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# Academia Open



By Universitas Muhammadiyah Sidoarjo

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# Study of The Frequency of Haemoglobinopathies at Premarital Health Screening In Basrah

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#### Abstract

Background: Hemoglobinopathies are increasingly recognized as a global public health concern, with β-thalassemia major and sickle cell disease posing significant health burdens, particularly in southern Iraq. Specific Background: In response, eight Middle Eastern countries, including Iraq, have implemented mandatory premarital screening and genetic counseling programs to mitigate the transmission of inherited blood disorders. Knowledge Gap: However, limited data exist regarding the prevalence and types of hemoglobinopathies detected through such screening in Basrah province. Aim: This study aimed to determine the frequency of hemoglobinopathies among individuals undergoing premarital screening in Basrah. Results: A retrospective cross-sectional analysis was conducted on 384 randomly selected participants screened between February and June 2018. Females comprised 53.7% and males 46.3% (mean age:  $22.8 \pm 7.78$  years). The prevalence rates were:  $\beta$ -thalassemia trait (2%), sickle cell trait (1.8%), sickle cell anemia (0.2%), sickle-thalassemia (0.5%), Hb D (0.1%), and Hb C (0.2%). A statistically significant association was found between hemoglobinopathies and both consanguinity (33.7%) and positive family history. Novelty: This study provides region-specific epidemiological data on hemoglobinopathies identified through premarital screening. Implications: Findings underscore the need to strengthen genetic counseling and raise awareness about consanguinity-related risks to reduce hereditary blood disorders in the region.

#### **Highlight:**

- Beta thalassemia trait was the most common disorder detected.
- Consanguinity showed significant correlation with hemoglobinopathies.
- Premarital screening is vital for early genetic risk detection.

**Keywords:** Premarital Screening, Premarital Counselling, Hemoglobinopathy, Thalassemia, Sickle Cell Anemia.

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## Introduction

A thorough test known as premarital screening, which must be completed before marriage, covers blood-borne illnesses, infectious diseases, genetic disorders, and clinical evaluations. Premarital medical exams have been suggested as a useful way to prevent several diseases [1]. Inherited hemoglobin disorders are emerging as a global public health concern [2].  $\beta$ -thalassemia major and sickle-cell disease are significant health problems in the southern region of Irag [3].

Premarital screening aims to protect spouses and their offspring against the risk of chronic illnesses [4]. It has been suggested that premarital medical exams are a useful way to prevent many illnesses. In addition, it provides a consultation service for those who are considering marriage. A history, a clinical examination, and laboratory tests are required to screen for inherited and communicable diseases [5].

A premarital screening program enables prospective married couples to find out if they are carriers of specific genetic illnesses, such as thalassemia and sickle cell disease. Although these carriers are typically asymptomatic, they may pass on these illnesses to their future offspring if both partners are carriers. Counseling sessions are usually provided to partners with incompatible premarital test results so they can make educated decisions regarding their marriage, including possibly ending it [6]. Premarital Counseling has shown evidence of effectiveness in reducing the incidence of genetic diseases such as  $\beta$ -thalassemia, as well as reducing the risk of atrisk couples getting married [7].

Hemoglobinopathies are a large, heterogeneous group of genetic abnormalities of hemoglobin. They are the most prevalent hereditary monogenic disorders in the world, and the number of cases is rising year by year. Carriers are typically clinically quiet because the majority of hemoglobinopathies exhibit recessive inheritance. In many endemic countries, preconception and antenatal carrier screening programs are beneficial, with the possibility of prenatal diagnosis [8].

An estimated 7% of the world population carries a DNA variant that causes defective hemoglobin synthesis [9]. Approximately 320,000 babies are born each year with clinically significant hemoglobin disorders. Hemoglobinopathies are most prevalent in certain malaria-prone regions, including Africa, all Mediterranean countries, the Middle East, the Indian subcontinent, and Southeast Asia. The most prevalent type of thalassemia in many Asian nations results from the co-inheritance of HbE and beta thalassemia. The most prevalent hemoglobin type in Bangladesh and other Southeast Asian countries, as well as in the eastern regions of the Indian subcontinent, is HbE [10]. In conclusion, the prevalence of  $\beta$ -thalassemia varies by region, with certain regions having greater rates.  $\beta$ -thalassemia is very common in parts of Asia (including India, Pakistan, and Bangladesh), the Middle East (including Saudi Arabia and Iraq), and the Mediterranean (including Greece, Italy, and Cyprus) due to genetic factors and historical migration patterns. SCD, on the other hand, is found in many African countries, such as those in the southern Sahara, the Middle East, and India, as well as among people of African heritage living in Europe, North America, Central America, and South America [11].

The World Health Organization estimates that carriers of various recessive genetic diseases are the majority, with hemoglobinopathies affecting approximately 7% of the world's population [12].

Eight Middle Eastern nations have mandated premarital screening and genetic counseling (PMSGC) programs to lower the number of at-risk marriages and, consequently, the frequency of disease [13].

β-thalassemia major and sickle-cell disease are significant health problems in the southern region of Iraq [3].

The prevalence of hemoglobinopathies represented 238 / 100000 of the Basrah population. The sex-specific prevalence rate was 247 / 100000 in males and 229 / 100000 in females [14]. Beta thalassemia is the most common diagnosed condition among hereditary hematologic disorders, accounting for 33.15% of the patients registered in the Al-Najaf Governorate's thalassemia center during the study period. This conclusion was reached based on data collected from 1,122 patients between October 2019 and March 2020. In contrast, only 9% of cases are caused by sickle cell disease [15]. With a prevalence of up to 78.71%, beta thalassemia is the most common hemoglobinopathy in the population of Erbil, northern Iraq, according to another study. In contrast, the prevalence of Sickle Cell Disease is only 6.23%. Overall [16].

In Oman, hemoglobinopathies are also rather prevalent; according to a study that used data from 19 hospitals, the prevalence of SCD was 2.7 per 1000 individuals and thalassemia was 0.4 per 1000 persons in a population sample of 1,450,000 people [17]. According to a Saudi Arabian study, the frequency of sickle cell trait was 45.8 per 1000 people overall, whereas sickle cell disease was determined to be 3.8 per 1000 people. In contrast, the prevalence rate for  $\beta$  thalassemia was 0.7 per 1000 and 12.9 per 1000 for the trait [18]. The prevalence of thalassemia is higher than that of sickle cell disease, with 21.1 and 18.1 cases per 1000, respectively, according to 11-year research conducted in Kuwait. However, in the 275,819-person population sample, most cases are of the thalassemia trait rather than  $\beta$  Thalassemia [19].

Classification of hemoglobinopathies:

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Hemoglobinopathies, which have a recessive autosomal dominant mode of inheritance, constitute some of the most prevalent genetic disorders worldwide.

The two primary categories of hemoglobinopathies are:

- a) Qualitative abnormalities: abnormal hemoglobin synthesis (sickle cell, Hb C, Hb D, and others), structural hemoglobin variations.
- b) Quantitative abnormalities: reduced alpha or beta globin chain synthesis rate (thalassemia). Thalassemia syndrome involves quantitative abnormalities in alpha and beta genes, which lead to  $\alpha$  and  $\beta$ -thalassemia, respectively.

These conditions necessitate medical treatment, including frequent blood transfusions [20].

Laboratory Investigation for diagnosis of hemoglobinopathies in a premarital screening program includes:

- 1) Complete blood counts: performed as an initial screening test (for low MCV and MCH), the result is available quickly and cheaply. They also show raised reticulocytes, target cells, and basophilic stippling in the blood film [21].
- 2) Target cells with reticulocytosis, sickle cells, and nucleated red blood cells are seen in peripheral blood smears [22].
- 3) Hb electrophoresis: absence of Hb A, with normal or slightly increased Hb A2 and increased Hb F for thalassemia [21], and the presence of HbS and (2-20%) HbF in sickle cell anemia [23].
- 4) Increase in serum iron and ferritin [21].

Routine screening is not currently offered in Iraq. However, this test can be suggested to the couple if one partner is at high risk of being a carrier (positive family history or one partner has sickling disorder [1].

Premarital screening is seen as the key preventive measure for couples who intend to have children, an essential step in preserving society and enabling individuals to enjoy life, and a way to lower the incidence of hereditary blood diseases such as hemoglobinopathy. In 2006, the World Health Organization (WHO) recommended that member countries set up national programs for treating and preventing hemoglobinopathies in order to lower the morbidity and mortality rates linked to these disorders. (19) The WHO wants to find carriers and offer genetic counseling along with practical ways to lower the number of these births. Iraq has a high rate of consanguineous marriages (47–60%) [24].

Prevention strategies of hemoglobinopathy: Hemoglobinopathy can only be avoided by preventing the genes from being passed on to a child through:

When both male and female are discovered to be heterozygous carriers, the pair receives premarital counseling.

To ascertain whether the fetus of two carriers is impacted, a prenatal diagnosis can be performed using genetic analysis or a tiny fetal blood sample.

Conceive through IVF using pre-implantation genetic diagnostics [25].

## **Methods**

Data were collected from premarital assessment forms and laboratory records at eight premarital medical examination centers, as well as premarital statistical reports from the Public Health Department in Basra during the study period, which spanned from February 1 to the end of June 2018.

Three hundred eighty-four people were included in the study.

Inclusion criteria: the partner who underwent an Hb electrophoresis test for hemoglobinopathy diagnosis; the policy used to do this test was only if one of the couple had a suspected result from a complete blood picture test or had a family history of hemoglobinopathies.

Exclusion criteria: individuals who are known cases of hemoglobinopathy.

The data were collected from the premarital medical examination records of eight hospitals in the Basra Governorate. The information was collected from three sources: the premarital assessment form, the Premarital laboratory results, and the Premarital statistics reports. These include their age, gender, occupation, Consanguinity (Blood relation), the family history of genetic diseases, and the result of the Laboratory Investigation.

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Mean corpuscular hemoglobin (MCH) normal ≥ 27pg

a. Hemoglobin value:

Normal value for Male 13 - 17 gm./dL

Female 12 - 16 gm./dL

- b. RBC indices: 1. Mean corpuscular volume (MCV) normal  $\geq$  80 fI
- c. Hb variant: For the detection of hemoglobinopathies.
- 1. Normal
- 2. Beta thalassemia trait (Hb A2>3.5)
- 3. Sickle cell trait (Hb AS)
- 4. Sickle cell anemia (HbSS)
- 5. Sickle-thalassemia
- 6. Hb D
- 7. Hb C

The statistical data analysis was performed using IBM SPSS Statistics version 26.0; The Pearson Chi-squared test is used to examine qualitative data, which are expressed as percentages (%) and frequencies. At p < 0.05, differences are considered statistically significant.

## **Result and Discussion**

The most common age of persons examined (47.1%) was 20-29 years, and the mean age was  $(22.8\pm7.78)$  as shown in Table 1, which also indicates that the percentage of females in the sample is more than that for males (52.6%) and (47.6%), respectively. Over three-thirds (76.7%) of females were housewives; the lowest percentage (13%) were governmental employees.

About one-third (35.6%) are residents of the Basrah center.

Age (years)		Male		Female	Total (%)			
		Number (%)		Number (%)				
< 20		38 (20.9)		104 (51.5)				
20-29		106 (58.3)		75 (37.1)				
30-39		25 (13.8)		18 (8.9)				
40-49		8 (4.4)		4 (1.9)	12 (3.1)			
50-59		3 (1.6)		1 (0.1)	4 (1.1)			
60-69		1 (0.5)		0 (0)	1 (0.3)			
70-79		1 (0.5)		0 (0)				
Occupation								
Housewife				155 (76.7)				
Self- employed		124 (68.1)						
Government al		38 (20.9)		12 (6.0)				
Student		20 (11.0)		35 (17.3)				
Total		182 (47.4)		202 (52.6)				
Residence		Number		%				
Basra center	127 35.1							
Basra Periphery	257		60	66.9				

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Total 384	100.0
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Table 1. Socio-demographic characteristics of the sample

The table below shows that the percentages of low hemoglobin values were (%) and (%) for females and males, respectively.

Hb v	value	Number	%	Total	
Male	Hb ≥ 13 mg/dL	49	12.8	182	
	<13 mg/dL	133	34.6		
Female	Hb ≥ 12 mg/dL	41	10.7	202	
	< 12 mg/dL	161	41.9		

Table 2. Distribution of the sample by Hemoglobin values.

Result of HB Variant	Number	%
Beta thalassemia trait	21	5.5
Sickle cell trait	19	5.0
Sickle cell anemia	2	0.5
Sickle-thalassemia	5	1.3
Hb D	1	0.3
Hb C	2	0.5
Normal Hb variant	334	86.9
Total	384	100

Table 3. Distribution of the sample according to the result of the Hb variant test

The table below shows that out of 384 individuals tested for Hb variants, the highest percentage (5.5%) was positive for the beta thalassemia trait, followed by the sickle cell trait (4.9%). Additionally, 86.9% of the samples have normal Hb variants.

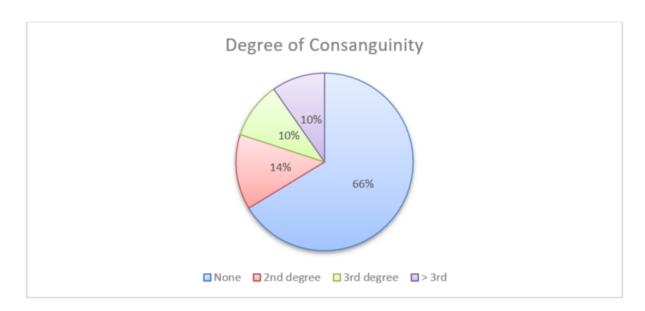


Figure 1. The sample distribution according to the degree of consanguinity between couples

It shows that most of the study sample (66.3%) were non-consanguineous with their partners. One-third (33.7%) shows a positive history of consanguinity, mostly of the second degree (40.6%)

This table shows a highly significant relation between hemoglobinopathies with consanguinity and family history of genetic diseases. P=0.0001

Cons	Hemoglobinopathies	To	tal	P
angui			ŀ	value
nity d				

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egree s	-		thalas	Beta thalassemia trait				Sickle cell anemia		Sickle cell anemia		kle- semia	Hł	D D	Hl	C C		
None	2	10	:	2	5		0		1		1		(	)	218	P= 0		
2nd	4	6	1	.2	5		0			1	0		1		65	.0001		
3rd	3	5	(	6	5		1		2	2	0		1		52	Highl y Sig		
Far	4	2		1	4		1			1	0		(	)	49	nifica		
Total	33	34	21 1		19	2			Ţ	5	=	1	2	2	384	nt X2 =66.9 83a		
histo gen	Family history of genetic diseases								P= 0 .0001 Highl y Sig									
No	one	197	13		15		0		2	(	)	2	2	22	29	nifica nt X2		
Thala	issemi a	60	2		0		0		0	(	)	(	)	6	52	=475. 488a		
S	CA	34	5		2		2	(	0	(	)	(	)	4	:3			
Sickle cell trait		17	0		2		0		0 0 0		1	.9						
thalas	Beta 23 1 0 1 0 1 0 thalassemia trait		(	)	2	:5												
	Sickle- thalassemia 0 0		0		2	(	)	(	)		5							
G6PD		0	0		0		0		0	1		(			1	]		
То	tal	334	21		19		2		5	1		2	2	38	84			

Table 4. Relation between consanguinity and family history of genetic diseases with hemoglobinopathies

#### **B.** Discussion

Premarital screening is a crucial preventive measure, particularly in very consanguineous communities [7].

Along with the negative health implications, they also present serious social, economic, and psychological challenges that have a significant influence on the quality of life for those who are impacted and their family. Primary health care strategies and prevention initiatives that prioritize education can reduce the health burden of these conditions [26].

In this study we screened 384 premarital partners (47.4%) of them were males, (52.6%) were females, their age were ranged from (13-72 years), most of them (47.1%) were age (20-29 years) with mean age (22.8±7.78) this reveals the social attitude towards encouraging the early marriage, this is comparable to previous study in Basra in which age ranged from (14-60 years) [27], and was similar to studying in Izmir/ Turkey [28], (41.9%) of the sample were females with low hemoglobin values; Among anemic people, genetic hemoglobin abnormalities seem to be prevalent. To ascertain the true prevalence of the illness, population screening is required [29].

A screening test helps identify and prevent high-risk marriages in nations where hemoglobinopathies are more prevalent. This study found the beta thalassemia trait in 5.5% of cases. It is higher than that previously reported in Basra (4.6%) in a study carried out in 2001 [27]. Also, it was higher than in another governorate; the prevalence of B-thalassemia carriers in a study in Karbala governorate of the Premarital Screening Program for Hemoglobinopathies was 3.8% [26] while it was lower than other Iraqi governorates, like the study in Erbil (6.94%) [16]; In other countries like Ras-Al Khaimah in UAE, about (2.98%) [30], Saudi Arabia (12.9%) [18], and it's higher than that reported in the Turkish study in Izmir (1.8%) [28].

It is well known that the treatment and health services for one B-thalassemia major patient cost US\$2500 to US\$10500 annually, depending on their age and weight. (One can imagine the total burden of these diseases on the Ministry of Health budget. This fact emphasizes the importance of launching a well-established nationwide prevention program [27].

The rate of sickle cell trait in this study was about 5%, which is lower than the previously reported figure in Basra (6.48%) [27] and sickle hemoglobin. This may be due to some missed cases because the Hb variant was not

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routinely performed for all cases. Sickle cell disease is the predominant disease in Basrah [31]. The prevalence of sickle cell carriers in this study was underestimated because all couples screened with CBC and hemoglobin electrophoresis should have undergone a sickling test to detect sickle cell carriers, but this was infeasible. This might be a weak point in the screening program. It requires both couples to have low MCV and low MCH to perform electrophoresis, which may lead to escape of some serious hemoglobinopathies like HbS or HbC when coinherited with thalassemia. This could be due to the reduced sickle hemoglobin detection rate in Basra, an endemic region with sickle cell hemoglobin. This could lead to lower high-risk marriages being detected in the study.

Also, it was lower than the result in Saudi Arabia (45.8%) [31], Nigeria (24%) [32], and India (3.36%) [33]. The result is higher than those reported in other Iraqi Governorates like Erbil (0.064%) [16] and other countries, such as Antalya, Turkey (0.31%) [34].

The rate of sickle cell anemia in this study is (0.5%) which is comparable to those reported in Karbala of 0.56% [26], and higher than that in Izmir/ Turkey (0.1%) [28] and in Nigeria (0.5%) [32] but lower than those reported in Saudi Arabia (3.8%) [18], Ras-Alkaima/ UAE (1.05%) [30].

The rate of Hb D in this study is (0.3%), which is higher than that reported in Antalya/Turkey (0.15%) (30) and lower than those reported in other countries like India (0.67%)[33].

The rate of Hb C in this study was 0.5%, which is lower than those reported in Nigeria (2.0%) [32].

The rate of sickle-thalassemia in this study is (1.3%). We couldn't compare this rate with other governorates or countries because similar data was unavailable.

There's a highly significant relationship between the family history of these diseases and consanguinity (P=0.001). These results agree with those of a study in Izmir /Turkey [28], which shows a significant relationship with consanguinity. This means those with a positive family history are more likely to have these genetic diseases; also, married couples who are consanguineous increase the chance of transmitting these diseases to their children [25].

This study shows that the consanguinity rate among married couples in Basra city is (33.7%). They are mostly in first cousin marriages (40.6%) (it's expected that the birth rate of homozygous for an inherited condition will be more than the rate expected for a population without those marriages), the rate in this result is higher than that reported in Kurdistan (26%) [35]. On the other hand, it's lower than that for Saudi Arabia (>50%) with a rate of first cousin marriage (40-50%) [36] and Pakistan (56%) [37].

According to the program's data, a similar project in neighboring nations did have more successful results. For instance, by issuing hazardous marriage licenses, the campaign successfully prevented 50.4% of risky couples from being married in Kuwait [7]. More work is still needed to properly accomplish the program's main objective of lowering high-risk marriages.

## **Conclusion**

The prevalence of marriages among high-risk couples has not decreased despite the nationwide mandatory premarital examination screening (PMSGC) program for thalassemia. However, according to the results of earlier research, targeting young adults and educating them about hemoglobinopathies and their effects may reduce the frequency of these conditions and marriages among carrier populations.

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