



Assessment of thyroid profile in children with thalassemia and its correlation with serum ferritin level

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Abstract

Background: Thalassemia is a group of hereditary anaemia characterized by reduced or absent globin chain, resulting in transfusion dependent anemia and iron overload.

Objectives: Evaluation of thyroid profile in thalassemia children and its correlation with serum ferritin in children.

Methods: This is a prospective study including 70 children of thalassemia who are on regular blood transfusion and whose ferritin is $>1000\mu\text{g}/\text{dl}$. Assessment of their thyroid profile and its correlation with serum ferritin was done.

Results: Hypothyroidism was found in around 38% children in our study. Amongst which 31.43% had subclinical hypothyroidism and 7.14% had overt hypothyroidism. We found statistically significant difference in mean serum ferritin level in euthyroid and hypothyroid group

Conclusion: Periodic thyroid testing must be done to detect hypothyroidism for planning timely replacement of hormone to prevent growth failure. There is strong association between ferritin and thyroid disorder which increases the need of chelation therapy to avoid iron toxicity.

Keywords: thalassemia, serum ferritin, hypothyroidism

1. Introduction

Thalassemia is the most common genetic disorder worldwide. In India, over 40 million people carry genes for beta thalassemia [1]. It refers to group of blood disorder characterized by decreased synthesis of either of polypeptide chains (α or β) that form the normal adult human hemoglobin (HbA, $\alpha_2\beta_2$), resulting in decreased filling of the red cells with hemoglobin and leading to anemia [2]. The homozygous state results in severe anemia, which needs frequent blood transfusion causing iron overload which further leads to hypogonadism, hypothyroidism, hypoparathyroidism, diabetes mellitus, liver fibrosis, and heart dysfunction [3, 4]. Iron overload leads to high mortality and morbidity in thalassemia patients. The dual therapy with blood transfusion and chelation therapy has dramatically prolonged the life expectancy of these patients to about third and fourth decades, thus transforming thalassemia from a rapidly fatal disease to a chronic disease [5]. Most common thyroid dysfunction in thalassemia is primary hypothyroidism. Subclinical hypothyroidism appear in 13-60% thalassemia patients after 10 years of age regardless of difference in the rate of prevalence [6]. We conducted this study to evaluate thyroid profile in children with thalassemia major and to study its correlation with serum ferritin.

2. Materials and methods

This study was done on 70 confirmed cases of thalassemia diagnosed on the basis of high performance liquid chromatography of age group 2 year to 18 years attending

inpatient and outpatient ward in department of Paediatrics Govt Multispeciality Hospital-16 Chandigarh, after taking informed consent from the parents during the time duration of February 2016 to February 2017. Data regarding age, gender, religion, region, disease duration, presenting clinical features, frequency of blood transfusion was taken. Physical examination of the patient included general and systemic examination for any evidence of iron overload and hypothyroidism. Laboratory tests included ferritin level and serum free T3, free T4, TSH level by chemiluminescence method.

Results were analysed statistically using SPSS software. Mean values with standard deviation were presented for continuous variables and numbers with percentages for categorical variables. P-value was considered as a parameter to assess significance of various observations and results. P-value <0.05 was taken as significant.

2.1 Groups according to thyroid profile

Group I: Euthyroid: Normal T3, T4 and TSH

Group II: Subclinical hypothyroidism: Normal T3, T4 and raised TSH

Group III: Overt hypothyroidism: Decreased T3 or T4 and increased TSH

3. Results

Out of 70 children of thalassemia, 75% were male and 25% were female. Majority patients were less than 5 years of age. Out of 70, 43(61.43%) were euthyroid, 22(31.43%) had

subclinical hypothyroidism and 5(7.14%) had overt hypothyroidism (Table 1).

Table 1: Case distribution according to thyroid profile

Thyroid profile	No of pts	% of pts
Euthyroid	43	61.43
Subclinical hypothyroid	22	31.43
Overt hypothyroid	5	7.14
Total	70	100

Out of 39 children in age group <5 years, 35 had normal thyroid profile, 4 had subclinical hypothyroidism and none had overt hypothyroidism. In age group 5-10 years,

majority(16) had subclinical hypothyroidism and 2 had overt hypothyroidism. In age group >10 years, none of the child had normal thyroid profile, 2 had subclinical hypothyroidism and 3 had overt hypothyroidism. Out of 39 children in age group <5 year, 35(89.74%) were euthyroid and 4(10.26%) had subclinical hypothyroidism. Out of 26 children in age group 5-10 year, 8(30.77%) were euthyroid, 16(61.54%) had subclinical hypothyroidism and 2(7.69%) had overt hypothyroidism. Out of 5 children in age group >10 year, all were hypothyroid, amongst which 2(40%) had subclinical hypothyroidism and 3(60%) had overt hypothyroidism (Table 2).

Table 2: Case distribution according to thyroid profile in different age group

Age group	Normal thyroid profile	Subclinical hypothyroidism	Overt hypothyroidism
<5 years	35	4	0
5-10 years	8	16	2
>10 years	0	2	3
Total	43	22	5

On comparison of euthyroid children with hypothyroid ones, we found that mean age in euthyroid group was 2.1 years whereas in hypothyroid group was 10.9 year, this was statistically significant. Mean units of blood transfusion in euthyroid group was 39.8 and in hypothyroid group was 88.9 which was also significant statistically (Table 3).

Table 3: Comparison of various parameters in euthyroid and hypothyroid patients

Parameters	Euthyroid patients	Hypothyroid patients	P value
Mean Age (Years)	2.1	10.9	0.0047*
Total units of Blood transfusion	39.8	88.9	0.0001*

Table 4: Mean value of T3, T4, TSH in different thyroid function group

Thyroid function group	T3 (ng/dl)	T4 (µg/dl)	TSH (mIU/l)
Euthyroid	141.78±24.52	6.92±1.09	2.87±1.76
Subclinical hypothyroidism	138.76±18.78	6.15±2.12	7.35±2.54
Overt hypothyroidism	78.65±6.75	1.34±1.02	53.78±20.78

Table 5: Serum ferritin levels in different thyroid groups

Serum ferritin (µg/dl)	Euthyroid		Subclinical hypothyroidism		Overt hypothyroidism	
	No. of pts	%	No. of pts	%	No. of pts	%
<2000	18	41.86	6	27.27	1	20
2001-3000	10	23.26	2	9.09	4	80
3001-4000	12	27.90	8	36.37	0	0
>4000	3	6.98	6	27.27	0	0
Total	43	100	22	100	5	100

On comparing serum ferritin levels in different thyroid groups, we found that amongst 43 children in euthyroid group, 18(41.86%) had ferritin value <2000µg/dl, 10(23.26%) had value 2001-3000 µg/dl, 12(27.90%) had value 3001-4000 µg/dl and 3(6.98%) had value >4000 µg/dl. Out of 22 children of subclinical hypothyroidism, 6(27.27%) had ferritin value <2000µg/dl, 2(9.09%) had value 2001-3000 µg/dl, 8(36.37%)

had value 3001-4000 µg/dl and 6(27.27%) had value >4000 µg/dl. Out of 5 children of overt hypothyroid group, 1(20%) had ferritin value <2000µg/dl and 4(80%) had value 2001-3000 µg/dl (Table 5). Mean serum ferritin value in euthyroid group was 1985.12µg/dl, in hypothyroid group it was 2989.09µg/dl and in overt hypothyroid group it was 1786.33µg/dl (Table 6).

Table 6: Comparison of mean serum ferritin values between different thyroid groups

Group	Serum ferritin Mean ± SD	P value
Euthyroid	1985.12±1534.74	Group I vs II 0.0001*
Subclinical hypothyroid	2989.09±1005.75	Group II vs III 0.0463
Overt hypothyroid	1786.33±798.07	Group III vs I 0.0001*

4. Discussion

In this era, thalassemic children can also have a near normal life span with good quality of life due to availability of good transfusion regimen, chelation therapy, proper management of complications and good supportive care. However, there is some drawback of this treatment as regular blood transfusion can lead to progressive iron overload, which if not adequately treated results in severe complications, including liver, endocrine damage and cardiac dysfunction. One important aspect of management in transfusion dependent β thalassemic patients is early recognition and treatment of endocrine dysfunction. Hypothyroidism which is associated with growth failure is most commonly present in thalassemic patients although the exact mechanism is unknown. It is postulated that thyroid disorder in these patients is due to iron overload which is due to high concentrations of labile plasma iron and labile cell iron. Both of these are responsible for the formation of free radicals and reactive oxygen species which lead to damage to various cell and organ [7].

Present study was undertaken to estimate the serum levels of total T3, T4, TSH in multi-transfused beta thalassemia major children and to find out the correlation of thyroid status with

serum ferritin value. We found that 61.43% children had normal thyroid profile and 38.57% had abnormal thyroid profile. Amongst 70 children of thalassemia, 31.43% had isolated elevation of TSH which was consistent with subclinical hypothyroidism. This was almost similar to Pirinccioglu AG *et al.* [6], Drema L *et al.* [8], Malik SA *et al.* [9], Neha D *et al.* [10]. Whereas 7.14% had decreased T4 and increased TSH which was consistent with overt hypothyroidism. Drema L *et al.* [8], Neha D *et al.* [10] and Solanki US *et al.* [11] also found overt hypothyroidism in less number of cases. On the other hand, Costin *et al.* [12] and Kuo *et al.* [13] found normal thyroid function in thalassemic patients. In thalassemia major, even if the prevalence of overt hypothyroidism is low, patient can manifest with milder forms of thyroid disorders. So we recommend regular follow-up for early detection and timely treatment of these complications so that we could improve the quality of life of these children.

On comparing euthyroid children and hypothyroid children with their mean T3 and T4, we found that mean T3 and T4 were almost normal in the subclinical hypothyroid group but was lower in the overt hypothyroid group than the euthyroid group whereas mean TSH was higher in both subclinical and overt hypothyroid children. This finding was similar to Drema L *et al.* [8].

Serum ferritin is used to assess the iron status in thalassemic patients. Similar to this study, Pirinccioglu *et al.* [6] showed statistically significant difference in mean serum ferritin level in euthyroid and hypothyroid group. Drema L *et al.* [8], Shamshirsaz A *et al.* [14] and Jaipuria R [15] did not show any statistically significant difference in mean serum ferritin between hypothyroid and euthyroid group. This difference can be correlated to difference in the mean age of the study population which might have overestimated the mean ferritin level in hypothyroid group as compared to euthyroid.

As the age and demand of blood transfusions increases, there is increase in iron overload which can be monitored by increase in serum ferritin level. In the thyroid gland, this affects the thyroid hormone production which manifests as hypothyroidism. So, monitoring of thyroid profile is required in all thalassemia patients.

5. Conclusion

Thalassemia is important cause of morbidity and mortality in children. We conclude that in thalassemia, thyroid disorders may start early in life. They go unrecognized as they occur in a low frequency and are clinically asymptomatic. So, regular physical examination and follow up for any overt sign of hypothyroidism along with their periodic thyroid profile testing must be done to detect overt hypothyroidism for planning timely replacement of hormone to prevent growth failure and pubertal delay which will definitely help to improve the life expectancy and quality of life in these patients. There is strong association between high serum ferritin and thyroid disorder which stresses the need for iron chelation therapy to avoid iron toxicity related complications.

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7. References

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