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Frequency of Hemoglobinopathies in Children Presenting with Pallor to Pediatrics Clinic HMC/IBP

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Abstract: The aim of this study was to collect data on different haemoglobin disorders in children who presented to the pediatric clinic at HMC/IBP with pallor and microcytic hypochromic anaemia on peripheral smears. This cross-sectional retrospective study was conducted in the HMC Pediatric IBP Clinic over a period of 4 years from 2018 to 2022. The blood samples were collected from patients with anaemia. All the data was analyzed using SPSS. A total of 48 children (21.6%) were diagnosed with various hemoglobinopathies, while 29 cases (13%) were classified as "undetermined" due to being borderline or requiring repeat electrophoresis. Additionally, 35 children (15.8%) were found to have other causes of anaemia. Hemoglobinopathies are a public health issue and more so in a resource-limited country like Pakistan. One of the contributing causes of anaemia in the pediatric age group is hemoglobinopathies.

Key Words: Beta Thalassemia, Hemoglobinopathies, Sickle Cell Disease, Anemia, Hb Electrophoresis

Introduction

Hemoglobinopathies and disorders related to globin genes encompass a broad range of genetic abnormalities that affect the structure or production of haemoglobin, an essential molecule found in red blood cells. These conditions have a significant global impact, with an estimated prevalence of approximately 7% (Origa, 2017). Thalassemia and sickle cell disease are the most commonly observed hemoglobinopathies, affecting a substantial number of individuals worldwide. Around 5% of the global population carries genes associated with these disorders, and in certain regions, the prevalence can reach as high as 25% (Akram, Khattak, Khan, & Khan, 2021). Thalassemia occurs as a result of imbalances in the synthesis of globin chains, whereas sickle cell disease is caused by a mutation in the beta-globin chain gene, leading to the distortion of red blood cells. These disorders give rise to various complications, including anaemia, excessive iron accumulation, and damage to multiple organs.

In Pakistan, beta thalassemia is the most prevalent form of hemoglobinopathy, accompanied by other variants such as HbS, HbE, and HbD-Punjab. The carrier rate for beta-thalassemia in the country is estimated to be around 5% (Hafeez, Aslam, Ali, Rashid, & Jafri, 2007). To prevent the occurrence of beta thalassemia major, primary prevention efforts are crucial, which involve raising awareness through campaigns and conducting premarital screening. Couples who carry the beta-thalassemia gene have a 25% risk of having a child with beta-thalassemia major (Akram et al., 2021). Screening programs utilize reliable laboratory methods to identify individuals who are asymptomatic carriers, and parameters like MCV and MCH measurements are valuable in identifying potential beta-thalassemia carriers (Hafeez et al., 2007).

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Limited research has focused on understanding the prevalence of hemoglobinopathies in specific regions, including Khyber Pakhtunkhwa. It is imperative to conduct thorough and comprehensive studies to gain a better understanding of the frequency and genetic variations of these disorders in remote areas. Such investigations are essential for informing policy decisions and improving the management and prevention strategies for hemoglobinopathies. The primary aim of this study is to assess the data pertaining to different haemoglobin disorders in children who displayed symptoms of pallor and microcytic hypochromic anaemia on peripheral smears and underwent haemoglobin electrophoresis at the pediatric clinic of HMC/IBP. By increasing awareness and promoting informed decision-making, this research aims to contribute to reducing the burden associated with haemoglobinopathies.

Material & Method

In this retrospective cross-sectional study, a total of 222 patients were enrolled between April 2018 and April 2022. All patients presenting to the clinic with symptoms of anaemia and microcytic hypochromic anaemia on smear were included in the study. The study was conducted in the pediatric department of the hospital, and a total of 222 patients were examined during the study period. Ethical approval was obtained from the hospital's review board prior to commencing the research. Patients aged between 6 months and 18 years were assessed for signs and symptoms of anaemia, as well as potential hemoglobinopathies, such as a family history of the condition, conjunctival pallor, irritability, hepatosplenomegaly, and failure to thrive. Initial laboratory investigations included a complete blood picture with red cell indices, haemoglobin (Hb) level, and mean corpuscular volume (MCV). If the Hb level was below 12g/dl, further investigations were conducted to determine the presence of hemoglobinopathies. Additional tests, such as haemoglobin electrophoresis (at alkaline pH), high-performance chromatography (HPLC), and sickling test, were performed on children to analyze their haemoglobin levels.

The laboratory tests for the complete blood picture, including red cell indices like haemoglobin (Hb) and mean corpuscular volume (MCV), were performed at the laboratory of HMC Hospital located in Peshawar. For the additional tests and haemoglobin studies, patients were referred to various reference pathology laboratories to undergo further investigations. All pertinent information, such as age, gender, and the specific type of haemoglobinopathy or disease, was carefully recorded and analyzed using the statistical package for social sciences (SPSS 21). The frequencies of the recorded data were expressed as percentages to present the findings accurately."

Results

During the duration of the research, a comprehensive examination was conducted on a total of 222 children at the outpatient department of Hayatabad Medical Complex Hospital. These children were clinically suspected of having anaemia and were advised a series of blood tests to diagnose hemoglobinopathies. Among the participants, there were 148 males (accounting for 65.9% of the sample) and 74 females (33.1%). The age range of the children varied from 6 months to 18 years, with an average age of 8.09±3.78 years. Figure 1 provides a visual representation of the frequency of different types of anaemia observed in pediatric cases, while Figure 2 presents the frequency of hemoglobinopathies. A total of 48 children (21.6%) were diagnosed with various hemoglobinopathies, while 29 cases (13%) were classified as "undetermined" due to being borderline or requiring repeat electrophoresis. Additionally, 35 children (15.8%) were found to have other causes of anaemia.

The most prevalent haemoglobinopathy identified was Beta-thalassemia trait (11.2%), followed by Beta Thalassemia Major (4.5%), Beta Thalassemia Major/Intermedia (2.7%), sickle cell disease (2.3%), sickle/beta-thalassemia (0.4%), and HbE (0.4%)

Figure 1

Frequency of Anemia

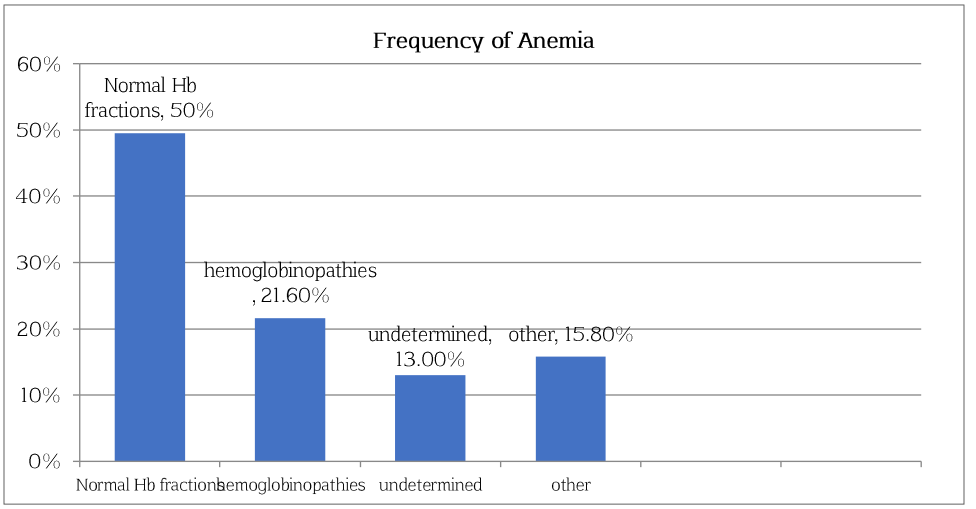
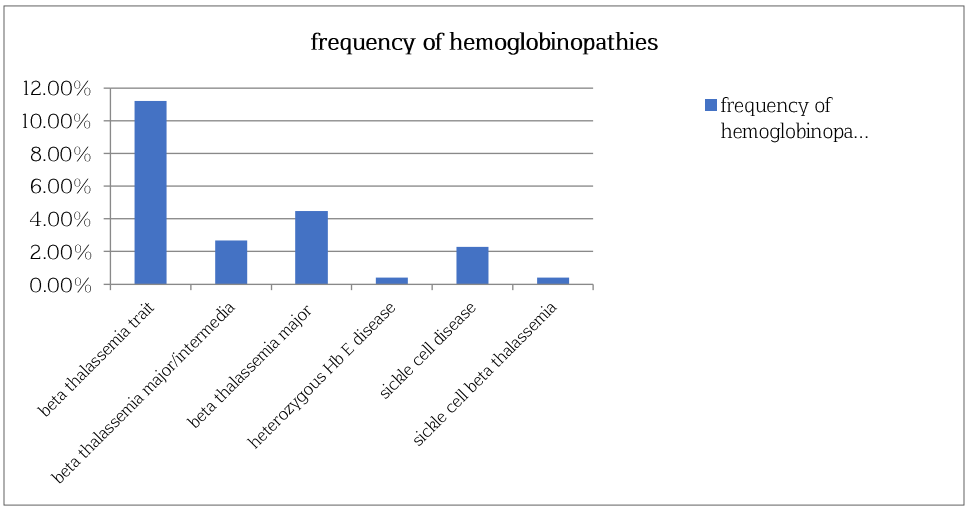


Figure 2

Frequency of hemoglobinopathies



Discussion

"Thalassemia poses a substantial public health concern worldwide, placing a particularly high burden on developing countries, particularly in Asia, where limited resources hinder effective mitigation of the issue (Brancaleoni, Di Pierro, Motta, & Cappellini, 2016). Pakistan is among these countries, currently facing the mounting challenges associated with beta thalassemia major.

In our research conducted at Hayatabad Medical Complex Hospital in Peshawar, we examined the prevalence rates of various haemoglobinopathies. The predominant cause of anaemia was identified as Beta-thalassemia trait (11.2%), followed by beta-thalassemia major (4.5%), Thalassemia Major/Intermedia (2.7%), sickle cell disease (2.3%), and sickle/beta-thalassemia (0.4%).

Numerous other studies have also investigated the frequency of hemoglobinopathies in different regions of Pakistan. For example, Waheed U 2012

(Waheed, Satti, Farooq, & Zaheer, 2012) reported a prevalence of 28.4% for various hemoglobinopathies among patients in Islamabad in 2012. Among them, 25.6% had thalassemia trait, 1.4% had thalassemia major, and 1.4% had sickle cell disease. In another study conducted in Karachi, Shabbir S. et al.(Shabbir et al., 2016) found that 34.2% of cases were affected by hemoglobinopathies. Among them, 51.8% had beta-thalassemia minor, 24.1% had beta-thalassemia major, 6.7% had HbD trait, 4.5% had sickle/beta-thalassemia, and 3.9% had sickle cell anaemia. Hussain J 2015 (Hussain, Khan, Ali, & Jan, 2015) studied the frequencies of hemoglobinopathies at the Department of Pathology, Gomal Medical College, Dera Ismail Khan in 2015. They discovered that beta-thalassemia major was the most prevalent haemoglobinopathy (25.8%), followed by beta-thalassemia trait (11.3%), sickle cell disease (9.7%), sickle cell trait (3.2%), and sickle/beta-thalassemia "double heterozygous" (3.2%) (Hussain et al., 2015).

In a study conducted by Ghani R in 2002 (Ghani, Manji, & Ahmed, 2002), the prevalence rates of various hemoglobinopathies were reported. They found a frequency of 20.6% for beta-thalassemia major, 13% for beta-thalassemia trait, 5.1% for sickle cell disease, and 0.76% for haemoglobin D (HbD Punjab). Arab countries also exhibit a high prevalence of these hemoglobinopathies, with carrier rates ranging from 1% to 11% for beta-thalassemia, 1% to 58% for alpha thalassemia, and 0.3% to 30% for sickle cell trait (Hamamy & Al-Allawi, 2013). This elevated prevalence is primarily attributed to consanguineous marriages. Similarly, the southern regions of Iran also demonstrate a significant prevalence of hemoglobinopathies, with rates of 35% for alpha thalassemia and 10% for beta-thalassemia (Abolghasemi et al., 2007).

Most of the reported frequency data on haemoglobinopathies in Pakistan originate from laboratories located in Karachi, Islamabad, and Dera Ismail Khan, as these cities have a higher concentration of reference laboratories. However, our study stands out as we presented the frequency rates of these haemoglobinopathies in an area where they are extensively prevalent. Our research revealed that 22.1% of children were affected by haemoglobinopathies, and it is anticipated that the carrier rate is even higher. Undetected carriers serve as a continuous source of homozygous haemoglobinopathies in future generations, especially through intermarriages.

The findings of our research hold significant value for policymakers involved in the thalassemia control program. These findings can guide them in redirecting their efforts towards the neglected areas and effectively addressing the issue of haemoglobinopathies. Managing haemoglobinopathies goes beyond treating anaemia and utilizing iron chelation therapy. It requires considering definitive therapeutic options, such as bone marrow transplants. Prevention should be a primary focus, emphasizing the implementation of pre-marital and extended family screening programs and the establishment of regional facilities for prenatal diagnosis.

These studies shed light on the variations in the frequencies of haemoglobinopathies across different regions of Pakistan, emphasizing the importance of understanding the local prevalence for implementing effective management and prevention strategies. We strongly recommend enforcing pre-marriage and prenatal counselling and screening as stringent laws in these areas. A successful example of such programs can be observed in Cyprus, where the occurrence of these disorders in newborns has been reduced to zero through the implementation of these measures (Bender et al., 2020). Additionally, it is crucial to educate healthcare professionals and the general population while raising awareness through various media platforms and influential individuals to prevent the occurrence of these genetic disorders."

Conclusion

In conclusion, hemoglobulin disorders remain a significant issue within various communities in Pakistan. If left unaddressed, these disorders could potentially escalate into an epidemic. The key to preventing the spread of the disease lies in identifying carriers and raising awareness among the population. Rather than discouraging cousin marriage outright, it is crucial to implement preventive measures such as mandatory pre-marriage carrier state detection. This proactive approach is essential in effectively controlling the disease and its impact.

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