Original article

Spectrum of Haemoglobinopathies in Population of Lahore District

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ABSTRACT

Background: Haemoglobinopathies describe a group of genetic disorders in which one or more globin chains are abnormally developed. Thalassemias are a common cause of hypochromic microcytic anemia, which arises from the reduced or absent synthesis of the globin chain of haemoglobin. Studies from various regions of Pakistan have indicated variable prevalence of the disease in Pakistani population with significant ethnic and geographical variations. This study was conducted to find the range of haemoglobinopathies among the population of Lahore District.

Patients and Methods: It was a descriptive cross-sectional study conducted at Haematology, Pathology Department, SIMS/Services Hospital, Lahore from 18-3-2021 to 18-9-2021. 364 Patients with both genders and age 1-65 years presenting with anaemia were enrolled in this study. A 5ml sample of intravenous blood was drawn and placed in an EDTA anticoagulant container. The data was analyzed using Statistical Package for Social Sciences (SPSS) version 22. Quantitative variables including age, haemoglobin was described as mean ± Standard Deviation, while qualitative variables including gender, haemoglobinopathies and their spectrum were described using frequencies and percentages.

Results: In this study the mean age of the patients was 18.18±13.92 years, 169 (48.84%) patients were male and 177(51.16%) females. The frequency of haemoglobinopathies was found in 76 (21.97%) patients. The most common spectrum of haemoglobinopathies was beta thalassemia trait found in 52 (68.42%) patients followed by Beta thalassemia major 6 (7.89%) and HbD Punjab trait 4(5.26%).

Conclusion: This study concluded that the frequency of haemoglobinopathies was 21.97% and the most common spectrum of haemoglobinopathies was Beta thalassemia trait followed by Beta thalassemia major & HbD Punjab Trait in patients referred to Haematology, Pathology Department, Services Hospital Lahore for workup of anaemia.

Keywords:

Haemoglobinopathies, Spectrum, Anaemia

INTRODUCTION

Haemoglobinopathies are inherited recessive disorders of globin gene. Haemoglobinopathies encompass all genetic disorders of the haemoglobin and are categorized into two types. These include less production of haemoglobin (thalassemia and its variants) and structurally abnormal haemoglobin variants. [1]

Haemoglobinopathies are the most common monogenic inherited disorders of the haemoglobin. Distribution of these disorders is highly variable between various geographical regions. Migration of human population among various regions and consanguineous marriages has led to increased burden of haemoglobinopathies across the globe.[2] The World Health Organization (WHO) estimates that 5.2% of all individuals worldwide carry defective haemoglobin. Around 3.4% of fatalities in children under the age of five are caused by inherited hemoglobin abnormalities.[3]

Three (3%) of the world population carries gene for beta-thalassemia and annually 60000 children with beta-thalassemia are born all over the world. Carrier rate of beta-thalassemia in Pakistan ranges between 5 – 8 % and approximately 5000 new cases are diagnosed each year. [4] The prevalence of α and β-thalassemia trait is 35.27% and highest in Badin District, Sindh while in ethnic-wise distribution, higher numbers of α- and β-thalassemia trait cases are seen in the Sindhi ethnic group.[5] In northern areas of Pakistan, overall prevalence of haemoglobinopathies is 25.69%. Distribution of thalassemia was general compared to abnormalities of haemoglobin chains mainly observed in tribal areas only. Beta-Thalassemia accounted for 83.23% of the cases (mostly homozygous) while structurally abnormal haemoglobin was observed in only 16.73% of the cases.[6]

Conflict of interest: The authors declared no conflict of interest exists.
Citation: Rahim A, Munir A, Bashir F, Zafar F, Zahid, Haseeb HM. Spectrum of Haemoglobinopathies in Population of Lahore District. J Fatima Jinnah Med Univ. 2023; 17(2):72-75.

DOI: https://doi.org/10.37018/JFJMU/ARR/9922

In a retrospective study conducted at National Institute of Blood Disease & Bone Marrow Transplantation, Karachi for the workup of anaemia or other blood-related disorders, haemoglobinopathies were reported in 34.2% of the patients. The commonest haemoglobinopathy was β-thalassemia major (51.8%) followed by β-thalassemia minor (24.1%) and HbD Trait in 6.7% of the cases. Sickle beta-thalassemia was reported in 4.5%, sickle cell disease in 3.9%, HbE trait in 1.9% and sickle cell trait in 1.7% cases only. [7] The prevalence of haemoglobin disorders in Peshawar is 40.30%. Thalassemia trait was the most prevalent disorder making 78.5% of the cases followed by thalassemia major in 11% of the diagnosed cases. HbD Trait was reported in 1.8%, HbD disease in 0.3%, HbE trait in 1.5%, HbE disease in 0.9%, sickle cell trait in 1.3% and sickle cell disease was found in 1.5% of the patients. [8]

PATIENTS AND METHODS

This descriptive cross sectional study was conducted at Haematology, Pathology Department, SIMS/Services Hospital, Lahore from 18-3-2021 to 18-9-2021. Following inclusion criteria 346 patients were enrolled after taking informed consent. A 5ml sample of intravenous blood was drawn and placed in an EDTA anticoagulant container. On an automated haematology analyzer, red cell indices were measured. The chromatographic separation of haemoglobin using high performance liquid chromatography enabled the study of HbA, HbA2, HbF, and other structural haemoglobin variants. Patients of both gender and age 1-65 years presenting with anaemia were enrolled in this study. Male patients with Haemoglobin less than 13g/dl and female patients with Haemoglobin less than 12g/dl were included. Pregnant females with Haemoglobin less than 11g/dl were enrolled. Children with Haemoglobin 2 Standard deviation below the mean Haemoglobin concentration for that age were included in our study population. The data was analyzed using Statistical Package for Social Sciences (SPSS) version 22. Quantitative variables including age, haemoglobin were described as mean ± Standard Deviation, while qualitative variables including gender, haemoglobinopathies and their spectrum were described using frequencies and percentages. Data was stratified by age, gender and weight. Post stratification chi square test was applied taking p-value ≤ 0.05 as significant.

RESULTS

Out of 346 cases, 76 (21.9%) patients had haemoglobinopathies, rest of the 270 patients had normal HPLC pattern. (Table 1) The age- and gender-wise distribution of the patients with haemoglobinopathies is described in (Table-2)

In this study the most common haemoglobinopathy was beta thalassemia trait found in 52(68.42%) patients followed by Beta thalassemia major and HbD-Punjab trait found in 6(7.89%) & 4(5.26%) patients respectively. HbE heterozygous, HbS trait, Beta-thalassemia intermedia, HbD-Punjab, HbJ, HbH & HbS was noted in 3(3.95%), 3(3.95%), 2(2.63%), 2(2.63%), 2(2.63%), 1(1.32%) and 1(1.32%) patients. (Fig 1)

Table 1: Frequency distribution of demographic characteristics and CB findings

Characteristics	Presence (Mean ± SD)
Age	
Mean ± SD	17.33 ± 13.19
Gender	
Male	169 (48.84%)
Female	177 (51.16%)
RBC Count(10⁶/µl)	4.52 ± 0.99
Hemoglobin (g/dl)	8.31 ± 2.9
MCV (fl)	62.9 ± 9.4
MCH (pg)	18.7 ± 4.63
MCHC(g/dl)	28.83 ± 4.67
RDW (%)	20.41 ± 4.92
Haemoglobinopathy	
Yes	76 (21.97%)
No	270 (78.03%)

Table 2: Comparison of Haemoglobinopathies between age groups and Gender

		Haemoglobinopathies		Total	P-value
		No	Yes		
Age Groups	≤ 25	185 (80.4%)	45 (19.6%)	230 (100%)	0.159
	>25	85 (73.3%)	31 (26.7%)	116 (100%)	
Gender	**Male**	140 (79.1%)	37 (20.9%)	177 (100%)	0.975
	Female	130 (76.9%)	39 (23.1%)	169 (100%)	

Spectrum of Haemoglobinopathies												
		A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	
Age Groups	≤ 25	2	6	29	3	1	2	1	0	1	0	0.534
	>25	0	0	23	1	1	1	0	2	2	1	
Gender	**Male**	0	4	30	3	1	1	0	0	0	0	0.014
	Female	2	2	22	1	1	2	1	2	3	1	

[A= Beta Thalassemia intermedia; B=Beta Thalessemia Major; C=Beta Thalessemia Trait, D= HbD Punjab Trait, E=HbD Punjab, F=HbE Heterozygous, G=HbH, H=HbJ, I=HbS Trait, J= Sickle cell Anaemia]

Figure 1: Frequency Distribution of Spectrum of Haemoglobinopathies

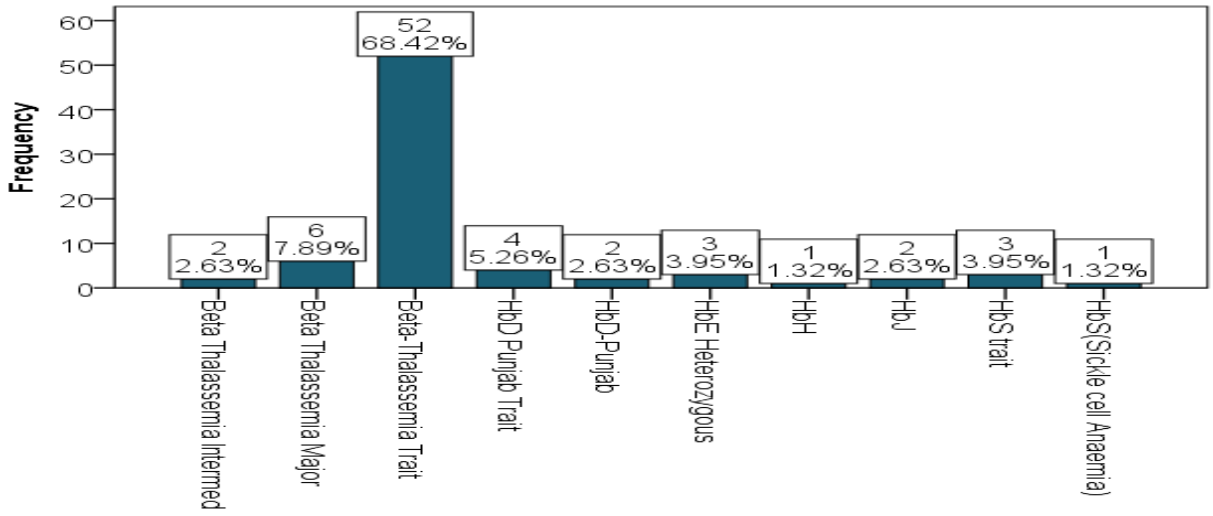

Table 3: Haematological Features of various haemoglobinopathies

Phenotype	Age (years)	RBC 10^6/µl	Hb (g/dl)	MCV (fl)	MCH (pg)	RDW (%)	HbA (%)	HbA2 (%)	HbF (%)	Others (%)
Beta - thalassemia trait	22.8±13.2	5.6±0.9	9.9±2.0	59.6±9.7	18.6±3.3	19.8±3.6	93.4±1.3	5.2±0.8	1.3±0.9	
Beta -Thalassemia Major	1.83±1.0	2.9±0.7	5.8±1.2	62.5±4.6	21.5±4.7	32.9±8.7	1.3±0.5	2.0±0.9	95.7±1.2	
HbD trait	20.7±10.5	4.2±0.5	7.0±1.2	59.3±4.2	16.4±1.3	31.9±7.1	64.2±5.8	2.5±0.7	0.65±0.4	HbD 24.2±13.7
HbE trait	11.6±15.9	4.4±0.9	8.5±4.1	70.5±19	21.1±9.5	21.2±7.4	59.9±4.9	2.6±0.4	0.9±0.3	HbE 35.2±6.3
HbS trait	26.3±15.3	5.5±0.6	12.4±0.5	72.4±5.6	25.6±0.9	13.6±0.4	55.6±6.4	2.7±0.3	3.5±1.7	HbS 32.7±3.7
Beta – Thalassemia Intermedia	4.0±2.8	2.6±0.2	5.9±1.2	62.6±3.3	17.3±4.6	28.9±15	30.8±1.7	2.4±1.1	61.2±5.4	
HbD – Punjab	21.0±9.8	5.4±0.2	9.8±1.0	64.7±6.9	20.1±1.4	16.4±0.9		2.6±0.1	0.05±0.7	HbD 97±0.7
HbJ	33.5±2.1	6.1±0.7	12±0.1	73.3±4.4	22.2±1.3	22±0.7	56.5±0.7	1.5±0.0	21.4±0.4	HbJ 20.3±0.3
HbH	18	3.15	8.2	99	26	22.6	79	1.9	2.8	HbH 16.3
HbSS	60	2.76	9.1	96	33	17.2	5.8	1	32.8	HbS 59.5

Severe anemia was observed in Beta-thalassemia major and Beta Thalassemia Intermedia with Hb 5.8±1.2 and 5.9±1.2 respectively. Among all the haemoglobinopathies, HbJ showed highest red blood cell count 6.1±0.7. The lowest values of MCV and MCH were found in HbD trait 59.3±4.2 and 16.4±1.3. Beta -Thalassemia Major showed the highest RDW=32.9±8.7. (Table 3)

Average values of haemogram and HPLC results are described in Table 3.

DISCUSSION

Haemoglobin (Hb) is an iron-containing protein found in RBCs. The human body relies on it to carry oxygen to all of its cells. WHO estimates that 7% of the global population carries a mutation that might lead to a haemoglobin disease. Approximately 300,000-500,000 infants born each year with clinically severe haemoglobin abnormalities are born in low-income countries. Both quantitative and qualitative inherited haemoglobin abnormalities contribute significantly to human suffering. [9]

In this study the frequency of haemoglobinopathies was 21.97%. The most common was beta thalassemia trait found in 68.42% patients followed by Beta thalassemia major 7.89% and HbD Punjab trait 5.26%. In contrast the prevalence of hemoglobinopathies was found to be 14.5% in the study

by Mansoor et al, (2022) which is not indicative of true figures. Reason of this is attributed to Iron Deficiency Anaemia in study cohort which restricts reliability of results of HPLC. Beta thalassemia trait was found in most of the cases 6.4%.[10]

Sharma et al. found that hemoglobinopathy affected 27.71 % (97/350) of their research population. There were a total of 36 (37.1%) patients who had β-thalassemia trait, followed by 16 (16.49%) who had Sickle cell trait, 9 (9.28%) who had β-thalassemia major, and 7 (7.22%) who had Sickle/β-thalassemia. Male to female ratio was 1.4:1 with slight male preponderance. Majority of the haemoglobinopathies were found in the age group of 21-30 years. [11]

In a study by Tariq et al, (2023) haemoglobinopathy was observed in 42.2% of the total population. Beta-Thalassemia minor accounted for 32.7% of the cases, and 8.4% cases had major B-thalassemia. [12]

Shaikh et al, conducted a study to find the incidence of hamoglobinopathies with regards to geographical distribution. Out of 10,297 samples, hemoglobinopathies were found in 9.7% cases. The most prevalent hemoglobinopathy identified was beta thalassemia trait, with a prevalence of 5%, amongst which maximum number of cases were from Lahore district. The next most prevalent hamoglobinopathy found was sickle cell disease, with a frequency of 1.43%. Sickle cell trait, Haemoglobin-D Punjab trait, and compound heterozygote for sickle and beta thalassemia were the other significant hemoglobinopathies identified. [13]

The results of this study reinforce the finding that Thalasssemia is most frequent form of haemoglobinopathy in Pakistan. This study is a step ahead in continuing efforts regarding estimation of burden of disease in various populations for effective control and management of disease. Adequate steps such as public awareness, carrier screening, extended family screening of Thalassemia patients will help reduce extent of the disease and in alleviating mental, psychosocial trauma to patients and their families as well as expenditure on treatment.

CONCLUSION

This study concluded that haemoglobinopathies were found in 21.97% and the most common spectrum of haemoglobinopathies was beta thalassemia trait followed by beta thalassemia major & HbD Punjab trait.

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