Original Article

Incidence Of Hemoglobinopathies In South Indian Population – 4 Year Study

Kavitha. A*, Kavita. V, Mukilarasi.

Metropolis Healthcare limited

DOI: 10.21276/APALM.3236

***Corresponding Author**:
Dr Kavitha. A
kavithaa.lm@metropolisindia.com

Submitted: 27-Nov-2022
Final Revision: 09-Jul-2023
Acceptance: 21-Jul-2023
Publication: 01-Sep-2023

This work is licensed under the Creative Commons Attribution 4.0 License. Published by Pacific Group of e-Journals (PaGe)

Abstract

Background

Hemoglobinopathies are very common, but majority being asymptomatic it is under diagnosed. Hemoglobinopathies are important health care threat in tropical countries. The present study analyzed the incidence of hemoglobinpathies in south Indian population reported in regional laboratory in Chennai catering Tamil nadu and Andhra Pradesh population.

Methods

A cohort of samples which was received for abnormal hemoglobinopathy studies for evaluation of anemia and prenatal screening from Tamil nadu and Andrapradesh population for 4 years was analyzed using capillary electrophoresis method in (Sebia Minicap instrument) for incidence of hemoglobinopathies.

Result

Total number of cases studied during 4 years (2018-2022) is 17678, Of which 1194(7%) were detected with hemoglobinopathy/ abnormal hemoglobin variant. Of which 56.28% were female and 43.72% were male. Common age group under study is 21-30(30.07%). Beta thalassemia trait was detected at the highest frequency (69.13%) followed by HbE-Beta thalaseemia(6.87%) and least being HbD homozygous.

Conclusion

Our study analyzed a cohort and reported a spectrum of hemoglobin variants and its incidence in Tamil nadu and Andhrapradesh population.

Keywords:

Anemia, Hemoglobinopathy, South India, Thalassemia

Introduction

Hemoglobinopathies are the most common single gene disorders [1]. The abnormal hemoglobin variants are genetic disorders that cause abnormalities in the structure or production of hemoglobin. More than 200 different mutations have been reported to date, resulting in marked differences in the molecular basis of β-thalassemia. However, population studies show that probably only 20 β-thalassemia alleles account for more than 80% of the β-thalassemia mutations worldwide.

Nationally, the five most common disease mutations, which account for approximately 82.5%, are IVSI-5 (GC), 619-bp del, IVSI-1 (GT), codon 41/42 (-TCCT), and codon 8/9 (-G). Codon 15 (GA), codon 30 (GC), cap site 1 (AC), codon 5 (-CT), and codon 16 (-C) account for an additional 11.0% of all mutant alleles. The four southern states (Andhra Pradesh, Karnataka, Tamil Nadu, and Kerala) have a high prevalence of hemoglobinopathies in India, predominantly in the Dravidian population, which is ethnically and culturally distinct from the largely Indo-European populations of the north. IVSI-5(GC) has a prevalence of 67.9%, the 619-bp deletion is present in only 1.8% of cases, whereas the second most common allele (8.8%) is codon 15 (GA). Poly A site (TC) is the third most common allele (4.7%) [2].

Approximately 450,000 infants worldwide are born with hemoglobinopathies, with approximately 80% of cases occurring in low- or middle-income countries. Hemoglobinopathies have developed among people in Asia, tropical Africa, and the Mediterranean region, and have spread throughout the world due to migration [3], making their detection significant from an epidemiological perspective, especially in India, which has a large multi-cultural population with distinct geographic distribution [4].

Materials and Methods

A total of 17,678 cases were received between January 2018 and July 2022 in the Hematology Department for screening of abnormal hemoglobinopathies or evaluation of anemia in the regional laboratory in Chennai, which serves the population of Tamil Nadu and Andhra Pradesh. The cases were referred from different peripheral hospitals, medical colleges, and hospitals from all districts of Tamil Nadu and Andhra Pradesh.

Approximately 5 ml of intravenous blood was collected from adults and 2-3 ml of blood from babies. Demographic details such as age, gender, and relevant clinical history were documented. Hematological indices were recorded using a Beckman Coulter instrument, and a peripheral smear was made for all cases.

If the blood count showed abnormalities with low hemoglobin and MCV, iron deficiency was considered as the probable cause. Post-correction of nutritional deficiency, the blood count was repeated, and if the MCV/MCH remained low, thalassemia was most likely.

In comparison to iron deficiency, hemoglobin concentration and RBC were significantly higher, and the mean corpuscular volume (MCV) and RDW were significantly lower in hemoglobinopathy cases. However, if hemoglobinopathy coexists with iron deficiency, the difference may not be significant. In such cases, microcytic hypochromic anemia with target cells observed in the peripheral blood smear may provide a clue to thalassemia trait, but these features are also associated with many other conditions.

Hemoglobin electrophoresis was carried out using capillary electrophoresis method with the Sebia Minicap instrument. All abnormal hemoglobin variants detected in capillary electrophoresis were further confirmed using the HPLC method with the Tosho instrument. A value greater than 3.5% of the A2 fraction of hemoglobin was considered the cutoff point for beta-thalassemia trait.

During the first year of life, the diagnosis of thalassemia is difficult based on hematologic studies. Other factors such as iron deficiency can distort the hematologic findings and lead to misdiagnosis. Molecular techniques help resolve the diagnostic problem.

Results

A total of 17,678 samples were received for abnormal hemoglobin studies among the south Indian population between 2018 and

2022. Among these, 1,194 samples (56.28% female, 43.72% male) were found to have abnormal hemoglobin variants. The maximum number of cases identified with abnormal hemoglobin was in the age group of 21-30 years (30.07%), followed by the pediatric age group (0-10 years) accounting for 22.61%. Thus, warranting early routine screening for hemoglobinopathies at an earlier age. (Fig.2)

Among all the abnormal hemoglobin variants, β-thalassemia trait was the most common, accounting for 69.13% (824 cases), followed by HbE β-thalassemia (6.87%), sickle beta thalassemia (4.61%), HbS Heterozygous (4.52%), HB D Heterozygous (4.36%), HbE Heterozygous (4.1%), HbE Homozygous & HBS Homozygous (1.68%), beta thalassemia Intermedia/HBF (1.08%), HB H Heterozygous (0.42%), beta thalassemia homozygous (0.17%), and HbD Homozygous (0.08%) (Table 1&Fig 1).

Table 1 Spectrum of abnormal hemoglobin variant and its incidence

Diagnosis	Total number of cases	%
Beta thalassemia trait	824	69.13
HbE beta thalasemia	82	6.87
Sicke beta thalasemia	55	4.61
HbS Heterozygous	54	4.52
HbE Heterozygous	49	4.1
HB D Heterozygous	52	4.36
HbE Homozygous	20	1.68
HbS Homozygous	20	1.68
Betathalasemia Intermedia/HBF	13	1.08
HB H Heterozygous	5	0.42
Beta thalasemia homozygous	2	0.17
HbD Homozygous	1	0.08

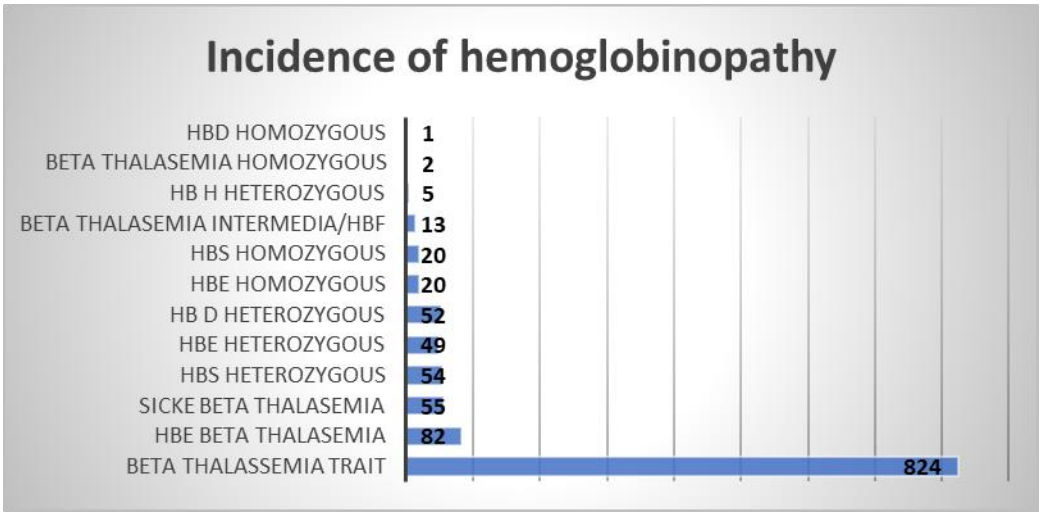

Figure 1 Spectrum of abnormal hemoglobin variant and its incidence

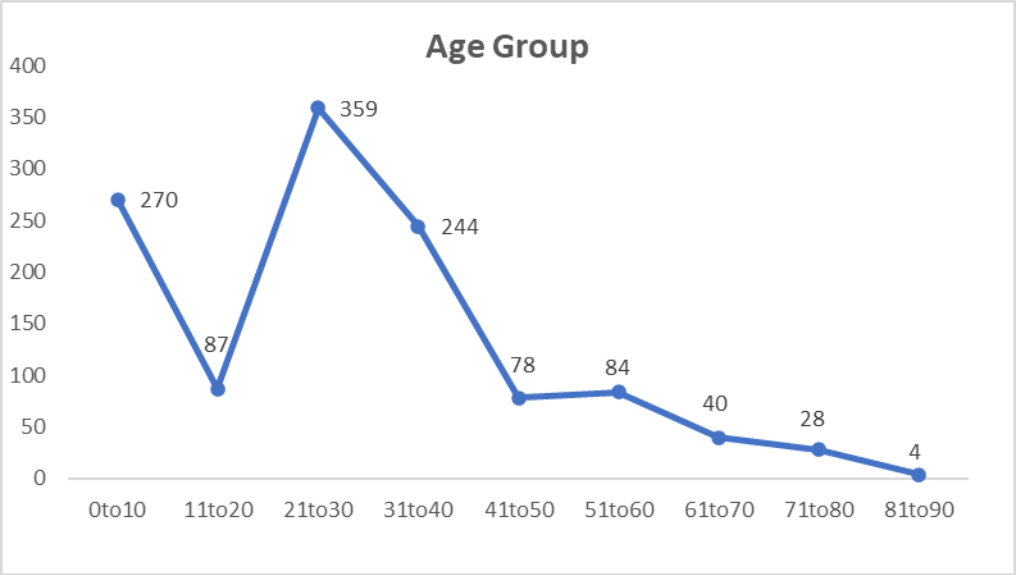

Figure 2 Incidence of hemoglobinopathy in different age group

Discussion

The most common genetic defect worldwide is hemoglobinopathy, with an estimated 269 million carriers. Some populations are at higher risk of having hemoglobinopathies due to their carrier state. In Southeast Asia, there are 90 million carriers, about 85 million in sub-Saharan Africa, and 48 million in the West Pacific region [6].

Patients with thalassemia major have severe anemia and become transfusion-dependent by 1 year of age. Thalassemia intermedia/trait patients have mild to moderate anemia and mostly require no or infrequent blood transfusions [7].

A study by Sandhya Iyer et al. states that sickle cell disease accounts for approximately 85.9% of hemoglobinopathies worldwide, β-thalassemia alone or combined with hemoglobin E accounts for 9.7%, and infants affected with Hb Barts and HbH disease account for 4.4% [4].

The prevalence of beta-thalassemia trait in India varies from 1% to 17% in different regions, with an average prevalence of about 3.3%. The prevalence of different types of hemoglobinopathy also varies in different regions of the country. HbD has been reported more in the Punjabi population, HbS is mainly reported in tribal populations, and HbE is more prevalent in the eastern region of India [8].

In our study, β-thalassemia trait was the most common hemoglobinopathy in the age group of 0-10 years among the south Indian population, with an incidence of 22.61%.

Various studies have reported different prevalence rates of hemoglobinopathies in different regions of India. For example, a multicentric study sponsored by the Indian Council of Medical Research showed beta-thalassemia carrier rates of 5.5%, 2.6%, and 10.2% among school children in Delhi, Bombay, and Calcutta, respectively [9].

In our study, the highest incidence of hemoglobinopathy was observed in the age group of 21-30 years (30.07%), with β-thalassemia trait being the most common.

The prevalence of hemoglobinopathies varies across different regions of India. For example, a study in rural areas of West Bengal

found the frequency of β-thalassemia trait to be 10.38%, HbE trait to be 4.30%, and sickle cell trait to be 1.12% [11].

Certain populations in India have a high prevalence of specific hemoglobinopathies. For instance, HbS is prevalent in central India with carrier rates varying from 1% to 40% in different tribal communities [12]. Hemoglobin E is widespread in northeastern states like Assam, Arunachal Pradesh, Mizoram, Manipur, and Tripura [13].

Our study identified the incidence of HbE disease, with HbE β-thalassemia accounting for 6.87% and HbE Heterozygous and HbE Homozygous accounting for 4.1% and 1.68%, respectively.

Migration plays a significant role in the global distribution of hemoglobinopathies. It has led to the emergence and spread of specific hemoglobin variants in different parts of the world. Sickle cell disease, a type of hemoglobinopathy, is more prevalent in populations of African descent due to the migration of people from Africa to other parts of the world spreading thalassemia to other parts of the world.

Globally, 80% of people affected by SCD are origins from central Africa. The condition also affects people from Central and South America, the Arabian Peninsula, Middle East, India, and eastern Mediterranean

In 1998, a questionnaire, requesting information about the cases of Sickle cell disease, A total of 696 cases were reported. The distribution of registered patients showed that, although the S gene originated mostly in Sicily, with an estimated mean frequency of 2% and a peak of 13%, and Southern Italy, 20% of patients with SCD lived in Central and Northern Italy

According to 2019 data from the National Registry of Thalassemia and Haemoglobinopathies, in Italy there are approximately 1,275 patients living with Sickle cell disease. The epidemiology of SCD has changed considerably in the country over recent years, in particular due to changes in migratory patterns and migration from countries with high sickle cell disease prevalence [17,18]

Genotype/phenotype correlation is helpful in predicting the phenotype and determining treatment options for thalassemia patients. Genetic analyses, including determining the type of β-globin gene mutation and co-inheritance of β-globin gene deletions/duplications, can provide valuable information for prognosis, response to therapy, and genetic counseling [7][16].

Conclusion

International migration has spread hemoglobinopathies from certain areas to different parts of the world. Early detection and characterization of hemoglobinopathies are crucial for providing appropriate counseling to at-risk couples and families. Our study highlights the prevalence of beta-thalassemia trait as the most common hemoglobinopathy, which is influenced by migration. It is important to understand the specific underlying abnormalities in each case to provide accurate health advice to individuals, offspring, and other family members. As hemoglobinopathies are usually inherited as autosomal recessive traits, there is a 25% risk of severe disorder inheritance in children of carrier parents.

Through mobility and migration flows, haemoglobinopathies have spread from the Mediterranean, Africa and Asia to the whole Europe, the America and Australia, and there is scientific evidence that they have become a global public health problem. Hemoglobinopathies pose a public health issue in multiethnic populations like India, requiring a range of diagnostic and therapeutic measures to provide adequate care for affected patients. Understanding the relationship between genotype and phenotype is valuable in clinical practice for predicting the phenotype, genetic counseling, making decisions regarding prenatal diagnosis, and planning appropriate treatment for β-thalassemia patients.

References

1. Flint J, Harding RM, Boyce AJ, Clegg JB. The population genetics of the haemoglobinopathies. Baillieres Clin Haematol. 1993 Mar;6(1):215-62.
2. Sinha S, Black ML, Agarwal S, et al. Profiling -thalassaemia mutations in India at state and regional levels: implications for genetic education, screening and counseling programmes. Hugo J. 2009;3:51–62.
3. Verma IC, Saxena R, Kohli S. Hemoglobinopathies in India—Clinical and Laboratory Aspects.
4. Iyer S, Sakhare S, Sengupta C, Velumani A. Hemoglobinopathy in India.
5. Surjawan Y, Tan HL, Setiabudy RD, Rositawati W. Early Screening of Hemoglobinopathy in Indonesia Using Erythrocyte Indices.
6. Angastiniotis M, Modell B. Global epidemiology of hemoglobin disorders. Ann N Y Acad Sci. 1998;850:251–69.
7. Verma IC, Saxena R, Kohli S. Hemoglobinopathies in India—Clinical and Laboratory Aspects.
8. Frequency of β-thalassemia trait and other hemoglobinopathies in Northern & Western India. Indian J Hum Genet. 2010 Mar;16(1):16-25.
9. Sood SK, Madan N, Colah R, et al. Collaborative study on thalassemia. Report of ICMR Task Force study on thalassemia. New Delhi: Indian Council of Medical Research; 1993.
10. Mohanty D, Colah R, Gorakshakar. Jai Vigyan S&T Mission Project on community control of thalassemia syndromes—Awareness, screening, genetic counseling and prevention. New Delhi: Indian Council of Medical Research; 2008.
11. Dolai TK, Dutta S, Bhattacharyya M, et al. Prevalence of Hemoglobinopathies in rural Bengal, India. Hemoglobin. 2012;36:57–63.
12. Serjeant GR. The case for dedicated sickle cell centres. Indian J Hum Genet. 2006; 12:148–51.
13. De M, Halder A, Podder S, et al. Anemia and hemoglobinopathies in tribal population of eastern and north eastern India. Hematology. 2006;11:371–3.
14. Ray GK, Jena RK. Spectrum of Hemoglobinopathies: A New Revelation in a Tertiary Care Hospital of Odisha.
15. Rangan A, Sharma P, Dadu T, et al. -Thalassemia mutations in subjects with borderline HbA(2) values: a pilot study in North India. Clin Chem Lab Med. 2011;49: 2069–72.
16. Thomas E, et al. Regional distribution of -thalassemia mutations in India. Hum Genet. 1997;100:109–13.
17. Russo G, De Franceschi L, Colombatti R, et al. Current challenges in the management of patients with sickle cell disease – A report of the Italian experience. Orphanet J Rare Dis. 2019;14:120.
18. Russo-Mancuso G, La Spina M, Schilirò G. The changing profile of sickle cell disease in Italy. Eur J Epidemiol. 2003;18:923–4.