Regional desk review of haemoglobinopathies with an emphasis on thalassaemia and accessibility and availability of safe blood and blood products as per these patients’ requirement in South-East Asia under universal health coverage
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CONTENTS

Acknowledgements iv
Abbreviations and acronyms vi
Foreword viii
Executive Summary x
1. Introduction 1
2. Haemoglobin disorders with a focus on thalassaemia 2
3. Thalassaemia – a global and regional perspective 7
4. Blood transfusion services – a global and regional perspective 7
5. Country scenarios 10
   • Bangladesh
   • Bhutan
   • Democratic People’s Republic of Korea 16
   • India 18
   • Indonesia 24
   • Maldives 27
   • Myanmar 31
   • Nepal 35
   • Sri Lanka 39
   • Thailand 43
   • Timor-Leste 46
6. Challenges and the way forward 48
7. References 54
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### Abbreviations and acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>α-thalassaemia</td>
<td>alpha-thalassaemia</td>
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<tr>
<td>β-thalassaemia</td>
<td>beta-thalassaemia</td>
</tr>
<tr>
<td>BTS</td>
<td>blood transfusion services</td>
</tr>
<tr>
<td>BTSC</td>
<td>blood transfusion service Centre</td>
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<tr>
<td>CBB</td>
<td>Central Blood Bank</td>
</tr>
<tr>
<td>CD</td>
<td>codon</td>
</tr>
<tr>
<td>CS</td>
<td>Constant Spring</td>
</tr>
<tr>
<td>CTP</td>
<td>clinical transfusion practices</td>
</tr>
<tr>
<td>CVTL</td>
<td>Timor-Leste Red Cross Society</td>
</tr>
<tr>
<td>DPR Korea</td>
<td>Democratic People’s Republic of Korea</td>
</tr>
<tr>
<td>EQAS</td>
<td>External Quality Assurance Schemes</td>
</tr>
<tr>
<td>FRU</td>
<td>first referral unit</td>
</tr>
<tr>
<td>GDBS</td>
<td>WHO Global Database on Blood Safety</td>
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<tr>
<td>Hb</td>
<td>haemoglobin</td>
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<tr>
<td>HbA</td>
<td>adult haemoglobin</td>
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<tr>
<td>HbC</td>
<td>haemoglobin C disease</td>
</tr>
<tr>
<td>Hb CS</td>
<td>haemoglobin Constant Spring</td>
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<tr>
<td>HbE</td>
<td>haemoglobin E disease</td>
</tr>
<tr>
<td>HbF</td>
<td>fetal haemoglobin</td>
</tr>
<tr>
<td>HbS</td>
<td>sickle cell haemoglobin</td>
</tr>
<tr>
<td>HPLC</td>
<td>high performance liquid chromatography</td>
</tr>
<tr>
<td>HSCT</td>
<td>haemopoietic stem cell transplant</td>
</tr>
<tr>
<td>IFRC</td>
<td>International Federation of the Red Cross and Red Crescent Societies</td>
</tr>
<tr>
<td>IGMH</td>
<td>Indira Gandhi Memorial Hospital (Maldives)</td>
</tr>
<tr>
<td>ISBT</td>
<td>International Society of Blood Transfusion</td>
</tr>
<tr>
<td>IVS</td>
<td>intervening sequence</td>
</tr>
<tr>
<td>MBS</td>
<td>Maldivian Blood Services</td>
</tr>
<tr>
<td>MoH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>MoHFW</td>
<td>Ministry of Health and Family Welfare (India)</td>
</tr>
<tr>
<td>MoHP</td>
<td>Ministry of Health and Population (Nepal)</td>
</tr>
<tr>
<td>MoPH</td>
<td>Ministry of Public Health (DPR Korea)</td>
</tr>
<tr>
<td>Acronym</td>
<td>Full Form</td>
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<tr>
<td>MRCS</td>
<td>Myanmar Red Cross Society</td>
</tr>
<tr>
<td>NACO</td>
<td>National AIDS Control Programme (India)</td>
</tr>
<tr>
<td>NBC</td>
<td>National Blood Centre</td>
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<tr>
<td>NBTC</td>
<td>National Blood Transfusion Council</td>
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<tr>
<td>NBTS</td>
<td>National Blood Transfusion Service</td>
</tr>
<tr>
<td>NDT</td>
<td>non-transfusion-dependent thalassaemia</td>
</tr>
<tr>
<td>NHI</td>
<td>national health insurance</td>
</tr>
<tr>
<td>NHM</td>
<td>National Health Mission (India)</td>
</tr>
<tr>
<td>NHSO</td>
<td>National Health Security Office</td>
</tr>
<tr>
<td>NPHL</td>
<td>National Public Health Laboratory</td>
</tr>
<tr>
<td>NRHM</td>
<td>National Rural Health Mission (India)</td>
</tr>
<tr>
<td>NTAC</td>
<td>National Technical Advisory Committee</td>
</tr>
<tr>
<td>NTC</td>
<td>National Thalassaemia Centre</td>
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<tr>
<td>NTDT</td>
<td>non-transfusion-dependent thalassaemia</td>
</tr>
<tr>
<td>PMI</td>
<td>Palang Merah Indonesia (Indonesian Red Cross Society)</td>
</tr>
<tr>
<td>POPTI</td>
<td>Association of Parents of Thalassaemia Patients Indonesia</td>
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<tr>
<td>QoL</td>
<td>quality of life</td>
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<tr>
<td>RBC</td>
<td>Regional Blood Centre</td>
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<tr>
<td>SEA Region</td>
<td>South-East Asia Region</td>
</tr>
<tr>
<td>SHE</td>
<td>Society for Health Education (Maldives)</td>
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<tr>
<td>SOP</td>
<td>standard operating procedure</td>
</tr>
<tr>
<td>TDT</td>
<td>transfusion-dependent thalassaemia</td>
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<tr>
<td>TFH</td>
<td>Thalassaemia Foundation Hospital (Bangladesh)</td>
</tr>
<tr>
<td>TOHC</td>
<td>Thalassaemia and Other Haemoglobinopathies Centre (Maldives)</td>
</tr>
<tr>
<td>TRCS</td>
<td>Thai Red Cross Society</td>
</tr>
<tr>
<td>TTI</td>
<td>transfusion-transmissible infection</td>
</tr>
<tr>
<td>UHC</td>
<td>universal health coverage</td>
</tr>
<tr>
<td>VNRBD</td>
<td>voluntary non-remunerated blood donors</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>YTI</td>
<td>Yayasan Thalassaemia Indonesia (Indonesian Thalassaemia Foundation)</td>
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</tbody>
</table>
Foreword

Thalassaemias are the most common monogenetic inherited disorders of haemoglobin (Hb). The inheritance of thalassaemias is autosomal recessive. Thalassaemias are globally prevalent, although prevalence varies widely between countries of the same region, and even within countries. Originally restricted to specific geographical locations, thalassaemias are now global due to population migration. α-thalassaemia is more frequent in the WHO South-East Asia Region than in other parts of the world. Up to 40% of genetic traits have been found in thalassaemia traits (1–30%). People living in the Mediterranean, African and South-East Asian regions are more likely to be affected by β-thalassaemia. Genetic prevalence of β-thalassaemia in the South-East Asia Region is 2.5–15%.

To provide life-long treatment to people with thalassaemia, and prevent serious complications and premature deaths, high-quality public health planning and policy making is required, for which high-quality epidemiological data is a must. In all countries of the Region, plans of action to manage and control Hb disorders are needed, covering community awareness and education, training of health care professionals, and infrastructure development to strengthen diagnostic and transfusion services. A holistic and cost-effective approach that includes family and population screening, a registry for epidemiological data, and a preventive programme that includes genetic counselling, prenatal diagnosis and preimplantation genetic diagnosis, has proven to be successful in reducing the frequency of thalassaemias in many countries globally.

To facilitate the development of such plans, this review aims to understand the prevalence of thalassaemic syndromes and the existent blood supply system available within each country of the Region. The review focuses on thalassaemic syndromes, since these disorders present mainly with transfusion-dependent anaemia and the need for periodic transfusions. The review will help health authorities plan for and provide adequate blood supplies for each patient with transfusion-dependent thalassaemia. The review was performed using data from thalassaemia societies, the nodal authorities dealing with blood product support, data published in the literature and data from WHO.

I encourage all stakeholders to leverage the information contained herein to develop national action plans to address thalassaemias, and to continue to increase access to sufficient and secure blood and blood products, and safe transfusion services, as a vital part of achieving universal health coverage. Together, in all countries of the Region, we must improve access to safe blood based on voluntary non-remunerated donations, for a fairer, healthier future for all.

Dr Poonam Khetrapal Singh
Regional Director
WHO South-East Asia Region
Executive summary

Disorders of haemoglobin, which affect the structure or function of haemoglobin, are one of the most common monogenic disorders prevalent across the world. While sickle cell disorders are more prevalent worldwide, the thalassaemic syndromes including α-thalassaemia, β-thalassaemia and haemoglobin-E disease are associated with high prevalence rates ranging from 2.5% to 15% in the 11 countries of the World Health Organization (WHO) South East-Asia (SEA) Region. The clinical presentation can vary from mild anaemia to severe transfusion-dependent anaemia and therefore poses considerable strain on health-care resources and blood supplies.

In this review, we have attempted to understand the prevalence of the thalassaemic syndromes and the existent blood supply system available within each country of the SEA Region. This review focuses on the thalassaemic syndromes since these disorders present mainly with transfusion-dependent anaemia and the need for periodic transfusions unlike sickle cell anaemia where the main manifestation is usually a painful crisis. This review will help health authorities in planning for adequate blood supplies for each patient with transfusion-dependent thalassaemia. This review was done using data from the thalassaemia societies from each country, the nodal authorities dealing with blood product support within each country, data published in the literature and data from WHO.

It is noted that within the countries of the SEA Region, there was a wide heterogeneity in the clinical and mutational spectrum of the thalassaemic syndromes. While the risk of β-thalassaemia major was high in India, Indonesia and Maldives followed by Bangladesh and Thailand, HbE-β-thalassaemia was as common as β-thalassaemia in India and Indonesia but much higher than β-thalassaemia in Bangladesh, Myanmar and Thailand. The risk of homozygous α0-thalassaemia and HbH disease (inheritance of only one out of the four normal alpha-globin genes [-α/--]) was highest in Thailand followed by Myanmar. The annual number of births with β-thalassaemia were highest in India (12 500 per 1391.99 million or 1.3 billion) followed by Bangladesh (9100 per 166.3 million or 0.1663 billion) while Thailand (4000 per 69 958 669 million), Myanmar (2500 per 54 409 800 million) and Nepal (120 per 29 136 808 million) reported more births with HbE-β-thalassaemia.
The availability of blood as a resource also varied considerably between the various countries of the SEA Region with the red blood cell units available per 100 000 population ranging from 3315 (Thailand) to 256 (Timor-Leste). Only four countries – Indonesia, Maldives, Sri Lanka and Thailand – have more than 1000 red cells units available per 100 000 population annually. It is seen that the countries that have a high number of annual births with thalassaemia such as India, Bangladesh and Myanmar have a lower number of red cells available for the population. In countries such as Maldives and Nepal, geographical constraints (either waterways or mountainous regions) play a key role in accessing blood transfusions. The under-5 mortality rates are a good indicator of health services being provided since several children with transfusion-dependent thalassaemia also belong to this age group. These rates are less than 10 per 1000 live births in Maldives, Sri Lanka and Thailand and more than 20 per 1000 live births in several other countries (Bangladesh, Bhutan, India, Indonesia, Myanmar, Nepal and Timor-Leste). While transfusion-dependent thalassaemia is not the sole contributor to the high under-5 mortality rates in some of the countries, it indeed plays a considerable part in contributing to these rates and, therefore, improving blood availability to these children should be useful in reducing these mortality rates.

A multipronged approach is needed in these countries to try and reduce the burden of thalassaemic syndromes through counselling and prenatal diagnosis, if feasible, and at the same time ensuring that the children who are already affected by this disease are taken care of adequately by ensuring timely and safe blood supplies. It is necessary to sensitize the government in each country to recognize transfusion-dependent thalassaemia as a major health problem so that adequate steps can be taken by these governments with support of WHO to improve health outcomes in children in this Region.
Introduction

Haemoglobinopathies are hereditary disorders affecting the structure, function or production of haemoglobin (Hb) and are among the commonest of clinically significant monogenic disorders (1). These are classified into two major groups: (i) thalassaemia syndromes consisting of α- and β-thalassaeemia and (ii) structural variants of Hb (abnormal Hb) including sickle cell disease (HbS), haemoglobin E disease (HbE), haemoglobin C disease (HbC) and haemoglobin Constant Spring disease (Hb CS). The prevalence of carriers of variants of the haemoglobin gene is very high among the populations of the African, South-East Asian, Eastern Mediterranean and the Western Pacific regions and much lower among the populations of the American and European regions (2). These disorders are common in 71% of countries that collectively account for 89% of all births and have a major impact on health-care needs of the affected countries. HbS accounts for 40% of carriers while about 20% of the world’s population carries a gene for α-thalassaemia. In some geographical areas, one can see a combination of a thalassaemia syndrome and a structural variant of Hb, the commonest type being HbE-β-thalassaemia with similar clinical presentations. It is therefore necessary to study the geographical distribution of severe illness since these diseases present a major health-care burden for the country.

The clinical spectrum of these Hb disorders can range from a silent carrier status to mild non-transfusion-dependent (NDT) anaemia to severe transfusion-dependent anaemia. Since anaemia is the predominant symptom, the major treatment consists of regular transfusions of red blood cells throughout life. The transfusion practice can range from transfusions every 2–4 weeks to once every 2–3 months depending upon the clinical severity of the disease. Blood transfusion corrects anaemia and promotes normal growth. Since blood transfusion is a key component of the clinical management of transfusion-dependent thalassaemia (TDT), it is essential that blood transfusion services in all the countries are strengthened to ensure the availability of a safe and adequate blood supply for all patients who need regular transfusions.
**Haemoglobin disorders with focus on thalassaemia**

The thalassaemia syndromes form one of the major groups of haemoglobinopathies. They are a group of monogenic disorders in which a genetic mutation interferes with the amount of protein that is produced and includes both α- and β-thalassaemia.

In a physiological state, the Hb molecule is a heterotetramer consisting of two α- and two non-α-globin chains, each carrying a haeme molecule with a central iron. The oxygen-carrying capacity of the Hb molecule is maximal in this state. The non-α-globin chains can either be β chains which coupled with α chains form adult Hb (HbA), while α chains and δ chains form a minor fraction of adult Hb (HbA2). Finally, α and γ chains form the fetal haemoglobin (HbF). The production of the globin chains is regulated by the α-globin cluster on chromosome 16 with the two α-globin genes HBA1 and HBA2, and the β-globin cluster on chromosome 11 with the genes for the γ, δ and β-globin chains. In a normal physiological state, there is a balanced production of the α- and the non-α-globin chains that ensures a reciprocal pairing into the normal tetramers. In the thalassaemias, this equilibrium is disrupted by the defective production of one of the globin chains. Any reduced production of one of the globin chains within the developing red cell will cause an accumulation of the normally produced chain that can no longer find the equivalent amount of its heterologous partner to assemble to the normal heterotetramer. If α-globin chains are not produced in adequate amounts, there will be an accumulation of β-globin chains (α-thalassaemia); alternatively, if β-globin chains are inadequately produced, then α-globin chains will accumulate (β-thalassaemia). The α-thalassaemias occur mainly due to deletions – a deletion of one of the globin genes is termed α+-thalassaemia, whereas if both the pairs are deleted it is termed α0-thalassaemia. Point mutations of the α genes are much less common; only one, Hb CS occurs at a very high frequency in some populations. The β-thalassaemias however result from more than 200 different mutations, and deletions are much less common.

In the premature red cells (erythroblasts), the presence of excess of α-globin chains in β-thalassaemia causes precipitation at the cell membrane leading to oxidative membrane damage and premature cell death by apoptosis (3). This happens within the tissue that promotes red cell formation and thus results in ineffective erythropoiesis. Some of the immature red cells however pass into the circulation and because of their membrane defect, they are fragile and prone to haemolysis. They
also exhibit an altered deformability and are trapped by the spleen where they are destroyed by macrophages. This leads to an enlargement of the spleen, which can become massive, leading to the development of functional hypersplenism with removal of platelets and white cells as well as red cells. The presence of ineffective erythropoiesis, the removal of abnormal cells by the spleen, and haemolysis all contribute to the anaemia of variable severity that is seen in β-thalassaemia (4).

β-thalassaemia can be classified into three groups based upon the clinical severity:

1. Transfusion-dependent β-thalassaemia (TDT) – leads to death in early infancy unless treated.
2. Non-transfusion-dependent β-thalassaemia (NDT) – occasional blood transfusions required but may become transfusion-dependent later in life.
3. Thalassaemia minor – mostly consist of carriers for thalassaemia genes but may also include some homozygotes/compound heterozygotes for mild β-thalassaemia mutations and HbE.

There can also be co-inheritance of different mutations involving the β-thalassaemia gene and the gene involving the structural variants leading to the genotypic and phenotypic manifestations as HbS-β-thalassaemia (sickle-β-thalassaemia) or HbE-β-thalassaemia (E-β-thalassaemia). The hallmark of thalassaemia major is severe anaemia that usually becomes apparent at 3–6 months after birth when the switch from fetal Hb (HbF) (α2γ2) to adult Hb (HbA) (α2β2) production should take place. Typically, the infant presents in the first year of life with severe pallor, failure to thrive and abdominal distension due to splenomegaly. Because of the ineffective erythropoiesis due to the genetic defect, there is repeated drop in Hb and this continuous fall leads to the need for repeated blood transfusions. Since anaemia is the predominant symptom in thalassaemia major, the treatment essentially consists of regular transfusions of red blood cells throughout life (5). Transfusion is usually administered every 2–4 weeks with the aim of maintaining a pre-transfusion Hb level of 9–10.5 g/dL. The strategy of repeated blood transfusion not only helps in the correction of anaemia but is also required for promotion of normal growth and prevention of physical abnormalities and to suppress bone marrow hyperactivity that is responsible for the characteristic skeletal changes seen with thalassaemia. Regular
lifelong transfusions however are associated with several possible adverse effects, which include immunological reactions, development of antibodies to red cell antigens and transmission of infectious agents (hepatitis B and hepatitis C). Since blood transfusion is one of the first and most critical components of the clinical management of TDT, it is imperative that blood transfusion services in each country, which have a burden of this disease, provide an adequate blood supply that is safe. A major side-effect, however, is the accumulation of iron from the transfused red blood cells. In patients receiving regular transfusions, the generation of free iron leads to organelle damage and cell death, especially in the liver, heart and endocrine glands leading to various clinical manifestations including short stature, hypothyroidism, impaired glucose tolerance, hypoparathyroidism and hypogonadism. The life-endangering effects of iron toxicity need close monitoring with quantification of the iron load in the tissues and removal of excess iron with the use of iron-chelating agents.

**Global perspective**

Collectively, the inherited disorders of Hb including sickle cell anaemia and its variants and the thalassaemias are the most common genetic disorders worldwide. These diseases occur mainly in the tropical and subtropical areas. There are several reasons for the high gene frequency in several tropical countries (1). First and foremost, the high gene frequency reflects natural selection through protection of carriers against severe malaria. Another major factor is the relatively high frequency of consanguineous marriages in many of these countries; this mechanism is known to have a key effect on increasing the gene frequency of any recessively inherited disorder. Epidemiological transition is another factor whereby as public health and nutritional standards improve in poorer countries, babies with these conditions who would otherwise have died in early life are now living long enough to present for diagnosis and management; an example of this being Cyprus. Finally, the varying distribution of some of the Hb disorders in different populations may reflect the strong founder effects by their original inhabitants as seen in populations of the Pacific Island. The α+-thalassaemias are more common worldwide compared to the β-thalassaemias (6). The α+-thalassaemias are present across the tropical belt from sub-Saharan Africa through the Middle East, South Asia, and South-East Asia with heterozygote frequencies in part of North India and South-East Asia reaching 75%. The more severe form of α-thalassaemia, α0-thalassaemia, is less common and is seen at a high
frequency in the Mediterranean region and in South-East Asia. The β-thalassaemias are less common in sub-Saharan Africa and spread across the rest of the tropical belt at varying frequencies. HbE is an extremely common structural Hb variant, occurring in South and South-East Asia and reaching very high frequencies in parts of South-East Asia with 70% heterozygote rates in the HbE triangle of North Thailand and Cambodia. It is therefore extremely common to see HbE-β-thalassaemia in this region. Worldwide estimates show that each year, over 40 000 new patients are born with a severe form of thalassaemia (β-thalassaemia major and HbE-β-thalassaemia) and nearly 80% of these births occur in developing countries (Table 1). The distribution of the thalassaemia genes stretches from the Mediterranean basin and sub-Saharan Africa through the Middle East to the Far East including South China and the Pacific Islands (Fig. 1). However, with constant migration that is occurring globally, Hb disorders, which were originally endemic in 60% of 229 countries, potentially affecting 75% of births, are now sufficiently common in 71% of countries among 89% of births (either in the whole population or among minorities). It is estimated that 80–90 million people are carriers for one of these genes, which is 1–1.5% of the population.

Table 1. Estimated annual births with severe β-thalassaemia in each WHO region (2)

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Estimated annual births with β-thalassaemia</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>African</td>
<td>1386</td>
</tr>
<tr>
<td>American</td>
<td>341</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>9914</td>
</tr>
<tr>
<td>European</td>
<td>1019</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>20 420</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>7538</td>
</tr>
<tr>
<td>World</td>
<td>40 618</td>
</tr>
</tbody>
</table>
**Regional perspective**

The SEA Region of WHO has 11 nations with a combined population of 2.02 billion. The ethnic origins of people living in these countries are also very heterogeneous. The Mon-Khmer and Thai language-speaking people occupy Thailand and some parts of Myanmar. The Malayopolynesians (Austronesian) live in Indonesia and several Pacific Island nations (7). The South Asian nations of Bangladesh, India and Sri Lanka are very heterogeneous and have their own specific ethnic populations. Therefore, the entire region is very heterogeneous leading to varying degrees of Hb disorders that are seen in these populations. β-thalassaemia is more common in the Mediterranean region while α-thalassaemia is more common in the Far East. Therefore, as one moves from South Asia to South-East Asia, one is likely to encounter a higher incidence of α-thalassaemia and the structural variants of thalassaemia. In South-East Asia, α-thalassaemia, β-thalassaemia, HbE and Hb CS are prevalent. The gene frequencies of α-thalassaemia reach 30–40% in Northern Thailand whereas β-thalassaemias vary between 1% and 9%. HbE is the hallmark of South-East Asia.
attaining a frequency of 70% at the junction of Thailand, Laos and Cambodia. Hb CS gene frequencies vary between 1% and 8%. These abnormal genes in different combinations lead to over 60 different thalassaemia syndromes, making South-East Asia an area with the most complex thalassaemia genotype. Interaction of the β-thalassaemia carrier gene with the structural variants can often result in non-transfusion-dependent form of thalassaemia that is commonly known as thalassaemia intermedia (e.g. compound heterozygous mutations involving β-thalassaemia and HbE disease leading to E-β-thalassaemia). A detailed understanding of the frequency distribution of these various phenotypes will help in planning transfusion strategies since a majority of patients with thalassaemia intermedia and all with thalassaemia trait do not require blood transfusions to sustain life while it is an essential requirement for patients with thalassaemia major.

**Blood transfusion services – global and regional perspective**

*Global perspective*

Since patients with thalassaemia major require monthly packed red cell transfusions to maintain their Hb at normal levels, an uninterrupted supply of blood and blood products should be ensured for these patients. To achieve this, there should be a robust programme of blood collection through various mechanisms for enhancing voluntary blood donations. It is also necessary that the blood collected is tested for transfusion-transmissible infections (TTIs) prior to transfusion.

The WHO Global Database on Blood Safety (GDBS) reported a marked variation in blood donation in various WHO regions (Table 2) (8). Of the 118.5 million blood donations collected globally, 40% were collected in high-income countries, home to 16% of the global population (9). About 13 300 blood centres in 169 countries reported collecting a total of 106 million donations and these collections at various blood centres varied according to income groups. The median annual donations per blood centre is 1300 in low-income countries, 4400 in lower middle-income countries and 9300 in upper middle-income countries, compared to 25 700 in high-income countries. There is a marked difference in the level of access to blood between low- and high-income countries. The whole blood donation rate is an indicator for the general availability of blood in a country. The median blood donation rate in high-income countries is 31.5
donations per 1000 people. This compares with 15.9 donations per 1000 people in upper middle-income countries, 6.8 donations per 1000 people in lower middle-income countries, and 5.0 donations per 1000 people in low-income countries.

Table 2. Estimated blood donation by WHO regions (2013) (8)

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Estimated whole blood donation (millions)</th>
<th>Estimated apheresis donations (millions)</th>
<th>Total (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>5.6</td>
<td>0.03</td>
<td>5.6</td>
</tr>
<tr>
<td>Americas</td>
<td>20.4</td>
<td>2.0</td>
<td>22.4</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>9.9</td>
<td>0.04</td>
<td>9.9</td>
</tr>
<tr>
<td>Europe</td>
<td>26.5</td>
<td>6.1</td>
<td>32.5</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>16.6</td>
<td>0.06</td>
<td>16.7</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>21.6</td>
<td>3.7</td>
<td>25.3</td>
</tr>
<tr>
<td>Global (Rounded totals)</td>
<td>100.6</td>
<td>11.9</td>
<td>112.5</td>
</tr>
</tbody>
</table>

To have an adequate and reliable supply of safe blood, it is necessary to have a stable base of repeat, voluntary, unpaid blood donors. These are also the safest group of donors as the prevalence of bloodborne infections is lowest among this group. Though 156 countries have reported an increase of 7.8 million blood donations from voluntary unpaid donors from 2013 to 2018, most of this increase was in the region of the Americas (25%) and Africa (23%). Only 79 countries (mainly high- and middle-income) are able to collect more than 90% of their blood supply from voluntary unpaid blood donations while in 56 countries (mainly middle-income and lower-income), more than 50% of the blood supply is still dependent on family/replacement donors. A modelling study involving 195 countries using data from the 2016 WHO Global Status Report on Blood Safety and Availability and estimates of the global disease-specific transfusion need suggested that in 2017, the global blood need was 304 711 244 and the global blood supply was 272 270 243 blood product units, with a need-to-supply ratio of 1.12 (95% UI 1.07–1.16). Of the 195 countries, 119 (61%) did not have a blood supply
sufficient to meet their needs (10). The WHO Global Status Report on Blood Safety and Availability has reported that in high-income countries, blood transfusion is mostly used for supportive care in cardiovascular surgery, transplant surgery, massive trauma, and therapy for solid and haematological malignancies while in low- and middle-income countries, it is used more often to manage perinatal haemorrhage, severe childhood anaemia and traumatic haemorrhage.

**Regional perspective**

Of the 11 countries that form the WHO SEA Region, one (Democratic People’s Republic of Korea) country belongs to the lower-income group, seven (Bangladesh, Bhutan, India, Myanmar, Nepal, Sri Lanka, Timor-Leste) belong to the lower middle-income group while three (Indonesia, Maldives, Thailand) belong to the upper middle-income group (10). Countries of the SEA Region reported the collection of 15% of global blood donations, though these countries represent 26% of the global population. Countries in the low-income and lower middle-income groups collected 2% and 22% of the global donations, respectively, though their populations represent 9% and 39% of the global population, respectively (Table 2). While the median whole blood donation rate was 32.1 donations per 1000 population per year in high-income countries, it is 14.9 (range 6.7–39.7) for upper middle-income countries, 7.8 in lower middle-income countries, and 4.6 in low-income countries. Across WHO regions, the donation rates ranged from 1.8 to 30.8 (median 7.9) in South-East Asia. As mentioned earlier, in several middle-income and low-income countries, more than 50% of the blood supply is still dependent on family/replacement and not through voluntary unpaid donors. A modelling study published in the *Lancet* in 2019 suggests that 119 (61%) countries (including Bangladesh, Bhutan, India, Indonesia, Maldives, Myanmar, Nepal and Timor-Leste but excluding Sri Lanka and Thailand) did not have a blood supply sufficient to meet their need (10). Across these 119 countries, the unmet need totalled 102 359 632 (95% UI 3 381 710–111 360 725) blood product units, equal to 1849 (1687–2011) units per 100 000 population globally. Every country in central, eastern and western sub-Saharan Africa, Oceania and South Asia had insufficient blood to meet their needs.
**Bangladesh**

Bangladesh is the eighth most populous country in the world. Bangladesh shares land borders with India to the west, north and east, Myanmar to the southeast and is narrowly separated from Nepal, Bhutan and China. A majority of the Bangladeshis (98.5%) belong to the Bengali ethno-linguistic group with ethnic minorities accounting for the rest. The country is divided into eight administrative divisions and 64 districts.

**Burden of thalassaemia in Bangladesh**

Noor et al. studied the carrier frequency of thalassaemia genes in a cohort of 1877 individuals in the age group of 18–35 years (11). The participants were from both rural and urban origins. About 4.32% of participants had consanguineous parents; 224 participants (11.89%) carried a single gene mutation for thalassaemia. Of the 11.89% carriers of β-globin gene mutations, 8.68% had HbE trait while 2.24% had β-thalassaemia trait. The carrier frequency among the participants with a history of consanguinity was 23.5%, whereas it was almost half (11.4%) among the children of non-consanguineous parents. The frequency of both HbE trait and thalassaemia trait varied across the eight divisions in Bangladesh. The frequency of HbE trait varied from as low as 4.2% in Khulna division to as high as 25% in Rangpur division. Conversely, the highest frequency of β-thalassaemia trait was found in Barisal division (3.9%). The highest frequency of β-thalassaemia trait and HbE trait was found in Rangpur division (27.1%) followed by Rajshahi division (16.4%).
Khan et al. published data in 2005 on the prevalence of thalassaemia among (n=735) schoolchildren in Bangladesh and showed a 4.1% prevalence of the β-thalassaemia trait and a 6.1% prevalence for the HbE trait (14). The same study revealed the regional variation of 2.9% to 8.1% for β-thalassaemia carriers and 2.4% to 16.5% for HbE carriers. Among tribal children, the prevalence of β-thalassaemia trait was almost identical but HbE was much higher (41.7%).

Between 2009 and 2014, Hossain et al. studied the patterns of thalassaemia among patients attending care at the Thalassaemia Foundation Hospital (TFH) located in Dhaka (12). Over the 5-year period, a total of 1594 thalassaemia patients were served by the TFH, of which 1178 complete cases were analysed. About 77.3% of patients were diagnosed as HbE-β-thalassaemia, while nearly 15% were β-thalassaemia major. About 91% of patients (n=971) required blood transfusion, where 66.9% of them were TDT patients and 24.3% were NTDT patients, thus requiring fewer transfusions than the former group. About 41.1% of TDT patients required blood transfusion every 2–4 weeks.
With the current HbE trait and β-thalassaemia trait carrier frequency of 10.92%, it is estimated that 9176 babies are born with thalassaemia each year. The overall estimates suggest 60–70 000 patients with β-thalassaemia or HbE-β-thalassaemia in Bangladesh (12). It should be remembered that the clinical manifestations of HbE-β-thalassaemia are varied. Based on clinical severity, they could be classified into three categories: mild (15% cases), moderately severe (majority of HbE-β-thalassaemia cases) and severe. Up to 50% of all patients with HbE-β-thalassaemia represent clinical manifestations like those of thalassaemia major.

**Blood transfusion services in Bangladesh**

Blood Transfusion Services (BTS) were established in Bangladesh in 1950 at the Dhaka Medical College Hospital and in 1976, the National Council of Blood Transfusion was set up. Until 2000, most of the country’s blood supply was obtained by professional donors (47%). The Safe Blood Transfusion Act was legislated in April 2002 and enforced from August 2004 as the regulatory law for blood transfusion centres. This law also encouraged the promotion of voluntary non-remunerated blood donation (VNRBD) through improved donor motivation and promotional campaigns. A national blood policy was approved in November 2013. However, there is no centralized blood collection system at the national level and no organization specifically supports and coordinates VNRBD. In 2019, the government launched the national guidelines on thalassaemia management for the physician.

In Bangladesh, there are 232 blood banks in the government sector and 150 in the private sector. Overall, the major providers of blood in Bangladesh include the government and private hospital-based blood banks (80%), Bangladesh Red Crescent Society (11%), medical college-based voluntary organizations (5%) and private organizations (4%). According to the Blood Transfusion Society of Bangladesh, approximately 600 000 units of blood are required annually (13). Most of the donations (70%) come from replacement through family relative donors while 30% come through voluntary donors, with no paid donors. Transfusion of children with thalassaemia occurs through organizations such as the Bangladesh Thalassaemia Foundation, Bangladesh Thalassaemia Samiti, Bangladesh Thalassaemia Society and the day-care transfusion centre in the Bangladesh Red Crescent Blood Centre. Transfusions also occur through individual hospitals.
Bhutan

Bhutan is a landlocked country in South Asia located in the Eastern Himalayas and is bordered by Tibet in the north and the west along with various states of India in the west, south and east. Bhutan is divided into 20 Dzongkhag (districts), administered by a body called the Dzongkhag Tshogdu. Bhutanese people primarily consist of the Ngalops and Sharchops, called the Western Bhutanese and Eastern Bhutanese, respectively while the Lhotshampa, meaning "southerner Bhutanese", are a heterogeneous group of mostly Nepalese ancestry. The Ngalops (also known as Bhote) constitute 50% of the population while ethnic Nepali (predominantly Lhotshampas) constitute 35% and indigenous or migrant tribes constitute 15%.

Burden of thalassaemia in Bhutan

Limited data are available on the prevalence of thalassaemia in Bhutan though a high incidence of anaemia has been reported (30–40% among children, adolescent girls, pregnant and non-pregnant women) (15). The reported frequency of β-thalassaemia and HbE disease in Bhutan is less than 1% (16). A survey done by University College, London in 2007 showed that among pregnant women, α+-thalassaemia carrier status was 31.9% with no α0-thalassaemia carrier status along with a 0.07% incidence of β-thalassaemia carrier status (2). Overall, among pregnant women who carried an abnormal thalassaemia gene, 92% were carriers of an α-globin gene variant while 0.16% were carriers of a β-globin gene variant and 7.8% were carriers of both α- and β-globin gene variants. In terms of the combinations of abnormal variants per 1000 conceptions, the births with haemoglobinopathies in Bhutan is very low – 0.001 with homozygous β-thalassaemia and 0.015 with HbE-β-thalassaemia.

Blood transfusion services in Bhutan

Bhutan has a coordinated National Blood Transfusion Service (NBTS), which is managed by the National Blood Centre (NBC) in the capital city of Thimphu. The NBC caters to blood needs of the 380-bedded Jigme Dorji Wangchuk National Referral Hospital where it is based and to the district hospitals in the western region of the country. There are 27 functional hospital-based blood centres throughout the country, which collect about 8028 units out of which voluntary donations are 3686 (46%) and family relative donors are 4342 (54%) (17). The functions of the NBTS include
recruitment and education of blood donors, blood donation, counselling and post-
donation care, blood component production, immunohaematology and testing for
TTIs, patient blood management, quality assurance and haemovigilance.

**Fig. 3.** Organizational structure of the NBTS, Bhutan

There has been a steady increase in the number of blood donations and the number
of VNRBDs. A status report issued in 2017 suggested that the total number of blood
donations annually had improved from 8175 in 2011 to 9917 in 2016 and the
respective percentage of VNRBDs has improved from 56% to 77% (8).

The annual blood report of 2019 revealed a total blood collection of 10 773 units (1.4%
of the total population) (18). Of these, 9302 (86.3%) were voluntary donations while
1471 (13.7%) were replacement donors. A total of 60 blood donation camps were
organized throughout the year and 3485 units were discarded with 43% of them being
expired blood units.

The NBTS has been playing a major role since 2009 in improving transfusion practices
in Bhutan, which includes developing various national documents such as national
standards, guidelines for clinical use of blood, blood donor selection and retention
criteria. In 2017, standard operating procedures (SOPs) on safe bedside clinical
transfusion practices (CTP) were developed through a technical working group
involving blood service personnel, nurses, nursing tutors and representatives of the blood safety programme. There are two qualified and dedicated transfusion medicine specialists in the country and there are other trained doctors to run the BTS. Trained doctors/technologists across the country manage the BTS efficiently; however, a few challenges still remain for the BTS in Bhutan. Some of them are: the difficult geographical terrain, to increase the number of voluntary donors, inconsistent supplies of test reagents and consumables, and awareness on rational use of blood/components by clinicians and nurses.
Democratic People's Republic of Korea (North Korea)

DPR Korea is situated in the northeastern part of Asia constituting the northern part of the Korean peninsula. The country is bordered to the north by China and Russia and to the south by Republic of Korea. According to The World Factbook, North Korea is racially homogeneous and contains a small Chinese community and a few ethnic Japanese. The 2008 census listed two nationalities: Korean (99.998%) and Other (0.002%). Administratively, the entire country is divided into nine provinces and two special cities: the capital city of Pyongyang and Nampo. Provinces are divided into cities (districts) and counties.

**Burden of thalassaemia in DPR Korea**

No data are available on the frequency of thalassaemia but based on data for DPR Korea, a low frequency of carrier rate for thalassaemia is expected possibly due to the absence of selection in favour of the β-thalassaemia genes (19). In neighbouring South Korea, thalassaemia is not a major problem; however, there has been an increase in prevalence due to increasing immigration (20). China is a neighbour in the north and the overall prevalence there of α-thalassaemia, β-thalassaemia and α+-β-thalassaemia was 7.88%, 2.21% and 0.48%, respectively; however, the geographical distribution of thalassaemia was highest in the south of China and decreased from south to north.

**Blood transfusion services in DPR Korea**

The Red Cross Society was initially involved in blood banking services including donor recruitment. However, since the mid-1950s, the Ministry of Public Health (MoPH) has taken over the responsibility. The blood banking service is nationally coordinated and centrally managed by the government under the MoPH (21).

In 1999, WHO completed a study of the blood transfusion system in DPR Korea (22). This study showed that nearly 25 000 volunteers donate blood every year without remuneration at the NBC in Pyongyang, out of a total pool of 40 000 blood donors. Despite occasional shortages, the blood supply is reported to be adequate for the country’s demand. The study also identified challenges with the blood transfusion system in DPR Korea. These included the following:
1. Use of glass bottles instead of disposable blood bags, which are required to be washed and sterilized before use
2. Use of latex tubing sets at least three times before being discarded
3. Lack of financial resources
4. Limited staff training and development
5. Inadequate physical infrastructure
6. Absence of back-up generators for domestic refrigerators in regional blood banks and hospitals.

Since then, there have been multiple levels of support to improve the blood transfusion system. WHO has been supporting the NBC with blood bags reaching 130,000 bags in the previous biennium of 2018–2019, which have contributed much to the National Blood Safety Programme to address the need for safe blood and improve health care of the people. During a visit to the Central Blood Centre in January 2020 by the WHO country team, the MoPH suggested their strong intention to have their own production of blood bags to attain self-sufficiency in the country, which is approximately 150,000 pieces every year (23). A plan is in place for the NBC which will have the first plant of its own to manufacture blood bags. The WHO country office will continue to support the supply of blood bags to address the ongoing need for 150,000 pieces even during 2020 as it will take time for the blood bag plant to start production.
India

India is the second-most populous country in the world, the seventh largest country by land area, and the most populous democracy. Bounded by the Indian Ocean on the south, the Arabian Sea on the southwest, and the Bay of Bengal on the southeast, it shares land borders with Pakistan to the west, China, Nepal and Bhutan to the north and Bangladesh and Myanmar to the east. In the Indian Ocean, India is in the vicinity of Sri Lanka and the Maldives; its Andaman and Nicobar Islands share a maritime border with Thailand and Indonesia. India is a federal union comprising 28 states and eight Union Territories.

Burden of thalassaemia in India

India, with 1.38 billion people, is a multi-ethnic and culturally and linguistically diverse population including around 8% of tribal groups according to the 15th Census of India 2011. The average prevalence of β-thalassaemia carriers is 3–4%, which translates to 35–45 million carriers. Estimates indicate that there would be around 100 000 patients with a β-thalassaemia syndrome, but the exact numbers are not known because of the absence of national registries (24). Extensive studies have provided data on haemoglobinopathies; these include multicentre studies covering different states conducted by the Indian Council of Medical Research, those undertaken by the Anthropological Survey of India or as a part of state thalassaemia control programmes as well as many Tribal surveys (25–27). At present, it is estimated that in India there are 150 000 people living with a severe form of thalassaemia. The expected annual number of affected births, estimated as 0.5/1000 live births for an average annual birth cohort of 25 million, predicted 12 500 thalassaemia major births per year. Over a period of 10 years, 125 000 more children will be added to the existing number of thalassaemia major cases (28).

Given the heterogeneous and diverse population in India, it is not surprising that there is a wide range of prevalence of thalassaemia in different states. In the eastern part of India, the influence of HbE mutations also plays a part in defining the clinical phenotype of the thalassaemia. In a multicentre study involving 56 780 individuals from six major cities (Bengaluru, Kolkata, Dibrugarh, Ludhiana, Mumbai and Vadodara) between 2000 and 2005, it was estimated that the prevalence of Hb
disorders ranged between 3.1% and 31.8% (29). The type of thalassaemia also varied with β-thalassaemia being the predominant disease seen in Bengaluru (overall 3.1%; β-thalassaemia 2.16%), Ludhiana (overall 5.2%; β-thalassaemia 3.96%), Mumbai (overall 3.48%; β-thalassaemia 2.55%) and Vadodara (overall 3.38%; β-thalassaemia 2.68%), while in Kolkata, both β-thalassaemia trait and HbE disease were equally prevalent (overall 8.3%; β-thalassaemia 3.64; HbE 3.92%) and in Dibrugarh, it was predominantly HbE disease (overall 31.8%; HbE disease 29.2%). In another study involving 1291 subjects in western Maharashtra, the incidence of Hb disorders was 11.43% with the main disease being β-thalassaemia major (30). An analysis of 1015 subjects with anaemia in Odisha between 1994 and 2003 revealed a prevalence of Hb disorders in 65.7% of the subjects with it predominantly being the sickle cell trait (29.8%) followed by the β-thalassaemia trait in 18.2% (31). A higher frequency has been observed in certain communities, such as Sindhis, Punjabis, Gujaratis, Bengalis, Mahars, Kolis, Saraswats, Lohanas and Gours (32). Within each state, the prevalence varies based on the presence of ethnic groups (33). Limited micromapping has shown an uneven distribution in frequencies of β-thalassaemia carriers in different districts of Maharashtra (1–6%) and Gujarat (0–9.5%) within small geographical regions (34). HbE is prevalent in the northeastern and eastern regions where the frequencies of HbE carriers range from 3% to over 50%, while HbS is predominantly seen among the Scheduled Tribes, Scheduled Castes and other backward castes with carrier frequencies varying from 5% to 35% in many groups (35). Co-inheritance of these Hb variants with β-thalassaemia is not uncommon particularly in regions where both are prevalent.

Guidelines for uniform management as well as prevention, screening of school and college students, antenatal screening and prenatal testing for thalassaemia were compiled and circulated by the blood cell of the National Health Mission (NHM) through the Ministry of Health and Family Welfare (MoHFW) in 2016 (36). Many facets of these guidelines have been implemented and training programmes are ongoing. The NHM document has also described the reported prevalence of haemoglobinopathies from several states of India.
Blood transfusion services in India

It has been estimated that 2 million units of packed red cells are needed for transfusion of thalassaemia patients in India (37). An assessment of blood banks across the country was performed by the MoHFW in 2016 (38). This assessment identified 2626 functional blood banks excluding military blood banks. The public and not-for-profit sectors together owned 76% of the blood banks in India and the private sector owned 24%. Around 61% of the blood banks were in located in eight states – Maharashtra (11.7%), Tamil Nadu (10.1%), Uttar Pradesh (9.4%), Karnataka (7%), Kerala (6.3%), Telangana (5.8%), Gujarat (5.1%) and Madhya Pradesh (5%). Except Maharashtra and Gujarat, these states do not have a very high prevalence of thalassaemia. If the number of blood banks per million population is considered, states such as Bihar (0.7 blood banks), Jharkhand (1.2), Uttar Pradesh (1.2), West Bengal (1.3), Rajasthan (1.5), Madhya Pradesh (1.8), Manipur (1.8), Odisha (1.9), Assam (2), Nagaland (2), Meghalaya (2) and Chhattisgarh (2) recorded less than the national average of 2.2. A majority of these states have a high prevalence of thalassaemia either in the entire state or within specific ethnic communities that are resident within the state. Between
January and December 2015, the annual blood collection reported from all the blood banks was 11,645,791, of which 71.9% (8,378,692) units were through voluntary blood donations and the remaining were from replacement donations. The average annual collection of blood units of each of the blood banks in the country was 4,789 units. The annual collection of blood units per 100 individuals was found to be around 1% in India, which meets the WHO recommendation that 1% of the population can meet a nation’s most basic requirements for blood. However, there are huge disparities in the collection of blood between various states. Bihar collected only 0.2 units of blood per 100 population followed by Arunachal Pradesh (0.4), Meghalaya (0.5), Nagaland (0.5), Jharkhand (0.5) and Uttar Pradesh (0.5). A recent estimate by the National AIDS Control programme (NACO) for the MoHFW has suggested that the annual demand is 14.6 million units whereas the collection in 2017 was 11.1 million units (39).

Though 91.5% of the blood banks reported adhering to the guidelines of the NBTC, only 12.6% and 11.2% of the blood banks in India have enrolled themselves for External Quality Assurance Schemes (EQAS) by recognized providers for immunohaematology and TTIs, respectively. The mean assessment score of blood banks in the country was 62 (SD 11.19). Most of the blood banks that scored less than or equal to 35 were in Uttar Pradesh (13; 5% of all blood banks), followed by Bihar (6; 8% of all blood banks) and Odisha (3; 4% of all blood banks). The blood banks that reported a higher proportion of voluntary blood donation indicated a higher mean assessment score. Nineteen states have recorded more than the national average of 71.9%. States and Union Territories such as Dadra and Nagar Haveli, Arunachal Pradesh, Maharashtra, Tripura, Tamil Nadu, Daman and Diu, Uttarakhand, Chandigarh, West Bengal, Kerala, Andaman and Nicobar, and Himachal Pradesh reported more than 80% voluntary blood donation. States and Union Territories such as Meghalaya, Uttar Pradesh, Manipur, Chhattisgarh, Delhi, Assam, Bihar, Jharkhand, Puducherry, and Jammu and Kashmir reported less than 60% of voluntary blood donation. This difference may be related to the incorrect practice of considering near relatives as voluntary donors. Repeat donations are also low (0–30%) due to lack of customer satisfaction and donor loyalty.

The National Blood Cell under the NHM, Government of India was set up in May 2014. It envisaged a comprehensive, efficient and total quality management approach for
building a sustainable, national, integrated and standardized blood programme to ensure the accessibility, adequacy, safety and quality of blood. The grant-in-aid provided under the NRHM/NHM to state governments for strengthening/setting up blood banks and blood storage centres is channelled through the National Blood Cell. The National Blood Cell also facilitates specialized services for chronically transfused patients and monitors and supports all aspects of blood services in the country. The National Blood Cell coordinates and liaises with the different arms of the MoHFW for efficient functioning. It has the following mandate:

- To adopt a comprehensive approach to the blood services rather than just focusing on disease transfusion through blood and blood products.
- To plan a long-term sustainable programme for blood services.
- To bring self-sufficiency in the blood services in all regions of the country.
- To ensure access to safe blood to far-flung and remote areas of the country so that the blood is available when and wherever required.
- To deal with issues of inequitable distribution of blood leading to surplus in some areas and severe scarcity in others.
- To organize continuous and periodic monitoring of all activities of blood services for providing support to the NHM.
- To conduct regular financial audit of all aspects of blood services for efficient use of resources.
- To strengthen the supply chain of critical consumables to ensure proper functioning.
- To address the issue of maintenance of equipment in government blood banks.
- To facilitate specialized services for chronically transfused patients.
- To establish coordination among the various divisions dealing with regulations and management of blood services.

To fulfil this mandate, the NHM has made 1599 blood storage units functional which are part of first referral units (FRUs) and subdistricts and some of the primary health centres which have a high load for delivery. The aim is to ensure that all districts have functional blood banks and all FRUs have at least blood storage centres. Eighty-nine districts still do not have blood banks and the NHM has supported the setting up of 74 blood banks in various states. To facilitate voluntary blood donation, the NHM has
been working towards strengthening blood services including mobile blood collection and transportation vans with dedicated workforce to augment the availability of blood. A detailed gap analysis carried out under the NHM in the states has revealed that most of the blood banks were facing shortage of human resource and equipment. Under the NHM, states have been supported with the required human resource and equipment in the blood banks and regular assessment is being done after 2 years for upgrading the blood services.

The NHM has also been working towards developing a network of blood banks and blood storage centres and the e-Raktkosh, which is an integrated Blood Bank Management Information System. This web-based mechanism interconnects all the blood banks of a state into a single network (40). This has been developed with the objectives of providing safe and adequate blood supplies, reducing the turnaround time, developing a network of blood banks, ensuring that all blood banks adhere to the Drugs and Cosmetics Act, having real-time availability of blood stock, a state-wise/district-wise donor database and generating various reports for blood bank officials and administrators. In the past 3 years, e-Raktkosh has made an impressive progress and more than 1900 blood banks across the country are using this application for their day-to-day activities with real-time updates of blood stock. The e-Raktkosh portal is extensively used by patients/citizens for their requirements related to blood, finding the location of blood banks, maintaining donation repository, details about blood donation camps, etc. The application has become a one-stop solution for both blood banks and patients who need blood and blood-related products. This platform has been recognized and awarded for its excellence and contribution to society in the “Gems of Digital India Award 2019”.

It is worth noting that many efforts may not trickle down to the grassroots. Dr J.S. Arora, General Secretary, National Thalassaemia Welfare Society expressed concern in a newspaper interview in 2019 on World Thalassaemia Day that despite the National Blood Transfusion Council (NBTC) issuing directions to provide free blood to all persons with thalassaemia in 2014 and NHM publishing guidelines on management and prevention of haemoglobinopathies in 2016, the optimum Hb level is not maintained in most patients with thalassaemia. It has been observed that 50–60% of persons with thalassaemia have Hb levels of less than 9 g/dL (41).
Indonesia

Indonesia is a country in South-East Asia and Oceania, between the Indian and Pacific oceans. It consists of more than 17,000 islands, including Sumatra, Java, Borneo, Sulawesi and New Guinea (Papua). Indonesia is the largest island country and has over 300 ethnic groups; 95% of those are of Native Indonesian ancestry. Javanese is the largest group with 100 million people (42%), followed by Sundanese, whose number is nearly 40 million (15%). Administratively, Indonesia is divided into provinces which are the 34 largest subdivisions of the country and the highest tier of the local government. Provinces are further divided into regencies and cities, which are in turn subdivided into districts.

Burden of thalassaemia in Indonesia

Early studies have estimated that there is a high prevalence of thalassaemia carrier status in the Indonesian population with a prevalence of 3–20% for α-thalassaemia carrier, 3% for β-thalassaemia carrier and 1–33% for HbE carrier (42). Because of the diversity of the genetic background, there is a difference in the carrier frequency of β-thalassaemia (5–10%), HbE (1–33%) and α-thalassaemia (6–16%) depending upon the ethnic population. This variation can result in unequal anticipated carrier testing and prenatal testing workload and therefore, the carrier screening protocol and prenatal testing must be designed on a regional basis (43).

Fig. 5. Distribution of thalassaemia trait in five provinces of Indonesia (44)
In a study, 241 volunteers were screened in the Yogyakarta special region between 2012 and 2015 (44). Among the 241 volunteers, 44 (18.2%) were diagnosed as β-thalassaemia carriers, 30 (12.4%) as α-thalassaemia carriers as well as HbE carriers, and 1 as α-β-thalassaemia carrier. There was no difference in the number of carriers detected during the 3 years of the study suggesting no increase in the prevalence (Fig. 5).

Because of the ethnic variation in frequency of thalassaemia in the Indonesian population, various studies have tried to identify specific genetic mutations in each population as this will help in genetic diagnosis and screening. Another study on 209 β-thalassaemia Javanese patients from Central Java, using a combination of multiple detection methods, identified 14 alleles that accounted for more than 85% of patients (45). Identification of the most prevalent alleles would help in improving the β-thalassaemia screening for the Javanese, which is one of the major ethnic groups in Indonesia. Specific variants have also been identified in the α-thalassaemia gene, which includes the identification of HbO mutation in Indonesia. Heterozygous mutations for HbO\text{Ina} were identified from the Bugis, Toraja, Makassar and Kajang ethnic populations, but not from the other populations (46).

The data from the Indonesian Thalassaemia Foundation/Association of Parents of Thalassaemia Patients Indonesia (YTI/POPTI) reveal that the number of patients with thalassaemia in Indonesia has increased from 4896 in 2012 to 9028 in 2018. According to the latest estimates, there are 10 531 thalassaemia patients, and more than 2500 newborns have thalassaemia each year in Indonesia (47). Since there is an absence of a national registry and the data available are fragmented, there may be many undiagnosed patients. Separate databases are available in major thalassaemia centres such as the Cipto Mangunkusumo Hospital, which is a national referral hospital.

The treatment of thalassaemia has been included in the benefits package of the government health insurance programme for the poor (JAMKSESMAS) since 2010 and the national health insurance (NHI) programme since 2014. Supportive measures such as blood transfusion and iron chelation are the mainstay of management of
patients with thalassaemia (48). National guidelines are available on the indications and frequency of transfusion based on international guidelines.

**Blood transfusion services in Indonesia**

The Indonesian Red Cross Society or Palang Merah Indonesia (PMI) is the national blood service agency which ensures that there is an adequate and safe supply of blood for all patients who require transfusions. The blood supply for all hospitals is performed by blood centres that either belong to the PMI or government hospitals. About 80% of blood donations occur through VNRBD, while the rest are replacement donations and occasionally through paid donations. The PMI targets 4.5 million blood bags annually in accordance with the national blood needs. Every week, Indonesia needs 60–70 000 blood donations to ensure enough supplies for people in need. However, with the current donation rate, Indonesia can only fulfil around half of the blood demand. The others must depend on blood provided by families, friends or even on paid donations. Moreover, there is an unequal distribution of blood supply in Indonesia. According to the MoH, in 2014 Jakarta had an excess supply of blood of 60%, while there was a 96.3% shortage of blood in West Papua. The variable quality of blood services throughout the country also reflects in the fact that 0.46% of national donations originate from paid donors and these paid donors were found in 34 remote areas (49). The transfusion rates in patients with thalassaemia are not encouraging and a study from the Cipto Mangunkusumo Hospital showed that only 30% of patients complied with the recommendation to come for a transfusion before their Hb levels fell below 9 g/dL (48). Studies on the quality of life (QoL) have also shown a reduced QoL compared to controls in children with thalassaemia (50).
Maldives

The Maldives is an island nation that comprises 20 natural atolls with only 200 inhabited islands, which are in the southwest of India. As of July 2020, the population of Maldives is 540,544. The population distribution varies considerably among the 200 islands. The population of atolls ranges from 5,000 to 20,000, and some islands have less than 500 people. Maldives was urbanized by immigrants from South Asia, mainly from South India and Sri Lanka (51). The largest ethnic group is Dhivehin, i.e. the Maldivians, native to the historic region of the Maldives Islands comprising today's Republic of Maldives and the island of Minicoy in the Union Territory of Lakshadweep, India. They share the same culture and speak the Dhivehi language. They are principally an Indo-Aryan people, having traces of Middle Eastern, South Asian, Austronesian and African genes in the population.

Burden of thalassaemia in Maldives

Initial studies from the early 1970s have suggested a thalassaemia carrier frequency of 10.1% (52). In 1985, a collaboration between the Government of Maldives and the Society for Health Education (SHE) established the National Thalassaemia Screening Programme. An analysis of this programme was published in 2020 (53). Blood samples were collected from 110,504 participants between 1992 and 2015, which is nearly 30% of the entire population. Hb and red blood cell indices were measured on automated haematology analysers. The quantitation of Hb, HbA2, HbF, and other abnormal Hb variants were assessed by HPLC. Molecular analysis was performed for the most common mutations in South-East Asia for only 874 individuals either heterozygous or homozygous for these mutations using reverse dot blot hybridization. The β-thalassaemia carrier frequency was estimated to be 16.2%. Molecular diagnosis of 874 β-thalassaemia carriers/major was performed for the most common seven mutations in South-East Asia; of these, 139 patients were diagnosed as β-thalassaemia major. This analysis showed that the most common mutations among the 874 individuals were IVS1+5G>C (678; 77.6%), followed by CD30 (136; 15.6%). The IVS1+5G>C (76%) mutation is consistent with what has been found in Sri Lanka and India. The second most common mutation was CD30 (13.3%), which is common among patients with β-thalassaemia in Italy. This indicates that Maldives might have its own distinct molecular genetic epidemiology profile. Besides β-thalassaemia, there
are α-thalassaemia carriers 2.1%, HbE carriers 0.9%, HbS carriers 0.13% and HbD carriers 0.43% (54).

The frequency of β-thalassaemia varies significantly among the 20 different atolls in Maldives. The carrier frequency ranged from 6.8% in the Meemu Atoll to 23.8% in the Noonu Atoll and Haa Dhalu Atoll (Fig. 6) (53). As per the 2018 Maldivian Blood Services Report, 874 patients have been registered in Maldives. About 10–15 new patients with thalassaemia are registered every year. A study performed in 2016 to understand the reasons for couples not testing for thalassaemia before or after marriage showed that participants did not undergo carrier tests because of poor awareness and a lack of understanding of the devastating consequences of the condition (55). The outcomes of not testing were distressing for most participants. In view of the high carrier frequency, the present regulations in Maldives make it compulsory for couples to test for thalassaemia before getting married. Authorities do not forbid marriage between two carriers, but it is discouraged.
Fig. 6. Prevalence of β-thalassaemia and mutation distribution among the 20 atolls in Maldives (53)
**Blood transfusion services in Maldives**

Maldivian Blood Services (MBS) was formed on 1 November 2012 by merging the National Thalassaemia Centre (NTC) and the National Blood Transfusion Services (NBTS). The aim was to provide better service to patients suffering from haematological disorders such as thalassaemia and other haemoglobinopathies and to provide safe blood to those who are in need. MBS, located in Male, has two main units: Thalassaemia and Other Haemoglobinopathies Centre (TOHC) and Central Blood Bank (CBB). The TOHC was till recently the only centre throughout Maldives serving exclusively to patients of thalassaemia and other haemoglobinopathies. In December 2018, the government in partnership with WHO inaugurated a nationwide system to facilitate convenient treatment to patients suffering from thalassaemia by improving access to safe blood, transfusion services and treatment for patients with thalassaemia. The Thalassaemia Society of Addu was inaugurated in October 2019 and is being operated in collaboration with the NTC and the Thalassaemia Society of Maldives. All patients with haemoglobinopathies can get registered at MBS to avail free services.

Blood donation occurs either through direct donations at the NBC and the Indira Gandhi Memorial Hospital (IGMH) or through outdoor blood donation camps. Mobile units are used for blood donation drives and three camps are organized each month. Each camp usually collects 35–40 units of blood although occasionally up to 120 units may be collected. Monthly blood collection is about 300 units by the IGMH and about 500 units by the NTC (17). About 70–80% of blood units are collected mainly from family replacement donors and directed donors for their own patients while there are only 10–30% voluntary donations and no paid donors. Family members are avoided as donors. A few blood banks on the other islands cater to their local population. A WHO Mission report in 2014 suggested that despite the allocation of the MBS as the NBC, there was less cooperation with the various blood banks in other hospitals, such as the IGMH, which could alleviate shortages, especially when a rare blood type or an antibody-free donor blood is sought (54). This lack of networking adds to delays in finding a suitable donor for a patient and allows drop in pre-transfusion Hb.
**Myanmar**

Myanmar is the largest of the Mainland South-East Asian states by area with a size of 676,578 sq. km (261,228 sq. miles). Myanmar is divided into seven states and seven administrative regions. Myanmar is composed of 135 ethnic groups in which Kachin, Kayah, Kayin, Chin, Mon, Bamar, Rakhine and Shan are the major indigenous races.

**Burden of thalassaemia in Myanmar**

Myanmar has a high prevalence of haemoglobinopathies: \( \alpha \)-thalassaemia 10–56.9%, HbE 1–28.3%, \( \beta \)-thalassaemia 0.54–4.07%. It was estimated that 1–4.9 births per 1000 infants are with a major haemoglobinopathy (56). In the 1960s and 1970s, the Anaemia Research project reported the prevalence of thalassaemia trait among the Burmese (Bamar) to be 4.3% and that of the \( \beta \)-thalassaemia trait 0.54% (57). Prevalence rates of \( \alpha \)-thalassaemia also ranged from 10% to 56.9%. A study in 2011 reported a \( \beta \)-thalassaemia carrier rate of 4.07% among asymptomatic Myanmar subjects aged 16–45 years (58). The prevalence of HbE trait was reported to be between 1% and 28% among the various races of Myanmar. There is no national thalassaemia registry, but hospital registries exist. According to hospital-based records, HbE-\( \beta \)-thalassaemia accounts for 46–58%, \( \beta \)-thalassaemia for 5.4–22% and \( \alpha \)-thalassaemia for 6–37%. Studies have also focused on the types of mutations prevalent in Myanmar. Molecular mutations associated with \( \alpha \)-thalassaemia were first described in 2001 and \( \alpha^{3.7} \) type of \( \alpha \)-thalassaemia mutation is the most common deletional type of mutations. The commonest genetic abnormalities in patients with HbH disease is \( \alpha^{3.7} / \alpha^{3.7} \) (53%) and \( \alpha^{4.2} / \alpha^{4.2} \) (30%) (59,60). In 2002, 18 different \( \beta \)-thalassaemia mutations were studied among patients with either thalassaemia major or thalassaemia intermedia. The common mutations seen include CD 41/42 (-TCCT), IVS1-1 (G-T), IVS1-5 (G-C) and CD17 (A-T) (61). A recent study compared the spectrum of \( \beta \)-thalassaemia mutations seen in Myanmar with five of its neighbouring countries – China, Laos, Thailand, India and Bangladesh (62). The common \( \beta \)-thalassaemia mutations were seen in all neighbouring countries though at different frequencies while several mutations described in other countries were rare in Myanmar. A molecular survey during annual check-up of 300 anonymous Myanmar workers in a factory in North-East Thailand revealed the presence of thalassaemia...
mutations in 61.5%, mainly α-thalassaemia (39%) and HbE (19.3%) with a very low prevalence of β-thalassaemia (2%) (63).

The prevalence of HbE disease has been estimated to be 25% in the general population in Myanmar but some studies have reported higher figures. In a study on 132 schoolchildren at the Yangon Children hospital, the prevalence of HbE disease was 63.6% (64).

Myanmar has four established haematology centres plus one new centre from the army. The thalassaemia registry is thus hospital-based only. In 2019, 496 new paediatric thalassaemia patients were registered in two paediatric centres, while about 400 new adult thalassaemia patients were registered in three adult centres. Yangong Children’s Hospital has 4000 registered thalassaemia patients – 1433 received transfusions in 2016, 1496 in 2017 and 1510 in 2018. Overall, five haematology centres provide services for transfusion of definite thalassaemia care, but patients get transfused at local hospitals as well.

**Blood transfusion services in Myanmar**

The first blood bank facility was established at the Yangon General Hospital in 1945 and is presently known as the NBC. In 1962, a national blood bank committee was created and the following year a voluntary blood donation programme was formalized. Set up in 1920, the Myanmar Red Cross Society (MRCS) initiated blood donation activities in 1961 to help improve blood donation. The MRCS supports the “national blood and blood product law” (enacted in January 2003) to save patient’s lives through blood transfusion of quality assured blood and blood products and to prevent TTIs through the promotion of VNRBD (65). Myanmar has a nationally coordinated BTS that is managed by the government and the NBC is the technical hub for developing BTS in the country. A blood and blood products law was enacted in 2003 to implement a regulatory mechanism in Myanmar. The Department of Health manages the NBC, which has two national blood banks at the Yangon General Hospital and Mandalay General Hospital, with an annual demand of 180 000 units of blood. Nationally, there are 359 hospital-based blood banks with an annual demand of 200 000 units of blood. Nearly 100 hospitals of varying levels and 324 townships and station level hospitals perform regular blood transfusions. Blood bank guidelines which represented the
country’s needs were launched in 2011. Training on these guidelines was started and covered the entire country by 2014. Since then, the blood transfusion service around the country developed a uniform registration system (66).

**Fig. 7.** Blood transfusion services connected to the National Blood Centre in Myanmar (66)
A survey done ahead of the World Blood Donor Day on 14 June showed that many people in Myanmar believed that the blood donation process was either too complicated or risky to get involved. In 2000, the percentage of voluntary donors was 34.9%. Several voluntary organizations assist in donor recruitment and blood donation. In 2018, Myanmar's NBC in Yangon provided 438,000 units of blood with 72% being donated by volunteers and 32% was used in Yangon. Presently, the voluntary blood donation in the country has improved to 85%. The NBC is supplying enough safe blood for 14 hospitals in the Yangon region and acting as a source of safe blood for other hospitals in the country. Despite this, shortage of blood is still a problem. During the World Blood Donor Day on 14 June 2019, it was reported by the National Blood Bank that it was around 100 litres short of the blood that was required by patients every day – the equivalent of 600 blood transfusions.
Nepal
Nepal is a landlocked country situated mainly in the Himalayas in South Asia and is bordered by China, India and Bangladesh. The Nepalis are descendants of three major migrations from India, Tibet and North Burma, and the Chinese province of Yunnan via Assam. Among the earliest inhabitants were the Kirat of the eastern region, Newars of the Kathmandu Valley, aboriginal Tharus of the Terai plains and the Khas Pahari people of the far-western hills. Nepal is composed of seven provinces, which are divided into 77 districts. Nepal has a diverse ethnic group of population. Though most of the geographical places of the country share mixed ethnicity, some ethnic group seems predominant in certain geographical locations of the country.

Burden of thalassaemia in Nepal
There has been no study to estimate the burden of thalassaemia in Nepal and a majority are hospital-based data (67). Sickle cell disease is commonly detected in Banke, Bardiya, Dang, Kailali and Kanchanpur, while thalassaemia cases can be found in any part of country. In Nepal, β-thalassaemia is more common and was found mostly in low land Terai region and some in the mid-hill region and, unlike sickle cell disease, it is believed to be prevalent in all ethnic communities.

A hospital-based study that examined 138 electrophoresis samples identified β-thalassaemia in 34 cases (β-thalassaemia trait in 26 and homozygous β-thalassaemia in eight), sickle cell anaemia in 21, α-thalassaemia in 11 and HbE disease in five. Incidentally, the Tharu community had the highest incidence of haemoglobinopathies (68). Another study done in Kathmandu on 163 electrophoretic samples showed the presence of a haemoglobinopathy in 47.3% with the common diagnosis being sickle-β thalassaemia in 14.1%, sickle cell disease (13.5%) and β-thalassaemia in 12.9% (69). Both studies carried the obvious bias of prevalence being estimated based on laboratory tests that were ordered for patients suffering from anaemia.

A recent study retrospectively analysed 4018 samples collected at five different Nepal government testing sites during 2016–2018. Of the 4018 cases, 1470 or 36.5% showed the presence of a haemoglobinopathy-related disorder (70). Sickle cell disease (homozygous or trait) was identified in 17.4% while β-thalassaemia
(homozygous and trait) was identified in 10% and HbE disease in 2.1%. It was observed that the types of haemoglobinopathy were not uniformly distributed in different geographical areas (Fig. 8). Sickle cell was more prevalent in Provinces 5, 6 and 7 while β-thalassaemia was more prevalent in Provinces 2, 3 and 4. In Province 1, HbE was the most common.

**Fig. 8.** Distribution of haemoglobinopathy among the various provinces of Nepal (70)

![Map of Nepal showing total number of haemoglobinopathy cases and common haemoglobinopathy types](image)

This study also recognized that all the ethnic groups did not have the same distribution of haemoglobinopathies (Table 1). The Tharus predominantly had sickle cell disease while the Newars, Chhetris, Brahmins and the Dalits predominantly had β-thalassaemia. The Rajbanshis predominantly had HbE disease while the Muslims had similar prevalence of HbE disease and β-thalassaemia. The Janjatis again had a combination of β-thalassaemia along with minor haemoglobinopathies.

Interestingly, studies in the early 2000s suggested that there was a correlation between the presence of malaria and the presence of α-thalassaemia (71). In a study involving four ethnic groups in a lowland area of Nepal, it was shown that the group that had lived for many decades in a malaria-endemic lowland area, the Danuwar, had a high prevalence of α+-thalassaemia (79.4%) and low prevalence of HbE and G6PD deficiency. On the other hand, much lower prevalence of α+-thalassaemia was observed in the Newar (20.5%), Parbate (16.5%) and Tamang (8.8%) regions, which
until the 1950s, all spent their hot-season nights in malaria-free areas at higher altitudes (72).

**Blood transfusion services in Nepal**

The National Policy for Blood Safety was approved in 1991 and the Government of Nepal mandated the Nepal Red Cross Society as the sole authority for conducting blood programmes in Nepal. The National Blood Policy has since been revised in 2006 and 2012, providing the regulations for ensuring the people of Nepal to have access to a safe and adequate supply of blood and blood products (21). There is a National Technical Advisory Committee (NTAC) which provides advice on blood-related technical matters, and falls under the National Steering Committee, part of the Ministry of Health and Population (MoHP). Under the MoHP, the National Public Health Laboratory (NPHL) functions as the reference centre and encourages all aspects of blood safety (policy, guidelines, protocols and SOPs). The draft guidelines for the management of thalassaemia and sickle cell anaemia was issued by the MoHP in 2017.

Voluntary blood collection was introduced in 1982 and the Central Blood Transfusion Service (BTS) in Kathmandu reached 90% VNRBD in 2009. According to the Nepal Red Cross Society (May 2020), there are 113 Blood Transfusion Service Centres (BTSCs) but only 13 blood banks have the blood component service. The BTSCs in Nepal are divided into the following: (i) Central BTSC (1) in Kathmandu; (ii) Regional BTSCs (4) in Biratnagar, Pokhara, Nepalgunj, Chitwan; (iii) district BTSCs; (iv) emergency BTSCs; and (v) hospital units.
More than 85–90% of blood is collected through VNRBD, but sometimes replacement is also being requested by blood banks at times of blood shortage mainly during or immediately after festivals such as Dussehra, Deepawali, Chhat and during the cold seasons. In 2009–2010, it was estimated that a total of 156,278 units of blood were collected, which was approximately 0.62% of the total population of the country. Though blood transfusion centres are present in 50 of the 77 districts in Nepal, many still lack in quality transfusion facilities and therefore several patients travel to Kathmandu for regular blood transfusions.
Sri Lanka

Sri Lanka is an island in the Indian Ocean about 28 km (18 miles) off the southeastern coast of India. The Sinhalese make up 74.9% of the population and are concentrated in the densely populated southwest and central parts of the island. The Sri Lankan Tamils, who live predominantly in the north and east of the island, form the largest minority group at 11.1% of the population. The Moors, descendants of Arab traders, form the third largest ethnic group at 9.3% of the population and are mostly concentrated in urban areas in the southern parts of the island with substantial populations in the central and eastern provinces. Indian Tamils form the other distinct ethnic group comprising 4.1% of the population. Other smaller minorities include the Malays, the Burghers and ethnic Chinese migrants. Administratively, there are nine provinces in Sri Lanka.

Burden of thalassaemia in Sri Lanka

de Silva et al. in a study published in 2000 studied blood samples from 703 patients with β-thalassaemia and 1600 schoolchildren (74). Although 23 different β-thalassaemia mutations were found, three accounted for the thalassaemia phenotype in about 70% of patients, most of whom are homozygotes or compound heterozygotes for IVS1-5 (G-->C) or IVS1-1 (G-->A). The third common mutation, codon 26 (G-->A), which produces HbE, interacts with one or other of these mutations to produce HbE-β-thalassaemia; this comprises 13.0–30.9% of cases in the main centres. As a subset from the above study, samples from 472 patients were analysed to determine the α-globin genotype and overall 15.5% patients were carriers for deletion forms of α+-thalassaemia. A study of the average gene frequencies estimated that there will be more than 2000 patients requiring treatment at any point of time in the future, of which those with HbE-β-thalassaemia will account for about 40%. Of the 1547 patients, genetic data were available for 1379 (75). A recent hospital-based survey described data on 1774 patients from 23 centres (76). Among these, 1219 patients (68.7%) had homozygous β-thalassaemia, 360 patients (20.3%) had HbE-β-thalassaemia, and 50 patients (2%) had sickle β-thalassaemia. This study also examined the annual births with thalassaemia between 1996 and 2014; the annual number of births of patients with β-thalassaemia varied from 45 to 55 with little evidence of reduction over 19 years. Ethnically, 1450 patients were Sinhalese (at 82.6%, higher than the national
representation at 72%), 211 were Moors (at 12.0%, higher than the national representation at 7.1%). Ninety-three were Tamils (at 5.3% less than one third of the national representation at 18%) and two patients were Burgher (0.11%). Overall, it is estimated that the carrier rate is 2–4%, estimated prevalence of 2000–3000 cases and annual incidence of 80–100 cases out of 350 000 births (77). In Sri Lanka, co-inheritance of either excess α-globin genes in β-thalassaemia heterozygotes or α-globin gene deletions in β-thalassaemia homozygotes is a significant factor in modulating disease severity (78).

The burden of thalassaemia in Sri Lanka is not uniform with a high burden of disease in the North West province, North Central Province and Central Province. To adequately manage these patients with thalassaemia, four regional thalassaemia centres are located in the provinces with the highest burden of disease. Since 1995, all thalassaemia patients were exempted from the requirement of finding donor replacements for blood transfusions, which considerably improved the quality of care for thalassaemia patients in Sri Lanka. As per the National Health Policy, all medications including blood and chelating agents are available free of charge for all patients in the country. Despite these efforts, patients with thalassaemia continue to have a lower QoL. In a study involving 271 children with TDT from the three largest thalassaemia centres of Sri Lanka, it was found that the mean health-related QoL scores was significantly lower in patients compared to controls. In addition, QoL scores in psychological health, emotional functioning and social functioning were significantly lower in patients with HbE-β-thalassaemia compared to those with β-thalassaemia major (79).
Blood transfusion services in Sri Lanka

Sri Lanka has one of the best blood transfusion services (BTS) in South Asia, which is nationally coordinated and managed by the government. The National Blood Transfusion Service (NBTS) Sri Lanka is a special campaign under the MoH. It has a unique role providing timely supply of quality assured blood and blood components and related laboratory, clinical, academic and research services for the entire government sector hospitals and for most of the private sector hospitals in the country. The NBTS was established in 1999 and is designated as a WHO Collaborating Centre for Blood Transfusion Service in 2018. The NBTS is the sole supplier of blood and blood products to all state hospitals and some of the private hospitals, which are registered under the MoH for supply of blood and blood products. There are 1042
government hospitals and 115 hospitals in the private sector. Having its headquarters at the NBC, the NBTS has 103 blood banks (both hospital-based in the public and private sectors) across the country, which are grouped into 19 clusters. There are no standalone blood banks in the nongovernment organization (NGO) or private sector. These blood banks are categorized as the NBC (headquarters), Cluster Centres and Peripheral Blood Banks.

The annual collections have been steadily growing with 450 640 units being collected in 2018; of these, 417 153 being mobile collections (80). The total discarded units for 2018 were 30 341 with the majority (23 617) being discarded post expiry. About 60–70% of donations are separated into blood components; 100% of Sri Lankan blood donors are VNRBDs and there is no paid donation. The NBC has established a system of functional hospital transfusion committee in all hospitals. It has also established a haemovigilance system and irradiation facility. In recognition of its services, the NBTS was awarded the International Society of Blood Transfusion (ISBT) Award for Developing Countries in 2012 from among 28 competitors and the NBTS Sri Lanka was selected as the best transfusion service among developing countries.

Though clear guidelines are laid down for transfusion in patients with β-thalassaemia major, guidelines are lacking for patients with HbE-β-thalassaemia. In a study on 328 patients (83% β-thalassaemia major, 16% HbE-β-thalassaemia), involving three large thalassaemia centres in Sri Lanka, it was observed that over 60% of regularly transfused patients with β-thalassaemia have low pre-transfusion Hb levels and did not maintain pre-transfusion Hb levels of >9 g/dL despite receiving large transfusion volumes (81). In addition, it was noted that patients with HbE-β-thalassaemia were also under-transfused. A companion study also noted that this disease had a significant impact on psychological health of the children and mothers with a large proportion reporting abnormal psychological symptom scores (82).
Thailand

Thailand has a diverse ethnic make-up and the Thai government officially recognizes 62 ethnic communities. The majority (34.1%) are Central Thai (with Khorat Thai) (83). Mountain people and ethnic communities in the northeast comprise about 24.9%. Other major ethnic communities include Khon Muang (9.9%, also called Northern Thais); Pak Tai (7.5%, also called Southern Thais) and Khmer Leu (2.3%, also called Northern Khmer). There is a significant number of Thai Chinese in Thailand and up to 14% of Thais may have Chinese origins. Another major group comprising one third of Thailand's population are the Isan people who are ethnic Lao with some belonging to the Khmer minority.

Burden of thalassaemia in Thailand

Thailand was the first country to report thalassaemia in the non-Mediterranean population in 1954 when they described a series of 32 cases (84). The prevalence of haemoglobinopathy varies in the Asia Pacific region and in Thailand the prevalence of α-thalassaemia varies between 5.5% and 30%, β-thalassaemia between 1% and 9% and HbE disease between 5% and 50% (85). The other type that is commonly seen is Hb CS. A hospital registry study involving 4303 patients between 1974 and 2013 showed that the majority were HbE-β-thalassaemia (61%) followed by HbH or α-thalassaemia (16%), Hb CS (15.7%) and β-thalassaemia (7.3%) (86). With the high prevalence and diverse heterogeneity of thalassaemia and haemoglobinopathies, around 60 thalassaemia syndromes are encountered in Thailand. A national prevention and control programme for thalassaemia was established throughout Thailand in 1992 with the support of the National Health Security Office (NHSO). Since the clinical manifestations of these genetic mutations can vary from their presentation as a transfusion-dependent disease to a mild asymptomatic illness, it is worth finding whether there are specific geographical distributions for each of the thalassaemic syndromes.

Chaibunruang et al. assessed the impact of the national control programme by studying 350 cord blood samples of newborns at the Maternal and Child Hospital, Khon Kaen province, northeast Thailand between January and May 2012 (87). Among the 350 newborns examined, thalassaemia genes were identified in 184 (52.6%) cases with as many as 22 different genotypes. The most prevalent one was HbE.
(39.1%) along with α^0^-thalassaemia (3.1%), α^-thalassaemia (25.9%), Hb CS (5.4%) and a very low incidence of heterozygous β-thalassaemia (0.6%).

Yamsri et al. in a study involving 21 068 unrelated subjects at a centre in northeast Thailand showed that 2637 patients (12.5%) had a β-thalassaemia mutation while only 177 (0.84%) had HbE-β-thalassaemia and all had a thalassaemia intermedia phenotype (88). In a study on 542 persons belonging to the four ethnic groups that inhabit the lower region of northeast Thailand, i.e. the Laos, Khmer, Suay and Yer, the prevalence of HbE disease was more than 50% along with a high incidence of α^+^-thalassaemia (48.2%) in the Khmer group and a high prevalence of Hb CS and Hb Pakse in the Yer and Suay ethnic groups (89). It is estimated that 3600 babies were born with severe α-thalassaemia in Thailand in 2020 though there is geographical variation. Heterogeneity is greatest in the north of the country. For α^0^-thalassaemia, the northernmost provinces of Chiang Rai, Phayao and Nan have predicted allele frequencies of up to 2% while the allele frequencies for the neighbouring provinces of Chiang Mai, Lampang and Phrae and the northeast are up to 4% (90). The predicted allele frequencies are below 1% in the southern zone. Nuinoon et al. in a study of 116 voluntary blood donors from southern Thailand showed an overall frequency of haemoglobinopathies of 12.9%, which were classified as follows: α-thalassaemia (3.4%), heterozygous β-thalassaemia (0.9%) and HbE disease (8.7%) (91).

**Blood transfusion services in Thailand**

The National Blood Programme in Thailand started in 1966 as a mission designated by the government to the Thai Red Cross Society (TRCS). The NBC TRCS was initiated with technical assistance from the French government and began to function in 1969. The TRCS has the responsibility for blood collection and delivery services throughout the 76 provinces of Thailand. Key to these services are the NBC in Bangkok and 12 Regional Blood Centres (RBCs) located in different provinces of the country, all of which offer facilities for donation of blood, screening and distribution. Both the NBC and RBCs distribute blood to hospitals in all provinces, as determined by the government. At present, there are 12 RBCs along with branches in 157 provincial hospitals. For a population of 65 900 000, there are around 1 800 000 whole blood collections annually. Overall, 2% of the adult eligible population donated blood. All donated blood was through voluntary blood donors and there were no private blood
collection centres (92). Nearly 94% of the blood collected is delivered to hospitals and patients while the rest are discarded either due to infections or expiry. In a survey of donor vigilance at the NBC TRCS between August and November 2011, of the 2789 responders, 81% indicated their willingness to donate every 3 months.

It is a challenge to make available and supply quality blood products in the periphery. The reverse occurs in the capital, necessitating the transportation of more than 40% of blood collected by the NBC in Bangkok out to areas of shortage throughout the country. Blood is sent by public transportation: aeroplane, bus and van depending on the available modes of transport and geographical locations of the provinces where the RBCs are located. Modelling studies have looked at establishing low-cost blood collection and distribution centres in areas where blood distribution centres are either lacking or are too far (93).

Fig. 11. Distribution of National Blood Centres in Thailand (92)
**Timor-Leste**

East Timor or Timor-Leste is an island country in South-East Asia. It comprises the eastern half of the island of Timor, the nearby islands of Atauro and Jaco, and Oecusse, an exclave on the northwestern side of the island surrounded by Indonesian West Timor. Australia is the country's southern neighbour, separated by the Timor Sea.

There are several distinct ethnic groups, most of whom are of mixed Austronesian and Melanesian/Papuan descent. The largest Malayo-Polynesian ethnic groups are the Tetum mainly in the north coast and around Dili and the Mambai in the central mountains along with the Tukudede, the Galoli Kemak and the Baikeno. The main tribes of predominantly Papuan origin include the Bunak, Fataluku and the Makasae. In addition, there is a population of mixed East Timorese and Portuguese origin and a small Chinese minority. Administratively, East Timor is divided into 13 municipalities, which in turn are subdivided into 65 administrative posts, 442 villages and 2225 hamlets.

**Burden of thalassaemia in Timor-Leste**

There are sparse data available on the prevalence of thalassaemia in East Timor (94). Chronic malnutrition, tuberculosis and anaemia among women seem to be the major health challenges. A 2007 WHO epidemiological study on Hb disorders in countries of the SEA Region estimated 25 births every year with β-thalassaemia major and HbE-β-thalassaemia (2).

**Blood transfusion services in Timor-Leste**

Blood donor recruitment and retention activities are coordinated nationally and funded by the National Society, which is the Timor-Leste Red Cross. As of 2011, the national blood bank in the capital Dili collected around 1500 units annually, while regional blood banks located in Baucau, Maliana and Oecusse collected and processed a small number of blood units (21). The national blood bank performs blood component separation and encourages clinicians to use blood responsibly. In 2014, blood transfusions were available only at six referral hospitals (Dili, Baucau, Suai, Maliana, Oecusse and Maubisse), with seven districts lacking access to blood products, resulting in a high number of deaths each year. To fast-track the development of blood
transfusion services, the MoH established the country’s first ever National Blood Policy in 2014 and National Blood Programme Strategic Plan 2015–2019 (95). The blood supply is well below the demand; about 2400 units of blood were required (mostly for managing pregnancy-related complications) in 2012, but only 1938 units were collected. In 2014, 63% of blood supplies were from VNRBD with the rest from patients’ relatives. Blood donation drives are organized only in the Dili district and blood is collected only when needed. Following establishment of the national policy and the strategic plan, the Timor-Leste Red Cross Society (CVTL) commenced its blood programme in 2016, engaging volunteer blood donors. It received technical assistance through the participation of a VNRBD workshop in Seoul, Korea (April 2016) and the Australian Red Cross. It receives financial support from the Australian Red Cross and the International Federation of the Red Cross and Red Crescent Societies (IFRC). It is in the process of expanding its level of involvement in blood-related activities.
**Challenges and the way forward**

Though the countries that form the SEA Region have a high prevalence of haemoglobinopathies (2.5–15%), each country is unique with its own prevalence and distribution of these diseases. Even within a single country, the prevalence of haemoglobinopathies varies depending on the ethnicity of the population in the region. While some countries have well documented prevalence data that are publicly available, other countries lack unified data for the entire country and have only fragmented regional data. In many countries, there is lack of available mutational data that would help both in carrier screening and in establishing a programme of prenatal diagnosis in some societies. There are several reasons for this including the absence of a unified action plan for the country for control of haemoglobinopathies such as a national thalassaemia control programme and lack of recognition of haemoglobinopathies as a major health problem especially when malnutrition, vaccine-preventable diseases and diarrhoeal diseases are widely prevalent. In addition, uniform guidelines for management of these disorders are not available. Regular blood transfusions play a major role in the management of a child with thalassaemia/haemoglobinopathy. The national blood services need to play an important role in ensuring that regular blood transfusions are given in a timely manner to the affected child. Some countries have a unified centralized blood collection programme (e.g. Sri Lanka). This may not be possible in certain other countries either because of size (e.g. India) or geographical constraints (e.g. Bhutan, Nepal, Maldives). Inadequate availability of VNRBD, the lack of uniform testing practices for TTI and the absence of cost-free blood availability for these patients are compounding factors. These factors contribute to inadequate and delayed transfusions leading to poor growth and a poor QoL in affected individuals.

The question arises how the MoH in each country along with WHO and other international stakeholders can help correct this situation? The solutions needed for each country may be unique depending upon their national strengths and weaknesses. Nevertheless, there are guiding principles that should govern the implementation of public health interventions for management of haemoglobinopathies. A combination of implementable structural and functional strategies should help in improving the detection and management of patients with
Establishment of national programmes for haemoglobinopathies

1. Recognition of haemoglobinopathies as a major health problem: It is important for each MoH to recognize haemoglobinopathies as a major health problem because recognition at the national level will lead to allocation of funds to help manage this disease.

2. Development of a national registry: It is important for each country to develop a unified national registry for haemoglobinopathies such as cancer registries/databases that are developed. It may be a single registry where data are submitted directly or there could be regional registries that collect the data and feed regularly to the national registry. All patients with haemoglobinopathies should be documented in this registry especially if they need government subsidies for their treatment.

3. Development of a national haemoglobinopathy diagnostic and prevention programme: Every country should develop, implement and mandate participation in its own haemoglobinopathy diagnostic and prevention programmes. This would entail planning studies to understand the patterns of mutation in various regions in the country and then setting up a comprehensive carrier detection programme. Each country should explore the possibility of starting programmes for genetic counselling and prenatal diagnosis if permitted by the society.

4. Development of a national haemoglobinopathy clinical management programme: Every country should develop its own national guidelines on diagnosis and clinical management of haemoglobinopathies in conformance with internationally recognized guidelines. There should be an inbuilt mechanism to do periodical audits of clinical practices. In addition, mechanisms for education and training of relevant health workers should be encouraged at the regional and national levels.

5. Development of specialized patient care centres: Multiple specialized patient care centres need to be established in areas where haemoglobinopathies are prevalent. These centres should take on the primary role of delivering appropriate management practices for children with thalassaemia and other haemoglobinopathies. In that context, the following recommendations may be helpful to national decision-makers and international stakeholders.
haemoglobinopathies, which include the provision of regular blood transfusion, monitoring of iron status, provision of iron-chelation therapy and facilitation of carrier testing. To facilitate patient access, each centre should cover a radius no greater than 50–100 km. If the centre is situated at the periphery, it should be suitably linked to a nearby blood bank/hospital to provide transfusion.

6. Establishing national blood services

The differences in geographical extent, population density and availability of resources make it challenging to implement uniform protocols for blood services. The general principles that may be adopted are:

a. To establish nationalized blood services: This could be either at the country level in smaller nations or at a regional level in larger nations.

b. To have uniform policy standards and quality practices starting from donor screening to testing for all blood banks both in the public and private sectors.

c. To develop national guidelines on optimal transfusion therapy for patients with thalassaemia major.

d. To ensure safety and quality of blood components by implementing sensitive TTI screening tests and provision of leukodepleted blood products to prevent allo-immunization.

e. To raise public awareness about blood donation and to work towards 100% VNRBD and eliminate the role of paid donors.

f. To make available legally cost-free blood for individuals with thalassaemia: This means that a family with a child affected by thalassaemia or any other clinically significant haemoglobinopathy should be able to obtain free blood for their regular transfusions at no cost to the family and without the need for the family to donate. This requires appropriate allocation of funds from the government to blood centres.
International collaboration

The countries of the SEA Region operate under significant constraints of infrastructure and resources, which limit their ability to recognize and respond to the challenges posed by the prevalence of haemoglobinopathies. International collaboration will help promote progress in this area of public health.

1. There is a specific need to promote intercountry collaboration for training and capacity building, and to promote transfer of affordable technologies to developing countries. National MoHs should seek to develop partnerships with countries that are more advanced in diagnosis and management of patients with haemoglobinopathies.

2. International societies and associations exist that provide advocacy and expert advice on identification and care of patients with haemoglobinopathies (e.g. Thalassaemia International Federation, Global Sickle Cell Disease Network). National MoHs should open communication with such organizations for knowledge transfer and technical support that they can provide to programme development for haemoglobinopathies.

3. WHO is uniquely positioned to promote international collaboration and to mobilize technical support for national programme development to address haemoglobinopathies including thalassaemia. MoHs should reach out to WHO with requests for technical support to advance their blood services and to facilitate development, implementation and monitoring of national programmes for haemoglobinopathies. This could include assistance with setting up genetic testing, establishment and running of patient registries, and formulation of clinical guidelines. Through their participation in the World Health Assembly, MoHs could seek a resolution for WHO to declare one year as the “Year of the thalassaemic child” to provide global impetus towards addressing the identified unmet needs.

4. World Thalassaemia Day is observed on 8 May every year. The theme for 2021 World Thalassaemia Day was “Addressing health inequalities across the global thalassaemia community”. The theme for 2020 was “The dawning of a new era for thalassaemia: time for a global effort to make novel therapies accessible and affordable to patients” and in 2019, it was “Universal access to quality thalassaemia health-care services: building bridges with and for patient”. All these reflect the ongoing global efforts to improve the care of individuals with thalassaemia.
### Table 3. Summary of thalassaemia and blood services in countries of the SEA Region

<table>
<thead>
<tr>
<th>Country</th>
<th>No. of thalassaemia cases</th>
<th>Annual births with thalassaemia</th>
<th>No. of red cells available per 100 000 population</th>
<th>Under-5 mortality rates (2019) (per 1000 live births)</th>
<th>Prevalence data available</th>
<th>Mutation data available</th>
<th>National registry</th>
<th>Thalassaemia centres</th>
<th>Centralized blood service</th>
<th>Free blood</th>
<th>Voluntary donors</th>
<th>Transfusion guidelines available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>60–70 000</td>
<td>9100</td>
<td>482</td>
<td>30.75</td>
<td>Yes</td>
<td>Yes</td>
<td>Nil</td>
<td>+/-</td>
<td>No</td>
<td>No</td>
<td>+/-</td>
<td>Yes</td>
</tr>
<tr>
<td>Bhutan</td>
<td>Very low</td>
<td>Low</td>
<td>713</td>
<td>28.49</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>Yes</td>
<td>+/-</td>
<td>Yes</td>
</tr>
<tr>
<td>DPR Korea</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>17.3</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>?</td>
<td>?</td>
<td>Yes</td>
</tr>
<tr>
<td>India</td>
<td>150 000</td>
<td>12 500</td>
<td>769</td>
<td>34.27</td>
<td>Yes</td>
<td>Yes</td>
<td>Nil</td>
<td>+/-</td>
<td>No</td>
<td>Yes</td>
<td>+/-</td>
<td>Yes</td>
</tr>
<tr>
<td>Indonesia</td>
<td>10 530</td>
<td>2500</td>
<td>1118</td>
<td>23.9</td>
<td>Yes</td>
<td>Yes</td>
<td>Nil</td>
<td>+/-</td>
<td>Yes</td>
<td>+/-</td>
<td>+/-</td>
<td>Yes</td>
</tr>
<tr>
<td>Maldives</td>
<td>12 652</td>
<td>28</td>
<td>2759</td>
<td>7.62</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes</td>
<td>+/-</td>
<td>Yes</td>
</tr>
<tr>
<td>Myanmar</td>
<td>4000</td>
<td>2500 (mainly HbE-β)</td>
<td>323</td>
<td>44.7</td>
<td>Yes</td>
<td>Yes</td>
<td>Nil</td>
<td>+/-</td>
<td>Yes</td>
<td>No</td>
<td>+/-</td>
<td>No</td>
</tr>
<tr>
<td>Nepal</td>
<td>300</td>
<td>120 (mainly HbE-β)</td>
<td>790</td>
<td>30.8</td>
<td>Yes</td>
<td>Yes</td>
<td>Nil</td>
<td>+/-</td>
<td>Yes</td>
<td>No</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>2000</td>
<td>45–55</td>
<td>1924</td>
<td>7.11</td>
<td>Yes</td>
<td>Yes</td>
<td>Nil</td>
<td>+/-</td>
<td>Yes</td>
<td>No</td>
<td>+</td>
<td>Yes</td>
</tr>
<tr>
<td>Thailand</td>
<td>98 460</td>
<td>4000 (mainly HbE-β)</td>
<td>3315</td>
<td>9</td>
<td>Yes</td>
<td>Yes</td>
<td>Nil</td>
<td>–</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Timor-Leste</td>
<td>NA</td>
<td>25</td>
<td>256</td>
<td>44.22</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Yes</td>
<td>No</td>
<td>+/-</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Table 4. Key metrics of SEAR countries

<table>
<thead>
<tr>
<th></th>
<th>Bangladesh</th>
<th>Bhutan</th>
<th>DPR Korea</th>
<th>India</th>
<th>Indonesia</th>
<th>Maldives</th>
<th>Myanmar</th>
<th>Nepal</th>
<th>Sri Lanka</th>
<th>Thailand</th>
<th>Timor-Leste</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total population in millions [2020]</strong></td>
<td>164.8</td>
<td>0.77</td>
<td>25.7</td>
<td>1380</td>
<td>273</td>
<td>0.54</td>
<td>54</td>
<td>29.1</td>
<td>21.4</td>
<td>69</td>
<td>1.3</td>
</tr>
<tr>
<td><strong>Population aged 0–14 in 2020 (%)</strong></td>
<td>26.8</td>
<td>24.9</td>
<td>19.8</td>
<td>26.2</td>
<td>25.9</td>
<td>19.6</td>
<td>25.5</td>
<td>28.8</td>
<td>23.7</td>
<td>16.6</td>
<td>36.8</td>
</tr>
<tr>
<td><strong>Estimated births (in 000) (in 2020–2025)</strong></td>
<td>14 111</td>
<td>62</td>
<td>176</td>
<td>119 707</td>
<td>23 569</td>
<td>32</td>
<td>4659</td>
<td>2798</td>
<td>1571</td>
<td>3339</td>
<td>193</td>
</tr>
<tr>
<td><strong>Crude birth rate (per 1000) (2020–2025)</strong></td>
<td>16.7</td>
<td>15.8</td>
<td>13.5</td>
<td>17.59</td>
<td>16.8</td>
<td>12.1</td>
<td>16.8</td>
<td>18.4</td>
<td>14.5</td>
<td>9.5</td>
<td>27.9</td>
</tr>
<tr>
<td><strong>World Bank category [2020]</strong></td>
<td>Lower middle income</td>
<td>Lower middle income</td>
<td>Low income</td>
<td>Lower middle income</td>
<td>Upper middle income</td>
<td>Upper middle income</td>
<td>Lower middle income</td>
<td>Lower middle income</td>
<td>Lower middle income</td>
<td>Lower middle income</td>
<td>Lower middle income</td>
</tr>
<tr>
<td>Estimated number of children with thalassaemia major [β-thalassemia and HbE-β thalassaemia]</td>
<td>60 – 70 000 (11)</td>
<td>No data but very low</td>
<td>No data available</td>
<td>150 000</td>
<td>10 531</td>
<td>861</td>
<td>4000</td>
<td>250–300</td>
<td>2000</td>
<td>98 460</td>
<td>No data</td>
</tr>
<tr>
<td><strong>Annual blood donations (2017)</strong></td>
<td>756 061 (10.12)</td>
<td>6825</td>
<td>130 000 (19)</td>
<td>11 100 000</td>
<td>2 886 233</td>
<td>12652</td>
<td>170 743 (10)</td>
<td>236 799</td>
<td>450 640</td>
<td>2 341 571 (10)</td>
<td>3291</td>
</tr>
<tr>
<td>Red blood cell units available per 100 000 (10)</td>
<td>482</td>
<td>713</td>
<td>17.3</td>
<td>769</td>
<td>1118</td>
<td>2759</td>
<td>323</td>
<td>790</td>
<td>1924</td>
<td>3315</td>
<td>256</td>
</tr>
<tr>
<td>Under 5 mortality rate [deaths per 1000 live births] 2019</td>
<td>30.75</td>
<td>28.49</td>
<td>17.3</td>
<td>34.27</td>
<td>23.9</td>
<td>7.62</td>
<td>44.7</td>
<td>30.8</td>
<td>7.11</td>
<td>9</td>
<td>44.22</td>
</tr>
</tbody>
</table>
References:


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National Guideline for Sickle Cell Disease and Thalassemia Management (Clinical Guideline for doctors, nurses and paramedics).


86. Group IW. Current management of Thalassemia Syndromes in Thailand : past , present and future Why Thailand ?


Disorders of haemoglobin are one of the most common monogenic disorders prevalent across the world. While sickle cell disorders are more prevalent worldwide, the thalassaemic syndromes including α and β-thalassaemia and haemoglobin-E disease are associated with high prevalence rates in the countries of the WHO SEA Region. This desk review was performed using data from thalassaemia societies, the nodal authorities dealing with blood product support, data published in the literature and data from WHO. Member states may find it useful to leverage the information contained herein to develop national action plans to address this problem in all possible ways including access to sufficient and secure blood and blood products, and safe transfusion services, as a vital part of achieving universal health coverage.