DOI: https://doi.org/10.54393/pbmj.v7i03.1051

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

ISSN (P): 2709-2798, (E): 2709-278X

Volume 7, Issue 3 (March 2024)

Original Article

Spectrum of Hemoglobinopathies in Tertiary Care Hospitals of Rawalpindi and Islamabad

Tanveer Ul Haq Zia[1], Ammar Ahmed[2], Muhammad Ilyas[3], Hira Siyar[4] and Haji Bahadar[4*]

[1]The University of Lahore, Islamabad Campus, Islamabad, Pakistan
[2]Ibadat International University, Islamabad, Pakistan
[3]Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan
[4]Institute of Pharmaceutical Sciences, Khyber Medical University, Peshawar, Pakistan

ARTICLE INFO

Keywords:
Hemoglobinopathies, Sickle Cell Anemia, Thalassemia, Hemoglobin, Electrophoresis

How to Cite:
Zia, T. U. H., Ahmed, A., Ilyas, M., Siyar, H., & Bahadar, H. (2024). Spectrum of Hemoglobinopathies in Tertiary Care Hospitals of Rawalpindi and Islamabad : Spectrum of Hemoglobinopathies . Pakistan BioMedical Journal, 7(03). https://doi.org/10.54393/pbmj.v7i03.1051

***Corresponding Author:**
Haji Bahadar
Institute of Pharmaceutical Sciences, Khyber Medical University, Peshawar, Pakistan
bahadar@kmu.edu.pk

Received Date: 28th February, 2024
Acceptance Date: 8th March, 2024
Published Date: 31st March, 2024

ABSTRACT

Hemoglobinopathies, including Thalassemia and sickle-cell syndromes are lifelong diseases with a significant impact on patients, families, and healthcare resources. Despite therapeutic progress, Pakistan, located within the Thalassemia belt, lacks comprehensive data on the epidemiology, clinical course, mortality, complications, and treatment outcomes of Thalassemia. **Objective:** To determine the frequency of haemoglobinopathies in Tertiary Care Hospital of Rawalpindi and Islamabad. **Methods:** A retrospective cross-sectional study of 7 months was conducted on the local population of Islamabad and Rawalpindi from January 2020 to July 2020. Total 600 patients referred for Hb electrophoresis were initially selected for study. Data from 300 patients were collected from PIMS Hospital, Islamabad, and 300 from Holy Family Hospital, Rawalpindi. Clinical information for each patient was recorded separately, data were statistically analyzed using Microsoft Excel version 2016 and graphs were made on GraphPad Prism version 08. **Results:** Out of 600 patients from Rawalpindi and Islamabad 227 (37.84%) patients were found to have hemoglobinopathies. Beta Thalassemia trait was the most common disorder among those with hemoglobinopathies (47.13%), followed by beta Thalassemia major (23.34%), sickle Beta Thalassemia (10.57%), sickle cell disease (6.6%), Hb D trait (5.28%), Hb D/beta Thalassemia (3.96%), Hb E trait (2.2%), and sickle cell trait (0.88%). **Conclusions:** The study showed a significantly high frequency of hemoglobinopathies in the capital city Islamabad and Rawalpindi. β- Thalassemia trait and β- Thalassemia major were found in high frequency among various hemoglobin disorders.

INTRODUCTION

Hemoglobinopathies are inherited blood disorders caused by mutations in genes responsible for making hemoglobin protein. These disorders can affect either the alpha (α) or beta (β) globin chains of the protein. Some of the most common syndromes include beta-Thalassemia, sickle cell disease (SCD), HbH disease (alpha-Thalassemia), and Hb E/β-Thalassemia [1]. Inherited hemoglobin disorders are a growing global public health concern, with approximately 320,000 babies born annually with clinically significant symptoms [2]. Developing countries suffer more from inherited hemoglobin disorders, which affect almost 80% of newborns with these problems. Around the world, a huge 5.2% of people (more than 360 million) have a major hemoglobin variation. Also, over 100 million people have the beta-Thalassemia trait, which has a global rate of 1.5% [3]. Thalassemia is a blood disorder characterized by decreased or absent production of globin chains, essential components of hemoglobin. The condition encompasses two primary types: alpha (α) and beta (β) Thalassemia. These can be subdivided into major, which is the most severe form involving the inheritance of two mutated genes, and minor, which is less severe and involves the inheritance of one mutated gene [4,5]. Sickle cell disease happens when mutation occurs in the β-globin chain

DOI: https://doi.org/10.54393/pbmj.v7i03.1051

results in the formation of hemoglobin S (HbS) [6]. However, if an individual inherits the HbS gene from one parent and the HbA gene from the other, they possess the sickle cell trait. In this case, they do not develop sickle cell disease and remain asymptomatic, without any associated health issues. Their blood tests yield normal results, and their life expectancy is comparable to that of individuals without the trait [7-9]. Similar to those with beta-Thalassemia, HbC carriers have mutations in the beta-globin chain. However, unlike sickle cell disease, these mutations lead to a different amino acid substitution that doesn't cause red blood cells to sickle, making it a less severe condition [10,11]. Hemoglobinopathies have varying rates throughout Pakistan, with beta-Thalassemia major (TM) being a particularly common inherited blood disorder. An estimated 5-7% of the population are carriers, meaning approximately 9.8 million Pakistani individuals carry the trait for this disease [12]. Pakistan is home to a considerable population of registered Thalassemia patients, estimated to be approximately 50,000 [13]. This substantial figure is influenced by multiple factors, including a notable prevalence of mutations in the hemoglobin beta-subunit gene (HBB), a large population size coupled with a high birth rate, and the common occurrence of consanguineous marriages [14].

METHODS

The research conducted was a 7 months retrospective cross-sectional study from January 2020 to July 2020. The study included a total of 600 patients who were referred for Hb electrophoresis to PIMS Hospital, Islamabad and Holy Family Hospital, Rawalpindi. Of these, 300 patients were from PIMS Hospital, Islamabad, and 300 were from Holy Family Hospital, Rawalpindi. The inclusion criteria required that patients must have been referred for Hb electrophoresis and were from the local population of Rawalpindi and Islamabad. After obtaining ethical approval and informed consents from all participants, comprehensive medical and clinical information of all participants were documented separately using special forms. The patients' medical profiles encompassed data from hematological, biochemical, and serological tests, comprising CBC parameters (Hb, RBC, MCV, MCH, MCHC), peripheral blood film analysis (for anisocytosis/poikilocytosis), Hb electrophoresis results, and DNA analysis if conducted. Statistical analysis of the data was performed using Microsoft Excel version 2016, while GraphPad Prism version 08 was used for generating graphs.

RESULTS

Table 1 shows the frequency of various haemoglobinopathies in the study participants.

Table 1: Frequency of various hemoglobinopathies (n=600)

Sr. No	Type	No. of Cases (%)
1	Normal	373 (62.166)
2	Beta Thalassemia Trait	107 (17.833)
3	Beta Thalassemia Major	53 (8.833)
4	Sickle cell disease	15 (2.5)
5	Sickle Beta Thalassemia	24 (4)
6	Hb D Trait	12 (2)
7	Hb D Beta Thalassemia	9 (1.5)
8	Hb E Trait	5 (0.833)
9	Sickle Cell Trait	2 (0.333)
Total		600 (100)

Out of 600 patients, 373 had normal hemoglobin levels while 227 had hemoglobinopathies. The ratio of male and female regarding hemoglobinopathies were 66% and 34% respectively. The frequency of hemoglobinopathies in male and female is shown in Figure 1.

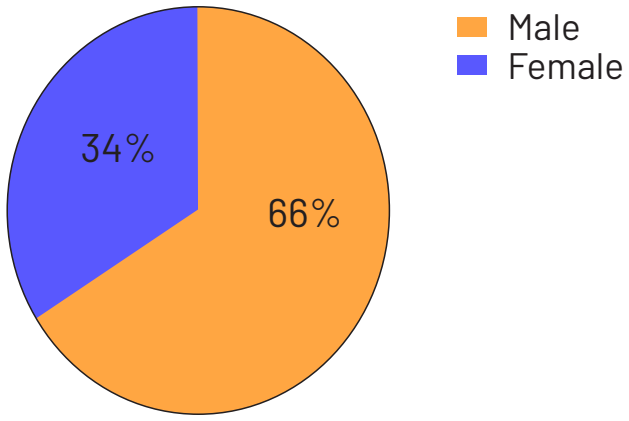

Figure 1: Gender wise distribution of hemoglobinopathies in patients

As shown in Figure 2, Beta Thalassemia trait was the most common, accounting for 107 cases (47.13%). This was followed by Beta Thalassemia major with 53 cases (23.34%), Sickle Beta Thalassemia with 24 cases (10.57%), Sickle cell disease with 15 cases (6.6%), Hb D trait with 12 cases (5.28%), Hb D/Beta Thalassemia with 9 cases (3.96%), Hb E trait with 5 cases (2.2%), and sickle cell trait with 2 cases (0.88%)

DOI: https://doi.org/10.54393/pbmj.v7i03.1051

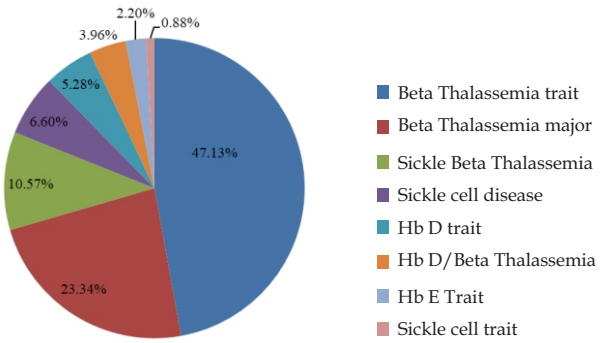

Figure 2: Percentage distribution of various types of hemoglobinopathies

All patients diagnosed with Beta Thalassemia major exhibited severe anemia, splenomegaly, and a history of blood transfusion before the age of 2 years. However, 13 cases were identified as Beta Thalassemia intermedia due to their minimal need for blood transfusions. Peripheral blood film analysis of Beta Thalassemia major cases revealed significant aniso-poikilocytosis, red cell fragmentation, and nucleated red blood cells. Hb electrophoresis consistently indicated elevated levels of HbF (fetal hemoglobin) in these cases. In patients diagnosed with Beta Thalassemia trait, HbA2 levels were elevated beyond 3.5%, RBC count exceeded 5x109/liter, and MCV was less than 70 fl. Peripheral blood film examination revealed a microcytic hypochromic blood picture with target-shaped red blood cells. Sickle cell disease cases presented with aches and pains in various body parts and joints, accompanied by anemia of lesser severity compared to Beta Thalassemia major cases. Conversely, sickle cell trait cases displayed mild anemia and were mostly asymptomatic, with the exception of one case experiencing aches and pains during exertion. The sickling test yielded positive results in all sickle cell disorders, but it displayed delayed sickling of red blood cells in carrier states compared to sickle cell disease. Sickle cells were frequently observed in peripheral blood smears of sickle cell disease cases, whereas they were less commonly observed in sickle cell trait cases. Patients with HbE disease, HbD/Beta Thalassemia, and Sickle cell/Beta Thalassemia exhibited clinical presentations similar to Beta Thalassemia major. However, sickle cell/Beta Thalassemia patients reported body aches in addition to other symptoms. Conversely, HbD trait cases were asymptomatic.

DISCUSSION

There are mainly two groups of hemoglobin disorders. One group is structural hemoglobin variants and second group is the thalassemias associated with defective globin synthesis. Hemoglobinopathies are one of the major genetic disorders of hemoglobin [15]. Traditionally seen in specific populations with endogamous marriage practices, these disorders have become more widespread due to the migration of diverse ethnic groups [16]. Our study showed that the overall frequency of hemoglobinopathies as 37.84 % in Rawalpindi and Islamabad; the results of our study, regarding the prevalence hemoglobinopathies, are almost similar to previously published reports from different area of Pakistan [17,18]. Our results show that the Beta Thalassemia trait was the most prevalent hemoglobinopathy (47.13%) followed by Beta-Thalassemia Major (23.34%), Sickle Beta-Thalassemia (10.57%), Sickle cell disease (6.6%), Hb D trait (5.28%), Hb D/Beta Thalassemia (3.96%), Hb E trait (2.2%) and sickle cell trait (0.88%). As compared to studies conducted in 2011 on the prevalence of hemoglobinopathies in Islamabad, the frequency of hemoglobinopathies has been increased [19]. Regarding the prevalence of hemoglobinopathies in other cities like Karachi, Peshawar, and the most prevalent hemoglobinopathies is Beta Thalassemia minor/trait with particularly in Peshawar. Similarly, a lower prevalence was observed for Sickle Beta Thalassemia (4.5%), Sickle cell disease (3.9%), and Hb E trait (1.9%), while a higher prevalence was reported for Hb D trait (6.7%) and sickle cell trait (1.7%) [16,18]. Data reported from Peshawar show that hemoglobinopathies in the form of Beta Thalassemia trait are highly prevalent. This variation may be attributed to the diverse ethnic communities in Peshawar [20].

CONCLUSIONS

The current study showed a significantly high frequency of hemoglobinopathies in the capital city Islamabad and Rawalpindi, Beta Thalassemia trait and Beta Thalassemia major were found in high frequency among various hemoglobin disorders. Our study showed the prevalence of different hemoglobin disorders in the capital region. This data may be valuable in making policies for preventing and managing these conditions.

Authors Contribution

Conceptualization: TUHZ
Methodology: TUHZ, MI
Formal analysis: AA, HB
Writing-review and editing: AA, HS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

DOI: https://doi.org/10.54393/pbmj.v7i03.1051

REFERENCES

[1] Piel FB. The present and future global burden of the inherited disorders of hemoglobin. Hematology/Oncology Clinics. 2016 Apr; 30(2): 327-41. doi: 10.1016/j.hoc.2015.11.004.

[2] Modell B, 1 Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bulletin of the World Health Organization. 2008 Jun; 86(6): 480-7.3. doi: 10.2471/BLT.06.03 667 3.

[3] Colah R, Gorakshakar A, Nadkarni A. Global burden, distribution and prevention of β-thalassemias and hemoglobin E disorders. Expert Review of Hematology. 2010 Feb; 3(1): 103-17. doi: 10.1586/ehm.09.74.

[4] Forget BG and Bunn HF. Classification of the disorders of hemoglobin. Cold Spring Harbor Perspectives in Medicine. 2013 Feb; 3(2). doi: 10.1101/cshperspect.a011684.

[5] Rosenfeld LG, Bacal NS, Cuder MA, Silva AG, Machado ÍE, Pereira CA *et al*. Prevalência de hemoglobinopatias na população adulta brasileira: Pesquisa Nacional de Saúde 2014-2015. Revista Brasileira de Epidemiologia. 2019 Oct; 22: E190007-SUPL. doi: 10.1590/1980-549720190007.supl.2.

[6] Aramayo-Singelmann C, Halimeh S, Proske P, Vignalingarajah A, Cario H, Christensen MO *et al*. Screening and diagnosis of hemoglobinopathies in Germany: Current state and future perspectives. Scientific Reports. 2022 Jun; 12(1): 9762. doi: 10.1038/s41598-022-13751-8.

[7] Odièvre MH, Verger E, Silva-Pinto AC, Elion J. Pathophysiological insights in sickle cell disease. The Indian Journal of Medical Research. 2011 Oct; 134(4): 532.

[8] Houwing ME, De Pagter PJ, Van Beers EJ, Biemond BJ, Rettenbacher E, Rijneveld AW *et al*. Sickle cell disease: clinical presentation and management of a global health challenge. Blood Reviews. 2019 Sep; 37: 100580. doi: 10.1016/j.blre.2019.05.004.

[9] Pecker LH and Little J. Clinical manifestations of sickle cell disease across the lifespan. Sickle Cell Disease and Hematopoietic Stem Cell Trans plantation. 2018: 3-9. doi: 10.1007/978-3-319-62328-3_1.

[10] Thein SL and Rees D. Haemoglobin and the inherited disorders of globin synthesis. Postgraduate Haematology. 2015 Dec: 72-97. doi: 10.1002/9781118853771.ch6.

[11] Kato GJ, Piel FB, Reid CD, Gaston MH, Ohene-Frempong K, Krishnamurti *et al*. Sickle cell disease. Nature Reviews Disease Primers. 2018 Mar; 4: 18010. doi: 10.1038/nrdp.2018.10.

[12] Ansari SH, Shamsi TS, Bohray M, Khan MT, Farzana T, Perveen K *et al*. Molecular epidemiology of β-thalassemia in Pakistan: far reaching implications. International Journal of Molecular Epidemiology and Genetics. 2011 Nov; 2(4): 403-8. doi: 10.4103/0971-6866.100762.

[13] Ehsan H, Wahab A, Anwer F, Iftikhar R, Yousaf MN. Prevalence of transfusion transmissible infections in beta-thalassemia major patients in Pakistan: a systematic review. Cureus. 2020 Aug; 12(8). doi: 10.7759/cureus.10070.

[14] El Goundali K, Chebabe M, Laamiri FZ, Hilali A. The determinants of consanguineous marriages among the Arab population: a systematic review. Iranian Journal of Public Health. 2022 Feb; 51(2): 253. doi: 10.18502/ijph.v51i2.8679.

[15] Kohne E. Hemoglobinopathies: clinical manifestations, diagnosis, and treatment. Deutsches Ärzteblatt International. 2011 Aug; 108(31-32): 532. doi: 10.3238/arztebl.2011.0532.

[16] Mir SA, Alshehri BM, Alaidarous M, Banawas SS, Dukhyil AA, Alturki MK. Prevalence of hemoglobinopathies (β-thalassemia and sickle cell trait) in the adult population of Al Majma'ah, Saudi Arabia. Hemoglobin. 2020 Jan; 44(1): 47-50. doi: 10.1080/03630269.2020.1729175.

[17] Shabbir S, Nadeem M, Sattar A, Ara I, Ansari S, Farzana T *et al*. Type and frequency of hemoglobinopathies, diagnosed in the area of Karachi, in Pakistan. Cogent Medicine. 2016 Dec; 3(1): 1188875. doi: 10.1080/2331205X.2016.1188875.

[18] Khan K and Zahoor S. Pattern of Hemoglobinopathies on HPLC among patients referred to selected centers in Peshawar, Pakistan. Rawal Medical Journal. 2018 Oct; 43(4): 623-6.

[19] Waheed U, Satti HS, Farooq N, Zaheer HA. Frequency of haemoglobinopathies: a single-centre, cross-sectional study from Islamabad, Pakistan. EMHJ-Eastern Mediterranean Health Journal. 2012; 18(12): 1257-9. doi: 10.26719/2012.18.12.1257.

[20] Riaz H, Shah MA, Rehan G, Azeem R. Types and frequency of hemoglobinopathies, diagnosed by HB electrophoreses in the lady reading hospital Peshawar, Pakistan. Khyber Journal of Medical Sciences. 2020 Jan; 13(1): 39-42.