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ORIGINAL ARTICLE

Magnetic Resonance Imaging Evaluation of Myocardial and Hepatic Iron Overload in Beta-Thalassaemia

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ABSTRACT

Background: Beta-Thalassemia major is an inherited condition characterized by a kind of anemia that causes the destruction of red blood cells, and a significant complication of this condition is the accumulation of excessive iron in body. Magnetic resonance imaging is the most commonly accessible modality that considered non-invasive for identifying or measuring the extent of iron buildup, as well as tracking the effectiveness of treatments that reduce iron levels. **Methods:** The current research was conducted as a prospective cross-sectional analysis and involved thirty-five participants that were diagnosed with beta thalassemia. Ferritin levels were measured from the serum of the studied participants and assessed as the initial screening test to assess presence of excessive iron in the body. 1.5 Tesla MRI machine was used to perform MRI scans of the liver and heart in all subjects to evaluate presence of excessive iron in the heart muscles or liver. **Results:** Serum ferritin levels among studied patients had a range from 300 up to 10000 ng/ml with a mean value of 3013.86 ± 3000.5 SD. There was no significant correlation exist between age or sex and hepatic or cardiac magnetic resonance imaging findings, butthere was a significant negative correlation between serum ferritin levels with hepatic MRI T2 *(P=0.037*). Also, it was reported a statistically significant positive correlation between seurm ferritin levels and R2 and LIC. It was noticed no significant correlation between ferritin levels assessed in the serum and cardiac MRI findings *(P >0.05).* As the grade of hepatic iron overload increase, serum ferritin levels increase*(P =0.02).*Also, patients with severe cardiac overload had a significant elevated levels of serum ferritin in comparison with patients with no cardiac iron overload**.** **Conclusions**: T2* MRI is currently the most preferred tool for early detection, measurement, and monitoring of iron overload in the liver and heart. It is used to guide chelation therapy, which helps prevent iron-related heart problems and minimize patient mortality.

Keywords: MRI; Beta-Thalassemia; Ferritin;Iron.

INTRODUCTION

Thalassemia major is known as an inherited condition that causes a debilitated kind of anemia defined as inefficient production of red blood cells and their subsequent destruction [1]. The fundamental cause is a malfunction in the formation of hemoglobin b-chains, leading to an excessive number of a-chains. The excessive accumulation of a-chain material inside cells leads to increased cell death of erythroid precursors and the destruction of red blood cells in the bloodstream [2]. Severe anemia occurs at the age of 3 months, will result in heightened absorption of iron from intestines. To keepthe level of hemoglobin around 10-12g/dl, patients diagnosed with b-thalassemia major will need regular frequent transfusions of blood [3]. One significant disadvantage of this management process is transfusion siderosis, which leads to excessive iron accumulation, leading to cell injury, toxic effect and malfunction of organs [4]. Iron initially is accumulating at the reticuloendothelial system, which includes the liver, Spleen and bone marrow. Subsequently, it accumulates in the liver cells, cardiac muscles, and endocrine glands as pancreas. The rate of iron turnover and removal in these organs is extremely low [5]. Excessive accumulation of iron in the heart results in various cardiac adverse events as cardiac dysfunction, cardiomyopathy (CMP), or heart failure (HF). This condition is thought to be the primary leading cause of mortality among affected individuals [3]. Early iron accumulation might potentially affect the liver. If liver iron accumulation and overload is not recognized and managed appropriately, it quickly progresses to cirrhosis., Pancreatic iron overload can impair the exocrine and endocrine functions of the pancreas which, unlike the liver, may not regenerate even after correction of hemosiderosis. This needs early detection of pancreatic iron and effective chelation that may prevent diabetes and preserve pancreatic reserve, to prevent hemosiderosis, it is necessary to chelate iron and eliminate it from the body. Chelation medications have been employed to eradicate it [5].

The successful treatment of individuals with thalassemia necessitates the careful evaluation and follow up of the harmful consequences of high iron accumulation and aggressive chelation therapy [6].

Serum ferritin is commonly employed as a substitute indicator; a goal ferritin level of 1,000mg/l is usually typically advised. Nevertheless, ferritin accounts for merely 1% of overall iron reservoir and, being an acute phase reactant (APR), it lacks specificity as its levels might be elevated in instances of inflammation (such as hepatitis) and liver injury [7].Utilizing non-invasive methods to monitor iron accumulation in affected organs is recommended. Among these methods, MR Imaging is the most accessible and noninvasive modality for evaluating iron levels in liver and heart. MRI has been found to have a strong correlation with biopsy results [8]. Combining both T2* MRI of the heart and liver is the most effective noninvasive technique for accurately measuring iron levels. This method is highly sensitive and specific, with reliable positive and negative predictive values. It also eliminates the need for repeated liver biopsies when monitoring therapy [9].

The main objective of the current analysis is to precisely assess accumulation of iron in liver and heart of individuals with B-Thalassemia using magnetic resonance imaging.

METHODS

This research was conducted as a prospective cross-sectional analysis and involved thirty-five participants that were diagnosed as beta-

thalassemia. This study was carried out in the radiology department of Zagazig University Hospital throughout the period from May 2023 to December 2024 after acquiring a local institutional review board (IRB) approval and informed written consent from all patients' parents before the start of the research.The Declaration of Helsinki, issued by the World Medical Association to ensure the protection of individuals participating in medical research, was strictly adhered to during this study.

Inclusion criteria comprised TM patients with history of hemolytic anemia, and other signs of hemosiderosis(Slowed growth and delayed puberty, Jaundice (a yellowish color of the skin or whites of the eyes,an enlarged spleen, liver, or heart, diabetes millets, Bone problems (especially with bones in the face), regular blood transfusions along with getting an iron chelation therapy.

Exclusion criteria were used to exclude patients with liver decompensation, patients with acute systemic infections, patients in whom MRI was contraindicated and patients who refused to be involved in the study.

Every patient underwent a comprehensive history assessment. The ferritin level was measured in the serum of the studied participants as the primary screening test for assessing the presence of iron overload.

Magnetic Resonance Imaging of the liver and heart were performed on all subjects using the 1.5 Tesla superconducting magnet (Philips Intera Achieva, Philips Medical System, Best, Netherlands) without any contrast material to assess presence of excessive iron in the liver and heart muscles.

No fasting or sedation was required before the examination. Respiratory triggering that triggers data acquisition at a fixed point of respiratory cycle (end expiration) requiring long repetition times, was implemented to guarantee minimal movement and reduce the occurrence of respiratory motion artifact. The ECG - cardiac gating used to compensate for cardiac motion, Where the technique details MRI examination was conducted with the patient lying in a supine posture, with the head positioned first, using a torso phased-array body coil. The field of view (FOV) spans from the carina towards the lower renal pole.

Cardiac T2*scanned as a single 10 mm mid-ventricular short axis slice at eight echo-times (ranging from 1.5 ms to 18.5 ms, increment 2.4 ms) with the following acquisition parameters: The repetition time (TR) was 199-125 ms, the flip angle used was 20°, a 128 × 256 matrix, the field of view was 40 cm, and the sampling bandwidth was 810 kHz.

The same mid-ventricular short axis cardiac slice used for both RBH T2* images, For white blood imaging, a multi gradient-echo sequence used for studying cardiac function and movement . For the black blood acquisitions, a double inversion recovery (DIR) pulse was applied generating a similar set of 8 images at increasing echo times to null the blood signal in the heart chamber.

Liver T2*: the acquisition consists of 5 slices collected through the center of the liver in a single breath-hold at 16 different echo times (TE 1.3 , 1.9, 2.7, 3.6, 4.4, 5.3, 6.1, 7, 7.8, 8.7, 9.5, 10.4, 11.3, 12.2, and 13.1 ms) with a gradient-echo sequence to ensure accurate measurement of liver T2* in cases with light liver iron burdens. Each image was acquired during an 11–13 s breath-hold, with the following acquisition parameters: The repetition time (TR) was 100 ms, a 128 × 256 matrix, the flip angle used was 20°, the field of view was 40*24 cm, and the sampling bandwidth was 810 kHz.

T2* measurement:

MR visuals were transferred to a specialized workstation (Philips magnetic resonance extended workspace, software version 2009) , All images will be checked and analyzed by two radiologists , in order to conduct cardiac studies, a uniform and complete region of interest (ROI) as large as possible approximately 5 mm in diameter was used without including any part of the cardiac cavities in the septum of the heart, encompassing both the endocardium and

epicardium layers. Efforts were made to specifically eliminate epicardial structures and blood pool from the outlines.

During hepatic evaluation, a mean region of interest of sufficient size, generally approximately 1 cm diameter. Was selected in uniform sections of the liver parenchyma, specifically omitting blood vessels.

For pancreatic iron load evaluation, the region of interest (ROI) is placed over the pancreatic head or tail (mostly pancreatic head) avoiding (large blood vessels or ducts) and areas with susceptibility artifacts from gastric or colic intra-luminal gas. Then, the ROI was copied across all 12 echo images

To evaluate RBH T2*, Each image showed a pair of numbers: The TE (echo time) and the mean Signal Intensity (SI) of the drawn ROI, that inserted in the two columns of the spread sheet program that supports an MS-Excel file,automatically a curve will be generated. that showed exponential decay. To minimize the potential for noise to cause over-estimation of T2* in heavily iron-loaded tissues, these later points are not used for curve fitting for very low values of T2* and we did truncation.

The T2*, R2 *, liver iron concentration (LIC), pancreatic iron concentration and myocardial iron concentration (MIC) were automatically computed from the datasets used in the analysis. Charts depicting the heart and liver were created, displaying the results in a color-coded format to indicate the severity of iron accumulation. Normal values were depicted in green, mild affection in yellow, moderate in orange, and severe in red.

Analysis of findings: The myocardial iron concentration (MIC) was determined by applying the equation (0.0254 × R2*) + 0.202, where R2* represents the reciprocal of T2* (1000/T2*), as proposed by Carpenter JP et al. [12]. MIC values ranging from 1.16 to 1.65 mg/g indicate mild cardiac siderosis, values between 1.65 and 2.71 mg/g indicate moderate cardiac siderosis and values exceeding 2.71 mg/g indicate severe cardiac siderosis.

Liver-T2* values less than 11.4 ms suggest iron overload, with mild being between 3.8 and 11.4, moderate between 1.8 and 3.8, and severe being less than 1.8 ms. The Liver iron concentration (LIC) was estimated using the formula developed by Garbowski MW et al. [13]. A LIC value of 2-7 mg/g suggests a mild iron burden, 7-15 mg/g shows a moderate iron burden, and a LIC value of less than 15 mg/g indicates a severe iron burden.

Grading of pancreatic iron loading according to Wood et al. (R2*): Normal: < 30 Hz, Mild: 30–100 Hz, Moderate: 100–400 Hz, and Severe: > 400 Hz

STATISTICAL ANALYSIS

The statistical analysis was conducted using SPSS 20 computer software. Qualitative information is expressed numerically and as percentages (N. %), and information that is quantitative, after undergoing normality testing using Shapiro-Wilk test, is represented with mean± standard deviation (SD)and (range) if it was normally distributed. Inferential statistics: The P value, also known as the significance level, is utilized to ascertain the statistical significance of a given outcome. If the P value is greater than 0.05, the result is considered non-significant. On the other hand, if the P value is less than or equal to 0.05, the result is considered significant. To analyze quantitative data, either a t-test or a Mann-Whitney test was used to compare two independent samples. The ANOVA test or Kruskal-Wallis's test was used to compare more than 2 independent samples. Pearson's correlation studies were used to assess correlations between two continuousvariables, spearman's correlation was used when the data was ordinal or non-parametric

RESULTS

This cross-sectional study comprised of 35 individuals who were diagnosed with ß thalassemia. The ages of the total participants had a range from eight to 50 years old and mean age of 24 years, as regard gender distribution among studied participants; 21 participants (60%) were females, and 14 patients (40%) were males. Among studied

patients, 14 patients (40%) had splenomegaly, 17 patients (48.6%) had splenectomy and 32 patients (91.4%) had hepatomegaly.

Serum ferritin levels among studied patients ranged from 300 to 10000 ng/ml with mean 3013.86 ± 3000.5 SD. Among studied 35 patients, 25 patients (71.4%) had serum ferritin levels ≤4000 and 10 patients (28.6%) had serum ferritin levels >4000.

As regards hepatic MRI results among studied patients; hepatic MRI T2* had a range from 2.2 up to 31 ms, mean of 7.77 ±6.94 SD. MRI R2 ranged from 29 to 450 with mean 207 ±113.6 SD. LIC ranged from 0.97 to 20 with mean 6.88 ±4.23SD. Out of the 35 patients examined, 18 patients (51.4%) exhibited mild iron excess, 9 patients (25.7%) displayed moderate, and 2 patients (5.7%) demonstrated severe iron overload.

Cardiac MRI T2* ranged from 3 to 28610 ms, with mean 855.4 ±4829.5 SD. Cardiac MRI R2 ranged from 0 to 175 with mean 37.9 ±31.7 SD. MIC ranged from 0.07 to 5.3 with mean 0.89 ±0.99 SD Out of the 35 patients examined, 31 patients did not show any excessive iron in their hearts, while only 4 patients (11.4%) had a significant amount of iron overload in their hearts. There were no significant correlations observed between the hepatic T2*, R2*, LIC and cardiac T2*, R2* and MIC, with a p-value greater than 0.05.

There was no evident correlation of age or sex with hepatic and cardiac MRI findings *(P >0.05)*, but there was a significant negative correlation between ferritin levels in serum with hepatic MRI T2* *(r=-0.354, P=0.037*). Also, there was a significant positive correlation between seum ferritin levels and R2 *(r=0.347, p=0.041)* and LIC *(r=0.490, p=0.003)*. There was no significant correlation between serum ferritin levels and cardiac MRI findings *(P >0.05)*.

As the grade of hepatic iron overload increases, serum ferritin levels increase (P =0.02). In addition, patients with severe cardiac overload exhibited significantly elevated blood ferritin levels compared to patients without cardiac iron overload (P <0.001).

Table 1: Patients' characteristics

Variable	Patients (N=35)
Age (years): mean±SD range	 24±9.4 (8 – 50)
Sex: *(N. %)* Male Female	 14 (40%) 21 (60%)
Splenomegaly *(N. %)*	14 (40%)
Splenectomy *(N. %)*	17 (48.6%)
Hepatomegaly *(N. %)*	32 (91.4%)
Serum ferritin (ng/ml) *mean±SD* *range*	 3013.86±3000.5 (300 – 10000)
≤4000 (ng/ml) >4000 (ng/ml)	25 (71.4%) 10 (28.6%)

Table 2: Hepatic and cardiac MRI findings among studied patients

Variable	Patients (N=35)
T2 *mean±SD*	7.77±6.94
R2 *mean±SD*	207±113.64
LIC *mean±SD*	6.88±4.23
Hepatic iron overload Normal Mild Moderate Severe	 6 (17.1%) 18 (51.4%) 9 (25.7%) 2 (5.7%)
T2 *mean±SD*	855.4±4829.5
R2 *mean±SD*	37.9±31.7
MIC *mean±SD*	0.89±0.99
Cardiac iron overload Normal Mild Moderate Severe	 31 (88.6%) 0 (0%) 0 (0%) 4 (11.4%)

Table 3: Correlation between serum ferritin levels with hepatic and cardiac MRI findings

Variable	Serum ferritin	
	r	P-value
Hepatic T2	-0.354	0.037
Hepatic R2	0.347	0.041
LIC	0.490	0.003
Cardiac T2	-0.170	0.328
Cardiac R2	0.281	0.102
MIC	0.203	0.243

Table 4: Correlation between age and hepatic and cardiac MRI findings

Variable	Age	
	r	P-value
Hepatic T2	0.084	0.630
Hepatic R2	-0.130	0.457
LIC	0.015	0.934

Variable	Age	
	r	P-value
Cardiac T2	0.241	0.163
Cardiac R2	-0.197	0.256
MIC	-0.173	0.319

Table 5: Association between sex distribution and hepatic and MRI findings

	Sex distribution		P-value
	Female (n=21)	Male (n= 14)	
Hepatic T2 *Median (IQR)*	6 (4.7)	4.1 (2.55)	0.36
Hepatic R2 *Median (IQR)*	162 (169)	237 (123.75)	0.4
LIC *Median (IQR)*	5 (5.5)	7.87 (4.2)	0.1
Cardiac T2 *Median (IQR)*	34 (17)	31 (4.3)	0.4
Cardiac R2 *Median (IQR)*	30 (15)	32.5 (2.23)	0.4
MIC *Median (IQR)*	0.6 (0.4)	0.7 (0.09)	0.4

Table 6: Correlation between MRI findings

Variable	LIC	
	r	*P*
Hepatic T2	-0.464	0.005
Hepatic R2	0.587	<0.001
	MIC	
	r	*P*
Cardiac T2	0.116	0.506
Cardiac R2	0.066	0.706

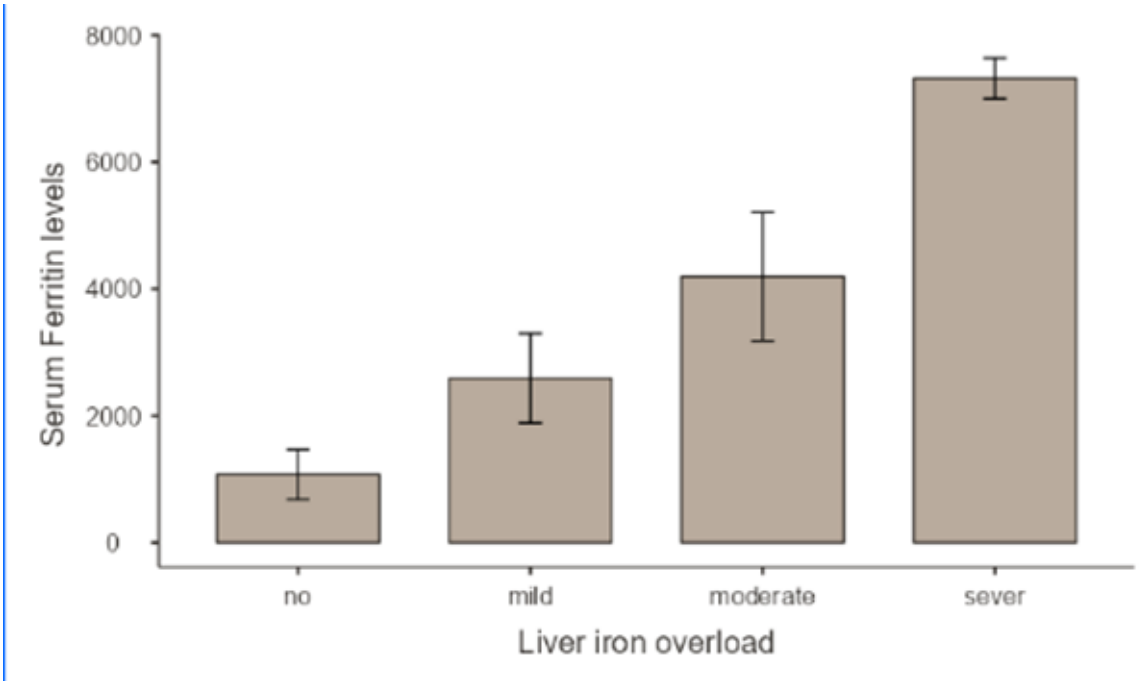

Figure 1: Association between hepatic iron overload and seum ferritin levels

DISCUSSION

Iron overload in thalassemia arises due to the repetitive administration of blood transfusions and the heightened absorption of iron from the gastrointestinal tract. The human body lacks a method to eliminate surplus iron, resulting in its accumulation in various tissues, including cardiomyocytes, and thus causing iron-induced heart illness [15].

When transferrin is fully saturated with iron, the excess iron leads to the formation of oxygen-free radicals, that produces oxidative stress. This, in turn, impairs the operation of the mitochondrial respiratory chain in the myocardium [15].

Excessive iron buildup in the heart can result in cardiac adverse effects and cardiac impairedfunctions, that is considered as a primary cause for mortality among people with thalassemia major [15] [16].

Before the establishment of cardiac T2*, there was no precise method to forecast the likelihood of iron-induced heart illness in individuals with TM [17]. Biopsy is an intrusive operation and thus not an optimal choice for evaluating iron accumulation. non-invasive techniques, such ferritin level, have certain limitations and exhibit weak connection with iron accumulation [15].

The non-invasive and reliable measurement of T2* is a method used to determine iron burden among different body organs such as the heart, pancreas and liver. It considered as a preferable modality [15] [16].

Hepatomegaly is a prevalent illness feature in patients with beta-thalassemia major. Our investigation revealed that 91.4% of the patients examined exhibited hepatomegaly. Hashemizadeh et al., [18] discovered that 46% of patients with beta-thalassemia major had hepatomegaly, with an average age of 10.8± 4.4 years. The acquired results varied due to discrepancies in the populations under study and the age range of the included patients.

Caocci et al. reported a higher frequency of hepatomegaly in patients diagnosed as thalassemia major, with 77% among patients affected. The median age of onset was 10 years. In contrast, Kirti et al., [20] discovered that hepatic problems were less significant (6.8%) in their study. This can be referred to the fact that 59.3% of their patients were under the age of 10.

The current research founded that the mean ferritin levels detected in the serum of the participants was 3013.86 ± 3000.5 ng/Ml SD. Higher percentage of serum ferritin in our study can be attributed to that we include only transfusion dependent thalassemia (thalassemia major) patients in our study

High ferritin levels were also reported by Thavorncharoensap et al. [21] and Torcharus and Pankaew [22] (2509± 1903.6 ng/ ml and 2473.92 ± 1247.38 ng/ ml respectively).

The findings of our study indicate an important inverse correlation between blood ferritin concentrations and hepatic MRI T2* values, as well as a notable direct correlation between serum ferritin concentrations and R2* and LIC. Nevertheless, there was no substantial link observed between the serum ferritin level and the amount of iron in the heart, as determined by T2*, R2*, and MIC.

Furthermore, Eghbali et al. [23],Shehata et al. [16] conducted a study on the correlation detected between liver and heart T2* with ferritin serum levels in thalassemia major studied patients. They found a strong association between ferritin serum level and liver T2*, while there was no correlation was observed with cardiac T2*. In concordance with another study conducted by Alexopoulou et al. [24], it was reported that R2* had a substantial positive correlation with Serum ferritin.

Majd et al., [25] and Shehata et al. [16] demonstrated that there is a statistically significant positive link between ferritin serum and hepatic iron concentration (LIC), also there was a substantial negative correlation between ferritin levels and liver T2* values. These findings are consistent with our own results.

Fahmy et al. [26] concluded a strong negative correlation between studied ferritin levels and liver T2* MRI (p= 0.007), which aligns with the findings of Fischer et al. [27]. Furthermore, Azarkeivan et al. [28] observed a significant inverse correlation between serum ferritin levels and liver MRI T2* values.

Puliyel M et al. [29] found that serum ferritin is not a reliable indicator of overall changes in body iron levels. They also observed a weak correlation between levels of ferritin in the blood and the level of iron in the heart and liver. Anderson et al. 2001 [1] similarly showed a non-significant association between cardiac T2* and levels of serum ferritin while Tanner et al. 2005 [30] reported a poor correlation between both.

These results can be attributed to various variables. Serum ferritin, also considered as an acute-phase protein produced in response to inflammation, has lower levels of iron compared to normal ferritin. This is particularly noticeable in patients with b-thalassemia and hepatitis C virus. Interpreting serum ferritin values can be challenging due to various factors that can affect its concentration independently of changes in the body's iron levels. These factors include fever, acute and chronic liver damage, hemolysis, and ineffective erythropoiesis, all of which are commonly observed in patients with b-thalassemia major [31].

Our data indicate that iron-loaded liver was present in 82.9% of patients with moderate and severe affection, and in 31.4% of instances, the liver was still normal. However, the myocardial iron remained normal in 88.6% of cases, and there were no significant connections between the MRI findings of the liver and heart. Consistent with our findings, Anderson [14] noted a significant discrepancy between the levels of iron in the liver and the heart. Shehata et al. [16], Tanner et al. [30]

and Wood et al. [17] observed no association between hepatic T2* and heart T2*.

Reitman et al. [32] and Ruccione et al. [33] could not find any magnetic resonance imaging (MRI) evidence of iron accumulation in the heart, even when there was excessive iron accumulation in the liver. Anderson et al. [14] showed a poor connection between heart and liver iron loading.

In contrast to the findings of Majd et al. [25] , who reported aberrant cardiac MR-T2* findings in 58% and 50% of patients, respectively. This can be ascribed to the varying chelation protocols employed. However, a significant number of patients are needed to confirm this theory.

Auger and Pennelle [34] Shehata et al. [16] noted that measurement of cardiac iron loading should be initiated between the ages of 6 and 10 years and that cardiac siderosis may appear at the age of 10 due to acute heart failure. The study found that the youngest participant who experienced cardiac siderosis, as indicated by aberrant cardiac T2* findings, was a 15-year-old female. Nevertheless, our investigation revealed no substantial association between patient age and the occurrence of hepatic or cardiac siderosis.

No significant associations were found between LIC and age or sex in our investigation. This finding is consistent with numerous prior investigations conducted by Musallam et al. [35] and Cappellini et al. [36], which indicated that there is no evident association between the characteristics of b-thalassemic patients and LIC (Liver Iron Concentration). Our investigation revealed a clear negative association between liver iron concentration (LIC) and T2* and a positive correlation between LIC and R2*. These findings agreed with other studies conducted by Anderson [14], Shehata et al. [16] and El Shanshory et al. [31] who reported that LIC is greatly associated with T2* and R2* and the larger the liver iron overload, the greater the decrease of Signal Intensity (SI) on MR images which is represented with T2* as liver parenchyma darkens progressively with increased TE.

These results can be attributed to the paramagnetic characteristics of iron, which can influence the susceptibility of tissue and cause alterations in the magnetic field. Consequently, excessive iron accumulation results in a drop in (T2, T2*) and an increase in (R2, R2*). An alternative interpretation of this discovery could be ascribed to the process of MRI, which does not directly visualize the iron, but rather visualizes the movement of water protons near iron deposits in certain tissues like the heart and liver. The iron functions as tiny magnets, destroying the uniformity of the magnetic field in iron laden tissues. one water proton undergoes distinct variations in its magnetic characteristics, causing them to lose synchronization with one other [18].

Our investigation found no statistically significant association between LIC and Cardiac T2* or R2 ($P > 0.05$). Consistent with our research, Wahidiyat et al., [37] discovered that there was no substantial association between LIC and cardiac T2* ($r=-0.163$). Also, Farhangi et al. [15], showed no significant connection between LIC and cardiac T2*. Hassan et al., [38] discovered a noteworthy inverse relationship between LIC and cardiac T2*, which was explained by variations in the transportation and accumulation of iron in these organs.

This study encountered several limitations. Firstly, there was a lack of consistent patient follow-up. Secondly, the inability to do

functional cardiac analysis using MRI was due to the unavailability of the necessary software in our institution. Lastly, there was a lack of a reference standard. Furthermore, the significant proportion of individuals exhibiting liver iron overload identified in this study necessitates a reassessment of the iron chelation approach employed.

CONCLUSIONS

T2* MRI is currently the preferred approach for early detection, measurement, and monitoring of iron levels in the liver and heart. It is also useful in guiding chelation therapy to prevent iron-related heart problems and reduce patient mortality.

Conflict of interests: -The authors declare that they have no conflict of interests

Financial Disclosures: There were no any financial interests, relationships and affiliations relevant to the subject of the study.

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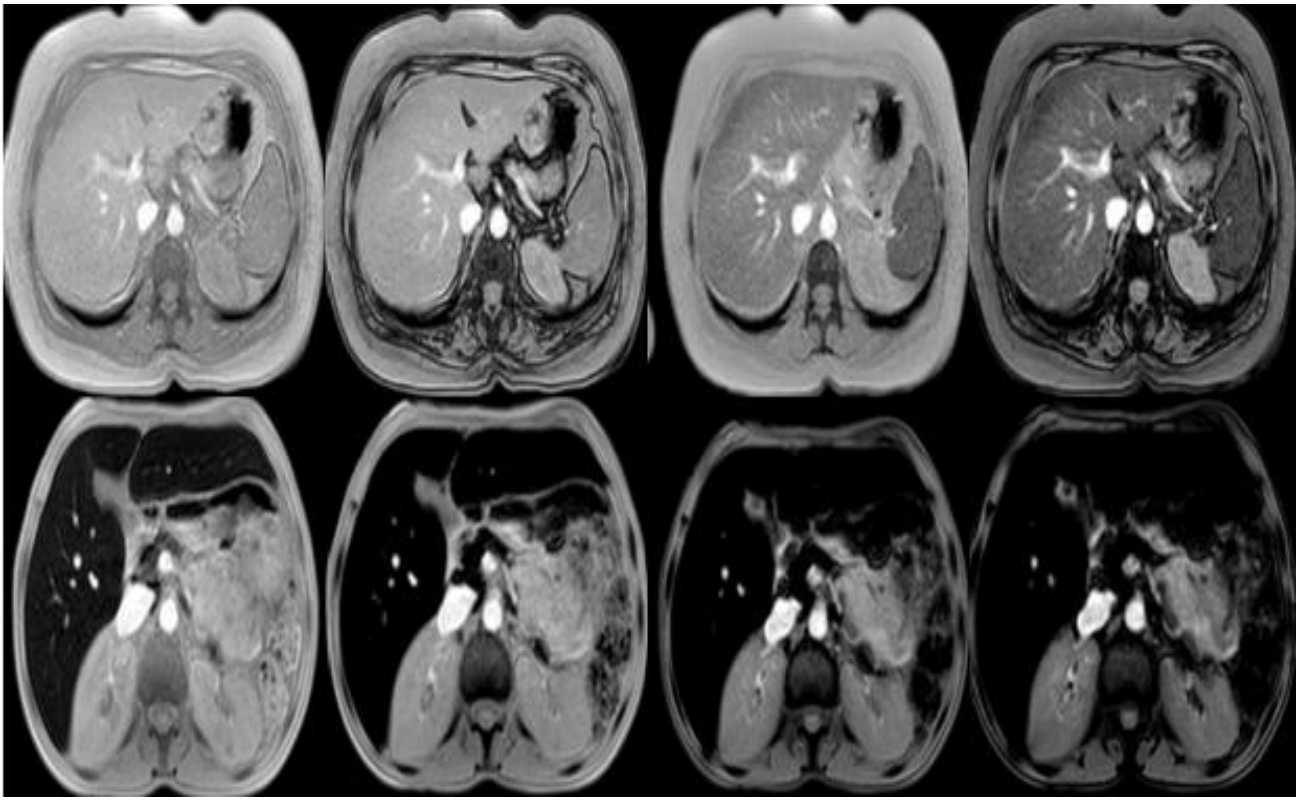
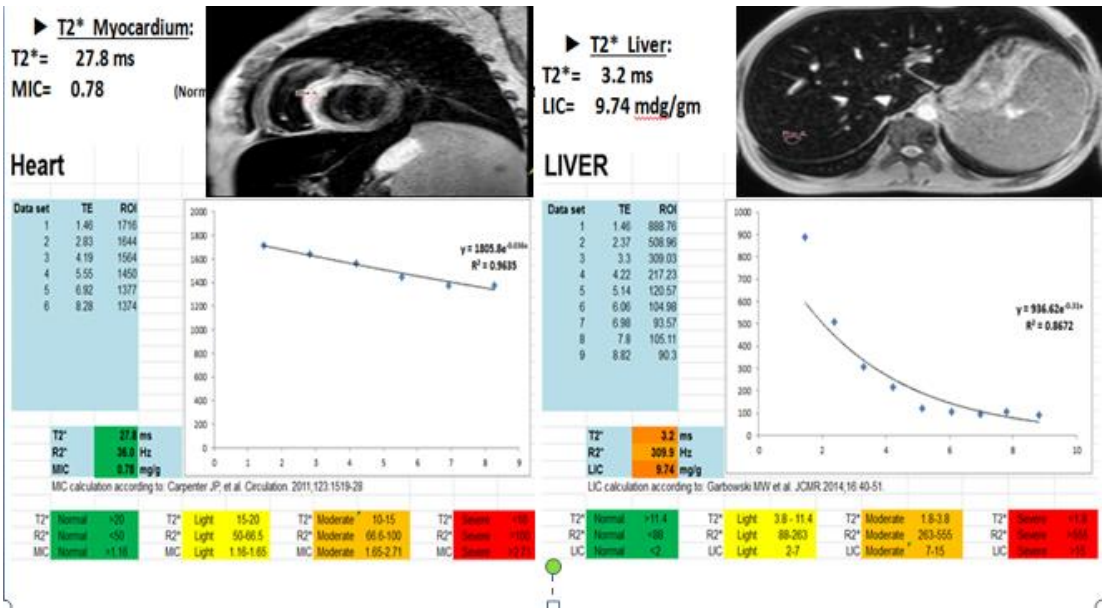
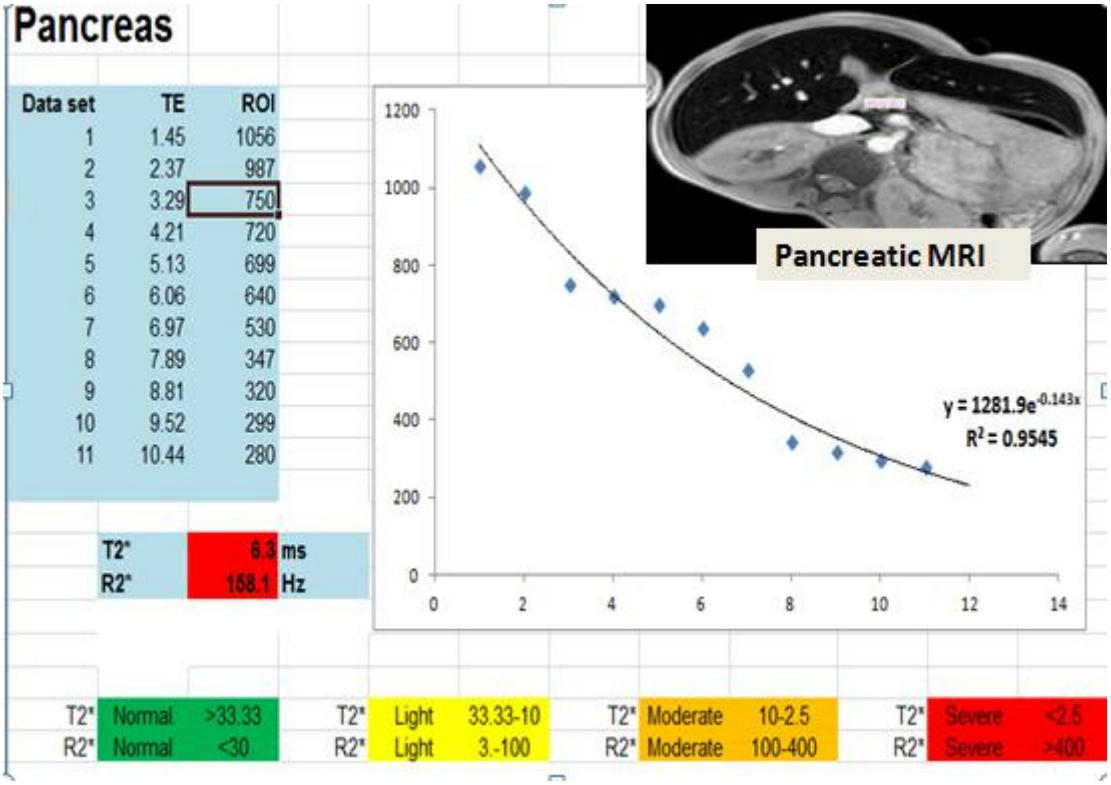


Figure S1:
Gradient echo T2* images of two thalassemic patients acquired at different TE (1.3 - 3,9 – 6,7 - 10) upper row images representing normal liver with no decay at t2* signal of the liver (normal value of t2* 15 ms and LIC 1,5 mg/g) indicating normal liver iron deposition, unlike the lower row images showing significant decrease in the signal of the liver with increasing echo time (t2* value 0,9 ms and LIC > 15 mg/g) that consistent with sever hepatic iron overload

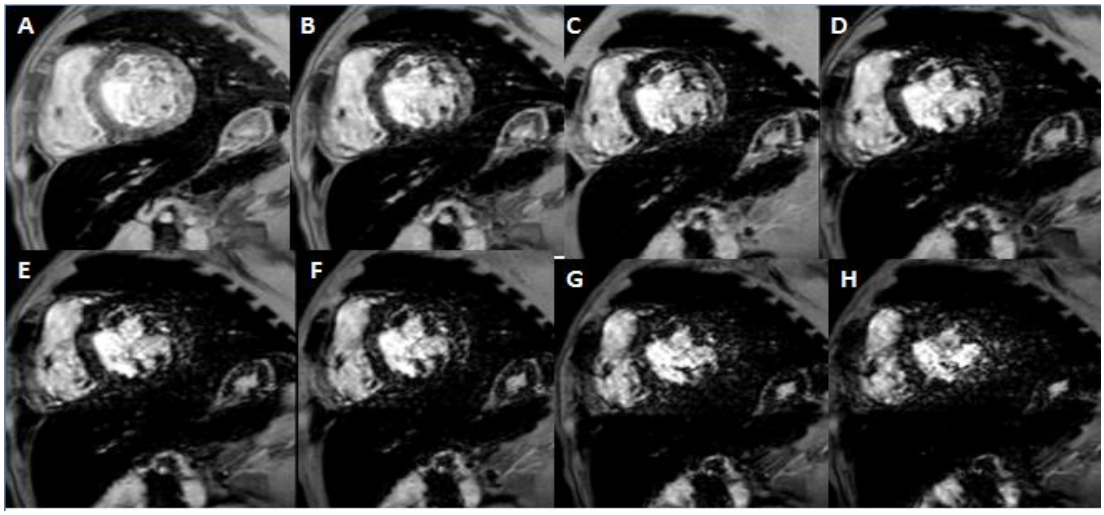


FigureS2: MRI of a transfusion-dependent patient with Beta-thalassemia with serum ferritin =3450 ng/ml using multiple gradient- echo time T2* sequence. A Left ventricular short-axis black blood MRI images of normal heart iron deposition with a region of interest drawn at mid-interventricular septum. B Axial MRI of moderate hepatic iron overload with a region of interest drawn in the periphery of the right lobe of the liver

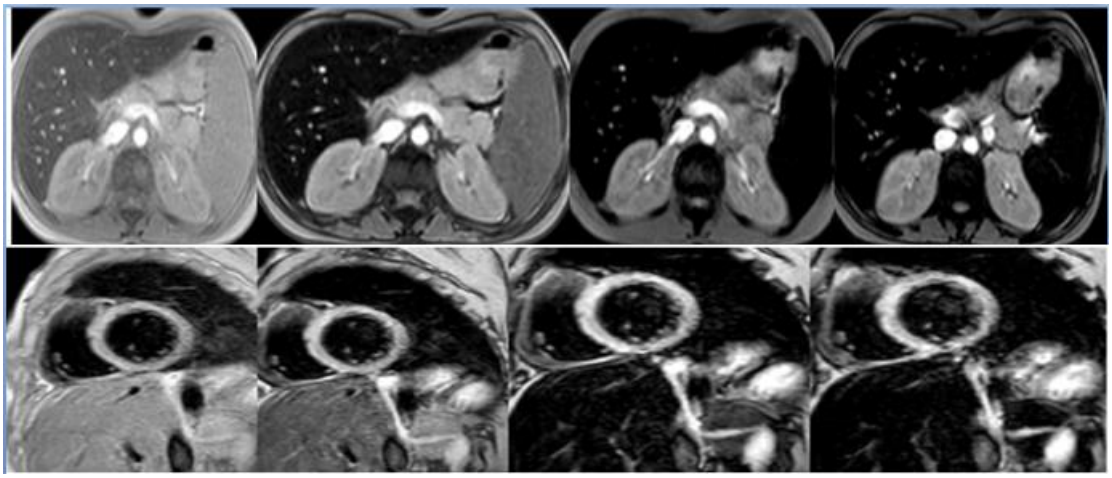


FigureS3:multiple gradient-echo times Axial MRI with a region of interest drawn in the head **of** the

pancreas, showing dark signal of pancreatic tissue with T2* value: 6.5 ms and R2* : 158 Hz indicate moderate pancreatic iron overload



FigureS4: Coronal images of gradient echo white blood sequence of the liver and heart at 8 different TE (1.6-18.7ms) reveal a significant decay in both hepatic and myocardial signal that increases on longer TE imaging sequences. The measured cardiac values were (T2*: value of 9.5 ms, R2*:146Hz , MIC: 9.5 mg/g) and hepatic values were (T2*: 0.6 ms, R2*: 61.8 Hz ,LIC: > 15 mg/g). The measured serum ferritin was >7000 ng/ml. These findings are consistent with sever hepatic and cardiac iron deposition.



FigureS5: Gradientecho axial images of the liver and pancreas (top images) and coronal black blood images of the heart (low images) of beta–thalassemic patient taken at different TE (1.6 - 4.1- 9.1- 12.6 ms) show a slow decay in hepatic signal along the increased TE imaging sequence . The measured hepatic values were (T2*: value of 2.9 ms, LIC: 11 mg/g) while pancreas and heart show no decay with measured values (pancreas: T2*: 40 ms, R2*: 25 Hz) (heart: T2*:33 ms, LIC: 2 mg/g). The measured serum ferritin was 1900 ng/ml. These findings are consistent with mild hepatic iron overload, normal cardiac and pancreatic iron deposition.

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