IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 3 Ver.17 March. (2018), PP 60-63
www.iosrjournals.org

Assessment of Vitamin D levels and Parathyroid Hormone levels in children with Beta Thalassemia major, and to compare their respective values with age and sex matched controls

Dr Vijay Kumar Aggarwal[1], Dr Vineet Popli[2], Dr Vibha Uppal[3]
[1,2]*Department of Paediatric Dr Baba Saheb Ambedkar Medical College & Hospital, India*
[3]*Department of Biochemistry, VMMC &Safdarjung Hospital, India*
Corresponding author: Dr Vineet Popli

Abstract: *Beta Thalassemia major (thalassemia) is a heterogeneous inherited disorder of haemoglobin synthesis[1]. There is ineffective erythropoiesis and anemia[2]. Regular blood transfusions and chelation therapy has noticeably prolonged survival in thalassemic patients[1] however they suffer growth, multiple endocrine and metabolic abnormalities. There is gross derangement of Calcium homeostasis in multi- transfused thalassemic patients. Both defective syntheses of 25 OH vitamin D (25OH D) and/or hypoparathyroidism are seen in these patients, which negatively affects their bone metabolism[3]. Sixty Beta Thalassemia children (cases) and an equal number of age, sex matched apparently healthy children (controls) were included in this study. After recording of history and thorough clinical examination blood samples from cases and controls were collected and tested for Vitamin D level, Serum Parathyroid level. Results were compared with age specific normal values. It was observed that Vitamin D levels were significantly deficient (66.67%) in thalassemic patients than controls (P value<.0001). Only 16.6% cases were having sufficient Vitamin D levels in comparison to 30% control. Most of the children cases and controls had insufficient vitamin D levels but it was far more in thalassemic children. There was no significant difference in the median PTH levels in cases (31.15) and controls (29.1) (P value 0.902).*

Date of Submission: 15-03-2018 Date of acceptance: 30-03-2018

I. Introduction

In India Beta Thalassemia affects over 1 lakh people and more than 8000 thalassemic children are born every year[1]. Thalassemia is a heterogeneous inherited disorder of haemoglobin synthesis[2]**.** There is ineffective erythropoiesis and anaemia. Beta-thalassemia major usually presents at 4 - 6 months of life, following weaning of protective effect of high Hb F concentration at birth. Most patients require blood transfusion every 2-4 weeks commencing at around 1 year of age[2].

Regular blood transfusions and chelation therapy have noticeably prolonged survival in thalassemic patients. Despite a significant increase in the lifespan of these patients, they suffer from multiple abnormalities probably due to iron overload, including endocrinal abnormalities such as hypogonadism, diabetes mellitus, hypothyroidism and hypoparathyroidism[1].

It is observed that calcium homeostasis is grossly deranged in β-thalassemic multi- transfused patients. Defective synthesis of 25 OH vitamin D (25OH D) and/or hypoparathyroidism are seen in these patients which negatively affects their bone metabolism[3].There is paucity of data in Indian population regarding the Vitamin D level and Parathyroid hormone levels in Beta-Thalassemia children. This prompted us to plan a study aiming to assess various parameters including, Vitamin D, Parathyroid hormone(PTH), Calcium, Alkaline Phosphatase(ALP), and Phosphorous levels in these children receiving regular packed red cells transfusion and chelation therapy.

II. Materials and methods

The present case-control study was conducted in Department of Paediatrics, at Dr.Baba Saheb Ambedkar Medical College and Hospital, during the period of August 2015 to November 2016.

The study was approved by the scientific and ethical committee of the Institute.

Sixty Beta Thalassemia children (cases) in the age-group of 1 to 12 years and an equal number of age, sex matched apparently healthy children (controls), were included in this study, after informed consent of parents/guardians. Healthy controls were children coming to hospital for minor illnesses and immunisations.

After recording of complete history and clinical examination on a predesigned Performa, blood samples from both cases and controls, were collected in Serum Separator Tubes (SST) and processed at the

designated testing facility, maintaining strict cold chain during transportation. All blood samples were tested for Vitamin D levels, Serum Parathyroid levels, Serum Calcium, Serum Phosphorous, and Serum Alkaline Phosphate (ALP).

The assays for Serum parathyroid hormone(PTH) levels and Serum 25 hydroxyvitamin D were measured by Chemiluminscence immunoassay(CLIA)[4]using Beckman coulter machine BECKMAN ACCESS2[@]and serum calcium levels, were measured by ARSENAZO 3 method[5], phosphate levels by Phosphomolybdate enzyme method[6] and Serum alkaline phosphatise(ALP) were measured by Para-Nitro Phenyl Phosphate AMP method[7]using OLYMPUS AU400[@].

Data was compiled in MS Excel sheet. Statistical testing was conducted with the Statistical Package for the Social Science system SPSS 20.0. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

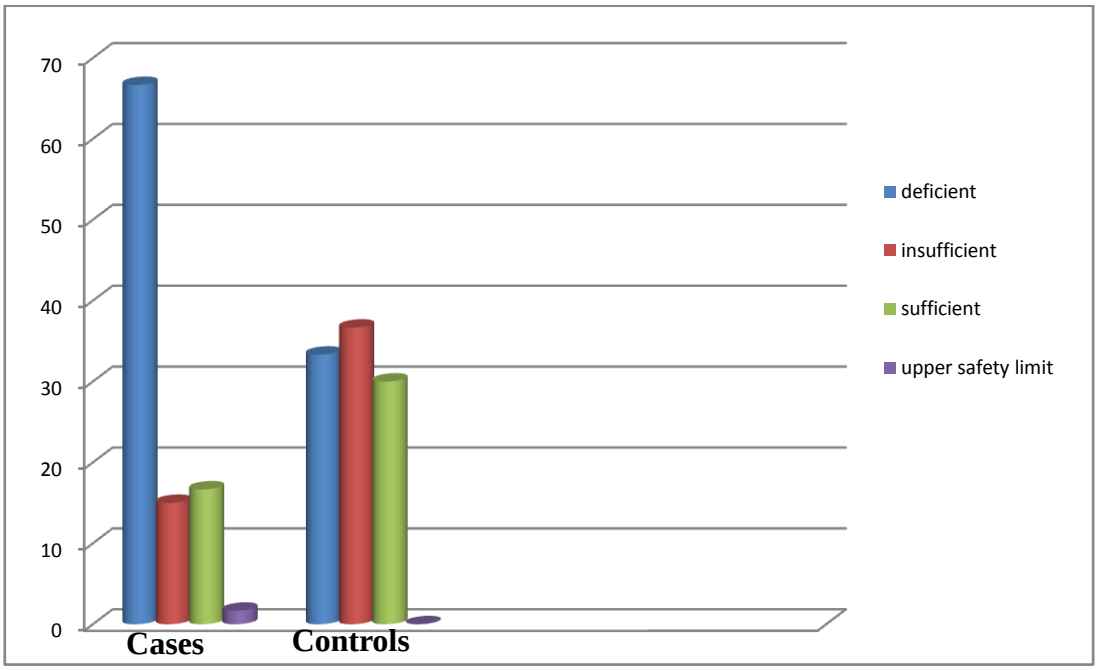
III. Results

The study included 60 Beta-thalassemia major children (**cases**) and 60 normal healthy children **(controls**).

Table no 1. Shows the descriptive characteristics and laboratory parameters.

Parameter	Cases (mean value)(60)	Controls (mean value)(60)	P-value
Age (years)	5.52+/-2.89	5.73+/-3.32	0.91
Sex	M:F 44:16	M:F 36:24	0,121
ALP(IU/L)	256.08+/-98.18	208.62+/-104.66	0.006
PHOSPHATE(MG/DL)	5.28+/-0.67	4.82+/-0.85	0.002
CALCIUM(MG/DL)	9.49+/-0.55	9.11+/-0.75	0.002
25 OH VITAMIN D(NG/ML	19.73+/-17.85	25.75+/-11.63	0.002
PTH (PG/ML)	39.31+/-40.14	33.94+/-22.95	0.902

The study showed significantly deficient Vitamin D levels in cases alongside with significantly higher phosphate levels and ALP levels than controls. The Calcium levels and PTH levels were not significantly different in both the groups



Graph no 1: Showing distribution of cases and controls on the basis of Vitamin D levels.

Vitamin D levels were significantly deficient (66.67%) in cases than in controls. Only 16.6% cases were having sufficient Vitamin D levels in comparison to controls (30%)..The mean value of vitamin D levels in cases was (19.73 ± 17.85ng/ml), as compared to controls (25.75 ± 11.63ng/ml).

IV. Discussion

Our study showed that there was significant Vitamin D deficiency in cases as compared to controls, which is in concurrence with many earlier studies mentioned below in Table no 2[2,8,9,10,11,12].

Table no 2: Depicting studies showing status of Vitamin D in Beta Thalassemic Children

STUDIES	DEFICIENT	INSUFFICIENT	P-VALUE
PRESENT STUDY	66.67%	15.00%	<0.001
Fahim FM(2013)	37%	54%	<0.001
Saffari F(2012)	45.5%	24.7%	<0.002
Wood JC(2008)	54.16%	41.16%	<0.001
Isik P(2014)	78.2%	-	<0.002
Nakavachara(2013)	89.9%	-	<0.01
Singh K(2012)	80.67%	-	<0.01

Low serum 25-OH vitamin D levels can be attributed to malabsorption of Vitamin D as well as hepatic dysfunction, which also leads to defective hydroxylation of vitamin D resulting in its paucity. Some researchers have attributed the etiology of Vitamin D deficiency to hepatic iron overload[3]. In our study, Vitamin D deficiency was recorded in more than 80% of cases. Multiple factors have been attributed to growth faltering in Thalassemia, some of which like Vitamin D deficiency can be easily monitored and corrected.

Table No 3: Showing Median Vitamin D levels and Parathyroid Hormone levels in cases and controls in present study:

Parameter	Case (Median)	Controls(Median)	P-Value
Vitamin D(ng/ml)	12.85	24.6	<0.001
Parathyroid Hormone (pg/ml)	39.31	33.94	0.902

There is gross deficiency of Vitamin D in cases. Serum PTH levels were not significantly different between cases (39.31 pg/ml) and controls (33.94 pg/ml). In different previous studies the incidence of hypo parathyroid varies from 0% to 22.5% of patients[13-20]although overt hypoparathyroidism is very rare and even subtle abnormalities are not well established in these cases. Majority of cases of hypoparathyroidism in Beta-Thalassemic children were seen in second decade of life[1,13-22].Parathyroid hormone levels is chiefly regulated by alteration in calcium levels in the body along with Calcitonin. Vitamin D directly affects calcium absorption and its excretion[1]. Hence, it is suggested that supplementation with Vitamin D and Calcium would greatly help in normalisation of function of parathyroid gland and serum parathyroid hormone levels.

In the present study, the serum level of calcium was found in eucalcemic range in both the groups. In literature, many studies have shown serum calcium level in thalassemic children to vary from hypocalcemia to hypercalcemia with no consensus. Normal serum calcium levels in this study can be explained, as in young children, during early stages of Vitamin D deficiency, decreased intestinal calcium absorption leads to moderate and/or intermittent increase of PTH and also stimulates the production of 1,25Dihydroxy Vitamin D that increases calcium absorption from the gut, and ensures maintenance of normal serum calcium concentration, important for adaptive stage[3].

The phosphate levels were found to be significantly high in cases (5.3 mg/dl) in comparison to controls (4.8 mg/dl) and these results were in agreement to various previous studies[1, 23,24]. ALP levels in our study were found statistically significantly high in cases than in controls. It basically represents the presence of high bone turnover rate in the cases[23,24].

V. Conclusion & Recommendations

We conclude that Vitamin D deficiency is significantly prevalent even among apparently healthy children in our country but it is far more in children affected by B-thalassemia, probably because of iron overload following repeated blood transfusions. Hence, it is suggested that Vitamin D supplementation in these children must be started early in life.

Due to very high prevalence of Vitamin D deficiency in these children, it would be a very cost effective therapy to supplement adequate vitamin D to all children with thalassemia major, even where the facilities for its estimation are not available. Therapy is relatively easier and with no adverse effects if instituted properly under medical supervision.

Supplementation with vitamin D in these children would also help in normalisation of various other growth markers such as calcium, phosphorous and ALP, as they are directly affected by vitamin D activity.

We should try to screen all B-thalassemic children for parathyroid hormone abnormalities at regular intervals especially from the end of first decade of life, so as to detect early alterations, if any and treat the same.

References

[1]. Basha KP, ShettyB, Shenoy UV. Prevalence of Hypoparathyroidism (HPT) in Beta Thalassemia Major. Journal of Clinical and Diagnostic Research. 2014 Feb; 8(2):24-26.
[2]. Fahim MF, Saad K, Askar EA, et al. Growth Parameters and Vitamin D status in Children with Thalassemia Major in Upper Egypt. IJHOSCR. 2013 Oct 1; 7(4):10-14.
[3]. Soliman A, De Sanctis V, Yassin M. Vitamin D status in thalassemia major-an update. Mediterr J Hematol Infect Dis. 2013; 5(1): e2013057.
[4]. Burtis CA, Ashwood ER, Bruns DE. Tietz Fundamentals of Clinical Chemistry. Optical techniques. 6th ed. St.Louis, Missouri: Elsevier; 2008. p.79-80.
[5]. Bauer PJ. Affinity and stoichiometry of calcium binding by arsenazo III. Anal Biochem. 1981;110:61-72
[6]. Daly JA, Ertingshausen G. Direct method for determining inorganic phosphate in serum with the "CentrifiChem". ClinChem 1972; 18(3):263-5.
[7]. Tietz NW, Rinker D, Shaw LM. IFCC methods for the measurement of catalytic concentration of enzyme Part 5.IFCC method for alkaline phosphatise. J ClinChemClinBiochem 1983; 21:731-48.
[8]. Saffari F, Mahyar A, Jalilolgadr S. Endocrine and metabolic disorders in B thalassemia major patients. Caspian J Intern Med. 2012; 3(3): 466-472
[9]. Wood JC, Claster S, Carson S, et al. Vitamin D deficiency, cardiac iron and cardiac function in thalassaemia major. Br J Haematol. 2008 Jun; 141(6):891–894.
[10]. Isik P, Yarali N, Tavil B, et al. Endocrinopathies in Turkish children with Beta thalassemia major: results from a single center study. PediatrHematolOncol. 2014 Oct; 31(7):607-15
[11]. 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 Oct; 60(10):1683-8.
[12]. Singh K, Kumar R, Shukla A, et al. 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.
[13]. Perignon F, Brauner R, Souberbielle JC, et al. Growth and endocrine function in major thalassemia. Arch Fr Pediatr. 1993; 50(8): 657-63.
[14]. Sharma R, Seth A, Chandra J, et al. Endocrinopathies in adolescents with thalassaemia major receiving oral iron chelation therapy. PaediatrInt Child Health. 2014 Oct 13.
[15]. G Meenu, Abrol P, Lal H. Parathyroid and Calcium Status in Patients with Thalassemia. Indian J ClinBiochem. 2010 Oct; 25(4):385–387.
[16]. Tantawy AA, El Kholy M, MoustafaT, et al. Bone mineral density and calcium metabolism in adolescents with beta-thalassemia major. PediatrEndocrinol Rev. 2008 Oct; 6 Suppl 1:132-5.
[17]. Angelopoulos NG, Goula A, Rombopoulos G, et al. Hypoparathyroidism in transfusion-dependent patients with beta-thalassemia. J Bone Miner Metab. 2006; 24(2):138-45.
[18]. Shamshirsaz AA, Bekheirnia MR, Kamgar M, et al. Metabolic and endocrine complications in B thalassemis major: multi centre study in Tehran. BMC EndocrDisord. 2003; 3: 4.
[19]. Aleem A, Al-Momen AK, Al-HarakatiMS, et al. Hypocalcemia due to hypoparathyroidism in beta-thalassemia major patients.Ann Saudi Med. 2000 Sep-Nov; 20(5-6):364-6
[20]. Gabriele O. Hypoparathyroidism associated with thalassemia. South Med J. 1971; 64:115-6
[21]. Vogiatzi MG, Macklin EA, Trachtenberg FL, et al. Differences in the prevalence of growth, endocrine and vitamin D abnormalities among the various thalassemia syndromes in North America. Br J Haematol. 2009 Sept; 146(5): 546-556
[22]. Chern JP, Lin KH. Hypoparathyroidism in transfusion dependent patients with B thalassemia. PediatrHematolOncol. 2002 May; 24(4): 291-3.
[23]. Salama OS, Al-tonbary YA, Shahin RA, et al. Unbalanced bone turnover in children with B. Thalassemia. Hematology. 2006; 11(3): 197-202. .
[24]. Mirhosseini NZ, Shahar S, Ghayour-Mobarhan M, et al. Bone-related complications of transfusion-dependent beta thalassemia among children and adolescents. J Bone Miner Metab. 2013 Jul; 31(4):468-76

Dr VINEET POPLI Corresponding Author "Assessment of Vitamin D levels and Parathyroid Hormone levels in children with Beta Thalassemia major, and to compare their respective values with age and sex matched controls."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 3, 2018, pp 60-63.