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Original Research Article

Thyroid Function in Beta Thalassemia Major Children: A Cross Sectional Hospital Based Study

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Abstract

Background: Thalassemia is most common Haematological genetic disease out of which 6-30 percent have hypothyroidism. Today patient has increased life expectancy and better quality of life because of hypertransfusion therapy but this has also lead to haemosiderosis. The thyroid gland is affected much before the thyroid pituitary axis which is less susceptible then the gonadal axis to iron induced damage and with the use of Iron chelators the survival rates have improved.

Objectives: To estimate thyroid function in Beta Thalassemia major children and to determine correlation of thyroid function with Serum ferritin level.

Methods: This is a cross sectional study done in the Thalassemia Day care centre, Department of Pediatrics, Kamlaraja Hospital and J.A. Group of hospitals of G.R. Medical College, Gwalior. All diagnosed thalassemia major children of 1 to 18 years of age group were included.

Results: Among 81 Thalassemia patients, 56 patients (69.14%) were Euthyroid and 25 patients (30.6%) have hypothyroidism. Out of 25 hypothyroidism patients 18 (22.2%) were having subclinical hypothyroidism, 7 patients (8.6%) were having Primary hypothyroidism and none of the patients have secondary hypothyroidism. There were no cases of hyperthyroidism.

Conclusion: From the study it was concluded that Beta thalassemia patients have a higher chance of developing hypothyroidism. Chronicity of disease, Number of blood transfusion and levels of serum ferritin are risk factors for hypothyroidism in beta thalassemia patients. Also, there is an increased risk of Stunting among the subjects.

Keywords: Hyperthyroidism, Hypothyroidism, Serum ferritin, Thalassemia.

Introduction

Iron overload is secondary to multiple blood transfusions and increase iron absorption leads to many complications including endocrine complication. Various transfusion regimes like Palliative, Conventional, Hyper transfusion and Supersaturation transfusion are followed to maintain target HB level. If a regular transfusion program that maintains a minimum hemoglobin concentration of 9.5 to 10.5 g/ dl is initiated, growth and development tends to be normal up to 10-12 years.[1]

Almost 6 – 30 percent of all thalassemia patients develops thyroid dysfunction[2] Thyroid dysfunction mainly occurs by gland

infilteration, chronic tissue hypoxia, free radical injury and organ siderosis. Thyroid dysfunction is characterized by an elevated TSH in face of normal or reduced T3 and T4.[3] Several studies have found that Primary and Subclinical hypothyroidism occurs more frequently than overt hypothyroidism and according to Thalassemia International Federation guidelines, free T4 and TSH need to be performed annually at > 9 years in all beta thalassemia patients[4]. There is association between Thyroid functions and factors like – Age, Gender, Weight, Height, Oral Chelation therapy, Frequency of transfusions and Serum ferritin.[5]

Hypertransfusion and Supertransfusion are followed to maintain target hemoglobin level at minimum baseline level of 10-12 mg/dl but Hypertransfusion and Supertransfusion leads to hemosiderosis because 500ml blood gives 200mg of Iron which cannot be excreated by physiological means. So, this comparative study to evaluate the thyroid function status in Beta Thalassemia major children in first decade of life is the need of the hour. This study is done to assess the Thyroid function in beta thalassemia patients and various factors affecting thyroid function.

Aims and Objectives

Aims: To estimate thyroid function in beta thalassemia major children.

Objective: To determine Correlation of thyroid function with serum ferritin level and determine Correlation of thyroid function with Blood transfusion and Correlation with chelation therapy.

Material And Methods

Study Centre: This descriptive cross sectional hospital based study was done between 2020-2022 in Thalassemia day care centre, Kamla Raja Hospital, Gajra Raja Medical College, Gwalior M.P.

Sample Size: 81.

Study Design: Descriptive Cross Sectional Hospital Based Study.

Inclusion Criteria:

1. All diagnosed thalassemia major children admitted in thalassemia ward Kamlaraja Hospital for blood transfusion.
2. Thalassemia patients of 1 to 18 years of age group.

Exclusion Criteria:

1. Patients on thyroxine or anti thyroid treatment.
2. Diagnosed Autoimmune Thyroiditis.

Methods

Approval for study was taken from institutional ethical committee and written informed consent was taken from their parents. Anonymity & Confidentiality was maintained.

Permission for conducting the study was taken from the Institutional Ethical Committee (IEC), GR Medical College, Gwalior. After taking consent from parents and assent from children, all diagnosed beta thalassemia major children with inclusion criteria were enrolled for study.

Data was collected from 3 following methods:

1. Interview of parents of thalassemia major parents were done on fixed questionnaire regarding socio – demographic variable and family history by records – information of chelation and blood transfusions were collected from available records.
2. Physical examinations – physical examinations of anthropometry, vitals parameters and systemic examinations were collected by thorough physical examinations and investigations like CBC, Serum ferritin and thyroid profile like CBC, Serum ferritin and thyroid profile.
3. Blood Sample collected with all aseptic

precautions and samples were sent to Laboratory of GR Medical College for thyroid function test and Serum ferritin levels.

4. All data was compiled, and statistical analysis was done.

Statistical Analysis

Data was entered in Microsoft Excel and analyzed using SPSS version 16.0 and EPI INFO version 7.0. Pearson's Chi-Square Test for association and trend (for categorical variables) for inferential statistics and Fischer's exact test wherever applicable. As needful t test will be applied for the testing of mean. A p-value of <0.05 will be considered to be statistically significant at 5% level of significance.

Results

Table 1: Demographic distribution of cases

Age groups (years)	Male		Female	
	No.	%	No.	%
1– 5	9	17.6	06	20
6 – 10	17	33.3	13	35.1
> 10	25	49.0	11	36.6
Total	51	62.9	30	37.1
Pearson Chi2 = 1.72 P-value = 0.4241				
Parents thalassemia status				
Yes	2		2.5	
No	79		97.5	
Total	81		100.0	
Sibling thalassemia status				
Yes	12		14.9	
No	69		85.1	
Total	81		100.0	

Among 81 cases, 51 (62.1%) were male and 30 (37.1%) were females. 15 children were of 1-5 years of age group. 09 (17.6%) were male and 06 (20%) were female. Thirty cases were of 6-10 years of age group. Among this age group 17(33.3%) were male and 13(35.1%) were female and >10 years 25 (49%) were males and 11(37.1%) were females.

Few number of parents found to be Thalasemia major patients. Out of total 81 cases, 79 cases (97.5%) were not having thalassemia and only 2 parents have Thalassemia.

Thalassemia status of siblings was also interviewed. Among 81 thalassemia patients, 69 (85.1%) cases siblings were not having Thalassemia whereas 12 cases siblings were suffering from thalassemia disease.

Table 2: Nutrition wise distribution of cases

	No of cases	% of cases
Nutritional status		
< 5 years		
Normal	4	20.00
MAM	12	60.00
SAM	4	20.00
Total	20	100.00
> 5 years		
Normal	36	59.02
Moderate thinness	13	21.31
Severe thinness	12	19.67
Total	61	100.00

Among the total 20 participants who were < 5 years of age: 60% were moderately malnourished and 20% were severely malnourished. Among the total 61 participants who were > 5 years of age: about 21.31% were moderately thin and 19.67% were severely thin.

Table 3: Association of Thyroid status with Serum Ferritin in Study cases.

	<1000	1000-2500	>2500	Total
Euthyroid	14 (100.0%)	37 (71.2%)	5 (33.3%)	56 (69.1%)
Hypothyroid	00	15 (28.8%)	10 (66.7%)	25 (30.9%)
Total	14 (100.0%)	52 (100%)	15 (100%)	81 (100.0%)
Pearson chi2(2) = 15.3600 P-value < 0.0001				

Figure 1(A): Association of Thyroid status with Serum Ferritin in Study cases

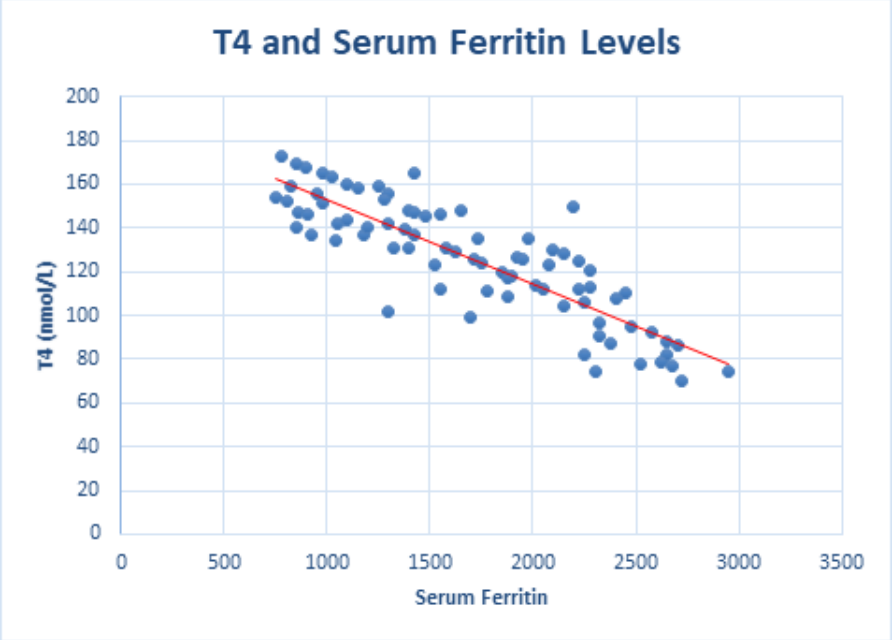

Figure 1(B): Association of Thyroid status with Serum Ferritin in Study cases

Range of Serum ferritin levels was categorized into 3 groups- <1000microgm/l, 1000-2500 microgm/l and >2500microgm/l respectively. As the serum ferritin levels increased the prevalence of hypothyroidism increased. Group 1 contains 14(100%) cases, none is hypothyroidism. Group 2 had 52 cases, out of which 37(71.2%) were euthyroid and 15(28.8%) were thyroid. Group 3 contains 15 cases out of which, 5(33.3%) cases were euthyroid and 10(66.7%) cases were hypothyroid. The distribution of participants across serum ferritin levels and thyroid status was statistically highly significant ($p < 0.0001$).

Table 4: Correlation of Thyroid profile with Weight for Age.

Thyroid Status	**Weight For Age**			
	–3 SD	**–2–3 SD**	**<–2 SD**	**Total**
Euthyroid	3 (37.5%)	34 (65.4%)	19 (90.5%)	56 (69.1%)
Hypothyroid	5 (62.5%)	18 (34.6%)	2 (9.5%)	25 (30.9%)
Total	8 (100.0%)	52 (100.0%)	21 (100.0%)	81 (100.0%)
Thyroid Status	**Height For Age**			
Euthyroid	2 (28.6%)	30 (66.7%)	24 (82.8)	56 (69.1%)
Hypothyroid	5 (71.4%)	15 (33.3%)	5 (17.2%)	25 (30.9%)
Total	7 (100.0%)	45 (100.0%)	29 (100.0%)	81 (100.0%)

Thyroid status was found to be correlated with weight for age of cases. Severely underweight (Weight for age Z < -3SD) was higher (62.5%) among hypothyroid participants in comparison to euthyroid participants (37.5%).

The distribution of participants across weight for age score categories and thyroid status was statistically significant. ($p = 0.14$)

Thyroid status was also correlated with the height for age of cases. severely stunted (Height for age < -3SD) was higher (71.4%) among hypothyroid participants in comparison to euthyroid

participants (28.6%). The distribution of participants across Height for Age score and thyroid status was statistically significant (p = 0.018).

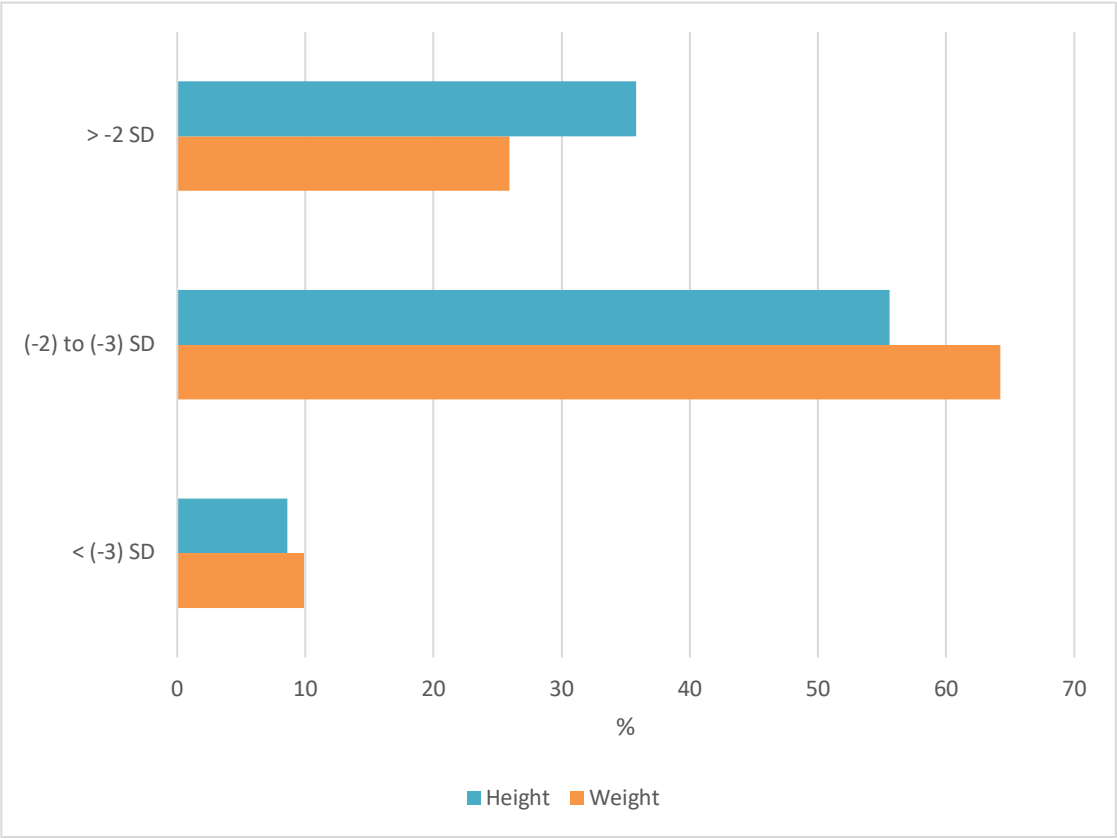

Figure 2 : Weight for Age Z and Height for age Z among participants

Figure 2 shows that patients with Weight for Age < – 3 SD have more incidence as compared to children having Weight for Age between -2SD & -3SD. Out of 8 patients with Weight for Age <-3SD, 3 (37.5%) were Euthyroid and 5 (62.5%) were hypothyroid. Out of 52 patients with Weight for age between -2SD to -3SD, 18 (34.6 %) were hypothyroid and 34(65.3%) were euthyroid. Out of 21 patients with Weight for age >-2SD, 19 (90.4%) were Euthyroid and 2 (9.06%) were Hypothyroid.

Out of 7 patients with Height for Age <-3SD, 5(71.4%) were hypothyroid and 2 (28.5%) were euthyroid. Out of total 45 patients with Height for Age between -2SD and -3SD, 15(33.3%) were Hypothyroid and 30 (66.6 %) were euthyroid.

Table 5: Thyroid status of thalassemia patients

Thyroid status	No.	%
Euthyroidism	56	69.14
Hypothyroidism	25	30.86
1. Subclinical hypothyroidism	18	22.2
2. Primary	7	8.6
3. Secondary	0	0
Hyperthyroidism	0	0.0
Total	81	100.0

Thyroid function were found to be deranged in thalassemia patients. The majority of participants were euthyroid 56 (69.14%) followed by hypothyroid 25 (30.86%). Among the 25 hypothyroid cases, 18 (22.2%) had subclinical hypothyroidism, 7 (8.6%) had primary hypothyroidism and none of the case had hyperthyroidism.

Discussion

The study group comprised of 81 thalassemia cases being regularly transfused at Department of Pediatrics, Kamla Raja Children Hospital, Gwalior.

Out of the 81 beta thalassemia major patients, 15 patients belongs to age group 1-5 years, 30 patients belong to age group 6-10 years, 36 patients belong to age group > 10 years. Males 51 (62.9%) were more than females 30 (37.1%), similar to the results obtained by Hananjassim *et al* [6], Suraj *et al* [7], Rahul *et al* [8] studies in which the males were 65%, 59%, 67% and females were 35%, 41%,33% respectively.

Physical growth is affected in large number of patients with transfusion dependent thalassemia. Thalassemia children show retardation of growth in the fetal, infantile, pre pubertal and pubertal period.

In the study, majority of the thalassemia patients are moderately underweight (64%) and around 9.9% of cases are severely underweight. Among 81 cases, 55% were moderately stunted and 8.6% were severely stunted. But other study done by Harish *et al* [9] revealed that approximately one – third (33.11%) of the patients had short stature, 13% were thin and 10.82% were very thin (Body Mass Index Z score < -3). Around 8% cases were overweight but in the present study none of the patient was overweight. According to study conducted by Ravi *et al* [10], it was observed that 65.71% had short stature and 77% were underweight. Study conducted by Gargi *et al* [11].

In this study, two–third of the patients were moderately malnourished, 21.3% were moderately thinness and 19.67 % were severely thin. Study done by Harish K *et al* [12] had approximately 24.19% of patients thin or severely thin.

This study is done to assess the efficiency and usefulness of serum ferritin level. In the present study, it is inferred that as the age of patient increases, the mean serum ferritin level also increases. The serum ferritin values among the youngest and the oldest age group participants were 1359 microgram/litre and 2065 microgram/litre respectively. Study done by Ravi, Amita *et al* [10] and Anna *et al* [13] also showed similar results. In another prospective study conducted by Ritu, Nigam RK *et al* [14] it was observed that 60 patients showed a mean TSH level of 4.65±2.41 micro Iu/ml. Mean serum ferritin level was 557.25±198.66ng/dl. There was a significant positive correlation of TSH levels with serum ferritin levels similar to the results shown in this study.

In this study, most of the cases had more than 1000 microgram/litre serum ferritin levels. Almost 17.28% had serum ferritin <1000microgram/litre, 64.20% had ferritin levels between 1000-2500 microgram/litre and 18.52% had >2500 microgram/litre.

Thyroid function were found to be deranged in beta thalassemia patients. In this study, it was seen that two – third (69.14%) of the patients were euthyroid and rest of the patients were hypothyroid (30.8%). Among hypothyroid patients, majority of the cases had subclinical hypothyroidism (72%) and few were primary hypothyroidism (28%). None of the patient had secondary hypothyroidism. No correlation was found between Thalassemia and hyperthyroidism. But study done by Chu *et al* [15] showed

results different from this study as among 51 thalassemia patients 21.6% had hypothyroidism among which 63.6% had central hypothyroidism, 27.3% had sub clinical hypothyroidism and remaining 9.1% had primary hypothyroidism. Other studies done by Abdel Fattah *et al* [16] also show similar results.

Ethical Committee Approval no – 107/IEC – GRMC/ 2020

Conclusion

This study concludes that:

1. There is worsening of thyroid function in 30% of the thalassemia patients from one to eighteen years of age.
2. Among the hypothyroid cases, subclinical hypothyroidism had the highest prevalence.
3. Serum ferritin levels were elevated in all these hypothyroid patients implying the positive correlation between Serum ferritin and Hypothyroidism in beta thalassemia patients.

Implications

1. Along with serum ferritin and liver function test, thyroid function monitoring should also be done.
2. Thyroid function monitoring along with serum ferritin and liver function, will improve morbidity and mortality of thalassemia patients.

WHAT IS ALREADY KNOWN

Beta thalassemia patients have deranged growth hormones and impaired glucose tolerance.

WHAT THIS STUDY ADDS

Apart from deranged growth hormones and impaired glucose tolerance thalassemia patients also have thyroid dysfunction which is equally common and should be taken care of.

References

1. Khandelwal R, Gundluru M, Mehta KL. Thyroid profile in patients of thalassemia with multiple blood transfusions and high serum ferritin: a cross-sectional study. Pediatrics Review- International Journal of Pediatrics Research. 2020;7(8):401-08.
2. Landau H, Matoth I, Landau-Cordova Z, Goldfarb A, Rachmilewitz EA, Glaser B. Cross-sectional and longitudinal study of the pituitary-thyroid axis in patients with thalassemia major. Clinical Endocrinology. 1993;38(1):55-61.
3. Cavallo L, Licci D, Acquafredda A *et al*. Endocrine involvement in children with β-thalassaemia major: Transverse and longitudinal studies. I. Pituitary-thyroidal axis function and its correlation with serum ferritin levels. J Acta Endocrinological. 1984;107(1):49-53.
4. Telfer PT, Warburton F, Christou S *et al*. Improved survival in thalassemia major patients on switching from desferrioxamine to combined chelation therapy with desferrioxamine and deferiprone. J Haematological. 2009; 94(12):1777-78.
5. Monge L, Pinach S. Multicentre study on prevalence of endocrine complications in thalassemia major. J Clinical Endocrinology. 1995;42(6):581-86.
6. Hammod H, Mokif TA, Al-Harbi HJ. The correlation between thalassemia with body mass index and blood groups in children and adult patient in the province of Babylon, Iraq. Asian Journal of Pharmaceutical and Clinical Research. 2018;11(9):509-12.
7. Upadya SH, Rukmini MS, Sundararajan S, Baliga BS, Kamath N. Thyroid Function in Chronically Transfused Children with Beta Thalassemia Major: A Cross-Sectional Hospital Based Study. International Journal of Pediatrics. 2018 Sep 16;2018: 9071213.

8. Panchal R, Patel A. Prevalence of hypothyroidism in children with β-thalassemia major in children coming to the New Civil Hospital, Surat, Gujarat. International Journal of Medical Science and Public Health. 2016; 5(12): 2475-2478.
9. Pemde HK, Chandra J, Gupta D, Singh V, Sharma R, Dutt AK. Physical growth in children with transfusion-dependent thalassemia. J Pediatrics Health, Medicine and Therapeutics. 2011; 2:13-19.
10. Shah R, Trehan A, Das R, Marwaha RK. Serum ferritin in thalassemia intermedia. Indian Journal of Hematology and Blood Transfusion. 2014 Dec;30(4):281-5.
11. Pathak G, Chauhan A, Badiyani J. A study of thyroid function in children with Beta thalassemia major. BJ Kines-National Journal of Basic & Applied Sciences. 2018;10(1):17-21.
12. Dey P, Kanwar G, Sarkar B. Body mass index in thalassemia children. Journal of Evolution Medical and Dental Science. 2019;8(19):1537-1539.
13. Spasiano A, Meloni A, Costantini S, Quaia E, Cademartiri F *et al*. Setting for "Normal" Serum Ferritin Levels in Patients with Transfusion-Dependent Thalassemia: Our Current Strategy. Journal of Clinical Medicine. 2021 Dec 20;10(24):5985.
14. Jaipuria R, Nigam RK, Malik R, Shrivastava A, Balani S *et al*. Assessment of thyroid function in children with beta thalassemia major and its correlation with serum ferritin and transfusion index. Journal of Evolution of Medical and Dental Sciences. 2014;3(4):847- 54.
15. Seow CE, Goh AS, Lim SL. High prevalence of central hypothyroidism among patients with transfusion dependent thalassemia in Hospital Pulau Pinang: A cross sectional study. Medical Journal of Malaysia. 2021 Nov;76(6):799-803.
16. Abdel-Razek AR, Abdel-Salam A, El-Sonbaty MM, Youness ER. Study of thyroid function in Egyptian children with β-thalassemia major and β-thalassemia intermedia. Journal of Egypt Public Health Association. 2013 Dec;88(3):148-52.