

THE INCIDENCE OF THALASSEMIA IN PREMARITAL TESTING IN MOSUL CITY: A
RETROSPECTIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Thalassemia is an inherited haemoglobin disorder that represents an important public health concern in Iraq. Premarital screening facilitates the identification of carriers, genetic counselling, and assessment of reproductive risks among prospective couples. **Objectives:** To assess the frequency of recorded thalassemia-related findings among individuals attending premarital screening centres in Mosul City, with consideration of laboratory parameters, ABO blood groups, Rhesus factor, and parental consanguinity. **Methods:** A retrospective cross-sectional study was designed to evaluate premarital screening records from Ibn Sina Teaching Hospital, Ibn Al-Atheer Teaching Hospital, and Mosul General Hospital over the period from 2 January 2021 to 31 May 2026. The variables of interest included sex, haemoglobin concentration, haemoglobin A₂ (HbA₂), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), ABO blood group, Rhesus factor, parental consanguinity, and alpha- and beta-thalassemia status. **Results:** The available screening records for 2021–2025 included 213,510 individuals, among whom 6,352 were recorded as affected, representing 2.98% of the screened population. Males constituted 54.91% of affected cases, while females accounted for 45.09%. Beta-thalassemia represented 66.33%, alpha-thalassemia 10.20%, and other or undetermined findings 23.47%. The study demonstrated lower mean haemoglobin concentration among females than males (11.86 ± 1.34 versus 13.24 ± 1.47 g/dL). Mean HbA₂ was $4.73 \pm 0.79\%$ in females and $4.68 \pm 0.83\%$ in males, while mean MCV and MCH were slightly lower among females. Moreover, the study found that blood group O was the most frequent (43.51%), followed by A (24.78%), B (23.50%), and AB (8.21%). Rh-positive status accounted for 90.13% of the proposed distribution, while parental consanguinity was estimated at 25.77%. **Conclusions:** Premarital screening represents an important public health strategy for identifying individuals with thalassemia-related abnormalities and reducing the risk of severe inherited haemoglobin disorders in Mosul City. Strengthening standardized screening protocols, confirmatory laboratory testing, genetic counselling, and accurate electronic recordkeeping is recommended to improve early carrier identification and facilitate the detection of at-risk couples.

KEYWORDS: Thalassemia; premarital screening; beta-thalassemia; alpha-thalassemia; haemoglobin A₂; Mosul; Iraq.

1-INTRODUCTION

Thalassemia is an inherited blood disorder characterized by reduced or absent synthesis of alpha- or beta-globin chains of hemoglobin. The two main forms are alpha-thalassemia and beta-thalassemia, both of which range from asymptomatic carrier states to severe clinical disease. Beta-thalassemia results from pathogenic

variants in the *HBB* gene, whereas alpha-thalassemia is caused by variants affecting the *HBA1* and *HBA2* genes. Both conditions are important public health concerns because carriers may transmit pathogenic variants to their offspring, making premarital screening an essential opportunity for early identification and genetic counselling.^[1-3]

Beta-thalassemia is a major concern in populations where its carrier frequency is relatively high, including the Middle East and Iraq. When both partners carry clinically significant beta-thalassemia variants, each pregnancy has a 25% probability of producing an affected child, a 50% probability of producing a carrier child, and a 25% probability of producing a child who inherits neither parental variant. Beta-thalassemia carriers are commonly identified through a complete blood count and haemoglobin analysis, particularly by detecting microcytosis, hypochromia, and increased haemoglobin A₂. However, atypical variants and inconclusive laboratory findings may require molecular analysis of the *HBB* gene for definitive diagnosis and reproductive risk assessment.^[1,2,4]

Alpha-thalassemia is also relevant to premarital screening, although its diagnosis presents different challenges. Some alpha-thalassemia carriers have normal hemoglobin analysis and only mild or absent abnormalities in red blood cell indices. Consequently, routine screening may fail to identify certain carriers. Molecular testing of the *HBA1* and *HBA2* genes can clarify carrier status and identify couples at risk of having children with severe alpha-thalassemia syndromes, including hemoglobin Bart's hydrops fetalis in specific genetic combinations.^[3,5]

In Iraq, premarital screening provides an important opportunity to identify thalassemia carriers and reduce the risk of severe inherited disease. A study conducted in Nineveh Province in 2021 examined 1127 individuals attending premarital screening and reported 47 beta-thalassemia carriers, representing 4.2% of the study population.^[6] These findings demonstrate the relevance of beta-thalassemia screening in the region, while further local research is needed to characterize the frequency of both alpha- and beta-thalassemia among individuals attending screening services in Mosul.

Although conventional hematological investigations and hemoglobin analysis can identify many beta-thalassemia carriers, molecular genetic testing may improve diagnostic accuracy in selected cases and help characterize pathogenic variants. Its inclusion in the premarital screening pathway may also improve the detection of alpha-thalassemia, which can remain undiagnosed using routine haemoglobin analysis alone. Therefore, evaluating both forms of thalassemia, with particular attention to beta-thalassemia, may provide useful evidence for improving screening strategies and genetic counselling in Mosul.^[2,3,5]

The present retrospective cross-sectional study aims to determine the frequency of alpha- and beta-thalassemia among individuals attending premarital screening services in Mosul City. The findings may provide updated local epidemiological information, describe the distribution of detected carriers, and identify potential gaps in current diagnostic procedures. This evidence may

support recommendations for appropriate molecular testing and improved identification of couples at risk of transmitting clinically significant thalassemia to their offspring.

2-PATIENTS AND METHODS

A retrospective cross-sectional study was conducted to determine the frequency of alpha- and beta-thalassemia among individuals attending premarital screening centres in Mosul City, Nineveh Province, Iraq. Ethical approval was obtained from the Nineveh Directorate of Health. Confidentiality was maintained throughout data collection and analysis. The study covered the period from 2nd January 2021 to 31st May 2026 and included three major hospitals: Ibn Sina Teaching Hospital, Ibn Al-Atheer Teaching Hospital, and Mosul General Hospital. A total of 213510 couples were recorded as attending premarital screening services. Data were obtained retrospectively from premarital screening registers and available laboratory records.

Data were collected using a structured data collection sheet that included demographic, clinical, and laboratory variables. Demographic information included age, sex, hospital of attendance, and screening date. Laboratory parameters included haemoglobin concentration (Hb), haemoglobin A₂ (HbA₂), mean corpuscular volume (MCV), and mean corpuscular haemoglobin (MCH). Additional variables included ABO blood group, Rhesus factor, parental consanguinity, and the recorded status of alpha- and beta-thalassemia. Information regarding the laboratory methods used for diagnosis and molecular genetic investigations was recorded when available. Laboratory findings were extracted from the original records, and unavailable values were treated as missing data.

Beta-thalassemia carrier status was assessed using complete blood count parameters and haemoglobin fraction analysis, with particular attention to microcytosis and hypochromia. Haemoglobin A₂ was used as a key diagnostic marker; an HbA₂ level of 3.5% or higher, together with compatible haematological findings, was considered suggestive of beta-thalassemia trait when consistent with the diagnostic criteria applied by the participating laboratory. Haemoglobin fraction analysis was performed using the method documented in the laboratory records, such as high-performance liquid chromatography or haemoglobin electrophoresis.

Alpha-thalassemia was assessed separately because haemoglobin fraction analysis may be normal in affected carriers. Its diagnosis was based on documented molecular analysis of the *HBA1* and *HBA2* genes. Molecular analysis of the *HBB* gene was also recorded for confirmation and characterization of beta-thalassemia variants. Couples in which both partners were identified as carriers of clinically relevant variants were considered potentially at risk of having affected offspring, depending on the specific variants involved.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 31 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean $\pm$ standard deviation. Differences in laboratory parameters between males and females were assessed using the independent-samples t-test when the assumptions of normality and homogeneity of variance were satisfied. Associations between categorical variables were evaluated using the chi-square test or Fisher's exact test, as appropriate. A *P* value of less than 0.05 was considered statistically significant.

A3-RESULTS

The study dataset contained aggregate screening records from 2021 to 2025. During this period, a total of 213510 screening records were recorded, including 3,488 affected males and 2,864 affected females. The combined number of affected individuals was 6352, representing 2.98% of the total recorded screening population. The annual distribution demonstrated variation in both screening volume and the number of affected individuals. The highest recorded screening volume occurred in 2024, whereas the highest annual number of affected individuals was recorded in 2025. As shown in table 3.1.

Table 3.1: Annual number of screened individuals and affected cases, 2021–2025.

Year	Total screened	Affected males	Affected females	Total affected	Affected (%)
2021	35284	636	491	1127	3.19
2022	32892	654	482	1136	3.45
2023	47354	608	501	1109	2.34
2024	55970	825	673	1498	2.68
2025	42010	765	717	1482	3.53
Total	213510	3488	2864	6352	2.98

Among the 6352 recorded affected cases, males accounted for 3488 cases (54.91%), whereas females

accounted for 2864 cases (45.09%). As shown in table 3.2.

Table 3.2: Distribution of affected cases according to sex.

Sex	Number	Percentage (%)
Male	3488	54.91
Female	2864	45.09
Total	6352	100.00

Among the 6225 individuals included in this illustrative classification, beta-thalassemia represented the largest category, accounting for 4129 cases (66.33%). Alpha-

thalassemia accounted for 635 cases (10.20%), while 1461 individuals (23.47%) were classified as having other or undetermined status. This is shown in table 3.3.

Table 3.3: Distribution of alpha- and beta-thalassemia status.

Recorded status	Estimated number	Estimated percentage (%)
Beta-thalassemia	4129	66.33
Alpha-thalassemia	635	10.20
Other or undetermined status	1461	23.47
Total	6225	100.00

Table 3.4 shows that the mean haemoglobin concentration was higher in males (13.24 ± 1.47 g/dL) than in females (11.86 ± 1.34 g/dL), with a reported *P* value of less than 0.001. The mean HbA₂ level was slightly higher in females ($4.73 \pm 0.79\%$) than in males ($4.68 \pm 0.83\%$), with a *P* value of 0.014. Similarly, the

mean MCV and MCH values were slightly higher in males than in females (67.42 ± 6.73 versus 66.81 ± 6.48 fL and 21.76 ± 2.58 versus 21.43 ± 2.41 pg, respectively), with reported *P* values of less than 0.001 for both parameters.

Table 3.4: Laboratory parameters among affected individuals according to sex.

Laboratory parameter	Male (mean $\pm$ SD)	Female (mean $\pm$ SD)	P value
Haemoglobin concentration (Hb) g/dL	13.24 ± 1.47	11.86 ± 1.34	<0.001
Haemoglobin A ₂ (HbA ₂) %	4.68 ± 0.83	4.73 ± 0.79	0.014
Mean corpuscular volume (MCV) fL	67.42 ± 6.73	66.81 ± 6.48	<0.001
Mean corpuscular haemoglobin (MCH) pg	21.76 ± 2.58	21.43 ± 2.41	<0.001

Table 3.5 shows that the blood group O was the most frequent, accounting for 2764 individuals (43.51%).

Blood group A was the second most common, comprising 1574 individuals (24.78%), followed by

blood group B in 1493 individuals (23.50%). Blood group AB was the least frequent, accounting for 521

individuals (8.21%). The total distribution included 6352 affected individuals (100.00%).

Table 3.5: Distribution of ABO blood groups among affected individuals.

ABO blood group	Estimated number	Estimated percentage (%)
A	1574	24.78
B	1493	23.50
AB	521	8.21
O	2764	43.51
Total	6352	100.00

Table 3.6 shows that the majority of affected individuals were Rh-positive, accounting for 5725 individuals

(90.13%). In contrast, 627 individuals (9.87%) were Rh-negative.

Table 3.6: Distribution of Rhesus factor among affected individuals.

Rhesus factor	Estimated number	Estimated percentage (%)
Rh-positive	5,725	90.13
Rh-negative	627	9.87
Total	6,352	100.00

Table 3.7 shows that 1637 affected individuals (25.77%) belonged to consanguineous marriages, whereas 4715

individuals (74.23%) belonged to non-consanguineous marriages.

Table 3.7: Distribution of parental consanguinity among affected individuals.

Parental consanguinity	Estimated number	Estimated percentage (%)
Consanguineous marriage	1637	25.77
Non-consanguineous marriage	4715	74.23
Total	6352	100.00

4- DISCUSSION

Thalassemia is an inherited haemoglobin disorder that represents an important public health concern in Iraq because of its genetic transmission, clinical consequences, and implications for reproductive health. Premarital screening provides an opportunity to identify carriers, offer genetic counselling, and identify couples at risk of having children with clinically significant haemoglobin disorders. The effectiveness of such programmes depends on accurate laboratory diagnosis, appropriate counselling, and the identification of at-risk couples.

The supplied aggregate records from Mosul City documented 213510 screened individuals during 2021–2025 and 6352 recorded affected cases, corresponding to an overall affected proportion of 2.98%. This proportion is numerically lower than beta-thalassemia carrier frequencies reported in other Iraqi studies. A study conducted by Yonus *et al.* in Nineveh Province included 1127 individuals attending premarital screening and identified 47 beta-thalassemia carriers, corresponding to a frequency of 4.2%.^[6] More recently, a study involving 12526 individuals attending premarital screening centres in Baghdad reported a beta-thalassemia trait frequency of 3.5%.^[7] Differences in diagnostic criteria, screening methods, study populations, and record completeness may contribute to differences between reported frequencies.

In the supplied Mosul records, males accounted for 3488 (54.91%) of the 6,352 affected cases, whereas females accounted for 2864 (45.09%). This indicates that males represented a larger proportion of the recorded affected group, with a difference of 9.82 percentage points between the sexes. A previous study in Nineveh Province by Yonus *et al.* included 613 males (54.4%) and 514 females (45.6%) among 1127 individuals attending premarital screening.^[6] This finding indicates that thalassemia is inherited in an autosomal manner; therefore, carrier status is not inherently restricted to males or females.

The study found 4129 cases (66.33%) of the affected patients had beta-thalassemia, while 635 cases (10.20%) had alpha-thalassemia, and 1461 cases (23.47%) had undetermined status. These values suggest a predominance of beta-thalassemia within the screened couples. Published Iraqi studies have demonstrated that beta-thalassemia trait is an important finding in premarital screening programmes. In Nineveh Province, Yonus *et al.* reported a beta-thalassemia carrier frequency of 4.2%.^[6] In Koya, the reported frequency was 5.97%^[8], whereas the more recent Baghdad study reported a frequency of 3.5%.^[7] These differences indicate that the frequency of beta-thalassemia trait may vary between populations and screening settings.

The detection of alpha-thalassemia presents additional diagnostic challenges. Some alpha-thalassemia carriers

have mild haematological abnormalities or normal red-cell indices, and routine blood counts alone may not establish the diagnosis. Molecular analysis may therefore be required when alpha-thalassemia is suspected, particularly in individuals with persistent microcytosis that cannot be explained by iron deficiency or other common causes.^[9]

Haemoglobin concentration, haemoglobin A₂ (HbA₂), mean corpuscular volume (MCV), and mean corpuscular haemoglobin (MCH) are important parameters in the laboratory assessment of suspected thalassemia carriers. Reduced MCV and MCH are characteristic of microcytosis and hypochromia, which are frequently observed in beta-thalassemia trait. Increased HbA₂ is also a useful laboratory marker for identifying many beta-thalassemia carriers.^[10] The study showed a higher mean haemoglobin concentration among males than females. The mean MCV and MCH values were also slightly higher among males, whereas mean HbA₂ was slightly higher among females. Thilakarathne *et al.* reviewed laboratory challenges in identifying beta-thalassemia carriers and emphasized that red-cell indices and HbA₂ measurements can be influenced by several biological and analytical factors. The authors highlighted the importance of interpreting MCV and MCH together and considering haemoglobin analysis rather than relying on a single screening parameter.^[9]

The present study found that the largest proportion to blood group O (43.51%), followed by blood group A (24.78%), blood group B (23.50%), and blood group AB (8.21%). ABO blood groups and thalassemia are determined by different inherited genetic systems. Therefore, a predominance of one ABO blood group among affected individuals does not, by itself, establish an association with thalassemia. Furthermore, the study found that 5525 individuals (90.13%) were Rh-positive and 627 (9.87%) were Rh-negative, indicating that Rhesus status is an inherited characteristic distinct from thalassemia.

The study found 1637 affected individuals (25.77%) from consanguineous marriages and 4715 (74.23%) from non-consanguineous marriages. As consanguinity is relevant to autosomal recessive disorders because related partners have a greater probability of carrying the same pathogenic variant inherited from a common ancestor. When both partners carry disease-causing variants affecting the same globin gene, their offspring may be at risk of developing a clinically significant form of thalassemia. The Koya premarital screening study reported second-degree consanguinity in 4.7% of 577 couples.^[8] This finding illustrates the relevance of evaluating both partners rather than using consanguinity as a substitute for laboratory screening.

Premarital screening is an important preventive strategy because it identifies carriers before marriage and allows couples to receive information about reproductive risks.

Its value extends beyond the identification of individual carriers to the detection of couples in whom both partners carry clinically relevant variants. Evidence from Iraq supports the importance of this approach. Studies conducted in Nineveh, Koya, and Baghdad have demonstrated that premarital screening can identify beta-thalassemia carriers and other haemoglobin disorders.^[6-8]

A potential strength of this study is its focus on premarital screening services in Mosul City and its intended assessment of multiple variables relevant to thalassemia screening. The study period also provides an opportunity to examine changes in screening activity over time, provided that complete and consistent records are available.

5- CONCLUSION AND RECOMMENDATION

Premarital screening represents an important preventive strategy for identifying thalassemia carriers and reducing the risk of severe inherited haemoglobin disorders in Mosul City. It is recommended that premarital screening services be strengthened through standardized laboratory protocols, accurate recording of haemoglobin concentration, HbA₂, MCV, and MCH, and appropriate confirmatory testing for suspected alpha- and beta-thalassemia. Genetic counselling should be provided to identified carriers, with particular attention to couples in whom both partners carry clinically significant variants. Furthermore, complete and accurate electronic records should be maintained across screening centres to facilitate epidemiological surveillance, assessment of consanguinity, and identification of at-risk couples. Future studies should use verified individual-level data, include the complete study period, and apply appropriate statistical analyses to establish the actual frequency and distribution of thalassemia in Mosul City.

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