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ORIGINAL ARTICLE

Frequency of Hypothyroidism in Beta Thalassemia Patients

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ABSTRACT

Aim: To find out the frequency of thyroid hypo-functioning in β-thalassemia patients presenting at Endocrinology Outpatient Department of Jinnah Hospital, Lahore.
Study design: Cross-sectional descriptive study
Place and duration of study: Allama Iqbal Institute of Diabetes and Endocrinology, Jinnah Hospital Lahore from 5th June 2019 to 4th January 2020
Methodology: One hundred diagnosed cases of β-thalassemia of both genders with age range of 5-19 years were included. Random blood samples were taken to measure serum thyroid stimulating hormone (TSH) and free T4 levels by Enzyme Linked Immunosorbent Assay (ELISA).
Results: Hypothyroidism was present in 32 (32%) patients. The frequency of hypothyroidism was same in 5-9 years versus 10-19 years age groups with no significant gender differences (p 0.434). The mean levels of ferritin were 5102±1134 ng/ml in thyroidhypo-functioning cases was 3687±1425 ng/ml in normal-functioning thyroid patients (P 0.001).
Conclusion: Hypothyroidism is highly prevalent in β-thalassemia patients. Periodic check-ups are recommended for early diagnosis and interceptive treatment.
Keywords: Thyroid; Hypothyroidism; Beta-thalassemia; Endocrinology

INTRODUCTION

Thalassemia is a heterogeneous group of genetic disorders (autosomal recessive) caused by mutations in hemoglobin producing genes and is one of the most common monogenic disorders in the world[1]. Thalassemia can be classified into alpha (α) and beta (β) thalassemia based on mutations of α or β hemoglobin chain genes. β-thalassemia is of 3 types: β-thalassemia silent carrier state, thalassemia intermedia and major type[2-4].

Severity of thalassemia may vary from silent carriers to severe phenotype requiring life-saving transfusions[1]. Out of 270 million carriers about 80 million are β-thalassemia carriers.[5] β-thalassemia is the most common inherited disorder in Pakistan having occurrence of 6 carriers out of every100 people and estimated carrier rate is 5-7%[6].

β-thalassemia major patients require regular blood transfusion for their survival. Frequent transfusion with poor chelating therapy can lead to iron overload which in turn may lead to various endocrine complications[7-10]. Thalassaemic subjects with hypo-functioning of thyroid are found to be having greater incidence of endocrinal issues and issues of other organ systems[11,12].

Frequency and complications of hypothyroidism in β-thalassemia patients on various organ systems is relatively understudied.

The current study was planned to find the frequency of thyroid disorders in diagnosed β-thalassemia Pakistani patients.

MATERIALS AND METHODS

This cross-sectional descriptive study was conducted after taking ethics approval from the institution and after taking informed consent from patients/parents at Allama Iqbal Institute of Diabetes and Endocrinology, Jinnah Hospital Lahore over a period of six months from 5th June 2019 to 4th January 2020. The sampling technique was non-probability consecutive sampling. Calculated sample size is 100 patients using world health organization (WHO) calculator was 75 patients with P 25.7%, confidence level 95%, and absolute precision required 10%[11].

Following patients were included: β-thalassemics of both genders with age range of 5-19 years and those who were on regular packed red cells transfusions at the rate of 2-4 weeks since infancy. Cases of α-thalassemia, minor or intermedia β-thalassemia and family history of thyroid disorders or acute illness were excluded from the study.

The study was conducted using specially designed questionnaire. Demographic information including age, gender and body mass index (BMI) was recorded. Family history of β-thalassemia, history of splenectomy, transfusion, chelating and other details was recorded. Random blood samples were taken to measure serum TSH and free T4 levels by ELISA. Pre-transfusion hemoglobin and ferritin levels were also recorded. β-thalassemia patients were diagnosed by complete blood count, peripheral film and Hb electrophoresis. The β-thalassemia patients having TSH level>4 IU/ml, and T4 levels <4.5g/dl were considered as hypothyroid. The β-thalassemia patients who were having increased TSH but normal T4 were further considered as compensated/sub-clinical hypothyroid and β-thalassemia patients who were having increased TSH butnormalT4 were considered as uncompensated/overt hypothyroid[11].

Qualitative variables results (gender, family history of β-thalassemia, history of splenectomy) were presented as frequencies and percentages and compared using Chi square test. Quantitative variables like Age, BMI, TSH & T4 levels, ferritin levels were presented as Mean±SD and compared using 't' test. The p-value of ≤0.05 was considered as statistically significantly.

RESULTS

There were 63 (63%) males and 37 (37%) were females with mean age13.45±3.43 years and mean BMI of16.35±2.39 kg/m^2 (Table 1). Nine patients had been splenectomised and 36 patients were having positive family history of β-thalassemia (Table 1). Hypothyroidism was present in 32(32%) patients with mean age of 13.11±3.29 years). Group 1 had patients ranging from 5-9 years whereas group 2 patients were of ages between 10 and 19 years. The frequency of hypothyroidism was same in both the age groups (p 0.411), with 19(59.37%) males and 13(40.62%) females and having no significant difference between males and females (p 0.434) [Table 2]. Similarly, there was no significant difference in hypothyroid versus euthyroid patients of BMI (p 0.841), history of splenectomy (p 0.544), and family history of β-thalassemia (p 0.312).However, there was significant difference in mean ferritin level of hypothyroid versus euthyroid patients(p 0.001), so the mean ferritin levels were significantly high in β-thalassemic patientsof hypothyroidism (Table 3). Among 32 hypothyroid β-thalassemics, 11 were patients compensated primary

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hypothyroidism, whereas 21 patients had uncompensated primary hypothyroidism (Fig. 1).

Table 1: Demographic data of all the patients (n=100)

Variable	No.	%
Gender		
Male	63	63.0
Female	37	37.0
Splenectomy	9	9.0
History of β-thalassemia	36	36.0
Mean age (years)	13.45±3.43	
Mean BMI (kg/m^2)	16.35±2.39	

Table 2: Gender distribution in hypothyroid patients (n=32)

Gender	No.	%
Male	19	59.37
Female	13	40.63
P value	0.434*	

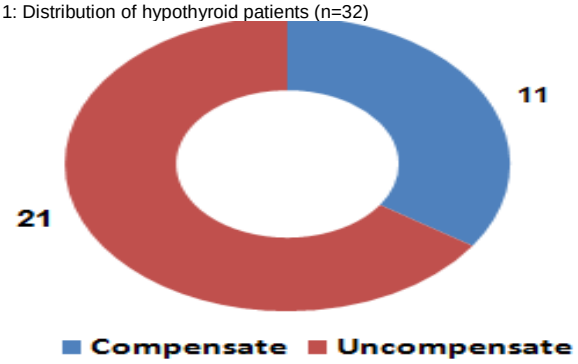
*Statistically not significant difference

Table 3: Comparison of mean ferritin levels

Gender	No.	%
Hypothyroid	19	59.37
Euthyroid	13	40.63
P value	0.001*	

*Statistically significant difference

Fig. 1: Distribution of hypothyroid patients (n=32)



DISCUSSION

Frequency of hypothyroidism in β-thalassemia patients on various organ systems during first and second decade of life is relatively understudied. The current study was planned to determine the frequency of hypothyroidism in diagnosed β-thalassemia patients having on-going blood transfusions. The β-thalassemia patients having TSH level >4 IU/ml, and T4 levels <4.5 g/dl were considered as hypothyroid. The methodology of present study is in accordance with previously conducted studies[7,10-15].

In Pakistan, the main treatment option in practice is blood transfusion along-with iron chelation therapy[11]. The mean age of patients with hypothyroidism in the present study was less than that was found in previously conducted studies[10,11,13-16] which may be linked to the insufficient chelation treatment, chronic Hb deficiency (anaemia) and related nutritional deficiencies, that is not rare in Indo-Pak region of the World&Asia[17].

In this study, there was significant difference in mean ferritin level of hypothyroid versus euthyroid patients, so the mean ferritin levels were significantly high in β-thalassemic patients of hypothyroidism. This may be due to the frequent blood transfusions but with poor chelating therapy, which leads to iron and ferritin overload which in turn damage thyroid cells at micro-levels due to formation of free radicals, reactive oxygen species and lipid peroxidation.[7-10] However, this is in contrast with the previously conducted several studies that have reported a lack of link between hypothyroidism and ferritin levels[1,11,12]. This is also in contrast with the previously conducted studies that have reported misleading ferritin levels due to chronic inflammatory disease and scurvy[15,16].

In the present study, the frequency of hypothyroidism was same in 5-9 years versus 10-19 years age groups and there was no significant difference in the frequency of hypothyroidism between boys and girls. Similarly, the frequency of hypothyroidism was not associated with BMI, history of splenectomy, and family history of β-thalassemia. These findings are in accordance with previously conducted studies[13-15] but in contrast with the findings of some other studies on same topic[7,10].

The frequency of hypothyroidism in the present study was found to be 32%. The frequency of thyroid dysfunction in thalassemia patients range from 6-30% and 13-60% depending on frequency of transfusion and chelation therapy was recorded. Frequency of primary hypothyroidism in β-thalassemia patients is reported to be 31.2% at Rahim Yar Khan[13]. Another large study from Karachi reported 11.8% over-all prevalence of hypothyroidism in thalassemia patients,[14] while in Faisalabad, hypothyroidism was reported in 29.3% of the patients.[15] Yet, in another study, frequency of primary hypothyroidism in homozygous β-thalassaemia patients was found 25.7%.[11]The frequency of hypothyroidism depends on factors such as region, the type and quality of therapy, and treatment strategies.

There are several limitations of present study such as present study was conducted at single endocrinology centre of Pakistan and with small sample size. However within these limitations, the results of present study showed that hypothyroidism is highly prevalent in β-thalassemia patients. Our suggestion is to do periodic check-ups in such patients for early diagnosis and interceptive treatment to avoid long-term complications[16-20].

CONCLUSION

Hypothyroidism is highly prevalent in β-thalassemia patients. Periodic check-ups are highly recommended for early diagnosis and interceptive treatment of associated issues to improve the life quality of such patients.

Conflict of interest: Nil

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