Original Article

Clinical Profile and Vitamin D Status in Beta Thalassemia Major Children at a Tertiary Care Institute of Central India: A Cross-Sectional Study

RM Meshram, MA Salodkar, SR Yesambare, SM Mohite, RB Gite, VR Rathod

Department of Paediatrics, Government Medical College, Nagpur, Maharashtra, India

Abstract

Background: In India, the prevalence of beta thalassemia is 3.74%, and sixty to eighty percent of thalassemic children have vitamin D deficiency syndrome. **Aim:** To estimate the prevalence of vitamin D deficiency and parathyroid levels in thalassemic children of Central India. **Methods:** This cross-sectional study was conducted on 61 diagnosed beta thalassemic children of 2-12 years of age at the pediatric department of the tertiary care institute of Central India for six months by consecutive sampling method. Demographic, transfusion, and clinical data were collected. Serum Vitamin D levels were estimated by electrochemical-luminescence technology and serum parathyroid hormone was by immunoassay. Complete blood count, serum ferritin/calcium/phosphorous, and liver functions test were performed. Frequency, mean, standard deviation, and correlation of various variables were performed. **Results:** Three-fourths of the participants were above 5 years of age and male to female ratio was 1.5:1. Most (88.5%) cases required blood transfusion every 3–4 weeks duration and 80.3% were receiving chelation therapy and all of them were on oral Deferasirox. About half of the participants had serum ferritin levels 1000–3000 ng/dl, and 27 (44.3%) had levels more than 3000- 5000 ng/dl. The total mean vitamin D and parathyroid hormone were 18.4 ± 9.9 ng/ml, and 13.1 ± 15.4 pg/ml respectively. The prevalence of low vitamin D was 63.9% and low parathyroid level in 21.3% of participants. Serum vitamin D level was inversely related to age, serum ferritin level, and transfusion frequency while directly related to serum calcium level. **Conclusion:** The prevalence of vitamin D deficiency is 63.9% and low parathyroid hormone is 21.3%. Serum vitamin D has a negative correlation with increased age and increased serum ferritin levels.

Keywords: *Beta thalassemia major, children, parathyroid hormone, serum ferritin, vitamin D deficiency*

Received: 04-Sep-2024;
Revision: 30-Nov-2024;
Accepted: 10-Dec-2024;
Published: 17-Mar-2025

Introduction

Thalassemia is an autosomal recessive inherited disorder of hemoglobin, and it is derived from the Greek word 'Thalassa' meaning sea. It is characterized by either the reduction or absence of production of one or more globin chains of tetramers of Hb resulting in uncontrolled destructions of RBCs leading to severe anemia. In beta thalassemia, β globin chain is involved which is encoded by Hbβ gene, located on chromosome 11 resulting in homozygous (major or intermediate beta-thalassemia) or heterozygous (minor or carrier) disease.[1] Children with beta-thalassemia major are chronically anemic, transfusion-dependent, prone to acquiring transfusion-associated infections, have poor growth, various endocrine diseases, metabolic bone diseases, and have a decrease in life expectancy when

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_592_24

Address for correspondence: Dr. RM Meshram, Department of Paediatrics, Government Medical College, Nagpur, Maharashtra, India.
E-mail: dr_rajmeshram@rediffmail.com

How to cite this article: Meshram RM, Salodkar MA, Yesambare SR, Mohite SM, Gite RB, Rathod VR. Clinical profile and vitamin D status in beta thalassemia major children at a tertiary care institute of central India: A cross-sectional study. Niger J Clin Pract 2025;28:107-12.

optimal care is compromised.[2-6] Recent meta-analysis reported that under 5 mortality is 7 times higher in severe thalassemia syndrome than in the general population and 3.4 times higher risk of death in patients of transfusion-transmitted infections while 4.6-time higher risk of mortality with serum ferritin higher than 4000 ng/dl compared to ferritin lower than 1000 ng/dl.[7]

The burden of beta thalassemia is measured by obtaining the prevalence of beta thalassemia carrier. Estimated global carrier prevalence ranges from 0.5 to 20%, and approximately 80 million are carriers of beta-thalassemia.[8,9] However, the major burden of thalassemia is distributed in the Indian subcontinents (including Bangladesh, Pakistan, and India), Mediterranean and Middle Eastern nations, and Southeast Asia. Nowadays, the disorder is also prevalent in Northern Europe, North Central and South America, and Australia probably due to migration.[10,11] Recent systematic review and meta-analysis reported a 3.74% pooled prevalence of beta thalassemia carrier in the general population and 4.6% among tribal groups of India.[12]

Metabolic bone diseases including osteoporosis, rickets, spinal deformities, and fractures are some of the major morbidities in beta thalassemic children due to impaired calcium homeostasis which is thought to be a consequence of iron overload, chronic endocrinopathies, malnutrition, and inadequate physical activities.[13-15] A report from the USA revealed 73% of thalassemic patients had either deficient or insufficient vitamin D levels, while a study from North India and South India reported 80% and 60% of patients, respectively had deficient/insufficient vitamin D. A study from Thailand showed 90% thalassemic patient had vitamin D deficiency.[14,16-18] Hence this study was planned to estimate the prevalence of low calcium, vitamin D deficiency, and parathyroid levels in thalassemic children of Central India.

Methods

This cross-sectional observational study was carried out at the Day Care Center of the Department of Pediatrics, tertiary care institute of Central India on diagnosed children of thalassemia major (age group 2-12 years) who were admitted for blood transfusion over six months. Considering the availability of patients within the data collection period, a total of 61 children and adolescents were included in the study by a consecutive sampling method. All the necessary information regarding the study was explained to parents/caregivers in vernacular language before enrolling the participants and informed written consent was obtained from those who were willing to participate in the study. The study was approved by the Institutional Ethics Committee (No. 2529/EC/Pharmac/GMC/NGP dated 25/10/2021).

Inclusion criteria

1) Diagnosed case of thalassemia major by Hb electrophoresis/HPLC of age group 2-12 years
2) Regularly transfused with packed RBCs with a minimum of 10 transfusions.

Exclusion criteria

1. Multi-transfused children of sickle cell anemia.
2. Poor compliance with packed cell transfusion.
3. Those who were sick and critically ill patients.
4. Those who were suffering from malnutrition.
5. Those who were on any calcium, phosphorus, or vitamin D-containing preparations.

Demographic details such as age, sex, residence, socioeconomic status, status of parents/sibling, age at first transfusion, frequency of transfusion, iron chelation therapy, duration of chelator therapy, and immunization status were collected. Routine hematological and biochemical investigations were done in the Central Clinical Laboratory of our institute. Serum Vitamin D level was estimated by electrochemical-luminescence technology for heterogenous immune assay on a fully automatic COBASe411 analyzer by Roche (Hitachi) disc system. Serum Vitamin D levels less than 20 ng/ml were considered deficient. Serum parathyroid hormone was estimated by immunoassay on COBASe immunoassay analyzer and the reference range was 15–51 pg/ml. A Serum PTH level of less than 15 pg/ml was considered deficient.

Collected Data was entered into a Micro software spreadsheet. Statistical software STATA version 14.0 was used for statistical analysis to determine the frequency, mean, standard deviation, and correlation of various variables. $P < 0.05$ was considered as statistically significant.

Results

In this study, a total of 61 participants of thalassemia major were included and three-quarters 46 (75.4%) were more than 5 years of age. The male-to-female ratio was 1.5:1. Almost two-thirds of participants 44 (72.1%) were from rural areas and 48 (78.7%) were from lower socio-economic classes. Family history of thalassemia was noted in 33 (54.09%); amongst 28 (45.9%) cases both parents were suffering from either thalassemia major or minor disease and in 5 (8.2%) either parent was suffering from disease while in 6 (9.8%) cases siblings were affected. Fifty-four (88.5%) cases required blood transfusion every 3-4 weeks duration. Chelation therapy was received in 49 (80.3%) cases and all of them were on oral Deferasirox [Table 1]. More than

two-thirds of 50 (81.9%) participants were completely immunized as per the National Immunization Schedule while 18 (29.5%) received the Pneumococcal and Meningococcal vaccine. Surgical splenectomy was done in 12 (20%) cases while spleen was not palpable in 5 (8.2%) cases. Chelation therapy was withheld in 2 (3.3%) cases due to toxicity. All participants were admitted for severe anemia while 2 participants presented with congestive cardiac failure. Signs of hemolysis, and liver dysfunction were noted in 51 (83.6%) and 7 (11.5%) participants, respectively, while none of them had renal or neurological complications. All participants were non-reactive to HIV and Hepatitis B while 5 (8.2%) were reactive to Hepatitis C virus.

Table 1: Demographic characteristics of study participants

Characteristics	Total participant *n*=61 (%)
Age (years) (Mean±SD)	6.6±2.8
2–5 years	15 (24.6)
5.1–12 years	46 (75.4)
Gender	
Male	37 (60.7)
Female	24 (39.3)
Residence	
Rural	44 (72.1)
Urban	17 (27.9)
Socio-economic Status	
Lower	48 (78.7)
Middle	13 (21.3)
Age at presentation (months) (Mean±SD)	11.6±9.9
Age at first transfusion (Months) (Mean±SD)	11.3±9.7
Transfusion frequency	
Every 2 weeks	4 (6.6)
Every 3-4 weeks	54 (88.5)
Every 2-3 months	3 (4.9)
Transfusion requirement (frequency)	
All participants (Mean±SD)	74.8±44
Chelation therapy received (yes)	49 (80.3)
Duration of chelation therapy (Mean±SD)	3.5±2.9
<5 years	30/49 (61.2)
>5.1 years	19/49 (38.8)

Analyzed serum ferritin levels showed that 30 (49.2%) had values in the range of 1000-2999 ng/dl, 27 (44.3%) were between 3000 and 4999 ng/dl while 3 (4.9%) cases had below 1000 ng/dl and one participant had serum ferritin level more than 5000 ng/dl.

The Vitamin D levels ranged from 3.0-56.5 ng/mL with a mean of 18.4 ng/ml. The serum Parathyroid hormone level varied between 1.2-93.5 pg/ml, with a mean of 13.1 pg/ml. The average serum calcium was 8.9 mg/dl and the mean phosphorus level was 4.3 mg/dl. Among the studied participants 39 (63.9%) had low Vitamin D levels (<20 ng/ml) while in 13 (21.3%) their parathyroid level was low (<15 pg/ml), as shown in Table 2.

The mean serum Vitamin D level for children in the age range of 2–5 years was 25.3 ± 14.5 ng/ml while in age group 5-12 years it was 16.1 ± 6.7 ng/ml and this difference was statistically significant (P = 0.001). In correlation of vitamin D level with serum ferritin, the mean values were 18.1 ± 14.0 ng/ml, 23.7 ± 10.5 ng/ml, 12.8 ± 4.3 ng/ml and 12.2 ± 12.9 ng/ml among the serum ferritin ranges of less than 1000 ng/dl, 1000–2999 ng/dl, 3000–4999 ng/dl, and ≥5000 ng/dl respectively and this was statistically significant (P = 0.0001). There was no statistically significant difference between the serum level of PTH, phosphorus, and magnesium level with vitamin D. It was also observed that children with serum calcium levels >8 mg/dl, and transfusion frequency <75 had statistically significantly higher mean vitamin D levels. The mean serum vitamin D level (18.8 ± 10.4 ng/ml) was observed in children receiving chelation therapy while it was 16.5 ± 1.9 ng/ml in children not receiving chelation therapy and the P value for this correlation was 0.46 [Table 3].

Table 2: Hematological and Biochemical Parameters in studied participants

Parameters	Minimum	Maximum	Median	Mean	SD
Serum Ferritin (ng/dL)	758	6532	2867	2922.3	1158.3
Serum calcium (mg/dL)	5.8	10.2	9	8.9	0.8
Serum Phosphorus (mg/dL)	2.5	11	4.4	4.3	0.6
Vit D (ng/mL)	3	56.5	16.2	18.4	9.9
Hemoglobin (g/dL)	1.9	9.9	5	5.2	1.6
Serum PTH (pg/mL	1.2	93.5	10.2	13.1	15.4
Serum Vit D level, *n* (%)			<20 ng/ml 39 (63.9)		
			≥20 ng/ml 22 (36.1)		
Serum PTH level, *n* (%)			<15 pg/ml 13 (21.3)		
			≥15 pg/ml 48 (78.7)		

Table 3: Correlation of Vitamin D level and other parameters

Parameters	*n* (%)	Vitamin D (ng/mL) mean	SD	Range	*P*
Age group (years)					
2–5	15 (24.6)	25.3	14.5	7.7-56.5	0.001
>5	46 (75.4)	16.1	6.7	3.0–32.1	
Serum Ferritin (ng/dL)					
<1000	3 (4.9)	18.1	14	9.25–34.2	0.0001
1000–2999	30 (49.2)	23.7	10.5	7.9–56.5	
3000–4999	27 (44.3)	12.8	4.3	3–22.1	
≥5000	1 (1.6)	12.2	12.9	12.2–12.2	
Chelation Therapy					
Yes	49 (80.3)	18.8	10.4	3–56.5	0.46
No	12 (19.7)	16.5	1.9	7.66–34.2	
Parathyroid hormone					
<15 pg/mL	48 (78.7)	19.3	9.6	3–56.5	0.15
≥1 5 pg/mL	13 (21.3)	15.1	10.8	3.37–45.3	
Serum calcium (mg/dL)					
<8	55 (90.2)	10.2	9.2	7.7–32.1	0.03
≥8	6 (9.8)	18.9	9.9	3–56.5	
Serum Phosphorus (mg/dL)					0.64
≥3	59 (96.7)	18.6	10.0	3–56.5	
<3	2 (3.3)	15.3	8.9	6.49–27.8	
Transfusion frequency					0.02
<75	30 (49.2)	21.8	12.3	3–56.5	
>75	31 (50.8)	16	6.3	3.37–32.2	
Serum Magnesium (mg/dl)					
	59 (96.7)	18	9.9	3–56.5	0.15
	2 (3.3)	28.2	5.6	22.4–32.1	

Discussion

The majority (three-quarters) of the participants were above 5 years of age and male children were dominant while almost two-thirds of children were from rural areas and belonged to lower socioeconomic classes. Our demographic findings agreed with the reported 77.35% and 78.4% by Tiwari *et al.* and Monem *et al*. Likewise, male gender dominance was reported by various authors.[19-24] Although, most of our participants are from rural areas; however, our finding was much lower than 92% observed by Tiwari *et al*.[19] Family history of thalassemia was observed in 54.1% of participants and siblings were affected in 9.8% of cases. Mahmoud *et al.*[23] revealed a family history of thalassemia in 39.16% of thalassemic children while Jena I *et al.*[24] observed 69% of fathers and 77.5% of mother's trait HPLC status in Indian children.

In this study, the mean age of the first transfusion was 11.3 ± 9.7 months, the majority of children required transfusion every 3-4 weeks, and the mean transfusion frequency was 74.8 ± 44. This agrees with earlier studies.[24,25] that reported more than 60% of thalassemic children were diagnosed in infancy and more than two-thirds of thalassemic children required monthly transfusion.

It is evident that iron overload leads to multiorgan dysfunction and increases the risk of death in thalassemic children. In this study, chelation therapy was received by 80.3% and all of them were on oral deferasirox due to this drug is freely available in hospitals, does not require hospitalization, avoids hospital stays, and minimizes the risk of complication. Similar to our findings Bazi *et al.*[5] noted the majority of their patients received deferasirox while in Mahmoud *et al.*[23] revealed majority of thalassemic children were on combined therapy of deferasirox and deferoxamine. Pallor was noted in all cases, signs of hyperhaemolysis and liver dysfunction were observed in 83.6% and 11.5% of children respectively and 8.2% of children had antibodies against hepatitis C virus. Similar types of presentations have been reported by various authors in their studies.[20,22,23,26] None of our patients had antibodies against hepatitis B, and this may not be surprising as the majority of the thalassemic children were completely

immunized as per the national immunization schedule and 29.5% had received pneumococcal/meningococcal vaccine; however, there is no effective vaccine against hepatitis C.

The mean Hb and serum ferritin levels were 5.2 ± 1.6 gm/dl and 2922.3 ± 1158.3 ng/dl respectively. More than two-fifths (44,3%) had serum ferritin between 3000-5000 ng/dl and only one participant had a value >5000 ng/dl. Such high ferritin levels because all the patients were on chronic blood transfusion and our results are concurrent with the findings of other authors.[14,26,27]

Vitamin D deficiency was noted in 63.9% and hypoparathyroidism in 21.3% of thalassemic children. The observed prevalence of vitamin D deficiency (63.9%) in our study is comparable to ranges between 49% to 79% reported by various earlier authors both within and outside India.[3,14,26,28] In the present study, the mean serum level of vitamin D was 18.4 ± 9.9 ng/ml. Various researchers noted that the level of 25-OH-vitamin D level was significantly lower among beta-thalassemia patients compared to the normal population.[3,4,26-30] Despite exposure to good sunlight and routine prescription of vitamin D, some of the possible reasons for such low levels of vitamin D in thalassemic children were endocrinopathies, defective hepatic hydroxylation of vitamin D, hepatic haemosiderosis, dark skin, poor nutrition, and vitamin D malabsorption. All the children in this study had high serum ferritin levels despite being on chelator.

Hypoparathyroidism (PTH <15 pg/ml) was noted in 21.3% of our patients which is similar to the reported incidence ranges of 2–38% in thalassemic children by previous authors.[3,5,14,31,32] Slightly higher incidence of hypoparathyroidism in this study might be because most of our thalassemic children were older, received monthly blood transfusions, and 20% of cases have had splenectomy done. Bazi *et.al.,*[5] also identified factors such as older age, the mean received a blood transfusion, total transfused blood per year, splenomegaly, hepatomegaly, chelation regimen, and splenectomy as independent risk factors of low PTH. In contrast to our findings Agrawal *et al.*[33] reported high mean PTH levels in thalassemic children [64.35 ± 16.01 pg/ml) compared to their control (42.61 ± 13.75 pg/ml).

In the current study, the total mean serum level of vitamin D was significantly higher in the age group 2–5 years compared age group of more than 5 years (P = 0.001). Vitamin D level statistically significantly decreases as serum ferritin level increases. It is also observed that serum vitamin D level increases in children with serum calcium level less than 8 mg/dl and transfusion frequency less than 75 while we could not find a significant correlation with parathyroid hormone, serum phosphorus, magnesium level, children on chelation therapy. A decrease in vitamin D level with an increase in serum ferritin and an increase in age group might be due to iron overload, endocrinopathy, poor nutrition, and no or inadequate supplementation of calcium and vitamin D. We could not correlate the relation of parathyroid hormone level with vitamin D probably due to small sample size. Shah B *et al.*[34] reported out of 72 patients with vitamin D level <30 ng/ml**,** 52% had ferritin level >2500 µg/l (OR = 2.23 P = 0.220, 95 CI) and 35% were <5 years (OR = 0.18, P = 0.01, 95 CI). While Jauhari *et al.*[35] reported strong negative correlation with serum ferritin level and serum vitamin D level (P = 0.008, r = −0.476).

Conclusion

Most of the participants were more than 5 years of age and required blood transfusion every 3-4 weeks duration. More than 80% were on chelation therapy and all of them were on oral deferasirox. All of them had pallor and almost 50% of cases had serum ferritin levels between 1000-3000 ng/dl, 63.9% had vitamin D deficiency and 21.31% had low PTH levels. Serum vitamin D level was inversely related to age and serum ferritin level and transfusion frequency with a positive correlation with serum calcium level. These abnormalities may be due to iron overload and poor nutrition and they require frequent monitoring for early detection and to prevent bone diseases.

Acknowledgment

We are sincerely thankful to the parents of the participants, and Head of the Department of Pediatrics, and the Dean of the Government Medical College for laboratory support and permission to carry out this research.

Ethical consideration

Written informed consent/assent was obtained from parents and children. The study was approved by the Institutional Ethics Committee.

Financial support and sponsorship

Authors use their funds for laboratory expenses.

Conflicts of interest

There are no conflicts of interest.

References

1. Thalassemia- Gene and Disease- NCBI Bookself. National Center for Biotechnology Information (US). Bethesda (MD): National Center for Biotechnology Information (US); 1998.

2. Yousuf R, Akter S, Wasek SM, Sinha S, Ahmad R, Haque M. Thalassemia: A review of the challenges to the families and caregivers. Cureus 2022;14:e32491.
3. Bulgurcu SC, Canbolat Ayhan A, Emeksiz HC, Ovali F. Assessment of the nutritional status, bone mineralization, and anthropometrics of children with thalassemia major. Medeni Med J 2021;36:325-32.
4. Fahim FM, Saad K, Askar EA, Eldin EN, Thabet AF. Growth parameters and vitamin D status in children with thalassemia major in upper Egypt. Int J Hematol Oncol Stem Cell Res 2013;7:10-4.
5. Bazi A, Harati H, Khosravi-Bonjar A, Rakhshani E, Delaramnasab M. Hypothyroidism and hypoparathyroidism in Thalassemia major patients: A study in Sistan and Baluchestan province, Iran. Int J Endocrinol Metab 2018;16:e13228.
6. Thiagarajan NR, Kumar CGD, Sahoo J, Krishnamurthy S. Effect of vitamin D and calcium supplementation on bone mineral content in children with Thalassemia. Indian Pediatr 2019:307-10.
7. Dhanya R, Sedai A, Ankita K, Parmar L, Agarwal RK, Hegde S, *et al*. Life expectancy and risk factors for early death in patients with severe thalassemia syndromes in South India. Blood Adv 2020;14:1448-57.
8. Weatherall D, Akinyanju O, Fucharoen S, Olivieri N, Musgrove P, Jamison DT, *et al*, editors. In: Disease Control Priorities in Developing Countries. 2nd edition. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; New York: Oxford University Press; 2006. Chapter 34. P.664-80.
9. De Sanctis V, Kattamis C, Canatan D, Soliman AT, Elsedfy H, Karimi M, *et al*. β-Thalassemia distribution in the old world: An ancient disease seen from a historical standpoint. Mediterr J Hematol Infect Dis 2017;9:e2017018.
10. Hossain MS, Hasan MM, Raheem E, Islam MS, Al Mosabbir A, Petrou M, *et al*. Lack of knowledge and misperceptions about thalassaemia among college students in Bangladesh: A cross-sectional baseline study. Orphanet J Rare Dis 2020;15:54.
11. Cao A, Kan YW. The prevention of thalassemia. Cold Spring Harb Perspect Med 2013;3:a011775.
12. Sumedha D, Anita K. Prevalence of beta thalassemia carriers in India: A systematic review and meta-analysis. J Community Genet 2023;14:527-541.
13. Soliman A, De Sanctis V, Yassin M. Vitamin D status in thalassemia major: An update. Mediterr J Hematol Infect Dis 2013;5:e2013057.
14. Handattu K, Aroor S, Kini P, Ramesh Bhat Y, Shivakumar G, Shastry P, *et al*. Metabolic bone disease in children with transfusion-dependent thalassemia. Indian Pediatr 2022;59:920-3.
15. Cahyadi A, Ugrasena IDG, Andarsini MR, Larasati MCS, Jauhari RMZ, Arumsari DK. Relationship between serum ferritin and growth status of pediatric transfusion dependent thalassemia. Caspian J Intern Med 2023;14:425-32.
16. Fung EB, Aguilar C, Micaily I, Haines D, Lal A. Treatment of vitamin D deficiency in transfusion-dependent thalassemia. Am J Hematol 2011;86:871-3.
17. Singh K, Kumar R, Shukla A, Phadke SR, Agarwal S. Status of 25-hydroxyvitamin D deficiency and effect of vitamin D receptor gene polymorphisms on bone mineral density in thalassemia patients of North India. Hematology 2012;17:291-6.
18. Nakavachara P, Viprakasit V. Children with hemoglobin E/β-thalassemia have a high risk of being vitamin D deficient even if they get abundant sun exposure: A study from Thailand. Pediatr Blood Cancer 2013;60:1683-8.
19. Tiwari D, Gupta SK, Thepa NB, Devkota K. Clinical profile of children with thalassemia admitted for blood transfusion at a tertiary health care center. JCMS-Nepal 2023;19:294-8.
20. Monem AA, Shehata S, Elsayed M, Ayad A. Descriptive clinical study of children with beta thalassemia at Damanhour Medical National Institute. Alex J Pediatr 2021;34:67-73.
21. Kumar D, Kinikar AA. Clinical profile of children with beta-thalassemia. Asian J Clin Pediatr Neonatol 2019;7:42-6.
22. Verma GK, Singh A, Chauhan CB, Singh MV. Clinical, hematological profile and status of iron overload in children with transfusion dependent thalassemia: A study from rural Northern India. Asian Hemat Res J 2021;5:20-6.
23. Mahmoud RA, Khodeary A, Farhan MS. Detection of endocrine disorders in young children with multi-transfused thalassemia major. Ital J Pediatr 2021;47:165.
24. Jena I, Ganguly S, Soren NN. Clinical profile of children with thalassemia major aged 5 to 14 years. WJPMR 2020;6:270-5.
25. Sudhakar C, Priyank S, Sudaram M, Rajashekar. Clinical profile of transfusion-dependent thalassemia major children with reference to serum ferrintin and liver function: A prospective observational study. Asian J Med Sci 2023;14:260-65.
26. Abdelmotaleb GS, Behairy OG, El Azim KEA, Abd El-Hassib DM, Hemeda TM. Assessment of serum vitamin D levels in Egyptian children with beta-thalassemia major. Egypt Pediatric Association Gaz 2021;69:20.
27. Sultan S, Irfan SM, Ahmed SI. Biochemical markers of bone turnover in patients with β-thalassemia major: A single center study from Southern Pakistan. Adv Hematol 2016;2016:5437609.
28. Ahmed Z, Pushpanjali, Kausar MS, Sinha D. Study of serum calcium, phosphorus and vitamin D status in multi-transfused β-thalassemia major children and adolescence of Jharkhand, India. Int J Contemp Pediatr 2019;6:598-601.
29. Gombar S, Parihar K, Choudhary M. Comparative study of serum ferritin and vitamin D in thalassemia patients with healthy controls. Int J Res Med Sci 2018;6:693-5.
30. Bashir A, Habib K, Lail A, Shah MA, Memon NA, Dahri ZA. Status of vitamin D and evaluation of growth parameters seen in the children suffering from thalassemia major. PJMHS 2023;17:587-9.
31. Tangngam H, Mahachoklertwattana P, Poomthavorn P, Chuansumrit A, Sirachainan N, Chailurkit L, *et al*. Under-recognized hypoparathyroidism in thalassemia. J Clin Res Pediatr Endocrinol 2018;10:324-30.
32. De Sanctis V, Soliman AT, Canatan D, Elsedfy H, Karimi M, Daar S, *et al*. An ICET- A survey on hypoparathyroidism in patients with Thalassaemia major and intermedia: A preliminary report. Acta Biomed 2018;88:435-44.
33. Agrawal A, Garg M, Singh J, Mathur P, Khan K. A comparative study of 25 hydroxy vitamin D levels in patients of thalassemia and healthy children. Int J Pediatr Res 2016;3:652-6.
34. Shah B, Gosai D, Shah H. Study of vitamin D status and bone age in children with thalassemia major. Int J Med Sci Clin Int (IJMSCI) 2017;4:2639-41.
35. Jauhari RMZ, Cahyadi A, Andarsini MR, Ugrasena IDG, Larasati MCS. Correlation between serum ferritin level and vitamin D Hydroxycholecalciferol (25OH) level in children with transfusion dependent thalassemia. IJRP 2021;83:103-9.