

Correlation between iron status and thyroid function in beta-thalassemia major of Iraqi patients

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ABSTRACT : Iron overload is an important issue in the state of thalassemic patients due to the harmful effect of high concentration of iron deposited in different tissues in the human body including endocrine glands. In the present work, an attempt is carried out to estimate the effect of different levels of iron body status on the function of thyroid glands in thalassemic major patients in relation to TPO antibodies. One hundred thirty beta-thalassemia major patients divided into three groups; two groups (low iron overload and high iron overload) and sixty-five healthy persons as control groups. Blood samples were taken in the fasting to check laboratory tests such as ferritin, T3, T4, TSH and TPO estimated by ELISA technique and iron status estimated by spectrophotometer technique. 119(61%) of patients had Euthyroid, 13(6.7%) subclinical hypothyroidism, 63 (32.3%) had hypothyroidism with a significant difference when compared to healthy control group while there was no significant statistical difference in TPO level between different studied groups (p -value ≤ 0.001). In the current study, there was no significant correlation between T3, T4 and TSH with different serum ferritin levels. Thyroid dysfunction (hypothyroidism and subclinical hypothyroidism) is common among Iraqi thalassemia major patients with iron overload, and it's unrelated to different serum ferritin levels, and the increasing presence of TPO antibodies among these patients with moderate correlation may be due to immunogenicity changes due to the direct effect of iron on thyroid tissue.

Keywords: Beta thalassemia major; Iron overload; Thyroid function

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I. INTRODUCTION

Beta thalassemia represents a group of recessively inherited haemoglobin disorders characterised by deficient synthesis of the β -globin chain. The homozygous state results in severe anaemia in infancy, which requires a regular blood transfusion. (Shamshirsaz et al., 2003) The combination of blood transfusion and chelation therapy has dramatically prolonged the life expectancy of these patients, thus transforming thalassemia from a rapidly fatal disease of childhood to a chronic disease compatible with prolonged life. (Khan, 2006) On the other hand, frequent blood transfusions, iron overload, poor compliance to therapy and chronicity of the disease have in turn contributed to a whole spectrum of complications including cardiac problems, hypogonadism, diabetes mellitus, hypothyroidism, hypoparathyroidism and other endocrine and metabolic problems in adolescents and young adults. (Satwani et al., 2005) In recent years, several authors reported a high incidence of endocrine abnormalities in children, adolescents and young adults suffering from thalassemia major. However the incidence of the various endocrinopathies changes among different series of the patients due to multiple reasons other than iron overloads. (Vullo et al., 1990) The commonest form of thyroid dysfunction, seen in thalassemia, is subclinical hypothyroidism. However, the frequency of hypothyroidism varies depending on the region, quality of management and treatment protocols. (Shamshirsaz et al., 2003) In the present work, an attempt is carried out to estimate the effect of different body iron overload status on the thyroid function in thalassemic patients with Thyroid peroxidase (TPO) antibodies evaluation.

II. Material and Method:

The study was carried out on 130 dependent beta thalassemia (TM) patients with a mean age (13.56 ± 4.72 years). The study includes three groups: sixty-five (65) TM patients with serum ferritin less than 2500 ng/ml (**group A**), sixty-five (65) TM patients with serum ferritin ≥ 2500 ng/ml (**group B**), and sixty-five (65) were healthy subjects (**group C**). All patients represented different ages and receiving a regular blood transfusion. No history of chronic infection or another chronic disease, negative history of viral hepatitis infection. The serum levels of ferritin, T3, T4, TSH and TPO assessed by ELISA (Reader & Printer Systems, USA) and ELISA (Washer system, Australia). Iron status levels assessed by spectrophotometry (Ce Cecil, England). Written

informed consent taken from all patients participated in the study, the study was approved by the local institutional board in our hospital.

III. Statistical methods:

Statistical analyses were conducted using the statistical software package of SPSS version 20.0. Differences between groups assessed by the Mann Whitney U test for nonparametric variables. Pearson's correlation coefficients were calculated to evaluate the association between relevant parameters. Statistical significance was set at $p < 0.05$.

IV. Results

The results in table (1) showed that 85.7% of patients had Euthyroid 119(61.0%), Subclinical hypothyroidism 13 (6.7%), and hypothyroidism 63 (32.3%) when compared with healthy group as the results revealed 64 (98.5%) Euthyroid, 1(1.5%) Subclinical hypothyroidism, 0 (0.0%) hypothyroidism, there was significant difference between patients and healthy individuals at (p -value < 0.001). In the current study, there was no significant correlation between T3, T4 and TSH with serum ferritin, while there was a moderate correlation between anti-TPO and serum ferritin, as illustrated in the table (2).

V. Discussion:

Early identification and management of endocrine dysfunction in patients with thalassemia is a recognized part of the whole management of thalassemia, in particular role of thyroid dysfunction, pituitary gland dysfunction, gonadal glands dysfunction, and diabetic mellitus as complications of thalassemia caused by iron overload. (Zervas et al., 2002) In the current study, the incidence of thyroid dysfunction was high (39%) of thalassemia patients, of these patients, 32.3% patients were with hypothyroidism while the 6.7% patients were with subclinical hypothyroidism. Eshragiet al, included 130 patients with thalassemia major in Babol/ Philippines in 2011, they reported 19 (14.6%) having hypothyroid (2 had primary hypothyroid, 3 had secondary hypothyroid, 14 had subclinical hypothyroidism), (Eshragi et al., 2011) while in another study in Iran (Tehran) 2003 which included 220 thalassemia patients, reported 7.7% patients having primary hypothyroidism, (Shamshirsaz et al., 2003) in another Iranian study in 2008 which included 56 patients primary hypothyroidism was present in 9 (16%) and subclinical hypothyroidism 10.7%. (Najafipour et al., 2008)

In these studies, the incidence of hypothyroidism was lower than that presented by our findings. While in a study that involved 50 patients with Hemoglobin E-beta-thalassemia (EBIT) in India they found 12% and 32% of studied patients had hypothyroidism and subclinical hypothyroidism respectively (Dolai et al., 2016) which is comparable to our findings. Hypothyroidism is one of the complications of thalassemia (especially in young adult and adolescent) which is caused by thyroid cells siderosis and start to develop during the 2nd decade of life in well treated thalassemic patients, with the advent of better management of iron overload and early initiation of therapy, the prevalence of thyroid dysfunction is declined especially compared to 70th and 90th where in it was frequently diagnosed in patients younger than 15 years (in these periods chelation therapy was started later and was not regularly used, and this led to chronic tissue hypoxia) which is still an issue in developing countries, and may explain the high rate of hypothyroidism in our patients (Delvecchio and Cavallo, 2010). The development of thyroid dysfunction is variable; in which in the precocious phase it is reversible, and become slowly progressive and stationary if intensive chelation therapy is offered (Toumba et al., 2007).

In the current study there was no significant correlation between T3, T4 and TSH with serum ferritin, Zervas et al and Derma et al indicate that there was no significant correlation between ferritin and thyroid function which is in agreement with our findings (Zervas et al., 2002, Drema et al., 2017), while Jaipuria et al in their study show that TSH directly and significantly correlated with ferritin, age, and TIBC which is in disagreement with our findings, while both T3 and T4 did not correlate with ferritin, age, and TIBC which is in agreement with our findings, the disagreement with our findings may be attributed to the type of patients included in their study which are thalassemia major and lower sample size (60 patients in total), (Jaipuria et al., 2014) however, the possibility of association of thalassemia major as a cause of the direct correlation between TSH and ferritin supported by another Iraqi study done in 2015 which included 50 patients with thalassemia major. (Hadeed et al., 2015)

Our study showed a significant moderate correlation of TPO antibodies and serum ferritin among major thalassemia patients, this result may be related to the effect of iron overload on the thyroid gland tissue immunogenicity leading to formation TPO antibodies, which may lead to increasing the risk of thyroid dysfunction as another mechanism besides the direct damage effect of the iron molecule on the thyroid gland.

VI. Conclusion

This study concludes that the iron overload and thyroid dysfunction (hypothyroidism and subclinical hypothyroidism) is common among beta-thalassemia major patients in Iraq. Presence of TPO antibodies may be

another cause of thyroid dysfunction in Thalassemia major patients which is related to change of the immunogenicity of thyroid tissue. Thyroid function evaluation must be carried out regularly in patients with beta-thalassemia major.

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Table 1: Assessment of thyroid function status among different studied groups

Variables	Healthy	All thalassemia	P value
Number	65	130	-
Euthyroid	64 (98.5%)	119 (61.0%)	
Subclinical hypothyroidism	1 (1.5%)	13 (6.7%)	<0.001
Primary hypothyroidism	0 (0.0%)	63 (32.3%)	

Chi-square test used

Table 2: assessment of thyroid function and TPO antibodies among different levels of serum ferritin in thalassemia major patients

Variables	Serum ferritin		p-value
	<2500 ng/ml	≥2500 ng/ml	
Euthyroid	29 (44.6%)	26 (40%)	0.858
Subclinical hypothyroidism	6 (9.2%)	6 (9.2%)	
Primary hypothyroidism	30 (46.2%)	33 (50.8%)	

Chi-square test

Table 3: Pearson correlation between ferritin test and various variables in all patients (n=130)

Variables	Ferritin	
	r	P-value
T3	0.022	0.808
T4	-0.030	0.733
TSH	0.102	0.246
TPO	0.268	0.002

r: correlation coefficient
Linear regression analysis

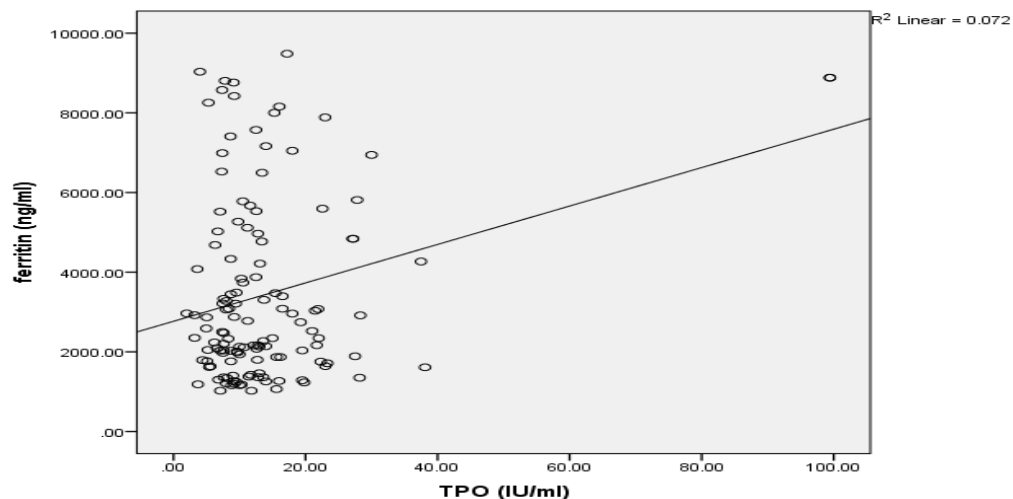


Figure 1: scatterplot of the correlation between TPO and ferritin

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