'Successful Implementation of Newborn Screening for Hemoglobin Disorders in the Philippines', *Int. J. Neonatal Screen.*, vol. 7, no. 2, Jun. 2021, doi: 10.3390/ijns7020030.

[153] E. d'J. Yuson and M. L. T. Naranjo, 'Thalassemia in the Philippines', *Hemoglobin*, vol. 46, no. 1, pp. 36–38, Jan. 2022, doi: 10.1080/03630269.2021.2023566.

[154] S. K. Kow Yin *et al.*, 'A Molecular Epidemiologic Study of Thalassemia Using Newborns' Cord Blood in a Multiracial Asian Population in Singapore: Results and Recommendations for a Population Screening Program', *J. Pediatr. Hematol. Oncol.*, vol. 26, no. 12, p. 817, Dec. 2004.

[155] J. C. M. Lam *et al.*, 'Clinical and health-related quality of life outcomes of transfusion-dependent thalassaemia patients in Singapore', *Blood Cells. Mol. Dis.*, vol. 88, p. 102547, May 2021, doi: 10.1016/j.bcmd.2021.102547.

[156] D. C. Tran *et al.*, 'Prevalence of Thalassemia in the Vietnamese Population and Building a Clinical Decision Support System for Prenatal Screening for Thalassemia', *Mediterr. J. Hematol. Infect. Dis.*, vol. 15, no. 1, p. e2023026, May 2023, doi: 10.4084/MJHID.2023.026.

[157] T.-T. Lam *et al.*, 'Combined Gap-Polymerase Chain Reaction and Targeted Next-Generation Sequencing Improve α- and β-Thalassemia Carrier Screening in Pregnant Women in Vietnam', *Hemoglobin*, vol. 46, no. 4, pp. 233–239, Jul. 2022, doi: 10.1080/03630269.2022.2096461.

[158] X.-H. To-Mai *et al.*, 'Prevalence of common autosomal recessive mutation carriers in women in the Southern Vietnam following the application of expanded carrier screening', *Sci. Rep.*, vol. 14, no. 1, p. 7461,

Mar. 2024, doi: 10.1038/s41598-024-57513-0.

[159] K. Q. Bach, H. T. T. Nguyen, T. H. Nguyen, M. B. Nguyen, and T. A. Nguyen, 'Thalassemia in Viet Nam', *Hemoglobin*, vol. 46, no. 1, pp. 62–65, Jan. 2022, doi: 10.1080/03630269.2022.2069032.

[160] B. Van Vien and D. Ba Truc, 'Treatment and growth of thalassemia patients in National Hospital of Pediatrics of Vietnam'.

[161] H.-T. Nhac-Vu, V. T.-N. Tran, T.-D.-T. Nguyen, V.-T. Pham, and T. Le, 'Economic burden of Thalassemia treatment: An analysis from the Vietnam Social Security perspective', *PLOS ONE*, vol. 18, no. 11, p. e0293916, Nov. 2023, doi: 10.1371/journal.pone.0293916.

[162] T. Chung, '[Preventing thalassemia in ethnic minority and mountainous regions]', Báo và Phát thanh, Truyền hình Nghệ An. Accessed: Jan. 19, 2026. [Online]. Available: https://baonghean.vn/phong-chong-benh-tan-mau-bam-sinh-tai-vung-dong-bao-dan-toc-thieu-so-va-mien-nui-10246116.html

[163] H.-P. Wu *et al.*, 'Survival and complication rates in patients with thalassemia major in Taiwan', *Pediatr. Blood Cancer*, vol. 64, no. 1, pp. 135–138, Jan. 2017, doi: 10.1002/pbc.26181.

[164] C.-H. Tang *et al.*, 'Relationship between transfusion burden, healthcare resource utilization, and complications in patients with beta-thalassemia in Taiwan: A real-world analysis', *Transfusion (Paris)*, vol. 61, no. 10, pp. 2906–2917, 2021, doi: 10.1111/trf.16636.

[165] H.-C. Wang *et al.*, 'The epidemiologic transition of thalassemia and associated hemoglobinopathies in southern Taiwan', *Ann. Hematol.*, vol. 96, no. 2, pp. 183–188, Feb. 2017, doi: 10.1007/s00277-016-2868-7.

[166] P. G. Georgiev, K. G. Sapunarova, V. S. Goranova-Marinova, and S. E. Goranov, 'Reduction of Liver Iron Load in Adult Patients with β-Thalassemia Major Treated with Modern Chelation Modalities', *Folia Med. (Plovdiv)*, vol. 62, no. 2, pp. 265–270, Jun. 2020, doi: 10.3897/folmed.62.e39518.

[167] A. R. Kyrri *et al.*, 'The Changing Epidemiology of β-Thalassemia in the Greek-Cypriot Population', *Hemoglobin*, vol. 37, no. 5, pp. 435–443, Oct. 2013, doi: 10.3109/03630269.2013.801851.

[168] P. Kountouris *et al.*, 'The molecular spectrum and distribution of haemoglobinopathies in Cyprus: a 20-year retrospective study', *Sci. Rep.*, vol. 6, p. 26371, May 2016, doi: 10.1038/srep26371.

[169] M. Angastiniotis *et al.*, 'The Outcomes of Patients with Haemoglobin Disorders in Cyprus: A Joined Report of the Thalassaemia International Federation and the Nicosia and Paphos Thalassaemia Centres (State Health Services Organisation)', *Thalass. Rep.*, vol. 12, no. 4, Art. no. 4, Dec. 2022, doi: 10.3390/thalassrep12040019.

[170] G. D. Efremov, 'Thalassemias and Other Hemoglobinopathies in the Republic of Macedonia', *Hemoglobin*, vol. 31, no. 1, pp. 1–15, Jan. 2007, doi: 10.1080/03630260601056726.

[171] E. Voskaridou *et al.*, 'National registry of hemoglobinopathies in Greece: updated demographics, current trends in affected births, and causes of mortality', *Ann. Hematol.*, vol. 98, no. 1, pp. 55–66, Jan. 2019, doi: 10.1007/s00277-018-3493-4.

[172] A. Kattamis *et al.*, 'Real-world complication burden and disease management paradigms in transfusion-related β-thalassaemia in Greece: Results from ULYSSES, an epidemiological, multicentre, retrospective cross-sectional study', *eJHaem*, vol. 4, no. 3, pp. 569–581, 2023, doi: 10.1002/jha2.695.

[173] K. Souliotis, C. Golna, S. Nikolaidi, G. Vatheia, and S. Hasurdjiev, 'Access to health care for patients with thalassaemia in Greece: a cross-sectional study.', *East. Mediterr. Health J.*, vol. 26, no. 12, p. 1482, Dec. 2020, doi: 10.26719/emhj.20.118.

[174] P. Klonizakis *et al.*, 'A Cross-Sectional, Multicentric, Disease-Specific, Health-Related Quality of Life Study in Greek Transfusion Dependent Thalassemia Patients', *Healthcare*, vol. 12, no. 5, p. 524,

Feb. 2024, doi: 10.3390/healthcare12050524.

[175] M. Geitona *et al.*, 'The Economic Burden of Treating Thalassemia In Greece', *Value Health*, vol. 17, no. 7, p. A526, Nov. 2014, doi: 10.1016/j.jval.2014.08.1661.

[176] 'Thalassemia and Other Hemoglobinopathies and Contemporary Bioethical Reflections. The Experience of Northern Greece', *ResearchGate*, Aug. 2025, doi: 10.26420/annhematoloncol.2022.1401.

[177] B. Gianesin *et al.*, 'Prevalence and mortality trends of hemoglobinopathies in Italy: a nationwide study', *Haematologica*, vol. 110, no. 5, pp. 1211–1216, Jan. 2025, doi: 10.3324/haematol.2024.286886.

[178] C. Borgna-Pignatti *et al.*, 'Survival and Disease Complications in Thalassemia Major', *Ann. N. Y. Acad. Sci.*, vol. 850, no. 1, pp. 227–231, 1998, doi: 10.1111/j.1749-6632.1998.tb10479.x.

[179] F. Longo *et al.*, 'Changing patterns of thalassaemia in Italy: a WebThal perspective', *Blood Transfus.*, vol. 19, no. 3, pp. 261–268, May 2021, doi: 10.2450/2020.0143-20.

[180] F. Bonifazi *et al.*, 'Pattern of complications and burden of disease in patients affected by beta thalassemia major', *Curr. Med. Res. Opin.*, vol. 33, no. 8, pp. 1525–1533, Aug. 2017, doi: 10.1080/03007995.2017.1326890.

[181] G. L. Forni *et al.*, 'Overall and complication-free survival in a large cohort of patients with β-thalassemia major followed over 50 years', *Am. J. Hematol.*, vol. 98, no. 3, pp. 381–387, 2023, doi: 10.1002/ajh.26798.

[182] V. M. Pinto, M. Poggi, R. Russo, A. Giusti, and G. L. Forni, 'Management of the aging beta-thalassemia transfusion-dependent population – The Italian experience', *Blood Rev.*, vol. 38, p. 100594, Nov. 2019, doi: 10.1016/j.blre.2019.100594.

[183] C. Udeze *et al.*, 'Mortality, Clinical Complications, and Healthcare Resource Utilization Associated with Managing Transfusion-Dependent β-Thalassemia and Sickle Cell Disease with Recurrent Vaso-occlusive Crises in Italy', *PharmacoEconomics - Open*, vol. 9, no. 1, pp. 115–124, Jan. 2025, doi: 10.1007/s41669-024-00532-4.

[184] R. Colombatti *et al.*, 'Results of a multicenter universal newborn screening program for sickle cell disease in Italy: A call to action', *Pediatr. Blood Cancer*, vol. 66, no. 5, p. e27657, 2019, doi: 10.1002/pbc.27657.

[185] A. Antmen, E. Angelucci, S. Losi, N. Burrows, C. Bartiromo, and X. H. Hu, 'Direct Medical Care Cost Associated with β-Thalassemia Care in Turkey', *Blood*, vol. 130, p. 2094, Dec. 2017, doi: 10.1182/blood.V130.Suppl_1.2094.2094.

[186] Y. Aydınok *et al.*, 'A National Registry of Thalassemia in Turkey: Demographic and Disease Characteristics of Patients, Achievements, and Challenges in Prevention', *Turk. J. Haematol. Off. J. Turk. Soc. Haematol.*, vol. 35, no. 1, pp. 12–18, Mar. 2018, doi: 10.4274/tjh.2017.0039.

[187] R. Talmaci *et al.*, 'Prenatal molecular diagnosis of β-thalassemia: report on the first two cases in Romania', *J. Med. Life*, vol. 1, no. 2, pp. 138–147, Apr. 2008.

[188] J. M. Marco Sánchez *et al.*, 'Haemoglobinopathies and other rare anemias in Spain: ten years of a nationwide registry (REHem-AR)', *Ann. Hematol.*, vol. 103, no. 8, pp. 2743–2755, Aug. 2024, doi: 10.1007/s00277-024-05788-8.

[189] D. Canatan *et al.*, 'Immigration and screening programs for hemoglobinopathies in Italy, Spain and Turkey', *Acta Bio Medica Atenei Parm.*, vol. 92, no. 4, p. e2021410a, 2021, doi: 10.23750/abm.v92i4.11965.

[190] J.-L. V. Corrons, 'Insights Into Hemoglobinopathies in Spain: A Comprehensive Review', *eJHaem*, vol. 6, no. 5, p. e70093, 2025, doi: 10.1002/jha2.70093.

[191] D. Rodrigues *et al.*, 'Newborn Screening for Sickle Cell Disease: Results from a Pilot Study in the Portuguese Population', *Int. J. Neonatal Screen.*, vol. 11, no. 1, p. 10, Jan. 2025, doi: 10.3390/ijns11010010.

[192] D. Santos *et al.*, 'Prevalence Rate of Thalassemia Carriers among Individuals with Microcytosis or Hypochromia in Portugal', *Acta Médica Port.*, vol. 36, no. 7–8, pp. 467–474, Mar. 2023, doi: 10.20344/amp.19162.

[193] M. Angastiniotis *et al.*, 'Hemoglobin disorders in Europe: a systematic effort of identifying and addressing unmet needs and challenges by the Thalassemia International Federation.', *Thalass. Rep.*, vol. 11, no. 1, p. 1, Jan. 2021, doi: 10.4081/thal.2021.9803.

[194] National Haemoglobinopathy Registry, 'National Haemoglobinopathy Registry (NHR) - Patient Information Leaflet'. United Kingdom, Nov. 20, 2020. Accessed: Jan. 20, 2026. [Online]. Available: https://nssg.oxford-haematology.org.uk/red-cell/documents/patient-information/nhr-patient-information-leaflet.pdf

[195] C. Udeze *et al.*, 'Clinical Burden and Healthcare Resource Utilization Associated With Managing Transfusion-dependent β-Thalassemia in England', *Clin. Ther.*, vol. 47, no. 1, pp. 37–43, Jan. 2025, doi: 10.1016/j.clinthera.2024.09.024.

[196] I. Thuret, 'The Value of Patient Registers: The Example of the French Register for Beta Thalassemia', presented at the 2nd Pan-European Conference on Haemoglobinopathies, Berlin, Germany: Thalassaemia International Federation, Mar. 2010.

[197] I. Agouti *et al.*, 'Data from the French Registry for Beta-Thalassemia Patients', *HemaSphere*, vol. 3, no. S1, p. 348, 2019, doi: 10.1097/01.HS9.0000561436.83737.79.

[198] J. Baldwin *et al.*, 'Clinical burden and healthcare resource utilization associated with managing transfusion-dependent β-thalassemia in France', *Curr. Med. Res. Opin.*, vol. 40, no. 8, pp. 1289–1295, Aug. 2024, doi: 10.1080/03007995.2024.2368197.

[199] H. Leleu *et al.*, 'Epidemiology and disease burden of sickle cell disease in France: A descriptive study based on a French nationwide claim database.', *PLoS ONE*, vol. 16, no. 7, pp. e0253986–e0253986, Jul. 2021.

[200] S. Lobitz *et al.*, 'Introduction of Universal Newborn Screening for Sickle Cell Disease in Germany—A Brief Narrative Review', *Int. J. Neonatal Screen.*, vol. 7, no. 1, Jan. 2021, doi: 10.3390/ijns7010007.

[201] M. S. Abreu de Miani and J. A. Peñalver, 'Incidencia de portadores βtalasémicos y de pacientes de la glucosa-6-fosfato dehidrogenasa (G6FD) en el área del Gran Buenos Aires', *Sangre (Barc.)*, vol. 28, no. 5, pp. 537–541, 1983.

[202] J. D. Luz *et al.*, 'Frequency and spectrum of hemoglobinopathy mutations in a Uruguayan pediatric population', *Genet. Mol. Biol.*, vol. 36, no. 3, pp. 316–322, Sep. 2013, doi: 10.1590/S1415-47572013005000027.

[203] C. R. Bonini-Domingos, 'Thalassemia screening in Brazil: results for 20 years', *Rev. Bras. Hematol. E Hemoter.*, vol. 26, no. 4, Dec. 2004, doi: 10.1590/S1516-84842004000400011.

[204] J. R. Zhou *et al.*, 'The Alberta Newborn Screening Approach for Sickle Cell Disease: The Advantages of Molecular Testing', *Int. J. Neonatal Screen.*, vol. 7, no. 4, Nov. 2021, doi: 10.3390/ijns7040078.

[205] O. J, H. Mm, P. Sn, G. Am, and undefined, 'Incidence of sickle cell trait - United States, 2010.', *MMWR Morb. Mortal. Wkly. Rep.*, vol. 63, no. 49, pp. 1155–1158, Dec. 2014.

[206] S. S. Vuma, H. Mayers, and G. Legall, 'Predictors of Thalassaemia Carriers in Trinidad and Tobago', *Blood*, vol. 126, no. 23, p. 4569, Dec. 2015, doi: 10.1182/blood.V126.23.4569.4569.

[207] D. A. Vargas-Hernández, A. C. Uscategui-Ruiz, A. J. Prada-Rueda, and C. Romero-Sánchez, 'Sickle Cell Trait, Clinical Manifestations and Outcomes: A Cross-Sectional Study in Colombia: Increasing Rate of Symptomatic Subjects Living in High Altitude', *Mediterr. J. Hematol. Infect. Dis.*, vol. 15, no. 1, p. e2023015, Mar. 2023, doi: 10.4084/MJHID.2023.015.

[208] C. Fong, M. A. Lizarralde-Iragorri, D. Rojas-Gallardo, and G. Barreto, 'Frequency and origin of haplotypes associated with the beta-globin gene cluster in individuals with trait and sickle cell anemia in the Atlantic and Pacific coastal regions of Colombia', *Genet. Mol. Biol.*, vol. 36, no. 4, pp. 494–497, Dec. 2013, doi: 10.1590/S1415-47572013000400005.

[209] B. Marcheco-Teruel, 'Sickle Cell Anemia in Cuba: Prevention and Management, 1982–2018', *MEDICC Rev.*, vol. 21, pp. 34–38, Nov. 2019.

[210] W. A. COLLIER and D. A. DE LA PARRA, 'Sickle-cell trait in Surinam creoles', *Doc. Med. Geogr. Trop.*, vol. 4, no. 3, pp. 223–224, Sep. 1952.

[211] M. Weiss, M. Parisi Jun, and S. Sheth, 'Clinical and economic burden of regularly transfused adult patients with β-thalassemia in the United States: A retrospective cohort study using payer claims', *Am. J. Hematol.*, vol. 94, no. 5, pp. E129–E132, 2019, doi: 10.1002/ajh.25429.

[212] World Health Organization, 'Supply of Blood for Transfusion in Latin America and Caribbean Countries 2016-2017 - PAHO/WHO | Pan American Health Organization', May 2020. Accessed: Jan. 19, 2026. [Online]. Available: https://www.paho.org/en/documents/supply-blood-transfusion-latin-america-and-caribbean-countries-2016-2017

[213] D. Langhi Jr *et al.*, 'Guidelines on Beta-thalassemia major - regular blood transfusion therapy: Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular: project guidelines: Associação Médica Brasileira - 2016', *Rev. Bras. Hematol. E Hemoter.*, vol. 38, pp. 341–345, 2016, doi: https://doi.org/10.1016/j.bjhh.2016.09.003.

[214] E. C. Chapchap *et al.*, 'Cardiac iron overload evaluation in thalassaemic patients using T2* magnetic resonance imaging following chelation therapy: a multicentre cross-sectional study', *Hematol. Transfus. Cell Ther.*, vol. 45, no. 1, pp. 7–15, Jan. 2023, doi: 10.1016/j.htct.2021.01.014.

[215] L. C. Rossetti, H. M. Targovnik, and V. Varela, 'The molecular basis of beta-thalassemia in Argentina. Influence of the pattern of immigration from the Mediterranean Basin', *Haematologica*, vol. 89, no. 6, pp. 746–747, Jan. 2004, doi: 10.3324/%25x.

[216] M. Arian, M. Mirmohammadkhani, R. Ghorbani, and M. Soleimani, 'Health-related quality of life (HRQoL) in beta-thalassemia major (β-TM) patients assessed by 36-item short form health survey (SF-36): a meta-analysis', *Qual. Life Res.*, vol. 28, no. 2, pp. 321–334, Feb. 2019, doi: 10.1007/s11136-018-1986-1.

[217] J. Chapin *et al.*, 'An update on the US adult thalassaemia population: a report from the CDC thalassaemia treatment centres', *Br. J. Haematol.*, vol. 196, no. 2, pp. 380–389, Jan. 2022, doi: 10.1111/bjh.17920.

[218] N. El-Haj, C. C. Hoppe, N. El-Haj, and C. C. Hoppe, 'Newborn Screening for SCD in the USA and Canada', *Int. J. Neonatal Screen.*, vol. 4, no. 4, Nov. 2018, doi: 10.3390/ijns4040036.

[219] C. Udeze *et al.*, 'Economic and clinical burden of managing transfusion-dependent β-thalassemia in the United States', *J. Med. Econ.*, vol. 26, no. 1, pp. 924–932, Dec. 2023, doi: 10.1080/13696998.2023.2235928.

[220] J. Y. Tan, Y. H. Yeo, K. H. Chan, H. S. Shaaban, and G. Guron, 'Causes of Death and Mortality Trends in Individuals with Thalassemia in the United States, 1999-2020', *J. Blood Med.*, vol. 15, pp. 331–339, Aug. 2024, doi: 10.2147/JBM.S470177.

[221] I. P. de S. Social, J. Castillo, E. Hazan, and M. del C. Márquez, '[Hemoglobinopathies in Peru]', *Hemoglobinopathies in Peru*, 1998, Accessed: Jan. 19, 2026. [Online]. Available: https://repositorio.essalud.gob.pe/handle/20.500.12959/5284

[222] A. Djenouni, S. Grifi, and M. T. Bougherira, 'Beta thalassemia in Algeria Multicenter National Study', presented at the 39th Congress of the French Society of Haematology, 2019.

[223] F. Grifi *et al.*, 'Epidemiological Study on β-Thalassemia in Algeria', *Blood*, vol. 132, no. Supplement 1, p. 4902, Nov. 2018, doi: 10.1182/blood-2018-99-112812.

[224] A. A. G. Tantawy, N. H. K. Elsherif, N. M. Habeeb, E. M. Hasan, and A. E. Abdelhameed, 'A two-dimensional speckle-tracking echocardiography for the diagnosis of early myocardial disease in beta-thalassemia major patients', *Ann. Pediatr. Cardiol.*, vol. 15, no. 3, p. 257, Jun. 2022, doi: 10.4103/apc.apc_91_21.

[225] F. Tedone, P. Lamendola, S. Lopatriello, D. Cafiero, D. Piovani, and G. L. Forni, 'Quality of Life and Burden of Disease in Italian Patients with Transfusion-Dependent Beta-Thalassemia', *J. Clin. Med.*, vol. 11, no. 1, p. 15, Dec. 2021, doi: 10.3390/jcm11010015.

[226] W. C. Foong, K. Y. Chean, F. F. Rahim, A. S. Goh, S. L. Yeoh, and A. A. C. Yeoh, 'Quality of life and challenges experienced by the surviving adults with transfusion dependent thalassaemia in Malaysia: a cross sectional study', *Health Qual. Life Outcomes*, vol. 20, no. 1, p. 2, Jan. 2022, doi: 10.1186/s12955-021-01897-4.

[227] V. Mehta *et al.*, 'Leg Ulcers: A Report in Patients with Hemoglobin E Beta Thalassemia and Review of the Literature in Severe Beta Thalassemia', *Acta Haematol.*, vol. 145, no. 3, pp. 334–343, May 2022, doi: 10.1159/000520731.

[228] S. Ekwattanakit, C. Hantaweepant, A. Khuhapinant, N. Siritanaratkul, and V. Viprakasit, 'An urgent need for improving thalassemia care due to the wide gap in current real-life practice and clinical practice guidelines', *Sci. Rep.*, vol. 11, no. 1, p. 13283, Jun. 2021, doi: 10.1038/s41598-021-92715-w.