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To study the difference of serum Vitamin D3 level and calcium profile in childhood multitransfused beta-thalassemia major between children receiving chelation therapy and those not receiving chelation therapy in a tertiary care hospital, Kolkata

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ABSTRACT

Background: Most cases of beta-thalassemia major in children are associated with potentially severe clinical characteristics such as poor growth, feeding difficulties, hepatosplenomegaly, bone metabolic disorders, and skeletal abnormalities. **Aims and Objectives:** In our study, we evaluated the demographic and clinical presentations with the serum ferritin level, serum calcium, serum Vitamin D3 level, and serum phosphate level of 85 patients who received blood transfusions at regular intervals. **Materials and Methods:** We recruited children with beta-thalassemia major, confirmed by hemoglobin electrophoresis, for this study. We recorded the demographic details and blood transfusion status. We estimated serum ferritin, serum Vitamin D3 level, serum calcium, and serum PO_4 using Enzyme-linked immunosorbent assay. **Results:** Of the 85 patients, 71 started chelation and 14 refused. 72 were non-consanguineous, and 13 were consanguineous offspring. 66% of the total patients had ferritin levels exceeding 1000 ng/mL. Marriage types did not show a significant association with ferritin. After 20 infusions, coagulation began at 83.53%. A significant link exists between chelation therapy and total transfusions. Nearly 40% of children (47.06%) had calcium levels <8 mg/dL. 23 (27.06%) of the 85 patients exhibited hypophosphatemia. **Conclusion:** In most people, chemotherapy does not impact their serum PO4 levels. We have found a significant association between frequent red cell transfusions during chelation therapy and increased levels of ferritin, Vitamin D3, calcium, and phosphate.

Key words: Multi-transfused; Beta-thalassemia; Vitamin D3; Calcium profile; Children; Chelation therapy

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INTRODUCTION

Thalassemia is a diverse group of hereditary hemoglobin diseases caused by the absence or decreased production of one or more globin chains. Alpha- and beta-thalassemia are the two major types. Severe beta-thalassemia requires regular blood transfusions to maintain hemoglobin levels above 10 G/dL, but multiple transfusions can cause citrate toxicity and iron deposition in the parathyroid gland.[1] Patients with hypoparathyroidism (HPT) have reported low calcium and low Vitamin D levels.

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People with thalassemia who get blood transfusions on a regular basis end up with too much iron in their bodies, which can cause heart failure, cirrhosis, liver cancer, slow growth, and problems with hormones.[2] Iron poisoning occurs when cells misuse iron after transfusions, causing long-term issues for beta-thalassemia patients. Iron overload accumulates tissue iron, leading to cell death and organ failure. Treatment with iron chelation gets rid of extra iron after a blood transfusion by increasing the excretion of iron through urine. This prevents iron buildup after a blood transfusion. Deferoxamine, deferiprone, and deferasirox are the primary iron chelators. In metabolic bone profile derangements, different chelation therapies significantly raise blood phosphorus levels. HPT, calcium, and Vitamin D3 metabolites are treatment staples.[3] HPT, characterized by decreased blood calcium, increased serum phosphorus, and decreased parathyroid hormone, is linked to Vitamin D3 insufficiency and bone metabolism issues in older children.[4] In thalassemia children, oral Vitamin D3 and calcium supplementation increase bone mineral density.

Chelation treatment may cure iron overload and toxicity caused by regular blood transfusions for thalassemia patients. In this present study, we were looking to compare blood Vitamin D3 and calcium levels in children with multitransfused beta-thalassemia major undergoing chelation treatment to those not getting it.

Aims and objectives

- To assess the effect on vitamin D3 and calcium level in children with beta thalassemia receiving multiple packed red cells transfusions and chelation therapy.
- To assess the effect on vitamin D3 and calcium level in children with beta thalassemia receiving multiple packed red cells transfusions and not on chelation therapy.
- To Compare the level of vit D3 level and calcium profile in between two groups.

MATERIALS AND METHODS

The Thalassemia Clinic in the Outpatient Department of the Indoor Department of Paediatric Medicine at R.G. Kar Medical College and Hospital in Kolkata conducted this institutional-based observational descriptive cross-sectional epidemiological study. We recruited 1–12 years old with beta-thalassemia major from this Institute's Thalassemia Clinic. We have obtained ethical clearance from the Institutional Ethical Committee (Memo no. RKC/673, dated November 16, 2022). We included children aged 1–12 who had blood transfusions at this institute's thalassemia unit and had a positive high-performance liquid chromatography (HPLC) result but were not on chelation treatment or had been on it for at least a year. We eliminated patients under 1 year old, more than 12 years old, children between 1 and 12 years old without an HPLC report and children with active infections or other inflammatory diseases. We eliminated children who used hormonal, Vitamin D3, calcium, or supplements for chronic liver or kidney disease. Parents of research children provided written informed consent. We computed 85 samples for this investigation using the formula: n=2 SD2 ($Z\alpha/2+Z\beta)2/d^2$; SD=standard deviation from prior research or pilots. $Z\alpha/2$–Z0.05/2–Z0.025=1.96 (Z table) at 5% type 1 error, $Z\beta$–Z0.20=0.842 (Z table) at 80% power, d-effect size-mean difference. This research uses Abdelmotaleb et al.,[5] because their methodology, process, and environment are identical. The chemiluminescence assay measured the patient's history, anthropometry, vitals, systematic exams, serum ferritin, calcium, phosphate, and Vitamin D3.

Statistical analysis

Data are expressed as frequency, percentage, mean, standard deviation, or range depending on distribution. When data departed from normality or had low frequency, we used the Chi-square test or Fisher's exact test to evaluate independence. Pearson correlation coefficient was used for correlation testing. R Studio 1.3.1056 analyzed. The figure was created in Graphpad Prism 9.5.1. We accepted statistical significance at $P<0.05$.

RESULT

We have found a total of 85 cases with children, all of whom were between the ages of 1 and 12. Out of the total, 37 individuals (43.53%) belonged to the age category of 1–6 years, whereas the remaining 48 individuals (56.47%) belonged to the age range of 7–12 years. Out of the whole population, 50 individuals (58.82%) were female, whereas 35 individuals (41.18%) were male. Table 1 summarises the clinical and biochemical characteristics of individuals with positive and negative chelation.

The majority of patients, around 83%, lived in rural regions, whereas 17% resided in metropolitan areas. We determined the ratio between urban and rural areas to be 4.8:1. We classified 72 (84.71%) of the various forms of marriage as non-consanguineous, and 13 (15.29%) as consanguineous. We have observed that the number of individuals with chelation-positive and consanguineous types was 11, whereas the number of individuals with chelation-negative and consanguineous types was only two. We identified 30 cases (35.29%) in individuals aged 1 year or less, and 55 cases (64.7%) in those older than 1 year. Those with a negative chelation condition had a significantly higher age at diagnosis. Out of 85 child patients, 39 (45.88%) had no

Table 1: Clinical and biochemical characteristics according to chelation positive and negative individuals

Characteristics	Chelation (positive) (n=71)	Chelation (negative) (n=14)	P-value
Age	7.81±2.55	4.07±1.21	<0.0001
Male (number)	29	6	>0.999
Female (number)	42	8	
Parental consanguinity (yes)	11	2	>0.999
Parental consanguinity (No)	60	12	
Age at diagnosis	14.54±5.21	16.71±2.58	0.045
Total No. of Transfusions	67.56±26.81	14.64±4.61	<0.0001
Weight (kg)	18.90±4.68	14.36±1.59	0.0002
Height (cm)	113.1±11.83	98.07±6.63	<0.0001
BSA	0.76±0.13	0.62±0.05	0.0001
Pallor (yes)	71	14	>0.999
Pallor (no)	0	0	
RR (yes)	0	0	>0.999
RR (No)	71	14	
HR (Trchy)	16	1	0.283
HR (No)	55	13	
BP (yes)	0	0	>0.999
BP (No)	71	14	
CVS (Yes)	0	0	>0.999
CVS (No)	71	14	
RS (Yes)	0	0	>0.999
RS (No)	71	14	
Liver (cm)	4.61±1.31	3.5±1.14	0.0031
Spleen (cm)	2.91±1.44	2.42±0.89	0.056
Hb (%)	6.92±0.76	7.32±0.75	0.097
MCV	76.25±3.83	77.08±3.36	0.265
MCH	25.45±1.39	26.53±2.32	0.152
Platelet	165915±47255	188571±52456	0.105
Ferritin (ng/dL)	1912±982.7	751.8±139.6	<0.0001
Serum Vit D3 (ng/dL)	16.76±9.04	15.36±9.77	0.326
Serum Ca (mg/dL)	8.53±1.09	8.54±1.24	0.771
Serum PO4 (mg/dL)	4.72±0.86	4.82±1.16	0.886

diseased sibling history, 24 (28.24%) had at least one normal sibling, 11 (12.94%) had one affected sibling, 8 (9.41%) had two normal siblings, 2 (2.35%) had three normal siblings, and 1 (1.18%) had a dead sibling history. Of the 85 child patients, 58.82% (50) received transfusions once a month, 21.18% (18) received them twice a month, 18.82% (16) received them once every 2 months, and 1.18% (1) received them once every 3 months. In situations where chelation was positive, the number of transfusions was notably higher. The majority of patients, around 84% (71 out of 85), had a prior record of undergoing chelation therapy, whereas the remaining 16% did not get chelation treatment. Children who undergo chelation therapy have noticeably greater body weight and height compared to children who do not undergo chelation therapy. Among the 85 child patients, 68 (80%) had a normal heart rate, whereas the remaining 17 (20%) had a heart rate indicative of tachycardia. Out of the whole study population, 8 individuals (9.41%) had a splenectomy. The study found that 56 children (65.88%) had a serum ferritin level of ≥1000 mg/dL, and there was a significant increase in serum ferritin level in cases where chelation was positive. Among the 72 child patients born to parents who are non-consanguineous, 27 (31.76%) had a ferritin level below 1000, whereas 45 (52.94%) had a ferritin level equal to or above 1000. Of the 13 child patients born to consanguineous parents, 2 (2.35%) had a ferritin level below 1000, whereas 11 (12.94%) had a ferritin level equal to or higher than 1000. There was no significant correlation between types of marriage and ferritin levels (P=0.121). Among the 85 patients, 56 individuals (65.88%) who had previously undergone chelation therapy had a ferritin level of 1000 ng/mL or higher. We observed a notable increase in serum ferritin levels in cases where we administered chelation. Out of the 71 patients, 83.53% had a history of more than 20 transfusions and began treatment with chelation therapy. Having had a total of <20 transfusions in the past, the treatment began with chelation therapy. The number of transfusions was notably greater in individuals who tested positive for chelation. The chelation therapy resulted in a significant increase in serum Vitamin D3 levels. Among the 85 patients, 45 (52.94%) had a serum calcium level of ≥8 mg/dL, whereas 40 (47.06%) had a serum calcium level of <8 mg/dL. In addition, we observed that the serum calcium level remained relatively consistent after the chelation therapy. We found that 23 (27.06%) of the 85 patients had hyperphosphatemia, whereas 62 (72.94%)

had serum PO_4 levels within a normal range. In addition, we observed that the serum PO_4 levels were comparable in both chelation-positive and negative cases. Out of the total of 85 patients, 40 exhibited the condition of hypocalcemia. Out of the 40 patients with hypocalcemia, approximately 57.50% (23 patients) have elevated serum PO_4 levels.

Figures 1 and 2 illustrate the correlation results. They had a strong positive relationship with serum ferritin (r=0.979; P≤0.0001) but not with serum PO_4, serum Vit D3, or serum Ca (r=0.204; P=0.479; r=−0.296; P=0.301; r=−0.191; P=0.509). These patients were not on chelation therapy and had multiple packed red cell transfusions. Patients who were getting chelation therapy and a lot of packed red blood cell transfusions had a strong positive relationship with both serum ferritin and serum PO_4 (r=0.9993; P≤0.0001; r=0.2954; P=0.0124). Patients on chelation therapy and multiple packed red cell transfusions had a significant negative correlation with serum Vitamin D3 and serum calcium (r=−0.6038; P≤0.0001; r=−0.4687; P≤0.0001).

DISCUSSION

In the present study, we measured serum ferritin level, serum calcium level, serum Vitamin D3 level, and serum

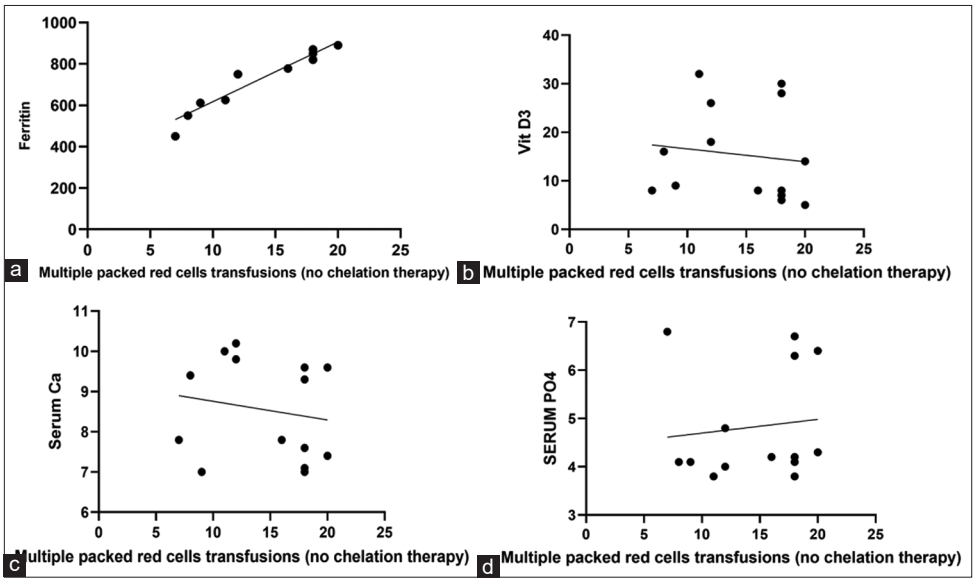

Figure 1: Correlation of multiple packed red cell transfusions (no chelation therapy) and (a) serum ferritin, (b) Serum Vit D3, (c) Serum Ca, (d) Serum PO_4

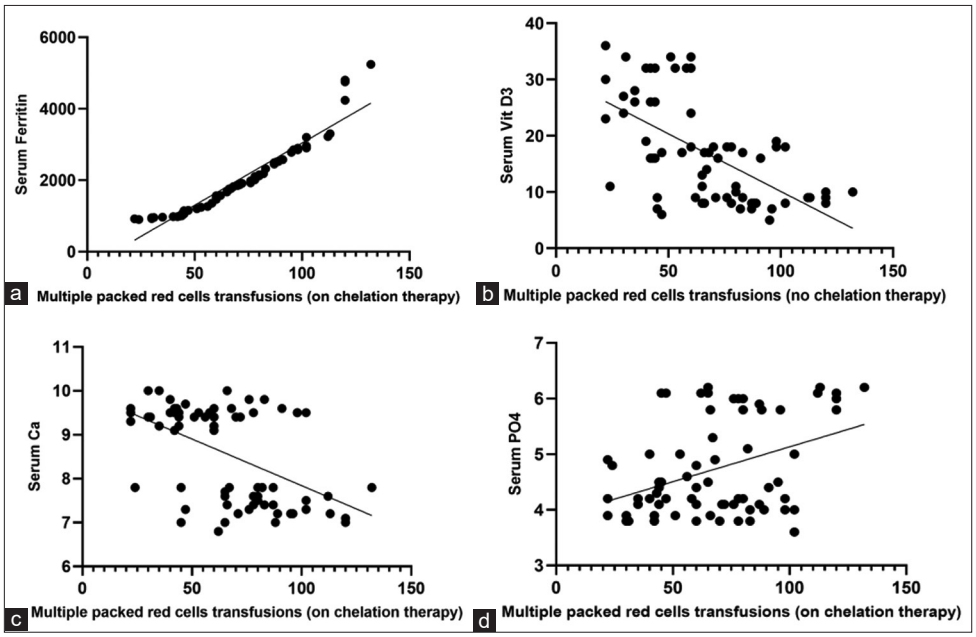

Figure 2: Correlation of multiple packed red cell transfusions (on chelation therapy) and (a) serum ferritin, (b) Serum Vit D3, (c) serum Ca, (d) Serum PO_4

phosphate level and evaluated the effect of chelation therapy on those values. We conducted the study on 85 transfusion-dependent patients with beta-thalassemia major to investigate the relationship between serum ferritin level and serum calcium profile in children with and without chelation therapy. Our study reveals a significant association between multiple packed red cell transfusions and serum ferritin, serum Vitamin D3, serum calcium level, and serum PO_4. We also found that most of the patients, with or without chelation history, have a normal range of serum PO_4. Our present study also shows that chelation therapy has a significant association with serum ferritin and the total number of transfusions.

In our study, 44% (n=37) were younger than 7 years, and the remaining 56% (n=48) were in the age group of 7–12 years. Ahmed et al. study revealed that 50.8% of the participants were between the ages of 6 and 10.[6] Out of 85 child patients, 50 (58.82%) were female and 35 (41.18%) were male. Studies done by Eghbali et al.,[7] showed a similar female preponderance (52% were female and 48% were male). Although some other studies, like those by Ahmed et al.,[6] and Usha et al.,[8] showed male preponderance, beta-thalassemia, which is an autosomal recessive disorder, does not show sex predilection. In this study, the majority of the patients were urban, and the urban–rural ratio was 4.8:1. Maji et al., study[9] revealed that the thalassemia belt encompasses rural areas of west Bengal and the eastern part of India. In the present study, 72 (84.71%) children were born from non-consanguineous parents, and 13 (15.29%) were born from consanguineous parents. A similar study by Sayed et al.,[10] showed around 32% of thalassemia patients were from consanguineous marriages, whereas 68% were from non-consanguineous marriages, where the prevalence is high. From this scenario, we can imply that the parents are heterozygous and obligate carriers, which, on the other hand, can be due to *de novo* mutations as well. In our study, 30 (35.29%) had ≤1 year of age, and 55 (64.7%) had >1 year of age at diagnosis. Children with thalassemia typically present in infancy at around 6 months of age, but some undergo screening earlier due to a history of sibling death. However, the majority of children receive a diagnosis by the age of 2 years. Sibling history in our study showed that out of 85 children, 39 (45.88%) did not have any diseased sibling history, 24 (28.24%) had one normal, 11 (12.94%) had one affected, 8 (9.41%) had two normal, and 2 (2.35%) had three normal, and out of them, only one child had lost his sibling due to disease. The results of our study align with those of Ameen Mosa et al.,[11] If one parent has the beta-thalassemia trait and the other parent has normal hemoglobin A, there is a 50% (1 in 2) chance with each pregnancy of having a child with the beta-thalassemia trait.[5] In this study, all 85 children were on regular blood transfusion therapy. Out of them, 50 (58.82%) went for transfusion once a month, 18 (21.18%) went for twice a month, 16 (18.82%) went for once every 2 months, and 1 (1.18%) went for once every 3 months. The Shah et al.[12] study presented a similar picture regarding the frequency of blood transfusions. In our study, almost 84% of the patients (71 out of 85) had a history of taking chelation therapy, whereas 16% (14 out of 85) were without chelation therapy. In our study, 24% of thalassemia patients were underweight and malnourished, and 37% had short stature as well. In the Usha et al.,[8] study, approximately one-third of their patients were underweight and had short stature. Splenectomy had been done in 9.41% of children, compared to 6.25–37% of children who had undergone splenectomy in a study conducted by Nisha[13] and Li et al.,[14] respectively. If the annual red cell requirement exceeds 180–200 mL/kg, splenectomy becomes necessary. To evaluate the extent of iron overload, this study categorized the patients into two groups based on their serum ferritin values: Those with values >1000 ng/mL and those with values <1000 ng/mL. 34% had a ferritin level <1000 ng/mL and 66% of the study population had a serum ferritin level >1000 ng/mL. However, the Sayed et al., study[10] revealed that 31.76% of the study population had a ferritin level <1000, whereas 52.94% had a ferritin level ≥1000. However, the types of marriage did not exhibit a significant association with ferritin. Out of 85 patients, 65.88% had a history of chelation therapy with a ferritin level ≥1000 ng/mL, and chelation therapy has shown a significant association with serum ferritin. Mobarra et al.,[15] and Cianciulli,[16] demonstrated the use of iron chelation therapy in reducing iron overload. In our study, 71 patients had a history of >20 total transfusions, and this patient started with chelation therapy. We found that chelation therapy and the total number of transfusions show a significant association. Poggiali et al.,[17] also demonstrated a correlation between multitransfusion and iron chelation therapy. In the present study, almost 45% of patients had Vitamin D3 deficiency, followed by 27% of patients with Vitamin D3 insufficiency and 28% of patients with a sufficient Vitamin D3 level. On the other hand, out of 85 patients, 52.94% have a serum calcium level of ≥8 mg/dL, 47.06% have a serum calcium level of ≥8 mg/dL, and 47.06% have a serum calcium level of <8 mg/dL. These types of similar findings were present in the studies done by Goyal et al.,[1] and Fahim et al.[18] Out of 85 patients, 27.06% have hyperphosphatemia, and 72.94% have a normal range of serum PO_4 levels. The majority of patients, both those with and without chelation (71.43% and 73.24%, respectively), exhibit normal serum PO_4 levels, and we found no correlation between these levels and chelation. In our study, among 71 chelation therapy patients, almost 72% had a low level of Vitamin D3, and among those without chelation therapy, 71% had a low

level of Vitamin D3. On the other hand, 46.48% had a level of serum Ca <8 mg/dL and 53.52% had a level of serum Ca ≥8. Among patients without chelation therapy, 50% had <8 mg/dL serum Ca level. Ahmed et al. study[6] revealed similar findings. We checked if there was a strong link between multiple packed red cell transfusions (during chelation therapy) and serum ferritin, serum Vitamin D3, serum calcium level, and serum phosphate level.

Despite some novel aspects, this study has some limitations. First, there were instances where patient follow-up was not possible due to unavoidable circumstances. Second, relatively small sample size. Third, because this is an institutional-based study, we cannot extrapolate our study findings to the community. Fourth, the evaluation did not cover all the endocrine parameters. Fifth, there was no baseline data available on the initial parameters at the start of the diagnosis.

Limitations of the study

In spite of every sincere effort, this study has some lacunae, as sometimes patient follow-up was not possible due to some unavoidable situation (like most of the patients belong to a remote area). Apart from that, another limitation of our study was the relatively small sample size, and the findings cannot be projected at a community level, as this is an institutional-based study. We did not evaluate all the endocrine parameters. Moreover, there was no baseline data available on the initial parameters at the start of diagnosis.

CONCLUSION

It is evident that most beta-thalassemia major patients on repeated blood transfusions have moderately to strongly elevated serum ferritin levels and serum levels of calcium and Vitamin D3 are deficient among them. Initiating stage of chelation therapy in patients with major beta-thalassemia is a key factor in their survival. This stage includes a change in the ferritin level to above 1000 ng/mL. As a result, effective chelation therapy trapped non-transferrin-bound iron and LPI to prevent the adverse consequences of iron overload. There is still some confusion about how Vitamin D3 and calcium levels affect the risk of bone disease in beta-thalassemia patients, but we do know that starting chelation therapy later is linked to a higher serum ferritin level.

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REFERENCES

1. Goyal M, Abrol P and Lal H. Parathyroid and calcium status in patients with thalassemia. Indian J Clin Biochem. 2010;25(4):385-387.
   https://doi.org/10.1007/s12291-010-0071-5
2. Needs T, Gonzalez-Mosquera LF and Lynch DT. Beta thalassemia. In: StatPearls Treasure Island, FL: StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK531481 [Last accessed on 2023 May 01].
3. De Sanctis V, Soliman AT, Canatan D, Elsedfy H, Karimi M, Daar S, et al. An ICET- a survey on hypoparathyroidism in patients with thalassemia major and intermedia: A preliminary report. Acta Biomed. 2018;88(4):435-444.
   https://doi.org/10.23750/abm.v88i4.6837
4. Yu U, Chen L, Wang X, Zhang X, Li Y, Wen F, et al. Evaluation of the vitamin D and biomedical statuses of young children with β-thalassemia major at a single center in Southern China. BMC Pediatr. 2019;19(1):375.
   https://doi.org/10.1186/s12887-019-1744-8
5. Abdelmotaleb, Ghada & Galal, Ola & Eid, Khaled & El-Hassib, Dalia & Hemeda, Tasbeh. (2021). Assessment of serum vitamin D levels in Egyptian children with beta thalassemia major. Egyptian Pediatric Association Gazette. 69. 20. 10.1186/s43054-021-00066y.
6. Ahmed Z, Pushpanjali P, Kausar MS and Sinha D. Study of serum calcium, phosphorus and vitamin D status in multitransfused β-thalassemia major children and adolescents of Jharkhand, India. Int J Contemp Pediatr. 2019;6:598-601.
   https://doi.org/10.18203/2349-3291.ijcp20190694
7. Eghbali A, Taherahmadi H, Bagheri B, Nikanjam S and Ebrahimi L. Association between serum ferritin level and diastolic cardiac function in patients with major β-thalassemia. Iran J Ped Hematol Oncol. 2015;5(2):83-88.
8. Usha BK, Stalin S, Ravi CT and Gnanasambandam S. Study of echocardiography in thalassemia (major/intermedia) patients at tertiary care center. Indian J Child Health. 2018;5(8):533-536.
   https://doi.org/10.32677/IJCH.2018.v05.i08.006
9. Maji SK, Mandal PK, Bera R and Dolai TK. The prevalence and characterization of β-thalassemia trait by using high-performance liquid chromatography among the rural population in West Bengal, India. Thalass Rep. 2014;4(1):2188.
   https://doi.org/10.4081/thal.2014.2188
10. Sayed SZ, Aly BA, El-Hakim A, Omar SM and Amin AS. The early cardiac involvement in patients with β-thalassemia major. Egypt Heart J. 2013;65(3):243-249.
    https://doi.org/10.1016/j.ehj.2013.01.002
11. Mohammad AM. Echocardiographic evaluation of thalassemia intermedia patients in Duhok, Iraq. BMC Cardiovasc Disord. 2014;14:183.
    https://doi.org/10.1186/1471-2261-14-183
12. Shah N, Mishra A, Chauhan D, Vora C and Shah NR. Study on effectiveness of transfusion program in thalassemia major patients receiving multiple blood transfusions at a transfusion centre in Western India. Asian J Transfus Sci. 2010;4(2):94-98.
    https://doi.org/10.4103/0973-6247.67029
13. Nisha MS. Study on Clinical Profile of Beta Thalassemia Major Children. Madurai: Masters Thesis, Madurai Medical College; 2013.

14. Li CK, Luk CW, Ling SC, Chik KW, Yuen HL, Li CK, et al. Morbidity and mortality patterns of thalassemia major patients in Hong Kong: Retrospective study. Hong Kong Med J. 2002;8(4):255-260.
15. Mobarra N, Shanaki M, Ehteram H, Nasiri H, Sahmani M, Saeidi M, et al. A review on iron chelators in treatment of iron overload syndromes. Int J Hematol Oncol Stem Cell Res. 2016;10(4):239-247.
16. Cianciulli P. Iron chelation therapy in thalassemia syndromes. Mediterr J Hematol Infect Dis. 2009;1(1):e2009034. https://doi.org/10.4084/MJHID.2009.034
17. Poggiali E, Cassinerio E, Zanaboni L and Cappellini MD. An update on iron chelation therapy. Blood Transfus. 2012;10(4):411-422. https://doi.org/10.2450/2012.0008-12
18. Fahim FM, Saad K, Askar EA, Eldin EN and Thabet AF. Growth parameters and vitamin D status in children with thalassemia major in upper Egypt. Int J Hematol Oncol Stem Cell Res. 2013;7(4):10-14.

Authors' Contributions:
SMH- Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, data collection, data analysis, manuscript preparation, and submission of the article; **SR**- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **DH**- Design of study, statistical analysis, and interpretation; **NR**- Review manuscript; **DH**- Review manuscript; **RA**- Literature survey and preparation of figures; **DH**- Coordination and manuscript revision.

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