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Study of Vitamin B12 Deficiency in Thalassemic Children with Special Reference to Clinical and Biochemical Correlation.

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ABSTRACT

Background: Beta Thalessemia is the most common hemolytic disease in children. The disease is characterized by microcytic hypochromic anemia. The bone marrow responds to chronic hemolysis by increased RBC production and therefore results in relative deficiency of vitamin B 12. The peripheral smear & blood indices does not pick up this deficiency due to predominant microcytic nature of anemia in this condition. **Methods:** We studied the level of vitamin B 12 in randomly selected 97 beta Thalassemic children enrolled in the regular blood transfusion programme at the tertiary care hospital to know the prevalence of vitamin B12 deficiency & its correlation with the clinical manifestations in the patients. ?. **Results & Conclusion:** This study illustrated the masked vitamin b12 deficiency amongst the beta Thalessemia patients included. A correlation too has been observed between the serum levels of vitamin b12 deficiency and its signs and symptoms in the Thalessemia children studied, though it was not found to be statistically significant may be due to less sample size.

Keywords: beta Thalessemia, vitamin b12.

INTRODUCTION

β – Thalassemia is the most common genetically transmitted hematological disorder in Indian children.[1] The thalassemia syndromes are a heterogeneous group of inherited disorders characterized by decreased either β or α globin chain synthesis. β homozygous thalassemia state presents with variable degree of anemia from early childhood and are generally transfusion dependent, a condition, clinically known as thalassemia major.[2]

The disease is characterized by microcytic hypochromic anemia. The bone marrow responds to chronic hemolysis by increased RBC production. Increased erythropoiesis results in relative deficiency of folic acid and vitamin B 12.

Vitamin B12 is classified as a water-soluble vitamin that is fundamental for cellular metabolism and appropriate nervous system functioning. Vitamin B12 deficiency can lead to inefficient erythropoiesis, megaloblastic anemia, and neuropsychiatric manifestations such as neuropathy, myelopathy, depression, and dementia,[3] Vitamin B12 level is generally evaluated in patients with macrocytic anemia; however, it ought to be remembered that its deficiency in some individuals could be unacknowledged due to other associated conditions as thalassemia minor or iron deficiency that would conceal the macrocytosis.[4] Many physicians and healthcare providers overlook cobalamin deficiency until the patient develops macrocytic anemia, which is often a late sign of advanced vitamin B12 disease.[5] MCV should not be the only parameter used to diagnose vitamin B12deficiency.[6,7]

The peripheral smear and blood indices does not pick up vitamin b12 deficiency due to predominant microcytic nature of anemia in this condition. All Thalessemic children are routinely supplemented with folic acid, calcium, zinc and multivitamins at our institute. Ferritin is a 450 kDa protein consisting of 24 subunits that is present in every cell type.[8] The ferritin levels measured have a direct correlation with the total amount of iron stored in the body including cases of anemia of chronic disease.[9] Ferritin is also used as a marker for iron overload disorders, such as hemochromatosis and porphyria in which the ferritin level may be abnormally raised.[10]

We studied the level of vitamin B 12 in randomly selected 97 Thalessemic children enrolled in regular

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blood transfusion programme at the tertiary care hospital (CIVIL HOSPITAL, AHMEDABAD) to know the prevalence of vitamin B12 deficiency and its correlation with clinical manifestations in them.

MATERIALS AND METHODS

The Study period was from November 2017 up to April 2018. The study is a prospective one.

Inclusion criteria:
All the confirmed cases of Beta Thalessemia major from the age of six months to 12 years were included.

Exclusion criteria:
The children with classical manifestation of infantile tremor syndrome were excluded.

The detailed history and complete examination was done after the informed consent of patient's relatives. The data were entered in the Performa. The serum sample for B12 was collected pre transfusion in all Beta Thalessemia patients. The data was analyzed. . Serum vitamin B12 concentration was evaluated by solid phase, competitive chemiluminescent assay method.[11]

RESULTS

Table 1: Comparison between male and female having thalessemia according to the age groups

Age (years)	Male	Female	Total (n)	Percentage (%)
1-5	11	06	17	17.53
5-10	21	16	37	38.14
	24	19	43	44.33
Total	56	41	97	100

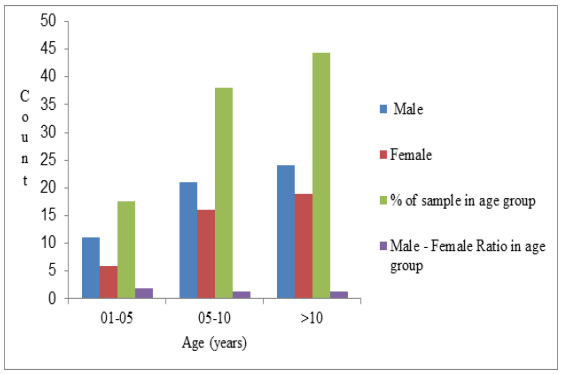

Figure 1: sample distribution according age and sex of thalessemia children.

Table 2: Gender wise distribution of thalessemic patients according to age at first transfusion.

Age	Male	Female	Total (n=97)	Percentage (%)
0-6 m	20	17	37	38.14
6 m-1yr	21	11	32	32.99
1-2yr	04	01	05	5.15
>2yr	16	07	23	23.72

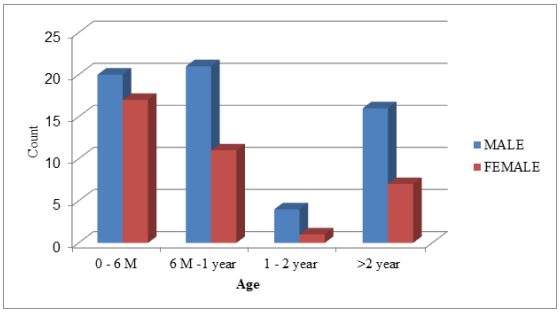

Figure 2: Graphical presentation of beta Thalessemia patients in accordance to age at first blood transfusion.

Table 3: Gender wise distribution of thalessemic patients and average pre blood transfusion level of hemoglobin.

Hemoglobin level	Male	Female	Total	Percentage (%)
9 -10 (moderate transfusion regime)	20	10	30	30.9
10-11 (hyper transfusion regime)	15	09	24	24.7
>11 (super transfusion regime)	02	04	06	6.1

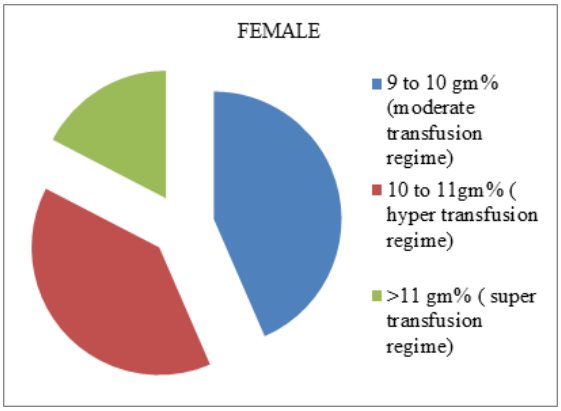

Figure 3(a): graphical presentation of average pre transfusion hemoglobin level amongst females

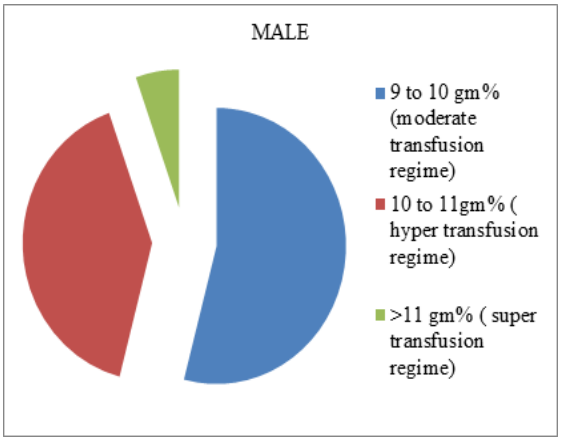

Figure 3(b): graphical presentation of average pre transfusion hemoglobin level amongst males

Table 4: Gender wise distribution of Thalessemia children taking blood transfusion at regular intervals.

Days	Male	Female	Total(n=97)	Percentage (%)
<15 days	15	14	29	29.9
15-21 days	25	06	31	31.96
>21 days	20	17	37	38.14

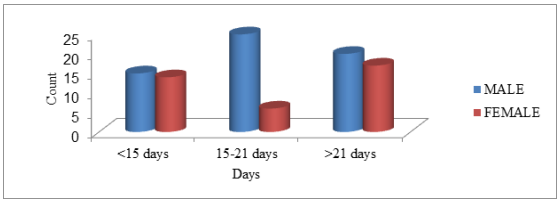

Figure 4: graphical presentation of Table IV.

Table 5: gender wise distribution of Thalessemia children taking tablet Deferasirox as an iron chelating agent.

Deferasirox dose (mg/kg)	Male	Female	Total (N=97)	Percentage (%)
<25	20	10	30	30.9
25-40	29	04	33	34.0
>40	10	24	34	35.1

Table 6: Average serum ferritin level in Thalessemia children.

Average ferritin level (measured quarterly)	Male	Female	Total (N=97)	Percentage (%)
<1000 mg/dl	02	04	06	6.1
1000-5000 mg/dl	40	33	73	75.3
5000-10000mg/dl	07	10	17	17.5
>10000 mg/dl	01	-	01	1.1

Table 7: serum vitamin b12 level amongst Thalessemia males and females.

Vitamin b12 level (pg/ml)	Male	Female	Total(n=97)	Percentage (%)
<206	33	18	51	52.8
>206	24	22	46	47.42

Normal reference range 206-678 pg/ml at institute lab.

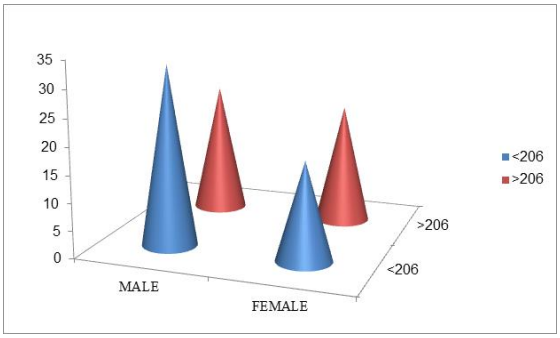

Figure 5: graphical presentation of Table 7.

Table 8: Signs of vitamin b12 deficiency amongst thalessemic children , male and females.

Signs of vitamain b12 deficiency	Male	Female	Total (N=97)	Percentage (%)
Knuckle hyper-pigmentation	38	22	60	61.8
Memory disturbances	07	09	16	16.5
Tingling sensation in hand and foot	11	03	14	14.4
Tremors	03	04	07	7.3

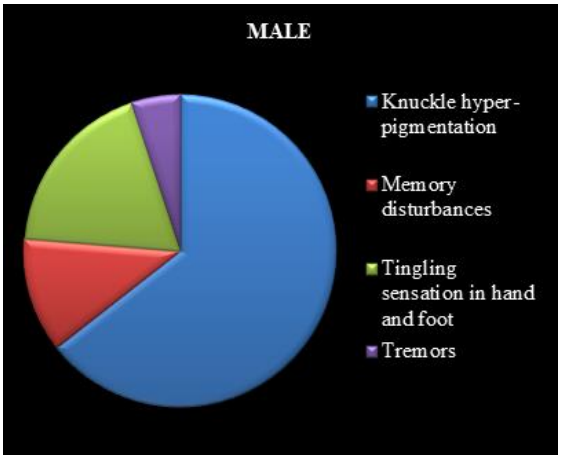

Figure 6(a): pie chart representing signs of vitamin b12 deficiency amongst beta Thalessemia males.

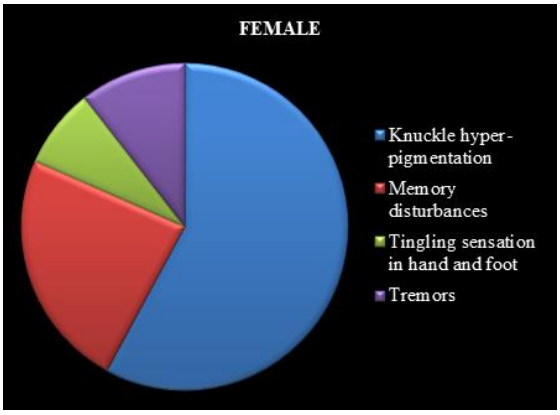

Figure 6(b): pie chart representing signs of vitamin b12 deficiency amongst beta Thalessemia females.

Table 9: Correlation between serum vitamin b12 level and signs of its deficiency amongst beta Thalessemia children.

Signs of vitamin B12 deficiency	Vitamin B12 level	
Present = 68	Normal	33
	Low	35
Absent = 29	Normal	13
	Low	16

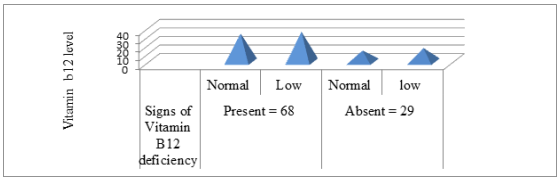

Figure 7: graphical representation of Table IX.

DISCUSSION

Out of total sample size, 56 were male and 41 were female with overall male: female ratio being 1.37:1. The maximum number of children were greater than 10 years of age.

76% children started receiving their first blood transfusion before 01 year of age. Although center was following hyper transfusion regimen and targeted to maintain pre-transfusion hemoglobin >10 gm%. The average pre-transfusion hemoglobin was observed in the range of 9.0 to 10.0 gm% in 30.9%, between 10 to 11 gm% in 24.7% and more than 11gm% in 6.2% thalessemic children. 38% of children were transfused at an average optimal interval of three weeks, the balance were required to be transfused at a shorter interval.All the children were receiving iron chelator (Deferasirox) of which 35.1% were prescribed dose more than 40 mg/kg/day to keep ferritin level low.

Only 6.1% of children could maintain their ferritin level below toxic range (<1000 mg/dl),75.3% of children had ferritin in the range of 1000-5000 mg/dl. 52.5% of the children showed deficient pre transfusion serum vitamin B12 level.

Out of total, 68 (70.1%) children had various clinical signs of vitamin B12 deficiency. The most common sign was knuckle hyper pigmentation of all four limbs (61.8%) followed by memory disturbance in 16.5%. Out of 68 children having clinical signs of vitamin B12 deficiency, 35 children also had low serum levels of vitamin B12. In 33 children vitamin B12 level was normal. In contrast 16 children with low levels of vitamin B12 level had no obvious clinical signs.

CONCLUSION

Out of total 97 patients of Beta thalessemia major studied; 68 patients were found to exhibit one or more clinical signs and symptoms of vitamin B12 deficiency. Amongst these 68 patients ,35 were found to have low levels of serum vitamin B12 and 33 were found to have the serum levels within the normal range. Amongst 29 patients having no clinical signs and symptoms of vitamin B12 deficiency, 16 were having low serum values for serum vitamin B12, which might be subjected to occult / preclinical stage of vitamin B12 deficiency.

However 33 patients were found to have levels of vitamin B12 within normal range, despite having one or more signs and symptoms of vitamin B12 deficiency, which might be due to prior therapy or false normal and which may require repeat measurement of serum levels. The Correlation between the serum vitamin B12 level and signs and symptoms of its deficiency was analyzed statistically using chi square test and p value . It was statistically not significant owing to the small size of sample included in the study.

Werbach MR,[12] have reported food and nutrient intake differences between Beta Thalessemia and healthy subjects. They also observed β Thalassemic patients have a lower intake of most vitamins and were less likely to have consumed fruit, vegetables, vitamins and mineral supplement.[13-15] Biochemical screening of ferritin and vitamin B12 is of paramount importance in all patients of Beta Thalessemia major. Increased levels of ferritin and vitamin B12 deficiency should be treated in the setting.

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