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STUDY OF PREVALENCE OF HYPOTHYROIDISM AND PHYSICAL GROWTH IN B THALASSAEMIA MAJOR CHILDREN

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ABSTRACT **INTRODUCTION:** Hypothyroidism and growth retardation are frequent complications in thalassaemia children. We investigated and reviewed the thyroid function and growth assessment in thalassaemia patients. **OBJECTIVE:** To study the prevalence of Hypothyroidism and its effect on growth parameters in children with beta thalassaemia major. **MATERIALS AND METHODS:** A case control study in which 100 cases and 100 healthy children of 6-18 years of age included. Children with primary endocrinopathies and other co morbid conditions were excluded. A detailed history regarding no. of blood transfusion, chelation, associated symptoms and growth parameters were taken.S.TSH,T3,T4 and s.ferritin level were done. Association of hypothyroidism and growth retardation in thalassaemia children was calculated by appropriate statistical test. **RESULTS:** Total 100 patients (58 male and 42 female) were included in this study. All cases were growth retarded. Total 44% cases had hypothyroidism (serum TSH >4.7mIU/ml).Out of them,63.64% cases were of subclinical and 36.37% cases were of primary hypothyroidism. None had central hypothyroidism. **CONCLUSION:** Hypothyroidism is common in beta thalassaemia major but its correlation with growth retardation was not found.
It is recommended to assess thyroid functions periodically to assess hypothyroidism early and their early management will improve the quality of life of these patient.

KEYWORDS : Hypothyroidism, growth retardation, s.ferritin, Beta thalassaemia ,organ siderosis

INTRODUCTION

Frequent blood transfusion in thalassaemia children lead to various complications and endocrinopathies are one of them. There is a possibility to have these complications due to poor compliance to regular blood transfusion and chelation therapy resulting in organ siderosis. In view of non-availability of pediatric Indian studies, increasing prevalence of endocrine disorders and the increasing concern among the patients regarding their stature there is a need to look into the burden of endocrine complications among them .Thyroid hormones are essential for growth development and metabolism. Thyroid dysfunction may affect growth directly or it may accentuates the ongoing growth retardation by affecting basal metabolism. For growth assessment, anthropometric measures including weight ,height and BMI are to be considered. Thus , we investigated and reviewed the thyroid function and growth assessment in thelessemic patients to determine the frequency of hypothyroidism and correlation with growth retardation.

AIMS AND OBJECTIVES

To study the prevalence of Hypothyroidism and its correlation with growth parameters in beta thalassemia major children.

MATERIAL AND METHOD

A case control study in which 100cases and 100healthy children of 6-18 years of age included. Study was conducted at JK lon hospital, kota Rajasthan over a period of December 2015 to November 2016. Children with primary endocrinopathies and other co morbid conditions were excluded. A detailed history regarding no,of transfusion,cheltion,associated symptoms and growth parameters were taken.

S.TSH,T3,T4 and s.ferritin level were done. Anthropometry including weight, height were taken and BMI was calculated. As the study population in this study were above five years and no comorbid conditions were included so head circumference was not considered.

Association of hypothyroidism and growth retardation in thalassaemia children was calculated by appropriate statistical test. Sample size was calculated according to prevalence of hypothyroidism in thalassaemia children.

Written informed consent was taken from either of parents or guardian. Two study groups were taken: case and control groups.

Cases were included 6-18 years age children diagnosed beta thelessemia major by HPLC method and had history of blood transfusion for five years.

Controls were healthy children of same age groups.

Total sample size was 200.

Children with ***TSH >4.7microU/L.*** **S.ferritin value >500ng/ml were included.**

Statistical Analysis:

Statistical analysis was done by using SPSS software version 18.Anthropometric parameters were analyzed according to WHO growth charts according to age and sex.

RESULTS

There was significant growth retardation among all ß thalassemic children on comparison with healthy controls. There were 28 (63.67%) cases of subclinical hypothyroidism and 16(36.33%) cases of primary hypothyroidism. None had central hypothyroidism. Correlation between hypothyroidism and growth retardation was not found.

Table 1 Comparison of weight of thalassaemia case and control groups

Weight (Kg)	Thalassaemia Boys /Girls(No. and %)	Healthy Boys/Girls No and %	Chi Square P-Value
<3th centile	37 (63.79%)/30 (71.43%)	11 (22%)/12(26%)	Chi-square= 41.53 P= <.001/ Chi-square= 2549 P= <.001
3-97th centile	21 (36.20%)/ 12(28.57%)	39 (78%)/38(76%)	
>97th centile	00/00	00/00	
Total	58 (100)/ 42(100%)	50 (100)/ 50 (100%)	

Table 2 Height of case and control groups

42Height (cm)	Thalassaemia Boys/girls No. and %	Healthy Boys/girls No and %	Chi Square P-Value
<3th centile	44(75.86%)/41 (97.62%)	08 (16%)/02 (04%)	Chi-square=63.80 P= <.001/ Chi-square=82.28 P= <.001
3-97th centile	14 (24.14%)/01 (2.38%)	42 (84%)/48 (96%)	
>97th centile	00/00	00/00	
Total	58 (100%)/42(100%)	50 (100%)/50 (100%)	

Table 3: Comparison of BMI of thalassaemia cases and control groups

S.No.		Mean ± SD	t- value	P- value
1.	**Healthy boys**	17.55 ± 1.53	**1.85**	>0.05 (NS)
	Healthy girls	17.25 ± 2.11		
2.	**Healthy boys**	17.55 ± 1.53	**2.05**	<0.05 (NS)
	Thalassaemia Boys	14.78 ± 4.82		
3.	**Healthy girls**	17.25 ± 2.11	**2.91**	<0.01 (HS)
	Thalassaemia Girls	14.86 ± 5.47		
4.	**Thalassaemia Boys**	14.78 ± 4.82	**0.68**	>0.05 (NS)
	Thalassaemia Girls	14.86 ± 5.47		

Table 4 Age & sex wise distribution of hypothyroidism (S.TSH>4.7) in thalassaemia patients

AGE (YEARS)	MALE	FEMALE	TOTAL
6-10	18	5	23
11-14	01	8	09
15-18	10	2	12
TOTAL	29	15	44

TABLE 5 Distribution of cases of hypothyroidism

SUBCLINICAL HT(HIGH TSH NORMAL T4)	PRIMARY HT(HIGH TSH LOW T4)	CENTRAL HT(LOW TSH LOW T4)
28(63.67%)	16(36.33%)	00

Table 6 Correlation of hypothyroidism and growth retardation

	Growth retardation present	Normal growth parameters	Odds ratio
Hypothyroidism present	44	00	
Euthyroid	56	00	
	100		0.76

DISCUSSION:

β-thalassaemia is the commonest single-gene disorder in the Indian population. They usually come to medical attention within first two years of life [1]. Over the past three decades, regular blood transfusions and iron chelation has dramatically improved the quality of life and transformed thalassaemia from a rapidly fatal disease in early childhood to a chronic disease compatible with prolonged life. Despite increased life expectancy, complications keep arising. These relate to inadequate transfusions, transfusion-related infections, allosensitization, iron-overload related cardiac, endocrine and liver disturbances and toxicities of iron chelators. Many of these problems are strongly age dependent [2].Transfusion related iron overload is the primary therapeutic complication in thalassaemia major. Other factors like hypoxia due to persistent anemia, perfusion defect and poor nutrition, chelating agents, liver disease and genetic susceptibility may also contribute to the derangement[3], [4], [5]. This study was conducted to access prevalence of hypothyroidism and physical growth pattern in thalassaemia major children. Total 100 cases of thalassaemia patients and 100 healthy children for control were included in the current study. Male and female ratio was almost same in both group (58:42 in cases and 50:50 in control).All cases and controls were of 6 to 18 year age group. This age group was select because growth pattern can be studied better in this age group and similarly complications would be more in higher age group as the need of blood transfusion increases with age[6] [7].

In all age groups, cases were growth retarded as campared to control. It is due to growth hormone neuro-secretary disturbance and secondary growth hormone insensitivity [8], [9]. Chronic anaemia, congestive cardiac failure, haemosiderosis and other endocrine and metabolic disturbances may also be contributory factors [10]. Similar results have been reported by Vahidi A. A. et al and others as well [6], [7].

Mean BMI in various age groups of cases less than control group and the difference is statically significant (<0.05). Patients with beta-thalassaemia major are prone to metabolic complications, including endocrine dysfunction which can occur as single or multiple endocrine glands involvement. Although the actual mechanism is not definitive, the most likely explanation is related to iron overload and its burden, in addition to lipid peroxidation, oxidative stress and free radicals release[9]. 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 endocrinopathies[10].

In this study, total 44 cases had serum TSH level more than 4.7mIU/ml. Out of them, 28 thalassaemia children had subclinical hypothyroidism which is in good agreement with the study done by Sharma et al[11].It was also found that 16 thalassaemia children had clinical hypothyroidism. Previous studies in transfused β thalassaemia patients showed a variable prevalence of hypothyroidism ranging from 0 to 35%, depending on the age of the study population, duration of blood transfusions, ferritin levels and dose and type of the iron-chelating agent [12], [13]. Not many studies are available from India and one among the very few studies done by Dr N. K. Anand, Dept. of Pediatrics, Safdarjang, New Delhi said that 32% of patients had subclinical hypothyroidism and 12% had clinical hypothyroidism. These findings were also comparable to present study. As the age increases, incidence of hypothyroidism increases. Subclinical HT is more common during early age but as the age advances, HT manifests with the symptoms also like constipation, cold intolerance, sleep cycle alteration and skin changes.

Thyroid hormones are important for the proper development, differentiation and metabolism of cells. A wide range of pathogenic mechanisms may be involved. Tissue chronic hypoxia and iron overload have a direct toxic effect on the thyroid gland. In severe iron overloaded thalassaemia patients the anterior pituitary may also be damaged and regulatory hormonal secretion (LH, FSH, and TRH) may be disrupted. Organ siderosis (liver, cardiac and skeletal muscle, kidney) may affect specific receptors, which regulate thyroid hormone action and convert T4 to the bioactive T3. Clinical hypothyroidism has been reported as 6.9% by Agrawal[14]]and his co-workers, 4% by Zervas et al, [15]18.3% by Magro et al, [15] and none by Phenekos et al[16]as the index study. Serum ferritin level was very high (>2000) in 55% cases and 43% cases had serum ferritin level in between 1000-2000. Such high level of ferritin indicates poor quality of chelation therapy . No significant difference was found in the iron overload as measured by serum ferritin in the thalassaemia euthyroid and hypothyroid patients. Similar findings were observed by Al-Hader et al, [17] Cavallo and his co-workers and Filosa et al[18], [19]. This suggests that other factors apart from iron over-load may play a role in the endocrine damage which may include chronic hypoxia secondary to chronic anemia and damage starts early before significant organ siderosis.

Limitations

Correlation between s.ferritin level and hypothyroidism is not being established where as it is well known to cause organ dysfunction associated with siderosis like cardiac, hepatic. Also there may be need to get complete blood count to take severe anemia and degree of organ dysfunction into consideration as chronic hypoxia is considered to be cause of organ dysfunction.

For thyroid dysfunction other parameters like anti TPO, anti peroxidase and assessment of hypopituitorism are needs to be taken into consideration for more detection of subclinical hypothyroidism. For all the above said limitations ,there will need to assess the parameters upon large group of population.

CONCLUSION

We concluded that hypothyroidism and growth retardation are commonly present in beta thalassaemia major patients, however its correlation was not found. Improvements in protocols of transfusion regime and chelating therapy should hopefully improve the care and quality of life of these patients. Regular follow-up is essential for the early detection and appropriate treatment of associated complications.

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