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Original Research Paper

Pediatrics

# STUDY OF THYROID FUNCTION IN CHILDREN LESS THAN 12 YEARS OF AGE WITH BETA THALASSEMIA

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## ABSTRACT

**Background:** The most common genetic disease in worldwide is thalassemia. Iron chelators have increased survivability, but they have also increased the frequency of endocrine problems. Between 6 and 30% of children with Beta-Thalassemia Major (BTM) have hypothyroidism. The major causes of thyroid dysfunction include gland invasion, long-term tissue hypoxia, damage from free radicals, and organs siderosis. **Objective:** To evaluated the thyroid dysfunction in kids with Beta thalassemia for Assessment of growth pattern in children with beta thalassemia. **Methodology:** Thyroid dysfunction and iron load status were estimate in 150 kids with a mean age of 7.02±3.31years with beta-thalassemia major by measuring serum free triiodothyronine (FT3), total thyroxin (T3), serum total triiodothyronine (T4), serum free thyroxin (FT4) , thyroid-stimulating hormone (TSH) and ferritin levels from serum of patients admitted to the Paediatric department of tertiary care hospital between August 2020 to December 2022. This study was performed after obtaining clearance from institutional ethics commission after a while, informed consent will be taken from the subjects willing to participate in the study. **Result:** There were 69 girls (46%), 81 boys (54%) among 150 kids in the research. Subclinical hypothyroidism was seen in 20.7% of the kids. Among them, two were in their first decade of life, while the other two were in their second. The mean TSH, FT4, and ferritin levels were 5.27–12.68 mIU/ml, 8.66–2.51 microgram/dl, and 2038.69–882.28 ng/ml, respectively, in children with thyroid dysfunction. With a p value of 0.004, higher serum TSH readings in kids in their second decade of life were statistically significantly correlated with the degree of thyroid dysfunction. No other significantly correlations were found between Oral chelation, the quantity and length of blood transfusions, or serum ferritin levels. **Conclusion:** Thus, the early diagnosis and prompt treatment of beta thalassemia major sufferers might be achieved with routine thyroid dysfunction testing and serum ferritin measurements.

**KEYWORDS :** Thyroid function, Iron Overload, Beta-Thalassemia, Chelation Therapy.

## INTRODUCTION

The most common genetic disease in worldwide is recognized is thalassemia. Depending on whether globin chain gene is damaged, there are mainly two types of this autosomal recessive disorder: alpha and beta.[1] Beta-thalassemia major causes fast erythrocyte breakdown and autosomal recessive erythropoiesis, which leads to progressive heart failure and early child mortality.[2,3]

According to the Census of India 2011, the overall prevalence of beta thalassemia carriers is 3%–4%, translating to 35–45 million carriers in our 1.21 billion-person multiethnic, culturally and linguistically diversified population, which also includes about 8% of tribal communities. There is an estimated 100,000 thalassemia sufferers, with a substantially greater frequency (4%–17%) in a few of the ethnic groups.[4,5]

Inherited diseases known as beta thalassemia syndromes are characterized by a shortage of beta globin chains, which impairs erythropoiesis and is worsened by circulating hemoglobin F's lack of affinity for 2,3-diphosphoglycerate. In order to preserve life, frequent blood transfusions are required. As a result, excessive iron gets stored in numerous organs, which causes early mortality. Depending on the chelation methods, the prevalence of hypothyroidism in Beta Thalassemia Major (BTM) patients ranges from 6 to 30% in different nations.[6]

Endocrinopathies are now among the most prevalent thalassemia problems, although identifying the incidence is challenging due to age variations at which chelation therapy was initially administered and the steady rising survival rates of well-chelated peoples.[7] While there are many factors that contribute to endocrine difficulties in the normal community, in Thalassemia major, the endocrine issues are caused by iron buildup in the endocrine glands as a result of transfusion dependence.[8] Following hypogonadism, hypothyroidism is the second-leading endocrine disease, being diagnosed in 5.6%–17percentage of individuals.[9,10,11] The principal source of injury to the endocrine glands, along the hypothalamic-pituitary axis, is iron accumulation. Endocrinopathies are more likely to develop in thalassemia that had splenectomy, high ferritin levels, and poor chelation compliance.[12,13]

All beta thalassemic patients should get a yearly thyroid dysfunction test in the lab since hypothyroidism's non-specific indications can impact numerous body organs. There are several studies which have investigated thyroid function in chronically transfused kids with beta thalassemia major in their second decade of lifespan, but relatively few examining thyroid dyfunction in chronically transfused kids in their first decade of lifespan. Consequently, it is necessary to conduct a comparison research to assess the thyroid dysfunction status in kids with beta thalassemia major in the first and second decades of lifespan.[14]

## METHOD

A Hospital based cross sectional descriptive research were conducted at Paediatric department of tertiary care hospital.150 diagnosed patients of BTM kids aged less than 12 years and those willing to participate in our research were examined. The research was performing from August 2020 to December 2022. Ethical approval letter was also obtained for the study. A sample size of 150 was calculated considering Prevalence of thyroid dysfunction which is 38% was considered here for sample size calculation. Applying the formula for sample size calculation $4^* P^* Q / L^2$ where P= 38% the sample size was calculated to be 105. All diagnosed patients of age 1 year to 12 years with Beta thalassemia and willing to participate were included in the study. People whose follow-up was not practical and who refused to contribute to the research were not included in it. After receiving approval from the institutional ethical committee (Government Medical College), people who met the original study inclusion requirements were enrolled in the investigation. Measurements of free triiodothyronine (FT3), free thyroxin (FT4), thyroid-stimulating hormone (TSH), blood total thyroxin (T3), total triiodothyronine (T4) and serum ferritin levels, as

well as BMI, height, and weight, were used to assess thyroid function and iron load status.

### Statistical analysis

The software packages SPSS 24.0 version IBM USA were used to conduct statistical studies, and Chi square and Fischer's exact test analyses were used in the assessments. A p value of less than 0.05 was recognized as statistical significance, and a p value of less than 0.001 was regarded as extremely significant.

## RESULT

We included 150 paediatric age patients with Beta thalassemia in the study. Mean age of the study population was 7.02 ± 3.31 years. Out of 150 patients 81 (54%) were males and 69 (46%) were females in our study.

Signs: Of the 150 individuals, 116 (77.3%) had pallor and 34 (22.7%) had both pallor and icterus.

Per-abdominal examination findings: Of the 150 individuals, 34 (22.7%) had hepatomegaly, 101 (67.3%) had hepatosplenomegaly, and 15 (10.0%) had splenomegaly.

Thyroid type: Of the 150 individuals, 117 (78.0%) were euthyroid, 2 (1.3%) had overt hypothyroidism, and 31 (20.7%) had subclinical hypothyroidism.

Chelation therapy status: Of the 150 individuals, 107 (71.3%) were on chelation therapy and 43 (28.7%) were not.(Table 1)

Mean T3 levels were measured in individuals with euthyroid, overt hypothyroidism, and subclinical hypothyroidism, and no statistically significant difference was found between the mean T3 levels across these three types of thyroid disorders whereas, The mean T4 levels were measured in individuals with different types of thyroid disorders. The results showed a statistically significant difference in the mean T4 levels across these three groups ($p<0.05$). Specifically, individuals with overt hypothyroidism had lower T4 levels, while individuals with euthyroid and subclinical hypothyroidism had normal T4 levels.(Table 2)

The study measured the mean TSH and serum ferritin levels in people with different types of thyroid disorders. The outcomes showed that there was a significant difference in the mean TSH levels between individuals with euthyroid, overt hypothyroidism, and subclinical hypothyroidism ($p<0.05$). However, there was no significant difference in the mean serum ferritin levels between these groups. Specifically, individuals with overt hypothyroidism had very high TSH levels, while individuals with euthyroid and subclinical hypothyroidism had normal TSH levels. These findings may help doctors in diagnosing and managing thyroid disorders.(Table 3)

## DISCUSSION

Children with BTM who have frequent transfusions and receive inadequate chelation are more likely to develop iron overload. Thyroid hemosiderosis is caused by iron being accumulated in the thyroid interstitium, as it is in all organs. This gradually deteriorates thyroid function. The purpose of this research is to determine the kind of thyroid dysfunction and its relationships to the length of time and number of blood transfusions, serum ferritin levels, and the effectiveness of chelation. It has been suggested that the most likely cause thyroid dysfunction in BTM sufferers is iron deposition from repeated transfusions. Iron buildup in the liver is directly correlated with serum ferritin. As an acute phase protein, serum ferritin is also a byproduct of hepatocellular injury. As an outcome, conditions including sepsis, congestive heart failure, and hepatitis may cause a falsely high reading. There is no clinical indication of hepatitis or heart failure in any of the research participants.[14] we included 150 paediatric age patients with Beta thalassemia in the study. Out of 150 children, majority i.e. 45.3% were from 6-10 years age group followed by 34% from 1-5 years and 20.7% from 11-15 years age group. Mean age of the research population was 7.02±3.31 years. Mean Age in years was 7.02±3.31. 54% were males and 46% were females were included in our study. 54% were from rural area and 46% from urban area.

Similar finding was observed in **Abdel-Razek AR et. al.**[15]study which enlisted 52 toddlers with beta thalassemia in his research, 27 of them (52%) were boys and 25 of whom (48%) were girls. They were between the ages of 12 and 18, with a mean age of 16.0±1.91 years.

In our study, the mean age of euthyroid, overt hypothyroidism and sub clinical hypothyroidism cases were 6.43±3.28, 11.00±1.41 and 9.00±2.49 years respectively. We observed statistically significant difference in the mean age with respect to types of thyroid disorders ($p<0.05$).

**Upadya SH et. al.**[16]indicated that subclinical hypothyroidism was present in 4.8% of the kids. Two of them belong to the first decade of existence, and the other two to the second. None of the kids from the BTM who had thyroid issues also had autoimmune thyroiditis**.**

In our study distribution according to weight revealed that 68% of the children had weight between 3rd-50th centile, 29.3% had below 3rd centile and 2.7% had between 50th-97th centile.

**Upadya SH et. al.**[16]reported weight distribution with those < $3^{RD}$ 66.9% having thyroid dysfunction are 4.8%, 10TH-$25^{TH}$-6%, 10TH-$3^{RD}$-4.8%, $10^{TH}$-3.6%, 25TH-$50^{TH}$-3.6%, $25^{TH}$-3.6%, 3RD-$10^{TH}$-1.2 $3^{RD}$-7.2%,50TH-$25^{TH}$-1.2% and $50^{TH}$-3.6%.

In our study, Distribution according to height revealed that 59.3% of the children had height between 3rd-50th centile, 38% had below 3rd centile and 2.7% had between 50th-97th centile.

**Upadya SH et. al.**[16]reported height distribution those with < $3^{RD}$ 66.3% having thyroid dysfunction are 2%, 10TH-$25^{TH}$-7.2%, 10TH-$3^{RD}$-6.0%, $10^{TH}$-2.4%, 25TH-$50^{TH}$-1.2%, $25^{TH}$-4.8%, 3RD-$10^{TH}$-6.0% $3^{RD}$-2.4%,50TH-$25^{TH}$-1.2% and $50^{TH}$-2.4%

In our study, Distribution according to BMI revealed that 84% of the children had BMI between 3rd to 85th centile, 9.3% had below 3rd centile, 4.7% had between 85th to 95th centile and 2% had >95th centile. Prevalence of overweight in our study was 4.7% whereas that of obesity was 2%.

Distribution according to thyroid type revealed that the prevalence of euthyroid was 78%, sub clinical hypothyroidism was 20.7% and overt hypothyroidism was 1.3%.

In our study, out of 117 euthyroid cases, majority were from 6-10 years age groups i.e. 43.6%, 41% were from 1-5 years and 15.4% from 11-15 years. Out of 2 overt hypothyroidism cases, 50% each were from 6-10 and 11-15 years respectively. Out of 31 sub clinical hypothyroidism cases, majority were from 6-10 years age groups i.e. 51.6%, 38.7% were from 11-15 years and 9.7% from 1-5 years. We observed statistically significant association between age and type of thyroid disorder in our study ($p<0.05$).

In our study, Proportion of euthyroid males and females were 53.8% and 46.2% respectively. Proportion of overt hypothyroidism males and females were 100% and 0% respectively. Proportion of sub clinical hypothyroidism males

and females were 51.6% and 48.4% respectively. We observed statistically non-significant association between gender and type of thyroid disorder in our study (p>0.05).

Mean T3 of euthyroid, overt hypothyroidism and sub clinical hypothyroidism cases were 120.72±24.76, 90.10±0.71 and 118.8±24.73 ng/dl respectively. We observed statistically no significant difference in the mean T3 with respect to types of thyroid disorders (p>0.05).

**Ayfer Gozu P et. al.**[17] reported the mean T3 of hypothyroidism and euthyroidism cases were 0.38±0.15 and 0.37±0.15 ng/dl respectively that was found statistically insignificant, as the difference in the mean T3 with respect to types of thyroid disorders was(p>0.05). These findings are comparable to our study findings.

**Abdel-Razek AR et. al.**[15] reported that mean fT3 (pg/ml) in beta thalassemia with thyroid dysfunction and normal cases was 2.14±0.89 2.11±0.73 respectively with statistically no-significant difference in the mean value (p-0.131). These findings are not comparable to our study findings.

**Ritu Jaipuria et. al.**[19] reported the mean T3 of hypothyroidism and euthyroidism cases were 1.25±0.62 and 1.39±0.43 ng/ml respectively hence the difference in the mean was found statistically insignificant difference in the mean T3 with respect to types of thyroid disorders (p>0.05). These findings are comparable to our study findings.

Mean T4 of euthyroid, overt hypothyroidism and sub clinical hypothyroidism cases were 9.04±2.57, 3.05±0.21 and 7.56±1.37 microgram/dl respectively. We observed statistically significant difference in the mean T4 with respect to types of thyroid disorders (p<0.05). ). It means T4 was lowered in overt hypothyroidism cases & normal in euthyroid and subclinical hypothyroidism cases.

**Ayfer Gozu P et. al.**[17] reported that mean T4 of hypothyroidism and euthyroidism cases were 9.0±18.8 and 10.3±2.1 ng/dl respectively. They found statistically insignificant difference in the mean T4 with respect to types of thyroid disorders (p>0.05). These findings are comparable to our study findings.

**Abdel-Razek AR et. al.**[15] reported that mean fT4 (pg/ml) in beta thalassemia with thyroid dysfunction and normal cases was fT4 (mg/dl) 11.52±2.02 10.48 ±2.77 respectively with statistically insignificant difference in the mean value (p-0.911). These findings are not comparable to our study findings.

**Ritu Jaipuria et. al.**[19] reported the mean T4 of hypothyroidism and euthyroidism cases were 7.44±2.59 and 7.39±1.72 ng/ml respectively that were found statistically insignificant difference in the mean T4 with respect to types of thyroid disorders (p>0.05). These findings are comparable to our study findings.

Mean TSH of euthyroid, overt hypothyroidism and sub clinical hypothyroidism cases were 1.81±1.36, 103.95±11.81 and 11.96±6.72 microgram/dl respectively. We observed statistically significant difference in the mean TSH with respect to types of thyroid disorders (p<0.05). It means TSH was significantly elevated in overt hypothyroidism and sub clinical hypothyroidism cases in our study.

**Ayfer Gozu P et. al.**[17] reported that mean TSH of hypothyroidism and euthyroidism cases were 3.4±3.8 and 2.31±1.8 IU/mL respectively. They found statistically insignificant difference in the mean TSH with respect to types of thyroid disorders (p>0.05). These findings are not comparable to our study findings.

**Abdel-Razek AR et. al.**[15] reported that the serum TSH of the studied patient ranged from 0.28 to 25 mIU/ml with the mean serum TSH of 4.5±4.8 mIU/ml.

**Ritu Jaipuria et. al.**[18] reported the mean TSH of hypothyroidism and euthyroidism cases were 8.15±1.20 and 3.59±1.50 mIU/ml. respectively that was found statistically significant difference in the mean TSH with respect to types of thyroid disorders (p<0.05). These findings are comparable to our study findings.

Mean serum ferritin of euthyroid, overt hypothyroidism and sub clinical hypothyroidism cases were 1856.55±913.9, 3000.0±0.0 and 2664.13±203.61 respectively. We observed statistically significant difference in the mean TSH with respect to types of thyroid disorders (p<0.05). It means serum ferritin was significantly elevated in overt hypothyroidism and sub clinical hypothyroidism cases in our study (p<0.05).

**Ayfer Gozu P et. al.**[17] reported that mean serum ferritin of hypothyroidism and euthyroidism patient were 2703±1649 and 81.5±15.5 ng/ml respectively. They found statistically no-significant difference in the mean serum ferritin with respect to types of thyroid disorders (p>0.05). These findings are comparable to our study findings.

**Ritu Jaipuria et. al.**[18] reported the mean serum ferritin of hypothyroidism and euthyroidism patient were 614.66±151.91 and 539.78±209.14 NG/dl respectively that was found statistically significant difference (p<0.05). These findings are comparable to our study findings.

**Panchal R et. al.**[19] reported the mean serum ferritin of hypothyroidism and euthyroidism patient were 3550.21 ± 1852.51 and 6262.27 NG/dl respectively that was found statistically non-significant difference (p>0.05). These findings are not comparable to our study findings.

Our study revealed that mean serum ferritin of euthyroid, overt hypothyroidism and sub clinical hypothyroidism cases were 1856.55±913.9, 3000.0±0.0 and 2664.13±203.61 respectively (p<0.05).

Our study found a link between iron overload and deteriorating thyroid function, so increasing chelation compliance, switching the chelator used, and routine thyroid function monitoring starting in the first decade of life will all have a big impact on stopping thyroid hemosiderosis and thyroid dysfunction later on. Also, it will be advantageous to regularly check the thyroid function of BTM kids and start hormone replacement therapy if necessary.

## CONCLUSION

Thalassemia patients have a high prevalence of endocrinological abnormalities. Primary hypothyroidism is due to iron deposition in thyroid gland which is due to frequent blood transfusions.

Earlier diagnosis and therapy of endocrine failure in sufferer multiple treatment with thalassemia sufferer is significant part of the holistic management of the disorder.

Hence regular screening of beta thalassemia major patients for thyroid function test and serum ferritin for early detection and timely therapy could raise the slandered of life.

**Tables:**

**Table-1: Distribution of sign, Per-abdominal, chelation therapy, Thyroid type and Thyroid type in given study.**

| Signs | No. Of cases | Percentage |
|---|---|---|
| Pallor | 116 | 77.3 |
| Pallor + Icterus | 34 | 22.7 |

| | | |
|---|---|---|
| Total | 150 | 100.0 |
| Per-abdominal examination findings | **No. of cases** | **Percentage** |
| Hepatomegaly | 34 | 22.7 |
| Hepatosplenomegaly | 101 | 67.3 |
| Splenomegaly | 15 | 10.0 |
| Total | 150 | 100.0 |
| Thyroid type | **No. of cases** | **Percentage** |
| Euthyroid | 117 | 78.0 |
| Overt hypothyroidism | 2 | 1.3 |
| Sub clinical hypothyroidism | 31 | 20.7 |
| On chelation therapy | **No. of cases** | **Percentage** |
| Yes | 107 | 71.3 |
| No | 43 | 28.7 |
| Total | 150 | 100.0 |

**Table-2: Comparison of mean T3 and T4, according to thyroid type**

| T3 (ng/dl) | N | Mean | Std. Deviation | F | p |
|---|---|---|---|---|---|
| Euthyroid | 117 | 120.72 | 24.76 | 1.56 | 0.21 |
| Overt hypothyroidism | 2 | 90.1 | 0.71 | | |
| Sub clinical hypothyroidism | 31 | 118.8 | 24.73 | | |
| Total | 150 | 119.91 | 24.76 | | |
| **T4 (micro gram/dl)** | **N** | **Mean** | **Std. Deviation** | **F** | **p** |
| Euthyroid | 117 | 9.04 | 2.57 | 10.5 | 0.0001* (<0.01) |
| Overt hypothyroidism | 2 | 3.05 | 0.21 | | |
| Sub clinical hypothyroidism | 31 | 7.56 | 1.37 | | |
| Total | 150 | 8.66 | 2.51 | | |

*= Significant

**Table-3: Comparison of mean TSH and serum ferritin according to thyroid type**

| TSH (micro IU/ml) | N | Mean | Std. Deviation | F | p |
|---|---|---|---|---|---|
| Euthyroid | 117 | 1.81 | 1.36 | 958.46 | 0.0001* (<0.01) |
| Overt hypothyroidism | 2 | 103.95 | 11.81 | | |
| Sub clinical hypothyroidism | 31 | 11.96 | 6.72 | | |
| Total | 150 | 5.27 | 12.68 | | |
| **Serum ferritin** | **N** | **Mean** | **Std. Deviation** | **F** | **p** |
| Euthyroid | 117 | 1856.6 | 913.9 | 13.37 | 0.0001* (<0.01) |
| Overt hypothyroidism | 2 | 3000 | 0 | | |
| Sub clinical hypothyroidism | 31 | 2664.1 | 203.61 | | |
| Total | 150 | 2038.7 | 882.28 | | |

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