DOI: https://doi.org/10.53350/pjmhs22167266

ORIGINAL ARTICLE

Hypothyroidism in Children with B-Thalassemia at a Tertiary Hospital of South Punjab, Pakistan

TAYYABA BATOOL[1], SHOMAILA IRIM[2], MALIK MUHAMMAD NAEEM[3], BADAR MEHMOOD[4], NADEEM SHAHID YOUNAS[5], MUHAMMAD IRFAN KHAN[6], KHADIJA NADEEM[7]

[1]Assistant Professor, Department of Biochemistry, Quaid-e-Azam Medical College / Bahawal Victoria Hospital, Bahawalpur.
[2]PHD Physiology Student, Government College University, Faisalabad.
[3]Assistant professor of Paediatric Medicine, Quaid-e-Azam Medical College, Bahawalpur.
[4]Medical Officer, Department of Hematological diseases, Thalassemia & Bone Marrow Transplant Centre. Quaid-e-Azam Medical College / Bahawal Victoria Hospital, Bahawalpur.
[5]Registrar, Department of Hematological Diseases, Thalassemia & Bone Marrow Transplant Centre. Quaid-e-Azam Medical College / Bahawal Victoria Hospital, Bahawalpur.
[6]Associate Professor, Department of Hematological Diseases, Thalassemia & Bone Marrow Transplant Centre. Quaid-e-Azam Medical College / Bahawal Victoria Hospital, Bahawalpur.
[7]A-Levels Roots IVY Science Society, Bahawalpur
Correspondence to: Tayyaba Batool, Email: drtayyababatool@yahoo.com

ABSTRACT

Objective: To determine the prevalence of hypothyroidism among children with β-thalassemia major.
Study Design: Cross-sectional study.
Place and Duration of the Study: The Department of Hematological Disorder, Thalassemia and Bone Marrow Transplantation Centre, and Department of Biochemistry, Bahawal-Victoria Hospital, Quaid e Azam Medical College", Bahawalpur, Pakistan from 1st January 2021 to 31st December 2021.
Methodology: A total of 125 children of both genders (2 to 18 years) with diagnosis of β-thalassemia major were analyzed. Two ml blood sample under strict aseptic conditions was obtained from every study participant and sent to Institutional Pathological Laboratory for thyroid-stimulating hormone (TSH), T3, and T4.
Results: In a total of 125 children with β-thalassemia major, 78 (62.4%) were male. Overall, mean age was 8.57±4.75 years while 57 (45.6%) children were aged between 6 to 10 years. Residential status of 84 (67.2%) children was rural. Parental consanguineous marriages were reported in 91 (72.8%) patients. Mean TSH, T3 and T4 levels were calculated to be 3.27±1.38 pmol/L, 4.71±0.75 pmol/L and 11.80±2.38 pmol/L respectively. Hypothyroidism was noticed in 38 (30.4%) children.
Conclusion: Prevalence of hypothyroidism in children with β-thalassemia major was high. Early identification and management of hypothyroidism in β-thalassemia major may improve overall quality of life among these affected children
Keywords: B-thalassemia major, hypothyroidism, thyroid-stimulating hormone.

INTRODUCTION

The most frequently observed single gene defect associated with haemoglobin chain production is known as thalassemia.[1] A series of hemolytic illnesses collectively known as thalassemia are estimated to affect 1.5% of the world's population as carriers. [2] The reduction or absence of -globin chain formation is a characteristic of the "autosomal recessive haemoglobin abnormalities" group known as -thalassemia. [3] In the second half of the first year of life, the homozygous state manifests symptoms that include severe anaemia and necessitate frequent blood transfusions.[4] Thalassemia is considered to be a frequent monogenic abnormality globally.[5] Among people of India sub-continent and middle eastern region, around 9,000 cases of beta-thalassemia are born annually.[6] In Pakistan, 8-10 million people are estimated to be carriers of thalassemia usually termed as thalassemia minor while around 100,000 cases of thalassemia major are estimated to be present in Pakistan and these numbers are increasing every year.[3,7]

In the recent decades, management of β-thalassemia has improved immensely while iron chelators have enhanced the overall survival rates of these patients but recent data advocates increase in long-term complications like cardiomyopathy, hypothyroidism, hypoganadism, diabetes mellitus and hypoparathyroidism.[8,9] Although, literature reports sub-clinical and central types of hypothyroidism in thalassemia major but sub-clinical types of hypothyroidism are more frequently reported.[10,11] A local study from Faisalabad reported 29.3% of pediatric thalassemia major cases to have hypothyroidism.[12] Not much data exists determining prevalence of hypothyroidism among children of South Punjab, Pakistan. Our aim was to determine the prevalence of hypothyroidism among children with β-thalassemia major at one of the leading tertiary care hospital of South Punjab, Pakistan.

MATERIAL AND METHODS

This cross-sectional study was conducted at "The Department of Hematological Disorder, Thalassemia and Bone Marrow Transplantation Centre, and Department of Biochemistry, Bahawal-Victoria Hospital, Quaid e Azam Medical College", Bahawalpur, Pakistan from 1st January 2021 to 31st December 2021. Approval from "Institution's Ethics Committee" was taken. Informed/written consents were acquired from parents/guardians. The sample size was calculated to be 125 with 95% confidence levels considering expected prevalence of hypothyroidism as 29.3%[12] with margin of error 8% using the formula: $n=z^2*p*(1-p)/e^2$

Inclusion criteria were children of both genders aged 2 to 18 years with diagnosis of β-thalassemia major. All children with thalassemia intermedia or minor or those having acute illness were excluded. Children having family history of hypothyroidism were also note included.

A total of 125 children as per inclusion/exclusion criteria were enrolled. Demographic characteristics including gender, age and residential status (urban/rural) were noted. Two ml blood sample under strict aseptic conditions was obtained from every study participant and sent to Institutional Pathological Laboratory for thyroid-stimulating hormone (TSH), T3 and T4 estimation. All TSH, T3 and T4 investigations were performed by"enzyme-linked immunosorbent assay (ELISA)". Hypothyroidism was labeled as serum TSH above 4.0 mIU/L, T3 below 3.1 pmol/L, and/or T4 below 12 pmol/L. For data analysis, "Statistical Package for Social Sciences (SPSS)" was used. Chi-Square (categorical data) and Independent sample t-test (numeric data) were applied considering $p<0.05$ as significant.

RESULTS

In a total of 125 children with β-thalassemia major, 78 (62.4%) were male. Overall, mean age was 8.57±4.75 years while 57 (45.6%) children were aged between 6 to 10 years. As per medical history and record, mean age at the time of diagnosis of β-thalassemia major was 5.51±2.46 months. Residential status of 84 (67.2%) children was rural. Parental consanguineous marriages were reported in 91 (72.8%) patients (table-1).

Table-1: Characteristics of Children with β-Thalassemia Major (n=125)

Characteristics of Children		Number (%) / Mean±SD
Gender	Male	78 (62.4%)
	Female	47 (37.6%)
Age		8.57±4.75 years
Age (years)	2-5	38 (30.4%)
	6-10	57 (45.6%)
	11-15	12 (9.6%)
	16-18	18 (14.4%)
Age of Diagnosis of β-Thalassemia Major		5.51±2.46 months
Residential Status	Rural	84 (67.2%)
	Urban	41 (32.8%)
Parental Consanguineous Marriage		91 (72.8%)

Mean TSH, T3 and T4 levels were calculated to be 3.27±1.38 pmol/L, 4.71±0.75 pmol/L and 11.80±2.38 pmol/L respectively. Hypothyroidism was noticed in 38 (30.4%) children as shown in figure-1.

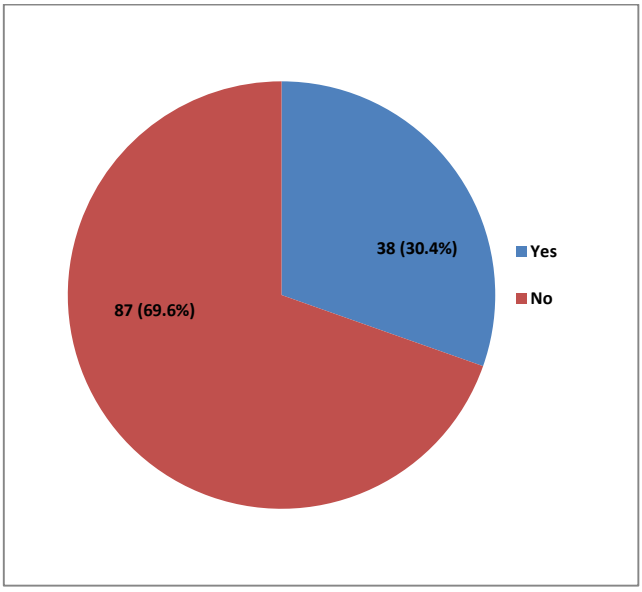

Figure-1: Prevalence of Hypothyroidism in Children with β-Thalassemia Major (n=125)

Stratification of characteristics of all children with β-thalassemia major with respect to prevalence of hypothyroidism is shown in table-2 and no statistically significant association of hypothyroidism was found with study variables (p>0.05).

Table-2: Stratification of Characteristics of Children with β-Thalassemia Major with respect to Prevalence of Hypothyroidism (n=125)

Characteristics		Hypothyroidism		P-Value
		Yes (n=38)	No (n=87)	
Gender	Male	24 (63.1%)	54 (62.1%)	0.9080
	Female	14 (36.9%)	33 (37.9%)	
Age Groups	2-5 years	12 (31.6%)	26 (29.9%)	0.8134
	6-10	16 (42.1%)	41 (47.1%)	
	11-15 years	5 (13.2%)	7 (8.0%)	
	16-18 years	5 (13.2%)	13 (14.9%)	
Age at Diagnosis of β-Thalassemia Major (months)		5.72±2.54	5.44±2.38	0.5544
Residential Status	Rural	22 (57.9%)	62 (71.3%)	0.4642
	Urban	16 (42.1%)	35 (28.7%)	
Parental Consanguineous Marriage		27 (71.0%)	64 (73.6%)	0.7717

DISCUSSION

Hyper-transfusion approach among cases of thalassemia has significantly enhanced overall life expectancy in the last few decades but chelation therapy is not cost-effective, has difficulty in administration and it is not always available so overall compliance is generally poor even in the presence of regular transfusions that further results in iron-overload.[13] Among hyper-transfused patients of thalassemia, experts advise early identification and management of endocrine related disorders. Histology based data has reinforced the hypothesis that thyroid related disorders are common among patients of β-thalassemia major.[14]

In this study, prevalence of hypothyroidism was high as observed to be 30.4% among patients of β-thalassemia major. A local study conducted by Yousaf HM et al revealed prevalence of hypothyroidism among children aged between 5-18 years receiving regular blood transfusions having β-thalassemia as 16% which is quite low that what was noted in this study.[15] Our findings are more aligned to what was found by Malik S et al where 25.7% patients of β-thalassemia major had hypothyroidism.[16] Rehman H et al showed prevalence of hypothyroidism as 29.3% in children aged 5-15 years with β-thalassemia which is very close to present findings.[12] Panchal R and Patel A from India noticed 10% of children between 3 to 16 years of age with β-thalassemia major to report hypothyroidism which is again lower that our findings.[17] A study from neighboring Iran showed prevalence of hypothyroidism to be 16% among patients of β-thalassemia.[18] Another study from Iran reported prevalence of hypothyroidism among patients of β-thalassemia to be 1% which is astonishing.[19] Data from the west reported prevalence of hypothyroidism to be 11% among patients of β-thalassemia major.[20] A study from Middle East has shown prevalence of hypothyroidism to be 19.2%.[9]

Literature also reports prevalence of hypothyroidism among thalassemic patients to be between 13 to 60% which shows large variation.[21] In light of all these studies, it can be stated that overall prevalence of hypothyroidism is high in patients of β-thalassemia major while the variation in prevalence of hypothyroidism in β-thalassemia major patients could be attributed to variation in patients characteristics, treatment protocols and adherence to overall management of β-thalassemia major. These β-thalassemic patients are also expected to have other endocrine dysfunctions while disruption in already compromised cardiac activity can further deteriorate the overall health quality of affected individuals and their families. Timely identification and management of these disorders can help clinicians improving overall health of β-thalassemia major children on regular blood transfusions.[22]

The limitations of this study included the fact that it was a single centre study and the limited sample size. We were unable to measure serum ferritin levels among children with β-thalassemia major which would have given us further insights about the role of serum ferritin in hypothyroidism and vice versa. Further studies incorporating large sets of patients with β-thalassemia major from multiple centers will further help us estimating the exact burden of hypothyroidism in these individuals.

CONCLUSION

Prevalence of hypothyroidism among children with β-thalassemia major was high. Early identification and management of hypothyroidism in β-thalassemia major may improve overall quality of life among these affected children but more studies exploring factors causing hypothyroidism are warranted to further guide us about various aspects of thyroid related disorders among children with β-thalassemia major.

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