MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.12.577.582

Correlation of Serum Ferritin Levels with Hepatic T2 MRI for Iron Deposition in Children with Beta Thalassemia

[1]Mrudula Yenepalli, [2]B. Vijaya Lakshmi, [3]V. Spandana, [4]B. Padmini Priya and [5]A.S. Kireeti

[1]Department of Pediatrics, Government Medical College, Nandyal, India
[2]Department of Radiology, SVIMS, Tirupati, India
[3,4]Department of Pediatrics, Sri Venkateswara Medical College, Tirupati, India
[5]Multi-Disciplinary Research Unit, Sri Venkateswara Medical College, Tirupati, India

ABSTRACT

In Thalassemia, Serum markers of iron overload, serum ferritin and transferring saturation are used to predict iron concentration in the body but have many shortcomings. Liver T2* MRI has been developed to replace Liver biopsy in assessing Liver iron concentration (LIC). This study was conducted to correlate Serum ferritin levels with Iron deposition in the liver by T2-MRI. This was a Hospital based Cross-Sectional study conducted on 36 children aged 2-18 with Beta Thalassemia major for over one year. They were subjected to T2 MRI evaluation of the Liver and also blood samples for Serum ferritin and CBC. The mean age of study participants was 9.69 years. The Mean Serum Ferritin level was 1677.28 mcg/L and the mean of hepatic MRI T2* results in the liver was 3.37ms. Thirteen patients (36.1%) patients had a Liver iron content of >15mg Fe/dry Liver calculated by using R2*at 1.5 T. On average, females have higher MRI T2 relaxation time with a mean difference being 0.94 msec (95% CI: -1.5-3.4, F (1,34)=0.61, P value=0.44). In Our study, 52.2% of male participants, 53.8% of females, 60% of participants with Serum Ferritin >2500 mcg/L and 58.4% of participants with Serum Ferritin 1000-2500 mcg/L had severe iron deposition in the Liver by T2 MRI. Spearman's correlation coefficient (rho-0.341, p-value-0.042) showed a moderately positive relation between Serum Ferritin and Liver Iron content. Scatter plots showed a weak negative relationship between Serum ferritin and T2 relaxation time and a weak positive relationship between Serum ferritin and Liver Iron content. Liver T2*MRI as a tool to identify iron deposition in the liver is important to include serum Ferritin. Assessment of Serum Ferritin alone may result in delayed initiation of chelation therapy, which may prolong patient exposure to high iron levels and associated morbidity and mortality risks. Further studies are required with a bigger sample size to give a definite recommendation.

OPEN ACCESS

Key Words
Thalassemia, serum, iron overload, liver iron concentration (LIC)

Corresponding Author
B. Padmini Priya,
Department of Pediatrics, Sri Venkateswara Medical College, Tirupati, Andhra Pradesh, India-517507
banothbaby123@gmail.com

Author Designation
[1]Associate Professor
[2]Professor and HOD
[3]Assistant Professor
[4]Associate Professor
[5]Professor of Pediatrics and Nodal Officer

Received: 29 October 2024
Accepted: 19 December 2024
Published: 26 December 2024

Citation: Mrudula Yenepalli, B. Vijaya Lakshmi, V. Spandana, Padmini Priya Banoth and A.S. Kireeti, 2024. Correlation of Serum Ferritin Levels with Hepatic T2 MRI for Iron Deposition in Children with Beta Thalassemia. Res. J. Med. Sci., 18: 577-582, doi: 10.36478/makrjms.2024.12.577.582

INTRODUCTION

Hemoglobinopathies are the most common single-gene disorders in humans[1]. Beta Thalassemia is a group of inherited blood disorders characterized by a genetic deficiency in the synthesis of the ß-globin chain[2]. The main complication of the multiple blood transfusions to these patients is iron overload and the deposition of iron in various organs, such as the reticuloendothelial system, the liver, the heart and the endocrine glands[3]. In iron overload states, unbound iron accumulates in the hypothecates and leads to severe oxidative stress with the overproduction of toxic ROS, which leads to severe hepatic inflammation and fibrosis[4]. Serum markers of iron overload, serum ferritin and transferrin saturation are inexpensive techniques and widely used to predict iron concentration in the body and to monitor therapeutic response after starting iron chelation therapy However, these techniques cannot be used solely to monitor iron levels in the body. Ferritin as an acute phase reactant will increase sharply in the presence of inflammation. Patients who have frequent transfusions will have fully saturated transferrin[5,6]. Liver biopsy was considered the gold standard for detecting iron overload. However, it is associated with several side effects and disadvantages such as pain, bleeding, infection, extensive sampling variability and inter-observer variability and is not suitable for related long-term follow-up. Therefore, a non-invasive examination T2* MRI has been developed to replace Liver biopsy in assessing Liver iron concentration (LIC). T2* MRI can measure the concentrations of iron in the liver and the heart and is particularly beneficial in tailoring the appropriate chelation treatment for each patient T2* MRI examination of the liver is now a validated examination in assessing LIC[7-11]. In 2012, the Thalassemia Clinical Research Network issued a recommendation stating that T2* imaging of the liver and heart should be performed at least annually, beginning at the age of 10 years old. The imaging may be performed more frequently in patients with dangerous levels of cardiac iron as demonstrated by T2* values <10 or excess levels between 10 and 20 ms[12]. Another study in China suggested that MRI evaluation of iron be performed from about 6 years of age[13] and a USA study recommends that it should be conducted even earlier[14].

Aims and Objectives: To correlate Serum ferritin levels with Iron deposition in the liver by T2* MRI in transfusion-dependent Beta Thalassemia major patients.

MATERIALS AND METHODS

A Hospital-based Cross-Sectional Study was conducted on children of age group 2-18 years already diagnosed with Transfusion dependent Thalassemia (TDT) admitted in the Department of Pediatrics, Sri Venkateswara Ramanarain Ruia Government General Hospital, a Tertiary care hospital attached to Sri Venkateswara Medical college over one year after getting clearance from Ethical Clearance Committee. Before collection of data, all subjects were briefed about the purpose of the study and written informed consent was obtained. All the tests and procedures were done free of cost and no financial burden was imposed on the patient. All thalassemia children who were younger than 2 years or who had <12 transfusions to date, were positive with HIV, Hepatitis B, Hepatitis C, Chronic inflammatory disease and associated malignancy were excluded from the study before selecting the Study subjects. Based on the previous study of Eghbali[15] the mean of hepatic T2-MRI was 26.46±9.19ms. The sample size was Calculated.

Sample Size Calculation is,

$$n = \frac{Z^2O^2}{d^2}$$

where,

z=1.96

o=9.19

d=3

$$n=\frac{(1.96)^2\,(9.19)^2}{3^2} = \frac{324.31}{9} = 36$$

All the study subjects satisfying inclusion criteria were enrolled in the study. After a detailed history and physical examination, the study subjects were subjected to T2 MRI evaluation of the Liver and also blood samples for Serum ferritin level along with investigations Complete Blood picture, C-Reactive Protein and Liver enzyme levels were collected. Serum Ferritin level was measured by ELISA. T2 MRI-Phillips Ingenia, 1.5 tesla performed MRI. A dedicated Iron quantification T2 weighted multi-echo sequence using a phased array surface coil. Each scan will be for about 20 minutes and includes the measurement of liver T2* relaxation. Fasting and sedation were not needed before the exam. The MRI instrument's cut-off points are as follows[16]: Liver: normal >16ms, mild: 4-8 ms, moderate: 4-2ms, severe <2 ms. Liver Iron content measured on 1.5 T, LIC (mg Fe/g dry liver)=0.026* R2*+ 0.07.

Statistical Analysis: Data was analyzed by descriptive statistics. The results were reported as number (percentage) for categorical variables, mean±standard deviation (SD) for normally distributed variables and median (inter quartile range (IQR)) for non-normally distributed variables. Spearman's tests were used to assess the correlation of liver T2* MRI with serum ferritin level. Categorical data were compared using the chi-square and Fisher exact test.

Ethical Considerations:

- Before the collection of data all the parents were briefed about the procedure and purpose of the study and then written informed consent was obtained from the parent of the subject.
- All investigations related to the study were done free of cost and no financial burden was imposed on parents of the subject.
- Confidentiality of individual information was maintained.
- No conflict of interest.

RESULTS AND DISCUSSIONS

We studied 36 patients with ß-thalassemia major who were transfusion-dependent. In the present study, it was found that 52.8% of study participants belonged to the age group of 11-18 years followed by the age group of 6-10 years (255) and the age group of 2-5 years (22.2%). The mean age of study participants was 9.69 years. Twenty-three (36.2%)were males. Only four (11.2%) patients had a history of parental consanguinity. Most patients around 50% already had transfusions between 100-200. In the present study, Serum Ferritin levels were in between 1000-2500 accounting for 66.6% of total study participants. The Mean Serum Ferritin level was 1677.28mcg/L The mean of hepatic MRI T2* results of iron overload in the liver was 3.37ms. Thirteen patients(36.1%) patients Had Liver iron content of >15 mg Fe/dry Liver calculated by using R2*at 1.5 T. The distribution of various variables among the study participants is shown in (Table 1).

Table 1: Distribution of Various Variables in the Study Participants Characteristics of Study Participants

Variable	Values
Age, Mean (years)	9.69
2-5 years n (%)	8 (22.2)
6-10 years n (%)	9 (25)
11-18 years n (%)	19(52.8)
Gender	
Male n (%)	23(63.8)
Female n (%)	13(36.2)
Parental Consanguinity	
Non Consanguineous n (%)	32 (88.8)
Consanguineous n (%)	4(11.2)
No of Transfusions	
<50 n (%)	9 (25)
50-100 n (%)	5(13.8)
100-150 n (%)	9 (25)
150-200 n (%)	9 (25)
>200 n (%)	4 (11.2)
S Ferritin (mcg/L) Mean	1511
Mild =<1000 n(%)	7 (19.4)
Moderate 1000-2500,n(%)	24(66.6)
Severe > 2500n(%)	5 (13.8)
T2 * at 1.5 T (ms) Mean	3.37
>16 n (%)	1 (2.8)
8-16 n (%)	4 (11.2)
4-8 (Mild) n (%)	2 (5.5)
2-4 (Moderate) n (%))	10 (27.8)
<2 (Severe) n (%)	19(52.8)
R2* at 1.5T (sec-1)	
<60 n(%)	1 (2.8)
60-120, n(%)	3(8.3)
120-270 (Mild)n (%)	4 (11.1)
270-580 (Moderate) n (%)	15 (41.7)
>580 (Severe) n (%)	13 (36.1)
Liver Iron Content (mg Fe/g dry liver) n (%)	
<1.8	1 (2.8)
1.8-3.2	3(8.3)
3.2-7 (mild Overload)	4 (11.1)
7-15(Moderate Overload)	15 (41.7)
>=15 (Severe Overload)	13 (36.1)

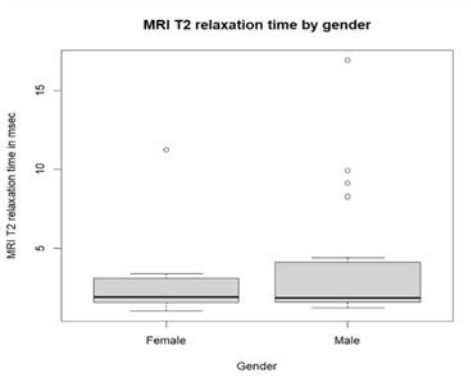

Fig. 1: Association of Hepatic MRI T2* Times and Gender in Beta Thalassemia Patients

There was no evidence of a statistical difference in MRI T2 relaxation time between the two genders. On average, females have higher MRI T2 relaxation time with a mean difference being 0.94 msec (95% CI: -1.5 -3.4, F (1,34) =0.61, P value =0.44). After adjusting for gender, there was no evidence of a difference in between number of transfusions and MRI T2 relaxation time as shown in (Fig. 1). For every 100 transfusions MRI T2 relaxation time would decrease by 1 milli second (95% CI: 0-2, LR Chi-Square =2.75, P value - 0.1) as shown in (Fig. 2)

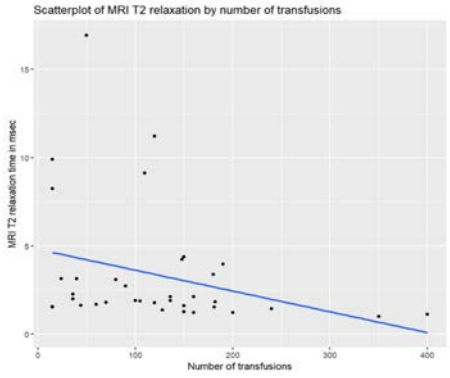

Fig. 2: Scatter Plot of Hepatic MRI T2* Times and Number of Blood Transfusions in Beta Thalassemia Patients

Table 2: Comparison of Sex, Number of Transfusions and Serum Ferritin Levels Among Four Groups of Patients with ß-thalassemia with Different Levels of Iron Deposition According to Hepatic T2* MRI

Variable	Normal	Mild	Moderate	Severe
T2 Median (ms)	>8	4-8	2-4	<2
Gender n(%)				
Male	3 (13)	3 (13)	5 (21.7)	12 (52.2)
Female	0	1 (7.7)	5 (38.5)	7(53.8)
Number of Transfusions n (%)				
<50	3 (30)	0	4(40)	3(30)
50-100	0	0	2(50)	2(50)
100-150	2(20)	2(20)	1(10)	5(50)
150-200	0	0	3(33.3)	6(66.7)
>200	0	0	0	3(100)
Ferritin mcg/L				
Mild (<1000) n (%)	2(28.6)	0	3(42.8)	2(28.6)
Moderate (1000-2500) n (%)	2(8.3)	2(8.3)	6(25)	14(58.4)
Severe (>2500) n(%)	1 (20)	0	1(20)	3(60)

Based on the results of liver T2*, patients were categorized into four groups: normal, mild, moderate

and severe iron load. The hepatic T2* times showed significantly different values among four groups of patients. In Our study, 52.2% of male participants and 53.8% of females had severe iron deposition in the liver. It was observed in the present study that all three cases with >200 blood transfusions had severe iron deposition in the Liver. In our study, 60% of participants with Serum Ferritin >2500 mcg/L and 58.4% of participants with Serum Ferritin 1000-2500 mcg/L had severe iron deposition in the Liver as shown in (Table 2).

Correlation Matrix

		S Ferritin	Liver Iron content
S Ferritin	Spearman's rho	—	
	df	—	
	p-value	—	
Liver Iron content	Spearman's rho	0.341	—
	df	34	—
	p-value	0.042	—

Fig. 3: Correlation Between Hepatic MRI T2* Times and Serum Ferritin Levels in Beta Thalassemia Patients (r=0.341, p-0.042)

As there are few extreme values (outliers) in the distribution of S. Ferritin, Spearman's correlation coefficient is used. Spearman's rho is 0.341 with a p-value of 0.042 which implies the relation is moderately positive (Fig. 3).

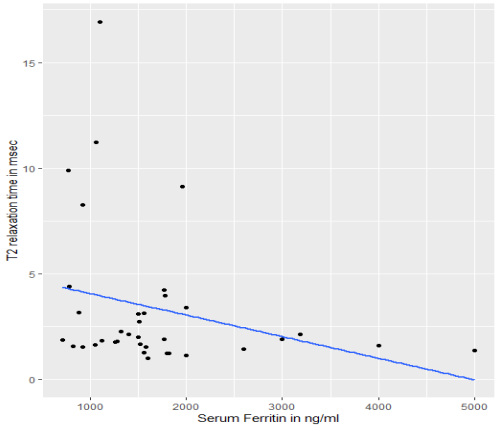

Fig. 4: Scatter Plot of Hepatic MRI T2* Times and Serum Ferritin Levels in Beta Thalassemia Patients

(Fig. 4) indicates a weak negative relationship on a scatter plot, with Serum ferritin on the X-axis and T2 relaxation time on the Y-axis.

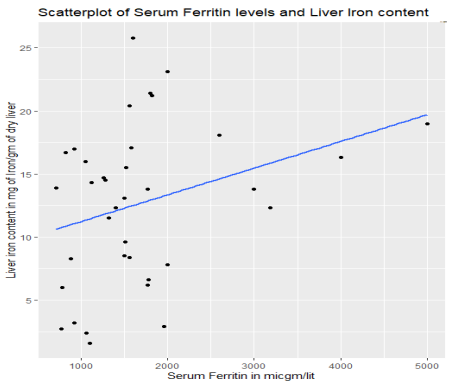

Fig. 5: Correlation Between Serum Ferritin Levels and Liver Iron Content in Beta Thalassemia Patients

(Fig. 5) indicates a weak positive relationship on a scatter plot, with Serum ferritin on the X-axis and Liver Iron content on the Y-axis.

Beta-thalassemia major is a hereditary genetic disorder of hemoglobin that leads to hemolysis., an effect makes these patients need repeated blood transfusions that lead to iron overloading including the liver, heart, spleen, bone marrow, pancreas and endocrine system[9,17,18]. The magnetic resonance signal of the hepatic tissue depends on the T1 and T2 relaxation times (TR) of its iron content. T2* is inversely related to intracellular iron. Increased tissue iron displays a moderate decrease in T1 signals and an extreme decrease in T2 signal intensities[19-21]. Owing to the late development of the clinical findings and echocardiographic abnormalities, MR-T2* has become the strongest biomarker for the simultaneous evaluation of liver and heart iron burden[22]. Measuring serum ferritin levels remains the primary screening test and is still used to monitor the efficacy of chelation therapy. A serum ferritin level greater than 2500ng/ml is considered an important risk factor for developing iron-induced complications such as liver cirrhosis, heart failure, arrhythmia, impaired growth and delayed puberty[23-26]. Our study observed that 60% of participants with Serum Ferritin >2500 mcg/L and 58.4% OF participants with Serum Ferritin 1000-2500 mcg/L had severe iron deposition in the Liver. In this study, the level of Serum ferritin ranged from 700-5000mcg/L. Our study shows the Spearman rank correlation coefficient between Serum ferritin and T2 relaxation time is -0.34, correlating negatively. Spearman's correlation coefficient is 0.341 with a p-value of 0.042 which implies the relation is moderately positive between Serum Ferritin and liver iron content. Also, Eghbali[15] studied the association between liver and heart T2* and levels of serum ferritin in TM patients and they reported a correlation between serum ferritin level and liver T2*MRI.

However, Puliyel[6] reported that ferritin cannot predict total body iron changes with little relevance between cardiac and hepatic iron content and levels of serum ferritin. Wood[27] reported that MR-R2* mapping could accurately estimate LIC in transfusion-dependent TM patients. Previous studies found that the frequency of MR-T2* relies on the iron concentration and chelation therapy used[28-30]. In this study, a moderate positive statistical significance was found regarding the association between Serum Ferritin and liver T2* (Fig 3, Fig 4). Zamani`s study revealed no reasonable correlation between the histological grade of siderosis (HGS) and serum ferritin. A moderate correlation was seen between serum ferritin levels and hepatic T2* levels. Iron concentration in the liver showed a significant correlation with hepatic T2*. These results indicated that T2* MRI measurement is of more value than HGS in patients with thalassemia[31].

Limitations of the Study:

- Further studies are required with a bigger sample size to give a definite recommendation.
- Serum Ferritin was assessed using a single measurement taken on the same day as the MRI examination., an average value of ferritin levels over the last 3-6 months might have more accurately reflected the true body iron status.

CONCLUSION

In our study, we observed that Serum Ferritin alone as a marker for Iron overload may not be adequate to assess the Iron overload in organ states-Liver Iron deposition and subsequently to guide Iron chelator therapy dosage adjustment. Therefore Liver T2*MRI as a tool to identify iron deposition in the liver is important to be included clinically. Assessment of Serum Ferritin alone may result in delayed initiation of chelation therapy, which may prolong patient exposure to high iron levels and associated morbidity and mortality risks.

Conflict of Interest: Nil.

Funding of Project: Multi-Disciplinary Research Unit, Sri Venkateswara Medical College, Tirupati.

ACKNOWLEDGMENTS

The authors are thankful and acknowledge to Department of Health Research (DHR) and the GOVT of India for providing MRU facility in our institution and CCT grant to MRU for projects. We are also thankful to MRU for aiding us financially for our research project. Data collection has been helped by junior doctors of SVMC, statistics helped by Dr Amrit Jeevan.

REFERENCES

1. Williams, T.N. and D.J. Weatherall, 2012. World Distribution, Population Genetics and Health Burden of the Hemoglobinopathies. Cold Spring Harbor Perspect. Med., Vol. 2 .10.1101/ cshperspect.a011692.
2. Taher, A.T., K.M. Musallam and M.D. Cappellini, 2021. ß-Thalassemias. New Engl. J. Med., 384: 727-743.
3. Gabutti, V., A. Piga, L. Sacchetti, A. Sandri, M. Biginelli, P. Saracco and M. Ferri., 1989. Quality of life and life expectancy in thalassemic patients with complications. Prog Clin Biol Res., 309: 35-41.
4. Sikorska, K., A. Bernat and A. Wróblewska, 2016. Molecular pathogenesis and clinical consequences of iron overload in liver cirrhosis. Hepatobiliary and Pancreatic Dis. Int., 15: 461-479.
5. Wang, W., M.A. Knovich, L.G. Coffman, F.M. Torti and S.V. Torti, 2010. Serum ferritin: Past, present and future. Biochim. Biophys. Acta (BBA) Gen. Subjects, 1800: 760-769.
6. Puliyel, M., R. Sposto, V.A. Berdoukas, T.C. Hofstra and A. Nord et al., 2014. Ferritin trends do not predict changes in total body iron in patients with transfusional iron overload. Am. J. Hematol., 89: 391-394.
7. Taher, A.T., V. Viprakasit, K.M. Musallam and M.D. Cappellini, 2013. Treating iron overload in patients with non-transfusion-dependent thalassemia. Am. J. Hematol., 88: 409-415.
8. Taher, A.T., K.M. Musallam, J.C. Wood and M.D. Cappellini, 2010. Magnetic resonance evaluation of hepatic and myocardial iron deposition in transfusion-independent thalassemia intermedia compared to regularly transfused thalassemia major patients. Am. J. Hematol., 85: 288-490.
9. Brittenham, G.M., 2011. Iron-Chelating Therapy for Transfusional Iron Overload. New Engl. J. Med., 364: 146-156.
10. Argyropoulou, M.I., D.N. Kiortsis, L. Astrakas, Z. Metafratzi, N. Chalissos and S.C. Efremidis, 2007. Liver, bone marrow, pancreas and pituitary gland iron overload in young and adult thalassemic patients: A T2 relaxometry study. Eur. Radiol., 17: 3025-3030.
11. Chirico, V., L. Rigoli, A. Lacquaniti, V. Salpietro and B. Piraino et al., 2014. Endocrinopathies, metabolic disorders, and iron overload in major and intermedia thalassemia: Serum ferritin as diagnostic and predictive marker associated with liver and cardiac T2* MRI assessment. Eur. J. Haematology, 1-9.
12. Yang, G., R. Liu, P. Peng, L. Long and X. Zhang et al., 2014. How Early Can Myocardial Iron Overload Occur in Beta Thalassemia Major? PLoS ONE, Vol. 9 .10.1371/journal.pone.0085379.

13. Berdoukas, V., A. Nord, S. Carson, M. Puliyel, T. Hofstra, J. Wood and T.D. Coates, 2013. Tissue iron evaluation in chronically transfused children shows significant levels of iron loading at a very young age. Am. J. Hematol., 88: 283-285.
14. Eghbali, A., H. Taherahmadi and M. Shahbazi, et al., 2014. Association between serum ferritin level, cardiac and hepatic T2-star MRI in patients with major ß-thalassemia. Iran J Ped Hematol Oncol., 17-21.
15. Labranche, R., G. Gilbert, M. Cerny, K.N. Vu and D. Soulières et al., 2018. Liver Iron Quantification with MR Imaging: A Primer for Radiologists. RadioGraphics, 38: 392-412.
16. Garbowski, M.W., J.P. Carpenter, G. Smith, M. Roughton and M.H. Alam et al., 2014. Biopsy-based calibration of T2* magnetic resonance for estimation of liver iron concentration and comparison with R2 Ferriscan. J. Cardiovasc. Magn. Reson., Vol. 16 .10.1186/ 1532-429x-16-40.
17. Wood, J.C., J.M. Tyszka, S. Carson, M.D. Nelson and T.D. Coates, 2004. Myocardial iron loading in transfusion-dependent thalassemia and sickle cell disease. Blood, 103: 1934-1936.
18. He, T., 2014. .Cardiovascular magnetic resonance T2* for tissue iron assessment in the heart Quant. Imaging Med. Surg., 4: 407-412.
19. Auger, D. and D.J. Pennell, 2016. Cardiac complications in thalassemia major. Ann. New York Acad. Sci., 1368: 56-64.
20. Anderson, L., S. Holden, B. Davis, E. Prescott, C.C. Charrier, N.H. Bunce, D.N. Firmin, B. Wonke, J. Porter, J.M. Walker and D.J. Pennell., 2001. Cardiovascular T2-star (T2*) magnetic resonance for the early diagnosis of myocardial iron overload. Eur. Heart J., 22: 2171-2179.
21. Wood, J.C., 2007. Magnetic resonance imaging measurement of iron overload. Curr. Opin. Hematol., 14: 183-190.
22. Carpenter, J.P., T. He, P. Kirk, M. Roughton and L.J. Anderson et al., 2014. Calibration of myocardial T2 and T1 against iron concentration. J. Cardiovasc. Magn. Reson., Vol. 16 .10.1186/s12968-014-0062-4.
23. Angulo, I.L., D.T. Covas, A.A. Carneiro, O. Baffa, J.E. Junior and G. Vilela, 2008. Determination of iron-overload in thalassemia by hepatic MRI and ferritin. Rev. Bras. Hematologia e Hemoterapia, 30: 449-452.
24. Telfer, P.T., E. Prestcott, S. Holden, M. Walker, A.V. Hoffbrand and B. Wonke, 2000. Hepatic iron concentration combined with long-term monitoring of serum ferritin to predict complications of iron overload in thalassaemia major. Br. J. Haematology, 110: 971-977.
25. Moussavi, F., M.A. Ghasabeh, S. Roodpeyma, S. Alavi, M. Shakiba, R. Gheiratmand and M. Omidghaemi, 2014. Optimal method for early detection of cardiac disorders in thalassemia major patients: Magnetic resonance imaging or echocardiography? Blood Res., 49: 182-186.
26. Wood, J.C., C. Enriquez, N. Ghugre, J.M. Tyzka, S. Carson, M.D. Nelson and T.D. Coates, 2005. MRI R2 and R2* mapping accurately estimates hepatic iron concentration in transfusion-dependent thalassemia and sickle cell disease patients. Blood, 106: 1460-1465.
27. Nienhuis, A.W., P. Griffith, H. Strawczynski, W. Henry, J. Borer, M. Leon and W.F. Anderson, 1980. Evaluation of cardiac function in patients with thalassemia major. Ann. New York Acad. Sci., 344: 384-396.
28. Anderson, L.J., 2011. Assessment of Iron Overload with T2* Magnetic Resonance Imaging. Prog. Cardiovasc. Dis., 54: 287-294.
29. PENNELL, D.J., 2005. T2* Magnetic Resonance and Myocardial Iron in Thalassemia. Ann. New York Acad. Sci., 1054: 373-378.
30. Zamani, F., et al., 2011. T2* magnetic resonance imaging of the liver in thalassemic patients in Iran. World J. Gastroenterol., Vol. 17 .10.3748/wjg. v17.i4.522.