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Assessment of Thyroid Profile in Thalassemia Major Patients

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Abstract:
Background: *Hypothyroidism is one of the most common endocrine complications in thalassemia major patients due to iron overload.*
Objective: *To evaluate thyroid profile in thalassemia major patients for early detection of hypothyroidism.*
Methodology: *This study was a hospital based prospective cross sectional study conducted from February 2015 to April 2016 in Department of Paediatrics and Neonatology, Rajendra Institute of Medical Sciences, Ranchi. In this study, 60 confirmed cases of thalassemia diagnosed on the basis of HPLC {High Performance Liquid Chromatography) were included for assessment of their thyroid profile and its correlation with serum ferritin level.*
Results: *Out of 60 thalassemic patients, majority of the patients i.e.39 children (65%) had normal thyroid profile, 18 children (30%) had subclinical hypothyroidism and 3 children (5%) had overt hypothyroidism.*
Conclusion: *Hypothyroidism occurs in a significant proportion of thalassemia major patients in the absence of obvious clinical signs of hypothyroidism. Regular follow-up for early detection and timely treatment of such complications could improve the quality of life of these patients.*
Keywords: *Hypothyroidism, Haemosiderosis*

I. Introduction

Thalassemia are the most common genetic disorder worldwide. In India, over 40 million people carry genes for beta thalassemia.[1] The thalassemias are heterogeneous group of disorders with genetically determined reduction in the rate of synthesis of one or more types of globin chain of haemoglobin (alpha or beta chain).[2] The high mortality and morbidity in patients of thalassemia is the consequence of iron overload. The combination of blood transfusion and chelation therapy has dramatically prolonged the life expectancy of these patients, thus transforming thalassemia from a rapidly fatal disease of childhood to a chronic disease compatible with a prolonged life[3] On the other hand, frequent blood transfusions, iron overload, poor compliance to therapy and chronicity of the disease have in turn contributed to a whole spectrum of complications including cardiac problems, hypothyroidism, hypogonadism, diabetes mellitus, hypoparathyroidism and other endocrine and metabolic problems[4]. Primary hypothyroidism that may affect thalassemic patients is mainly due to gland infiltration by iron overload. Central hypothyroidism caused by decreased secretion of thyrotropin stimulating hormone (TSH) from the anterior pituitary gland or by decreased secretion of thyrotropin-releasing hormone (TRH) from the hypothalamus is less common[5].

II. Methodology

This study was done on 60 confirmed cases of thalassemia diagnosed on the basis of HPLC (High Performance Liquid Chromatography) of age group 8 months to 12 years attending inpatient and outpatient ward, Department of Paediatrics and Neonatology, Rajendra Institute of Medical Sciences, Ranchi., during the period of February 2015 to April 2016 for the assessment of their thyroid function and its correlation with serum ferritin level.

The following information were taken from each patient: name, age, sex, religion, region, age at the time of diagnosis of thalassemia, total units of blood transfusions, whether the patient is on iron chelators, if yes, duration of therapy. Physical examination of the patient included general and systemic examination. Laboratory tests included pre and post transfusional haemoglobin, serum iron and ferritin level and serum free T3, free T4, TSH level by chemiluminescence method. Patients having severe systemic illness were excluded from this study.

III. Results

In this study, out of 60 patients of thalassemia, majority of the patients (70%) were males. Patients age ranged from 8 months to 12 years. Majority of patients were less than 5 years (56.6%). Among 60 thalassemic children, the youngest case was diagnosed at 4 months of age and oldest at 18 months of age and mean age of

diagnosis was around 7 months. Mean serum ferritin level in age group < 5 years who were not on iron chelators was 392.63 ng/ml and in those with iron chelators was 1815.46 ng/ml. Out of 60 thalassemic patients, majority of the patients i.e.39 children (65%) had normal thyroid profile, 18 children (30%) had subclinical hypothyroidism and only 3 patients (5%) had overt hypothyroidism.

Table 1: Case distribution according to thyroid profile

THYROID PROFILE	NO OF PTS	% OF PTS
NORMAL	39	65%
SUBCLINICAL HYPOTHYROIDISM	18	30%
OVERT HYPOTHYROIDISM	3	5%
TOTAL	60	100%

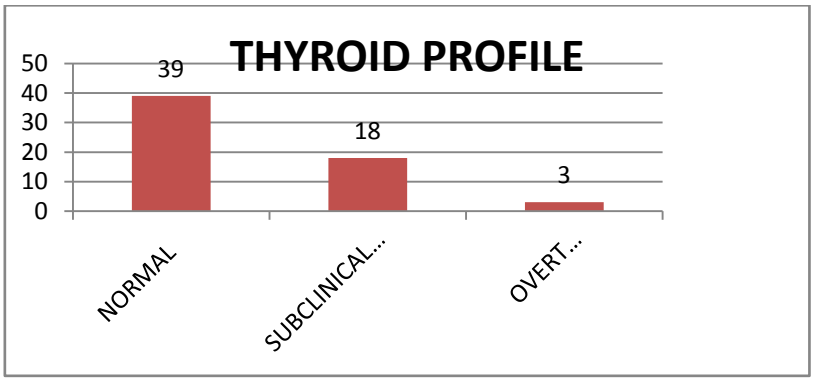


Fig 1: Thyroid profile in thalassemia patient

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

Age Group	Normal Thyroid Profile	Sub-Clinical Hypothyroidism	Overt Hypothyroidism
<5yrs	32	2	0
5-10yrs	7	14	1
>10yrs	0	2	2
Total	39	18	3

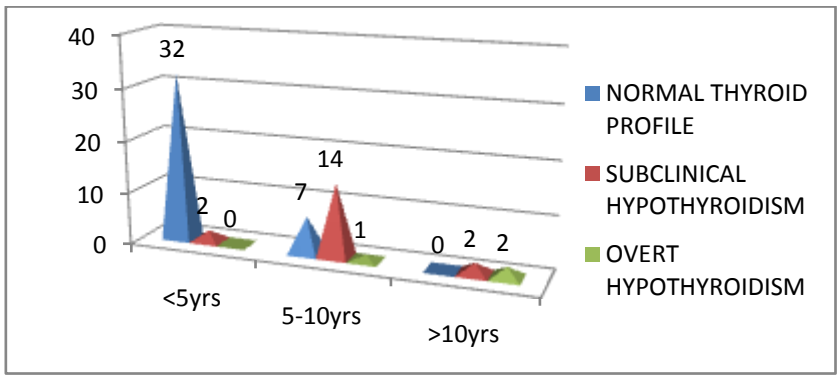
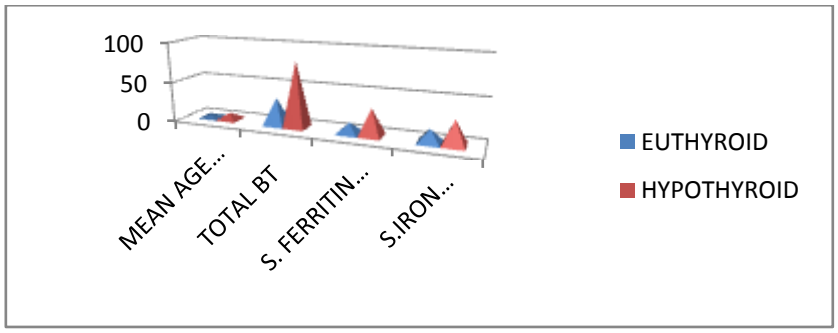


Fig 2: Case distribution according to thyroid profile in different age groups

Out of 34 children in age group < 5 years, 32 children (53.3%) had normal thyroid profile, 2 (3.3%) had subclinical hypothyroidism. Out of 22 children in the age group 5-10 years, 7 children (11.6%) had normal thyroid profile, 14 children (23.3%) had subclinical hypothyroidism, 2 children (3.3%) had overt hypothyroidism. Out of 4 children >10 years, 2 children (3.3%) had subclinical hypothyroidism, 2 (3.3%) had overt hypothyroidism.

Table 3: Comparison of various parameters in euthyroid & hypothyroid pts

Parameters	Euthyroid Patients (Mean Value)	Hypothyroid Patients (Mean Value)	P Value
Mean Age (Yrs)	3.6	8.5	<0.05
Total Units Of Bt	34.7	82.1	<0.05
S.Ferritin(Ng/Dl)	1251.53	3293.76	<0.05
S.Iron(µg/Dl)	162.1	304.7	<0.05



Comparative study between Euthyroid patients and Hypothyroid patients showed mean age of the patients in euthyroid group was 3.6 years and in hypothyroid group was 8.8 years, this difference was statistically significant.($p<0.05$). Also there was statistically significant difference ($p<0.05$) between hypothyroid and euthyroid patients in relation to total units of BT, serum iron and serum ferritin level.

IV. Discussion

In the present study, minimum age of diagnosis was 4 months and maximum age as 18 months, the mean being around 7 months. This implies that thalassemia major patients present symptoms early in childhood, an early as 3 to 6 months with progressive pallor being the most common manifestation.

Table 4: Comparison of thyroid profile in various studies

Studies	**Normal thyroid profile (%)**	**Subclinical hypothyroidism (%)**	**Overt hypothyroidism (%)**
Geeta Gathwala etal 2009[7]	70%	18%	12%
Malik et al 2010[6]	73.2%	25.7%	1.4%
Solanki US et al 2014[12]	64%	34%	2%
Hashemizadeh H et al 2009[9]	92%	7%	1%
Garadah T et al 2010[10]	84.6%	15.4%	8.1%
Anand NK et al 1995[11]	56%	32%	12%
Somchit J 2007[8]	78.5%	17.6%	3.9%
Present study	65%	30%	5%

Table 5: Comparison of mean age and S. Ferritin level in hypothyroid pts in various studies

Studies	**Mean age of hypothyroid patients (yrs)**	**S. Ferritin (mean) in hypothyroid patients (ng/dl)**
Gathwala G et al 2009[7]	7.97 ± 2.83	3394.46
Hashemizadeh H et al 2009[9]	10.2 ± 5.5	3942
Somchit J et al 2007[8]	13.9 ± 2.2	4,825 + 2,064
Present study	8.5 ± 3.7	3293.76

In the present study, out of 60 thalassemics, 41 patients (68.3%) were on chelation therapy, all were on single oral iron chelator, deferasirox and 19 patients (31.6%) were not on chelation therapy. In the age group <5 years, iron overload in these patients as suggested by serum iron and ferritin level is less owing to less duration of illness and total number of blood transfusions. Serum iron and ferritin level in patients on iron chelators appears to be rising with age. This finding suggests that though the patients are on oral iron chelators, but serum iron and ferritin level is increasing due to increasing number of blood transfusions which contributes to iron overload in thalassemic patients and single oral iron chelators is not effective in reducing iron overload in these patients.

The present study showed majority of the thalassemic patients (65%) had normal thyroid profile. Similar results with majority of the patients with normal thyroid function were observed by other workers. Subclinical hypothyroidism was seen in 30% in the present study. Similar results were seen by Solanki US et al 2014[12] (34%), Malik et al 2010[6] (25.7%), Anand NK et al 2012[11] (32%).

In the present study, overt hypothyroidism was found in 5% of the cases. Other workers like Malik et al 2010[6], Solanki US et al 2014[12], Somchit J 2007[8] found overt hypothyroidism in less number of patients.

It is important to note that even in the studies in which the prevalence of overt hypothyroidism as a complication of thalassemia major is relatively low, milder forms of thyroid dysfunction are much more common. Hypothyroidism occurs in a significant proportion of thalassemia major patients in the absence of obvious clinical signs of hypothyroidism. Regular follow-up for early detection and timely treatment of such complications could improve the quality of life of these patients.

In the present study, comparison was made between the patients who had normal thyroid profile and those who were hypothyroid (subclinical/overt). Statistically significant difference ($p<0.05$) was found between the two groups in terms of mean age, total units of blood transfusions, serum iron and ferritin level.

This could be due to the fact that with increasing age and increasing units of blood transfusions in thalassemic patients, there is increase in transfusional iron overload which is reflected by increase in serum ferritin level. In the thyroid gland, this affects the production of thyroid hormones and manifests as varying degrees of hypothyroidism. So, monitoring of thyroid function is required in all thalassemic patients, particularly who receive suboptimal chelating agents.

V. Conclusion

Thalassemia syndromes are important cause of morbidity and mortality in children. Though thyroid dysfunction secondary to iron overload in thalassemic patients may start early in life, clinical signs are not observed in most patients. Thyroid dysfunction was present in significant proportion of the patients without obvious clinical signs. Regular follow up of thyroid function should be done for early detection and timely replacement of hormone to prevent growth failure and pubertal delay. There was also strong association between high serum ferritin level and thyroid dysfunction which stresses the need for intensive iron chelation therapy to avoid iron toxicity related complications.

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