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Original Research Article

Clinical Study of Growth, Nutrition and ThyroidDysfunction in Children with Beta Thalassemia

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Abstract

Background: Thalassemia is a hereditary anaemia resulting from defect in haemoglobin production and the most common genetic disorders worldwide. The aim of this case control study was to know the growth patterns and thyroid dysfunction in beta thalassemia major patients.

Materials and Methods: This study was conducted in the Department of Paediatrics, BMIMS Pawapuri, over a period of two years. The study included 50 homozygous thalassemia major patients, receiving regular blood transfusion and 50 normal children were taken as controls.

Conclusion: Thalassemia major patients with iron overload had decreased weight for age, height for age and increased TSH suggestive of subclinical hypothyroidism. Awareness of these findings is helpful to avoid unnecessary evaluation in patients with beta thalassemia. Better evaluation of iron toxicity can protect patients fromcomplications associated with treatment.

Keywords: Thalassemia; Anaemia; Growth; Thyroid Dysfunction.

Introduction

Thalassemia refers to a spectrum of diseases characterized by the reduction or absence in the synthesis of the globin chains of haemoglobin. Worldwide, approximately 15 million people are estimated to suffer from thalassemic disorders. Reportedly, there are about 240 million carriers of β-thalassemia worldwide [9-11], i.e. 1.5% of world population, and in India alone, the number is approximately 30 million with 505 in S.E.Asia [9-11]. The burden of Haemoglobinopathies in India is high with nearly 12,000 infants being born every year with a severe disorder. These numbers imply that every hour 1 child is born who will suffer with this genetic disorder. The carrier rate for β - thalassemia varies from 1-17 % in India with an average of 3.2% [12-13]. This means that on an average 1 in every 25 Indians is a carrier of thalassemia. Thalassemia exists in 3 forms:

Thalassemia trait or the asymptomatic carrier stage – The carrier does not exhibit any symptoms and leads an absolutely normal life

Thalassemia intermedia – Genotypically the patient is similar to a thalassemia major but differs phenotypically in that they do not require regulartransfusions

Thalassemia major – In β thalassemia major, the production of β-globin chainsis severely impaired, because both β-globin genes are mutated.

The severe imbalance of globin chain synthesis results in ineffective erythropoiesis and severe microcytic, hypochromic anaemia. Clinical presentation of thalassemia major occurs at 6 months of age. Affected infants fail to thrive and become progressively pale. Feeding problems, diarrhoea, irritability, recurrent boutsof fever, and progressive enlargement of the abdomen due to splenomegaly may occur. Patients are treated by lifelong blood transfusion every 15 to 30 days alongwith iron chelation therapy. The cost of treatment of a 4-year-old thalassemic child is around Rs.90,000 – 1,00,000 annually. The only cure available today is bone marrow transplantation which is largely unaffordable to the large majority of the Indianchildren. Thyroid dysfunction has been reported in 13 – 60% of patients with thalassaemia, but its severity is variable. This variation has been attributed to difference in treatment protocols including different transfusion rates and chelation therapies in different centres. The commonest form of thyroid dysfunction seen in thalassaemics is primary hypothyroidism which leads to insufficient production of the thyroid hormones. Prevalence of overt hypothyroidism as a complication of thalassaemia major is relatively low, milder forms of thyroid dysfunction are much more common. Thalassaemic patients having thyroid dysfunction have shown a greater incidence of other complications including multiendocrine dysfunction, worsening of already compromised cardiac function, more pronounced growth retardation, liver disease and need for splenectomy during the course of the disease Hence, I intend to do a study on the evaluation of the growth and nutritional status and thyroid dysfunction in children with beta thalassemia major.

Objectives

To assess growth patterns and nutritional status in children with betathalassemia

To assess thyroid hormone function in children with beta thalassemia

Materials and methods

The proposed study was a hospital-based case control study conducted in the Department of Paediatrics, Bhagwan Mahavir Institute of Medical Science Pawapuri**,** over a period of two years. The study included 50 homozygous thalassemia major patients, receiving re Source of data was children between 3 years to 18 years diagnosed with beta thalassemia attending the Paediatric OPD or IP patients.

Inclusion criteria

Children between 3 years to 18 years diagnosed with beta thalassemia.

Exclusion criteria

Children with other haematological disorders.

Age > 18 years.

It included obtaining history from the parents of thalassemic children followed by thorough clinical examination including anthropometry followed by blood investigations which include haemoglobin levels, serum ferritin and thyroid function tests. Nutritional status of the subjects will be classified by percent weight and height for age. gular blood transfusion and 50 normal children were taken as controls.

The haematological investigations were carried out before transfusion. Diagnosis of subclinical hypothyroidism is made when the T3 and T4 levels are within normal range and TSH is elevated. Overt hypothyroidism is termed when the T3 & T4 levels are decreased and TSH levels are elevated.

Therefore the sample size is rounded to 50 cases and 50 controls.

This formula is based on 5% level of significance and 80% power of the study.

Results

The aim was to study the growth and nutrition patterns and thyroid dysfunction in patients with beta thalassemia major. The

outcomeof 50 cases were compared with 50 controls during a two year.

Table 1 Age Distribution

Age (Yrs)	Cases (n=50)		Controls (n=50)	
	No.	%	No.	%
3 – 6	16	32.0	21	42.0
6 – 12	25	50.0	26	52.0
12 – 16	9	18.0	3	6.0
Total	50	100.0	50	100.0
Mean ± SD	7.9 ±3.9		6.8 ±3.0	
Range	3 -16 yrs		3 - 14 yrs	
Cases v/s Controls	**t = 1.59, P = 0.12, NS**			
Unpaired t test				
P > 0.05, Not Sig.				

Table 1 shows age wise distribution, 50% of cases and 52% of controls were between6 – 12 years.

Table 2 Sex wise Distribution

Gender	Cases (n=50)		Controls (n=50)	
	No.	%	No.	%
Male	32	64.0	28	56.0
Female	18	36.0	22	44.0
Total	50	100.0	50	100.0
Cases v/s Controls	**X^2 = 0.67, P = 0.41, NS**			
Chi-square test				
P > 0.05, Not Significant				

Table 2 shows sex wise distribution, 64% of cases and 56% of controls were males.

Table 3 Religion wise Distribution

Religion	Cases (n=50)		Controls (n=50)	
	No.	%	No.	%
Hindu	39	78.0	43	86.0
Muslim	11	22	7	14.0
Total	50	100.0	50	100.0
Cases v/s Controls	X^2 = 1.08, P = 0.30, NS			
Chi-square test				
P > 0.05, Not Significant				

Table 3 shows religion wise distribution, 78% of cases and 86% of controlswere Hindus.

Table 4 Weight for age percentile distribution for two groups

Wt. for agepercentile	Cases (n=50)		Controls (n=50)	
	No.	%	No.	%
$<3^{rd}$	10	20.0	0	0.0
$>3^{rd}$ & $<15^{th}$	11	22.0	2	4.0
$>15^{th}$ & $<50^{th}$	28	56.0	42	84.0
$>50^{th}$ & $<85^{th}$	1	2.0	4	8.0
$>85^{th}$ & $<97^{th}$	0	0.0	2	4.0
Total	50	100.0	50	100.0

Cases v/s Controls	**X^2 = 22.83, P < 0.001, HS**
Chi-square test	
P < 0.001, Highly Significant	

Table 4 shows weight for age distribution: Among cases 20% were < 3rd centile, 22% were between 3rd and 15th centile and 56% were between 50th and 85th centile.

Table 5 Haemoglobin Level

Hb level(g/dl)	**Cases (n=50)**		**Controls (n=50)**	
	No.	**%**	**No.**	**%**
5.0 - 7.0	16	32.0	0	0.0
7.0 - 10.0	34	68.0	0	0.0
10.0 - 12.0	0	0.0	17	34.0
12.0 - 16.0	0	0.0	33	66.0
Total	50	100.0	50	100.0
Mean ± SD	7.53±1.05		12.18±1.42	
Range	5.4 - 9.2		10.0 - 15.6	
Cases v/s Controls	**t = 18.64, P < 0.001, HS**			
Unpaired t test				
P < 0.001, Highly Significant				

Table 5 shows Haemoglobin level distribution:among cases 32% had hb between 5.0-7.0g/dl and 68% had Hb between 7.0 – 10.0 g/dl. All controls had Hb levels withinnormal limits.

Table 6 T3 levels in two groups

T3 (ng/dl)	**Cases (n=50)**		**Controls (n=50)**	
	No.	**%**	**No.**	**%**
60-100	15	30.0	19	38.0
100-150	29	58.0	23	46.0
150-200	6	12.0	8	16.0
Total	50	100.0	50	100.0
Mean ± SD	118.4 ± 28.3		115.5 ± 31.9	
Range	66 - 183 -		71 - 195	
Cases v/s Controls	**t = 0.47, P = 0.64, NS**			
Unpaired t test				
P > 0.05, Not Significant				

Table 5 shows T3 distribution: both cases and controls had normal T3 levels

Table 7 T4 levels in two groups

T4 (µg/dl)	**Cases (n=50)**		**Controls (n=50)**	
	No.	**%**	**No.**	**%**
2.5-6.0	12	24.0	5	10.0
6.0 - 9.0	24	48.0	30	60.0
9.0 - 12.0	14	28.0	15	30.0
Total	50	100.0	50	100.0
Mean ± SD	7.63 ± 2.19		8.03 ± 1.61	
Range	2.6 - 12.0		5.2 - 11.0	
Cases v/s Controls	**t = 1.05, P = 0.30, NS**			
Unpaired t test				
P > 0.05, Not Significant				

Table 7 shows distribution of T4: both cases and controls had normal T4 levels.

Table 8 TSH Levels in two groups

TSH (µIU/ml)	Cases (n=50)		Controls (n=50)	
	No.	%	No.	%
0.3 - 5.0	42	84.0	50	100.0
> 5.5	8	16.0	0	0.0
Total	50	100.0	50	100.0
Mean ± SD	3.11 ± 2.85		2.20 ± 1.18	
Range	0.76 - 12.8		0.72 - 4.56	
Cases v/s Controls	**t = 2.08, P = 0.04, S**			
Unpaired t test				
** P < 0.05, Significant*				

Table 8 shows TSH distribution:16% of cases had elevated TSH levels and allcontrols had TSH within normal limits.

Table 9. Comparison of Mean levels of study variables between two groups

Parameter	Mean ± SD		Cases v/s Controls
	Cases	Controls	P value
Hb level (g/dl)	7.53±1.05	12.18±1.42	< 0.001, HS
S. Ferritin (ng/ml)	1744.6 ± 530.6	91.6 ± 49.7	< 0.001, HS
T3 (ng/dl)	118.4 ± 28.3	115.5 ± 31.9	0.64, NS
T4 (µg/dl)	7.63 ± 2.19	8.03 ± 1.61	0.30, NS
TSH (µIU/ml)	3.11 ± 2.85	2.20 ± 1.18	< 0.05, S
Unpaired t test			
** P < 0.05, Significant*			
*** P< 0.001, HS*			
P > 0.05, Not Significant			

Table 9 shows that among cases Hb levels were decreased and Serum Ferritin andTSH levels were elevated and found to be statistically significant.

Discussion

Beta thalassemia syndromes are a group of hereditary disorders characterized by a genetic deficiency in the synthesis of beta-globin chains. In the homozygous state, beta thalassemia (ie, thalassemia major) causes severe, transfusion-dependent anaemia [1]. In the heterozygous state, the beta thalassemia trait (ie, thalassemia minor) causes mild to moderate microcytic anemia. (See Etiology.) Patients in whom the clinical severity of the disease lies between that of thalassemia major and thalassemia minor are categorized as having thalassemia intermedia. Treatment for patients with thalassemia major includes long-term transfusion therapy, iron chelation, splenectomy, allogeneic hematopoietic transplantation, and supportive measures. the growth patterns and thyroid dysfunction in patients with beta thalassemia major [2]. In this study the mean age among cases was 7.9 years with range 3 – 16 years and among the controls was 6.8 years ranging from 3 – 14 years and was statistically comparable. Mean age of the patients in other studies are approximately similar to the present study [3]. The study group had 64% males and 36% females whereas the control group had 56% male and 44% females which was statistically comparable. In the present study 84% (P < 0.001, highly significant) of the cases were offsprings of consaginuosly married couples [4]. Whereas only 14% of controls were offsprings of consaginously married couples. As thalassemia is inherited as an autosomal recessive condition it is therefore more common in

children of consagniously married couples. The mean age of diagnosis of beta thalassemia in this study was 7.7 ±2.7 months [range: 6 – 18 months] In this study 10 cases [i.e 20%] were below the 3rd centile for weight for age; 22% of cases were between the 3rd and 15th centile; 56% were between 15th and 50th centile. Of the controls 84% were between 15th and 50th centile. 15 cases [i.e 30%] were below the 3rd centile for height for age and 34% each between 3rd and 15th centile and 15th and 50th centile. 94% of controls were between 15th and 50th centile. The mean Hb level among the cases was 7.53 ±1.05 g/dl [range: 5.4 - 9.2g/dl]and among the controls was 12.18 ±1.42 g/dl [range: 10.0 - 15.6 g/dl] [5]. This shows that thalassemia patients were significantly [p<0.001] anaemic. Serum ferritin among cases were significantly elevated [p < 0.001] with a mean of 1744.6 ±530.6 ng/dl [range: 1002-2981 ng/dl]. 62% of cases had serum ferritin between 1000 to 2000 ng/dl. Mean serum ferritin among controls was 91.6 ±49.7 ng/dl with a range between 14 to 190 ng/dl [6]. The mean T4 among cases [7.63 ±2.19 µg/dl] was comparable with that of cases [8.03 ±1.61 µg/dl]. However, in the study by Geetha et al T4 among cases [7.36 ±1.61µg/dl] was significantly lower than that of controls [9.30 ±2.15 µg/dl]. This was not comparable with our study. The mean TSH among cases [3.11 ±2.85 µIU/ml] was significantly higher [p<0.05] when compared to controls [2.20 ±1.18 µIU/ml]. This was comparable to thestudy done by Geetha et al. In this study the serum ferritin among the cases correlated with the age, Hband TSH. This was statically significant [p<0.05]. [7,8,14]

Conclusion

The mean age of diagnosis of beta thalassemia was 7 months

Beta thalassemia patients had significant undernourishment, stunting and anaemia

Those with iron overload have subclinical hypothyroidism which can in the long run lead to overt hypothyroidism, Though thyroid dysfunction in thalassemia may start early in life, hypothyroidism is not clinically observed in most thalassemia major patients. Therefore thyroid function should be followed periodically, particularly when other iron overload associated complications occur. Early recognition and hence prevention of these complications might help improve the quality of life of these patients.

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