REVIEW ARTICLE

Assessing the Need for a Population-based Screening for Thalassemia in Pregnancy: Systematic Analysis of Evidence from Uttar Pradesh

Ayesha Ahmad[1], Fareha Khatoon[2], Amrita Singh[3], Shweta Kumari[4]

Abstract

Introduction: Thalassemia and other structural variants of hemoglobin are among the commonest hereditary disorders in India. They pose a great burden on the existing health resources with an estimated 300,000–400,000 babies born every year with a major hemoglobin disorder. The best strategy for reducing the burden of thalassemia is prenatal screening. However, there are no existing universal guidelines for thalassemia screening in pregnancy. This study was planned to evaluate the extent of published work on the subject in the state of Uttar Pradesh (UP), in order to suggest recommendations for the same. The aim of this study is to examine the data on prevalence of thalassemia in the state of UP, find out the cost burden of treating patients with thalassemia major, and to assess data on knowledge, attitude, and practices (KAP) among healthcare professionals dealing with antenatal women with regard to thalassemia screening.

Methodology: The study was planned as a systematic review with literature search done using relevant MeSH terms as well as Free-text terms to run a search. The papers were assessed for relevant questions on prevalence, cost analysis, and KAP, from the state of UP.

Results: Studies were limited in the designated research period with varying prevalence. Much of the data has the bias of being hospital based which precludes to the assessment of actual prevalence in the state. There are no studies on knowledge, attitude, and practices of healthcare professionals involved in antenatal care with respect to thalassemia. Only one study has looked into the detailed aspects of socio-economic burden imposed on the family due to a member affected by thalassemia major.

Conclusion: There is significant economic impact caused by having a thalassemia sufferer in the family. However, the approximate financial burden is difficult to estimate because we have lack of sufficient studies on the subject. There are no studies on knowledge, attitudes, and practices of healthcare practitioners dealing with antenatal women with regard to thalassemia screening and management.

Keywords: Down syndrome, Genetic disorders, Neural tube defects, Thalassemia, Uttar Pradesh prevalence.

Journal of South Asian Federation of Obstetrics and Gynaecology (2022): 10.5005/jp-journals-10006-2018

Introduction

Thalassemia and other structural variants of hemoglobin are among the commonest hereditary disorders worldwide, with data estimates of 7% pregnant women being gene carriers of a hereditary hemoglobin disorder. However, there are wide variations in incidence and suspected under-reporting from resource limited countries, with paucity of advanced laboratory tests and financial constraints.[1] The past few decades have seen India witnessing a gradual demographic shift from communicable to noncommunicable diseases as a result of which genetic disorders have attained exponential importance. Conservative estimates of Indian data show a carrier frequency of beta-thalassemia as 3–17%, and hemoglobin HbE and HbS up to 40% in some regions.[2] With every one in eight thalassemia affected living in India, we account for 10% of the world's total incidence of thalassemia.[3] Viewed in terms of absolute numbers, given the high birth rate of India, the average accepted prevalence of 3–4% translates to 35–45 million carriers, with 300,000–400,000 babies being born every year with a major hemoglobin disorder.[4] This becomes highly significant in overburdening an evolving and already stretched healthcare delivery system.[5]

The prevalence estimates show a wide variation in thalassemia and other hemoglobinopathies, with frequencies as high as 6% for beta-thalassemia in some regions to 35% for HbS and 50% for HbE in some populations.[6–8] This may be contributed in part by the immense heterogeneity of population in this vast country, diverse ethnic groups with different degrees of prevalence, presence of many pockets of consanguineous population, and limited resources for population screening and micromapping. The best strategy for reducing the burden of thalassemia is prenatal testing.

Despite the observed fluctuations in prevalence statistics of thalassemia, we do have sufficient published data to appreciate the need to initiate population based screening for them. However, despite recommendations for screening by standard obstetrical and fetal medicine societies, we have no existing national or regional guidelines for prenatal screening of thalassemia.

[1–4]Department of Obstetrics and Gynecology, Era's Lucknow Medical College and Hospital, Lucknow, Uttar Pradesh, India

Corresponding Author: Shweta Kumari, Department of Obstetrics and Gynecology, Era's Lucknow Medical College and Hospital, Lucknow, Uttar Pradesh, India, Phone: +91 9430604966, e-mail: dr053shweta@gmail.com

How to cite this article: Ahmad A, Khatoon F, Singh A, *et al.* Assessing the Need for a Population-based Screening for Thalassemia in Pregnancy: Systematic Analysis of Evidence from Uttar Pradesh. J South Asian Feder Obst Gynae 2022;14(2):218–222.

Source of support: Nil

Conflict of interest: None

The objective of this study is to analyze the extent of published work on thalassemia in order to suggest recommendations for prenatal screening in the state of UP.

Aim of the Study

To examine the data on prevalence of thalassemia in the state of UP, find out the cost burden of treating patients with thalassemia major, and to assess data on knowledge, attitudes, and practices (KAP) among healthcare professionals dealing with antenatal women with regard to thalassemia screening.

Methodology

Literature search was conducted using the relevant MeSH terms as well as Free-text terms. Databases searched were PubMed, Scopus, Medline, Google Scholar, SCI and SCI expanded, and ICI. All articles in English language and pertaining to human studies were scanned, from 2010 to 2020. The papers were assessed for relevant questions on prevalence, cost analysis, and KAP, from the state of UP. The data were entered in the Data Extraction Form and results were extrapolated to draw conclusions.

Results

A total of 30 papers were scanned, out of which 26 were original studies, 1 was editorial communication, and 1 was review. There was no systematic review or meta-analysis. The inclusion criteria of our systematic review did not match in 22 studies, so they were excluded. Seven studies were finally included in the analysis (Table 1).

Of these, only one study dealt with the economic impact on the family of a thalassemia sufferer.[9] Seven studies dealt with the prevalence of thalassemia.[10–16] There was no study assessing KAP of healthcare practitioners dealing with antenatal women with regards to thalassemia. Meena et al.,[10] 2.8% BTT, Nagar et al.,[11] 3.41% BTT and 3.41% other hemoglobinopathies; Singh et al.,[15] 42% BTT, 2% beta thalassemia major, 3% hereditary persistence of fetal hemoglobin, Verma et al.[14] 5.04% BTT, 0.43% beta thalassemia major, 6.54% other hemoglobinopathies (Table 2).

Problem Burden

The burden of hemoglobinopathies is a challenge not just for the patient but the entire family, at physical, cognitive, emotional, and economic levels. Indian data show the prevalence ranging from 3.4% (Nagar et al.) to 19.5% (Verma et al.), with beta-thalassemia being the commonest. This study was done to consolidate the existing literature about epidemiological aspects of thalassemia in UP, which is the most populous state of India. There are significant gaps in knowledge from UP,[11] which contributes to 16.26% (23.15 crore) of Indian population.[17] The authors had restricted the study period to 10 years, from 2010 to 2020, to ensure that only recent literature is considered for the purpose of evaluation. We found that population-based studies are very limited with most of the studies being hospital-based or largely limited to certain population groups. Majority of data is from the more developed cities, with scanty primary data from aspirational districts. Therefore, there remains an inherent bias in the available literature and it does not reflect the exact status of thalassemia prevalence in general population.

With regard to data from the state of Uttar Pradesh (UP), Verma et al.[16] found the prevalence of hereditary hemoglobin disorders to be 19.5% in Lucknow District. Other regions with a high prevalence were Faizabad (6.99), Basti and Barabanki (5.59), Gonda and Ambedkar Nagar (4.89), Maharaj Ganj (4.79), Bahraich (3.49), etc. Gupta et al. collected data from Eastern UP found beta-thalassemia as the commonest hemoglobinopathy, not restricted to any specific community or caste in the region.[18] They found the relative prevalence of hemoglobinopathies as follows: homozygous

Table 1: Analysis of studies studying prevalence of thalassemia in UP

Authors	*Study*	*Type of study*	*No. of subjects*	*Study period*	*Outcome measured*	*Outcome in detail*
Kumar et al.[13]	Mediterr J Hematol Infect Dis 2013;5	Prospective, Observational	300	3 years (2007–2010)	Prevalence	Relative prevalence of thalassemia mutations calculated
Verma et al.[14]	Biomed Res 2013;24(3): 377–382	Prospective, Observational	933	3 years (2009–2012)	Prevalence	Distribution pattern of hemoglobinopathies, ABO, and Rh blood groups in Northern UP
Meena et al.[10]	J Clin Diagn Res 2013;7(7):1394–1396	Prospective, Observational	1,000	2 years (2008–2010)	Prevalence	β-thalassemia trait among blood donors in eastern Uttar Pradesh, India
Nagar et al.[11]	J Commun Genet 2014	Prospective, Observational	1,592	Not mentioned	Prevalence	Prevalence of hemoglobinopathies in eastern Indian states
Kumar et al.[12]	Adv Hematol 2015	Observational	516	Not mentioned	Prevalence	Profiling β-thalassemia mutations in consanguinity and nonconsanguinity
Singh et al.[15]	Natl J Lab Med 2016;5(3):PO70–PO75	Observational	100	1.5 years (2014–2015)	Prevalence	Diagnosis of hemoglobinopathies and thalassemia by use of HPLC
Verma et al.[16]	Asian J Med Sci	Cross sectional	1,180	2 years (2011–2013)	Prevalence	Prevalence of hemoglobinopathies in different regions and castes of UP

Table 2: Risk of bias calculation

Authors	*Eligibility criteria defined*	*Exclusion criteria defined*	*No. of centers*	*Bias in patient recruitment*	*Is sample representative*	*Statistical methods used*	*Sampling method*
Kumar et al.[13]	No	No	Single	Yes, Hospital-based study	No	No	Random sampling
Verma et al.[14]	Yes	No	Single	Yes, Hospital-based study	No	No	Random sampling
Meena et al.[10]	Yes	No	Single	Yes, Hospital-based study	No	Fisher's exact test	Random sampling
Nagar et al.[11]	Yes	Yes	Nine	No	Yes	Median (IQR)	Random sampling
Kumar et al.[12]	No	No	Single	Yes, Hospital-based study	No	No	Random sampling
Singh et al.[15]	Yes	Yes	Single	Yes, Hospital-based study	No	No	Random sampling
Verma et al.[16]	Yes	Yes	Single	Yes, Hospital-based study	Yes	*p* value	Random sampling

beta-thalassemia (78.7%), e-beta-thalassemia (11.7%), sickle cell beta-thalassemia (3.3%), homozygous sickle cell disease (3.2%), beta-thalassemia trait (BTT) (2.1%), and hemoglobin-H disease (1.1%). It is to be noted that with such a high birth incidence of Thalassemia, we have only one designated Thalassemia Treatment Centre in UP, which caters to a projected population of 23.15 crore.[17–19] Although we have some schools in UP for specially abled children, dedicated educational institutions for children affected with genetic disorders are still not the norm.

Known risk factors for hemoglobinopathy include high risk ethnicity, history of chronic anemia or stillbirth, a family history of hemoglobinopathy and consanguinity. In the aftermath of globalization, with wide heterogeneity in population, universal screening is recommended instead of selective screening based on race and ethnicity. However, while this can be practiced in developed countries, the cost effectiveness of such an exercise on a global basis is questionable.[20] Surprisingly, there are no studies on KAP of healthcare professional dealing with pregnant women. This becomes cogent considering that prenatal screening is the best way of avoiding birth of thalassemia afflicted babies. Hemoglobinopathy screening is most useful before pregnancy or in early pregnancy, so that fetal diagnosis can be confirmed and parents have the option of deciding for continuation or termination of an affected pregnancy. In selected cases, early diagnosis could prompt changes in pregnancy management, for example, monitoring for fetal hydrops, serial fetal transfusions, or stem cell therapy.

Antenatal women should be advised to get a CBC done at the earliest, and in women with low MCH and MCV values and a relatively high RBC count in relation to hemoglobin and/or normal RDW; estimation of HbA2 and HbF should be done by cation exchange high performance liquid chromatography (CE-HPLC). The cut-off value of HbA2 for the diagnosis of thalassemia carriers is taken as 3.5%, although this may vary with clinical situations such as iron deficiency and HIV positive patients on antiretroviral therapy, etc. Reduced MCV (<80 fl) and MCH (<27 pg) with a relatively high RBC count and a normal RDW are highly suggestive of thalassemia. If both partners are found to be carriers of beta-thalassemia or hemoglobinopathy, the fetus has a 25% chance of suffering from beta-thalassemia major or other hemoglobinopathies. In such a case, mutation testing of both partners needs to be done to determine homo- or heterozygosity of mutation. The prenatal testing will need to be done in each pregnancy, irrespective of the result of the previous pregnancy. It is best done in the first trimester of pregnancy by chorionic villus sampling and DNA analysis. The mutations are characterized by allele-specific priming (ARMS) or by reverse dot blot hybridization (RDB). Around 80 mutations have been characterized with IVS 1–5 (G>C) being predominant in most parts of India. Eighty to ninety percent of the problem burden is carried by 6–7 common mutations.[4]

Economic Impact

We planned to scrutinize studies assessing the economic burden imposed by having a member with thalassemia major and compared it with the average per capita income in India which stands at 1,35050 INR.[21] However, we came across only one study in the said time period from UP. Moirangthem[9] estimated the cost of thalassemia in a dedicated government unit to be around US$ 1135 (INR 74,948) per annum in UP. However, these numbers grossly underestimate the ground situation in most of the regions of India, because such centers with subsidization in medical care are very limited. Besides, as the authors themselves point out, the study did not take into account the actual days of earning lost and the cost of additional treatment such as chelation, etc., besides the cost incurred in treatment. The average cost of thalassemia treatment often escalates to several lakh rupees per annum in different parts of India, depending on the type of hospital and care available.[22]

Genetic Counselling

Genetic counselling is the process by which individuals at risk of acquiring an inherited disorder are given information regarding nature and effects of the disorder, probability of developing or transmitting it, and any ways to prevent, avoid, or ameliorate the manifestations. It involves personnel trained to the purpose. While counselling, it is essential that the healthcare provider understands the advantages as well as the limitations of the available tests, whether the test is a screening or a diagnostic test, economics involved, and feasibility of the test for a particular couple. It goes without saying that all available options have to be explained and discussed, and the couple should be allowed to make take an informed decision. The crux of counselling is to make the couple aware of the genetic disorder, its clinical spectrum, the available healthcare, and the options, if any, for termination of an affected pregnancy. An important aspect of counselling is to get the message across that screening tests are limited to certain genetic disorders and a negative screening test does not ensure a normal baby. Both

pre- and post-test counselling are equally important components of prenatal screening programs. Needless to say that Uttar Pradesh, with its lower literacy and per capita income as compared to the Indian average will present a challenge with regard to counselling.

Areas that Need to be Addressed

The first step toward tackling the problem would be getting the actual statistics of the disease prevalence, awareness in the healthcare workers, as well as general population and understanding the knowledge gaps. The lack of information regarding prevalence precludes a realistic estimate of the disease burden which reflects in formulation of state policies for management, counselling, and rehabilitation of affected families. We need large-scale population-based studies to understand the real status of thalassemia in Uttar Pradesh.

Madan et al.[23] conducted a large multicentric study evaluating 11,090 school children from Delhi, Mumbai, and Kolkata. The investigators concluded that the birth rate of thalassemia homozygotes is highly underestimated and the actual prevalence would be much higher. The authors categorized school children according to the state of origin and found the prevalence of BTT to be 4.1% in children from UP, which stood at ninth place in comparison to other states. However, if we talk of sheer numbers, UP is ahead of all the states due to its dubious distinction of being the most populous state.[24] The authors found the prevalence of anemia in school girls (Delhi) to be 18.6% (without hemoglobinopathy) and 58.4% (with BTT). Interestingly, in 3.2% girls, the hemoglobin concentration was >14 g/dL. This underscores the importance of universal screening without dependence on hemoglobin and blood picture.

There have been a few isolated questionnaire-based KAP studies about beta-thalassemia.[25–27] However, till date we do not have any such studies from UP. The existing data show that knowledge among general population is highly limited with only about 10.07% having idea about beta-thalassemia. Importantly, more than 50% individuals from a Delhi-based study were not willing for premarital screening for beta-thalassemia due to fear of stigmatization. It is imperative that such studies are undertaken, coupled with the aim of improving awareness about thalassemia and its screening methods.

A screening program instituted for thalassemia will have a significant impact in determining the incidence and prevalence of the disorders and will have a long-term effect in improved delivery of care for mother and baby. For a screening program to be effective, it needs to be integrated into the existing healthcare delivery system as part of a national program. This proves challenging in states with a large population and limited resources like UP. The program should encompass preventive, curative, as well as rehabilitative aspects. While it is essential that couples at risk of having fetuses with congenital abnormalities be identified, screened, and counselled, it is equally important that existing patients are treated in the best possible manner. Maintaining a disease register should be mandatory to ensure that all individuals affected with thalassemia and other hemoglobinopathies are provided appropriate healthcare pertaining to their situation.

Due to the scope and complexity involved, a rational planning, with the involvement of multitude of healthcare staff, patients, and parents, is essential. A thorough system of evaluation of the program should be in place from the outset, which can measure and report progress in patient care and preventive strategies. This is essential to ensure stimulation of all personnel involved and to identify problem areas so that continuing support can be extended from the relevant authorities.

The thalassemia prevention program of Cyprus can serve as an excellent example of how a well-planned program can lead to decrease in the incidence of a genetic disorder. The program involved improvement of curative services with defined management protocols, establishment of thalassemia centers, and availability of adequate and safe blood. Improvement in prenatal screening facilities was done, with integration of thalassemia screening and counselling into the existing basic health services. There was planned community participation with increased public awareness campaigns and involvement of "Patient Support Associations".[28]

Suggestions for Implementation

- A regional multidisciplinary team should be constituted, comprising experts involved in the care of individuals with thalassemia. This could include obstetricians, fetal medicine specialists, geneticists, genetic counselors, pediatricians, etc.
- The local database should be strengthened by improving collection of epidemiological information so that the actual health burden can be assessed. This would require policy making, legislation, and funding at the level of government.
- Other sources of help apart from government agencies should be actively enlisted such as WHO consultancy, support from funding bodies, patient support associations, parent welfare groups, and other nongovernment organizations should be constituted and encouraged to focus on increasing awareness, providing psychological, logistical, and occasionally, economic support to patients and their families. These philanthropic organizations could work in collaboration with the state and national organizations.
- Encouragement of research in the area of hereditary hemoglobin disorders should be encouraged, with focus on the socio-demographic characteristics of population, frequency and distribution of common mutations, correlation between local mutations and severity of affliction, demand-supply discrepancy in prenatal diagnostic services, and management of affected children, etc.
- School-based screening of adolescents for assessment of beta thalassemia status along with education and awareness would be a good idea. This segment of population would be most amenable to screening and counselling. This may serve as a good alternative to the concept of premarital screening as is practiced in other countries such as Iran, Turkey, UAE, etc.
- Capacity building workshops need to be encouraged, and NGOs, parents forum, patient societies, etc., need to be brought together under a single roof in order to increase awareness and community participation in combating thalassemia.

Anticipated Benefits of Population-based Screening

Presently, there is no nation-wide consensus regarding prenatal screening protocols. Several benefits of the same have been purported. For instance, an important corollary of population-based screening will be a collection of data on a large scale which will help in estimation of true prevalence and distribution of specific genetic disorders in Uttar Pradesh. This knowledge will be of use in formulation of screening policies, establishment of treatment, and rehabilitation services for the sufferers. Pre- and post-test counselling, an integral component of such an undertaking will serve the dual purpose of creating awareness and helping couples with reproductive choices. In the process, healthcare staff will be trained who will also serve to disseminate the knowledge to general population. Awareness will be the first step toward reduction of

genetic disorders in offspring, mental, and physical trauma of affected patients and socio-economic burden of the family.

Conclusion

- There is lack of data on prevalence of thalassemia in Uttar Pradesh.
- The existing studies show high prevalence but the statistics are variable due to lack of properly planned population-based studies.
- There is significant economic impact caused by having a thalassemia sufferer in the family. However, the approximate financial burden is difficult to estimate because we have insufficient studies on this subject.
- There are no studies on knowledge, attitudes, and practices of healthcare practitioners dealing with antenatal women with regard to thalassemia screening and management.

References

1. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ 2008;86:480. Available from: https://pubmed.ncbi.nlm.nih.gov/18568278/.
2. Edison ES, Shaji RV, Devi SG, et al. Analysis of beta globin mutations in the Indian population, presence of rare and novel mutations and region-wise heterogeneity. Clin Genet 2008;73:331–337. Available from: https://pubmed.ncbi.nlm.nih.gov/18294253/.
3. Sengupta M. Thalassemia among the tribal communities of India. Internet J Biol Anthropol 2007;1(2):1–9. Available from: https://www.researchgate.net/publication/289231722_Thalassemia_among_the_tribal_communities_of_India.
4. Colah R, Italia K, Gorakshakar A. Burden of thalassemia in India: The road map for control. Pediatr Hematol Oncol J 2017;2:79–84. Available from: https://www.sciencedirect.com/science/article/pii/S2468124517300748.
5. Verma IC. Burden of genetic disorders in India. Indian J Pediatr 2000;67(12):893–898. Available from: https://pubmed.ncbi.nlm.nih.gov/11262988/.
6. Mohanty D, Colah RB, Gorakshakar AC, et al. Prevalence of β-thalassemia and other haemoglobinopathies in six cities in India: a multicentre study. J Commun Genet 2013;4:33–42. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3537975/.
7. Baruah MK, Saikia M, Baruah A. Pattern of haemoglobinopathies and thalassemia in upper Assam of north eastern India: high performance liquid chromatography studies in 9000 patients. Indian J Pathol Microbiol 2014;57:236–243. DOI: 10.4103/0377-4929.134680.
8. Colah R, Mukherjee M, Ghosh K. Sickle cell disease in India. Curr Opin Hematol 2014;21:215–223. Available from: https://pubmed.ncbi.nlm.nih.gov/24714525/.
9. Moirangthem A, Phadke SR. Socio-demographic profile and economic burden of treatment of transfusion dependent thalassemia. Indian J Pediatr 2018;85(2):102–107. Available from: https://pubmed.ncbi.nlm.nih.gov/29119463/.
10. Meena LP, Kumar K, Singh VK, et al. Study of mutations in β-thalassemia trait among blood donors in Eastern Uttar Pradesh. J Clin Diagn Res 2013;7(7):1394–1396. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3749643/.
11. Nagar R, Sinha S, Raman R. Haemoglobinopathies in eastern Indian states: a demographic evaluation. J Community Genet 2015;6:61–68. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4286564/.
12. Kumar R, Arya V, Agarwal S. Profiling β-thalassemia mutations in consanguinity and nonconsanguinity for prenatal screening and awareness programme. Adv Hematol 2015:625721. Available from: https://pubmed.ncbi.nlm.nih.gov/26576156/.
13. Kumar R, Singh K, Panigrahi I, et al. Genetic heterogeneity of beta globin mutations among Asian-Indians and importance in genetic counselling and diagnosis. Mediterr J Hematol Infect Dis 2013;5(1):e2013003. Available from: https://pubmed.ncbi.nlm.nih.gov/23350016/.
14. Verma P, Singh S, Krishna A, et al. Prevalence of hemoglobin variants, ABO and rhesus blood groups in Northern Uttar Pradesh, India. Biomed Res 2013;24(3):377–382. Available from: https://www.biomedres.info/biomedical-research/prevalence-of-heamoglobin-variants-abo-and-rhesus-blood-groups-innorthern-uttar-pradesh-india.html.
15. Singh J, Saxena M, Ahmad F, et al. Spectrum of haemoglobinopathies and thalassemias diagnosed on HPLC in a tertiary teaching hospital of Northern India. Natl J Lab Med 2016;5(3):PO70–PO75. DOI: 10.7860/NJLM/2016/19972.2149.
16. Verma P, Ghildiyal A, Verma D, et al. Prevalence of haemoglobinopathies in different regions and castes of Uttar Pradesh, India–a hospital based study. Asian J Med Sci 2015;6(5):21–26. DOI: 10.3126/ajms.v6i5.12339.
17. Census 2011. Uttar Pradesh Population 2011-2021. Available from: https://www.census2011.co.in/census/state/uttar+pradesh.html [Last accessed on July 26, 2020].
18. Gupta V, Shukla J, Tilak V, et al. Spectrum of haemoglobinopathies in Eastern Uttar Pradesh. Indian J Pediatr 2009;76(8):857. Available from: https://pubmed.ncbi.nlm.nih.gov/19381515/.
19. Thalassemia treatment centres in India. Available from: http://www.curethalassemia.org/thalpedia/thalassemia-treatment-centers-india/ [Last accessed on July 26, 2020].
20. Ahmed S, Saleem M, Modell B, et al. Screening extended families for genetic haemoglobin disorders in Pakistan. N Engl J Med 2002;347:1162. Available from: https://pubmed.ncbi.nlm.nih.gov/12374877/.
21. Economic survey 2020-21 statistical appendix. Available from: https://www.indiabudget.gov.in/economicsurvey/doc/Statistical-Appendix-in-English.pdf [last accessed on February 26, 2021].
22. Financial Express. Modi government, Coal India to help in treatment of kids suffering from thalassemia. Available from: https://www.financialexpress.com/health-3/modi-government-coal-india-to-help-in-treatment-of-kids-suffering-from-thalassemia/631121/ [last accessed February 26, 2021].
23. Madan N, Sharma S, Sood SK, et al. Frequency of β-thalassemia trait and other hemoglobinopathies in Northern & Western India. Indian J Hum Genet 2010; 16(1):16–25. Available from: https://pubmed.ncbi.nlm.nih.gov/20838487/.
24. India Today. Indian states with highest population. Available from: https://www.indiatoday.in/education-today/gk-current-affairs/story/indian-states-with-highest-population-1358414-2018-10-08.
25. Mohanty D, Colah R, Gorakshakar A, editors. Report of the Jai vigyan S & T mission project on community control of thalassemia-awareness, screening, genetic counselling and prevention. Indian Council of Medical Research; 2008.
26. Shrivastava JK, Sinha N, Behera SK, et al. Knowledge, attitude and practice study of β-thalassemia in rural Bengal. Genet Clin 2011;4:13–15.
27. Chawla S, Singh RK, Lakkakula B, et al. Attitudes and beliefs among high and low risk population groups towards β-thalassemia prevention: a cross sectional descriptive study from India. J Community Genet 2017;8:159–166. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5496837/.
28. Bozkurt G. Results from the North Cyprus thalassemia prevention program. Hemoglobin 2007;31(2):257–264. Available from: https://pubmed.ncbi.nlm.nih.gov/17486509/.