

## Evaluation of Delayed Puberty of Patients with Beta Thalassemia Major in –Diyala Governorate

Alaa A Mahmud (BSc)<sup>1</sup>, Ali M Al-Gharawi (PhD)<sup>2</sup> and Falah M Mustafa (PhD)<sup>3</sup>

### Abstract

**Background:** The absence of secondary sexual characteristics are known complications in patients with beta thalassemia major.

**Objective:** Evaluation the effects of frequent blood transfusions on puberty in patients afflicted with beta thalassemia ( $\beta$ -thal) major.

**Patients and Methods:** Eighty patients with beta thalassemia major were categorized into two groups, 51 male and 29 female, and 40 normal individuals were chosen as a control group. The concentrations of the luteinizing hormone (LH), follicle stimulating hormone (FSH) in both genders, Estradiol in female and testosterone in male were evaluated in the sera of patients and controls by ELISA method.

**Results:** The mean concentrations of serum FSH, LH, estradiol in female, and testosterone in male showed highly significant decrease in patients with beta thalassemia major in comparison with control group. Hypogonadotropic hypogonadism was reported in 67.5% of all  $\beta$ -thalassemia patients (70.6% of male and 62.1% of female).

**Conclusion:** Delayed puberty is caused by the effect of excess iron on the anterior lobe of pituitary gland.

**Key words:** Delayed puberty, Blood transfusion, Hypogonadotropic hypogonadism.

**Corresponding Author:** alaa.alzuhary@yahoo.com

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<sup>1</sup> Baqubah Teaching Hospital -Diyala - Iraq.

<sup>2</sup> Foundation of Technical Education- Section of Medical Laboratory Science Technology- College of Health and Medical Technology-Baghdad I-Iraq.

<sup>3</sup> Al-Batool Teaching Hospital for Obstetrics and Pediatrics -Diyala -Iraq.

### Introduction

Beta-thalassemia ( $\beta$ -thal) syndromes are grouping of inherited blood disorders characterized by reduce or missing of beta globin chain synthesis, resulting in reduced amounts of haemoglobin (Hb) in the red blood cells (RBC), decrease RBC creation and anemia. The majority of thalassemias are inherited as recessive traits [1].

Frequent blood transfusions with increased gastrointestinal iron absorption lead to an iron overload in the body [2]. Human are

unable to remove the iron, and the overload iron is deposited as hemosiderin and ferritin in the liver, spleen, endocrine organs and myocardium [3]. Poor growth and manifold endocrinopathies, include hypogonadotropic hypogonadism (HH), growth hormone deficiency, are recognized complications in beta thalassemia major (TM), and are considered the result of iron excess [4]. Failure of pubertal growth, delay or lack of sexual progress, amenorrhea, sexual

dysfunction and infertility due to hypogonadism are well-known disorder of the hypothalamic - pituitary - gonadal axis in  $\beta$ -thal patients[5].

### Patients and Methods

Eighty patients(51males and 29 females) with  $\beta$ - thalassemia major with an age range of 14–30 years (mean  $18.80\pm 4.58$ years)for male and 13–30 years (mean  $17.48\pm 4.83$ ) for females were studied. Sera were collected from the patients at Baqubah Teaching Hospital - The Specialized Center of Hereditary Blood Diseases ,Baquba-Diyala.The diagnosis of  $\beta$  thalassemia major was made by the consultants, considering the results of hemoglobin electrophoresis ,laboratory investigations and clinical features of the patients.

The data were collected about sex, age, ,socio-economic state, marital status, parent consanguinity, family history, medical and surgical history (e.g.splenectomy),date of diagnosis, date of first blood transfusion, period, between blood transfusions , medication history ,puberty information including questions about the presence of secondary sexual characteristics .In female ,menstruation history was reported .Forty healthy subjects(23male and 17 female) were taken as a control group for comparison. Chi-square test and T-test were used to the distinction between two independent means.

### Sample collection

About 5 milliliters venous blood were obtained from all subjects(patients and controls). In thalassemic patients ,sampling was done just before the blood transfusion. In menstruating thalassemia major female patients and controls, venous blood samples were drawn through the mid-follicular phase of the menstrual cycle (days 5–8). The blood samples were centrifuged at 3000 rpm for 10 minutes and sera were freezed at about  $-20^{\circ}\text{C}$ ( until examination )didn't exceed 10 weeks [6].

### Statistical analysis

Basic serum biochemical parameters including, follicular stimulating hormone(FSH) ,luteinizing hormone (LH), serum estradiol in female and serum testosterone in male were assayed for patients and control groups within eight weeks by ELISA method [7].

### Results

In this study fifty four  $\beta$ -thal patients (67.5%) were suffering from hypogonadotropic hypogonadism ,while twenty six (32.5%)were eugonadism, Table(1). A high significant decrease ( $p < 0.001$ ) was seen in patients in serum follicle stimulating hormone FSH , luteinizing hormone(LH), testosterone and estradiol,when compared with healthy control , Table(2).

**Table (1):** Distribution of Thalassemic Patients and Healthy Controls According to Hypogonadotropic Hypogonadism and eugonadism.

Secondary hypogonadism		Male				Female			
		Thalassemia		Control		Thalassemia		Control	
		No	%	No	%	No	%	No	%
Yes	36	70.6	-	-	18	62.1	-	-	
No	15	29.4	23	100	11	37.9	17	100	
P value		0.0001				0.0001			
*Highly Significant using Pearson Chi-square test at 0.05 level of significance									

**Table (2):** Mean Concentration of the hormones in the Sera of Studied Groups.

	Male		Female	
	Thalassemia	Control	Thalassemia	Control
LH (mIU/ml)	2.19 ±1.19 (0.3-5.3)	7.01±2.14 (4.1-12.0)	2.98±2.77 (0.2-12.0)	10.73±3.93 (6.1-21.9)
FSH (mIU/ml)	2.78±1.94 (0.3-10.5)	6.97±2.63 (4.0-12.2)	3.41±1.36 (1.1-6.6)	12.15±2.39 (8.3-17.0)
Testosterone (ng/ml)	1.64±1.75 (0.2-6.2)	3.89±1.31 (1.7-6.7)	-	-
Estradiol (pg/ml)	-	-	14.77±20.22 (1.3-101.0)	59.65±45.70 (21.0-185.0)

## Discussion

Delayed puberty and hypogonadism are the most common iron-related endocrinological complications reported in almost all studies from a range of countries[8]. Primary hypogonadism is associated with low levels of testosterone /estradiol and high-normal to high levels of LH and FSH. Secondary hypogonadism(hypogonadotrophic hypogonadism HH) is associated with low levels of testosterone /estradiol and normal to low levels of LH and FSH[9, 10]. In the present study 70.6% of male and 62.1% of female

patients with  $\beta$ -thal major developed hypogonadotropic hypogonadism .

The similar study was defined by Soliman *et al* [11], who reported that thalassaemic patients had a total absent of pubertal changes in 73% of boys plus 42% of girls with thalassemia between the ages of 13 and 21 years. De Sanctis *et al*[12] , reported that there is a considerable percent (30%) of patients with  $\beta$ -thalassemia major having hypogonadotropic hypogonadism . Kwan *et al*[13], have recorded that 62% of boys with 75% of girls above the age of 12 years had hypogonadotropic hypogonadism .

## Conclusion

In  $\beta$ -thal. major patients the majority of the studied patients were at age range of (15-19 year) for both sexes. Therefore, early diagnosis of hypogonadism is crucial to ensure normal sexual development and puberty and avoid irreversible complications. Although therapy with Deferoxamine to treat iron overload, the threat of secondary hypogonadism remained elevated.

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