Razi Med J. 2025;1(4):312-316
https://doi.org/10.69667/rmj.25405
Razi Medical Journal
https://razi.edu.ly/rmj/index.php/hm

Original article

Serum Testosterone and Estradiol Profiles in Patients with β-Thalassemia Major

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Abstract
β-thalassemia major is the most common chronic hemolytic anemia in Iraq, treated with multiple transfusions. The present study was carried out to evaluate Serum testosterone in male patients and estradiol in female patients with β-Thalassemia major and the effects of frequent blood transfusions. In this study, eighty patients were employed and categorized into two groups: 51 males (63.7%) with age range 14–30years and 29 females (36.3%) with an age range 13–30 years, while 40 normal healthy individuals were chosen as a control group, 23 male (57.5%) and 17 female (42.5%) for comparison. ELISA was used to measure the levels of testosterone and estradiol in the serum. The mean levels of serum testosterone (1.64 ± 1.75) and estradiol (14.77 ± 12.30) were significantly lower in β-thalassaemia patients than in controls ($p < 0.001$). In patients with hypogonadism, the mean age for the start of blood transfusion was significantly lower compared to those with eugonadism, with a P value of 0.003. There was a significant decrease in height percentile in hypogonadism thalassemic patients compared to eugonadism patients (p value = 0.01). In contrast to healthy controls, the study shows that patients with β-thalassemia major have significantly lower serum levels of testosterone and estradiol, suggesting that hypogonadism is quite prevalent in this population.
Keywords. *Testosterone; Hypogonadism; Estradiol; β-thalassemia; Eugonadism.*

Received: 11/08/25
Accepted: 11/10/25
Published: 21/10/25

Introduction

A severe microcytic, hypochromic anaemia (Cooley's anaemia) is a hallmark of the most severe variant, β-thalassemia major [1]. Peripheral erythrocyte haemolysis is caused by an imbalance in globin chain production towards increased production of the α-chain, which results from depletion or reduced synthesis of the β-globin chain. This causes haemoglobin to change from a normal oxygen-transporting role into poisonous inclusion bodies. This condition is autosomal recessive [2,3].

Early initiation of a regular transfusion program that maintains a minimum Hb concentration of 9.5 to 10.5 g/dl usually results in normal growth and development for 10 to 12 years [4]. Transfusion recipients may have issues related to iron excess. Excess iron in children can lead to growth retardation and failure or delay in sexual development. Later complications from iron overload include problems with the liver (fibrosis and cirrhosis), the heart (dilated myocardiopathy or infrequent arrhythmias), and the endocrine glands (diabetes mellitus, hypogonadism, and insufficiency of the parathyroid, thyroid, pituitary, and, less commonly, adrenal glands) [5,6].

When iron buildup surpasses physiological needs, extra iron is deposited in tissues, resulting in iron overload. The effect of subsequent parenchymal damage is organ dysfunction [7]. Disorders that are acquired or inherited can cause iron overload. It is important to differentiate acquired iron overload from hereditary hemochromatosis since it encompasses several clinically unique diseases. A patient who has received multiple transfusions is a typical example [8]. One of the androgen group's steroid hormones is testosterone. Although the adrenal glands also secrete tiny amounts, the testicles of males and the ovaries of females are the primary locations for their secretion. With a molecular weight of 288.47 Dalton, it is an anabolic steroid and the primary male sex hormone [9]. The steroid hormone estradiol (17-beta-estradiol; E2) is made from cholesterol. The molecular weight of this steroid hormone is 272.4 Daltons. Targets tissues found in the skeletal and cardiovascular systems, the mammary gland, and the reproductive tracts of both men and women [10]. It is mostly produced by the placenta and the female ovary's Graafian follicle, with the adrenal glands producing trace amounts as well [11]. Low testosterone/estradiol levels that cause delayed puberty, insufficient reproduction, or both were referred to as hypogonadism [12]. Assessing the levels of testosterone and oestradiol in patients with beta thalassaemia major and comparing them to healthy controls is the aim of this study.

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Methods

Study Population

Eighty patients with β-thalassemia major (51 males with an age range of 14–30years) (mean 17.90±4.35) and 29 females with an age range of 13–30 years (mean16.98±3.93) were studied. For contrast, 40 subjects in the same age range—23 men and 17 women—who made up the control group were selected. Between March 2025 and July 2025, blood samples were taken from patients at the AL-Batool Teaching Hospital for Obstetrics and Paediatrics in Baquba, Diyala, Iraq.

Diagnostic and Classification Criteria

Expert consultants used laboratory testing, haemoglobin electrophoresis data, patient clinical characteristics, and age at the onset of blood transfusion to diagnose beta thalassaemia major. Additionally, the height percentile of controls and thalassaemia patients was determined.

Sample Collection

All individuals (patients and controls) had venous blood drawn in amounts of around 5 millilitres. Sampling was done right before the blood transfusion in thalassemic patients. Blood samples were taken during the mid-follicular phase of the cycle (days 5–8) in both the control group and the menstrual female patients. For the hormonal assay, the blood samples were centrifuged for 10 minutes at 3000 rpm, and each serum was stored in two locations and frozen at roughly -20°C.

Laboratory Analyses

Within eight weeks, serum levels of male testosterone and female oestradiol were measured in both the patient and control groups using the enzyme-linked immunosorbent assay (ELISA) technique (MyBioSource, USA).

Exclusion criteria

The other sixty β-thalassemia major patients were excluded because they were under 14years for boys and under 13 years for girls. Patients with Hb <8 gm% were also excluded.

Ethical Clearance

Each participant group received an explanation of the study's goals and procedures, and subsequently provided their consent. The research received approval from the Training and Human Development Centre Research Committee of the Diyala Health Department (No. 3540).

Results

The data illustrated in (Table 1) revealed that those with low testosterone hormone levels in male patients and estradiol in female patients were higher (70.6% and 62.1%) when compared with healthy controls (4.3% and zero). Furthermore, there was a high percentage of normal levels of testosterone and estradiol in the control group (95.4% and 100%) in comparison with a low percentage in thalassemic patients (29.4% and 37.9%) in males and females, respectively. There was a highly significant difference with a P value = 0.0001 between thalassemic patients and healthy controls at the 0.05 level of significance.

Table 1. Distribution of healthy controls and thalassemic patients based on hormone levels.

Parameter		*Male*				*Female*			
		Thalassemia		**Control**		**Thalassemia**		**Control**	
		No	%	No	%	No	%	No	%
Testosterone (ng/ml)	Low	36	70.6	1	4.3	-	-	-	-
	Normal (2 - 6.9)	15	29.4	22	95.7	-	-	-	-
	High	-	-	-	-	-	-	-	-
	P value	0.0001*				-			
Estradiol (pg/ml)	Low	-	-	-	-	18	62.1	-	-
	Normal (13-191)	-	-	-	-	11	37.9	17	100

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	High	-	-	-	-	-	-	-	-
	P value	-				0.0001*			
* Highly significant at the 0.05 level of significance using the Pearson Chi-square test									

Data illustrated in Table 2, the mean value of testosterone in thalassemic males (1.64) and estradiol in thalassemic females (14.77) was significantly decreased when compared with their mean values of healthy controls (3.89 in males and 59.65 in females), p value =0.0001.

Table 2: Comparison of Serum Testosterone and Estradiol Levels (Mean ± SD) in Thalassemic and Control Subjects.

Parameter	Sex	Thalassemia (Mean ± SD)	Control (Mean ± SD)	P-value
Testosterone (ng/ml)	Male	1.64 ± 1.75	3.89 ± 1.31	0.0001**
	Female	–	–	
Estradiol (pg/ml)	Male	–	–	
	Female	14.77 ± 12.30	59.65 ± 45.70	0.0001* *
* Significant difference between two independent means using Student's t-test at the 0.05 level.				

Table 3 revealed that the mean age of the start of blood transfusion in eugonadism patients with β-thalassemia major was 1.6 of males and 2.98 of females. The mean age of the start of blood transfusion in hypogonadism patients was 1.0 in males and 0.86 in females. There was a highly significant decrease in the mean age of the start of blood transfusion in patients with hypogonadism in comparison with eugonadism patients at P value =0.003.

Table 3: Mean Age at the Start of Blood Transfusion (years) in Eugonadal and Hypogonadal Thalassemic Patients.

Group	Eugonadism (Mean ± SD)	Hypogonadism (Mean ± SD)	P-value
Male thalassemia	1.60 ± 1.10	1.00 ± 0.91	0.003 **
Female thalassemia	2.98 ± 2.12	0.86 ± 0.71	
All thalassemia patients (Male + Female)	2.15 ± 1.70	0.96 ± 0.90	
Significant at the 0.05 level (difference between two independent means using Student's t-test).			

The data illustrated in Table 4, a high percentage of height percentile less than the 3rd was found in thalassemia patients with hypogonadism (70.4%). Followed by 3rd -25percentile (24.0%), the last was 25-50th percentile (5.6 %). There was a low percentage of height percentile less than the 3rd in eugonadism patients (42.3%). Followed by the 3rd-25 percentile (34.6%), then 25-50 percentile (15.4%) in each male and female eugonadism thalassemia patients. There was a significant decrease in height percentile in hypogonadism thalassemic patients when compared with eugonadism patients (p value =0.01).

Table 4: Distribution of eugonadism and hypogonadism thalassemia patients according to height percentile.

Height Percentile	Thalassemia (Male and Female)			
	Eugonadism		Hypogonadism	
	No	%	No	%
<3rd	11	42.3	38	70.4
3rd-25	9	34.6	13	24.0
25-50	4	15.4	3	5.6
50-75	-	-	-	-
75-97	2	7.7	-	-
>97	-	-	-	-
P value			0.01*	
*Significantly using the Pearson Chi-square test at 0.05 level of				

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Discussion

β-thalassemia major is the most common chronic hemolytic anemia in Iraq, treated with multiple transfusions. The goal of the current study was to assess how frequent blood transfusions affected the puberty of a group of Iraqi patients who had β-thalassaemia (β-thal) major. The damage to the hypothalamic-pituitary-gonadal axis is probably limited to the central area. It is well known that elevated iron deposition in the pituitary gland causes cytotoxicity in transfusion-dependent β-thal patients, primarily resulting in hypogonadotropic hypogonadism (HH) because of the pituitary's decreased responsiveness to gonadotropin-releasing hormone (GnRH) [13]. In addition to lipid peroxidation, oxidative stress, and the generation of free radicals, the most plausible reason is associated with iron overload and its burden, even though the precise process is not entirely clear [14].

Iron deposition has been shown to cause hypofunction of the pituitary-gonadal axis, particularly in the form of secondary hypogonadism, which iron chelation therapy seldom reverses [15,16]. In the current study, neither male nor female patients were found to have hypergonadotrophic hypogonadism. More recent studies have shown that hypogonadism is common in transfusion-dependent β-thalassemia patients (usually 60–70 percent). This is in line with secondary (central) hypogonadism, which is marked by low sex steroid levels and low or unusually normal LH/FSH levels [17,18].

Early blood transfusion led to increased iron accumulation in the body and increased complications of the endocrine system. Patients with delayed age of blood transfusion may have less genetic defect than others with early transfusion, leading to the need for blood transfusion at a later age. These results agreed with Moayeri [19], who found that there was a significant difference between patients with normal puberty and impaired puberty in age at the start of blood transfusion and age at the start of chelation therapy.

Growth failure in adolescents with thalassemic disorders is frequently caused by delayed puberty. Iron overload, the harmful effects of deferoxamine, or the emergence of other endocrinopathies, such as growth hormone insufficiency or intrinsic hypothyroidism, could be the cause of the growth retardation and aberrant body proportions with truncal shortening that are frequently observed in beta thalassemic patients [20]. It has been noted that a common consequence of transfusion-dependent thalassaemia is short stature [21].

Patients with thalassaemia experience growth retardation due to a variety of reasons. The primary ones were iron overload, folate deficiency, hypersplenism, chronic anaemia, and endocrine disorders (hypogonadism, hypothyroidism) brought on by iron overload [22,23]. The results agreed with Dhouib *et al* [24], who asserted that patients in their pubertal years were more likely to have growth anomalies.

Conclusion

The reduction in serum testosterone in males and estradiol in females suggests that gonadal function and hypothalamic-pituitary regulation might be affected by chronic anemia, repeated blood transfusions, and subsequent iron excess, potentially resulting in delayed puberty and reproductive failure.

Conflict of interest. Nil

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