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Frequency of carrier state of thalassemia and various hemoglobinopathies in tertiary care hospital of Pakistan.

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Abstract

Background: It has been estimated that 5% of the global population are carriers of Hemoglobin (Hb) disorders. These disorders may cause hemolytic anemia leading to the critical condition of the patients. The current research was designed to identify spectrums of thalassemia minor and carriers of other hemoglobinopathies patients presenting at the tertiary care center to evaluate anemia.

Methodology: A total of 3289 patients' data with low Hb values and suspicion of hemoglobinopathies were included in this cross-sectional retrospective study. Complete blood count (CBC), High-performance liquid chromatography (HPLC), and sickling test were utilized in this study. At the same time, Patients with normal Hb as per HPLC analysis were excluded from this study.

Results: Of the total, 708 (21.5%) patients had hemoglobin disorder and the mean age of patients with thalassemia minor was 24.0 ± 14.7 years. Out of 708 carriers, 646 (19.6%) cases showed traits of thalassemia minor, 12 (0.36%) showed Hb S trait, 43 (1.30%) showed Hb D trait, 07 (0.21%) showed Hb E trait, whereas there were no cases of Hb C recorded in this study.

Conclusion: Thalassemia trait was the highest among other variants in our study population. It is recommended that to decrease the frequency of hemoglobinopathies, pre-marriage screening should be conducted, and family marriages should be restricted.

Keywords

Hemoglobinopathies, Hemoglobin D, Hemoglobin E, Hemoglobin S, Thalassemia Minor

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Introduction

Disorders of hemoglobin (Hb), also called hemoglobinopathies, comprise thalassemia and other inherited disorders of Hb variants with defects in the folding structure of globin chain[1]. Hb is a tetrameric globular protein with two alpha and two beta chains composed of 141 and 146 amino acids. These chains are held together by noncovalent bonds. Each chain contains one heme group that consists of an iron molecule that binds to oxygen present in the center of the protoporphyrin ring. The alpha chain is present in different forms of hemoglobin, such as embryonic, fetal, and adult. However, the non-alpha chain includes the beta chain of adult Hbα2β2, HbA_2 Hbα2δ2, HbF, Hbα2γ2[2].

World Health Organization (WHO) has estimated that 5% of the worldwide population are carriers of Hb disorders (Executive board session 118th agenda point 5.2, 2006). These disorders may cause hemolytic anemia, leading to the critical condition of the patients, and may even cause death. Some geographical areas are at higher risk of having these genetic disorders, reaching up to 25%[3]. The expected carrier rate of hemoglobinopathies is 5–7% (9.8 million) in the entire population of Pakistan[4]. Thalassemia is defined as the decrease in the production of normal Hb due to the absence or reduction in the synthesis of globin chains. It is a heterogeneous group of inherited blood disorders, which may cause blood transfusion-dependent anemia[3].

Worldwide, the prevalence of thalassemia is about 5–8%, and it causes significant healthcare issues. It runs in families where intermarriages are shared[3]. To date, 1600 Hb variants have been recognized, and most of them are asymptomatic, but few variants produce symptoms that can be difficult to manage[5]. Furthermore, some variants are more prevalent in particular racial groups.

Overall, hemoglobinopathies cause anemia with divergent severity. The terminology of the various types of hemoglobinopathies is usually done according to the family name of the first discovered case or residence of the persons, e.g., Hb-Lepore and HbD-Punjab. Commonly studied variants are HbS, HbE, and HbC worldwide[5,6]. Regular revealing and documentation methods for Hb variants and β-thalassemia traits to prevent more problems such as thalassemia major (homozygous) are needed. Recently, screening programs for thalassemia in Pakistan's neighboring countries, namely, the Islamic Republic of Iran and Turkey, have presented a marked decrease in freshly recorded cases of thalassemia[3].

The current study was designed to identify spectrums of thalassemia minor and carriers of other hemoglobinopathies.

Methodology

A cross-sectional retrospective study was conducted on 3289 patients with anemia detected on complete blood count (CBC), from January 2017 to December 2017. Ethical clearance was obtained from Dow University of Health Sciences Institutional Review Board (IRB-1353/DUHS/Approval/2019 dated August 1, 2019).

Samples were collected to screen and diagnose hemoglobinopathies from DUHS hospital OPDs and (other than DUHS) laboratories and clinics from all over Karachi. Samples were received for testing of CBC, High-performance liquid chromatography (HPLC), and Sickling test. The samples were analyzed at Dr. Ishrat ul Ebad Khan Institute of Blood Disease (DIEKIBD), Dow University of Health Sciences Ojha Campus Karachi, Pakistan.

CBC was conducted on the Sysmex XN 1000 analyzer. HbA_2 value >3.5% was measured as a cut-off point for beta-thalassemia trait, and <50% was estimated as a cut-off point for carrier state of other hemoglobinopathies such as HbS, HbD, and HbE. Patients with normal Hb as per HPLC analysis were excluded from this study. SPSS version 21.0. was utilized for statistical analysis, and the data were presented as mean and standard deviation.

Results

Out of 3289 cases, 708 (21.5%) patients were carriers of various hemoglobinopathies. Mean age in the case of patients with thalassemia minor was 24.0 ± 14.7 years, Hb S was 13.8 ± 14.6 years, Hb D trait was 20.0 ± 13.8 years, whereas the mean age of Hb E trait was 16.0 ± 16.8 years. Out of 708 carriers, 646 (19.6%) cases showed traits of thalassemia minor, 12 (0.36%) showed Hb S trait, 43 (1.30%) showed Hb D trait, 07 (0.21%) showed Hb E trait, whereas there were no cases of Hb C recorded in this study.

Table 1: Age and gender wise distribution of patients with hemoglobinopathies

Hemoglobinopathies	β-thalassemia minor	HbS Trait	HbD Trait	HbE Trait
Age (years)	24.0±14.7	13.8±14.6	20.0±13.8	16.0±16.8
Female (N = 2098)	385(59.6)	04(33.3)	24(55.8)	05(71.4)
Male (N = 1191)	261(40.4)	08(66.7)	19(44.2)	02(28.6)

Values are given as mean±SD or n(%).

Table 2: Hematological parameters in common hemoglobinopathies

Hematological Parameters	β-thalassemia minor (N = 646)	HbS Trait (N = 12)	HbD Trait (N = 43)	HbE Trait (N = 7)
RBC ($\times 10^{12}$/L)	5.1±1.1	4.1±0.9	4.6±1.0	4.3±0.6
HGB g/dl	10.3±2.3	9.3±2.3	10.3±3.2	9.3±2
HCT (%)	33.2±7.5	29.3±6.9	33.6±9.2	30.3±4.6
MCV (fl)	65.3±8.5	71±10.8	72.8±14.0	70.4±9.5
MCH (pg)	20.3±3.0	22.7±4.4	22.6±5.8	21.6±3.9

Values are given as mean±SD.

Table 3: Hb electrophoresis results in various hemoglobinopathies

Hb Electrophoresis	β-thalassemia minor (n=646)	HbS Trait (n=12)	HbD Trait (n=43)	HbE Trait (n=7)
HbA%	90.6±15.1	54.5±22.2	66.5±10.1	69.6±26.5
HbA_2%	5±1.5	2.5±0.9	1.9±0.4	0.9±1.6
HbF%	3.3±11.3	8.5±9.9	0.7±1.0	0.5±0.4
HbS%	0.6±6.6	29.1±12.9	-	-
HbD%	0.3±4.9	-	31.2±10.1	-
HbE%	-	-	-	20.8±5.4

Values are given as mean±SD.

According to our results, the mean Hb level (%) was 10.3 ± 2.3, 9.3 ± 2.3, 10.3 ± 3.2, 9.3 ± 2.0 in thalassemia minor, HbS trait, HbD trait, and HbE trait, respectively. The mean value of RBC was found 5.1 ± 1.1 in thalassemia trait and 4.1 ± 0.9, 4.6 ± 1, and 4.3 ± 0.6 in Hb S, HbD, and HbE, respectively. The average value of mean corpuscular volume (MCV) was 65.3 ± 8.5 in thalassemia carrier, 71 ± 10.8 in HbS, 72.8 ± 14 in HbD, and 70.4 ± 9.5 in HbE. Table 3 shows the results of electrophoresis of Hb. The average HbA_2 level in thalassemia minor, HbS trait, HbD trait, and HbE trait was 5 ± 1.5, 2.5 ± 0.9, 1.9 ± 0.4, and 0.9 ± 1.6, respectively. HbS and HbD levels were also detected in minor thalassemia cases. HbF level was also seen in various traits (Table 3).

Discussion

Hemoglobinopathies are among the most frequent genetic disorders of the blood. In this study, we determined the rate of occurrence of different traits in multiple groups in extensive data. The incidence and prevalence of different types of hemoglobinopathies vary in other regions of the world[7,8]. The diversity is based on genetic variations in different ethnic and racial groups even within the same country[9]. Hb disorders have a recessive genetic origin and are categorized into structural variants and thalassemia. Carriers of single defective genes remain asymptomatic until two carriers marry, where the mutated gene will get expressed in 1 in every 4 of their offspring.

In this study, the overall occurrence of carriers of hemoglobinopathies was 21.5%, which is similar to a previous study conducted by Khan et al[10]. Another study by Shabbir et al. showed a frequency of 34.2% carriers, which is slightly higher than our study[4]. In this study, most cases were positive for the thalassemia trait, and the least cases were with the HbE trait (0.21%).

Thalassemia is common in the Southeast Asian and Mediterranean zones due to the lack of awareness and the closed family system where consanguineous marriages are preferred[11-13]. We identified more cases of thalassemia minor (19.6%), which is higher than that of a previous study conducted in Bangladesh (6.6%) and various Indian states (2.78–9.59%) respectively[14-16]. HbE is another major variant detected worldwide, and it is expressed with thalassemia that causes an extremely common condition known as HbE thalassemia.

While HbE thalassemia is a major medical issue in many parts of the world, especially in Asia, its homozygous and heterozygous states are relatively harmless[17]. In contrast to its common occurrence in the Indian subcontinent and throughout Southeast Asia, where it ranges from 23% to 66%[15], we found very few cases (0.2%) of HbE, consistent with Pakistan's reported cases [11,18]. Followed by thalassemia trait, HbD trait (1.3%) was most frequently recorded in this study; however, from sub-Saharan Africa to the Middle East and Indian subcontinent, it ranges from 5% to 40%[17].

According to gender-wise distribution, thalassemia minor (59.6% of the females and 40.4% of the males) and HbD (55.8% of the female and 44.2% of the male), previous studies conducted in NIBD, also showed female preponderance[4]. However, a previous study conducted by Khan K et al. and Yasmeen H et al. in Peshawar showed that the male population had more thalassemia minor and HbD[10,11]. Female preponderance is postulated due to the higher female population, level of awareness and availability of advanced diagnostic facilities in Karachi compared to other parts of the country. Another factor is negligence and restriction on females to healthcare facilities due to poor socio-economic background and literacy rate, particularly in rural areas of Pakistan[19,20].

Age-wise distribution of carriers of hemoglobinopathies was identified in this study with a mean age of around 24 years in thalassemia minor and HbD. In contrast, HbS and HbD mainly were found in adolescence, which is similar to the previous study[11]. Average Hb concentration revealed in thalassemia minor, and HbD trait cases were 10.3 g/dL which is slightly higher than other variants in this study, consistent with a study conducted by Greene et al. in India[21]. We found certain parameters of hemograms such as Hg and MCV decreased among various traits, which suggests that anemia should be investigated carefully.

Hb electrophoresis results identified HbA_2 level as higher in thalassemia minor than other variants of hemoglobinopathies. We found HbA_2 in sickle cell trait with a mean value of 2.5 ± 0.9. Sickle hemoglobin polymerization can be inhibited by HbA_2. Although our study is more related to a trait, it can be considered that patients with sickle cell disease can take benefit from high HbA_2, which was described by Griffin et al [22].

Conclusion

Thalassemia trait was the highest among other variants in our study population. It is

recommended that to decrease the frequency of hemoglobinopathies, pre-marriage screening should be conducted, and family marriages should be restricted. This strategy may help in the prevention of disease. Moreover, early detection and diagnosis can save thousands of lives, and the rate of survival and quality of life will be improved. However, our data is not reflective of the general population but a cohort of the patients diagnosed with anemia.

Conflicts of Interest

The authors have declared that no competing interests exist.

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