Journal of Community Genetics (2020) 11:39–45
https://doi.org/10.1007/s12687-019-00410-1

ORIGINAL ARTICLE

# Haemoglobinopathies in India: estimates of blood requirements and treatment costs for the decade 2017–2026

Sujata Sinha[1,2,3] · Tulika Seth[1,4] · Roshan B. Colah[5] · Alan H. Bittles[6,7]

Received: 10 August 2018 / Revised: 8 January 2019 / Accepted: 29 January 2019 / Published online: 12 February 2019


## Abstract

The Government of India is presently engaged in the implementation of a prevention and control programme for two major forms of haemoglobinopathies, thalassaemia major and sickle cell disease, with guidelines for their prevention and management formulated under the National Health Mission. Based on projections for the population up to the year 2026, the annual blood requirement for treatment will increase to 9.24 million units, together with an 86% increase in budgetary requirements which then would account for over 19% of the current National Health Budget. To avert a public health crisis there is an urgent need to fully implement the prevention programme for haemoglobinopathies.

**Keywords** Thalassaemia · Sickle cell disease · India · Transfusion needs · Health budget · Public health

## Introduction

The current population of India is estimated to be 1.37 billion (PRB 2018), equivalent to 18% of the global total and despite rapid urbanisation some 67% of people in India continue to live in rural areas. In terms of health indicators, the rural population significantly lags their urban counterparts, as reflected by the rural infant mortality rate of 38/1000 live births compared with 23/1000 in towns and cities (RGI 2017). Further, differences within the country, both in terms of the prevalence and causes of diseases across the 29 states, are highlighted in the recent comprehensive report on the burden of disease at the individual state level. The report also confirms a significant overall shift from communicable to non-communicable diseases, with congenital defects listed among the 20 commonest causes of disease listed (India State-Level Disease Burden Initiative Collaborators 2017). The genetic diversity of the Indian population, with large numbers of endogamous ethnic, geographical, religious and social groupings each with extended, unbroken genealogical histories, adds to the complexity of the prevalence and burden of genetic disorders (Basu et al. 2016; Nakatsuka et al. 2017), as observed in regional and caste-specific analyses of mutation data on haemoglobinopathies (Sinha et al. 2009; Black et al. 2010; Trehan et al. 2015).

**Electronic supplementary material** The online version of this article (https://doi.org/10.1007/s12687-019-00410-1) contains supplementary material, which is available to authorized users.

✉ Sujata Sinha
sujatasinha64@gmail.com

Tulika Seth
drtulikaseth@gmail.com

Roshan B. Colah
colahrb@gmail.com

Alan H. Bittles
abittles@ccg.murdoch.edu.au; a.bittles@ecu.edu.au

[1] Genomics and Public Health Foundation, Dehradun, India

[2] PHG Foundation, Cambridge, UK

[3] Dehradun, India

[4] Department of Hematology, All India Institute of Medical Sciences, New Delhi, India

[5] National Institute of Immunohaematology, ICMR, Mumbai, India

[6] Centre for Comparative Genomics, Murdoch University, Perth, Australia

[7] School of Medical and Health Sciences, Edith Cowan University, Perth, Australia

## Background

The prevention of inherited haemoglobinopathies has been internationally recognised as a health priority for several decades (Cousens et al. 2010). Both voluntary programmes to identify carriers in high school students (Mitchell et al. 1996; Amato et al. 2014) and mandatory premarital testing (Bozkurt 2007; Loukopoulos 2011; Alswaidi et al. 2012) have been successfully employed, with the reduction in affected births achieved via an informed decision made by carriers either regarding their choice of partner or early prenatal testing and selective termination of pregnancy (Giordano 2009; Miri et al. 2013).

The Government of India is presently engaged in implementing a prevention and control programme for haemoglobinopathies at the National level. Guidelines for the prevention and management of these disorders have been formulated under the terms of the National Health Mission and published by the Ministry of Health and Family Welfare (2016), with a final policy currently under deliberation. Severe forms of thalassaemia and sickle cell disease (SCD) are the two major clinical disorders constituting the burden of disease due to haemoglobinopathies. The benefits of prevention strategies, based largely on avoidance of the birth of affected babies, may not become fully apparent at the population level until some years after their implementation (Old et al. 2013; Amato et al. 2014). Yet, in the intervening period, many more affected children will be born, and a significantly larger number of community members are likely to share the burden of meeting transfusion requirements through voluntary blood donation. Hence, it is important that along with policymakers, administrators and healthcare providers, the community at large is made aware of the magnitude of the impending disease burden in readily comprehensible terms. In order to highlight the scale of the burden and the urgent need to fully implement the planned prevention programme for these disorders, we have attempted to project the blood and budgetary requirements for a cumulative cohort of haemoglobinopathy patients over the decade from 2017 to 2026.

## Subjects and methods

### Sources of input population data

The projected annual birth cohorts are based on year-wise population projections and five-yearly projections of the crude birth rate (CBR) up to the year 2026 by the Technical Group on Population Projections (RGI 2017), Census data for 2001 and 2011, and Sample Registration Survey Bulletins from 2008 to 2017, each of which is published by the office of the Registrar General and Census Commissioner, India, which also provided actual data on the population and the CBR (RGI 2017). Total population figures for 2011 onwards have been sourced from the Population Reference Bureau website (www.prb.org/Publications/Datasheets.aspx), including the data for 2016 (PRB 2016). A review of the available data shows that up to 2016 the actual population marginally exceeded the projected figures, as did the estimated annual birth cohorts based on actual population data. However, in 2016, a decrease in the annual birth cohort was registered and this trend is expected to extend over the following decade, approximating closely to the projected annual birth cohort figures. Thus, the Registrar General's projections were deemed to be fit for this purpose

The estimated annual birth cohorts, derived as a product of the total population and CBR, are 27.11 million for 2016 and 22.38 million for 2026. The projected average annual birth cohort of 25 million for the decade has been derived by rounding off the figure of 24.75 million, i.e. the simple mean of the two annual birth cohorts (Supplementary Table 1). This annual birth cohort has been used for further estimations and in the projections provided below. As the requirements for management and the ensuing burden differ significantly for β-thalassaemia and sickle cell disease, separate projections have been made for each disorder.

## Projected blood and budgetary requirements

### β-Thalassaemia

During the course of the last six decades, there has been little change in the therapeutic options for people in India affected with a severe form of thalassaemia (thalassaemia major), although there has been a substantial improvement in terms of survival outcomes (Sharma et al. 2017). Management by regular transfusion of packed red blood cells and iron chelation to eliminate the excess iron remains the standard mode of therapy that should be accessible to every affected child. While a large majority of such cases need to continue this therapy for life, a very small number, fortunate enough to have a matching donor, can hope to be cured by haematopoietic stem cell transplantation (HSCT). It is, however, pertinent to note that while a successful HSCT does help to improve the life experience of a treated individual, it does not spare them from having to confront marital and reproductive choices on attaining adulthood. Only a gene-based therapy could change these prospects.

#### Estimation of the number of people affected with thalassaemia requiring treatment

On the basis of carrier prevalence rates, the WHO Guidelines on Haemoglobin Disorders provides a straightforward method to estimate the number of affected births (Modell 1989). Thus, for the average carrier prevalence rate of 4% in India (Colah and Gorakshakar 2014; National Health Mission 2016), the expected annual number of affected births can be estimated

as 0.5/1000 live births. Over the last decade, with increased accessibility to blood transfusions, the number of thalassaemia major cases in India surviving the first decade of life has steadily increased, with a conservative estimate in 2012 of 100,000 children living with thalassaemia (Sharma et al. 2017). However, according to a personal communication from the Federation of Indian Thalassemics (FIT), there are currently some 150,000 people living with a severe form of thalassaemia. Hence, for an average annual birth cohort of 25 million, and with a 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. By 2026, the cumulative number of people with thalassaemia requiring treatment will therefore be approximately 275,000 persons (Table 1), although future changes in reproductive behaviour may influence the actual number of affected individuals.

### Projected blood requirement for thalassaemia patients

Voluntary blood donation has improved considerably in India over the last three decades and all blood banks are required to provide blood to thalassaemia patients free of processing costs. Nevertheless, despite an increase in the number of thalassaemia patients being enrolled for treatment, adequate treatment is accessible to only a limited proportion of cases. To estimate the actual blood requirement to ensure adequate treatment, we solicited blood requirement records of 42 adequately managed patients from four centres during 2016–2017 (Supplementary Table 2). The mean blood requirement for these patients with a mean age of 20.0 years was 29.5 + 11.75 units. This compares with a recent comprehensive study in Hong Kong that showed an average requirement of 38.7 units at a mean age of 23 years and a mean weight of 46.5 kg (Lau et al. 2013).

To estimate the blood requirements for the treatment of thalassaemia major in India in 2026, with assumed improvements in the survival outcomes of patients from poor and rural areas, the mean age of thalassaemia patients has been taken as 20 years with an annual blood requirement of 30 units/patient. Accordingly, if all of the 150,000 patients with thalassaemia major currently estimated by FIT were receiving adequate transfusions, the national requirement would be for 4.5 million units of packed red cells, and this requirement is projected to increase to 8.25 million units for 275,000 patients by 2026 (Table 1).

### Projected annual costs for treatment by transfusion and chelation

With improvements in blood banking services and more options for iron chelation, this modality of treatment can be made available to all patients through district level care centres. In 2008, the cost of transfusing and chelating a child of 30-kg body weight was estimated to be INR200,000/year (USD2985) (Chandy 2008). As the child matures, a multidisciplinary approach is required to ensure their quality of life, which further increases the cost of management. Thus, if the entire present cohort of 150,000 thalassaemia patients was receiving adequate care, the annual cost would be INR30,000 million (USD448 million), and with an added cohort of 125,000 cases over a decade by 2026, the annual cost of care is predicted to escalate to INR55,000 million (USD820 million) (Table 2).

### Estimated annual cost of treatment by haematopoietic stem cell transplant

In the National Health Mission guidelines (NHM 2016), the cost of a HSCT has been estimated at INR1.4 million (USD21,000) per patient. Even under ideal circumstances, for an average annual cohort of 12,500 patients, only some 10% of patients would be eligible for HSCT, given the limited number of available matched donors and the success rate of the procedure. For 10% of the existing 150,000 patients, the cost would be INR21,000 million (USD313 million) rising to INR38,500 million (USD575 million) by 2026 (Table 2). Even among patients eligible for a HSCT, only those individuals who are adequately managed by transfusion and chelation have a good transplant success rate. As many of the existing patients would therefore no longer be eligible for HSCT, a more realistic cost estimate for transplantation in the year 2016 would be for 10% of the annual affected cohort of

**Table 1** Estimated blood requirements for patients with β-thalassaemia major and sickle cell disease (SS genotype), assuming an average annual birth cohort of 25 million from 2017 to 2026

| Projected annual blood requirement of haemoglobinopathy patients for an estimated average of 12,500 TM and 37,500 SCD affected births annually | | Year 2016 | Year 2026 |
|---|---|---|---|
| I a | Number of patients with TM | 150,000 | 275,000 |
| I b | Blood units required (in millions) | 4.50 | 8.25 |
| II a | *Number of patients with SCD (SS genotype) | 120,000 | 495,000 |
| II b | Blood units required (in millions) | 0.24 | 0.99 |
| Total blood unit requirement (in millions) (I b + II b) | | 4.74 | 9.24 |

*TM* β-thalassaemia major, *SCD* sickle cell disease

*Number of patients from Supplementary Table 3

**Table 2** Estimated annual treatment costs for patients with β-thalassaemia major and sickle cell disease (SS genotype) with an estimated average of 12,500 TM and 37,500 SCD births annually from 2016 to 2026

| Estimated number of patients and projected costs of treatment | | | | | |
|---|---|---|---|---|---|
| | | Year 2016 | | Year 2026 | |
| I | Number of patients requiring treatment | | | | |
| a | TM patients | 150,000 | | 275,000 | |
| b | SCD patients (SS genotype) | 120,000 | | 495,000 | |
| II | Annual cost of treatment | INR (in million) | **USD (in million) | INR (in million) | **USD (in million) |
| a | Annual cost of care | 30,000 | 448 | 55,000 | 820 |
| b | Annual cost of HSCT of 10% of patients | *21,000 | *310 | *38,500 | *575 |
| c | Annual cost of treatment of SCD patients | 360 | 5.4 | 1485 | 22.2 |
| | Total annual cost of treatment (a + b + c) | 51,360 | 766 | 94,985 | 1418 |

*TM* β-thalassaemia major, *SCD* sickle cell disease

*A more realistic estimate would be INR1,750 million/USD26 million for 1250 patients (10% of annual cohort of 12,500) for 2016 and INR17,500 millions/USD261million for 12,500 new eligible patients for 2026

**Conversion rate, 1USD = 67 INR

12,500 patients, i.e. INR1,750 million (USD26 million), increasing to INR17,500 million (USD261 million) for a cumulative 12,500 patients added over 10 years by 2026, assuming that all or most patients henceforth would be maintained adequately by transfusion and chelation (Table 2).

## Sickle cell disease

In India, although many more people are affected by SCD than thalassaemia major, the causative mutation mainly is linked to the Arab-Indian haplotype, which is considered to be clinically much less severe than the African haplotypes. Severe haplotypes have been reported in some Indian communities, more commonly in non-tribal populations, but to date, there have been limited data available from newborn screening programmes to provide information on the natural history of the disease, especially early neonatal and infant mortality (Colah et al. 2018). Those patients with SCD who survive childhood usually require supportive treatment in the form of penicillin prophylaxis and hospitalisation for blood transfusion for anaemia and sickle cell crises.

### Estimation of the number of people affected with SCD

Given the highly variable prevalence of HbS trait across the country (Hockham et al. 2018), national estimates of people with SCD are at best approximate. Published data suggest that some 50% of all homozygotes for HbS are born in the states of Karnataka, Tamil Nadu and Maharashtra (Piel et al. 2013; Colah et al. 2014) where consanguineous marriages are widely favoured (Bittles 2012) and with high rates in the western, eastern and central states of Gujarat, Odisha, Madhya Pradesh and Chhattisgarh (NHM 2016). In 2016, an estimated 120,000 people in India were living with SCD and an equal number were born with the HbS-β-thalassaemia genotype that contributed to the SCD phenotype (Rees and Brouse 2016).

In the absence of accurate national data on the overall numbers affected with SCD, we have projected requirements only for the SS genotype. According to the global epidemiology report on the number of neonates in India with AS and SS in 2010 (Piel et al. 2013), neonates with the SS genotype would account for 1.5/1000 live births. Hence, in an annual birth cohort of 25.0 million, there would be 37,500 SS neonates, resulting in a total of 375,000 neonates with SS genotype over the decade 2017–2026 (Supplementary Table 3).

Based on the relatively small mortality numbers in the few available newborn screening and follow-up studies reviewed by Colah et al. (2014), a survival rate of 100% for first 10 years of life has been assumed in estimating the number of people with SCD in 2026. The exclusion of people with the HbS-β-thalassaemia genotype would compensate for mortality occurring within the first decade of life in the HbSS genotype cohort over the decade. On this basis, even by conservative estimates, the total number of people living with SCD by 2026 would be 495,000, with 375,000 added over the course of the decade to the existing 120,000 persons with the disorder in 2017 (Supplementary Table 3).

### Projected annual blood requirement and cost of treatment for SCD

Following the review by Colah et al. (2014), the average annual requirement of blood for a SCD patient in India is assumed to be 2 units. On this basis, the current annual blood requirement of 0.24 million units would increase to 0.99 million units per year, thus raising the total national blood

transfusion requirement for haemoglobinopathies to 9.24 million units by 2026.

In the National Guidelines for Hemoglobinopathies (NHM 2016), the annual medical care costs for SCD including penicillin prophylaxis have been estimated at INR3,000/year/child (USD45), but this figure does not take into account expenditure incurred on hospitalisation for transfusions and the management of SCD crises. With the addition of a birth cohort of 37,500 affected persons yearly over a decade to the existing 120,000 SCD patients, the annual cost of care would expand to INR1,485 million (USD22.2 million) (Table 2).

## Limitations of the projected estimates

As noted in the Introduction, the compilation of credible prevalence estimates for disorders such as β-thalassaemia and SCD in India is problematic, given the overall population size and the uniquely marked levels of genetic diversity within the national population due to sub-community endogamy (Bittles 2002; Basu et al. 2016; Nakatsuka et al. 2017). For that reason, the projected estimates for both disorders are intentionally conservative, e.g. with the large number of compound heterozygotes of β-thalassaemia and the abnormal haemoglobins E and S giving rise to thalassaemia major and SCD excluded.

However, with the relative paucity of the estimated numbers even for homozygotes with β-thalassaemia mutations and for the HbSS genotype, due caution is merited in assessing the projections on the scale of the disease burden, especially as the incidence of haemoglobinopathies differs significantly across ethnic, religious, geographical and social minorities, and given the tacit but mistaken assumption that all affected persons will have access to effective treatment.

## Assessment of resources for requirements

### Availability of blood

To meet the all-cause requirement for blood transfusions in India, over the last decade there has been an attempt to improve blood banking services and increase the availability of safe blood. According to the Blood Transfusion Services Report of the Ministry of Health and Family Welfare and based on the WHO donor norm of 1% of the population (http://naco.gov.in/blood-transfusion-services) (NACO 2016), in 2015–2016, a total of 10.9 million units of blood were donated nationally, resulting in a shortfall of 1.15 million units to meet the projected total blood requirement. In 2016–2017, the volume of blood collection increased to 11.09 million units (NACO 2017). Significantly, if all children affected with haemoglobinopathies were being adequately treated, 43% of this blood would be used in meeting their transfusion requirements (Table 3).

Thus, even if the Health and Family Welfare authorities succeed in their objective to recruit 1% of the national population as blood donors, by 2026, 66% of the envisaged 14 million units collected would be required for the treatment of haemoglobinopathy patients alone. Clearly, when only a small proportion of thalassaemia patients are being adequately treated by transfusion, the actual and burgeoning needs of haemoglobinopathy patients have been very substantially underestimated.

### Budgetary allocations for health

In 2016–2017, the national budgetary allocation for health in India was INR398,880 million (USD5,950 million), which was increased to INR488,800 million (USD7,300 million) for 2017–2018. According to current estimates for the management of haemoglobinopathies, if all haemoglobinopathy patients were provided with adequate treatment, the cost would account for some 10% of the national health budget. However, as shown in the projected estimates (Table 2), in the absence of effective prevention, there would in fact be an 85% increase in the budget requirements for the treatment of haemoglobinopathy patients to INR94,985 million (USD1,420 million), thus accounting for 19.4% of the current health budget.

In summary, all pregnant women, estimated to number 11.61 million in the year 2021, can be screened at an annual cost of approximately INR1,200 million (USD18 million). By 2026, if preventive strategies are fully implemented, with voluntary premarital adolescent screening in schools, antenatal

**Table 3** Annual blood requirement (million units) for treatment of all affected persons with β-thalassaemia major and sickle cell disease

| Year | Blood required (million units*) | Blood donated (million units*) | Blood requirement as percentage of donated blood units (%) |
|---|---|---|---|
| 2016 | 4.74 | 9.24 | 42.7 |
| 2026 | 11.09 | 14.0 | 66.0 |

*Both requirement and availability of blood are reported in number of units, with one unit donated per session. A unit of blood may contain 350 or 450 ml of blood, dependent on whether the donation is collected at a camp site or in hospital

**Table 4** Estimated annual cost of screening for carrier status in adolescent students and pregnant women and of prenatal diagnosis in pregnancies of carrier couples (Census 2011; RGI 2006; MHRD 2016; NHM 2016)

| | | Year | | |
|---|---|---|---|---|
| | | 2016 | 2021 | 2026 |
| Estimated annual cohorts | | | | |
| Students of class IX available for carrier screening (in millions) | | 19.1 | 18.5 | 18.5 |
| Pregnant women available for carrier screening (in millions) | | – | 11.61 | 2.2 |
| Pregnancies for prenatal diagnosis (*n*) | | – | **50,000 | **50,000 |
| Estimated annual costs | | | | |
| Screening of students at INR96/student | INR (millions) | 1833 | 1776 | 1776 |
| | USD (millions) | 28.65 | 27.75 | 27.75 |
| Antenatal screening at INR104/woman | INR (millions) | – | 1207.4 | 228.8 |
| | USD (millions) | – | 18.86 | 3.57 |
| Prenatal diagnosis for @INR5000/pregnancy | INR (millions) | – | 250.0 | 250.0 |
| | USD (millions) | – | 3.90 | 3.90 |
| Estimated annual cost of screening and PND (excluding HR costs) | INR (millions) | 1833 | 3233.4 | 2254.8 |
| | USD (millions) | 28.65 | 50.51 | 35.22 |

*Due to the limited current availability of prenatal diagnosis, no estimates have been presented for 2016

**The number of pregnancies in which prenatal diagnosis will be required will be approximately four times the annual cohort of estimated affected births in accordance with the 25% risk in each pregnancy

screening and prenatal diagnosis, the cost would be approximately INR2250 million (USD35 million) (Table 4), i.e. < 4% of the estimated cost for one year of treatment.

## Conclusion

Given the sharply increasing demand within health budgets imposed by non-communicable diseases, including rare genetic disorders, where possible, it is imperative for the Government of India to devise cost-effective preventive strategies to reduce the burden of disease. From the above projections and the assessment of available resources, it is evident that effective implementation of well-designed and efficiently implemented prevention strategies is urgently required. In India, screening for the detection of carriers in an annual cohort of adolescents in schools and/or of all pregnant women is the most feasible prevention strategy available for reducing the birth of children affected with thalassaemia. Besides improving genetic literacy in the population, an important side benefit of such screening programmes would be the capacity to derive accurate, representative data on the incidence of the major haemoglobinopathies at state and community levels which, in turn, would facilitate the compilation of comprehensive disease registries (Sinha et al. 2011).

The experience with thalassaemia in other countries has repeatedly shown that a significant reduction in affected births is fully achieved after some 20 years of implementation (Old et al. 2013; Amato et al. 2014). Even by conservative estimates, by spending 6–7% of the annual cost of treatment on prevention and control strategies, the birth of children with thalassaemia could be reduced by 50–70%, and the simultaneous implementation of newborn screening for HbSS could significantly reduce the cost of care for SCD births.

**Authors' contributions** SS prepared the first draft with calculation of projected estimates, data sources and other literature references. TS checked all the initial data, helped in preparing first draft and contributed in revising the manuscript. RC provided inputs, rigorously cross-checked all source data and estimates and contributed in editing the text and tables. AHB majorly contributed in providing context to the expressed opinion and in revising the manuscript to its final format.

## Compliance with ethical standards

**Ethical clearance** Permission for the use of anonymised data on blood requirements of thalassaemia patients was provided by each of the four collaborating centres.

**Conflict of interest** In 2017, AHB acted as consultant on consanguinity for Merck, Sharp and Dohme. SS, TS and RC have nothing to disclose.

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

## References

Alswaidi FM, Memish ZA, O'Brian SJ, Al-Hamdan NA, Al-Enzy FM, Alhayani OA, Al-Wadey AM (2012) At-risk marriages after compulsory premarital testing and counseling for β-thalassemia and sickle cell disease in Saudi Arabia. J Gen Counsel 21:243–255

Amato A, Cappabianca MP, Lerone M, Colosimo A, Grisanti P, Ponzini D, Di Biagio P, Perri M, Gianni D, Rinaldi S, Piscitelli R (2014) Carrier screening for inherited haemoglobin disorders among secondary school students and young adults in Latium, Italy. J Commun Genet 5:265–268

Basu A, Sarkar-Roy N, Majumder PP (2016) Genomic reconstruction of the history of extant populations of India reveals five distinct ancestral components and a complex structure. Proc Natl Acad Sci U S A 113:1594–1599

Bittles AH (2002) Endogamy, consanguinity and community genetics. J Genet 81:44–50

Bittles AH (2012) Consanguinity in context. Cambridge University Press, Cambridge

Black ML, Sinha S, Agarwal S, Colah R, Das R, Bellgard M, Bittles AH (2010) A descriptive profile of β-thalassaemia mutations in India, Pakistan and Sri Lanka. J Commun Genet 1:149–157

Bozkurt G (2007) Results from the north Cyprus thalassemia prevention program. Hemoglobin 31:257–264

Census of India (2011) Figures at a glance. http://censusindia.gov.in/2011-prov-results/indiaatglance.html

Chandy M (2008) Developing a national programme for India. In: Ghosh K, Colah R (eds) Control and Management of Thalassemia and other Hemoglobinopathies in the Indian Subcontinent_ Synoptic Views. National Institute of Immunohaematology, Mumbai

Colah RB, Gorakshakar A (2014) Control of thalassemia in India. Thal Reports 4(s1):1955. https://doi.org/10.4081/thal.2014.s1.1955

Colah R, Mukherjee M, Ghosh K (2014) Sickle cell disease in India. Curr Opin Hematol 21:215–223

Colah RB, Mehta P, Mukherjee MB (2018) Newborn screening for sickle cell disease: Indian experience. Int J Neonatal Screen 4:31. https://doi.org/10.3390/ijns4040031

Cousens NE, Gaff CL, Metcalfe SA, Delatycki MB (2010) Carrier screening for Beta-thalassaemia: a review of international practice. Eur J Hum Genet 18:1077–1083

Educational Statistics at a Glance (2016) Department of School Education and Literacy, Ministry of Human Resource Development. Government of India, New Delhi

Giordano PC (2009) Prospective and retrospective primary prevention of hemoglobinopathies in multiethnic societies. Clin Biochem 42:1757–1766. https://doi.org/10.1016/j.clinbiochem.2009.06.027

Hockham C, Bhatt S, Colah R, Mukherjee MB, Penman BS, Gupta S, Piel F (2018) The spatial epidemiology of sickle-cell anaemia in India. Sci Rep 8:17685. https://doi.org/10.1038/s41598-018-36077-w

India State-Level Disease Burden Initiative Collaborators (2017) Nations within a nation: variations in epidemiological transition across the states of India, 1990–2026 in the Global Burden of Disease Study. Lancet 390:2437–2460

Lau EHY, He X-Q, Lee C-K, Wu JT (2013) Predicting future blood demand from thalassemia major patients in Hong Kong. PLoS One 8(12):e81846. https://doi.org/10.1371/journal.pone.0081846

Loukopoulos D (2011) Haemoglobinopathies in Greece: prevention programme over the past 35 years. Ind J Med Res 134:572–576

Miri M, Tabrizi Namini M, Hadipour Dehshal M, Sadeghian Varnosfaderani F, Ahmadvand A, Yousefi Darestani S, Manshadi M (2013) Thalassemia in Iran in last twenty years: the carrier rates and the births trend. Iran J Blood Cancer 6:11–18

Mitchell JJ, Capua A, Clow C, Scriver CR (1996) Twenty-year outcome analysis of genetic screening programs for Tay-Sachs and β-thalassemia disease carriers in high schools. Am J Hum Genet 59:793–798

Modell B (ed) (1989) Guidelines for control of haemoglobin disorders. WHO Working Group on Haemoglobinopathies. WHO_HDP_HB_GL_94.1.pdf

NACO (2016) Blood Transfusion Services (BTS) data for FY 2015–2016. National AIDS Control Organization, Government of India http://naco.gov.in/sites/default/files/BTS%20Data%202015-16.pdf

NACO (2017) Blood Transfusion Services (BTS) data for FY 2016–2017. National AIDS Control Organization, Government of India http://naco.gov.in/blood-transfusion-services-publications

Nakatsuka N, Moorjani P, Rai N, Sarkar B, Tandon A, Patterson N, Bhavani GS, Girisha KM, Mustak MS, Srinivasan S, Kaushik A, Vahab SA, Jagadeesh SM, Satyamoorthy K, Singh L, Reich D, Thangaraj K (2017) The promise of discovering population-specific disease-associated genes in South Asia. Nat Genet 49:1403–1407

National Health Mission Guidelines on Hemoglobinopathies in India (2016) Prevention and Control of Hemoglobinopathies in India. National Health Mission, Ministry of Health & Family Welfare, Government of India http://nhm.gov.in/images/pdf/programmes/RBSK/Resource_Documents/Guidelines_on_Hemoglobinopathies_in%20India.pdf

Old J, Angastiniotis M, Eleftheriou A, Hartveld C, Petrou M, Traeger-Synodinos J (2013) Prevention of thalassaemias and other haemoglobin disorders Volume 1: principles, 2nd edn. Thalassaemia International Federation, Cyprus

Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Dewi M, Temperley WH, Williams TN, Weatherall DJ, Hay SI (2013) Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates. Lancet 381:142–151

Population Projections for India and States 2001-2026 (2006) Report of the technical group on population projections constituted by the National Commission on Population, Registrar General & Census Commissioner, India. Office of the Registrar General & Census Commissioner, New Delhi

Rees DC, Brouse VAM (2016) Sickle cell disease: status with particular reference to India (Editorial). Ind J Med Res 143:675–677

Registrar General of India (2017) Sample Registration System, Vital Statistics Division, Office of the Registrar General of India, New Delhi. SRS Bulletin 51(1):1 http://censusindia.gov.in/vital_statistics/SRS_Bulletins/Bulletins.html

Sharma S, Seth B, Jawade P, Ingale M, Setia MS (2017) Quality of life in children with thalassemia and their caregivers in India. Ind J Pediatr 84:188–194

Sinha S, Black ML, Agarwal S, Colah R, Das R, Ryan K, Bellgard M, Bittles AH (2009) Profiling β-thalassaemia mutations in India at state and regional levels: implications for genetic education, screening and counseling programmes. HUGO J 3:51–62

Sinha S, Black ML, Agarwal S, Das R, Bittles AH, Bellgard M (2011) ThalInd, a β-thalassaemia and hemoglobinopathies database for India: defining a model country-specific and disease-centric bioinformatics resource. Hum Mutat 32:887–893

SRS Bulletins, Sample Registration System, Registrar General, India. Published by office of the Registrar General, India, Ministry of Home Affairs, Government of India. http://censusindia.gov.in/vital_statistics/SRS_Bulletins/Bulletins.html

Trehan A, Sharma N, Das R, Bansl D, Marwaha RK (2015) Clinico-investigational and demographic profile of children with thalassemia major. Ind J Hematol Blood Transfus 31:121–126

World Population Data Sheet (2018) Population Reference Bureau, Washington DC. http://www.prb.org/wp-content/uploads/2018/08/2018_WPDS.pdf

World Population Datasheet (2016) Population Reference Bureau, Washington DC. http://www.prb.org/pdf16/prb- wpds2016-web-2016.pdf