Original Article

# Significance of 2D Echocardiography in Thalassemia Major/Intermedia Patients at a Tertiary Care Centre: A Cross-Sectional Observational Study

**Dakavaram Hema Manvi[1], Manasa R[2], Padmajarani V[3], Manohar Badur[4], Rajashaker Venkatappa[5]**

[1]PG, Department of Paediatrics, S.V. Medical College, Tirupati, India, [2]Assistant Professor, Department of Paediatrics, SV Medical College, Tirupati, India

[3]Assistant Professor, Department of Paediatrics, SV Medical College, Tirupati, India, [4]Professor, Department of Paediatrics, S.V. Medical College Tirupati, India, [5]Assistant Professor of Paediatrics, SV medical College, Tirupati, India.

## Abstract

**Background:** Beta-thalassemia major is the commonest transfusion-dependent hemoglobinopathy in South Asia. Cardiac iron overload is the leading cause of mortality, yet early non-invasive cardiac surveillance remains inconsistently practiced in resource-limited settings. The objective is to evaluate the role of 2D echocardiography in detecting cardiovascular complications in pediatric thalassemia patients and correlate findings with serum ferritin. **Material and Methods:** Hospital-based cross-sectional observational study of 57 transfusion-dependent beta-thalassemia patients aged 1–18 years at SVRRGGH Tirupati (June 2023–October 2024). All underwent 12-lead ECG, 2D echocardiography (48 hours post-transfusion), and pre-transfusion serum ferritin estimation. **Results:** 56% male; 98.2% thalassemia major. Echocardiographic abnormalities in 33% of patients; PAH in 5.26%, dilated LA/LV in 7.01%, tricuspid regurgitation in 22.8%. Mean EF 62.91%. Ferritin ≥1000 ng/mL in 89.47%. ECG abnormal in 22.8%. Echocardiography: sensitivity 72.22%, specificity 100%, diagnostic accuracy 91.23% vs ECG. **Conclusion:** 2D echocardiography is a sensitive, specific, accessible tool for early cardiac surveillance in thalassemia. Routine echocardiographic screening should be integrated into standard management protocols. **Keywords:** Thalassemia major; 2D echocardiography; iron overload; pulmonary hypertension; serum ferritin; pediatric cardiology.

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## Introduction

Beta-thalassemia major is an autosomal recessive disorder characterized by absent or severely reduced beta-globin chain synthesis, resulting in transfusion-dependent hemolytic anemia. It represents a significant public health burden in South and Southeast Asia, the Mediterranean, and the Middle East, with an estimated 100,000 children born with the condition annually worldwide.[1]

India contributes approximately 10,000–15,000 new cases of thalassemia major per year.[2] The hallmarks of the disease are chronic anemia, ineffective erythropoiesis, and transfusional iron overload, which collectively drive its major complications. Among these, cardiovascular disease is the leading cause of death, accounting for over 50% of mortality in affected individuals.[3]

Iron overload cardiomyopathy arises from two mechanisms: chronic anemia-driven high-output cardiac state, and direct myocardial iron deposition through L-type calcium channels once transferrin saturation is exceeded. This leads to dilated or restrictive cardiomyopathy, arrhythmias, and pulmonary arterial hypertension (PAH).[4] Pulmonary hypertension in thalassemia is multifactorial, involving hemolysis-induced nitric oxide scavenging, vascular remodeling from iron-mediated oxidative stress, and porto-pulmonary hypertension secondary to hepatic cirrhosis.[5]

Cardiac T2* MRI is the gold standard for quantifying myocardial iron deposition, but is costly, time-consuming, and unavailable in most Indian tertiary centers.[6] In contrast, 2D echocardiography provides real-time assessment of ventricular dimensions, systolic and diastolic function, and pulmonary artery pressures non-invasively and affordably. Despite this, routine echocardiographic screening in the first decade of life remains underutilized in Indian practice.

This study was conducted to establish the role of 2D echocardiography in early detection of cardiovascular complications in pediatric thalassemia patients, and to evaluate its correlation with serum ferritin as an indirect marker of iron burden.

## Materials and Methods

**Study Design and Setting:** A hospital-based cross-sectional observational study was conducted in the Department of Pediatrics, S.V.R.R. Government General Hospital and Sri Venkateswara Medical College, Tirupati, Andhra Pradesh, from June 2023 to October 2024. Institutional Ethics Committee approval was obtained (Ref No: 143/2023) and written informed

**Address for correspondence:** Dr. Rajashaker Venkatappa, Assistant Professor, Department of Paediatrics, SV Medical College, Tirupati, India. E-mail: vrajesh2001@gmail.com

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parental consent was secured for all participants.

**Participants:** Patients aged 1–18 years with confirmed thalassemia major or intermedia (by hemoglobin electrophoresis) on regular transfusion therapy were enrolled. Exclusion criteria included known congenital heart disease, critically ill patients, and refusal of consent.

**Sample Size:** Sample size was calculated based on a reported cardiac complication prevalence of 24%, 95% confidence interval, and 20% relative precision, yielding an adjusted finite population sample of 57 patients (population N=701).

**Clinical and Laboratory Assessment:** Clinical history, anthropometric measurements, and complete blood count were recorded. Pre-transfusion serum ferritin was measured; levels ≥1000 ng/mL were classified as elevated. Serum ferritin was measured by electro chemiluminescent immunoassay (ECLIA).

**Electrocardiography:** Standard 12-lead ECG was performed in all patients. QTc interval was calculated using Bazett's formula. Findings were assessed for rhythm abnormalities, QTc prolongation, RVH, and LVH.

**Echocardiography:** 2D M-mode and Doppler echocardiography was performed 48 hours post-transfusion per American Society of Echocardiography guidelines. LVIDd, LVIDs, IVS thickness, posterior wall thickness, EF, %FS, LV mass index, E/A ratio, and pulmonary artery systolic pressure (PASP) were measured. PAH was defined as PASP >25 mmHg by modified Bernoulli equation from TR jet velocity.

**Statistical Analysis:** Data were analyzed using SPSS v25.0. Categorical variables are reported as frequencies and percentages. Fisher's exact test and chi-square tests were used for association analyses. Sensitivity, specificity, PPV, NPV, and diagnostic accuracy of echocardiography relative to ECG as reference were calculated. A p-value <0.05 was considered statistically significant.

## Results

**Demographic and Clinical Profile:** Fifty-seven patients were enrolled. Males constituted 56% (n=32) and females 44% (n=25). The majority were from rural areas (85%; n=48) and had consanguineous parentage (44%; n=25). Thalassemia major was confirmed in 98.2% (n=56). Mean age at diagnosis was 1 year 5 months; 53% were diagnosed by 6 months of age. Demographic and clinical characteristics are summarized in [Table 1 and Figure 1].

**Table 1: Demographic and clinical characteristics of study participants (N=57)**

| Parameter | Category | n | % |
|---|---|---|---|
| Gender | Male | 32 | 56.1% |
| | Female | 25 | 43.9% |
| Age Group | 1–6 years | 14 | 24.6% |
| | 7–12 years | 24 | 42.1% |
| | 12–18 years | 19 | 33.3% |
| Residence | Rural | 48 | 84.2% |
| | Urban | 9 | 15.8% |
| Consanguinity | Yes | 25 | 43.9% |
| | No | 32 | 56.1% |
| Thalassemia Type | Major | 56 | 98.2% |
| | Intermedia | 1 | 1.8% |
| Transfusion Frequency | Monthly | 45 | 78.9% |
| | Every 20 days | 6 | 10.5% |
| | Bimonthly | 5 | 8.8% |
| | Every >2 months | 1 | 1.8% |
| Chelation Therapy | Deferasirox | 40 | 70.2% |
| | Deferiprone | 7 | 12.3% |
| | DFO+DFP (combined) | 5 | 8.8% |
| | None | 5 | 8.8% |
| Nutritional Status | Height <–3 SD | 19 | 33.3% |
| | Weight <3rd centile | 17 | 29.8% |
| | Normal anthropometry | 21 | 36.9% |

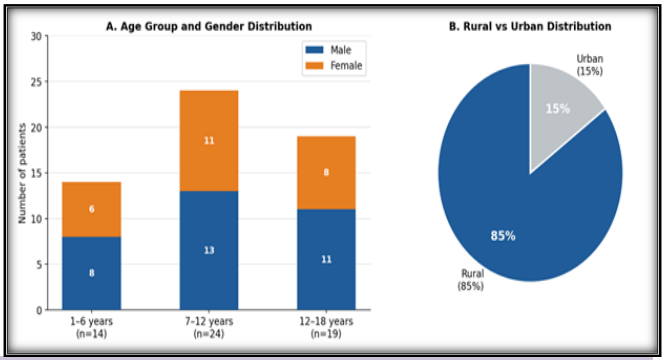


**Figure 1. A: Stacked bar chart showing age-group and gender distribution. B: Rural vs urban distribution of enrolled patients.**

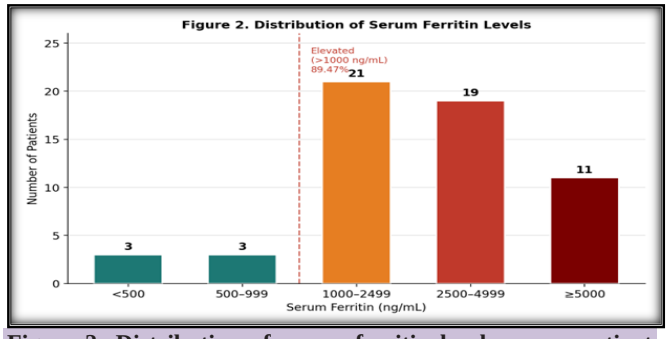


**Figure 2: Distribution of serum ferritin levels across patient cohort. The dashed red line marks the 1000 ng/mL threshold; 89.47% of patients exceeded this level.**

**Serum Ferritin Distribution:** Serum ferritin was elevated (≥1000 ng/mL) in 89.47% (n=51) of patients. The distribution of ferritin levels across groups is shown in Figure 2. Despite ongoing chelation therapy in 91.2% of patients, most patients had persistently high ferritin, reflecting inadequate chelation efficacy or compliance.

**Electrocardiographic Findings:** ECG was normal in 77.2% (n=44) and abnormal in 22.8% (n=13). Tachycardia was identified in 54.4% of patients at presentation. Among abnormal ECGs: RVH was found in 7.0% (n=4), LVH in 3.5% (n=2), prolonged QTc in 5.3% (n=3), and non-specific ST-T changes in 7.0% (n=4). No statistically significant association was found between ferritin levels and ECG abnormalities [Table 3 and Figure 3].

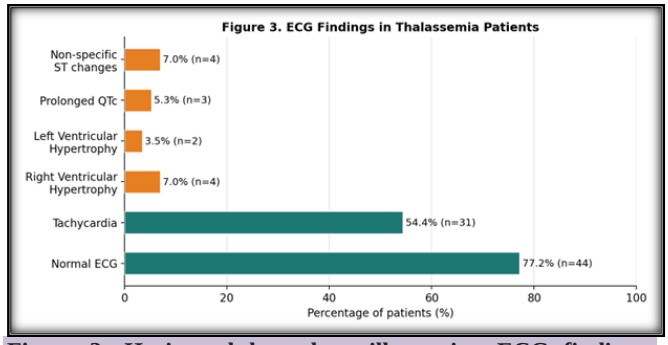


**Figure 3: Horizontal bar chart illustrating ECG findings. Tachycardia and normal ECG predominated; structural ECG changes were present in 22.8% of patients.**

**Table 2: Electrocardiographic findings in the study cohort**

| ECG Finding | n | % Total (N=57) | % Abnormal (n=13) |
|---|---|---|---|
| Normal ECG | 44 | 77.2% | – |
| Tachycardia | 31 | 54.4% | – |
| Right Ventricular Hypertrophy (RVH) | 4 | 7.0% | 30.8% |
| Left Ventricular Hypertrophy (LVH) | 2 | 3.5% | 15.4% |
| Prolonged QTc interval | 3 | 5.3% | 23.1% |
| Non-specific ST-T changes | 4 | 7.0% | 30.8% |
| Total with ≥1 abnormality | 13 | 22.8% | 100% |

**Echocardiographic Findings:** Overall, 33% (n=19) of patients had echocardiographic abnormalities. The mean, ejection fraction was 62.91% (SD ±4.10, range 55–76%) and mean fractional shortening was 31.45%. Systolic function was preserved in all patients. The spectrum of echocardiographic abnormalities is summarized in [Table 3 and Figure 4]. Detailed quantitative echo parameters are presented in [Table 4].

**Table 3: Echocardiographic findings in the study cohort (N=57)**

| Echocardiographic Finding | n | % Total (N=57) | % Abnormal (n=19) |
|---|---|---|---|
| Normal echocardiogram | 38 | 66.7% | – |
| Tricuspid Regurgitation – Mild | 4 | 7.0% | 21.1% |
| Tricuspid Regurgitation – Trivial | 3 | 5.3% | 15.8% |
| Dilated Left Atrium & Left Ventricle | 4 | 7.0% | 21.1% |
| Pulmonary Arterial Hypertension – Mild | 2 | 3.5% | 10.5% |
| Mitral Regurgitation – Mild | 2 | 3.5% | 10.5% |
| Pulmonary Regurgitation – Trivial | 2 | 3.5% | 10.5% |
| Diastolic Dysfunction with LVH | 1 | 1.8% | 5.3% |
| Dilated Right Atrium & Right Ventricle | 1 | 1.8% | 5.3% |
| Patent Foramen Ovale (Small) | 1 | 1.8% | 5.3% |
| Aortic Regurgitation – Trivial | 1 | 1.8% | 5.3% |
| Total Abnormal | 19 | 33.3% | 100% |

**Table 4: Quantitative echocardiographic parameters (Mean ± SD)**

| Parameter | Mean ± SD | Reference | Abnormal Cutoff |
|---|---|---|---|
| Ejection Fraction (%) | 62.91 ± 4.10 | 55–76 | <55 |
| Fractional Shortening (%) | 31.45 ± 3.50 | 25–43 | <25 |
| LVIDd (mm) | 40.12 ± 5.20 | Indexed to BSA | – |
| LVIDs (mm) | 26.80 ± 4.10 | Indexed to BSA | – |
| IVSd (mm) | 7.40 ± 1.20 | Age-specific | – |
| PWd (mm) | 7.20 ± 1.10 | Age-specific | – |
| LV Mass Index (g/m²) | 88.3 ± 18.5 | <115 | ≥115 |
| PASP (mmHg) | 21.4 ± 5.8 | <25 | ≥25 |
| E/A Ratio | 1.42 ± 0.30 | >1.0 | <1.0 |

**Pulmonary Arterial Hypertension:** Mild PAH (PASP 25–40 mmHg) was identified in 5.26% (n=3) of patients; all had serum ferritin ≥1000 ng/mL. Two of three PAH cases were diagnosed with thalassemia before 12 months of age. No statistically significant association was found between PAH and age at diagnosis ($\chi^2$=4.997, p=0.082), gender (p=0.594), consanguinity (p=0.454), or ferritin level (p=0.411).

**Chelation Therapy and Transfusion Compliance:** Deferasirox was the most common chelation regimen (70.2%). Monthly transfusions were received by 78.9% of patients. The distribution of chelation and transfusion compliance is shown in [Figure 5].

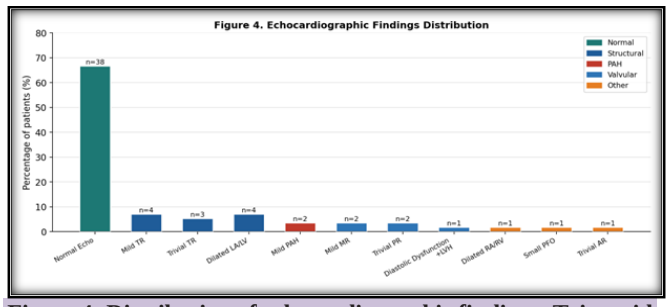


**Figure 4: Distribution of echocardiographic findings. Tricuspid regurgitation (mild+trivial combined, 12.3%) and dilated LA/LV (7.0%) were the most common structural abnormalities. PAH was identified in 5.26%.**

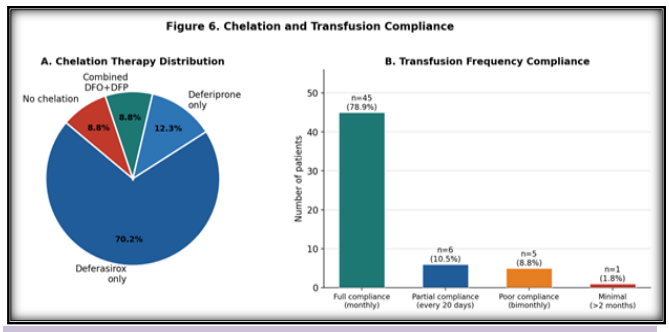


**Figure 5. A: Chelation therapy distribution. Deferasirox constituted the majority of regimens. B: Transfusion frequency compliance among enrolled patients.**

**Table 5: Correlation of serum ferritin (≥1000 vs <1000 ng/mL) with cardiac parameters (Fisher's Exact Test)**

| Cardiac Parameter | Ferritin ≥1000 ng/mL (n=51) | Ferritin <1000 ng/mL (n=6) | p-value (Fisher's Exact) |
|---|---|---|---|
| Pulmonary Arterial Hypertension | 3/51 (5.9%) | 0/6 (0%) | p = 0.411 |
| Dilated LA and/or LV | 4/51 (7.8%) | 0/6 (0%) | p = 0.487 |
| Elevated LV Mass Index | 4/51 (7.8%) | 0/6 (0%) | p = 1.000 |
| Tricuspid Regurgitation (any) | 6/51 (11.8%) | 1/6 (16.7%) | p = 0.598 |
| ECG: RVH | 4/51 (7.8%) | 0/6 (0%) | p = 0.887 |
| ECG: LVH | 2/51 (3.9%) | 0/6 (0%) | p = 0.548 |

### Correlation of Serum Ferritin with Cardiac Parameters

No statistically significant correlation was identified between serum ferritin level and any individual echocardiographic or ECG parameter, as detailed in [Table 5]. Trends in EF, LVIDd, and PASP across ferritin groups are shown in [Figure 6].

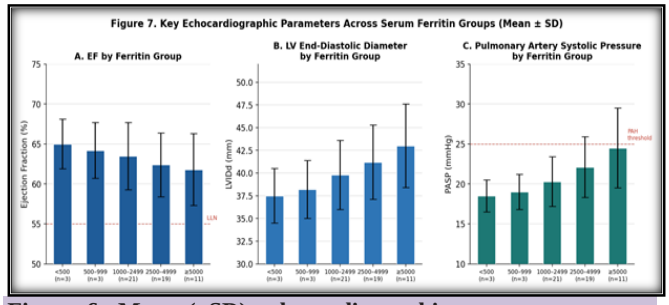


**Figure 6: Mean (±SD) echocardiographic parameters across serum ferritin groups. A: Ejection fraction (EF%) remained above the lower limit of normal (55%) across all groups. B: LV end-diastolic diameter showed a trend of increase with higher ferritin. C: Pulmonary artery systolic pressure (PASP) showed a trend towards the PAH threshold (25 mmHg) in the highest ferritin group; none reached statistical significance.**

**Diagnostic Performance of Echocardiography:** Compared to ECG as the reference standard, 2D echocardiography demonstrated a sensitivity of 72.22% (95% CI: 48.98–87.42%), specificity of 100% (95% CI: 91.03–100%), PPV of 100%, NPV of 88.64%, and overall diagnostic accuracy of 91.23% (95% CI: 81.06–96.19%). These data are presented in [Table 6 and Figure 7].

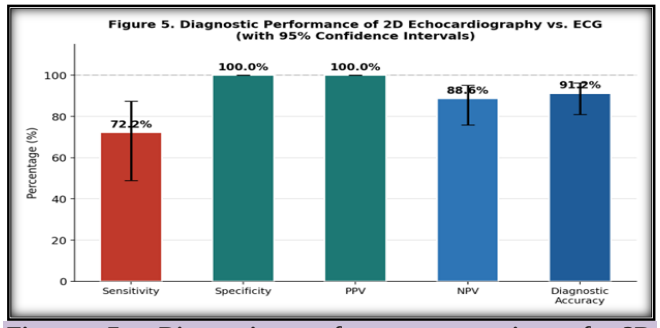


**Figure 7: Diagnostic performance metrics of 2D echocardiography versus ECG as the reference standard, with 95% confidence interval error bars. Perfect specificity (100%) and high diagnostic accuracy (91.23%) are demonstrated.**

**Table 6: Diagnostic performance of 2D echocardiography relative to ECG (reference standard)**

| Parameter | Estimate | 95% Confidence Interval |
|---|---|---|
| Sensitivity | 72.22% | 48.98% – 87.42% |
| Specificity | 100.0% | 91.03% – 100% |
| Positive Predictive Value (PPV) | 100.0% | 77.18% – 100% |
| Negative Predictive Value (NPV) | 88.64% | 75.93% – 95.19% |
| Diagnostic Accuracy | 91.23% | 81.06% – 96.19% |

## Discussion

This study provides systematic echocardiographic characterization of cardiovascular complications in a cohort of pediatric transfusion-dependent thalassemia patients at a tertiary care center. The 33% overall rate of echocardiographic abnormality underscores the significant cardiac burden in this population, corroborating international data.

The male predominance (56%) is consistent with findings from Samira Z. Sayed et al. (male 64%) and Ameen Mosa et al. (male

49%).[7,8] The high consanguinity rate (44%) in our cohort emphasizes the need for premarital screening and genetic counseling in South Indian rural communities. The rural predominance (85%) reflects geographical distribution of disease and barriers to local care, compounding iron-mediated organ damage through delayed and inconsistent chelation.

Nearly 90% of our cohort had elevated ferritin (>1000 ng/mL) despite chelation with deferasirox, aligning with observations by Azarkeivan et al. and Abbas et al., who noted persistent ferritin elevation even on chelation.[9,10] The absence of statistically significant correlation between ferritin and echocardiographic parameters confirms the recognized limitation of serum ferritin as a cardiac iron surrogate.[11] The mean EF of 62.91% and preservation of systolic function likely reflect early-stage cardiac involvement in a predominantly young cohort, mirroring Rodrigues et al. and Noori et al.[12,13] Our finding of diastolic dysfunction in one patient and dilated LA/LV in four (7.01%) is consistent with established knowledge that diastolic dysfunction precedes systolic impairment in iron overload cardiomyopathy. The 5.26% prevalence of mild PAH is lower than the 30–40% reported in thalassemia intermedia populations but consistent with well-transfused thalassemia major cohorts, where regular transfusion is protective against pulmonary vascular remodeling.[14] Two of three PAH cases were diagnosed before 12 months, suggesting heightened pulmonary vascular risk from early, heavy iron exposure.

Echocardiographic sensitivity of 72.22% and specificity of 100% versus ECG are clinically meaningful. Perfect specificity implies that a positive echocardiographic finding reliably identifies true cardiac pathology. Five patients with normal ECGs had abnormal echocardiograms, demonstrating that ECG alone would miss early structural and hemodynamic changes — an important finding for surveillance protocols in resource-constrained settings.[15,16]

**Limitations**

**Key limitations include:** (1) single-centre design with modest sample size (n=57) limiting subgroup analyses; (2) absence of cardiac T2* MRI validation; (3) tissue Doppler imaging for comprehensive diastolic assessment was not systematically performed; (4) cross-sectional design prevents longitudinal evaluation of cardiac progression; and (5) referral centre bias may overestimate complication rates relative to community prevalence.

## Conclusion

2D echocardiography is a highly specific, accessible, and cost-effective tool for early detection of cardiac complications in pediatric thalassemia patients. It identified cardiac abnormalities in one-third of patients — including cases missed by ECG. Serum ferritin is insufficient as the sole monitor of cardiac iron burden. Annual echocardiographic surveillance from the first decade of life should be integrated into standard thalassemia management guidelines, supplemented by cardiac MRI T2* where available. Community-level premarital and prenatal thalassemia screening programs remain imperative to reduce the disease burden in India.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Weatherall DJ, Clegg JB. Inherited haemoglobin disorders: an increasing global health problem. Bull World Health Organ. 2001;79(8):704–12.
2. Verma IC, Saxena R, Thomas E, Jain PK. Regional distribution of beta-thalassemia mutations in India. Hum Genet. 1997;100(1):109–13.
3. Malik S, Syed S, Ahmed N. Complications in transfusion-dependent patients of beta thalassemia major. Pak J Med Sci. 2009;25(4):678–82.
4. Kremastinos DT, Farmakis D, Aessopos A, Hahalis G, Hamodraka E, Tsiapras D, et al. β-Thalassemia cardiomyopathy: history, present considerations, and future perspectives. Circ Heart Fail. 2010;3(3):451–8.
5. Farmakis D, Aessopos A. Pulmonary hypertension associated with hemoglobinopathies: prevalent but overlooked. Circulation. 2011;123(11):1227–32.
6. Barzin M, Kowsarian M, Akhlaghpoor S, Jalalian R, Taremi M. Correlation of cardiac MRI T2* with echocardiography in thalassemia major. Eur Rev Med Pharmacol Sci. 2012;16(2):254–60.
7. Sayed SZ, Aly BA, Abd El-Hakim I. The early cardiac involvement in patients with beta thalassemia major. Egypt Heart J. 2013;65(1):29–36.
8. Mosa AM. Echocardiographic evaluation of thalassemia intermedia patients in Duhok, Iraq. BMC Cardiovasc Disord. 2014;14:183.
9. Azarkeivan A, Mehrvar A, Faranoush M. Cardiac involvement in patients with transfusion-dependent beta thalassemia. Res J Biol Sci. 2009;4(2):195–9.
10. Abbas AA, Najeb B, Abdulhussein A, Jassim HJ, Falih MA, Jubiaer H, et al. Echocardiographic parameters of LV systolic and diastolic function in β-thalassemia major. Iraqi Postgrad Med J. 2012;11(4):467–72.
11. Harrison PM, Arosio P. The ferritins: molecular properties, iron storage function and cellular regulation. Biochim Biophys Acta. 1996;1275(3):161–203.
12. Rodrigues A, Guimaraes FV, Braga JCF, Rodrigues CSC, Waib P, Fabron A, et al. Echocardiography in thalassemic patients on blood transfusions and chelation without heart failure. Arq Bras Cardiol. 2013;100(1):75–81.
13. Noori NM, Mahjoubifard M, Nakhaee-Moghadam M, Pezeshki M. Echocardiographic evaluation of systolic and diastolic heart function in patients with beta-thalassemia major. Acta Haematol. 2007;118(2):86–92.
14. Meloni A, Detterich J, Pepe A, Harmatz P, Coates TD, Wood JC. Pulmonary hypertension in well-transfused thalassemia major patients. Blood Cells Mol Dis. 2014;53(4):242–6.
15. Papadopoulou-Legbelou K, Varlamis SG, Athanassiou-Metaxa M, Karamperis S, Malaka-Zafiriou A. Cardiac complications in children with beta-thalassemia major. Hellenic J Cardiol. 2009;2(3):132–8.
16. Kliegman RM, Stanton BF, Geme JWS, Schor NF, Behrman RE. Nelson's Textbook of Pediatrics. 20th ed. Philadelphia: Elsevier; 2015. p.2349–53.