Original Article

FREQUENCY OF HEMOGLOBINOPATHIES AND ITS RELATION WITH CONSANGUINITY AT TWO HEALTHCARE CENTERS OF PESHAWAR

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ABSTRACT

Background: One of the most prevalent genetic disorders and major problems in Pakistan is hemoglobinopathies. Every year, 5,000 additional patients are added to the pool. Considering the medical and social implications of this familial condition, it is important to evaluate the prevalence of hemoglobinopathies across members of the family.

Material and Methods: This cross-sectional study included 263 samples with the diagnosis of anemia and complete blood count referred for screening of HB disorder from March 2021 to February 2022 at two general hospitals Rehman medical institute (RMI) and Peshawar Institute of medical sciences (PIMS). The institutional review board approved the study then blood specimens were collected in EDTA anti-coagulated tube: a complete blood picture with a peripheral blood smear was stained with a Leishman stain was performed. Hemoglobin electrophoresis was performed at pH 8.8 (Fisher Biotech) using a commercially available electrophoresis kit.

Result: Out of 263 Samples, Hemoglobinopathies affected 111(42.2%) people; the remaining 152(57.8%) people had a normal profile of Hb Electrophoresis. Of these 111 people with hemoglobinopathies, 86 (32.7%) had minor B-thalassemia and 22 (8.4%) had major B-thalassemia, while the rate of recurrence of sickle cell disease was 3 (1.1%). Among these, 40.3% of patients' parents are relatives with which consanguinity frequency was 37.3% and 22.4% of patients' parents are not relatives or cousins.

Conclusion: According to our research, cousin marriages frequently have a significant role in the development of B thalassemia minor, which affects the majority of patients. Relatives of known cases of thalassemia can be screened for hemoglobinopathies to reduce the financial and medical burden of transfusions and treatment.

Key Words: Electrophoresis, Hemoglobinopathies, Thalassemia, Sickle cell disease

doi: https://doi.org/10.51127/JAMDCV5I2OA06

How to cite this:
Tariq M, Rehman F, Rahman A, Hanif M, Umar S, Abid S. Frequency of hemoglobinopathies and its relation with consanguinity at two healthcare centers of peshawar. JAMDC. 2023;5(2): 97-101
doi: https://doi.org/10.51127/JAMDCV5I2OA06

INTRODUCTION

Sickle cell diseases (SCDs), α and β-thalassemia, and other inherited blood illnesses known as hemoglobinopathies are caused by abnormalities in the globin genes.[1] Hemoglobinopathies are a genetic disorder of the globin component of the hemoglobin protein. genetic modification of the globin protein code that alters protein output produces thalassemia syndrome.[2] They currently occur most commonly in the tropical belt; a type of micro mapping will be necessary to determine their true prevalence and the likely cost of management for the governments of these countries.[3] Sickle cell disease (SCD) is a term used to describe a collection of inherited blood disorders characterized by chronic anemias and a variety of acute and chronic issues, such as

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episodes of discomfort, strokes, and early death.[4]

Thalassemia, which is a widespread genetic illness around the world, is mostly caused by a variety of mutations in the globin genes. Though it varies greatly from region to region, Iran has a high gene frequency of -thalassemia. The North and South coasts show the highest prevalence, which can exceed 10% in some places. Iran has more than 50 distinct mutations, which shows how the population's genotype is diverse.[5,6] One of the most common heredity hemoglobinopathies in Pakistan is thalassemia major (TM). With an essential 100,000+ current cases. It has one of the largest prevalences of transfusion-dependent TM patients worldwide.[7]

Some Hemoglobinopathies particularly having mutations in regulatory regions such as promoters and enhancers alters the globin protein production and leads to a well-known disorder thalassemia syndrome. If mutations are in the regulatory regions of globin, then globin proteins are normally made but at a modified rate. On the contrary, if the mutations are in the coding regions, then proteins may be produced in normal amounts, but proteins will not be normal as amino acid sequences are altered and lead to a decrease in the quality of globin proteins. Quantitative defects present as thalassemia, while the qualitative changes are collectively known as Hb variants, which result in great health problems ranging from sickle cell disease to unstable Methemoglobinemia encompassing many variants.[8] There have been more than 200 distinct point mutations and uncommon deletions of the gene described to date. Consanguineous marriage patterns, high birth rates, high fertility rates, poor levels of education, and early marriages without consent have contributed to Pakistan having one of the highest rates of transfusion-dependent Thalassemia in the world. A lack of screening facilities and 40% of cousin marriages in cultural norms have increased the likelihood of congenital transfer of the thalassemia trait.[9]

Our main purpose of the study was to discover the different types of hemoglobin disorders, consanguinity ratio, and their prevalence of Peshawar in the northern part of Pakistan which may be beneficial in various techniques for potent management and prevention of this hereditary disease in the general population of Khyber Pakhtunkhwa

MATERIAL AND METHODS

This cross-sectional study included 263 samples with the diagnosis of anemia and Complete Blood Count (CBC) referred for screening of Hb disorder from March 2021 to February 2022 at two general hospitals Rehman Medical Institute (RMI) and Peshawar Institute of Medical Sciences (PIMS). A reference lab that gets samples for the evaluation and diagnosis of hemoglobinopathies from the OPD and numerous minor labs. The study was given institutional review board approval, and after obtaining patient consent, information about their age, gender and marital status (consanguinity) was recorded.

Blood samples were collected from patients of low HB, with suspicion of hemoglobinopathies who visited these two healthcare hospitals. Using a completely automated blood cell counter, samples were examined within 120 minutes of being taken. (Sysmex KX-21), Leishman's stain was used to stain peripheral blood smears, and the conventional criteria were followed for evaluating the presence of hyperchromasia, anisocytosis, microcytosis, macrocytosis, and polychromasia.

For Thalassemia and sickle cell anemia samples, hemoglobin electrophoresis was performed at pH 8.8 (Fisher Biotech) using a commercially existing electrophoresis set with a cellulose acetate membrane in a tris-EDTA-borate buffer. Band density is measured by the Turboscan Digital Densitometric Analysis System (Fisher Biotech). Beta-thalassemia symptoms are considered present if the HbA2 measurement is greater than 3.5%. Red blood cell counts are positive for thalassemia in all

circumstances where the HbA2 gene is elevated.

RESULT

There were 140 (53.2%) Females and 123(46.8%) males in this study. Among these patient's majority were children (1-10 years) 85 (32.4%), Adults (18-30 years) 28 (10.7%), and more than 30 years old 58 (22.1%), Infant (1-12 months) 28 (10.7%), 12-18 years' children's 20 (7.6%). The socio-demographic profile has been identified in (Table-1). Out of 263 Samples, Hemoglobinopathies affected 111(42.2%) people; the remaining 152(57.8%) people had a normal profile of Hb Electrophoresis. Of these 111 people with hemoglobinopathies, 86 (32.7%) had minor B-thalassemia and 22 (8.4%) had major B-thalassemia, while the rate of recurrence of sickle cell disease was 3 (1.1%). Diverse Hemoglobinopathy wise distributions are shown in Table-2.

Among these 111, 40.3% of patients' parents are relatives with which consanguinity frequency was 37.3% and 22.4% of patient's parents are not relatives or cousins. The parent's relative, consanguinity frequency was described in table-3.

Table-1: Socio-demographic profile of study participants

		Frequency	Percent
Gender	Female	140	53.2
	Male	123	46.8
	Total	263	100
Age	1-10 years	82	31.1
	18-30 years	72	27.3
	Above 30 years	59	22.3
	1-12 months	29	11
	12-18 years	21	8
	Total	263	100

Table-2: Diverse Hemoglobinopathy in study participants

	Frequency	Percent
Normal patients	152	57.8
Beta thalassemia minor	86	32.7
Beta thalassemia major	22	8.4
Sickle cell disease	3	1.1
Total	263	100.0

Table-3: Consanguinity Frequency in study participants

	Frequency	Percent
Relatives	106	40.3
Cousins	98	37.3
Not relatives or Cousins	59	22.4
Total	263	100.0

DISCUSSION

In Pakistan, family marriages are more frequent, particularly marriages to first cousins who have a family history of hemoglobinopathy while also being homozygous. Thalassemia is the most prevalent hemoglobin disorder in one situation. There are more than 5000 homozygotes born in Pakistan every year, and they may be found all around the nation. In numerous areas of the country, the prevalence of Carriers varies from 4.0% to 5.0% for various populations. A family with a main patient of beta thalassemia is more likely to have more than 30% carriers.[10] In our study 111 (42.2%) people with hemoglobinopathies, 86 (32.7%) had minor B-thalassemia, and 22 (8.4%) had major B-thalassemia, while the rate of recurrence of sickle cell disease was 3 (1.1%). According to a study done in Lahore, the prevalence of various thalassemia diseases is 61%, with - Thalassemia trait at 51.9%.[9] Thalassemia major and minor were highly common at; 36.5% (n=301) and 47.5% (n=301)

respectively.[11] According to a 2020 study by Huma Riaz, 115 (32.9%) patients received a diagnosis of beta thalassemia trait, 45 (12.9%) patients received a diagnosis of beta thalassemia major, and 3 (0.8%) patients received a diagnosis of sickle cell anemia.[8] Which is close to our result. First cousin marriages accounted for 68.69% of consanguineous unions in the Moroccan study and 49 (18.1%) families had more than one child with thalassemia major. The study found that the rate of consanguinity in the parents' generation of children with hemoglobinopathies was 50.25 percent.[12,13] And according to our study 40.3% of patients' parents are relatives with which consanguinity frequency was 37.3%. Another study was conducted in Karachi, where minor beta thalassemia made up 51.8% of cases, major beta thalassemia 24.1%, HbD trait 6.7, sickle cell disease 3.9%, and sickle/beta thalassemia 4.5%. Another investigation was conducted in western Iran, where 56 (16.2%) of the patients had minor beta thalassemia.[2,14] Hemoglobinopathies were reported to affect 3.7% of the population in the 2014–15 Brazilian National Health Survey. Thalassemia mild (0.30%), probable thalassemia major (0.80%) and sickle cell trait (2.49%) were the most prevalent.[15] According to a study done in Saudi Arabia, the prevalence of the -thal trait is higher in the adult population of Al Majma'ah than that of the sickle cell trait[16] In 2018 another study conducted in Islamabad in which out of the 175 participants, 33 (or 18.9%) had hemoglobinopathies. the most common hemoglobinopathies were thalassemia major 8 (4.6%) and thalassemia trait 18 (10.1%).[17] Additionally, this research supports the hypothesis that thalassemia minor is the most prevalent hemoglobinopathy in Pakistan.

Although precise statistics on the prevalence of hemoglobin disorders in Pakistan are not yet available, it is possible to reduce their vertical transmission by conducting population surveys, inductive screenings using the HPLC technique and special care facilities in major cities that provide access to genetic counseling, prenatal diagnosis, genetic studies, diagnostic services, and treatment using cutting-edge techniques for restriction enzyme analysis and management. Young individuals must become aware of their carrier status as early as possible to weigh all of their options, including getting married and having children.

CONCLUSION

According to our research, cousin marriages frequently have a significant role in the development of B thalassemia minor, which affects the majority of patients. Relatives of known cases of thalassemia can be screened for hemoglobinopathies to reduce the financial and medical burden of transfusions and treatment to create a regional database, further investigation on the prevalence of various features is needed.

AUTHOR'S CONTRIBUTION

MT: Manuscript writing & data collection
FR: Conceived design, and final approval
AR: Performed data analysis
MH: Manuscript writing
SU: Manuscript writing
SA: Performed data analysis and data collection

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