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Hemoglobinopathies Among Saudi adults at Taif city, Saudi Arabia

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Haemoglobinopathies are a group of haematological disorders, which are responsible for pathological variants and medical complications. On the other hand, some haemoglobin variants couldn't make any detectable illnesses. About 30 to 50% of the variant hemoglobin in red blood cells detected among carriers was reported with structural abnormalities. Multi-research studies have been found that hemoglobin S is the most common variant hemoglobin between carriers, accounting for 40% and associated with more than 80% of patient's clinical manifestations. The World Health Organization (WHO) reported that 948 000 couples were newly diagnosed with hemoglobin variants annually. Thus, carrier screening program within the highly affected population are essential to reduce or /and prevent the prevalence of such blood hemoglobin variant. This study, investigated a total of 9008 blood samples of Saudi male and female, who visiting the Centre of premarital screening center in Taif city, western region of Saudi Arabia from October 2017 to August 2018. Abnormal haemoglobin fractions were detected among 122 (1.3%) cases when screened with HPLC. This study also showed that 72 (59%) of participant were presented with Hb S heterozygous as major abnormality followed by beta thalassemia minor with 25 (20%). Studying the incidence and distribution of hemoglobin variants and their genetic mutations will provide opportunities for prevention and lower incidence. In addition to the massive efforts accomplished by the Saudi government to prevent at-risk marriages, this study suggests that the early diagnosis and detection for these hemoglobin variants offered for young couples as they can discuss the issue in the primary period of the marriage proposal.

Keywords: Beta thalassemia minor, Genetic variations, hemoglobinpathies, Hb S heterozygous, Sickle cell anemia

INTRODUCTION

Hemoglobin consists of four globin chains: fetal hemoglobin (Hb F) has two α and two gamma chains (α2γ2) while the adult hemoglobin (Hb A) has two α and two β chains (α2β2). Genes in the α-globin and β-globin gene are responsible to control globin-chain production. Genetic variations in these genes, which might lead to alterations in the amino acid substitution in a globin chain, are the main reason behind the mutant form of the hemoglobin variants. Such genetic changes can generate structural variants that affect the amino acid sequence and either produce abnormal haemoglobin or reduce the production of globin chains (Trent, 2006) (Urbinati et al., 2006). Some of the hemoglobin variants are considered hemoglobinopathies and responsible for diseases occurrence such as sickle cell anemia (SCA) and beta thalassemia. In addition, individuals who inherit combinations of hemoglobin S, C, E, D Punjab, β thalassemia, or α zero (α0) thalassemia may have a serious hemoglobin disorder (Angastiniotis and Modell, 1998). On the other hand, some hemoglobin variants considered non-pathological variants and couldn't make any detectable disorder, which means that they are harmless and without signs or symptoms.

Carriers (person has one normal beta gene and

one abnormal beta gene) of structural variant haemoglobin have 30–50% of the variant haemoglobin in their red blood cells (RBCs). For example, thalassemia carriers have small RBCs and in some cases mild anemia and more than 3.5% of HbA2β are detected in thalassemia carriers. In 2008, World Health Organization (WHO) showed that 75% of births were having haemoglobin disorders in of 229 countries. Moreover, among the world population at least 5.2% (and over 7% of pregnant women) carry a significant variant (Weatherall and Clegg, 2001). The most common variant haemoglobin is haemoglobin S, which accounts for 40% of carriers and responsible for more than 80% of disorders because of the very high prevalence of carrier: accounting over 70% of all affected births occur in Africa. It has been estimated that there are at least 948 000 new carrier couples, and more than 1.7 million pregnancies to carrier couples every year. Modell and colleagues, reported 19 countries where haemoglobin disorders occur primarily as a result of migration were obtained by combining data on residents' ethnicity or country of birth with gene frequencies in countries of origin (Modell et al., 2007). The mortality rate from haemoglobin disorders in children younger than five years was 3.4% and 6.4% worldwide and in Africa respectively. Early detection as well as accurate diagnosis of variant haemoglobin play an important role in preventing the occurrence of different serious disorders like thalassemia major in offspring. Thus, systematic carrier screening must be provided among many countries through primary health care, where the disorders affect primarily ethnic minorities (Modell et al., 2000). The prenatal screening program has been established in parts of Asia, parts of the Caribbean and most of southern Europe (except Albania). Moreover, in the United Kingdom this diagnosis is recommended and provided through primary health care for at-risk couples (Modell et al., 2000).

In 2003, the Saudi government adopted effective strategies aimed to minimize at-risk marriages and reduce the incidence of the hemoglobinopathies, through the optional premarital screening program for all new couples. A year after, the marriage license was given only after completing the mandatory screening tests for all couples planning to marry (AlHamdan et al., 2007). Moreover, carriers were offered to have a free genetic counseling service by qualified therapists and consultants. Zaini (2016) reported that these government facilities were effective in educating the public and improving the quality of life of those affected and carriers. This is also support primary, secondary and tertiary prevention of such common hemoglobinopathies in Saudi Arabia (Zaini, 2016).

The aim of this study was to assess the variant haemoglobin among Saudi's, who attending the Centre of premarital screening in Taif city. This will help in prevention and management of various hemoglobinopathies.

MATERIALS AND METHODS

This study is a cross sectional study performed from October 2017 to August 2018. A total of 9008 healthy Saudi male and female (who attending the Centre of premarital screening and aged between 19 to 40 years old were participating in this study. Venous blood (2-3 ml) was collected in EDTA-K2 tube (Guanazhou, Improne, Medical Instruments, Co. LTD.) and mixed well. Samples were analyzed in automated cell counter (Symex-CellDyne) for complete blood counts (CBC). Samples were then analyzed by High Performance Liquid Chromatography (HPLC) on the BIO-RAD VARIANT II Haemoglobin Testing System using the VARIANT II β-thalassemia Short Program. No sample preparation was required unless sample was less than 500 µl. In such case, sample was manually pre-diluted. The sample tubes were loaded into sample racks and placed on the sampling station. A whole Blood Primer was used at the beginning of each run to condition the cartridge for analysis.

Haemoglobin A_2/F calibrator and two levels (Level 1 and 2) of controls (BIO-RAD Laboratories) were used at the beginning of each run. The haemoglobin control level 1 containing A_2 and F (normal) and level 2 containing A_2, F and S (Abnormal). The total area acceptable was between one to three million µVolt/second. The Variant II Clinical Data Management (CDM) Software (BIO-RAD Laboratories) performs reduction of raw data collected from each analysis. To aid the inter-pretation of results. For each sample a chromatogram/ sample report is generated by CDM showing all haemoglobin fractions eluted. The integrated peaks are assigned to manufacturer-defined windows derived from specific retention time (RT) of normal haemoglobin fractions and common variants (Table 1).

Table 1: Shows Manufacturer Assigned Windows for BIO-RAD Variant II HPLC System.

Window	Retention Time (Min)
P_1	0.63 – 0.85
F	0.98 – 1.20
P_2	1.24 – 1.40
P_3	1.40 – 1.90
A_0	1.90 – 3.10
A_2	3.30 – 3.90
D	3.90 – 4.30
S	4.30 – 4.70
C	4.90 – 5.30

Statistical Analysis

Data was analyzed by SPSS version 19. Frequencies and percentages were calculated.

RESULTS

A total of 9008 blood samples were studied. Of these, 122 (1.4%) cases displayed abnormal haemoglobin fractions on HPLC. The result of this study showed that Hb S heterozygous was presented as the major abnormality with 59% (72 cases). Beta thalassemia minor was detected at higher range among female when compared to male with 64% and 36% respectively. However, the prevalence of haemoglobin D heterozygous was only detected among male participants. The result of this study also showed that the hereditary persistence of fetal haemoglobin (HPFH) detected among 14 cases (11.5%) with female predominance. Three cases of adults were diagnosed with Hb S homozygous, which indicated the presence of sickle cell anaemia. Similarly, only three cases reported with Hb E (2.4%). The number and percentage of haemoglobin abnormalities were summarized in table 2**.**

Table 2: Shows the number and percentage of HB variants among Saudi male and female participants

HB variants	Number	Male	Female
Beta thalassemia Minor	25 (20.5 %)	9	16
Hb D	4 (3.3%)	4	0
Hb E	3 (2.4%)	1	2
Sickle cell trait	72 (59%)	35	37
Sicke cell anemia	4 (3.3%)	2	2
HPFD	14 (11.5%)	4	10
Total	122	55	67

DISCUSSION

This is the first study to be done in the Taif city in the western region of the King dome of Saudi Arabia to detect various Hb variants among Saudi male and female who attending the pre-marriage clinic at Taif city during six months from October 2017 to August 2018. Since, the high mortality rate and the financial, social, and psychological cost related to patients with hemoglobinopathies disorders, thus early detection as well as accurate diagnosis of variant haemoglobin plays an important role in preventing the occurrence of such serious disorders including sickle cell disease in offspring (Sachdev et al., 2010).

In 2011, a study was performed at north border region of Saudi Arabia and found that the prevalence of hemoglobinopathies was 2.8% and the majority of the participants were diagnosed as beta thalassemia carrier (Alenazi et al., 2015). However, the result of this study showed that the Hb S heterozygous was presented as the major abnormality followed by beta thalassemia minor. Another study has performed during February 2004 to January 2005 among all the individuals who applied for a marriage license at 70 laboratories of Ministry of health all over Saudi Arabia and found that 4.20% had sickle cell trait, 3.22% had thalassemia trait, 0.26% had sickle cell disease, and 0.07% had thalassemia disease (AlHamdan et al., 2007). Moreover, within the same study they found that Thalassemia trait was highest in the eastern region followed by Qunfudah (15.85%) while Thalassemia disease was highest in Jazan (0.39%), followed by the northern region (0.27%).

This study showed clearly the low prevalence of Hb E compared to Hb S hetrozygous and beta thalassemia minor disorders among Saudi's male and female. This result is in agreement with the finding of Al-jaunt (2014), which showed that the prevalence of haemoglobin E trait was the least frequents compare to the other investigated hemoglobin disorders (Al-Jaouni, 2010).

Memish and Saeedi, have reported that there was highest detection of at risk marriage and also greater increase in marriage cancellation among at-risk couples in eastern region compared to other regions of Saudi Arabia between 2004 and 2009 (Memish and Saeedi, 2011). Studying the pathophysiology, genetic and distribution of these hemoglobin disorders will help to reduce their incidence.

CONCLUSION

Since the haemoglobinopathies are one of the common genetic blood disorders among Saudis with very high financial management and treatment coast, studying their prevalence and distribution is a crucial step to suggest effective strategies to minimize and prevent their incidence. In this study, it had been suggested that additionally to the enormous efforts already adapted by the Saudi government to prevent at-risk marriages through mandatory premarital investigation program, the early diagnosis for these disorders might be offered for individuals with high risk as well as high school level students. Subsequently, they can discuss the issue in the early stage of the marriage proposal.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

Haytham Dahlawi designed and submits the research to the research committee and analysing the results data. Omer Zamzami collected the data from the hospitals. Rana Zaini wrote the manuscript. Mazen Almehmadi reviewed the manuscript. All authors read and approved the final version.

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