Family Medicine and Primary Care: Open Access
Alqahtani A, et al. J Family Med Prim Care Open Acc 7: 230.
www.doi.org/10.29011/2688-7460.100230
www.gavinpublishers.com

Research Article

# Prevalence of Hemoglobinopathy in Adult Population at KAMC, Riyadh, Saudi Arabia

**Abdulhadi Alqahtani[1*], Salih Bin Salih[2], Areej Almoghairi[3], Ali Alaklabi[4], Mada Alshamrani[5], Hanan S Alghamdi[6], Mohammed Altuwaijri[7], Ahmed Alanazi[8]**

[1]Resident, Prince Sultan Military Medical City, Saudi Arabia

[2]Professor and Chairman, Medicine Department – Principal Investigator (PI) at King Abdullah International Medical Research Center (KAIMRC), Ministry of National Guard Health Affairs, Saudi Arabia

[3]Consultant, Head of Hematopathology, Ministry of National Guard Health Affairs, Saudi Arabia

[4]Consultant, Internal Medicine, Department Of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Saudi Arabia

[5]Nurse, King Fahad Medical City - Ministry of Health, Saudi Arabia

[6]Clinical Laboratory Specialist, King Saud University, Saudi Arabia

[7]Resident, Ministry of National Guard Health Affairs, Saudi Arabia

[8]Resident, Ministry of Health, Saudi Arabia

[*]**Corresponding author:** Abdulhadi Alqahtani, Resident, Prince Sultan Military Medical City, Saudi Arabia

**Citation**: Alqahtani A, Salih SB, Almoghairi A, Alaklabi A, Alshamrani M, et al. (2023) Prevalence of Hemoglobinopathy in Adult Population at KAMC, Riyadh, Saudi Arabia. J Family Med Prim Care Open Acc 7: 230. DOI: 10.29011/2688-7460.100230

**Received Date:** 24 July, 2023; **Accepted Date:** 02 August, 2023; **Published Date:** 07 August, 2023

## Abstract

**Rationale and Objectives:** Hemoglobinopathies are among the most commonly inherited genetic disorders in humans and are considered as a major public health problem in Saudi Arabia. The prevalence of hemoglobinopathies is a severe health threat to the society and future generations if the assessment of hemoglobinopathies in pre-marriage cohorts is not monitored. The purpose of this study is to analyze the type of hemoglobinopathies in relation to age, gender and genetic mutations and to assess the prevalence of hemoglobinopathies in pre-marriage cohort. **Materials and Methods:** This is a retrospective study including a sample of 7054 patients who are older than 14 years (i.e. age ≥ 14 years) and were diagnosed with hemoglobinopathies. This study includes adults of both genders (male and female) from pre-marriage screening cohorts at King Abdul- Aziz Medical City, Ministry of National Guard – health affairs, Riyadh, Saudi Arabia. Patients were analyzed over a period of 4 years i.e. 2013 o 2017. **Results:** The comparative analysis of patient's clinical characteristics were recorded and among 7054 patient sample, 3822 (54.2%) were male while 3232 (45.8%) were females. The results of the proposed study showed that Saudi Arabia has a high prevalence rate of Sickle Cell Anemia (30.7%) and β-thalassemia (12.8%). The sickle cell trait was the most repeated hemoglobinopathy in this research. **Conclusion:** According to the results of this cohort study B-thalassemia and SCA are the most common hemoglobinopathy disorders in Saudi Arabia with a higher prevalence. In countries with a high prevalence of hemoglobinopathies, premarital screening is helpful for identification and prevention of high-risk marriage challenges. There is need for preventive measures and future comprehensive program with reference to the management, diagnosis and prevention of β-thalassemia and sickle cell diseases among patients in Saudi Arabia.

**Keywords:** Hemoglobinopathies; Iron Deficiency Anemia; Pre-marital screening; Sickle Cell Anemia; Thalassemia

## Introduction

Hematopoiesis is the process of making and producing matured blood cells from multipotent Hematopoietic Stem Cells (HSCs) [1]. Hematopoiesis is regulated via intrinsic and extrinsic cellular factors that control variable pathways affecting DNA methylation, which plays a critical role in hematopoiesis. Also mutations at this stage can result in a hematological malignancy [2]. DNA methylation basically maintains the persistence of transcription factors in Hematopoietic Stem and Progenitor Cells (HSPC) required for determining their fate [3]. Thalassemia and sickle cell disease are two well-known hemoglobinopathies. Thalassemia is caused by impaired production of either the alpha or beta hemoglobin chain and is accordingly classified as alpha or beta thalassemia. Alpha thalassemia is relatively rare, whereas beta thalassemia is quite common in certain parts of the world. Beta thalassemia clinically presents as thalassemia trait (thalassemia minor) or thalassemia major. Compared with patients with thalassemia major (HbA2 2%, HbF 98%, HbA Nil) who present with severe illness and require periodic blood transfusions, patients with thalassemia trait (HbA2>3.5%, HbF Nil) are clinically well and are usually only detected through routine blood testing. However, the children of such patients could inherit the disease if the patient's partner also has the beta thalassemia trait. Because of the high mortality associated with thalassemia especially, and the financial, social, and psychological cost of maintenance of patients with these illnesses, prenatal and neonatal screening programs for hemoglobinopathies have been considered cost-effective in populations with a high prevalence [4].

Referring to Hemoglobinopathies, these are inherited disorders of hemoglobin caused by mutations in the genes required for hemoglobin synthesis [5]. The defects usually take place in the α- or β-globin genes [6]. Hemoglobinopathy is one of the most common hereditary diseases worldwide; mostly in the orient and black African people. Recently this disease has become more frequent in North America and Europe, secondary to the immigration of Asian and Sub-Saharan African population [7]. The literature of hemoglobinopathies in Saudi Arabia is very limited and exiguous. In general, the most prevalent monogenic diseases in Saudi Arabia are β- thalassemia and Sickle Cell Anemia (SCA) [8]. In the western region of Saudi Arabia, α thalassemia is the most common prevalent disease [9]. According to previous studies, the prevalent frequency of Sickle Cell Anemia is higher among males (56.4%) as compared to females in Saudi Arabia [10]. Moreover, the study of Elsayid also reveals that the incidence of SCA was highly frequent in children (with 48.5% chances of occurrence) when compared to the adult age group [10]. In the eastern and southern region of Saudi Arabia, SCA is broached as the greatest public dominant disease [11].

## Material and Methods

### Patients and Study Design

This is a retrospective study including patients who are older than 14 years (i.e. age ≥ 14 years) and were diagnosed with hemoglobinopathies. This study includes adults of both genders (male and female) from pre-marriage screening cohorts at King Abdul- Aziz Medical City, Ministry of National Guard – Health Affairs, Riyadh, Saudi Arabia. Patients were analyzed over a period of 4 years i.e. 2013 to 2017. A total of 7054 patients were used as a sample in the study and among them 3822 (54.2%) were male while 3232 (45.8%) were females. This retrospective study follows ethical policies and regulations conscientiously.

### Data Collection

The medical records of adult male and female patients were collected using Laboratory Information System (LIS) and electronic chart review using best-care system. All data was gathered from the medical record of patients from King Abdul-Aziz Medical City in Ministry of National Guard – Health Affairs in Riyadh city, Saudi Arabia. The data was collected by two medical students and reviewed by hematologist for duration of four years i.e., 2013 to 2017. Following collection and reviewing phase, all data was entered in excel sheets. Statistical analysis was then conducted using SPSS package. Appropriate statistical tests were used to analyze the findings of this study.

### Eligibility Criteria

The research design included medical evidence of all male and female adult patients at King Abdul- Aziz Medical City in Ministry of National Guard – health affairs, Riyadh. The medical record included the diagnosis results of patient's age, percentage of hemoglobin variants, hemoglobin concentration and RBC indices. The data from 2013 to 2017 was gathered for this cohort study. Any adult patient (age>14 years) who was diagnosed with hemoglobinopathies and belonged to pre-marriage cohort was considered eligible for the study. On the contrary pediatric patients (age<14 years) with hemoglobinopathies were excluded from the study design.

### Statistical Analysis

The baseline characteristics which include age of the patient, percentage of hemoglobin variants, hemoglobin concentration and RBC indices were recorded during the diagnosis. These continuous variables were presented using n%, mean and Standard Deviation (SD) values. Frequencies and percentages were also calculated for categorical variables like gender. The student sample t-test was used for comparing the mean of continuous variables and the Chi-square test was used for the categorical variables. Fisher's exact test was used for categorical variables if the expected cell count was less than 5 (i.e. count <5). A two-tailed p- value less than 0.05 was considered as statistically significant. All data were entered and analyzed through statistical package SPSS 25 (SPSS Inc., Chicago, IL, USA).

### Ethical Approval

This study was performed in accordance with the Declaration of Helsinki of 1975 (revised in 1983) [12]. There is no personal interest of the researcher in this study objective. Ethical policies and regulations will be followed conscientiously. Collected data were anonymously analyzed and reported solely in aggregate form. No identifiable participant information such as patients' images, faces or names was disclosed in the study. All the medical records and data will be kept in a secure place within at King Abdul- Aziz Medical City premises, both the hard and soft copies.

## Results

A total of 7054 patients were collected from chart review and among them 3822 (54.2%) were male while 3232 (45.8%) were females. The baseline characteristics and their recorded n% values are displayed in Table 1. According to the findings 531 patients (12.8%) were tested positive for Thalassemia with 179 patients (33.71%) having β Thalassemia, 305 patients (57.4%) having α Thalassemia and 48 patients (9.04%) showing Thalassemia traits. On the other hand, 2076 patients (30.7%) were found positive for Sickle Cell Anemia (SCA) while 1046 patients (14.8%) were positive for Iron Deficiency Anemia (IDA).

| Characteristics | Description | n (n %) |
|---|---|---|
| Gender | Male | 3822 (54.2%) |
| | Female | 3232 (45.8%) |
| Thalassemia | Positive | 531 (12.8%) |
| | Negative | 0 (0.0%) |
| β Thal. | Positive | 179 (33.71%) |
| | Negative | 0 (0.0%) |
| α Thal. | Positive | 305 (57.4%) |
| | Negative | 0 (0.0%) |
| Thal trait | Positive | 48 (9.04%) |
| | Negative | 0 (0.0%) |
| SCA | Positive | 2076 (30.7%) |
| | Negative | 4686 (69.3%) |
| IDA | Positive | 1046 (14.8%) |
| | Negative | 6008 (85.2%) |

**Table 1:** Demographic and clinical characteristics of patients (n=7054).

From the results depicted in Table 2, the mean age of all patients was recorded to be 33.82 years with a standard deviation (SD) of 12.61 and the mean hemoglobin level (HGB) of all patients was found to be 131.45 (g/dl).

| Variables | Mean ± SD |
|---|---|
| Age (years) | 33.82 ± 12.61 |
| HGB level | 131.45 ± 30.29 |
| HGB level 10 | 12.33 ± 2.98 |
| Hgb A2 | 2.85 ± 1.05 |
| Hgb F | 3.14 ± 8.24 |
| Hgb S | 39.83 ± 14.62 |

**Table 2:** Descriptive analysis of continuous variables.

Table 3 indicates that concerning the association between SCA positive and negative patients with the baseline characteristics was significant. From Table 3 it can be determined that gender was statistically significant with sickle positive and negative patients. More than half of the male patients i.e. n= 1889 were negative for SCA while n=1807 male patients were positive for sickle cell. On the other hand, 2797 (59.69%) female patients were recorded negative for sickle cells whereas 269 (12.96%) female patients had positive sickle

cells. Also the mean value of HGB for positive SCA patients (mean=144.64) was statistically significant (i.e. P < 0.001) with mean HGB for negative SCA patients (mean=125.73). Hence, Table 3 shows a statistically significant association between the SCA patients and the baseline characteristics.

| Characteristics | Description | SCA patients | | *P - value* |
|---|---|---|---|---|
| | | Positive (n = 2076) | Negative (n = 4686) | |
| Gender | Male | 1807 (87.04%) | 1889 (40.31%) | *< 0.001 |
| | Female | 269 (12.96%) | 2797 (59.69%) | |
| Age (years) | Mean ± SD | 27.62 ± 7 | 35.67 ± 12.51 | *<0.001 |
| HGB level | Mean ± SD | 144.64 ± 25.72 | 125.73 ± 30.29 | *<0.001 |
| HGB LEVEL_/10 | Mean ± SD | 10.71 ± 2.6 | 12.5 ± 2.98 | *<0.001 |
| Thalassemia | Positive | 266 (50.3%) | 263 (5.61%) | *<0.001 |
| BETA THAL. | Positive | 17 (0.82%) | 160 (3.41%) | *<0.001 |
| ALPHA THAL. | Positive | 249 (11.99%) | 56 (1.20%) | *<0.001 |
| Thal trait | Positive | 1 (0.05%) | 47 (1.00%) | *<0.001 |
| IDA | Positive | 81 (3.90%) | 953 (20.34%) | *< 0.001 |
| | Negative | 1995 (96.10%) | 3733 (79.66%) | |
| A2HGB | Mean ± SD | 3.28 ± 0.77 | 2.65 ± 1.12 | *<0.001 |
| FHGB | Mean ± SD | 3.82 ± 7.65 | 1.42 ± 5.87 | *<0.001 |
| SHGB | Mean ± SD | 39.91 ± 14.47 | 14.08 ± 24.37 | *<0.001 |

**Table 3:** Significant association between sickle cell patients and clinical characteristics of the study variables.

The association between IDA and the baseline characteristics of patients is displayed in Table 4. The results show that gender was statistically significant with IDA positive and negative patients. The majority of 3641 (60.60%) male patients were negative IDA while 181 (17.30%) male patients were positive IDA, and 2367 (39.4%) female patients negative IDA whereas 865 (82.7%) female patients were recorded positive IDA. Patients with IDA were more likely to be older with a mean age of 36.39 compared to 33.38 years in patients without IDA (P<0.001). In addition, they had lower hemoglobin (Hgb) levels with a mean Hgb level of 95.43 g/l vs. 138 g/l in patients without IDA (P<0.001). Hence, Table 4 shows a statistically significant association between the IDA patients and the baseline characteristics.

| Characteristics | Description | IDA | | *P - value* |
|---|---|---|---|---|
| | | Positive (n = 1046) | Negative (n = 6008) | |
| Gender | Male | 181 (17.30%) | 3641 (60.60%) | *< 0.001 |
| | Female | 865 (82.70%) | 2367 (39.40%) | |
| Age (years) | Mean ± SD | 36.39 ± 13.11 | 33.38 ± 12.47 | *< 0.001 |
| HGB level | Mean ± SD | 95.43 ± 24.87 | 138.01 ± 26.32 | *< 0.001 |
| HGB LEVEL_/10 | Mean ± SD | 9.05 ± 2.12 | 13.14 ± 2.59 | *< 0.001 |
| Thalassemia | Positive | 68 (6.50%) | 463 (7.71%) | *< 0.001 |
| BETA THAL. | Positive | 7 (0.67%) | 172 (2.86%) | *< 0.001 |
| ALPHA THAL. | Positive | 48 (4.59%) | 257 (4.28%) | *< 0.001 |

| | | | | |
|---|---|---|---|---|
| Thal trait | Positive | 13 (1.24%) | 35 (0.58%) | *< 0.001 |
| A2HGB | Mean ± SD | 2.35 ± 0.64 | 2.92 ± 1.08 | *< 0.001 |
| FHGB | Mean ± SD | 1.56 ± 3.76 | 3.21 ± 8.36 | *< 0.001 |
| SHGB | Mean ± SD | 31.19 ± 7.29 | 40.18 ± 14.74 | *< 0.001 |

**Table 4:** Significant association between IDA patients and clinical characteristics of the study variables.

## Discussion

### Interpreting the research findings

The results of the proposed study showed that Saudi Arabia has a high prevalence rate of Sickle Cell Anemia (30.7%) and β-thalassemia (12.8%) as shown in Table 1. The results from our sample identified an adult population with some type of hemoglobinopathy. The SCA and IDA thalassemia were the most frequent observations. The sickle cell trait was the most repeated hemoglobinopathy in this research.

However, the past report covering the first two years of the PMSGC program in Saudi Arabia showed a lower prevalence of SCA (4.2% carriers and 0.26% cases) and a more significantly decreased prevalence of β-thalassemia (3.2% carriers and 0.07% cases) in contrast to current study [13]. It is important to note that the incidence of the sickle cell trait does not identify the disease and the carrier does not need treatment [14]. However, its genetic condition should be communicated, particularly during the procreant age [15].

Generally, doctors, physicians, researchers and clinicians sometimes misinterpret statistically significant result as being practically or clinically important. In fact, statistical significance is not the same as practical significance or importance. With the large samples, you can find statistical significance even when the differences or associations are small / weak. Thus, in addition to statistical significance, normally we determine effect size. As in the case of the proposed study, it is quite possible with large sample, to have a statistically significant result that is weak (i.e. has small effect size). Remember that the null hypothesis is that there is no difference or no association. A significant result with a small effect size means that we can be very confident that there is some difference or association, but it is probably small and may not be practically important.

## Correspondence with Literature

There are several studies reporting outcomes concerning the prevalence of hemoglobinopathies. As per the literature, a premarital screening program for the period between 2004 and 2005 was conducted in Saudi Arabia [16]. The national premarital screening program provided an opportunity for researchers to study the prevalence and distribution of hemoglobinopathies. At the beginning of the program, it was apparent that counseling had limited benefit in reducing the probability of marriage in risky couples (i.e. when both male and female are diagnosed with hemoglobinopathies). It was discovered that about 90% of risky couples continued with their marriage despite being aware of the likelihood of having children affected with hemoglobinopathies [16]. Likewise, another research study reported to have examined a limited sample of 129 couples who were identified by the premarital screening program as couples with risk of hemoglobinopathies [17]. This study also showed similar results, revealing that 98% patients proceeded with their marriage despite the risk of both partners having hemoglobinopathies. Furthermore, studies were carried out to examine factors that why do positive patients proceed with marriage despite being informed about the risks of having children with hemoglobinopathies. It was observed in literature that cultural pressure was one of the main reasons behind rejecting the counseling advice and proceeding with marriage of positive hemoglobinopathies patients [18].

According to recent research, approximately 1.5% of the global population is considered as heterozygote (carriers) of the β-thalassemia. There is a high incidence of β-thalassemia in populations from the Mediterranean basin, throughout the Middle East, the Indian subcontinent, Southeast Asia, and Melanesia to the Pacific Islands [19]. Moreover the prevalence of SCA in Saudi Arabia is irregular but several studies have reported that sickle cell disease is a relatively common genetic disorder in this part of the world. The carrier status for sickle cell disease ranged from 2% to 27% and up to 1.4% had sickle cell disease in some areas of Saudi Arabia [20].

The rate of prevalence of sickle cell disease in previously published studies appears to be much lower than studies done before the PMS & GC program. For instance, the national study of males and females, for the age of 2 and 60 years old in the 1980s and the early 1990s estimated sickle cell disease carriers and cases to be 73.6 and 10.6 per 1000 patients respectively [15]. However the current study estimated the SCA carrier and cases to be 42.4 and 2.7 respectively, which is significantly lower and could be moderately explained by the exclusion of the pediatric population in this study

In a more recent study, Al-Qurashi, et al. estimated sickle cell disease cases at 2.4 per 1000 patients, which is much lower than from our study findings. Similarly, the same results were observed in El-Tayeb, et al. reported during the first 2-year period of the time [21,22].

The differences in sickle cell disease rates in this study and pre-PMS&GC program studies may be distinguished by the differences in the sample point and by methodology. Furthermore, adult-based parameters in the current study should be lower or

higher than rates estimated from neonates or children as the earlier rates reflect incidence whereas the later rates replicate prevalence and survival. Unlike sickle cell disease, the regional and overall prevalence of β-thalassemia in the current study was much higher than previously published rates regardless of the scheduling of the PMS&GC program, with a probably broader difference after the program than before it. For example, between the 1980s and the 1990s, β-thalassemia rates were estimated at 130 and 36 per 1000 examined persons in Eastern and Central regions compared to the current estimated rates of 58.5 and 9.3 respectively. B-Thalassemia carriers per 1000 were estimated earlier from the PMS&GC program to be 32 in all regions of SA and 34 in the Al-Hassa region compared with the rates of the current study i.e. 18 and 26 respectively [23].

There are several factors leading to hemoglobinopathy prevalence sickle and one of the most common is consanguinity and inter-family marriages. The accomplishment of 48% marriages that were likely to have been affected by hemoglobinopathy in 2009 specifies the extreme cultural influence that remains to be addressed. Among the high frequency of consanguineous marriages, 55% were observed in large family size settings. The Eastern region that had 58% of all identified at-risk marriages during the program period had a lower overall cancellation of at-risk marriages in contrast to other regions (22.6% vs 34.3%). This may be explained by the fact that the cancellation of at-risk marriages at the beginning of the program operation (2004) was lower in the Eastern region compared to other regions (5% vs 21%). This might be due to the screened development of at-risk marriage prevention in the Eastern region compared to other regions (8.0-fold vs 1.7 fold). Furthermore, potential elucidation is the higher positivity of sickle-cell disease and/or β-thalassemia in the Eastern region compared to other regions (19.3% vs 3.8%), which could make it challenging for at-risk couples to find an alternative socially and suitably safe match [24].

## Recommendations and Future Scope

The Saudi MOH has already put forward immense efforts to prevent at-risk marriages for hemoglobinopathy patients, specifically sickle-cell disease and β-thalassemia. Some of these efforts include increasing the number of specialized health care reception clinics to cover more regions. Further endeavors are required to connect all clinics in the country with state-of-art web-based database software that will enhance instant rate calculation and research. This will overcome the limitation of aggregate data as seen in the current study because there was no access to raw or individual data for analysis. Saudi MOH must also enhance the effects of counseling by encouraging couples to seek testing earlier in the marriage process, engage religious figures in counseling, include program information in high school curriculum, allow singles to voluntarily seek genetic testing, and finally augment the help of community figures to publicize the program in media and religious gatherings [25].

## Conclusion

According to the results of this cohort study B-thalassemia and SCA are the most common hemoglobinopathy disorders in Saudi Arabia. There is a severe health threat to the society and future generations if the assessment of hemoglobinopathies in pre-marriage cohorts are disdained and considered unworthy and there is an exigency to take preventive measures. In countries with a high prevalence of hemoglobinopathies, premarital screening is helpful for identification and prevention of high-risk marriage challenges. There is need for preventive measures and future comprehensive program with reference to the management, diagnosis and prevention of β-thalassemia and sickle cell diseases among patients.

# References

1. Warr MR, Pietras EM, Passegué E (2011) Mechanisms controlling hematopoietic stem cell functions during normal hematopoiesis and hematological malignancies. Wiley Interdiscip Rev Syst Biol Med 3: 681-701.
2. Celik H, Kramer A, Challen GA (2016) DNA methylation in normal and malignant hematopoiesis. Int J Hematol 103: 617-626.
3. Gore AV, Athans B, Iben JR, Johnson K, Russanova V, et al. (2016) Epigenetic regulation of hematopoiesis by DNA methylation. Elife 5: e11813.
4. Al Sulaiman A, Saeedi M, Al Suliman A, Owaidah T (2010) Postmarital follow-up survey on high risk patients subjected to premarital screening program in Saudi Arabia. Prenat Diagn 30: 478-481.
5. Kohne E (2011) Hemoglobinopathies: clinical manifestations, diagnosis, and treatment. Dtsch Arztebl Int 108: 532-540.
6. Kohne E, Kleihauer E (2010) Hemoglobinopathies: a longitudinal study over four decades. Dtsch Arztebl Int 107: 65-71.
7. Weatherall D (2008) Hemoglobinopathies worldwide: present and future. Curr Mol Med 8: 592-599.
8. Alsaeed AH (2012) Prevalence of hemoglobinopathy disorders in adult patients sent for diagnosis of anemia in Saudi Arabia. Genet Test Mol Biomarkers 16: 25-29.
9. Jaouni SK Al (2010) Prevalence of thalassemia disorders and hemoglobinopathies in Jeddah, western Saudi Arabia. J Appl Hematol 1: 43-46.
10. Elsayid M, Al-Shehri MJ, Alkulaibi YA, Alanazi A, Qureshi S (2015) Frequency distribution of sickle cell anemia, sickle cell trait and sickle/beta-thalassemia among anemic patients in Saudi Arabia. J Nat Sci Biol Med 6: S85-S88.
11. Jastaniah W (2011) Epidemiology of sickle cell disease in Saudi Arabia. Ann Saudi Med 31: 289-293.
12. WMA (1975) Declaration of Helsinki 1975 – WMA – The World Medical Association.
13. Al-Muammar AM, Kalantan H, Azad TA, Sultan T, Abu-Amero KK (2015) Analysis of the SOD1 Gene in Keratoconus Patients from Saudi Arabia. Ophthalmic Genet 36: 373-375.
14. Rosenfeld LG, Bacal NS, Cuder MAM, da Silva AG, Machado ÍE, et al. (2019) Prevalence of hemoglobinopathies in the Brazilian adult population: National Health Survey 2014-2015. Rev Bras Epidemiol 22: E190007.

**15.** El-Hazmi MAF, Al-Hazmi AM, Warsy AS (2011) Sickle cell disease in Middle East Arab countries. Indian J Med Res 134: 597-610.

**16.** AlHamdan NAR, AlMazrou YY, AlSwaidi FM, Choudhry AJ (2007) Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. Genet Med 9: 372-377.

**17.** Al Sulaiman A, Saeedi M, Al Suliman A, Owaidah T (2010) Postmarital follow-up survey on high risk patients subjected to premarital screening program in Saudi Arabia. Prenat Diagn 30: 478-481.

**18.** Al-Qurashi MM, El-Mouzan MI, Al-Herbish AS, Al-Salloum AA, Al-Omar AA (2008) The prevalence of sickle cell disease in Saudi children and adolescents. A community-based survey. Saudi Med J 29: 1480-1483.

**19.** Al-Marzouki AF, Alrefaie NI, Aljohani NA, Alandanusi RA, Alghamdi AA, et al. (2021) The Prevalence of Depression and Anxiety Among Sickle Cell Disease Patients in King Abdulaziz University Hospital. Cureus 13: e18374.

**20.** Thom CS, Dickson CF, Gell DA, Weiss MJ (2013) Hemoglobin variants: biochemical properties and clinical correlates. Cold Spring Harb Perspect Med 3: a011858.

**21.** Al-Qurashi MM, El-Mouzan MI, Al-Herbish AS, Al-Salloum AA, Al-Omar AA (2008) The prevalence of sickle cell disease in Saudi children and adolescents. A community-based survey. Saudi Med J 29: 1480-1483.

**22.** El-Tayeb E-NH, Yaqoob M, Abdur-Rahim K, Gustavson K-H (2008) Prevalence of beta-thalassaemia and sickle cell traits in premarital screening in Al-Qassim, Saudi Arabia. Genet Couns 19: 211-218.

**23.** Al-Gazali L, Hamamy H, Al-Arrayad S (2006) Genetic disorders in the Arab world. BMJ 333: 831-834.

**24.** Bener A, Al-Mulla M, Clarke A (2019) Premarital Screening and Genetic Counseling Program: Studies from an Endogamous Population. Int J Appl Basic Med Res 9: 20-26.

**25.** Al-Shahrani M (2009) Steps toward the prevention of hemoglobinopathies in the kingdom of Saudi Arabia. Hemoglobin 33: S21-S24.