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The prevalence Diabetes Among Patients with Thalassemia Major

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Abstract

Background: Thalassemia major requires lifelong transfusions, which often lead to iron overload and pancreatic damage. This increases the risk of glucose intolerance and diabetes mellitus, with prevalence rates ranging from 10% to over 30%. Early diagnosis and management are essential to reduce morbidity and improve outcomes. Iron chelation therapy and insulin treatment remain key components in preventing and managing diabetes in these patients**.**

Patients and Methods: This cross-sectional study was conducted at the Thalassemia Centre in Erbil to assess the prevalence of diabetes mellitus among transfusion-dependent thalassemic patients. A total of 100 patients aged ≥10 years were included, with data collected through structured interviews and clinical records. The study found an 18% prevalence of diabetes, with younger age and poor chelation adherence as notable factors. Statistical analysis revealed no significant association between diabetes and adherence levels. These findings highlight the need for early screening and comprehensive management in this high-risk group**.**

Results: Out of the 100 patients included in the study, most were aged <20 years (65%), with a slight female predominance (51%). Adherence to chelating agent therapy in thalassemic patients 51% showed medium adherence. The prevalence of DM in the thalassemic patients was 18.0%, participants who are underweight, were significantly 2.99 times with a lower risk of diabetes. **Conclusion:** This study found an 18% diabetes prevalence in thalassemia patients, with higher rates in younger individuals, moderate chelation adherence, being underweight and younger have lower risk of developing DM

Key words: Adherence, Diabetes mellitus, Iron overload, Prevalence, Thalassemia major, Transfusion-dependent.

Introduction:

Thalassemia major is a severe inherited anaemia caused by defective haemoglobin synthesis, resulting in ineffective erythropoiesis and chronic anaemia. Lifelong blood transfusion therapy is necessary to

maintain haemoglobin levels and suppress ineffective erythropoiesis. [1] However, chronic transfusions lead to systemic iron overload, which accumulates in various organs, including the pancreas, liver, and heart. [2] Pancreatic iron deposition impairs insulin secretion and promotes insulin resistance, significantly increasing the risk of glucose intolerance and diabetes mellitus (DM) in these patients. [3,4] According to the literature, the prevalence of thalassemia patients with diabetes mellitus is between 20% and 30% worldwide. According to some researchers in a multicentre study, 4.9% of patients with thalassemia major had diabetes mellitus (DM) (sample size 1861). In a different study, 17% of patients with beta thalassemia major had diabetes. [5,6] Studies have reported a variable prevalence of glucose abnormalities and DM among patients with thalassemia major, ranging from 10% to over 30%, depending on the population and diagnostic criteria.[7] Early identification and management of diabetes are critical to improving long-term outcomes and reducing morbidity in this vulnerable population. [8]Iron chelation treatments and frequent blood transfusions were used to treat patients with beta thalassemia major. However, the pancreatic beta cells still had excessive iron deposition, which subsequently destroyed the beta cells of the pancreas. Insulin treatment is required because this results in the death of pancreatic beta cells and insufficient insulin secretion.[9] Deferoxamine (DFO) and deferiprone were used in iron chelation therapy to reverse glucose intolerance and postpone the onset of diabetes. [10] According to recent studies, deferasirox helped thalassemia major patients. Additionally, losing weight and engaging in physical activity can help prevent the onset of diabetes. One of the main determinants of diabetes management is the extent of beta cell destruction and, consequently, the decrease in insulin secretion. [11-13] Present two systematic treatment plans. Prior to breakfast and dinner, premixed insulin is used. Second, prandial rapid-acting insulin is prescribed with every meal, and basal slow-acting insulin is administered once daily like Levemir or Glargine. [14] Aim of the Study is to determine the prevalence of diabetes mellitus among patients with thalassemia major. Moreover, the objectives of the study are to find out the association between DM and. serum Ferritin level group in thalassaemic patients, DM and chelation adherence in thalassaemic patients, and (DM and duration of blood transfusion in thalassaemic patients).

Methodology

This study is a Cross-sectional, observational study, meaning the researcher studied thalassaemic patients over 1 month and observed their outcome and prognosis over a brief time. The study was performed in the outpatient department of the Thalassemia Centre of Erbil city, which is a tertiary health care facility in Erbil/ Kurdistan/ Iraq, for patients who came for admission and blood transfusion. The researcher collected data through a structured questionnaire designed for patients from Apr. 2024 to Jun 2025. Inclusion Criteria were patients (aged ≥10 years) with a confirmed diagnosis of transfusion-dependent thalassemia,

whereas patients diagnosed with other endocrinopathies or chronic conditions affecting glucose metabolism, patients with pre-existing type one diabetes mellitus, and those receiving blood transfusion for less than 5 years were excluded from the study. A sample size of approximately 100 was calculated using Epi-Info software, considering a population size of 1000 thalassemia patients who receive regular blood transfusions, with an expected frequency of 50%, a 95% confidence interval, and a 5% acceptable margin of error. A total of 100 patients were included in the study. This number will allow for a comprehensive description and analysis of data. After obtaining every participant's approval, on some occasions, their parents' approval in case of child cases, and the scientific and Ethical Committee of the Kurdistan Higher Council of Medical specialties approval, convenient data were collected by direct face-to-face interviews of the patients using a structured questionnaire and by reviewing the patients laboratory, imaging results and reviewing their form and case sheets, the questionnaire was divided into 3 parts including demographic information. clinical presentation, and laboratory data**.** The data that had been collected were analysed using appropriate statistical methods to describe frequencies and proportions of different variables. Descriptive statistics were used to summarize the sociodemographic and other characteristics of the participants, while the Chi-square and Fisher Exact test were used to explore the association between variables. SPSS version 26 was used for this purpose.The study had several limitations, including incomplete or inaccurately recorded data for some patients, limited patient enrolment due to time restrictions confined to morning hours, and the relocation of some internally displaced individuals to southern Iraqi governorates, which may impact the generalizability of the findings.

Results

Out of the 100 patients included in the study, most were aged <20 years (65%), with a slight female predominance (51%). Regarding BMI, 44% were overweight, 36% had normal weight, and 20% were underweight. Details are shown in Table 1. Out of 100 patients, 18% were diabetic, and 19% had a history of endocrine disorders. A family history of diabetes mellitus (DM) was present in 38% of the participants. Regarding HbA1c levels, 75% had normal values, while 15% were borderline, and 10% had high HbA1c levels, indicating poor glycaemic control in a minority of cases**.** Details are shown in Table 2.

Table 1: Sociodemographic Characteristics of Patients

Variables	**Groups**	**No (%)**
Age group	<20 years	65 (65.0)
	20-39 years	25 (25.0)
	40- 60 years	10 (10.0)
Sex	Male	49 (49.0)
	Female	51 (51.0)

BMI	Underweight (<18.5)	20 (20.0)
	Normal weight 18.5-24.9)	36 (36.0)
	Over weight	44 (44.0)
Total		100 (100.0)

Table 2: Clinical Characteristics and Comorbidities

Variables	Groups	No (%)
Diabetes status	Diabetic	18 (18.0)
	Non-diabetic	82 (82.0)
History of endocrine disorder	Yes	19 (19.0)
	No	81 (81.0)
Family history of DM	Yes	38 (38.0)
	No	62 (62.0)
HbA1c (%)	Normal	75 (75.0)
	Border line	15 (15.0)
	High	10 (10.0)
Total		100 (100.0)

Among the 100 patients, 40% were receiving a single chelating agent, 40% used two agents, and 20% were on triple therapy. Regarding the type of chelating agents, Desferal (65%) was the most commonly used, followed by Exjade (60%) and Keilfer (50%).

In terms of adherence to chelation therapy, 51% showed medium adherence, 33% high, and 16% low adherence. Regarding blood transfusion frequency, the majority (56%) received 12–24 transfusions per year, while 24% had fewer than 12, and 20% received more than 24.The age at diagnosis of thalassemia was 1–5 years in 65% of patients, under 1 year in 30%, and over 5 years in only 5%. The most recent serum ferritin levels were high in the vast majority (51%), borderline in 46%, and only 3% had normal ferritin levels, indicating a high prevalence of iron overload in the study population. Details are shown in Table 3.

Table 3: Thalassemia-Related History and chelating agent

Variables	Groups	No (%)
Chelating agent	Single chelating agent	40 (40.0)
	Tow chelating agent	40 (40.0)
	Triple chelating agent	20 (20.0)
Type of chelating agent	Exade	60 (60.0)
	Keilfer	50 (50.0)
	Desferal	65 (65.0)
Adherence to chelating agent	Low	16 (16.0)
	Medium	51 (51.0)
	High	33 (33.0)
Frequency average of regular blood transfusions/year	< 12	24 (24.0)
	12-24	56 (56.0)
	>24	20 (20.0)
Age of diagnosis of Thalassemia	<1 year	30 (30.0)
	1-5 years	65 (65.0)
	>5 years	5 (5.0)
Most Recent Ferritin level	Normal	3 (3.0)
	Borderline	46 (46.0)

	High	51951.0)
Total		100 (100.0)

Among the 100 patients, 40% received a single chelating agent, 40% received two agents, and 20% received triple therapy. There was **no statistically significant association** between the type of chelation regimen and the presence of diabetes mellitus among thalassemia major patients. Details are shown in Table 4.

Table 4: Association of Chelation Regimens with Diabetes Status

Chelation Regimen	Diabetic no (%)	Non-Diabetic no (%)	Total no (%)	Chi-square (χ^2)	p. value
Single agent	7 (7.0)	33 (33.0)	40 (40.0)	0.915	0.633
Two agents	6 (6.0)	34 (34.0)	40 (40.0)		
Triple agents	5 (5.0)	15 (15.0)	20 (20.0)		
Total	18 (18.0)	82 (82.0)	100 (100.0)		

Among the 100 thalassemia major patients, analysis of adherence to chelation therapy in relation to diabetes status revealed that 5 diabetic patients (5.0%) had low adherence compared to 11 (11.0%) non-diabetic patients; 9 (9.0%) diabetic patients had medium adherence versus 42 (41.0%) non-diabetics; and 4 (4.0%) diabetic patients had high adherence compared to 29 (29.0%) non-diabetics. Although a higher proportion of diabetic patients demonstrated low adherence than non-diabetics, the association between adherence level and diabetes status was not statistically significant. Details are shown in Table 5.

Table 5: Comparison of chelating agent adherence levels between Diabetic and Non-Diabetic patients

Adherence Level	Diabetic no (%)	Non-Diabetic no (%)	Total no (%)	Chi-square (χ^2)	p. value
Low	5 (5.0)	11 (11.0)	16 (16.0)	2.68	0.262
Medium	9 (9.0)	42 (41.0)	51 (51.0)		
High	4 (4.0)	29 (29.0)	33 (33.0)		
Total	18 (18.0)	82 (82.0)	100 (100.0)		

The distribution of HbA1c levels among the study participants showed that 10% of diabetics and 65% of non-diabetics had normal HbA1c levels, while 5% of diabetics and 10% of non-diabetics were in the borderline range. High HbA1c levels were observed in 3% of diabetics and 7% of non-diabetics. Overall, 18% of the participants were diabetic and 82% were non-diabetic. Although there appears to be a difference in HbA1c level distribution between diabetic and non-diabetic groups, the association was not statistically significant. Details are shown in Table 6.

Table 6: Distribution of HbA1c levels among Diabetic and Non-Diabetic patients**"**

HbA1c Level	Diabetic no (%)	Non-Diabetic no (n)	Total no (%)	Chi-square (χ^2)	p. value
Normal	10 (10.0)	65 (65.0)	16 (16.0)	4.47	**0.107**
Borderline	5 (5.0)	10 (10.0)	51 (51.0)		
High	3 (3.0)	7 (7.0)	33 (33.0)		
Total	18 (18.0)	82 (82.0)	100 (100.0)		

Participants who aged younger than 20 years and those who are underweight, were significantly with a lower risk of diabetes, while having a family history of diabetes was significantly associated with a higher

risk. Endocrine disorders showed a borderline association. Most diabetics were aged 20–39, and being overweight showed a slight, non-significant positive association with diabetes.

Table7: Logistic Regression Analysis of Factors Associated with Diabetes Status

Factors		Diabetic no (n)	Non-Diabetic no (%)	Total no (%)	Coefficient (β)	p. value
Age	Age < 20	0 (0.0)	5 (5.0)	5 (5.0)	-2.995	0.001
	Age 20–39	15 (15.0)	70 (70.0)	85 (85.0)	1.204	
	Age 40–60	3 (3.0)	7 (7.0)	10 (10.0)	0.693	
BMI	Underweight	3 (3.0)	17 (17.0)	20 (20.0)	-1.500	0.045
	Normal	6 (6.0)	30 (30.0)	36 (36.0)	0.000	
	Overweight	9 (9.0)	35 (35.0)	44 (44.0)	0.405	
Family history	Positive	10 (10.0)	28 (28.0)	38 (38.0)	1.203	0.032
	Negative	8 (8.0)	54 (54.0)	62 (62.0)	0.000	
Endocrine disorder	Positive	8 (8.0)	11 (11.0)	19 (19.0)	0.500	0.067
	Negative	10 (10.0)	71 (71.0)	81 (81.0)	0.000	
Total		18 (18.0)	82 (82.0)	100 (100.0)		

Discussion

Because of the intricate interactions between iron overload, endocrine dysfunction, and continuous transfusion treatment, the frequency of diabetes mellitus among thalassemia patients has become a major clinical issue. Several studies have shown that thalassemic patients, especially those with transfusion-dependent thalassemia major, have a greater prevalence of glucose metabolism abnormalities than the general population. Iron accumulation in the pancreas, which causes β-cell malfunction and insulin resistance, is mostly to blame for this elevated prevalence. Since diabetes increases overall morbidity and calls for early screening and multidisciplinary management options to enhance long-term results, it is imperative to comprehend the burden of diabetes in this group. The current study indicates a prevalence of diabetes mellitus (DM) at 18%, which aligns closely with findings from previous research conducted by Al Ani et al in Iraq, who reported a prevalence of (15%).[15], and in Turkey by Mahgoub et al., who found a prevalence of (11%).[16] This consistency across studies suggests a significant and concerning trend in the prevalence of DM among thalassemic patients in these regions. The similarities in prevalence rates may be attributed to common risk factors associated with thalassemia, such as iron overload due to frequent blood transfusions, which can lead to pancreatic damage and subsequent insulin deficiency. Furthermore, the socio-economic and healthcare contexts in Iraq and Turkey may also play a role in these findings, as they both face challenges related to healthcare access and management of chronic diseases. In the current study, a notable 65% of patients were aged <20 years, indicating a higher prevalence younger individual, while the gender distribution showed a slight female predominance at 51%. similarly, Almahmoud R et al from the Dubai [17] Thalassemia Centre, reported (50.7% male and 49.3% female) and a more diverse age range, with only 11.1% of patients aged 2-9 years and a significant 67.7% aged 19-45 years. This disparity in age distribution highlights the importance of targeted healthcare strategies for younger populations, as

early intervention can significantly improve outcomes. In current study adherence to chelating agent therapy in thalassemia patients, 51% showed medium adherence this is in agreement with Mohamed et al in Jordan who reported 51.4% adherence level.[18] on the other hand and unexpectedly Al-Jabory et al from Iraq[19] reported adherence level of 79% this differences in the result may be attributed to the difference in study sample and classification of adherence level and type of questionnaire. In current study a higher proportion of diabetic patients demonstrated low adherence than non-diabetics, the association between adherence level and diabetes status was not statistically significant similarly Al-Jabory et al(19) reported diabetic patients exhibited lower adherence, the overall association between adherence and diabetes status was statistically not significant. This lack of significant association may be attributed to various factors, including the complexity of treatment regimens, individual patient circumstances, and the multifaceted nature of adherence, which can be influenced by psychological, social, and economic factors rather than just the presence of diabetes. Thus, while diabetes may complicate health management, it does not necessarily dictate adherence levels to iron chelation therapy. In this study participants who are underweight, were significantly 2.99 times with a lower risk of diabetes, this is in alignment with a similar study carried out in India by Maniyara et al [20] who reported that being obese have 4 times risk of developing DM. Further-more Bae et al [21] from Korea reported that lower BMI have lower risk of developing DM. on the other hand patients with family history of DM have 1.2 times higher risk of developing DM than those with no family history this in agreement with a study done in Saudi Arabia by Alrashed et al [22] who reported that patients with family history of DM have a 1.9 risk of developing DM than those with no family history.

Conclusion

This study found an 18% diabetes prevalence in thalassemia patients, with higher rates in younger individuals, moderate chelation adherence, being underweight and younger have lower risk of developing DM.

Recommendations

1. Implement routine diabetes screening for thalassemic patients, especially younger individuals.
2. Enhance patient education to improve adherence to iron chelation therapy.
3. Monitor BMI and family history as part of risk assessment.
4. Strengthen multidisciplinary care to manage and prevent diabetes in this population.

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Availability of data: The corresponding author can provide the datasets used and/or analyzed during the current study upon reasonable request.

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