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Frequencies of Hemoglobinopathies in Pakistan: A Single Center Study

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Abstract

Objectives: This study aimed to determine the frequencies of different hemoglobinopathies to assess the disease burden in our population.
Methodology: We conducted a descriptive cross-sectional study at The CITI Lab in Rawalpindi from August 2021 to November 2024. After obtaining clinical and family histories, we evaluated 5,961 patients. Laboratory analysis included complete blood count using a Beckman Coulter UniCel DxH 800 analyzer, red blood cell morphology examination through Giemsa-stained peripheral smears, and hemoglobin electrophoresis performed on a Sebia Capillarys 2 Flex Piercing system.
Results: Among 5,961 cases analyzed, 5,254 (88.14%) showed normal results while 707 (11.86%) demonstrated hemoglobinopathies. The most frequent abnormality was beta thalassemia trait (9.5%), followed by Hb D trait (1.39%), thalassemia major (0.64%), thalassemia intermedia (0.07%), sickle cell trait (0.07%), Hb E trait (0.07%), Hb D/beta thalassemia (0.05%), fast-moving hemoglobin variants (0.05%), sickle cell disease (0.02%), and Hb E/beta thalassemia (0.02%).
Conclusion: The high prevalence of hemoglobinopathies in Pakistan appears strongly associated with consanguineous marriages, limited health literacy, socioeconomic challenges, and inadequate access to healthcare services. We recommend implementing comprehensive public health strategies including population education initiatives, expanded screening programs particularly in high-prevalence regions, and enhanced genetic counseling services to mitigate this growing health burden.
Keywords: Thalassemia, sickle cell disease, hemoglobinopathies, prevalence, capillary electrophoresis

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Introduction

The hemoglobinopathies are the genetic diseases of hemoglobin which fall into two main groups: thalassemia syndromes (α and β thalassemia) and structural hemoglobin variants (HbS, Hb D, HbE and HbC).[1] They have autosomal recessive pattern of inheritance and carriers are usually silent. α and β thalassemia are caused by decreased production of alpha and beta chains respectively whereas structural variants are caused by amino acid substitution in beta globin chains. In sickle cell disease glutamic acid is replaced by valine at position 6, in Hb C glutamic acid is replaced by lysine at position 6, in Hb D glutamic acid is replaced by glutamine at position 121 and Hb E is caused by replacement of glutamic acid by lysine at position 26.

Beta thalassemia can be further divided into thalassemia minor, intermedia and major depending upon the amount of globin chain produced. Alpha thalassemia which is caused by decreased production of alpha chains is common in Southern China and South East Asia and cannot be diagnosed by Hb Electrophoresis.

In world there are 269 million carriers of hemoglobinopathies and therefore they are regarded as the most prevalent genetic defect. About 5% of population of the world has a gene for sickle cell anemia or thalassemia, this percentage can reach up to 25% in some regions.[2] Mediterranean, Middle East, Indian subcontinent, Southeast Asia and South China regions show a high incidence of thalassemia carriers.[3] In Iraq beta thalassemia is the most prevalent hemoglobinopathy. The frequency of beta thalassemia trait in Iraq is 3.7-6.9% and sickle cell trait is 0.06-1.2%.[4] In India the prevalence of beta thalassemia trait is 3-4% however in some ethnic groups this percentage increases up to 8%.[5]

Beta thalassemia major is an inherited disorder that requires lifelong red blood cell transfusions and iron chelation therapy.[6] Sickle cell disease is also a genetic disorder whose complications start to manifest in childhood.[7] Sickle cell anemia is common in areas like Africa, the Middle East and parts of India.[8] In Pakistan sickle cell anemia is common in Layari (Karachi), in some

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areas of Khyber Pakhtunkhwa (KPK) and Balochistan. Due to the severity of these diseases it is important to detect the traits so that we can halt the inheritance to future generations.

The estimated population of Pakistan is approximately 225 million.[9] The frequency of beta thalassemia trait in Pakistan is 5-8% and each year 5000 children are born with thalassemia major which puts a significant burden on our health care system.[10] Families with consanguineous marriages have high incidence of having beta thalassemia major children. Most of population in Pakistan belong to lower socioeconomic class so blood transfusion is the mainstay of management in these cases.[9] Parents of these children face physical, emotional and financial challenges.[11] Currently in Pakistan some legislation has been approved for premarital screening in its provinces Sindh, KPK and Baluchistan but implementation of this legislation is still an issue.[9]

Furthermore in Punjab (which is a highly populated province) only one government funded project exists" Punjab Thalassemia Prevention Program" which is providing services for beta thalassemia screening and prenatal diagnosis.[10] The aim of the study is to determine the frequencies of different hemoglobinopathies so that disease burden can be identified.

Methodology

A descriptive cross-sectional study was conducted at The CITI Lab, Rawalpindi from August 2021 to November 2024 after ethical approval from institutional review board. The WHO sample size calculator was used to determine the sample size, based on population prevalence of 9.7%, with a confidence interval of 95% and a margin of error of 5%. Five thousand nine hundred and sixty-one (5961) referred cases for Hb electrophoresis from all collection points were included in study using non probability consecutive sampling. Verbal consent was taken from patient while taking the history.

Detailed history like patient age, gender, history of blood transfusion, consanguinity and family history of hemoglobinopathies were noted. Patients with recent history of blood transfusion within 3 months were excluded. Physical examination for splenomegaly was done. Three ml of blood sample was collected in EDTA and analysed on automated hematology analyzer (Beckman Coulter unicel DxH 800) to determine peripheral cell counts and RBC indices. Peripheral blood smear was examined for red blood cells morphology. Hb electrophoresis was carried out on Sebia Capillary 2 Flex- piercing (SEBIA capillary electrophoresis system). Recommended cut off points for different variants were considered using standard recommended guidelines. Quantitative variables like frequency of different hemoglobin variants were calculated. Data was analyzed using Libre Office Calc software (version 24.2.6.2). Prevalence of hemoglobinopathies was calculated in percentages and data was presented in form of tables and pie charts.

Results

A total of 5961 blood samples were received for hemoglobin electrophoresis during the study period. Out of which 5254 cases (88.14%) were normal and 707 cases (11.86%) had hemoglobinopathies as shown in figure 1.

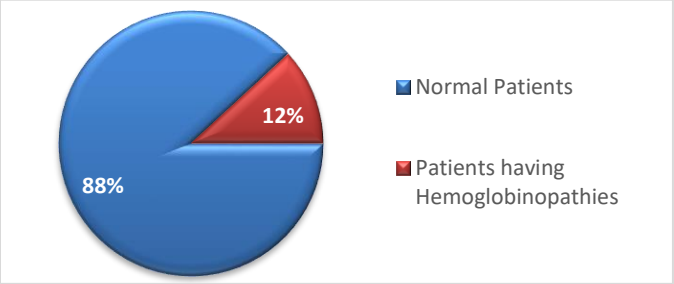

Figure 1. Patients affected by Hemoglobinopathy

Table 1: Prevalence and Distribution of Hemoglobinopathies

Hemoglobinopathy Type	N	(%)	Distribution (%) (Out of abnormal cases)
Beta Thalassemia Trait	566	9.50	80.06
Hb D Trait	83	1.39	11.74
Thalassemia major	38	0.64	5.37
Sickle Cell Trait	04	0.07	0.57
Sickle Cell Anemia	01	0.02	0.14
Thalassemia Intermedia	04	0.07	0.57
Hb E Trait	04	0.07	0.57
Fast Bands	03	0.05	0.42
Hb D/ Beta Thalassemia	03	0.05	0.42
Hb E/ Beta Thalassemia	01	0.14	0.14

Beta thalassemia trait was found in 566 patients (9.5%), Hb D in 83 patients (1.39%), thalassemia major in 38 patients (0.64%), thalassemia intermedia in 4 patients (0.07%), sickle cell trait in 4 patients (0.07%), sickle cell anemia in 1 patient (0.02%), Hb E trait in 4 patients (0.07%), Hb D/ Beta thalassemia in 3 patients (0.05%), Hb

E/ Beta Thalassemia in 1 patient (0.02%) and fast moving bands were also seen in 3 patients (0.05%). Table I

Among 707 patients about 80.06% patients were beta thalassemia trait, 11.74% Hb D trait and 5.37% beta thalassemia major as shown in figure 2. Table 1 shows the prevalence of hemoglobinopathies in study population and the distribution of hemoglobinopathies among 707 affected patients.

Discussion

Hemoglobinopathies are a group of genetic disorders with autosomal recessive pattern of inheritance. Our study showed that the prevalence of various hemoglobinopathies was 11.86% which was close to studies done in Indus hospital Karachi (14.5%)[12], Shaukat khanum hospital Lahore (9.7%)[13] and India (11.26%)[14] whereas studies done by Hussain et al (75.6%), Riaz et al (48.9%), Ghani et al (40%) and Shabbir et al (34.2%) showed high prevalence of hemoglobinopathies. [15-18.]

The most predominant hemoglobinopathy in our study was beta thalassemia trait followed by Hb D trait. Beta thalassemia trait prevalence in our study was 9.50% which was slightly higher than the studies done in Indus Hospital (6.4%) and Shaukat Khanum hospital (5.0%).[12,13] Prevalence of beta thalassemia trait in our study was also higher than some of our neighbouring countries like India (4.52%)[14], Bangladesh (4.1%)[19] and Iraq (3.7-6.9%).[4]

However it was lower than some studies conducted at Peshawar(32.9%)[18], Karachi (19.6%)[20] and Islamabad (25.6%).[2] Hb D trait in our study was 1.39% which was similar to values of Hb D trait seen from Dow Hospital (1.3%), Chughtai lab (1.11%) and Shaukat khanum hospital (1.5%)[13,20,21] whereas studies done in Dera Ismail Khan (0.3%) and Peshawar(0.2%) showed low values of Hb D trait. [16,18]

The frequency of beta thalassemia major in our study was low (0.64%) as compared to some other studies done in Dera Ismail Khan (29%)[16], Karachi (20.6%)[15] and Peshawar(12.9%)[18] but was similar to the frequency of beta thalassemia major seen in Shaukat Khanum hospital (0.37%)[13] and India (0.94%).[22] The frequency of thalassemia major might have been reduced because of awareness and preventive strategies being employed among study population. Sickle cell trait and sickle cell anemia frequency was low in our study. Studies from Indus Hospital and Iraq also showed low frequency for defective sickle genes.[4,12] Low frequency of sickle cell disease was seen because our study was not done near sickle cell prevalent areas of KPK and Karachi as shown by some studies.[15,16]

The studies conducted in Pakistan over the years showed that the frequency of hemoglobinopathies had reduced in Pakistan in some places mostly in urban areas but rural areas and areas with poor access to health facilities are still having high frequency of hemoglobinopathies. Most of the studies conducted in Pakistan showed that the hemoglobinopathy frequency in Pakistan is still more than our neighboring countries (Iraq, Bangladesh, India).

The main cause of high frequency of hemoglobinopathies in Pakistan is illiteracy, poverty, poor access to health facilities and consanguineous marriages. Therefore, in order to reduce the disease, burden we need to put more effort to educate our people about hemoglobinopathies and introduce not only antenatal screening but also premarital screening although legislature has already been approved but no practical steps are taken especially in rural areas. Population screening can be done but is less powerful and is not cost effective. Family studies of affected children should be done. Premarital and antenatal screenings should be done in relatives of affected children.[23]

Limitation: There was sample bias as our study was not done on general public but on patients that presented to us for antenatal screening or as a part of anemia work up.

Conclusion

Hemoglobinopathies put a lot of burden on Pakistan which is a poor country so as to avoid this we need to educate our people and screen them for hemoglobinopathies. Screening entire population is not efficient and cost effective so antenatal and premarital should be done. Family screening of index cases should be done. Population screening can be done by government only in disease prevalent areas because undetected carriers can become a source of homozygous hemoglobinopathies especially in cousin marriages. If these measures are not taken in near future, hemoglobinopathies will remain endemic in our country.

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