

# Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

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## ABSTRACT

**Background:** Thalassemia and hemoglobinopathies have significant complications on children's health. Also, they have a higher cost for treatment. The prevalence of these diseases differs from one area to another in Saudi Arabia.

**Aims:** To detect the different hemoglobin abnormality and their frequency in the premarital Saudi population in Makkah city.

**Methods:** A cross-sectional study was conducted, which included 473 subjects who attended the premarital screening tests at the maternity and children Hospital laboratory and Herra hospital. We were collected the complete blood count, hemoglobin electrophoresis, and iron profile from the participants. The statistical analysis was achieved by statistical product and service solution (SPSS) program version 20.

**Results:** 74.8% of the participants were normal, 9.3% had iron deficiency anemia (IDA), 6.3% were suspected to be alpha thalassemia trait, 3.4% had sickle cell trait, 3% were polycythemia, 1.5% had hereditary persistence fetal hemoglobin (HPFH), 1.1% were IDA with thalassemia trait, 0.4% were beta thalassemia trait, 0.2% had hemoglobin E trait.

**Conclusion:** thalassemia trait and hemoglobinopathies are present in the premarital Saudi population in Makkah city at a low prevalence. The highest frequency was for the alpha thalassemia trait, then sickle cell trait, then HPFH, then beta-thalassemia trait, and lastly, hemoglobin E trait. IDA is present at a high frequency. Education to the Saudi population at Makkah city is essential to decrease the prevalence of these disorders.

**Keyword:** thalassemia trait, hereditary persistence of fetal hemoglobin, sickle cell trait.

## Introduction

Premarital screening is a program conducted for all married couples to detect genetic and infectious diseases [1]. Thalassemia, sickle cell disease (SCD), and sickle thalassemia are the most common hemoglobin hereditary disorders that have significant complications on the affected person. The incidence of hemoglobin abnormalities in Saudi Arabia has shown wide geographical variation [2-6]. Thalassemia is

Inherited as a recessive trait. It is named according to the deficient chain production. The most common types are  $\alpha$ - and  $\beta$ -thalassemia [7]. Alpha thalassemia causes different manifestations or no symptoms according to the numbers of the affected genes and chains.  $\beta$ -thalassemia is highly prevalent. It includes three forms: major (TM), intermedia (TI), and trait or carrier (TT). The number of carriers worldwide is 80

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## Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

to 90 million (1.5% of the whole population). The patients with  $\beta$ TM are blood transfusion dependents, while those with TI are non-transfusion dependent. The patients with beta-thalassemia major and intermedia have hemolytic anemia, hepatosplenomegaly, bone expansion, and osteoporosis [8]. SCD is inherited as an autosomal recessive disorder. It is characterized by abnormal hemoglobin S. It is common in Sub-Saharan Africa, the Mediterranean basin, and Saudi Arabia [9]. The prevalence of genetic hemoglobin abnormalities in Saudi Arabia (SA) is higher than in other countries [10]. In one study in SA, the prevalence rate for  $\beta$  thalassemia trait and SC trait was 12.9 and 45.8%, respectively. On the other hand, the prevalence rate for  $\beta$  thalassemia and SC diseases was 0.7% and 3.8%, respectively. The highest rate is found in the East and South regions of SA. [11]. Also, the interaction of alpha and beta-thalassemia with the sickle cell gene is observed in SA [11]. Thalassemia, SCD, and sickle thalassemia result from consanguineous marriages. The frequency of consanguineous marriages in SA ranged from 57.7% to more than 80% [12]. As the consanguineous marriages increased the development of these diseases, the Saudi government made the Premarital Screening Program many years ago. It is aimed to detect the frequency of these diseases in different areas in SA. Also, to decrease the cases by increasing the population's awareness about the effects of these diseases [1]. The aim of the study is to detect the different hemoglobin abnormality and their frequency in the premarital Saudi population in Makkah city.

### Methods

This cross-sectional study was carried out from November 2019 to June 2021; it included 473 Saudi premarital screening attendants of both sex, who attended the maternity and children Hospital, and Heraa hospital lab, Makkah, Saudi Arabia, for testing before marriage. The institutional review board (IRB) of Makkah research approved the protocol of this study, and the approval number was H-02-K-076-0919-217. The calculation of the sample size of this study was done according to Slovin's Formula. All Saudi premarital screening attendants were included in the study without any exclusion. Non-Saudi nationality were excluded.

The followings informations were collected:

- 1- Clinical data, which included age and sex.
- 2- Complete hemogram analysis data, which included hemoglobin (Hb), red blood cells (RBC), hematocrit (HCT), mean cell volume (MCV), mean corpuscular

hemoglobin (MCH), total leucocytic count (TLC), and platelets.

3- Data of hemoglobin electrophoresis. It was performed by high-performance liquid chromatography and capillary electrophoresis.

4- Data of serum iron, ferritin, and total iron-binding capacity (TIBC).

### Statistical analysis

The statistical product and service solution (SPSS) program version 20 was used in this study. Normally distributed quantitative data were expressed as mean  $\pm$  SD. The skewed quantitative data were described as median and range. The student t-test, the Mann-Whitney U test, or the Kruskal-Wallis test were used to compare groups.

### Results

The results are summarized from table 1 to table 5. The descriptive data of all participants are shown in (Table 1): 74.8% were normal, 9.3% were iron deficiency anemia (IDA), 6.3% were suspected to be alpha thalassemia trait (ATT), 3.4% were sickle cell trait (SCT), 3% were polycythemia, 1.5% were hereditary persistence of fetal hemoglobin (HPFH), 1.1% were IDA with suspected ATT or BTT, 0.4% were beta thalassemia trait (BTT), 0.2% were hemoglobin E carrier. The suspected cases of the alpha thalassemia trait had normal hemoglobin with low MCV and MCH, high RBC count  $>5.5 \times 10^{12}$ , with normal iron profile and normal hemoglobin A2. Cases with combined IDA with suspected ATT or BTT had low to normal hemoglobin with low MCV and MCH, high RBC count  $>5.5 \times 10^{12}$ , with affected iron profile and normal hemoglobin A2. The laboratory investigations of the male participants in different groups are found in (Table 2). The SCT group showed a significant rise in RBC count and a significant reduction of the MCV compared to the normal group. The IDA group exhibited a significant reduction of RBC count, Hb, and HCT compared to the normal group. The suspected ATT group displayed a significant increase in RBC count and a significant decrease in Hb, MCV, and MCH compared to the normal group. In the polycythemia group, there was a significant rise in RBC count, Hb, and HCT compared to normal. There was only one patient in BTT and Hb E carrier groups, so there was no comparison between them and the control group. The laboratory investigations of the female participants in different groups are illustrated in (Table 3). The SCT showed a significant rise of RDW and a significant reduction of the MCV and hematocrit compared to the normal group. The IDA versus the normal group showed a significant decrease

Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

in Hb, Hct, MCV, MCH, and a significant increase in RDW, RBC count, and platelets. The suspected ATT group versus the normal group displayed a significant increase in RBC count and RDW and a significant decrease in MCV and MCH. The polycythemia group showed a significant increase in RBC count and Hb compared to normal. The combined group versus normal exhibited a significant increase in RBC count and a significant decrease in MCV and MCH with an impaired iron profile. There was one patient only in BTT, so no comparison was made between her and the control group. The data of the hemoglobin electrophoresis of the different groups studied are shown in (Table 4). The descriptive data of classic sickle cell trait (SCT) and various combinations with SCT are shown in (Table 5).

**Discussion**

Thalassemia and hemoglobinopathies have significant complications on the health of the affected subjects and have a high cost for treatment. The prevalence of these diseases differs from one area to another in Saudi Arabia. This study aimed to detect the different hemoglobin abnormalities in the premarital population in Makkah city. Also, to catch the frequency of these hemoglobin abnormalities. In our study, the highest prevalence of abnormality in the premarital screening Saudi population in Makkah city was iron deficiency anemia 9.5%, followed by alpha thalassemia trait (not confirmed by genetic study) 6.3%, then sickle cell trait 3.4%, then polycythemia 3%, then HPFH 1.5%, then IDA with ATT or BTT 1.1%, then beta-thalassemia trait 0.4% and lastly, hemoglobin E carrier 0.2%. As reported previously, in Saudi Arabia, congenital hemoglobin disorders are mainly found in two-zone, one in the eastern of the country (the Eastern region and Ahsa) and the other in the southwestern of the country (Jazan and Qunfudah) [13]. Makkah city is in western Saudi Arabia. The Saudi population lives in Makkah city originated from different nationalities as many peoples in the past migrated to live in Makkah. In our study, 6.3% of our cases were suspected to be alpha thalassemia and needed a genetic analysis for confirmation. This agrees with previous authors who reported that the highest percentage in Saudi Arabia (SA) is  $\alpha$ -thalassemia [14], and up to 45% in the Eastern region are alpha thalassemia trait [15]. The second frequency in our work is the sickle cell trait which constitutes 3.4%. Our results are consistent with previous works, which stated that the frequency of the sickle-cell trait in Makkah city was 4.5%, 4.2%, and 3.1%, respectively [16, 17, 18]. This prevalence is lower than the prevalence in Ahsa, Qunfudah, the Eastern and Jazan regions, which showed a higher prevalence of 16.8%, 13.52%, 13.4%, and 12.7%

**Table 1:** Descriptive data of the participants.

groups	No.	%	Sex		Age Mean± SD
			M	F	
Normal	354	74.8%	19		31.8± 10.7 26.2 ± 7.6
Male			7	15	
Female				7	
HPFH	7	1.5%	4	3	26.8 ± 2.1 29.7 ± 6.8
Male					
Female					
SCT	16	3.4%	7	9	28.0 ± 4.2 25.6 ± 4.2
Male					
Female					
IDA	44	9.3%	2	42	26.0 ± 4.2 25.5 ± 4.9
Male					
Female					
suspected ATT	30	6.3%	14	16	27.6 ± 4.4 26.1 ± 9.7
Male					
Female					
Polycythemia	14	3 %	12	2	30.3 ± 10.7 27 ± 9.9
Male					
Female					
Beta TT	2	0.4%	1	2	23 23
Male					
Female					
HB E carrier	1	0.2%	1	0	66
Male					
IDA +BTT or ATT	5	1.1%	0	6	27.8 ±9.0
Female					
Total	473				

Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

**Table 2:** Laboratory investigations of the male participants in different groups studied.

Groups	WBC X10 <sup>9</sup> /l	RBC X10 <sup>12</sup> /l	Hb g/dl	HCT%	MCV /fl	MCH /pg	RDW CV	Platelets X10 <sup>9</sup> /l
Normal(no. 197)								
Mean ± SD	6.8±1.9	5.4±0.4	15.6±0.9	45.9±2.8	85.7±3.9	29.5±4.6	14±9.9	284.7±65.2
Median	6.4	5.4	15.7	46.3	86	29.2	13.1	275
Min-Max	3.4-13.9	4.4-6.4	12.6-18.2	38.2-55.1	68-99	20.8-89.2	11-142	133-599
HPFH (no.4)								
Mean ± SD	7.6±3.2	5.2±0.4	15.5±0.9	44.4±2.6	84.9±4	29.6±1.7	12.8±0.5	314.8±60
Median	6.7	5.4	15.7	44.9	86.3	30	12.7	316
Min-Max	5-11.9	4.6-5.6	14.3-16.1	40.7-46.8	79.2-87.7	27.4-31	12.4-13.6	246-381
SCT (no.7)								
Mean ± SD	6.4±1.9	<b>5.9±0.4<sup>a</sup></b>	16.3±1.1	47.1±2.4	<b>79.9±3.4<sup>a</sup></b>	27.6±1.1	13.4±0.8	319.9±79.2
Median	6.1	6.0	16.2	46.1	79.9	27.0	13.5	342.0
Min-Max	4.4-8.9	5.1-6.4	14.9-18.4	44.1-51.4	76.2-86.4	26.4-29.2	12.3-14.3	206.0-437.0
IDA (no.2)								
Mean ± SD	5.6±0.2	<b>4.4±0.2<sup>a</sup></b>	<b>11.3±0.9<sup>a</sup></b>	<b>34.1±1.8<sup>a</sup></b>	76.9±0.1	25.4±0.7	15.4±2.6	290.0±79.2
Median	5.6	4.4	11.3	34.1	76.9	25.4	15.4	290.0
Min-Max	5.4-5.8	4.3-4.6	10.6-11.9	32.9-35.3	76.9-77.0	24.9-25.9	13.5-17.2	234.0-346.0
ATT (no.14)								
Mean ± SD	6.3±1.5	<b>6.1±0.3<sup>a</sup></b>	<b>15.0±0.6<sup>a</sup></b>	45.9±1.4	<b>75.4±3.4<sup>a</sup></b>	<b>24.7±1.8<sup>a</sup></b>	14.5±1.4	314.3±101.1
Median	6.5	6.0	15.1	46.1	77.0	25.4	14.3	285.0
Min-Max	3.2-9.3	5.6-6.9	13.6-15.9	43.5-48.2	69.1-70.2	21.4-26.7	12.3-16.8	284.0-599.0
Polycythemia(no.12)								
Mean ± SD	7.0±1.6	<b>6.1±0.3<sup>a</sup></b>	<b>18±0.4<sup>a</sup></b>	<b>52.7±2.1<sup>a</sup></b>	85.7±3.6	29.3±1.4	14.6±2.5	272.5±74.6
Median	7.1	6.1	18	52.2	86	29.3	13.9	254
Min-Max	4.36-10.1	5.70-6.6	17.00-19	49.1-57.3	80.10-90.9	26.10-31.3	12.00-19.8	171.00-402
BTT (no.1)	5.1	7.2	13.6	43	59.6 <sup>a</sup>	18.9 <sup>a</sup>	19.6	211
Hb E carrier (no.1)	8.7	5.5	14.3	42.4	77.8 <sup>a</sup>	26.2	13.2	288.0

N.B. the superscript a denote significance between the normal group and other groups

Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

**Table 3:** Laboratory investigations of the female participants in different groups studied.

Groups	WBC X10 <sup>9</sup> /l	RBCX10 <sup>12</sup> /l	Hb g/dl	HCT%	MCV /fl	MCH /pg	RDWCV	Platelets X10 <sup>9</sup> /l
Normal(no=157)								
Mean ± SD	7.6±2.4	4.7±0.3	13.7±3.2	39.9±2.5	84.9±3.9	28.1±2.8	14.1±9.5	326.2±67.3
Median	7.2	4.7	13.3	39.5	85	28.3	13.3	316
Min-Max	3.2-15	4-5.9	11.3-43.3	34.6-50.2	77.2-95.2	0-32.5	11.5-129	189-522
HPFH (n=3)								
Mean ± SD	7.5±0.9	4.5±0.3	12.9±1.1	37.4±2.4	83.2±4.1	28.5±0.9	13.9±1.9	262±54
Median	7.6	4.7	12.9	36.6	85.5	28.3	13.9	287
Min-Max	6.6-8.5	4.2-4.7	11.8-13.9	35.5-40.1	78.5-85.6	27.7-29.6	12.5-15.2	200-299
SCT (n=9)								
Mean ± SD	7.1±2.1	4.9±0.5	12.5±1.3	<b>37.3±3.6<sup>a</sup></b>	<b>76.6±4.9<sup>a</sup></b>	25.6±2.3	<b>14.6±1.9<sup>a</sup></b>	325.9±70.9
Median	7.1	5	12.1	38.9	77.3	24.9	14.8	288.0
Min-Max	3.6-11.5	4.1-5.5	10.2-14.3	31-42.3	69.5-82.4	22.9-29.0	11.6-17.6	241.0-456.0
IDA (n=43)								
Mean ± SD	6.9±1.9	<b>4.8±0.3<sup>a</sup></b>	<b>10.7±1.3<sup>a</sup></b>	<b>34.7±2.9<sup>a</sup></b>	<b>72.4±5.8<sup>a</sup></b>	<b>22.4±2.7<sup>a</sup></b>	<b>17.1±2.9<sup>a</sup></b>	<b>382.9±97.4<sup>a</sup></b>
Median	6.7	4.8	11.1	35.0	73.7	22.8	16.9	367.0
Min-Max	3.6-11.2	4.2-5.5	8.0-12.9	29.2-40.7	56.5-81.1	15.4-26.4	12.9-26.7	176.0-542.0
ATT (n=16)								
Mean ± SD	7.9±2.9	<b>5.7±0.5<sup>a</sup></b>	13.1±0.8	40.5±2.1	<b>71.2±5.2<sup>a</sup></b>	<b>23.0±2.3<sup>a</sup></b>	<b>14.9±1.2<sup>a</sup></b>	321.5±64.8
Median	7.8	5.6	13.3	41.6	69.4	22.2	14.9	306.5
Min-Max	4.6-15.4	4.9-6.5	11.8-14.3	36.5-42.8	64.5-78.4	20.2-26.7	13.2-17.2	212.0-436.0
Polycythemia (n=2)								
Mean ± SD	8.6±0.5	<b>6.2±0.02<sup>a</sup></b>	<b>16.8±1.3<sup>a</sup></b>	49.6±0	79.2±0.3	26.9±1.9	13.7±2.2	<b>228.5±0.7<sup>a</sup></b>
Median	8.6	6.2	16.8	49.6	79.2	26.9	13.7	2285
Min-Max	8.8	6.2	17.8	49.6	79.5	28.3	15.3	229
BTT(n=1)								
Mean ± SD	8.2	5.4	10.4	33.2	61.1	19.2	16±0.9	371±56.1
Median	8.2	5.4	10.4	33.2	61.1	19.2	16.2	367
Min-Max	8.2	5.4	10.4	33.2	61.1	19.2	16.9	429
IDA +BTT orATT(n=6)								
Mean ± SD	7.0±1.7	<b>5.7±0.2<sup>a</sup></b>	12.5±1.1	39.6±3.2	<b>69.4±7.4<sup>a</sup></b>	<b>21.9±2.3<sup>a</sup></b>	<b>16.5±2.1<sup>a</sup></b>	<b>402.2±95.6<sup>a</sup></b>
Median	7.3	5.7	12.9	40.6	74.4	23.3	15.5	391.5
Min-Max	5.2-8.9	5.5-6.0	11.2-13.6	34.7-42.7	58.3-74.8	18.8-23.8	15.1-20.3	317-557.0

N.B. the superscript a denote significance between the normal group and other groups

Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

**Table 4:** Hemoglobin electrophoresis of the different groups studied and serum iron.

groups	No.	Hb A %	Hb A2%	Hb F%	Hb S% or E or iron
Normal	354				Iron
Male (mean±SD)	197	96.8±0.34	2.8±.27	0.3±0.17	23.5± 2.5
Median(min-Max)		96.9(95.9-98.4)	2.8(1.4-3.6)	0.3(0.1-1.10)	
Female (mean±SD)	157	96.8±0.3	2.8±0.2	0.4±0.2	19.4 ±2.7
Median(min-Max)		96.8(95.7-97.5)	2.8(2.2-3.3)	0.3(0.2-1.3)	
HPFH	7				
Male (mean±SD)	4	93.6±3.4	2.7±0.4	3.7±3.2	
Median(min-Max)		95.1(88.5-95.0)	2.0(2.2-3.0)	2.5(1.5-8.4)	
Female (mean±SD)	3	95.8±0.1	2.8±0.1	1.4±0.1	
Median(min-Max)		95.8(95.7-95.8)	2.8(2.7-2.9)	1.4(1.4-1.5)	
SCT	16				Hb S
Male (mean±SD)	7	60.8±3.1	3.6±0.2	0.4±0.3	35.3±2.9
Median(min-Max)		62.2(57.2-64.1)	3.6(3.3-3.9)	0.2(0.1-1.0)	33.6(32.4-38.8)
Female (mean±SD)	9	61.0±2.7	3.7±0.3	0.4±0.2	34.9±2.7
Median(min-Max)		61.6(56.9-64.5)	3.7(3.4-4.1)	0.4(0.2-0.8)	34.2(31.1-38.4)
IDA	44				Iron
Male (mean±SD)	2	97.3±0.4	2.4±0.4	0.3±0.0	8.5 ±0.7
Median(min-Max)		97.3(97.0-97.5)	2.5(2.2-2.7)	0.3(0.3-0.3)	
Female (mean±SD)	42	97.2±0.4	2.5±0.5	0.4±0.3	6.7±3.1
Median(min-Max)		97.2(95.8-98.0)	2.5(1.5-3.2)	0.3(0.2-1.2)	
Suspected ATT	30				Iron
Male (mean±SD)	14	97.0±0.6	2.6±0.4	0.4±0.3	22.8± 2.1
Median(min-Max)		97.1(95.3-98.2)	2.5(1.6-3.2)	0.3(0.2-1.5)	
Female (mean±SD)	16	97.0±0.4	2.5±0.3	0.4±0.2	19.1± 2.7
Median(min-Max)		97.0(96.6-98.2)	2.7(1.6-3.0)	0.4(0.2-0.8)	
Polycythemia	14	97±0.5	2.6±0.5	0.3±0.1	
Male (mean±SD)	12	96.9(96.2-98)	2.7(1.6-3.3)	0.3±(0.1-0.5)	
Median(min-Max)		97.3±0.4	2.5±0.1	0.3±0.2	
Female (mean±SD)	2	97.3(97-97.5)	2.5(2.4-2.6)	0.3(0.1-0.4)	
Median(min-Max)					
Beta TT	2	94.1	4.9	1.0	
Male (mean±SD)	1	94.1(94.1-94.1)	4.9(4.9-4.9)	1.0(1.0-1.0)	
Median(min-Max)		94.6	5.0	0.4	
Female (mean±SD)	1	94.6(94.6-94.6)	5.0(5.0-5.0)	0.4(0.4-0.4)	
Median(min-Max)					
HB E carrier					Hb E
Male	1	71.7	2.2	0.4	25.7
IDA +BTT or ATT	5				
Female (mean±SD)		97.4±0.2	2.3±0.2	0.4±0.1	
Median(min-Max)		97.5(94.1-97.7)	2.4(2.1-2.4)	0.4(0.2-0.5)	

Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

**Table 5:** Descriptive data of classic sickle cell trait (SCT) and different combinations with SCT.

	Male (7)(mean ±SD)				Female (9) (mean ±SD)		
	Classic (4)	Polycythemia (1)	IDA (1)	Suspected ATT(1)	Classic (4)	IDA (3)	Suspected ATT (2)
WBC X10 <sup>9</sup>	5.9±2.0	8.9	4.8	7.1	6.0±1.7	8.5±2.5	6.9±1.2
RBCX10 <sup>12</sup>	5.7±0.4	6.4	6.2	6.0	4.7±0.5	4.7±0.3	5.5±0.0
Hb g/dl	15.8±0.7	18.4	16.4	16.1	13.1±1.3	11.2±0.9	13.1±0.4
Hct %	46.3±2.0	51.4	47.7	45.9	38.0±3.8	34.9±3.9	39.4±0.4
MCV fl	81.6±3.4	79.9	76.8	76.2	81.2±1.4	73.7±3.9	71.7±0.8
MCH pg	27.9±1.1	28.7	26.4	26.7	28.0±1.0	23.8±1.0	23.8±0.6
MCHC %	34.1±1.3	35.9	34.4	35.1	34.4±1.3	32.2±1.6	33.1±0.6
Platelets X10 <sup>9</sup>	313.5±58.5	437.0	206.0	323.0	270.5±20.4	374.0±89.8	335.7±53.2
RDW %	13.5±1.0	14.2	12.7	13	12.9± 1.0	16.56±1.16	14.8±.07
HbA%	60.3±3.2	57.6	62.6	64.1	59.4±2.9	62.9±1.4	61.3± 3.0
HbA2%	3.7±0.2	3.5	3.7	3.3	3.7±0.3	3.76± 0.32	3.7± 0.0
HbF%	0.50± 0.40	0.10	0.20	0.2	0.40± 0.05	0.53± 0.23	0.33± 0.07
HbS%	35.5± 3.1	38.8	33.60	32.4	36.4± 2.6	32.8± 1.5	34.8± 3.1
Iron umol/l Male 14-32 female11-29	24.5 ±3.0	23	8.0	14	22.0±2.8	6.6±1.2	18.0± 2.8

## Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

[16, 18, 19]. The cause of higher prevalence in Ahsa, Qunfudah, the Eastern and Jazan regions is due to the higher rate of consanguineous marriage. The combination of the sickle cell gene with other abnormal hemoglobin was recorded earlier. In our work, 0.6% of our sickle cell trait cases combined with alpha thalassemia trait cases (Table 5). This is in agrees with previous results ([13]. This study's third frequency of abnormal hemoglobin is HPFH which constitutes 1.5%. It is like the previous author in SA [20]. The fourth frequency in our work was the beta-thalassemia trait which constitutes 0.4%. It is lower than previous results in Makkah city, which showed the prevalence of 1.8%, 3.2%, and 2.7%, respectively [16, 17, 18]. The cause of lower prevalence in our work may be that our study is a cross-sectional study done one year, and the previous studies collected the data in many years. Makkah is not located in the higher frequency of hemoglobinopathies in SA [13]. This explains the lower prevalence of the beta-thalassemia trait in our work and other studies done in Makkah. Our result is nearer to a study done in Al Majma'ah, which showed a prevalence of 0.69% [21]. Also, Al Majma'ah is not located in the higher frequency zone in SA. The fifth and last frequency in our work was hemoglobin E carrier which constitutes 0.2%. Our result is like previous results in SA, where they reported a frequency of 0.9% and 0.08%, respectively [19, 22]. Hemoglobin E is found mainly in Southeast Asian descent [23]. Of our participants, 9.3% and 1.1% were IDA and combined IDA with suspected thalassemia trait, respectively. IDA masks the beta-thalassemia trait as it decreases hemoglobin A2. A study done in 4 regions in Saudi Arabia reported that the highest frequency of IDA (59.2%) was in Dammam, followed by Makkah, Riyadh, and Medina [24]. Lastly, 3% were polycythemic out of our participants, which is not our scope.

### Limitation of the study

No genetic detection of the suspected cases of alpha thalassemia and sickle alpha thalassemia.

### Conclusion

Thalassemia trait and hemoglobinopathies are present in the premarital Saudi population in Makkah city at a low prevalence. The highest frequency was for the alpha thalassemia trait, then sickle cell trait, then HPFH, then beta-thalassemia trait, and lastly, hemoglobin E trait. IDA is present at a high frequency. Increasing the knowledge about thalassemia and hemoglobinopathies could decrease marriage between the carriers and reduce the incidence of the diseases. Genetic detection of the suspected cases of the alpha thalassemia trait is recommended to confirm the diagnosis. Pay attention to the cases of IDA as it interferes with hemoglobin electrophoresis results.

### Conflict of Interest

None

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None

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Prevalence of hemoglobin abnormality in the premarital screening Saudi population in Makkah city in a cross-sectional study

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