

# International Journal of Radiology and Diagnostic Imaging



E-ISSN: 2664-4444  
P-ISSN: 2664-4436  
[www.radiologypaper.com](http://www.radiologypaper.com)  
IJRDI 2023; 6(1): 115-124  
Received: 08-01-2023  
Accepted: 13-02-2023

**Omnia Mohamed Elrakaiby**  
Radiodiagnosis Department,  
Faculty of Medicine, Tanta  
University, Tanta, Egypt

**Manal Fathi Hamisa**  
Radiodiagnosis Department,  
Faculty of Medicine, Tanta  
University, Tanta, Egypt

**Mohamed Ramadan El-Shanshory**  
Pediatric Department, Faculty  
of Medicine, Tanta University,  
Tanta, Egypt

**Rasha Mahmoud Dawoud**  
Radiodiagnosis Department,  
Faculty of Medicine, Tanta  
University, Tanta, Egypt

**Corresponding Author:**  
**Omnia Mohamed Elrakaiby**  
Radiodiagnosis Department,  
Faculty of Medicine, Tanta  
University, Tanta, Egypt

## The impact of liver iron overload determined by T2\* MRI on liver fibrosis determined by FibroScan in patients with thalassemia major

**Omnia Mohamed Elrakaiby, Manal Fathi Hamisa, Mohamed Ramadan El-Shanshory and Rasha Mahmoud Dawoud**

DOI: <https://dx.doi.org/10.33545/26644436.2023.v6.i1b.315>

### Abstract

**Background:** Thalassemia major (TM) is a form of hemolytic anemia requiring monthly blood transfusions from early childhood with each RBC introducing 200mg of iron to the patient system. The prognosis of liver iron overload is highly dependent on the one hand on both liver iron content (LIC) and the extent of liver fibrosis. In recent years, non-invasive methods were developed in order to replace liver biopsy. Magnetic resonance imaging (MRI) with T2\*-weighted sequences has the potential to become a non-invasive standard technique in assessing tissue iron. Transient elastography TE (Fibroscan) is a new non-invasive and reliable bedside method used to measure liver stiffness (LS) caused by fibrosis.

**Methods:** This is a prospective study which was conducted on 40 patients diagnosed with a  $\beta$ -thalassemia major (22 males and 18 females) with age from 6 to 16 years old, regular blood transfusion and Iron chelation therapy for at least 18 months. All patients underwent evaluation of clinical manifestations, laboratory investigations and MR imaging techniques: liver to muscle signal intensity ratio and T2\* and R2\* Relaxometry.

**Results:** R2\* was significantly higher among severe iron overload stage than the other stages. T2\* is reverse proportion with iron overload, but R2\* is direct proportion with iron overload in liver. Age was significantly increased among severe iron overload group than mild and moderate groups. Also, there was significant relation between consanguinity and family history with iron overload stages among the studied patients. Virus C and splenectomy were significantly higher among severe iron overload stage than mild and moderate stages. Also, age at diagnosis was significantly higher among moderate iron overload stage than the other stages. There was highly significant relation between iron overload stages and fibrosis stage Also, Fibrosis reading was significantly higher among moderate iron overload stage than the other stages.

**Conclusions:** MRI T2\* is the best noninvasive method for assessment and evaluation of hepatic iron overload and determine its severity in  $\beta$  thalassemia major patients. There was significant relation between iron overload stages with MRI T2\* and R2\*.

**Keywords:** MRI T2\*, thalassemia, iron overload, fibroscan

### Introduction

Thalassemia major (TM) is a type of hemolytic anaemia needing monthly blood transfusions beginning in infancy, with each red blood cell (RBC) containing 200 mg of iron that the patient's body lacks the natural ability to clear <sup>[1]</sup>. However, both transfusion and high iron absorption have aggravated iron excess <sup>[2]</sup>.

Despite the introduction of iron-chelating medications during the past three decades, hemosiderosis continues to be one of the top causes of mortality among TM patients <sup>[3]</sup>. Iron accumulation may impact all organs, including the heart, liver, and pancreas <sup>[4]</sup>. Risk for developing hepatic fibrosis and cirrhosis has been linked to liver iron concentration (LIC) and length of iron exposure by the liver <sup>[5]</sup>.

Liver failure is the third main cause of mortality in people with iron overload behind heart failure and infectious illnesses <sup>[6]</sup>. The prognosis of liver iron overload is greatly reliant on liver iron content (LIC), hepatic fibrosis, and hepatotoxic co-factors such as viruses and alcohol <sup>[7]</sup>.

There is a need for methods to assess total body iron reserves, and serum ferritin is a trustworthy measure but can provide false positives in the context of inflammation, fever, and liver illness. Iron content in the liver is regarded as the standard direct detection technique for body iron overload [8].

In individuals with thalassemia, liver biopsy is the gold standard for assessing the state of fibrosis and measuring the liver iron content (LIC) of hepatic tissue [9]. However, this invasive approach has several procedure-related risks, as well as broad results variances and sampling inaccuracies [10].

In recent years, non-invasive alternatives to liver biopsy have been developed. Magnetic resonance imaging (MRI) with T2\*-weighted sequences has the ability to become a non-invasive standard method for assessing tissue iron [11] and is a reliable method for detecting iron deposition in the liver, demonstrating a high correlation with the values found in liver biopsy specimens [12].

In addition to LIC measurement, an accurate estimate of hepatic fibrosis has significant consequences for patient care, prognosis evaluation, and long-term follow-up [13]. Transient elastography TE (fibroScan) is a novel, non-invasive, and dependable bedside technique for measuring liver stiffness (LS) due to fibrosis [14].

The objective of this study was to assess the relationship between liver iron overload identified by T2\* (MRI) and hepatic fibrosis measured by FibroScan in individuals with TM.

### Patients and Methods

This is a prospective study which was conducted on 40 patients diagnosed with a  $\beta$ -thalassemia major (22 males and 18 females) with age range of 6-16 years old, regular blood transfusion and Iron chelation therapy for at least 18 months referred to Radiodiagnosis and medical imaging Department at Tanta University Hospital from pediatric department during the period from July 2018 to July 2022.

The study was approved by the Ethical Committee of the Faculty of Medicine, Tanta University. A written informed consent was obtained from the guardian of the patient after simple and clear explanation of the research objectives.

Exclusion criteria include the following: patients younger than 6 years old, advanced hepatic and cardiac disease, patients with ascites and contraindication to MRI (including severe claustrophobia, patients with pacemaker or metal implants).

All patients were subjected to the following: clinical examination including: pallor, hepatomegaly, splenomegaly, splenectomy, age at diagnosis and blood transfusion interval., laboratory examination including: Complete blood count, serum ferritin, liver functions and virus C markers (hepatitis markers), and radiological imaging including: U/S examination, MRI liver with T2\* weighted gradient echo and liver transient elastography.

### MR Imaging Techniques:

Liver to muscle signal intensity ratio and T2\* and R2\* Relaxometry

### Techniques

Two broad groups of techniques used for iron estimation are the signal intensity ratio method and the relaxometry method. Both of these methods can use spin-echo and/or

GRE sequences.

### Signal intensity ratio

In the signal intensity ratio method, the signal intensity of the liver and heart, is divided by the signal intensity of a reference tissue, such as muscle or fat, by drawing a region of interest. and includes four GRE sequences with different TEs (T1-weighted, intermediate-weighted, T2-weighted, and long-TE T2-weighted) and one T1-weighted spin-echo sequence. Signal intensity measurements from each of these sequences are used to calculate iron concentration.

### Relaxometry

Signal intensity loss in the image from dephasing of transverse magnetization follows a pattern similar to radioactive decay (160). Hence, iron-mediated darkening can be characterized by time constants such as T2 or T2\* or by relaxation rates such R2 (1/T2) and R2\* (1/T2\*). Relaxometry methods include calculation of T2 or R2 (spin-echo sequence) and T2\* or R2\* (GRE sequence) by acquiring multiple images at different TEs.

A relaxometry method to calculate hepatic and myocardial T2\*, developed by Anderson *et al.* [11], includes acquisition of GRE images with eight different TEs (2.2-20.1 msec) for liver and nine different TEs (5.6-17.6 msec) for the heart.

### Transient Elastography:

To achieve a minimum of 4 cm of penetration into the liver parenchyma using the TE method, the transducer is positioned between the 9<sup>th</sup> and 11<sup>th</sup> right intercostal gaps. The equipment provides an A-mode picture, which can help the examining physician decide which liver segment to take. The TE probe's specialised (cylinder-shaped) piston will apply a calibrated force to the liver, producing an elastic shear wave. The probe is sensitive enough to measure the speed with which shear waves go into the liver, which is indicative of liver stiffness.

The scale operates between 1.5 and 75 kilopascals (kPa). If the system finds faults in the acquisition process, it will automatically reject the measurement. The quality metrics and the median of 10 measures are presented at the conclusion of the test (IQR, SR). For more reliable assessments, manufacturers produced M, XL, and S probes that are advised in order to eliminate the confounding factor of obesity and thoracic circumference fluctuations.

### Serum ferritin

The serum ferritin was measured using a routine laboratory technique. Approximately 3 mL of blood was extracted from the patient by a sterile venous puncture. The blood was let to coagulate. Separated serum was kept at -200C.

### Statistical analysis

Using microsoft excel 2017 and SPSS V.25 for microsoft windows 10, the results were compiled and statistically evaluated using conventional computer programmes. Descriptive statistics was done using mean and SD for quantitative data, and frequency and proportion for qualitative data. Non-normally distributed numerical data were presented as median (IQR). Analytical statistics: Chi-Squared ( $\chi^2$ ), ANOVA (f) test and Mann-Whitney test. P value <0.05 was considered statistically significant

**Results**

The mean age of the studied patients was 12.78±2.02 years, (55%) of them were males. Most of them had negative family history and positive consanguinity (90% and 60%), respectively. Most of the patients had positive virus C and

splenectomy (60%). All patients had pallor and hepatomegaly. The mean age at diagnosis and blood transfusion interval were (18.48±9.58 and 1.4±0.53) months, respectively. (Table 1)

**Table 1:** Demographic and clinical data of studied patients.

Variables	Studied patients (N=40)	
<b>Age/ year</b>		
Mean ± SD	12.78±2.02	
<b>Gender</b>	<b>No.</b>	<b>%</b>
Male	22	55.0
Female	18	45.0
<b>Family History</b>		
Negative	36	90.0
Positive	4	10.0
<b>Consanguinity</b>		
Negative	16	40.0
Positive	24	60.0
<b>Virus C</b>		
Negative	8	20.0
Positive	32	80.0
<b>Pallor</b>		
Negative	0	0
Positive	40	100
<b>Hepatomegaly</b>		
Negative	0	0
Positive	40	100
<b>Splenomegaly</b>		
No	24	60
Yes	16	40
<b>Splenectomy</b>		
No	16	40
Yes	24	60
<b>Age at diagnosis (months)</b>		
Mean ± SD	18.48±9.58	
<b>Blood transfusion interval (month)</b>		
Mean ± SD	1.4±0.53	

Mean Hb level among the studied thalassemia patients was 6.43±2.08 g/dl, platelets count was 367.08±172.54, the

mean ferritin level was 7965.90±4359.79 ng/ml and Hb F was 56.20±23.86 g/dl (Table 2)

**Table 2:** Laboratory investigations and signal intensity ratio of liver

Variables	Studied patients
	Mean ± SD
Hb (g/dl)	6.43±2.08
Platelets x 10 <sup>-3</sup>	367.08±172.54
Ferritin level (ng/ml)	7965.90±4359.79
Hb-F (g/dl)	56.20±23.86
T2* /ms	3.47±2.41
R2*/Hz	502.20±350.22

About half of the studied patients (47.5%) had severe iron over load, followed by (32.5%) had moderate iron overload and (20%) had mild iron over load. Also, (45%) of the studied patients had moderate fibrosis stage, followed by

(25%) had mild stage, (17.5%) had severe stage while, and (12.5%) had normal stage. The mean fibrosis reading and F stage among the studied patients were (8.38±2.10 and 1.90±0.84), respectively. (Table 3)

**Table 3:** Iron overload and fibrosis stages of studied thalassemia patients.

Variables	Studied patients, N=40	
	No.	%
<b>% of iron overload</b>		
Mild	8	20
Moderate	13	32.5
Severe	19	47.5
<b>Fibrosis stage</b>		
Normal	5	12.5
Mild	10	25.0
Moderate	18	45.0
Severe	7	17.5
Fibrosis Reading Median	Mean ± SD	
	8.38±2.10	
Fibrosis Reading IOR*	1.77±3.27	
Fibrosis Reading IQR*/med	10.85±5.75	
F stage score	1.90±0.84	

Age was significantly increased among severe iron overload group (15.82±1.84) than mild and moderate groups (P=0.002). Also, there was significant relation between consanguinity and family history with iron overload stages among the studied patients (p<0.001). While gender showed no significant relation with iron overload stages (p =0.777). Virus C and splenectomy were significantly higher among

severe iron overload stage than mild and moderate stages (p<0.001). Also, age at diagnosis was significantly higher among moderate iron overload stage (27.00±3.56 month) than the other stages (p<0.001). While pallor, hepatomegaly, splenomegaly and blood transfusion interval showed no significant relation with iron overload stages (p>0.05). (Table 4)

**Table 4:** Relation between iron overload stages and demographic & clinical data of the thalassemia patients.

	% Of iron overload (N=40)						X <sup>2</sup>	P value
	Mild (N=8, 20%)		Moderate (N=13, 32.5%)		Severe (N=19, 47.5%)			
<b>Age/ years</b>								
Mean ± SD	12.88±2.47		14.00±1.2		15.82±1.84		H= 7.265	0.002*
Gender	No	%	No.	%	No.	%	0.505	0.777
Female	3	37.5	4	30.76	11	57.89		
Male	5	62.5	9	69.23	8	42.10		
<b>Family History</b>								
Negative	8	100.0	12	92.30	16	84.21	14.0	<0.001*
Positive	0	0.0	1	7.69	3	15.79		
<b>Consanguinity</b>								
Negative	0	0.0	13	100.0	3	15.78	21.818	<0.001*
Positive	8	100	0	0.0	16	84.20		
<b>Virus C</b>								
Negative	8	100	0	0.0	0	0.0	40.0	<0.001*
Positive	0	0.00	13	100.0	19	100.0		
<b>Pallor</b>								
Negative	0	0	0	0.0	0	0.0	NA	---
Positive	8	100	13	100.0	19	100.0	NA	
<b>Hepatomegaly</b>								
Negative	0	0	0	0	0	0.0	NA	---
Positive	8	100	13	100	19	100.0	NA	
<b>Splenomegaly</b>								
No	8	100	13	100	15	78.94	NA	---
Yes	0	0	0	0	4	21.60		
<b>Splenectomy</b>								
No	6	75	0	0	0	0.0	40.0	<0.001*
Yes	2	25	13	100	19	100.0		
<b>Age at diagnosis/ month</b>								
Mean ± SD	8.50±4.99		27.00±3.56		18.23±9.17		H= 13.728	<0.001*
Range	1.0-13.0		22.0-30.0		2.0-28.0			
	P1=0.003*, p2=0.004*, p3<0.001*							
<b>Blood transfusion interval/ month</b>								
Mean ± SD	1.81±1.28		2.50±1.35		1.87±0.92		H= 1.280	0.290
Range	0.5-3.0		1.0-4.0		0.5-3.0			
	P1=0.908, p2=0.144, p3=0.201							

P1= severe compared mild, P2= severe compared moderate, P3= mild compared moderate, X<sup>2</sup>: Chi square test, H: Kruskal Wallis test, \*significant

MRI T2\* was significantly higher among mild iron overload stage (14.9±1.20) than other stages, (p=0.002). While, R2\* was significantly higher among severe iron overload stage (717.3±156.9) than the other stages (p=0.001). Platelet's count was significantly higher among moderate iron overload stage (449.20±128.07) than the other stages

(p=0.015). and ferritin level was significantly higher among severe iron overload stage (7300 ±2180) than the other stages (p=0.002). On the other hand, Hb and Hb F levels didn't show any significant relation with iron overload stages (p>0.05). (Table 5)

**Table 5:** Relation between iron overload stages and signal intensity ratio of liver & laboratory data of the studied patients

Variables	% Of iron overload (N=40)			H	P value	Post hoc
	Mild (N=8, 20%)	Moderate (N=13, 32.5%)	Severe (N=19, 47.5%)			
<b>T2*/ ms</b>						
Mean ± SD	14.9±1.20	3.65±0.19	1.45±0.34	7.30	0.002*	-
Range	14.1-15.9	2.8-3.8	1.1-1.9			
Median (IQR)	14(2.2)	3.6 (0.35)	1.3 (0.65)			
<b>R2*/Hz</b>						
Mean ± SD	67.1±4.52	274.2±14.5	717.3±156.9	42.3	0.001*	-
Range	62-71.1	260-292	526-898			
Median (IQR)	70 (60.3)	272 (27.7)	720 (302)			
<b>Hb (g/dl)</b>						
Mean ± SD	7.00±2.24	6.33±2.22	6.20±1.75	0.373	0.691	P1=0.448 P2=0.873 P3=0.431
Range	3.5-9.5	3-9.75	4-8	0.373	0.691	
<b>Platelets</b>						
Mean ± SD	223.7± 104.6	449.20 ±128.07	381.8± 182.6	4.734	0.015*	P1=0.020* P2=0.271 P3=0.005*
Range	170-480	350.0-598.0	90.-595	4.734		
<b>Ferritin level (ng/ml)</b>						
Mean ± SD	1800±700	4600±1270	7300±2180	6.80	0.002*	P1=0.003* P2=0.002* P3=0.927
Range	1000-3000	2000-10000	2000-12000			
<b>Hb F (g/dl)</b>						
Mean ± SD	63.75±7.44	64.40±17.56	49.73±28.45	1.882	0.167	P1=0.154 P2=0.108 P3=0.953
Range	50.0-70.0	44.0-78.0	3.0-88.0			

P1= severe compared mild, P2= severe compared moderate, P3= mild compared moderate

MRI: magnetic resonance imaging, Hb: Hemoglobin, Hb F: Fetal hemoglobin, H: Kruskal Wallis test, \*significant

There was highly significant relation between iron overload stages and fibrosis stage (p<0.001). Also, Fibrosis reading IQR\*/med was significantly higher among moderate iron overload stage (15.13±1.89) than the other stages (p=0.024).

While, fibrosis reading median, fibrosis reading IOR\* and F score didn't show any significant relation with iron overload stages (p>0.05) (Table 6).

**Table 6:** Relation between iron overload stages and fibrosis stages among the studied patients.

Variables	% of iron overload (N=40)						X <sup>2</sup>	P value
	Mild (N=8, 20%)		Moderate (N=13, 32.5%)		Severe (N=19, 47.5%)			
Fibrosis stage	No	%	No	%	No	%	25.921	<0.001*
Normal	3	37.5	2	15.38	0	0		
Mild	5	62.5	4	30.76	6	31.57		
Moderate	0	0.00	3	23.07	10	52.63		
Severe	0	0.00	4	30.76	3	15.78		
<b>Fibrosis Reading Median</b>								
Mean ±SD	8.08±1.82		7.66±1.68		9.60±2.63		H= 2.568	0.090
Range	5.6-11.7		4.0-9.1		5.8-11.4			
P1=0.622, p2=0.056, p3=0.051								
<b>Fibrosis Reading IOR*</b>								
Mean ± SD	2.45±4.32		1.14±0.18		0.77±0.54		H= 1.104	0.342
Range	0.3-13.0		0.7-1.2		0.3-1.4			
P1=0.335, p2=0.184, p3=0.814								
<b>Fibrosis Reading IQR*/med</b>								
Mean ± SD	10.64±6.38		15.13±1.89		7.90±4.41		HF= 4.108	0.024*
Range	3.0-20.0		13.0-18.0		4.0-13.0			
P1=0.049, p2=0.187, p3=0.007								
<b>F score</b>								
Mean ± SD	1.73±0.77		1.75±0.71		2.40±0.97		H= 2.544	0.092
Range	0.0-3.0		0.0-2.0		1.0-3.0			
P1=0.946, p2=0.036, p3= 0.099								

X<sup>2</sup>: Chi square test, H: Kruskal Wallis test,

\*significant, CI: Confidence interval



Relation between MRI T2\* with demographic data, iron overload and fibrosis stages of the studied patients is shown in table.7

Data in Table 7 demonstrated that, there was significant

relation between MRI T2 with consanguinity and fibrosis stage ( $p < 0.05$ ). While, gender, family history and iron overload stage didn't show any significant relation with MRI T2 ( $p > 0.05$ ). (Table 7)

**Table 7:** Relation between MRI T2\* with demographic data, iron overload and fibrosis stages of the studied patients.

Variables	MRI T2	U	P-Value
	Mean ± SD		
<b>Gender</b>			
▪ Male	3.58±2.59	0.292	0.801
▪ Female	3.05±2.19		
<b>Family history</b>			
▪ Positive	3.34±2.52	0.472	0.649
▪ Negative	4.6±0.0		
<b>Consanguinity</b>			
▪ Positive	4.49±2.17	4.128	0.006*
▪ Negative	1.10±0.0		
<b>% Of iron over load</b>			
▪ Mild	4.6±0.0	0.223	0.649
▪ Moderate	0.0±0.0		
▪ Severe	3.34±2.52		
<b>Fibrosis stage</b>			
▪ Normal	4.6±0.0	6.792	0.023*
▪ Mild	1.20±0.20		
▪ Moderate	5.06±2.10		

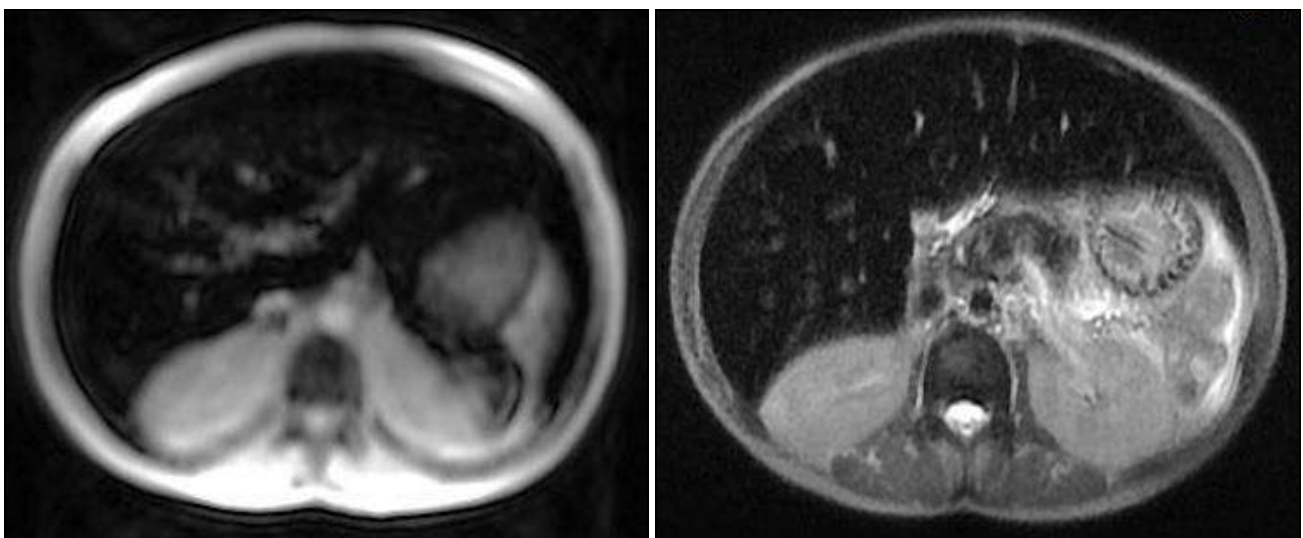
U test: Mann-Whitney U test, \*significant

**Case No. 1**

Male patient, aged 15 years old, diagnosed as β-thalassemia major at 1.5 year with Hb=6 g/dl, transfusion of blood every month and serum ferritin level from 3000-12000 ng/ml, positive virus C with splenectomy. Negative family history and positive consanguinity. The patient was pale and jaundiced, he received deferoxamine and desferasirox as

chelation therapy. T2\* of liver= 1.3 ms, R2\* of liver= 770.5 Hz, Diagnosis: sever hemosiderosis of liver.

The reading of 8.6 K Pascal in this examination correlates with a fibrosis stage of F2 on the Metavir histological index of grading fibrosis. Which classifies fibrosis on a scale of F0 to F4 where F0 is normal liver without fibrosis and F4 represents liver cirrhosis.



**Fig 1:** MRI T2 axial section of upper abdomen (FS=1.5, TR=1494 ms, TE=80.8 ms) showing hepatomegaly with low signal intensity of liver, spleen not visualized (Surgically removed), the kidneys show no abnormal enhancement.

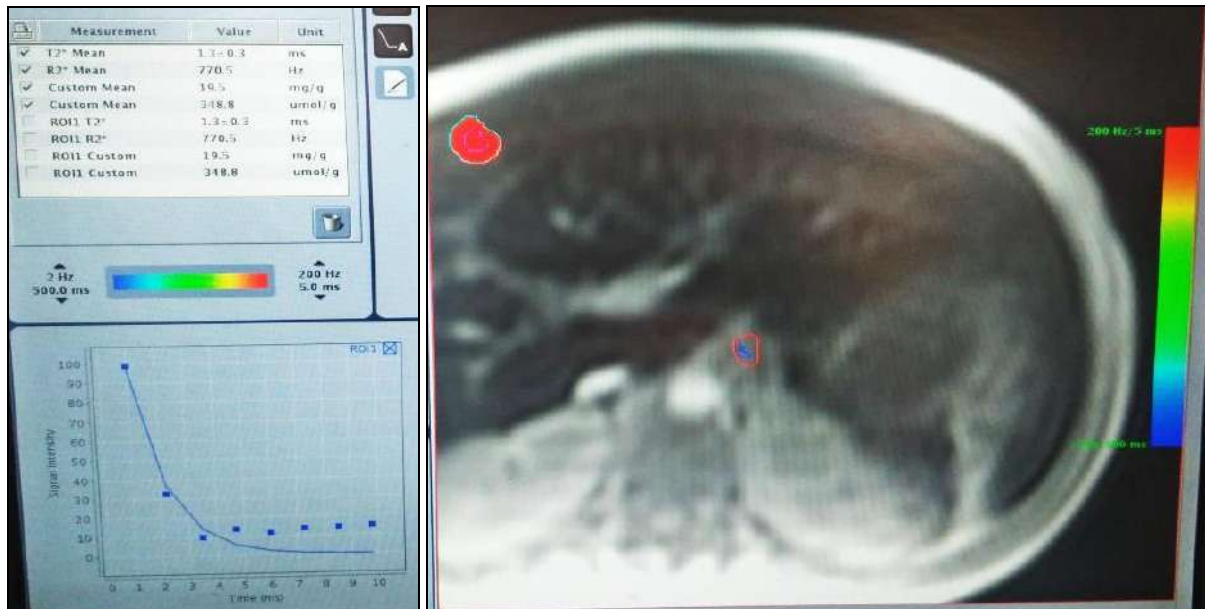


Fig 2: Manually drawn ROI of liver

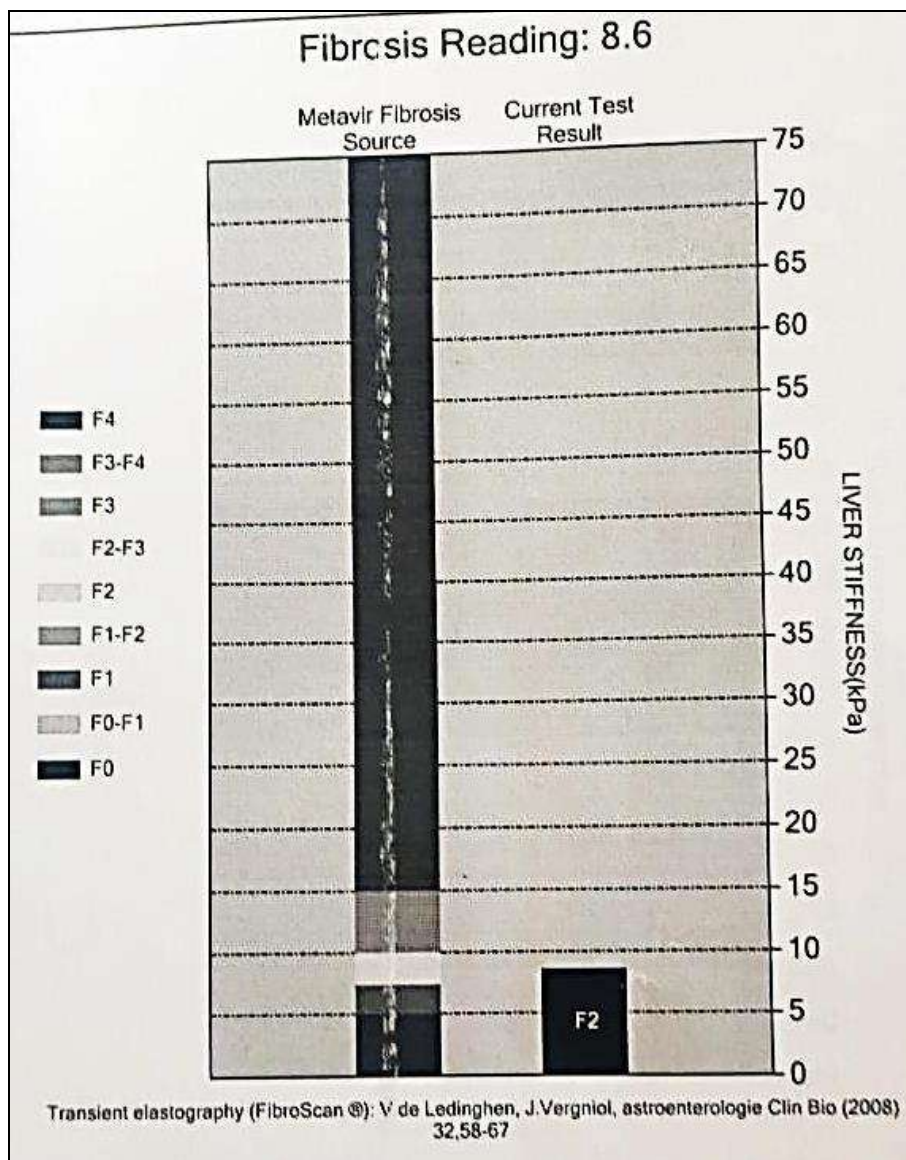
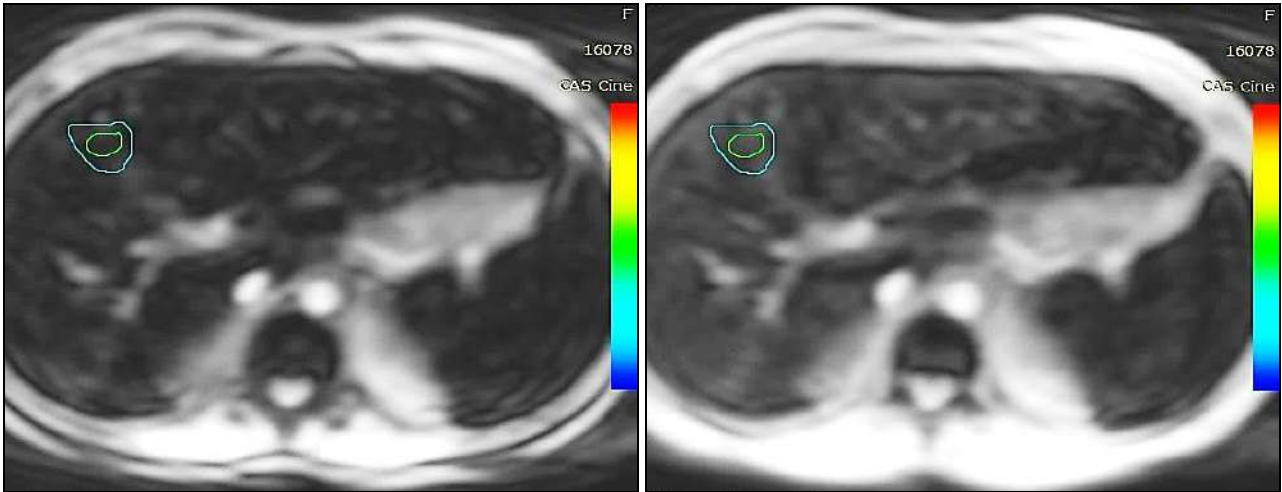


Fig 3: Fibrosis reading measured by fibroScan of case 1

**Case No.2**

Female patient, aged 13 years old, diagnosed as  $\beta$ -thalassemia major at 1 year with Hb=7 g/dl, transfusion of blood every two months and serum ferritin level 2000 ng/ml, negative virus C not splenectomized. Negative family history and positive consanguinity, the patient was pale and jaundiced, she received deferasirox and

desferasirox as chelation therapy. The reading of 4 k Pascal in this examination correlates with a fibrosis of F0 on the Metavir histological index of grading fibrosis. Which classifies fibrosis on a scale of F0 to F4 where F0 is normal liver without fibrosis and F4 represents liver cirrhosis. T2\* of liver= 3.6 ms, R2\* of liver= 280 Hz, Diagnosis: Moderate hemosiderosis of liver.

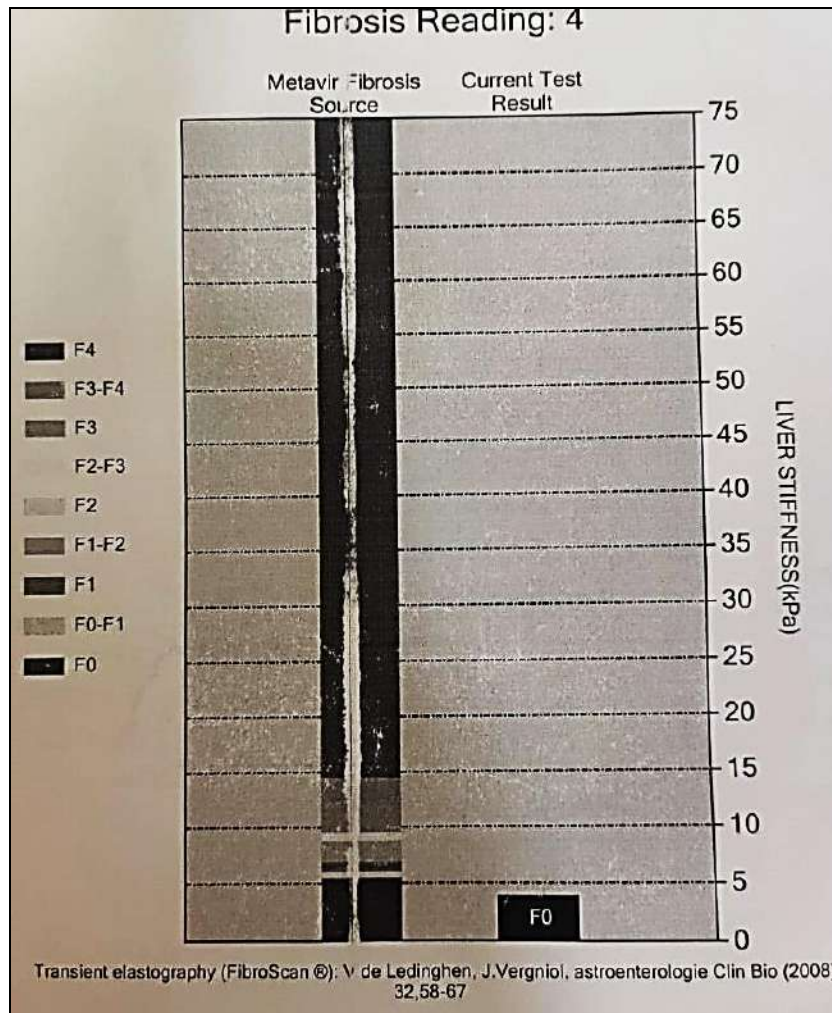


**Fig 4:** MRI T2\* of upper abdomen (FS= 1.5, TR= 1494 ms, TE= 80.8ms) showing hepatosplenomegaly with low signal intensity of liver and spleen.



**Fig 5:** Manually drawn ROI of liver.





**Fig 6:** Fibrosis reading measured by fibroScan of case 2

**Discussion**

Magnetic resonance imaging (MRI) with T2\*-weighted sequences is a viable tool for identifying iron deposition in the liver, exhibiting good correlation to the levels observed in specimens from biopsy, and may become a non-invasive standard technique in measuring tissue iron [2].

The present study found a significant relation between iron overload stages with Virus C, age at diagnosis, platelets count and ferritin level while blood transfusion interval, Hb and Hb F levels didn't show any significant relation with iron overload stages. In agreement Tziomalos and Perifanis, [3] found that, iron overload can result in the development of liver cirrhosis and hepatocellular carcinoma (HCC) in patients with thalassemia major. Also, in accordance with the current findings, Vichinsky, [4] and Cohen *et al.*, [5] exhibited that; Due to increased intestinal absorption of iron, overload can occur even in cases who do not require frequent transfusions.

In agreement with Chui *et al.*, [6] reported that, regular transfusions are infrequently required for iron overload to develop and can occur in transfusion naive cases. Another agreement with Atmakusuma and Lubis, [7] revealed that, Serum ferritin fluctuates and varies in conjunction with variations in body iron burden. The mean ferritin amount per year was 2831±1828 ng/mL. 60% of the individuals suffered a significant iron overload in ferritin levels >2000 ng/mL.

Also, Angelucci *et al.*, [8] found that, Serum ferritin levels are not a reliable indicator of total body iron stores,

especially in individuals with a high iron load. Also, Viprakasit *et al.*, [9] and Sengsuk *et al.*, [10] concluded that Iron load fluctuates dramatically with time, based on the strength of the transfusion, administration of iron chelator, and iron absorption, which is highly impacted by the degree of inefficient erythropoiesis and chronic anaemia

The current findings showed that, MRI T2\* and R2\* show significant relation with iron overload stages. In this line, more recent studies by Ooi *et al.*, [11] and Christoforidis *et al.*, [12] also have found only weak associations (r = 0.65–0.89) between SIR and LIC. Cases with thalassemia intermedia had less liver iron overload as measured by the T2\* relaxation time compared to those with TM [13]. In agreement with our findings, Tziomalos and Perifanis, [3], found liver R2 was strongly correlated with LIC measured in biopsy (r = 0.98, p<0.0001). However, R2 variability increased with increasing LIC. Also, Mohamed *et al.* [14] showed that, There was also a considerable shift in other MRI parameters (a large drop in T2\* and a marked increase in R2\*), which correlated with the marked increase in LIC. This finding is consistent with the findings of Alstiza *et al.* (28), who found that the bigger the liver iron overload, the greater the reduction in Signal Intensity (SI) on MR images, as shown by T2\*.

This study found highly significant relation between iron overload stages and fibrosis stage. In agreement with Elalfy *et al.*, [15] Hepatic iron overload is a serious issue for transfusion-dependent TM cases because of the frequent transfusion regimen that causes iron overload. Additionally,

Perifanis *et al.*,<sup>[16]</sup> and Ardalan *et al.*,<sup>[17]</sup> According to reports, the development and severity of hepatic fibrosis are highly associated to the degree of iron excess in the liver and the existence of chronic HCV infection. In addition, Marco *et al.* found that the advancement of hepatic fibrosis is closely correlated with iron excess and chronic HCV infection.

Further studies with large sample size are needed to evaluate the impact of liver iron overload detected by T2\* Magnetic Resonance Imaging (MRI) on Hepatic fibrosis detected by fibroscan. Monitoring of liver iron concentration should be done regularly, if possible, to achieve optimal iron chelation. We recommend T2\*MRI as noninvasive tool that have no complication and more accurate than serum ferritin needed to assess the hepatic iron overload.

### Conclusion

The risk of hepatic fibrosis is associated with iron overload in patients with TM. There was significant relation between iron overload stages and ferritin level. Blood transfusion interval and hemoglobin levels didn't show any significant relation with iron overload stages. MRI T2\* is the best noninvasive method for assessment and evaluation of hepatic iron overload and determine its severity in  $\beta$  thalassemia major patients. There was significant relation between iron overload stages with MRI T2\* and R2\*.

### Conflict of Interest

Not available

### Financial Support

Not available

### References:

1. Barrera CA, Otero HJ, Hartung HD, Biko DM, Serai SD. Protocol optimization for cardiac and liver iron content assessment using MRI: What sequence should I use? *Clin Imaging*. 2019;56:52-57.
2. Fischer R, Harmatz PR. Non-invasive assessment of tissue iron overload. *Hematology Am Soc Hematol Educ Program*. 2009;215-21.
3. Tziomalos K, Perifanis V. Liver iron content determination by magnetic resonance imaging. *World J Gastroenterol*. 2010;16(13):1587-1597.
4. Vichinsky E. Hemoglobin e syndromes. *Hematology Am Soc Hematol Educ Program*. 2007:79-83.
5. Cohen AR, Galanello R, Pennell DJ, Cunningham MJ, Vichinsky E. Thalassemia. *Hematology Am Soc Hematol Educ Program*. 2004:14-34.
6. Chui AK, Rao AR, Wong J, Mann D, Leung KF, Lau WY. *Ex situ ex vivo* liver resection, partial liver auto transplantation for advanced hilar cholangiocarcinoma: A case report. *Transplant Proc*. 2003;35:402-3.
7. Atmakusuma TD, Lubis AM. Correlation of Serum Ferritin and Liver Iron Concentration with Transient Liver Elastography in Adult Thalassemia Intermedia Patients with Blood Transfusion. *J Blood Med*. 2021;12:235-243.
8. Angelucci E, Barosi G, Camaschella C, Cappellini MD, Cazzola M, Galanello R, *et al.* Italian Society of Hematology practice guidelines for the management of iron overload in thalassemia major and related disorders. *Haematologica*. 2008;93(5):741-752.
9. Viprakasit V, Tyan P, Rodmai S, Taher AT.

Identification and key management of non-transfusion-dependent thalassaemia patients: not a rare but potentially under-recognised condition. *Orphanet Journal of Rare Diseases*. 2014;9:131.

10. Sengsuk C, Tangvarasittichai O, Chantanaskulwong P, Pimanprom A, Wantaneeayawong S, Choowet A, *et al.* Association of Iron Overload with Oxidative Stress, Hepatic Damage and Dyslipidemia in Transfusion-Dependent  $\beta$ -Thalassemia/HbE Patients. *Indian J Clin Biochem*. 2014;29:298-305.
11. Ooi GC, Khong PL, Chan GC, Chan KN, Chan KL, Lam W, *et al.* Magnetic resonance screening of iron status in transfusion-dependent beta-thalassaemia patients. *Br J Haematol*. 2004;124:385-390.
12. Christoforidis A, Perifanis V, Spanos G, Vlachaki E, Economou M, Tsatra I, *et al.* MRI assessment of liver iron content in thalassamic patients with three different protocols: comparisons and correlations. *Eur J Haematol*. 2009;82(5):388-392.
13. Mavrogeni S, Gotsis E, Ladis V, Berdousis E, Verganelakis D, Toulas P, *et al.* Magnetic resonance evaluation of liver and myocardial iron deposition in thalassemia intermedia and b-thalassemia major. *Int J Cardiovasc Imaging*. 2008;24:849-854.
14. Agaln AEA, Mohamed MA, Badraia EM, Darwish AE-MN, Badraia EM. MRI Evaluation of Hepatic Iron Overload in b-thalassemia Children. *The Medical Journal of Cairo University*. 2018;86:4537-4545.
15. Elalfy MS, Esmat G, Matter RM, Abdel Aziz HE, Massoud WA. Liver fibrosis in young Egyptian beta-thalassemia major patients: relation to hepatitis C virus and compliance with chelation. *Ann Hepatol*. 2013;12(1):54-61.
16. Perifanis V, Tziomalos K, Tsatra I, Karyda S, Patsiaoura K, Athanassiou-Metaxa M. Prevalence and severity of liver disease in patients with b thalassemia major. A single-institution fifteen-year experience. *Haematologica*. 2005;90(8):1136-1138.
17. Ardalan FA, Osquei MR, Toosi MN, Irvanloo G. Synergic effect of chronic hepatitis C infection and beta thalassemia major with marked hepatic iron overload on liver fibrosis: a retrospective cross-sectional study. *BMC Gastroenterol*. 2004;4:17.

### How to Cite This Article

Elrakaiby OM, Hamisa MF, El-Shanshory MR, Dawoud RM. The impact of liver iron overload determined by T2\* MRI on liver fibrosis determined by fibroscan in patients with thalassemia major. *International Journal of Radiology and Diagnostic Imaging*. 2023;6(1):115-124.

### Creative Commons (CC) License

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0) License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.