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Gonadal dysfunctions in Beta Thalassemia Major Adults in association with anemia and iron overload

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ABSTRACT

Background: Endocrine dysfunctions, particularly hypogonadism, are among the most common complications in adults with β-thalassemia major (BTM), significantly impairing quality of life.

Objective: To evaluate the effect of anemia and iron overload on gonadal dysfunction in Beta Thalassemia Major Adults in Suez Canal University hospitals

Methods: A cross-sectional observational study was conducted at the Endocrinology and Hematology clinics of Suez Canal University Hospital. Sixty participants were divided equally into three groups: (1) BTM patients with gonadal dysfunction, (2) BTM patients without gonadal dysfunction, (both aged more than 18 years) and (3) Age - matched healthy control group. Gondal dysfunction assessed by medical history and lab evaluation, complete blood count and serum ferritin levels was done.

Results: Both thalassemia groups showed markedly lower hemoglobin levels compared to the control group, The difference in anemia between thalassemia patients with and without gonadal dysfunctions was not statistically significant ($p = 0.174$).

Serum ferritin was extremely elevated in both thalassemia groups compared to controls, reflecting iron overload, but no statistically significant difference in ferritin levels between thalassemia patients with and without gonadal dysfunctions. ($p = 0.989$).

Conclusion: Hemoglobin level and serum ferritin cannot be used as sole predictors for gonadal dysfunctions in β-thalassemia major (BTM) adults

Keywords: *β-thalassemia major, gonadal dysfunctions*

1. INTRODUCTION

Endocrine complications are a major problem for patients with transfusion-dependent β-thalassemia, with pituitary iron deposition thought to be the main cause of hormonal alterations in thalassemia patients (Karadag et al., 2020)

Hypothalamic- pituitary- gonadal dysfunction in beta thalassemia major both anemia and iron overload were involved in the pathophysiology of hypogonadism in thalassemia.

The mechanisms involved in the development of hypogonadism in TM patients are complex. Chronic anemia, iron overload and chronic liver disease seem to play an important role in the development of this complication. (De Sanctis et al., 2017)

Low hemoglobin (Hb) levels can affect HPG function, and blood transfusions can cause significant changes in the hormonal milieu in thalassemia patients.

(Soliman et al., 2018) investigated the effect of packed red blood cell (PRBC) transfusions in 10 young adults with TM, aged 17-32 years, who had completed pubertal development (Tanner stage 5, eugonadal), on gonadal function and sperm parameters, and ejaculatory ability after Packed RBCs transfusion, hemoglobin increased significantly from 8.7 ± 0.86 g/dL to 11.1 ± 0.82 g/dL, also testosterone levels (from 16.5 ± 8 nmol/l to 20 ± 8.8 nmol/l), and gonadotropin concentrations. Total sperm count increased significantly from 57.80 ±38.3 million/ml to 166 ± 132 million/ml, and fast progressing sperm motility increased from 20.6 ± 16.6% to 79.7 ± 67.4%. (Soliman et al., 2018)..

pituitary-gonadal function, which in thalassemia is exacerbated by the presence of iron overload. **(Soliman et al., 2018).**

2. SUBJECTS AND METHODS

cross-sectional observational study was conducted at Suez Canal University Hospital, Ismailia, Egypt. Ethical approval was obtained, and written informed consent was provided by all participants.

3. STUDY GROUPS:

- Group 1: BTM patients with gonadal dysfunctions

- Group 2: BTM patients without gonadal dysfunctions

- Group 3: Healthy, age- and sex-matched controls (Hb ≥13 g/dL in males, ≥12 g/dL in females)

Inclusion Criteria: Egyptian adults (≥18 years) with confirmed BTM (Groups 1 and 2); healthy, non-anemic controls (Group 3).

Exclusion Criteria: Thalassemia minor, liver/kidney disease, autoimmune or chronic inflammatory diseases.

Participants (n=60; 19 males, 41 females) underwent medical/reproductive history taking, and blood sampling (2 x 2 mL).

4. LABORATORY ANALYSIS:

1. First blood sample for CBC and hemoglobin level measurement.

2. Second blood sample centrifuged for assessing serum ferritin level before blood transfusion done by ELISA KIT (Enzyme-linked fluorescent assay method on VIDAS system) and measurement of serum levels of:

LH, FSH, Estrogen in females, Free testosterone in males (early morning sample was taken (done by equilibrium dialysis followed by direct assessment) and serum ferritin.

5. STATISTICAL ANALYSIS:

SPSS v22.0 used. ANOVA, t-tests, chi-square tests applied, Significance: $p \leq 0.05$.

6. RESULTS:

Both thalassemia groups showed markedly lower hemoglobin levels compared to the control group, The difference in anemia between thalassemia patients with and without gonadal complications is not statistically significant (p = 0.174).

Serum ferritin was extremely elevated in both thalassemia groups compared to controls, reflecting iron overload, but no statistically significant difference in ferritin levels between thalassemia patients with and without gonadal complications (p = 0.989).

Hemoglobin level and serum ferritin cannot be used as sole predictors for gonadal dysfunctions in β-thalassemia major (BTM) adults

Table (1):

Hematological	**Thalassemia patients with gonadal dysfunction[1]** **Mean ±SD**	**Thalassemia patients without gonadal dysfunction [2]** **Mean ±SD**	**Control group [3]** **Mean ±SD**	**p-value**
Hemoglobin level**(gm/dl)**	7.129 ±0.82	7.52 ± 0.79	12.9 ± 0.71	0.174[b]
Serum ferritin **(ng/ml)**	2621.52 ± 1288.88	2383.39 ± 706.84	101.52 ± 20.24	

				0.989[b]

Table (1): Demonstrated that no statistically significant difference in ferritin levels between thalassemia patients with and without gonadal complications (p = 0.989).

7. DISCUSSION:

In this study the mean serum ferritin level in thalassemic patients with hypogonadism was 2621.52 ng/mL ± 1288.88. VS thalassemia patients without complications showed a lower mean serum ferritin level of 2383.39 ng/mL ± 706.84, the same as in **(Mahwi et al., 2023)** the mean ferritin level in thalassemic patients with hypogonadism and thalassemic patients without hypogonadism was 2326±2625 ng/ml vs. 1220±2625 ng/ml, suggesting higher ferritin levels in BTM patients with complications.

Unlike a study in Bangladesh investigating the role of serum ferritin level as a diagnostic tool for hypogonadism in BTM patients by **(Romana Chowdhury., etal.2023)**, Hypogonadism was common (~35%) among thalassemia patients, Patients with hypogonadism had significantly higher serum ferritin levels than those who were eugonadal (mean ~3,572 vs ~2,175 ng/mL; $p < 0.001$), and Serum ferritin showed strong predictive power (AUC ~0.83) for gonadal dysfunction

Cross-sectional analysis from Pakistan by (Shahid Z, etal.2021) revealed elevated ferritin was associated with sexual underdevelopment by Tanner staging. A ferritin cutoff ~4,900 ng/mL was moderately sensitive and specific to predict sexual immaturity in patients with β-thalassemia major.

8. CONCLUSION:

Although serum ferritin correlates with gonadal dysfunction in beta thalassemia major patients but can not be used as a sole specific and sensitive predictor marker.

Declarations

The authors express their sincere gratitude to the staff of the Endocrinology and Hematology clinics at Suez Canal University Hospital for their assistance in participant recruitment and data collection. We also thank all study participants for their valuable time and cooperation.

Ethics approval and consent to participate: Approved by Suez Canal University Faculty of Medicine Ethics Committee in accordance with the declaration of Helsinki. Written informed consent obtained.

Consent for publication: Not applicable.

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Dr. Nada Mosafa Ahmed and dr. Mohamed A. Greash are responsible for the integrity of the work as a whole from inception to published article, are considered as 'guarantor'

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