http://www.pjbs.org

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

OPEN ACCESS Pakistan Journal of Biological Sciences

ISSN 1028-8880
DOI: 10.3923/pjbs.2022.1094.1099

Research Article
Hemoglobinopathy Patterns in Anemic Patients with a Strong History of Sickle Cell Disease in Eastern Province, Saudi Arabia: A Cross-Sectional Study

[1]Eihab Idris Mohammed, [2]Yousif Mohammed Elmosaad and [3]Hisham Ali Waggiallah

[1]Department of Hematology and Immunohaematology, College of Medical Laboratory Science, Sudan University of Science and Technology, Khartoum, Sudan
[2]Department of Public Health, College of Applied Medical Sciences, King Faisal University, Saudi Arabia
[3]Department of Medical Laboratory Science, College of Applied Medical Science, Prince Sattam Bin Abdulaziz University, Alkharj 11942, Saudi Arabia

Abstract

Background and Objective: The most common genetic disease in humans is hemoglobinopathies, also known as hemoglobin hereditary diseases. The purpose of this study was to look at the hemoglobinopathy patterns in anemic patients with a history of sickle cell disease in Saudi Arabia's Eastern Province. **Materials and Methods:** This prospective cross-sectional study was conducted on anemic patients attending the hospital with a strong family history of hemoglobinopathy and general signs and symptoms, as well as mild to moderate anemia crises. One hundred and ten people were chosen to participate in this study. The research was carried out between September, 2019 and October, 2020. **Results:** The sickle cell trait was the most common hemoglobinopathy in males (31.1%) and sickle cell trait+beta thalassemia minor was the most common in females (18%). The gender of patients and the distribution of hemoglobinopathy types were found to have a significant relationship (p-value of 0.001). **Conclusion:** A significant correlation was discovered between the gender of patients and the distribution of hemoglobinopathy types. More efforts must be made to raise the prevention of endogamy awareness among Saudis.

Key words: Hemoglobinopathies, anemic patients, sickle cell disease, thalassemia, Hb H

Citation: Mohammed, E.I., Y.M. Elmosaad and H.A. Waggiallah, 2022. Hemoglobinopathy patterns in anemic patients with a strong history of sickle cell disease in Eastern Province, Saudi Arabia: A cross-sectional study. Pak. J. Biol. Sci., 25: 1094-1099.

Corresponding Author: Hisham Ali Waggiallah, Department of Medical Laboratory Science, College of Applied Medical Science, Prince Sattam Bin Abdulaziz University, Alkharj 11942, Saudi Arabia

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Hemoglobinopathies or hemoglobin genetic disorders, are the most frequent genetic disease in humans[1]. Because of their increased morbidity and mortality among affected persons, the international public health community has focused on two hemoglobinopathy disorders, thalassemia and sickle cell disease[2,3]. Some of these disorders, such as beta-thalassemia (β-thal) major, are classified as serious autosomal recessive phenotype disorders[4]. The β-thalassemia, Hb C disease, Hb E disease and sickle-cell disease are the clinically significant types[5]. The precise clinical picture in such a condition is mostly defined by an underlying genotype. The phenotype can display as a silent carrier, a calm state or moderate to severe anemia[6,7].

The incidence of sickle cell disease and thalassemia in the Arab population is unknown, even though research findings have shown that these genetic disorders are relatively common in this region[8]. Several research findings in Saudi Arabia discovered that the incidence of these diseases differed considerably. Across the country, with the Eastern Province with the greatest incidence, accompanied by the Southwestern Provinces[9]. This increased incidence of hemoglobinopathies is similar to the structure of autosomal recessive inherited disorders, which is evident in a country where endogamy accounts for more than half of all marriages[10,11].

Nonetheless, the value of neonatal screening programs is restricted because they can only provide secondary protection to sick children. Despite the fact that a prenatal screening program has the potential to reduce the occurrence of the disorder, many societies do not accept it. In this situation, a premarital screening program seems to have a high chance of lowering the occurrence of genetic conditions[12]. With these factors in mind, the Saudi Government decided to establish a mandatory premarital screening program in 2003 in order to decrease the occurrence of sickle cell disease and thalassemia[13]. The goal of this research was to evaluate the hemoglobinopathy patterns in anemic patients with a strong history of sickle cell disease in the Eastern Province, Saudi Arabia.

MATERIALS AND METHODS

Settings and participants of the study: This prospective cross-sectional study was conducted on anemic patients attending Health clinics with a strong family history of hemoglobinopathy and general signs and symptoms, as well as mild to moderate anemia crises. One hundred and ten people were chosen to participate in this study. The research was carried out between September, 2019 and October, 2020.

Sampling and HPLC technique: The CE-HPLC was used to analyze the hemoglobinopathy work-up (BioRad Laboratories, California, USA). Five milliliters of blood was collected in EDTA vacutainers and analyzed in batches within one week. On the Variant II Sampling Station (VSS), the samples were automatically mixed and diluted before being injected into the analytical cartridge. The dual pumps of the Variant II Chromatographic Station (VCS) deliver an ionic strength buffer gradient. The HbA2/F/S/H are isolated in the cartridge based on their ionic interaction with the cartridge substance. The isolated HbA2/F/S/H was then gone through the flow cell of the filter photometer, where the adjustments were evaluated. Variant II CDM (CDM) Software reduces original information from each assessment. The CDM generates a sample report and a chromatogram for each specimen, displaying all hemoglobin fragments eluted, their retention times, peak area and amounts of fractions[14].

Ethical approval: The aim of the research was clearly addressed to the lab managers and the administrative unit provided informed consent to participate. Each participant provided written consent.

Statistical investigation: The Statistical Package for Social Sciences (SPSS) version 20 was used to examine the data. According to the type of variables, descriptive statistics (frequency, proportion estimation and mean) was used to tabulate and describe the data. Inferential statistics like the chi-square test and fisher exact test explain the association between age and gender prevalence of hemoglobinopathies. All statistical analyses were set at a 95% confidence interval (CI) and $p<0.05$ level of significance.

RESULTS

Table 1 showed that the percentage of males and females who participated in the study, as well as their age distribution. The percentage of female participants in the study was higher, at 56.6% than the percentage of male participants, at 43.4%. The most common age group among males and females was under 18 years old. There was no significant correlation between any of the age groups, gender, or the presence of hemoglobinopathy.

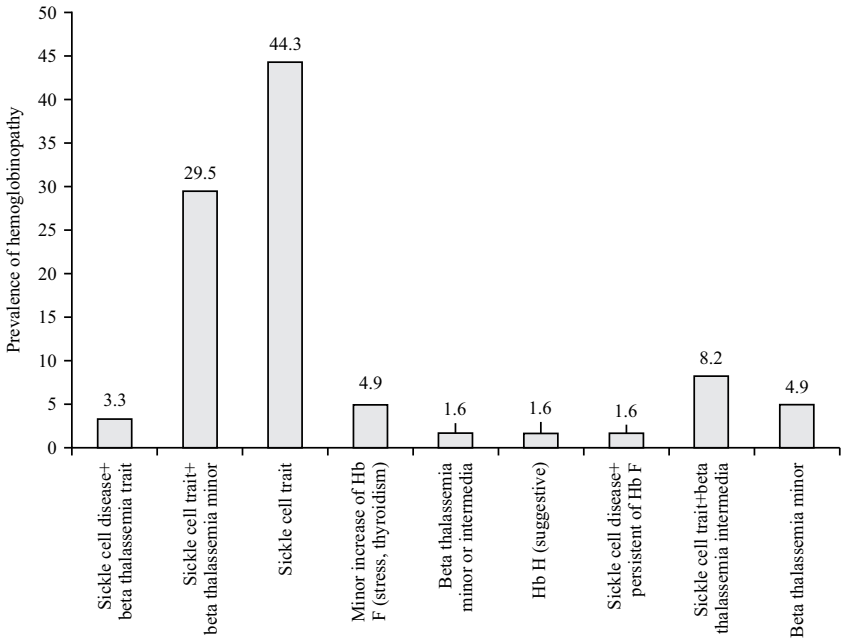

Fig. 1: Prevalence for hemoglobinopathy for both genders

Table 1: Distribution of age and gender percentage in respondents participated in the study

Gender	Percentage (%)	Age range	Age Mean±SD	<18	18-25	26-35	36-45	>46	Total
Male	43.4	1-47	16.0±13.6	25 (46.3%)	10 (66.7%)	5 (25.0%)	4 (33.3%)	1 (25.0%)	45 (42.9%)
Female	56.6	1-52	21.0±14.3	29 (53.7%)	5 (33.3%)	15(75.0%)	8(66.7%)	3(75.0%)	60 (57.1%)

Table 2: Displays the distribution of hereditary hemoglobin disorders in both genders

	Prevalence for hemoglobinopathies					
Hemoglobinopathies	Both gender (No./%)	95% CI	Male (No./%)	95% CI	Female (No./%)	95% CI
Sickle cell disease+beta thalassemia trait	2 (3.3)	1.4-5.2	1 (1.6)	0.3-2.9	1(1.6)	0.3-2.9
Sickle cell trait+beta thalassemia minor	18 (29.5)	24.7-34.3	7 (11.5)	8.2-14.8	11 (18.0)	14.0-22.0
Sickle cell trait	27 (44.3)	39.1-49.5	19 (31.1)	26.3-35.9	8 (13.1)	9.6-16.6
Minor increase of Hb F (stress, thyroidism)	3 (4.9)	2.6-7.2	0 (0.0)	0	3 (4.9)	2.6-7.2
Beta thalassemia minor or intermedia	1(1.6)	0.3-2.9	0 (0.0)	0	1 (1.6)	0.3-2.9
Hb H (suggestive)	1(1.6)	0.3-2.9	0 (0.0)	0	1 (1.6)	0.3-2.9
Sickle cell disease+persistent of Hb F	1 (1.6)	0.3-2.9	1 (1.6)	0.3-2.9	0 (0.0)	0
Sickle cell trait+beta thalassemia intermedia	5 (8.2)	5.3-11.1	1 (1.6)	0.3-2.9	4 (6.6)	4.0-9.2
Beta thalassemia minor	3 (4.9)	2.6-7.2	1 (1.6)	0.3-2.9	2 (3.3)	1.4-5.2
Total	61(100.0)	100-100	30 (49.2)	44.0-54.4	31(50.8)	45.6-56.0

Table 2 showed that the different types of hemoglobinopathy found in the patients who took part in the study, as well as their gender. The sickle cell trait was the most common hemoglobinopathy in males (31.1%) and the most prevalent in females was sickle cell trait+beta thalassemia minor, accounting for 18%. A significant relationship was discovered between the distribution of hemoglobinopathy types and the gender of patients (p-value of 0.001).

Figure 1 showed the prevalence of hemoglobinopathy in the study sample, with sickle cell trait representing the highest percentage of 44.3%, while beta-thalassemia minor or intermedia, hemoglobin H, sickle cell disease and persistent hemoglobin F constituted the lower percent (1.6%).

Table 3 presented the relationship between hemoglobinopathy prevalence and the age groups participating in the study. It turned out that there was no significant relationship between them (P-value 0.184), but we found that sickle cell trait and thalassemia minor were more prevalent (10%), specifically in the age group 26-35 years, while sickle cell trait was the most prevalent (15%), especially in the age group less than 18 years old.

Table 3: Illustrates the prevalence for hemoglobinopathy in age groups

		Age groups (years)*				
Hemoglobinopathies	All age groups	<18	18-25	26-35	36-45	>46
Sickle cell disease+beta thalassemia trait	2 (3.3)	0	0	1 (1.7)	1(1.7)	0
Sickle cell trait+beta thalassemia minor	17(28.3)	4 (6.7)	2(3.3)	6(10.0)	2(3.3)	3(5.0)
Sickle cell trait	27(45.0)	9(15.0)	8(13.3)	6(10.0)	4(6.7)	0
Minor increase of Hb F (stress, thyroidism)	3(5.0)	0	0	3(5.0)	0	0
Beta thalassemia minor or intermedia	1(1.7)	1(1.7)	0	0	0	0
Hb H (suggestive)	1(1.7)	0	0	0	1(1.7)	0
Sickle cell disease+persistent of Hb F	1(1.7)	1(1.7)	0	0	0	0
Sickle cell trait+beta thalassemia intermedia	5 (8.3)	3 (5.0%)	0	1(1.7)	1(1.7)	0
Beta thalassemia minor	3 (5.0)	3 (5.0)	0	0	0	0
Total	60(100)	21(35.0)	10 (16.7)	17(28.3)	9(15.0)	3(5.0)

*Age group of study participants not statistically associated with hemoglobinopathies p = 0.184

DISCUSSION

The study was conducted among patients with a strong family history of sickle cell disease in order to detect other hemoglobin inherited disorders, as known hemoglobinopathies are centered in two geographical areas of Saudi Arabia: The Eastern and Southern Regions[9]. Since Saudi Arabia is mainly a tribal society with a significant number of endogomy marriages, recessive genes have occurred, accumulated and induced illness for centuries. This phenomenon has been identified as the primary cause of increased autosomal recessive disorder prevalence in similar populations[15].

Many types of hemoglobinopathies associated with the sickle disease have been discovered in the current study, including all thalassemia types, Hb H and persistent Hb F. Results revealed that the proportion of female study participants was higher, at 56.6%, than the proportion of male study participants, which was 43.4%. Results showed that the most common age group among both males and females was under the age of 18, which was consistent with a previous study conducted by Alsaeed *et al.*[16], which revealed a high rate of Hb variants in subjects aged ≤17 years old. In Saudi Arabia, there was no information on the impact of sickle cell disease on under-five mortality, there were few studies on death patterns. Furthermore, research findings from the Eastern Province revealed that 73% of mortality occurred in individuals under the age of 30, as a result of the respiratory syndrome. being the leading cause of death, followed by infection[17]. According to a recent WHO statement, the most reliable measure to investigate the effects of sickle cell disease on public health was under 5 years old death[18]. The SCD kills approximately 5% of African children under the age of five, more than 9% in West Africa and up to 16% in person West African countries. A rising number of affected children stay alive to the age of five but were at risk of dying prematurely and 48% of patients who survive into adulthood have chronic organ failure[19].

According to this study, sickle cell trait is the most common hemoglobinopathy in males (31.1%) and sickle cell trait+beta thalassemia minor is the most common in females (18%). The gender of patients and the distribution of hemoglobinopathy types were found to have a significant relationship. The reported incidence rate for sickle cell disease[20] is 0.3-30%. Familial marriages were the most common cause of recessive hemoglobinopathies (homozygous or compound heterozygous mutations), which can increase the occurrence rate by up to 60%[21]. The prevalence of sickle cell disease and β-thalassemia in Saudi Arabia was thought to be among the highest in the Middle East (0.05 and 4.50%, respectively)[21].

Sickle cell disease was a complex disorder with incidence ranging from 1-44% in different regions in India. Recurrent RBC sickling, causes hemolytic anemia, acute vaso-occlusion and organ failure[22].

Numerous countries have launched various programs to increase public knowledge of hemoglobinopathies and monitor the incidence of hemoglobin disorders, for instance, thalassemia awareness campaigns in Cyprus, Greece and Italy have been effective[23]. However, in Italy, the initiatives and premarital consultation only participated in a provisional reduction in thalassemia cases in the 1970s and 1980s[24].

In 2004, Saudi Arabia launched a program called premarital screening (PMS) and genetic counseling (PMSGC). The program's objective was to decrease the couple's and progeny's risk of genetic illnesses. The goal of these PMS and genetic counseling programs was to reduce the prevalence of hemoglobinopathy through the prevention of high-risk

marriages. The PMS is a very valuable method in health promotion and it is the only primary preventative measure in diseases like hemoglobinopathy, there were strong measures of increased knowledge on the importance of PMS in the identification and avoidance of genetic illnesses[23].

CONCLUSION

The sickle cell trait was the most common hemoglobinopathy in males (31.1%) and sickle cell trait+beta thalassemia minor was the most common in females (18%). The gender of patients and the distribution of hemoglobinopathy types were found to have a significant correlation. More efforts should be made to raise preventive measures of endogamy awareness in the Saudi community.

SIGNIFICANCE STATEMENT

The sickle cell trait is the most common hemoglobinopathy in males and sickle cell trait+beta thalassemia minor is the most common in females. The gender of patients and the distribution of hemoglobinopathy types were found to have a significant correlation. This study will help the researcher to uncover the further efforts that should be taken in the Saudi community to raise endogamy prevention awareness.

ACKNOWLEDGMENT

This publication was supported by the Deanship of Scientific Research at Prince Sattam Bin Abdulaziz University.

REFERENCES

1. Chatterjee, T., A. Chakravarty and S. Chakravarty, 2015. Population screening and prevention strategies for thalassemias and other hemoglobinopathies of Eastern India: Experience of 18,166 cases. Hemoglobin, 39: 384-388.
2. Cao, A., M.C. Rosatelli, G. Monni and R. Galanello, 2002. Screening for thalassemia: A model of success. Obstet. Gynecol. Clin. North Am., 29: 305-328.
3. Weatherall, D.J., 2011. The challenge of haemoglobinopathies in resource-poor countries. Br. J. Haematol., 154: 736-744.
4. Flint, J., R.M. Harding, A.J. Boyce and J.B. Clegg, 1993. The population genetics of the haemoglobinopathies. Bailliere's Clin. Haematol., 6: 215-262.
5. Goonasekera, H.W., C.S. Paththinige and V.H.W. Dissanayake, 2018. Population screening for hemoglobinopathies. Annu. Rev. Genom. Hum. Genet., 19: 355-380.
6. Tshilolo, L., L.M. Aissi, D. Lukusa, C. Kinsiama, S. Wembonyama, B. Gulbis and F. Vertongen, 2009. Neonatal screening for sickle cell anaemia in the democratic republic of the Congo: Experience from a pioneer project on 31 204 newborns. J. Clin. Pathol., 62: 35-38.
7. Weatherall, D.J., 2001. Phenotype-genotype relationships in monogenic disease: Lessons from the thalassaemias. Nat. Rev. Genet., 2: 245-255.
8. Hamamy, H.A. and N.A.S. Al-Allawi, 2013. Epidemiological profile of common haemoglobinopathies in Arab countries. J. Community Genet., 4: 147-167.
9. Jastaniah, W., 2011. Epidemiology of sickle cell disease in Saudi Arabia. Ann. Saudi Med., 31: 289-293.
10. Kohne, E., 2011. Hemoglobinopathies: Clinical manifestations, diagnosis, and treatment. Dtsch. Arztebl Int., 108: 532-540.
11. Meyer, B.F., 2005. Strategies for the prevention of hereditary diseases in a highly consanguineous population. Ann. Hum. Biol., 32: 174-179.
12. Gosadi, I.M., G.A. Gohal, A.E. Dalak, A.A. Alnami, N.A. Aljabri and A.J. Zurayyir, 2021. Assessment of factors associated with the effectiveness of premarital screening for hemoglobinopathies in the South of Saudi Arabia. Int. J. Gen. Med., 14: 3079-3086.
13. AlHamdan, N.A.R., Y.Y. AlMazrou, F.M. AlSwaidi and A.J. Choudhry, 2007. Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. Genet. Med., 9: 372-377.
14. Pant, L., D. Kalita, S. Singh, M. Kudesia, S. Mendiratta, M. Mittal and A. Mathur, 2014. Detection of abnormal hemoglobin variants by HPLC method: Common problems with suggested solutions. Int. Scholar Res. Not., Vol. 2014. 10.1155/2014/257805.
15. Madi, S.A., R.L. Al-Naggar, S.A. Al-Awadi and L.A. Bastaki, 2005. Profile of major congenital malformations in neonates in Al-Jahra Region of Kuwait. East. Mediterr. Health J., 11: 700-706.
16. Alsaeed, E.S., G.N. Farhat, A.M. Assiri, Z. Memish and E.M. Ahmed *et al*., 2018. Distribution of hemoglobinopathy disorders in Saudi Arabia based on data from the premarital screening and genetic counseling program, 2011–2015. J. Epidemiol. Global Health, 7: S41-S47.
17. Al-Suliman, A., N.A. Elsarraf, M. Baqishi, H. Homrany, J. Bousbiah and E. Farouk, 2006. Patterns of mortality in adult sickle cell disease in Al-Hasa Region of Saudi Arabia. Ann. Saudi Med., 26: 487-488.
18. WHO, 2006. ASA Fifty-Ninth World Health Assembly. Provisional Agenda Item 11.4, World Health Organization, Geneva.
19. Powars, D.R., L.S. Chan, A. Hiti, E. Ramicone and C. Johnson, 2005. Outcome of sickle cell anemia: A 4-decade observational study of 1056 patients. Medicine, 84: 363-376.

20. Al-Gazali, L., H. Hamamy and S. Al-Arrayad, 2006. Genetic disorders in the Arab world. BMJ, 333: 831-834.
21. Umair, M. and M. Alfadhel, 2020. Prevention of hemoglobinopathies in Saudi Arabia: Efficacy of national premarital screening and the feasibility of preimplantation genetic diagnosis. J. Biochem. Clin. Genet., 3: 94-99.
22. Warghade, S., J. Britto, R. Haryan, T. Dalvi and R. Bendre *et al.*, 2018. Prevalence of hemoglobin variants and hemoglobinopathies using cation-exchange high-performance liquid chromatography in central reference laboratory of India: A report of 65779 cases. J. Lab. Physicians, 10: 73-79.
23. Binshihon, S.M., M.O. Alsulami, W.M. Alogaibi, A.H. Mohammedsaleh, H.N. Mandourah, B.S. Albaity and M.H. Qari, 2018. Knowledge and attitude toward hemoglobinopathies premarital screening program among unmarried population in western Saudi Arabia. Saudi Med. J., 39: 1226-1231.
24. Chakravorty, S. and M.C. Dick, 2019. Antenatal screening for haemoglobinopathies: Current status, barriers and ethics. Br. J. Haematol., 187: 431-440.