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Study of Glucose Tolerance Test and Thyroid Profile in Tranfusion Dependent Thalassemic Children and Their Correlation with Serum Ferritin Level

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Abstract

Background: The present study was designed to estimate the serum levels of total T4, total T3, TSH, glucose level and serum ferritin in multi-transfused thalassaemic patients and to see any correlation between thyroid hormone dysfunction, glucose dysfunction and high serum ferritin value.

Methods: Hospital based observational study conducted at Department of Pediatrics, S.P. Medical College and P.B.M. Associated Group of Hospitals, Bikaner.

Results: The mean age of patients was 9.55±3.76 years. The age ranged from 5 years to 18 years. 41.3% were male in age group 5-10 years, 45% male were in 11-15 years and 47.2% males were in age group 16-18 years. 42.5% Hindu patients, 50.7% patients were Muslims and 6.8% patients includes Sindhi and Jews etc. 78.1% patients belong to urban area and 21.9% patients belong to rural area. 43.8% patients belong to lower class, 31.5% patients belong to lower middle, 13.7% patients belong to middle class, 9.6% patients belong to upper middle and only 1.4% patients belong to upper class. 5.5% patients had splenectomy and rest 94.5% did not had splenectomy. 16.4% patients had Family history of diabetes mellitus and 83.6% had no family history. 35.6% patients had family history of thalassemia and 64.7% had no family history. 45.2% patients had history of consanguinity and these patients were Muslims. 54.8% patients had no family history of consanguinity. 6.8% had serum ferritin level >2000 ng/ml, 17.8% had serum ferritin level between 2000-3000 ng/ml, 19.2% had serum ferritin level between 3000-4000 ng/ml, 12.3% had serum ferritin level between 4000-5000 ng/ml, 13.7% had serum ferritin level between 5000-6000 ng/ml and 30.2 had serum ferritin level >6000ng/ml. <10 centile there were 5 (45.4%) patients having thyroid dysfunction, in 10-50 centile there were 5 (45.4%) patients having thyroid dysfunction, in 50-90 centile there were 1 (9.2%) patients having thyroid dysfunction and in >90 centile there were 0 patients having thyroid dysfunction. In males there were 5 (45.5%) patients having thyroid dysfunction, in females there were 6 (54.5%) patients having thyroid dysfunction. In patients having monthly transfusion there were 4 (36.4%) patients having thyroid dysfunction, having bi-monthly transfusion there were 5(45.4%) patients having thyroid dysfunction and having tri-monthly transfusion there were 2 (18.2%) patients having thyroid dysfunction. 10 patients having

thyroid dysfunction Thalassemia were diagnosed at below 1 year, 1 patients having thyroid dysfunction Thalassemia were diagnosed at age between 1-5 year. 2 (18.2%) patients having thyroid dysfunction blood transfusion occur from last 5 year and from 5-10 years each, 7 (63.8%) patients having thyroid dysfunction blood transfusion occur from more than 10 years.

Conclusion- High prevalence of HT among thalassemic patients signifies the importance of regular screening for evaluation of endocrine function in these patients.

Introduction

The thalassaemias are a heterogeneous group of disorders with a genetically determined reduction in the rate of synthesis of one or more types of normal haemoglobin polypeptide chain. In β-thalassaemia the inadequate production of β chain leads to a reduction in the amount of Hb-A in the red cells.

Thalassaemia was originally described in people of Mediterranean origin. Now it is a disorder with a widespread geographical distribution1. The world population of carriers of β -thalassaemia trait is reported to be more than 100 million and about 70,000 children with thalassaemia major are born each year.

Beside various causes, iron overload is an important, although rare etiological factor in thyroid failure13, 14. The thyroid gland function in thalassaemia major has been reported to be normal, decreased reserve, or primary hypothyroidism. The total serum T4 and T3 are measured by radioimmunoassay. Serum TSH levels reflect the anterior pituitary gland sensing the level of circulating free T4, is measured by immune-radiometric assay which is the most sensitive, convenient, and specific test for the diagnosis of both hyperthyroidism and hypothyroidism15. Serum ferritin estimation is the most widely used method for monitoring the total iron load16.

Glucose intolerance is a common consequence of transfusion therapy in patients with TM, but the relative contribution of pancreatic damage and insulin resistance to glucose intolerance is unclear.12-15 The exact mechanism of ironinduced diabetes is unclear, but it most likely occurs through these 3 mechanisms: (1) insulin deficiency, (2) insulin resistance, and (3) hepatic dysfunction.9 Although numerous studies have been performed on endocrine and liver complications in thalassemia, the number of published studies about Iranian patients is significantly small.

The present study was designed to estimate the serum levels of total T4, total T3, TSH, glucose level and serum ferritin in multi-transfused thalassaemic patients and to see any correlation between thyroid hormone dysfunction, glucose dysfunction and high serum ferritin value.

Material and Methods

Study Design: Hospital based observational study.

Study Place: Department of Pediatrics, S.P. Medical College and P.B.M. Associated Group of Hospitals, Bikaner.

Sample Size: Total 50 cases of transfusion dependent thalassemia major aged between 5-18 years.

Sampling Method: Convenience Sampling

Inclusion Criteria

1. Transfusion dependent thalassemic major children between 5-18 years age admitted in P.B.M. Hospital.

Exclusion Criteria

1. Transfusion dependent thalassemic children between 5-18 years age admitted in P.B.M. Hospital not willing to participate in study.

Data Collection

Children between 5-18 years with transfusion dependent thelesemia major admitted in Hospital and willing to participate in study were examined for serum ferretin

level, thyroid function test and glucose tolerance test by blood sampling method. Written informed consent was obtained from each patient and the parents for using their clinical data for study purpose.

Detailed history was obtained from each patient and details of their demographic data, age of diagnosis, frequency of transfusion, and chelation therapy etc. will be noted.

Serum ferritin level was determined by immunometric enzyme immune assay (ELISA kit), level of serum ferritin between 25-350ng/ml in male between 13-232 ng/ml in females were considered as normal. Thyroid function test (free T_4, TSH) was assessed by assessed by ELISA method in children.

Oral glucose tolerance test

- The patient was instructed to fasting overnight for 8-12 hours prior to test only water is allowed and then blood glucose level will be recorded.
- Patient will be given 1.75gm/kg/body weight maximum 75gm in water to drink within 5 minutes time frame and then blood glucose level will be tested after 2 hours of drinking solution by glucose peroxydase and glucose oxidase method.

Data Analysis

To collect required information from eligible patients a pre-structured pre-tested proforma will be used. For data analysis Statistical software SPSS version 17.0 will be used and data were analyzed with the help of frequencies, figures, proportion measures of central tendency, appropriate statistical test.

Results

Observations

Table: 1 Gender wise distribution

Age group	Male		Female		Total
	Number	Percentage	Number	Percentage	
5-10 years	19	41.3	27	58.7	46
11-15 years	9	45	11	55	20
16-18 years	4	47.2	3	42.8	7
Mean age ±Sd	10.2±3.8		9.1±3.6		73

Here, 41.3% were male in age group 5-10 years, 45% male were in 11-15 years and 47.2% males were in age group 16-18 years. The mean age of male patients was 10.2±3.8. 58.7% were female in age group 5-10 years, 55% female were in 11-15 years and 42.8% females were in age group 16-18 years. The mean age of female patients was 9.1±3.6. There were total 32 males and 41 females i.e. there were female preponderance.

Table: 2 Serum T3 level

T3	No.	%	Mean ± SD	p-value
<0.8 n mol/L	9	12.32877	0.48±0.18	0.0001
0.8-3.54 n mol/L	64	87.67123	1.79±0.60	
Total	73	100		

Table: 3 Serum T4 level

T4	No.	%	Mean±SD	p-value
>54 n mol/L	12	16.4	45±5.84	0.0001
54-175 n mol/L	61	83.6	86.4±21.1	
Total	73	100		

Table: 4 Serum TSH level

TSH	No.	%	Mean±SD	p-value
0.5-5.0 IU/L	62	85	3.65±1.1	0.0001
5-10 IU/L	11	15	5.98±0.44	
>10 IU/L	0	0		
Total	73	100		

Table: 5 Fasting glucose level

Fasting glucose	No.	%	Mean±SD	p-value
<110 mg/dl	57	78.1	91.4±9.7	0.0001
>110 mg/dl	16	21.9	137.4±19.6	
Total	73	100		

Table: 6 postprandial glucose levels

postprandial glucose	No.	%	Mean±SD	p-value
<140 mg/dl	58	79.5	125.9±9.2	0.0001
>140 mg/dl	15	20.5	217.6±43.6	
Total	73	100		

Table: 7 Correlation between Ferritin and T3, T4, TSH, Fasting glucose and PP glucose

	T3	T4	TSH	Fasting	PP
Ferritin (r)	-0.169	-0.292	0.412	0.22	0.333
p-value	0.154	0.012	0.0001	0.061	0.004

Discussion

Endocrine dysfunction is the second most frequent complication, over 60% of thalassaemics after the age of 10 years have at least one endocrine gland dysfunction and about 40% have multiple endocrinopathies6. In our study, maximum thalassemic children had subclinical hypothyroidism which is in good agreement with the study done by Sharma et al 7. The reason for the lower frequency may be attributed to the fact that the majority of patients in the present work were under 10 years old. Not many studies are available from India and one among the very few studies done by N. K. Anand revealed that 32% of patients had subclinical hypothyroidism and 12% had clinical hypothyroidism.8 This finding is comparable to our study in terms of subclinical hypothyroidism.

Hyper-transfusion has improved the life expectancy of thalassemic patients, over the decades. However, chelation therapy is expensive, difficult to administer and not as readily available, hence the compliance is often poor despite regular transfusions resulting in iron overload [9]It has been demonstrated that thyroid abnormalities in these patients are related to iron overload. Histological studies have supported this hypothesis [10]. However, the serum ferritin is the most widely used test for assessment of iron status in these patients. Iron overload of tissue is the most important complication of beta-thalassemia and is a major subject of management[11]. Although most clinical signs of iron loading do not appear until the second decade of life in patients with inadequate chelation, evidence from serial liver biopsies in very young patients present that the toxic effects of iron begins much earlier. After approximately one year of transfusions, iron starts accumulating in parenchymal tissues, where it may bring about substantial toxicity as compared with that within reticulo-endothelial cells. Despite the reports relating endocrine dysfunction with iron overload, it was recently demonstrated that the degree of iron overload, at least reflected by ferritin levels, was not associated with the development of endocrine complications [11] In this study, a significant association was found between ferritin levels and thyroid functional status; the ferritin levels of hypothyroid patients being significantly higher than euthyroid patients. The precise mechanism by which iron overload causes tissue damage is not completely understood, though it is suggested that tissue iron deposits act at the cellular level causing damage via free radical formation and lipid peroxidation resulting in mitochondrial, lysosomal and sarcolemmal membrane damage. In the thyroid gland, this affects the production of thyroid hormones and manifests as varying degrees of primary hypothyroidism. Hence, it is postulated that higher serum ferritin levels predispose to a greater risk of developing endocrine-pathies like hypothyroidism. It has been suggested that thyroid dysfunction may be reversible by intensive chelation.

Apart from iron overload, other factors responsible for organ damage have been previously pointed out including anemia and chronic hypoxia that may potentiate the toxicity of iron deposition in endocrines [12]. Also, viral infections as well as individual susceptibility have been implicated in causing endocrine dysfunction.

Conclusion

High prevalence of HT among thalassemic patients signifies the importance of regular screening for evaluation of endocrine function in these patients.

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