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ORIGINAL RESEARCH

Serum Ferritin Levels and Other Associated Parameters with Diabetes Mellitus in Adult Patients Suffering from Beta Thalassemia Major

Ahmed Saleh Ibrahim[1], Azza Hasan Abd El-Fatah[2], Ayman Fathy Abd El-Halim[3], Farid Fawzy Mohamed[2]

[1]Department of Internal Medicine, Faculty of Medicine, Mansoura University, Mansoura, Egypt; [2]Department of Internal Medicine, Faculty of Medicine, Zagazig University, Zagazig, Egypt; [3]Department of Hematology, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Correspondence: Ahmed Saleh Ibrahim, Tel +20 109 232 6689, Email abadawi70@yahoo.com

Background: Although beta thalassemia major (BTM) patients are properly treated with blood transfusions in accompany with iron chelation therapy, they suffer from complications, such as diabetes mellitus (DM).

Purpose: The purpose was to detect the critical serum ferritin level and other parameters correlated with DM among adult BTM patients. Also, it was to study whether each of these parameters is associated with a certain period of age.

Patients and Methods: This study included 200 adult BTM patients. A cross-sectional study was carried out. Patients clinical and laboratory variables, such as ferritin levels, and fasting blood glucose (FBS) were extracted from medical records at Zagazig University Hospital, Egypt. Liver and cardiac iron contents were assessed using MRI T2* methods. Statistical analysis was performed using IBM SPSS V26.0 software package.

Results: The overall frequency of DM over the total sample equals 6.5%. There were no impaired fasting glucose (IFG) in the medical records. Statistical significance between serum ferritin and DM was (P = 0.014). The serum ferritin 2500 ng/mL with age group (27–<32) years-old were risk factors. The distributions of DM according to BMI were (3.5%) of class overweight. Significant association between DM and BMI was (r = 0.357, P < 0.001). Liver MRI T2* has significant correlation with serum ferritin, but cardiac MRI T2* was poorly correlated. Association between liver and cardiac MRI T2* was not found.

Conclusion: Age group (27–<32) years-old and ferritin >2500 ng/mL should be properly treated immediately. The serum ferritin and BMI of class "overweight" were risk factors for DM. Factors such as diet should be followed. Serum ferritin can be used for estimating liver iron content for economic factors. But cardiac MRI T2* must be performed for evaluating cardiac iron accurately.

Keywords: hemoglobin, iron chelation, blood glucose, endocrinopathy

Introduction

Frequency of thalassemia patients with diabetes mellitus lies in the range 20% to 30% worldwide as stated in the literature. Some researchers in a multicenter reported that the prevalence of diabetes mellitus (DM) among thalassemia major patients was 4.9% (sample size 1861). In another work, diabetes was detected in 17% of beta thalassemia major patients.[1,2]

Although the management of beta thalassemia major patients with frequent blood transfusion and iron chelation treatments, there was an excess of iron deposition in beta cells of pancreas. This leads to destruction of pancreatic beta cells and deficiency of insulin secretion[3,4] so, treating with insulin is necessary. Iron chelation treatment with desferrioxamine (DFO) and deferiprone were used to reverse glucose intolerance and to delay the beginning of diabetes.[5]

Recent works reported that deferasirox was effective for BTM patients. Moreover, physical activity and weight reduction are beneficial for preventing the development of diabetes. The degree of destruction of beta cells and hence reduction of insulin secretion are key factors determining the management of diabetes.[6–8] two systematic plan for

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treatment. First, premixed insulin is used before breakfast and dinner. Second, basal slow acting insulin once daily (eg, levemir or glargine) and prandial rapid acting insulin prescribed with each meal.[9]

Motivations for this research can be summarized as follows: First to get more information on the prevalence of the studied endocrine complication because there is a lack of information in our area. Second, to be able to install a database system for those BTM patients as a foundation stone of a whole database network in Egypt. Finally, to clarify the underlying endocrine disorder (eg, DM in this work) for optimal management and treatments.

Materials and Methods

The current work is cross-sectional study. The study depends on collecting data reported in the patient's medical reports including hematologists and endocrinologists as well as biochemical laboratory checkup. The assessment was done on the data of the patients with beta-thalassemia major attending outpatient clinic of Zagazig University Hospitals.

The patients with beta thalassemia major were enrolled and their medical records were studied following the inclusion and exclusion criteria. The number of records for patients fulfilling the inclusion criteria from 2016 to 2020 was 200 records. Patients ≥18 years old were considered in the study. Patients <18 years old, and patients with hemolytic anemia other than beta-thalassemia major were excluded. Also, patients who died were deleted from patient's records; subsequently, 40 patients were excluded and 200 patients remained in the study. So, two hundred patients from Zagazig University Hospitals, with confirmed diagnosis of beta-thalassemia major entered in the study. The patients were classified according to age into the following groups: First group: 18–<22 years old; Second group: 22–<27 years old; Third group: 27–< 32 years old; Forth group: ≥32 years old.

Inclusion and exclusion criteria: patients diagnosed with beta-thalassemia major with ages ≥18 years old were included in the study. Also, both sex are considered. The exclusion criteria was specified as follows: Patients with chronic hemolytic anemia other than beta-thalassemia major were excluded. Moreover, patients with ages <18 years old were not considered in the study.

Data collection: all patients' records must include the following items: (a) Full medical history and through physical examination reported in the medical files. (b) Assessment of anthropometric measures, such as length, weight, body mass index, etc. (c) Routine investigations according to our local standards, eg, serum ferritin, liver function tests, kidney function tests, etc.

Biochemical laboratory data: serum calcium (Ca), phosphorus (P), serum 25-OH vitamin D and fasting blood sugar (FBS) were assessed and serum ferritin levels were measured and collected.

Body measurements and body mass index: Body mass index (BMI) was invented by Prof. Adolphe Quetelet in 1830. Height was measured by a standard wall-mounted meter and rounded to the nearest 0.5 cm. The weight was assessed via a standard scale, while the patient was wearing light clothes with no shoes. Using the standard formula, BMI was calculated as follows:

$$\mathrm{BMI} = \mathrm{weight(in\ kg)/height\left(in\ m^2\right)}$$

BMI was classified into the following classes: underweight (BMI < 18.5), healthy (18.5–<25), overweight (25–<30), and obese (BMI ≥30).[11]

Diagnostic Criteria

Diabetes mellitus (DM) diagnosis was based on the American Diabetes Association criteria, which defines impaired fasting glucose (IFG) for FBS 100–125 mg/dl, also known as pre-diabetic and DM in patients with FBS ≥ 126 mg/dl (American diabetes association ADA2018).[10]

Magnetic Resonance Imaging (MRI T2*)

MRI T2* was performed using Magneto, 1.5 T, Siemens medical systems. The measurements of liver and cardiac MRI T2* were included. The cut-off time values that showed the degree of severity of iron overload in the heart and liver were as follows:[37]

For liver: Normal ≥6.3 milliseconds (msec.), mild 2.8 - <6.3 msec, moderate 1.4 - <2.8 msec, and severe <1.4 msec.

For heart: Normal ≥20 milliseconds (msec.), mild 14 - <20 msec. moderate 10 - <14 msec. and severe <10 msec. The correlation between serum ferritin levels with both the liver and cardiac iron by MRI T2* were assessed.

Statistical Analysis

Data were analyzed by SPSS software package version 26. Descriptive data are presented as mean, standard deviation, and percentages. Inferential analysis was done using Chi square test to compare categorical variables among different groups, Student's *t*-test to compare quantitative variables between the two groups, and ANOVA test to compare quantitative variables among three or more groups.

The associated variables with DM were investigated to determine their correlations with that endocrinopathy. In this work, we suggested the correlated factors including age, ferritin level, BMI, gender and hemoglobin (Hb). Correlation and bivariate analysis of DM with those factors were studied. A two-tailed P-value < 0.05 was considered to be statistically significant.

Results

A total number of 200 β-thalassemia major patients were enrolled in this study. The general sociodemographic and medical characteristics of the sample are shown in Table 1. The mean serum ferritin level among BTM patients was 3909.0200 ± 1935.72465 (ng/mL). Also, the mean of body mass index BMI (kg/m^2) was 20.4995 ± 3.12525.

The study sample with beta-thalassemia major (BTM) patients with the total mean age over the whole sample N (200 patients) was 24.6840± 5.30761 (Table 2). The patients were 115 males and the 85 females. The gender distribution over the sample N is given in (Table 3) where 57.5% represents males and 42.5% females.

Table 1 General Characteristics and Laboratory Data of the Patients in This Study

Variables	N	Mean	Median	Standard Deviation
Age (years)	200	24.6840	23.5000	5.30761
Weight (kg)	200	53.9950	56.0000	11.52733
Length (cm)	200	161.6500	162.5000	11.33046
Gender: F/M (115/ 85)	200	–	–	–
BMI (kg/m2)	200	20.4995	20.3800	3.12525
Hb (g/dL)	200	7.1290	7.1000	0.91386
S.Ferritin (ng/mL)	200	3909.0200	3410.0000	1935.72465
S.calcium (mg/dL)	200	7.9371	8.1000	1.30125
S. phosph (mg/dL)	200	4.9985	4.9450	0.99161
Vitamin D (ng/mL)	200	19.6673	18.3000	9.57021
ALT (U/L)	200	31.1830	27.0000	23.69074
AST (U/L)	200	32.1016	30.6000	13.42624
Cr (mg/dL)	200	0.7742	0.6650	0.36617
Iron Chelation Therapy (ICT)	n/N			
Deferoxamine	24/200			
Deferasirox	33/200			
Combined	17/200			
Splenectomy	20/200			

Table 2 Mean Age Distribution

Mean Age				
		Mean	**N**	**Std. Deviation**
Valid	Male	24.9678	115	5.53956
	Female	24.3000	85	4.98316
	Total	24.6840	200	5.30761

Table 3 Gender Distribution

Gender					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Male	115	57.5	57.5	57.5
	Female	85	42.5	42.5	100.0
	Total	200	100.0	100.0	

The distribution of age groups are also given in Table 4. In the age group (18 - <22) years old the frequency was 85 (42.5%). The occurrence of patients was 55 (27.5%) in the age group (22 - <27) years old. Also, the frequency of patients was 43 (21.5%) in the age group (27-<32) years old. For the age group (≥32) years old, the frequency was 17 (8.5%).

The serum ferritin levels among BTM patients are divided into four ranges (Table 5) as follows: (0–1500 ng/mL); ferritin level range (1501–2500 ng/mL); ferritin level (2501–3500 ng/mL); and ferritin level range (>3500 ng/mL). It

Table 4 Age Groups Distribution

Age Groups (Years)					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	18 -<22	85	42.5	42.5	42.5
	22-<27	55	27.5	27.5	70.0
	27-<32	43	21.5	21.5	91.5
	≥32	17	8.5	8.5	100.0
	Total	200	100.0	100.0	

Table 5 Distribution of Ferritin Levels Among BTM Patients

Ferritin Level (ng/mL)					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	0–1500	20	10.0	10.0	10.0
	1501–2500	35	17.5	17.5	27.5
	2501–3500	49	24.5	24.5	52.0
	>3500	96	48.0	48.0	100.0
	Total	200	100.0	100.0	

should be noted that iron chelation therapy (ICT) and splenectomy were not completely recorded in the patients' medical records.

Distribution of Serum Ferritin Levels Among BTM Patients

The distribution of ferritin level was given in (Table 5). The frequency of patients was 20 (10%) had serum ferritin level range (0–1500) ng/mL. Also, 35 (17.5%) patients were in the ferritin level range (1501–2500) ng/mL. In the range (2501–3500) ng/mL the patients were 49 (24.5) %. The frequency of patients was 96 (48%) found in the ferritin level range (>3500) ng/mL. This information reflected poor compliance with iron chelation therapy (ICT), and the patients did not follow up the instruction regarding monitoring the ferritin level and continuously taking ICT. Also, this might be happened because of patients' economic reasons.

Iron chelation therapy (ICT) for BTM patients was not completely recorded in the medical records. It was found that 24 patients took deferoxamine, while 33 patients prescribed deferasirox and 17 followed combined ICT. Moreover, splenectomy was not completely registered in the patient files.

The body mass index (BMI) distribution among the patients with beta –thalassemia major in the studied sample was as follows: one hundred thirty four of the patients 134 (67%) had normal BMI while the others had underweight 47 (23.5%) and overweight were 19 (9.5%) in (Table 6 and Figure 1). There were no obese patients in the sample under consideration (N =200).

General characteristics, laboratory data, and more information about distribution of age, gender, ferritin levels and body mass index are summarized in the (Table 1).

Distribution of Diabetes Mellitus Among BTM Patients According to Certain Parameters and Its Correlation

The overall frequency of diabetes mellitus among the BTM patients over the total sample size (N=200) was 6.5%. This result was represented visually in (Figure 2). Distribution of DM according to the age groups was studied. The maximum frequency was 2.5% found in the age group (27–<32) years old, while the minimum frequency 1% was found in the age group (18–<22) years old. It was noted that a frequency of (1.5%) was found in each of the age group (22–<27) years old and the age group (≥32) years.

According to the ferritin level, the maximum frequency of this endocrine dysfunction was 9 (4.5%) that found in patients with ferritin level range >3500 ng/mL (Figure 3). The median frequency was 1.5% with the associated ferritin level range (2501–3500) ng/mL. It was shown from (Figure 3) that the minimum serum ferritin level range at which DM had appeared was (1501–2500 ng/mL). So, the upper bound of this range was 2500 ng/mL which can be considered as a risk factor.

The body mass index (BMI) was studied with this endocrine disorder. It was found that the maximum frequency of that endocrinopathy was 7 (3.5%) found in the class of overweight patients (Figure 4). Those patients (their number was 7) need physical activity and weight reduction besides the treatment of DM. The minimum frequency of DM was 3% with BMI of class normal weight.

Study of DM in lean groups (underweight and normal weight classes) among adult BTM patients was given (Table 7). Underweight group with DM was not found in the studied samples, only diabetic normal weight was detected. In the lean

Table 6 Body Mass Index Distribution

		Frequency	Percent
Valid	Under weight	47	23.5
	Normal weight	134	67.0
	Over weight	19	9.5
	Total	200	100.0

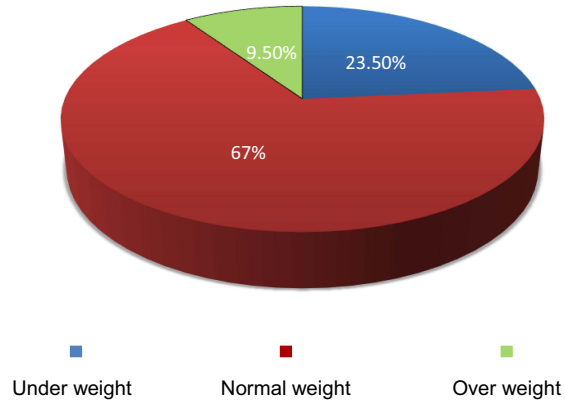

Figure 1 Frequency distribution of body mass index.

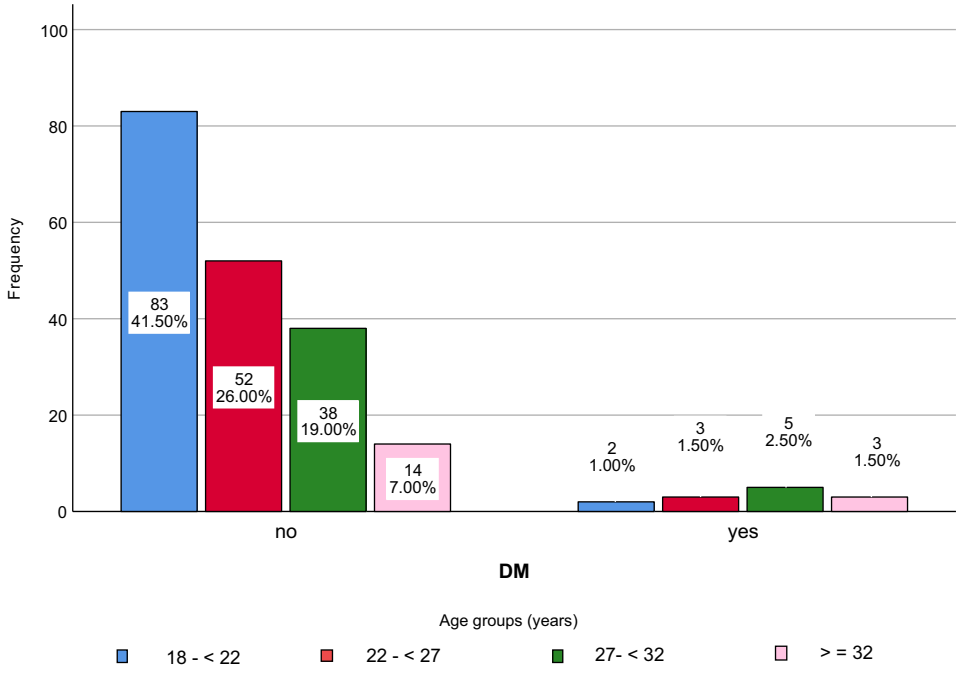

Figure 2 Distribution of Diabetes mellitus among the patients according to age groups.

groups with and without DM, the mean of ages (years), BMI (kg/m^2), ferritin levels (ng/mL) and fasting blood glucose (mg/dL) were computed.

Using bivariate statistical method, it was detected a high correlation between DM and serum ferritin in the group with BMI of class normal weight (r =0.912, P=0.011). But in the normal weight group and underweight one without DM, weak correlations with ferritin (r =0.295) and (r = 0.178) was found, respectively. This interpreted that serum ferritin was the risk factor in the lean diabetic group with minimum ferritin level was 2600 ng/mL (Table 7).

Moreover, the distribution of DM according to gender was given in (Figure 5). The maximum frequency of DM was 4% found in females, while the frequency of 2.5% found in males.

DM and the Correlated Parameters

Using the correlation analysis with the bivariate method and Pearson correlation, BMI was statistical significance with that endocrine dysfunction (P < 0.001), and given in (Table 8). Also, it was found that there was an association between

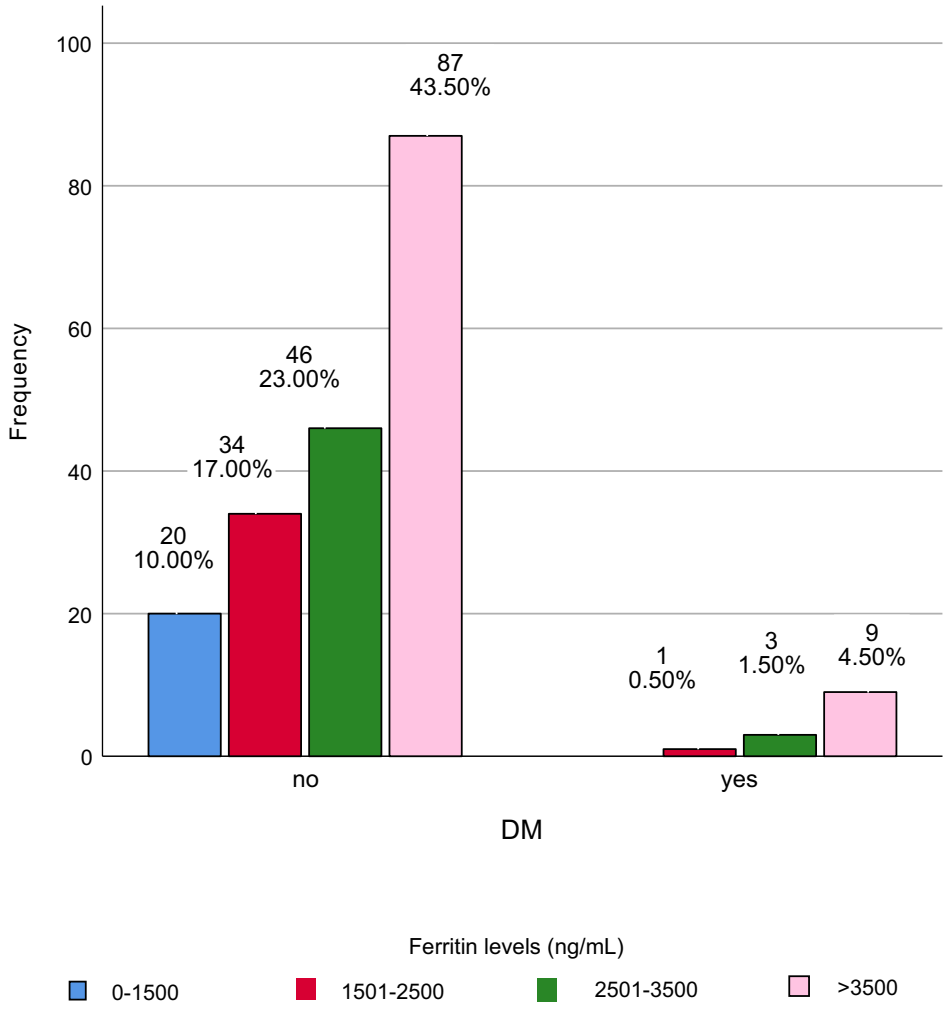

Figure 3 Distribution of Diabetes mellitus among the patients with different ferritin levels.

serum ferritin level and DM (P= 0.014). From the previous discussion and the results given in (Figure 3), it can be concluded that the serum ferritin level 2500 ng/mL can be considered as a risk factor of that endocrinopathy.

Also, from Table 8, the statistical P-value of the patients′ age groups was (P =0.006). Also, the most prevalent of DM was (2.5%) in the age group (27–<32) years old. So, this parameter was statistically significant. However, there was no association between DM and gender. Also, it was found that DM had no correlation with Hb.

Correlation Between Serum Ferritin and Both Liver and Cardiac Magnetic Resonance Imaging –T2-Star (MRI T2*)

The correlations between serum ferritin levels and both liver and cardiac MRI T2* are shown in Table 9. There was a moderate negative correlation between liver MRI T2* and serum ferritin readings (r = –0.681, P < 0.001) (Table 9 and Figure 6). Also, there was a negative poor correlation between cardiac MRI T2* and serum ferritin level (r = –0.284, P = 0.002) (Table 9 and Figure 7). The poor correlation between heart MRI T2* and serum ferritin readings reflected that the serum ferritin level could not predict the heart iron contents. This result ensures the importance of MRI T2* as a more accurate technique for predicting the cardiac iron overload. The moderate correlation between liver MRI T2* and serum ferritin level, which had statistical significance (P < 0.001) proved that the serum ferritin can be applied for estimating the liver iron level for economic factors.

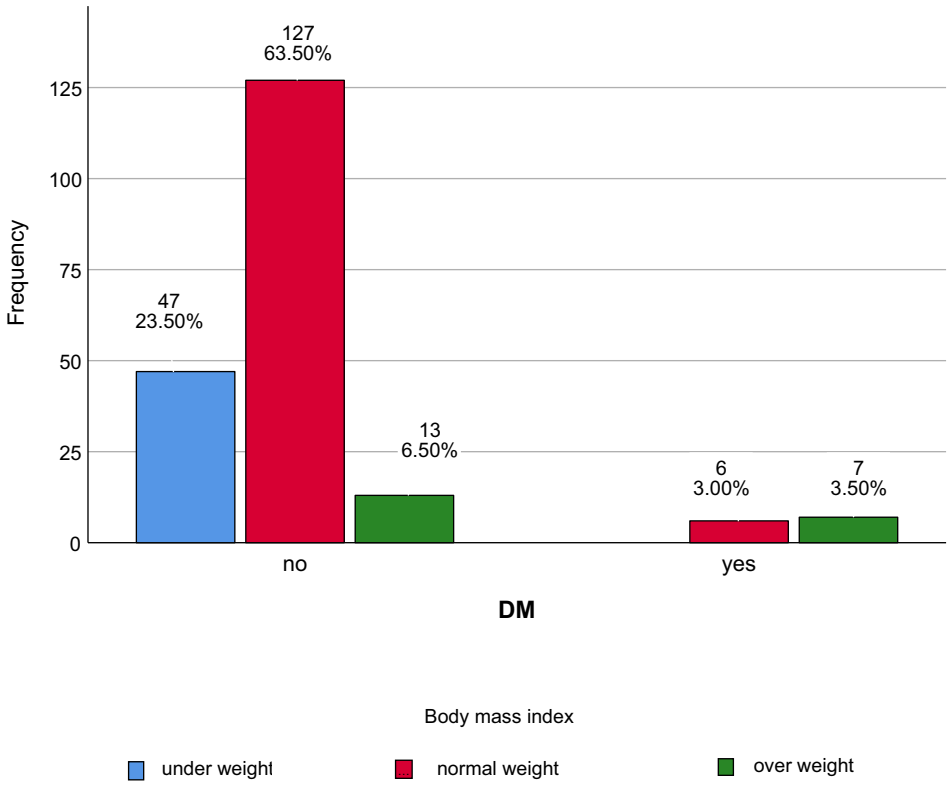

Figure 4 Distribution of Diabetes mellitus among the patients with different classes of BMI.

From Table 10, the correlation between cardiac MRI T2* and liver MRI T2* was (r=0.064, p=0.367). This means that there was a very poor correlation between cardiac and liver MRI T2* readings among BTM patients with no statistical significance. These results were similar to other studies.[38,39] This important result emphasizes the role of cardiac MRI T2* for early predicting the heart iron contents among thalassemia patients instead of depending only on liver MRI T2*.

Discussion

In this work, we evaluated the prevalence and associated parameters which can be considered as risk factors with DM. It showed that the overall frequency of diabetes mellitus (DM) in adult beta thalassemia major patients greater than or equal

Table 7 Study of DM Among Lean Groups of Adult BTM Patients

Variables		Lean Group With DM (DM=Yes) (Underweight Group with DM not Found)	Lean Groups Without DM (DM=No)	
		Normal Weight	Underweight	Normal Weight
Age	Mean ±SD	29.5500±3.9098	21.1323±2.3794	25.0654±4.3367
(years)	Min.	25.00	18.30	18.00
	Max.	35.60	26.50	32.00
BMI (kg/m^2)	Mean ±SD	22.0083±1.5822	16.7560±1.2898	20.7257±1.3470
	Min.	20.30	14.20	18.60
	Max.	24.70	18.30	23.50

(*Continued*)

Table 7 (Continued).

Variables		Lean Group With DM (DM=Yes) (Underweight Group with DM not Found)	Lean Groups Without DM (DM=No)	
		Normal Weight	Underweight	Normal Weight
S.Ferritin (ng/mL)	Mean ±SD	5926.8333±2323.5822*	2190.8723±425.143	2691.2913±709.010
	Min.	2600.00	1268.00	1120.00
	Max.	9863.00	2900.00	3980.00
Fasting Blood glucose (mg/dL)	Mean ±SD	168.6667±20.2649*	115.2553±4.05113	116.7244±5.8141
	Min.	137.00	104.00	103.00
	Max.	195.00	121.00	124.00

Note: *Statistically significant at *P*-value < 0.05.

18 years old was 6.5% with the mean age (24.6840± 5.30761). In other studies, DM has been reported with frequency of 3–26% in BTM patients.[6,19,20] DM has also been reported with frequencies of 10.5% in United Arab Emirates,[21] 9.4% in Brazil,[22] 15.9% in Iran.[12]

In Italian working group on endocrine complications (sample size was 1861),[23,24] the overall frequency of diabetes mellitus was 4.9%. Furthermore, and the frequency of DM in the age group (18–30 years old) was much more prevalent than in the age group >30 years (approximately double).[23] This result was in direction with our result where the frequency of age group (18–32 years) was 5% (Figure 2) and in the age group (>32 years) 1.5%, ie, the frequency was approximately 3.3 times of the latter. This may be due to a number of patients with thalassemia major had been died after age >32 years. So, the frequency of DM in last age group was decreased. It should be noted that, the wide range of variation in prevalence depends on the patients′ age, duration of red blood cells transfusion, iron overload, organ disorder, iron chelation protocol, compliance to treatment.[6,25]

In 2017, a published work reported that the prevalence of diabetes mellitus among adult beta- thalassemia major patients is greater than or equal to 18 years (4/56) 7.1%, which is close to our result.[26] In 2010, a work

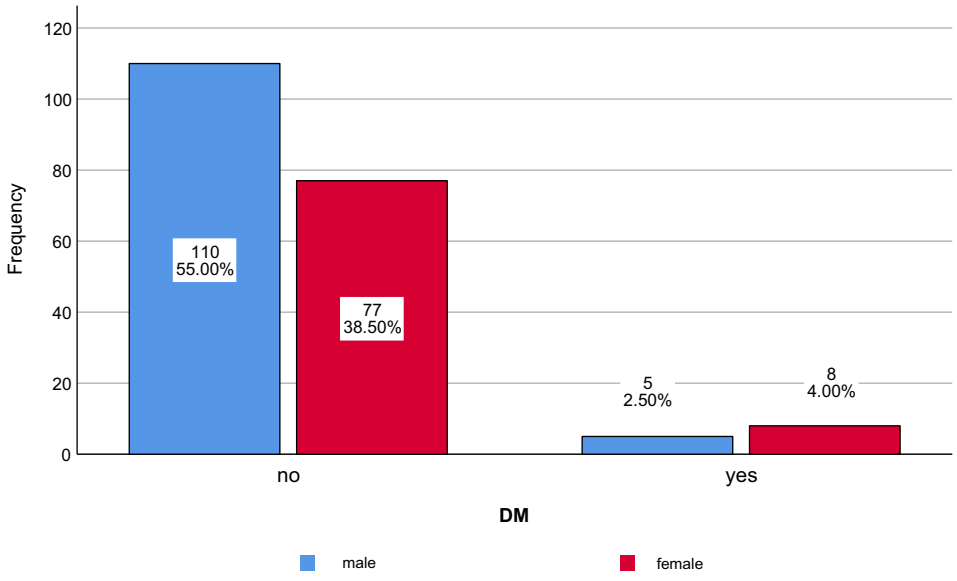

Figure 5 Distribution of Diabetes mellitus among the patients according to gender.

Table 8 Association Between DM and Various Parameters

		Age groups	BMI	Gender	Hb	S. Ferritin
DM	Pearson Correlation	0.195**	0.357**	0.102	0.004	0.174*
	Significance (2-tailed)	0.006	< 0.001	0.153	0.951	0.014
	N	200	200	200	200	200

Notes: *Statistically significant at P-value < 0.05, **High level of significance at *P*-value < 0.01.

Table 9 Correlation Between Serum Ferritin and Hepatic and Cardiac MRI T2*

		Liver MRI T2*	Cardiac MRI T2*
	N	200	200
Ferritin	Pearson Correlation	−0.681**	−0.284**
	Significance (2-tailed)	0.000	0.002

Notes: *Modified technique where MRI signal decay rates are proportional to liver or cardiac iron concentration, **Statistically significant at *P*-value < 0.01.

done by Royal Australasian College of Physicians, the frequency of DM among patients′ age >18 years was (2/29) 6.89%, (sample size 29 patients).[27] Also, this latter result was very close to our results. Regarding the assessment of ferritin level, we found a statistical significance for serum ferritin level among the patients with DM, and those patients need proper iron chelation protocol;[28–34] in combination with DM treatments. When making a comparative study with previous reports, we observed that serum ferritin was associated with DM in BTM patients.[4–6,19]

In the Italian work, the mean serum ferritin level associated with DM was (3790 ±2566 ng/mL), P < 0.05. Our result was in agreement with that work where the mean serum ferritin was 3909.0200 ±1935.72465 ng/mL; P-value = 0.014. In a previous work,[12,23] the ferritin level was greater than 2500 ng/mL, P < 0.001.

Concerning the evaluation of BMI with the development of diabetes mellitus, we found out that BMI was associated with DM (P < 0.001). This result was in the same direction of the previous work where BMI was statistically significant with DM,[12] P= 0.046.

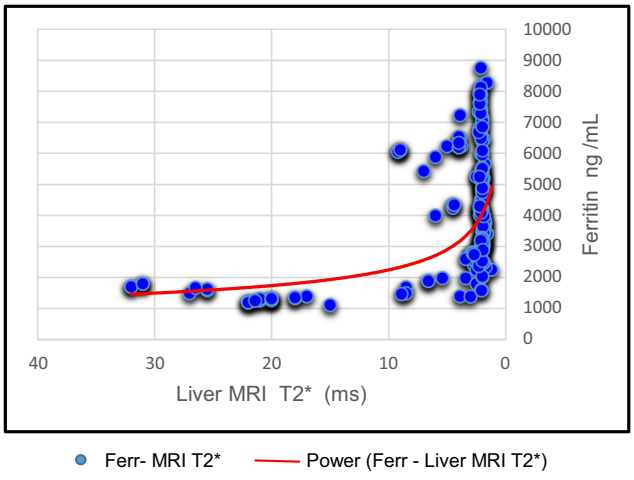

Figure 6 Correlation between liver MRI T2* and ferritin.
Note: The red curve is the trend-line of type (power) to fit the data.

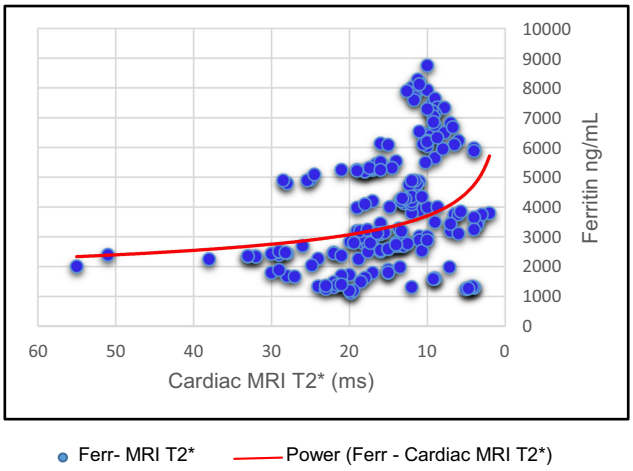

Figure 7 Correlation between cardiac MRI T2* and ferritin.
Note: The red curve is the trend-line of type (power) to fit the data.

Moreover, in the current study, we found that gender was not statistically significant with DM where P=0.153. This result agreed with the result of a previous research,[12] where gender had no significance with DM; P= 0.129. Also, in the work done by the Italian group, gender was not associated with DM.[12,23]

Some papers indicated that T2* Magnetic Resonance Imaging (MRI) is a sensitive method for detecting iron content in body organs. The cardiac T2* MRI is considered as predictors of diabetes,[35,36] and it is correlated with the pancreatic values of T2*.

In the current work, a significant moderate negative correlation between liver MRI T2* and serum ferritin level was observed. This means that the serum ferritin level is predictive of liver iron level. Other work had shown a significant association between ferritin level and iron level of liver MRI T2*.[40] Another study exhibited that serum ferritin levels had moderate negative correlation with liver MRI T2* values ($r = -0.586$, $P < 0.0001$).[41]

In another research using hepatic MRI R2 method (FerriScan®) with sample size (N=24) and age ranges 9–35 years old, the liver iron concentrations (LIC) had significant moderate correlation with serum ferritin levels ($r = 0.512$; $p = 0.011$).[42] In the current study with sample size (N=200) and ages ≥18 years), there was a moderately negative correlation, which had statistical significance between liver MRI T2* and serum ferritin readings ($r = -0.681$, $P < 0.001$). Although this method was different from the previous one (LIC using MRI R2 method; FerriScan®), they had similar prediction that both techniques indicated significant moderate correlation with serum ferritin levels.

In the current study, a poor correlation between cardiac MRI T2* and serum ferritin level was observed. A recent study used cardiovascular magnetic resonance with T2-weighted sequences (CMR T2*) for thalassemia major patients, to determine the association between (CMR T2*) and serum ferritin in thalassemia major patients. It proved that no

Table 10 Bivariate Correlations Analysis of Liver and Cardiac MRI T2*

		Liver MRI T2*	Cardiac MRI T2*
Liver MRI T2*	Pearson Correlation	1	0.064
	Significance (2-tailed)		0.367
	N	200	200
Cardiac MRI T2*	Pearson Correlation	0.064	1
	Significance (2-tailed)	0.367	
	N	200	200

Notes: *Modified technique where MRI signal decay rates are proportional to liver or cardiac iron concentration.

significant correlation was found between CMR T2* and the serum ferritin (P = 0.158, r = 0.201).[43] Another work showed that no correlation was found between serum ferritin and cardiac iron levels using MRI T2* in BTM patients.[44]

Moreover, our study proved that there was very poor correlation between cardiac and liver MRI T2* readings among BTM patients with no statistical significance (r=0.064, p=0.367). A work with sample size (N = 180) has showed significant but very poor correlation between liver MRI T2* and cardiac MRI T2* (r = 0.18, P < 0.05).[45]

Based on the above discussion, since there was a significant correlation between serum ferritin and liver MRI T2*serum ferritin can be used for evaluating liver iron levels for economic reasons. But cardiac MRI T2* is preferred for accurate measuring cardiac iron levels instead of using serum ferritin levels.

Comparative Study of Distribution of DM with Previous Studies

In this section, comparative study of distribution of DM with previous studies. This is given in (Table 11). The overall prevalence of DM among our BTM patients was 6.5%. The endocrinopathy was studied with the available and suggested parameters model. Recently, a work was done by a multicenter clinic revealed that the prevalence of DM among TDT patients (transfusion-dependent thalassemia) with sample size 713 patients was 15.8%. The parameters including age, ICT and splenectomy were studied in the research.[12]

Some researchers reported that the age and duration of blood transfusion were significantly associated with DM, while others stated that the prevalence of DM was 8.9% among 56 BTM patients, and neither serum ferritin nor gender was associated with that endocrine disorder.[13] This may be due to small sample size.

Table 11 Comparative Study of Our Work with Previous Studies

DM in Current and Previous Works	Sample Size N	% Prevalence	Correlated Parameters With DM	Status
DM (in current work)	200	6.5	Age groups	(Correlated)
			(27-< 32) years old	Most prevalent
			Ferritin	(Correlated)
			Level >2500 ng/mL	(Critical)
			BMI	(Correlated)
			Hb	(Not correlated)
			Gender	(Not correlated)
DM in work[12]	713	15.8	Age	(Correlated)
			Ferritin	(Correlated)
			Splenectomy	(Correlated)
			ICT	(Not Correlated)
			Gender	(Not Correlated)
DM in work[13]	56	8.9	Ferritin	(Not Correlated)
			Gender	(Not Correlated)
DM in work[15]	64	4.7	Ferritin (Not correlated)	(Not correlated)
DM in work[17]	267	10	Ferritin (Correlated)	(Correlated)
DM in work[18]	148	8.8	Age (Correlated)	(Correlated)
			Splenectomy	(Correlated)
			Ferritin (Correlated)	(Correlated)

In another work, serum ferritin and hemoglobin levels are related to IGT (impaired glucose tolerance).[14] The work done in previous studies[15,16] revealed that the prevalence of DM was 4.7% among sample size of 64 patients, and their results showed that the serum ferritin was not correlated. It is worth noting that, in the previous mentioned works, there were different variables, eg, ferritin, that truly correlated with the endocrinopathy such as DM. However, serum ferritin is of critical importance and leads to damage the endocrine glands and the BTM patients should be immediately medically treated using iron chelation therapy.

Conclusion

The overall frequency of Diabetes mellitus among the BTM patients was 6.5%. The maximum occurrence of this endocrine dysfunction was 4.5% that associated with ferritin level range (>3500 ng/mL). The minimum serum ferritin level was 2501 ng/mL.

It was found that there was an association between serum ferritin level and that endocrine dysfunction (P = 0.014). The serum ferritin level 2501 ng/mL can be considered as a risk factor of that endocrinopathy. The maximum frequency of that endocrinopathy was found in the BTM patients with BMI of class "overweight". Since BMI had significant association with DM, then factors such as diet and physical activity should be advised.

In a few words, DM was found among BTM patients and the following critical points should be taken into considerations: (a) Age group (27–<32) years old and severe serum ferritin >2500 ng/mL should be properly managed and treated immediately to stop or reduce that endocrine complication. Proper ICT protocol must be used especially to those BTM patients. (b) More research should be done to find out the correlation of different parameters with DM. This requires longitudinal observations of the BTM patients taking ICT and different managements.

Serum ferritin can be used for estimating liver iron levels for economic factors. It is preferred to perform cardiac MRI T2* for measuring cardiac iron level instead of using serum ferritin level. It is important to evaluate precisely the iron level in both the liver and heart for tailoring optimal chelation treatment protocol to avoid or minimize mortality in BTM patients. Based on the above results, it is recommended to do scanning for cardiac MRI T2* every six months in severe cases and annually for moderate cases.

Abbreviations

S.Phosph, serum phosphorous; Hb, hemoglobin; ALT, aminotransferase alanine; AST, aminotransferase aspartate; Cr, creatinine; n, number; Std, standard; BTM, beta thalassemia major; BMI, body mass index; Sig, significance; Ferr, ferritin; MRI, magnetic resonance image.

Data Sharing Statement

No data sharing os this manuscript and the data were not published elsewhere.

Ethical Approval

This work complies with the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board (IRB) Faculty of Medicine, Zagazig University, Egypt (Approval IRB #: 5895- 8-3-2020). The data are accessed confidentially by the authors. The information was not specific to certain patients and the work was cross-sectional study. The patient informed consent was waived for this research.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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