

## Prevalence of Hypogonadism in $\beta$ -Thalassemia Major Patients from Gaza Strip

Amin T. Hamed<sup>1</sup>, Mohammed R. Zughbur<sup>2</sup> and Elham A. Shaheen<sup>3</sup>

<sup>1</sup>Associate Professor of Pharmacology, Faculty of Pharmacy, Al-Azhar University, Gaza-Palestine.

<sup>2</sup>Associate Professor of Endocrinology, Faculty of medicine, Al-Azhar University- Gaza-Palestine.

<sup>3</sup>Master of pharmaceutical sciences, Sheikh Hamad Bin Khalifa Al Thani Rehabilitation & Prosthetics Hospital, Gaza-Palestine

### ABSTRACT

This study was conducted to determine the prevalence of hypogonadism among  $\beta$ -Thalassemia Major ( $\beta$ -TM) adolescent patients, and the role of iron chelation therapy (ICT) in its prevention. Data was collected from 60  $\beta$ -TM patients and 35 controls aged 13–30 years through a questionnaire and a review of medical history to collect sociodemographic characteristics, transfusion regimen, chelating history and pubertal status. Complete blood count, serum ferritin, and pituitary-gonadal function tests were analyzed 1–2 weeks after blood transfusion. Logistic regression, independent t-test, and chi-square test were used to analyze our results and the significance was tested at  $p \leq 0.05$ . The overall prevalence of hypogonadism among  $\beta$ -TM patients was 75%, the mean of serum ferritin was  $6704.83 \pm 2849$  ng/ml and all patients had serum ferritin above 2000 ng/ml indicating a severe iron overload. Low hemoglobin level ( $p=0.006$ ), high ferritin level ( $p=0.018$ ), high blood transfusion per year (24-blood transfusions) ( $p=0.007$ ), and poor compliance to iron chelation therapy programs ( $p=0.001$ ), were detected had significant partial effect in hypogonadism. In conclusion, hypogonadism is highly prevalent among Gaza strip  $\beta$ -TM patients. Its presence being associated with lower hemoglobin values, iron overload, high blood transfusion and low compliance of iron chelation therapy.

**Keywords:**  $\beta$ -thalassemia major, Hypogonadism, Iron overload, Chelation therapy, Gaza strip.

### 1. INTRODUCTION

$\beta$ -Thalassemia major ( $\beta$ -TM) is the term applied to patients who have no effective or severely limited production of  $\beta$ -globin chains. This type is the most severe form of thalassemia which is often associated with life-long blood transfusion dependent anemia<sup>1</sup>. More than five decades ago,  $\beta$ -TM was fatal in the first decade of life, this poor prognosis changed since the survival rates started to increase progressively; thanks to intensive blood transfusion programs combined with chelation therapy<sup>2</sup>. Humans have a very limited ability to excrete iron, so regular blood transfusion inevitably leads to iron overload. Evidence of marked iron

deposition in the liver, heart, pancreas, pituitary, thyroid, parathyroid, adrenal, gonads, renal medulla, bone marrow, and spleen are commonly reported<sup>3</sup>. To date, there are 3 major classes of iron chelators. The first is Deferoxamine (DFO), which cannot be orally absorbed, so, it must be administered subcutaneously or intravenously. Having a short plasma half-life of 20–30 minutes, DFO should be administered by slow subcutaneous (SC) infusion over a span of 8–12 hours using an infusion pump for 6 nights per week<sup>4</sup>. The second iron chelator is Deferiprone (DFP), which can be administered orally once daily<sup>5</sup>. Also, the third iron chelator Deferasirox (DFX) is recommended orally once or twice daily and is characterized by its high affinity for iron<sup>6</sup>.

Abnormalities in pubertal onset and hypogonadism are the most frequently reported endocrine complications that

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affect 50–100% of  $\beta$ -TM patients<sup>7</sup>, and is likely to result from impaired gonads (primary), pituitary gland (secondary), and hypothalamus (tertiary). Secondary hypogonadism, often referred to as hypogonadal hypogonadism, is the most common cause of hypogonadism in thalassemia major. Several worldwide studies examined the risk factors for these complications, and the results varied between them. Some of them showed that pituitary iron overload due to intensive blood transfusion and low efficient chelation is the main risk factor for hypogonadism<sup>8,9</sup>. These studies observed significant relationship between serum ferritin level and hypogonadism rate, however other studies did not observe significant relationship between serum ferritin and hypogonadism rate, these studies attributed hypogonadism for factors other than iron overload like multi-endocrine dysfunction, chronic anemia, infections, and malnutrition<sup>10,11</sup>.

In Gaza Strip,  $\beta$ -thalassemia is a major public health problem where the screening studies estimated the prevalence of  $\beta$ -thalassemia gene carriers between 2.6% and 4.3%. The relatively high consanguinity rate, as well as the remarkable prevalence of the defects in HBB gene, resulted in more than 300  $\beta$ -TM patients currently being managed through blood transfusions and iron chelation at the government hospitals<sup>12,13</sup>.

The present study evaluated the prevalence of hypogonadism among  $\beta$ -thalassemia major patients from the Gaza Strip, and how it associates to the level of ferritin, the main indicator for body iron overload. The outcomes of our evaluation study could be used to improve or modify the management protocols, such as blood transfusions and iron chelation, for our patients in Gaza Strip.

## 2. SUBJECTS, AND METHODS

### 2.1. Study design

This study is a quantitative analytical retrospective case control study in which the prevalence of hypogonadism among  $\beta$ -TM patients from the Gaza Strip was evaluated, and correlated with ferritin level to detect the main risk factors for the resulted rate of hypogonadism,

thus the main measures for its prevention could be determined.

### 2.2. Patients

#### 2.2.1. Study Population and Sample Size

Sixty  $\beta$ -thalassemia major patients were selected randomly from two hospitals in the Gaza strip, where thalassemia patients are usually monitored and attend regularly for blood transfusion and iron chelation therapy administration, in Al Shifaa hospital, and European Gaza hospital.

Also, thirty-five healthy subjects with the same age and sex distribution as the experimental group served as the control group. Clinical and laboratory evaluation of patients and controls was performed in the same way after taking written consent to participate in this study after explaining its objectives to them.

#### 2.2.2. Inclusion criteria

Patients were considered eligible in this study upon meeting the following criteria: (1)  $\beta$ -TM with 13-30 years old. (2) on a regular blood transfusion program. (3) subjected to suitable iron chelating program.

#### 2.2.3. Exclusion criteria

Exclusion criteria were as follows: (1) non-transfusion-dependent thalassemia's. (2) mental illness. (3) bone marrow transplanted patients. (4) acute diseases as a sudden increase in serum ferritin may be caused by infections, or inflammatory conditions<sup>14</sup>. (5) treatment with hormones or anabolic steroids within the last 3 months.

### 2.3. Data collection.

Data was collected through questionnaire and a review of medical history records. The questionnaire included major sets of questions that include demographic characteristics, age at first transfusion and the interval between transfusions, age of starting iron chelation therapy (ICT), and compliance rate with ICT programs which was defined as percent of doses administered in the week out of those prescribed (The use of DFO regularly 5–7 days a week was considered as excellent, while the use of DFO

less than 5 days a week and less than two days a week was considered as good and poor compliance, respectively according to Haghpanah, et al.(2014)<sup>15</sup> and Trachtenberg, et al. (2011)<sup>16</sup>.

#### **2.4. Blood sampling and analytical procedures**

All blood samples were collected in the morning (08.00 – 09.00 am) after an overnight fasting, and 1–2 weeks after blood transfusion. The investigations included complete blood count, serum ferritin analysis, liver function tests, pituitary-gonadal function analysis which included follicle-stimulating hormone (FSH) analysis, Luteinizing hormone (LH) analysis, estradiol analysis in females and testosterone analysis in males.

#### **2.5. Assessment of hypogonadism and delayed puberty:**

##### **2.5.1. Laboratory evidence for hypogonadism**

Laboratory evidence for hypogonadism was based on finding of low FSH and LH with low estradiol or testosterone (hypogonadotrophic hypogonadism), or normal FSH and LH with low estradiol or testosterone (normogonadotrophic-hypogonadism) according to Noetzli et al.<sup>17</sup>.

##### **2.5.2. Pelvic ultrasound and careful physical examination**

Hypogonadism and delayed puberty in males was defined by absence of testicular enlargement (>4ml) by the age of 18 years or the lack of complete pubertal development for more than 5 years after the start of puberty. While in females it is defined as: Absence of breast development by the age of 13 years, Primary amenorrhea or Secondary amenorrhea<sup>18,19</sup>.

##### **2.5.3. Tanner staging**

According to Tanner staging which known as Sexual Maturity Rating (SMR), and defined as an objective classification system that providers use to document and track the development and sequence of secondary sex characteristics of children during puberty according to separate scales for the development of external genitalia: phallus, scrotum, and testes volume in males; breasts in females; and pubic hair in both males and females,

hypogonadism is diagnosed by Tanner stage 2 or 3<sup>20</sup>.

#### **2.6. Data analysis**

Statistical package for social science (SPSS) version 22 was used for analysis of data, and statistical relationship between hypogonadism and all variables were assessed using logistic regression chi-square and independent t-test and with (CI) of 95%.

### **3. RESULTS**

#### **3.1. Sociodemographic characteristics**

As shown in table (1) out of 60 patients included in this study; 29(48.3%) patients were males, while 18(51.5%) of controls were males. The mean age of study patients was 21.08±3.8 years and study controls was 21.11 ± 3.86 years. BMI in thalassemic patients was about 19.97 ± 2.74 that significantly lower than controls ( $P = 0.001$ ) and high percentage of thalassemic patients about 28(46.67%) were underweight. Splenomegaly was reported to be a major complication among our  $\beta$ -TM patients that was mainly managed by splenectomy in 75% of them.

#### **3.2. Hemoglobin level and iron status of the study sample**

Reviewing the medical files of the studied patients revealed that all of them were diagnosed in the first year of life through hemoglobin electrophoresis and began blood transfusion. The mean age at the first transfusion was four months (range 1–10 months).

Table (2) shows that the mean current pre-transfusion hemoglobin (Hb) levels was about 7.64 ± 0.87 g/dl, and 7.48 ± 0.86 g/dl for males and females respectively, which was significantly lower than the mean Hb levels of study controls ( $P < 0.005$ ). The distribution of study sample according to three Hb level intervals showed about 56(93.33%) of thalassemic patients were below the expected pre-transfusion hemoglobin level (9-10) g/dl. To correct the anemic status among thalassemic patients, all of them were given packed red blood cells. Data shown in table (2) represents the distribution of patients according to the number of blood transfusions per year which estimated from the week interval between transfusions

and range between 12-24 blood transfusions per year.

Frequent transfusions are associated with iron overload that usually is reflected by serum ferritin. The mean serum ferritin concentration for  $\beta$ -TM males was  $6381 \pm 2813$  ng/ml significantly higher than the mean serum ferritin concentration of study control males  $170 \pm 25$  ng/ml ( $P < 0.005$ ). Also, the mean serum ferritin concentration for thalassemia females was  $7007 \pm 2895$  ng/ml was significantly higher than the mean serum ferritin concentration of study control females  $106 \pm 29$  ng/ml ( $P < 0.005$ ). This revealed that all thalassemic patients of the study sample had severe iron overload with ferritin level more than (2000 ng/ml) which serves as a risk factor for multiple endocrine dysfunctions.

### 3.3. Iron chelating therapy characteristics and compliance rate

All patients who participated in this study were using iron chelating agents, specifically Deferoxamine (Desferal)<sup>®</sup> due to unavailability of other chelators at the ministry of health for about one year. The mean dose of (Desferal)<sup>®</sup> for study patients was  $49.27 (\pm SD 23.6)$  mg/kg/day (range 1500-5000mg/day) administered by slow subcutaneous (SC) infusion over a span of 8-12 hours using an infusion pump for 5-7 nights per week. As shown in table (2) only about 40(66.67%) of patients used chelating agents at earlier dates before the age of 10 years, and the majority of patients 32(53.33%) had poor compliance to the therapy regimen, that resulted from practical issues such as difficulty with DFO infusions, or from psychological / psychosocial issues, socio-economic status, and lack of family support.

### 3.4. Characteristics of patient's liver function test levels

Table (3) shows significantly worsened liver function test levels results for  $\beta$ -thalassemia major patients compared to controlled persons (ALT  $82.68 \pm 38.9$  IU/l; AST  $76.5 \pm 41.4$  IU/l; ALP  $355.42 \pm 108.98$  U/l; and INR  $1.25 \pm 0.12$ ,  $P < 0.001$ ).

### 3.5. Patient's Gonadal hormones level

In the gonadal profile, LH, FSH, total testosterone and estradiol were significantly different between cases and controls in males and females as shown in table (3).

### 3.6. Patients distribution according to gonadal function status

The prevalence of hypogonadism in  $\beta$ -TM was about 75%, while it was only 11.5 % in the control group. About 53.33% of  $\beta$ -TM patients had hypogonadal hypogonadism, while 21.67 of them had normo-gonadal hypogonadism.

### 3.7. Symptoms of hypogonadism

The main symptoms of hypogonadism in our  $\beta$ -TM females were menstrual irregularities as primary amenorrhea and secondary amenorrhea which applied to 29% and 42% of females respectively. In male's hypogonadism was in the form of sexual infantilism: this applied to 72% of them. Also, a grossly impaired pattern of sexual maturity rating (SMR) was found in our  $\beta$ -TM patients. About 2 (3.33%), 6 (10%), 19 (21.6%) of cases group had an SMR of T1, T2, and T3 respectively.

### 3.8. Risk factors for hypogonadism

In order to predict risk factors for hypogonadism, simple and multiple logistic regression analyses were employed after taking into consideration the absence of multicollinearity between the variables of interest.

The predictor variables in first multiple logistic regression analysis were age, gender, hemoglobin level, BMI, ferritin level, blood transfusion rate per year and age of using iron chelation therapy. A test of the full model versus a model with intercept only was statistically significant,  $\chi^2 = 44.434$ ,  $p < 0.001$ . The model was correctly classified 88.3% of cases.

Table(4) shows the logistic regression coefficient, Wald test, and odds ratio for each of the predictors. Employing a 0.05 criterion of statistical significance, hemoglobin level ( $p=0.006$ ), ferritin( $p=0.018$ ), and one blood transfusion program had significant partial effect.

The odds ratio for different variables indicates that 1% increment in hemoglobin level will decrease

hypogonadism risk about 98% when holding all other variables constant, while 1% increment in ferritin level will increase hypogonadism risk about 0.1% also when holding all other variables constant. Regarding to different programs of blood transfusion only there was significant difference between 12-blood transfusion program per year and 24- blood transfusion program per year ( $p=0.007$ ) with odds ratio about (0.000) which indicates that patients who need blood transfusion once monthly (12-blood transfusion per year) were at very low risk to have hypogonadism compared to patients who need blood transfusion twice monthly (24-blood transfusion per year).

Second logistic regression was employed to predict the effect of compliance to ICT on hypogonadism. A test of the full model versus a model with intercept only was statistically significant,  $\chi^2 = 23.88$ ,  $p < 0.001$ . The model was correctly classified 83.3% of cases. As shown in Table(4) significant difference was predicted between groups with poor and excellent compliance to ICT program ( $p=0.001$ ), and patients with poor compliance to ICT program will have hypogonadism 28.6 times more than patients with excellent compliance to ICT program when holding ferritin constant. Finally, there was no significant difference between hypogonadism and normal groups in percentage of splenectomy, and presence of other endocrine disease or levels of liver enzymes (Table5).

## 4. DISCUSSION

### 4.1. Prevalence of hypogonadism

This is, to the best of our knowledge, the first study that focused on endocrinopathies of  $\beta$ -TM in the Gaza strip. Our findings regarding the range of hypogonadism in patients with  $\beta$ -TM are consistent with findings in previous studies as in the West Bank and Saudi Arabia with rate about 46.7%, and 52.7% respectively<sup>21,22</sup>. while these findings are much higher than findings in Dubai and Taiwan with rate about 25%, and 23.1% respectively. This lower rate could be explained by the availability of treatment according to the latest guidelines to all patients including the latest medical

treatments such as deferasirox (DFX) iron chelator which can be administrated orally once daily thus ensuring patient continuity with treatment<sup>23,24</sup>.

### 4.2. Symptoms of hypogonadism and delayed puberty

Primary amenorrhea and secondary amenorrhea were the main symptoms of hypogonadism in our  $\beta$ -TM females, while sexual infantilism was the main symptom of hypogonadism in male participants with  $\beta$ -TM which was applied to 72% of them. This become in agreement with different studies carried out by Merchant & Shirodkar, 2011; Moayeri, H. & Oloomi, Z., 2006 in India and Iran respectively<sup>25,26</sup>.

Also, a grossly impaired pattern of sexual maturity rating (SMR) which was found in our  $\beta$ -TM patients become in agreement with different studies carried out in India and Egypt<sup>25,27</sup>.

### 4.3. Relationship between hypogonadism and other variables

The main risk factors associated with hypogonadism were anemic status and the overloaded iron due to chronic blood transfusion regimen associated with inadequate chelation therapy. This study revealed that most of the study patients about 93% had Hb level lower than (9g/dl) that is recommended by Thalassemia International Federation (TIF) and also lower than median baseline of 10.0g/dl reported by previous studies<sup>14,28</sup>. This reflects a severe anemic presentation of the study group. These results were consistent with the results of across sectional study in Tunis among twenty-eight  $\beta$ -TM patients and showed chronic hypoxia due to anemia could be a mechanism involved in pituitary-gonadal dysfunction<sup>29</sup>.

The measurement of serum ferritin concentration used in this study to assess the iron status of patients as it is an easy, cost effective and noninvasive indicator of iron overload. The average of serum ferritin level for patients in the current study was 6704.83ng/ml ( $\pm$ SD 2847.8) and all patients had serum ferritin  $\geq 2000$ ng/ml. Such increase in serum ferritin level is well known to put these patients at a great risk of developing

iron overload complications. According to TIF guidelines, serum ferritin cut off limit must be kept below 1000ng/ml<sup>14</sup>. This rise of serum ferritin in our participants resulted despite the fact that all patients were on standard regimen of iron chelation therapy but the main problems were that Deferoxamine (Desferal)<sup>®</sup> chelator which need parenteral administration was the only available drug and oral chelators were unavailable to replace it at the ministry of health for long period of time, which resulted in that majority of patients with poor adherence to the chelation regimen.

Other risk factor for hypogonadism was frequency of blood transfusion which indicates that patients who need blood transfusion twice monthly (24-blood transfusion per year) were at very high risk to have hypogonadism compared to patients who need blood transfusion once monthly (12-blood transfusion per year). The present results were consistent with the results of a retrospective cohort analysis of  $\beta$ -TM patients attending an ambulatory transfusion clinic in Australia which showed that the age of first transfusion and frequency of blood transfusion correlated with the number of endocrinopathies<sup>30</sup>, while these results were inconsistent with other cross sectional study in India among 35 patients with  $\beta$ -TM which stated that there was no direct relationship between the amount of iron accumulated and organ dysfunction, and it is possible that endocrine glands are extremely sensitive to iron toxicity that even small amounts of iron accumulated in the early years of life can cause irreversible damage<sup>25</sup>.

In our survey also, compliance to ICT program was detected as significant predictor for hypogonadism and majority of patients with poor compliance at high risk for hypogonadism. This result attributed mainly to the availability of only DFO as an iron chelators at the MOH, that is only given either subcutaneously through the pump or by intravenous infusion.

Both ways of therapy were not preferable by patients who found it painful. In addition, the pump was not always provided and sometimes broken down and need a long period of time to be repaired. All of the studied patients,

said that they hope to use oral therapy to avoid the harmful pain. Despite that iron overload of tissues is the most important complication of  $\beta$ -thalassemia and is a major subject of management iron chelation therapy is still not efficient in Gaza Strip as indicated by the high ferritin level observed in our patients even after desferrioxamine chelation therapy. Thus, strategies to improve chelation regimens should be of the highest priority. These strategies must include continuance providing of oral iron chelators such as deferasirox (Exjade) and deferiprone to improve compliance.

### **5. Conclusion and Recommendations**

Results of the current study revealed a high prevalence of hypogonadism as well as a gross impairment of pubertal development in  $\beta$ -TM patients in Gaza strip which was associated with iron overload and severe anemia. Higher blood transfusion and low compliance of iron chelation therapy was particularly associated with pubertal abnormalities. Such findings emphasize the need for a protocol for early detection and prevention of iron overload which leads to cell damage in various endocrine glands. Assessment of blood transfusion frequency, early (prepubertal), monotherapy, or combined chelation therapy, together with appropriate monitoring and continuous health education programs can protect or ameliorate such consequences.

### **ACKNOWLEDGMENT**

We would like to thank directors in thalassemia awards at Al Shifaa hospital and European Gaza Hospital for their recommendations and facilities provided to conduct this study.

### **Limitations**

This study was carried out, with all its blood tests at the student's personal expense, without any financial donation from anyone. Therefore, blood tests were limited and did not include any other endocrine disorder.

### **Ethical Approval**

The study was approved by Helsinki Committee of ministry of health-Palestine at 4/12/2017.

### **Conflict of Interest**

There is no conflicts of interest.

**Table (1). Sociodemographic characteristics of patients and control groups**

Variables		Cases (n=60)	Controls (n=35)	P-Value <sup>a</sup>
Gender	Male	29 (48.3)	18(51.5)	0.833 (X2)
	No. (%) Female	31 (51.7)	17(48.5)	
Age	Mean ± SD	21.08 ± 3.9	21.11± 3.9	0.970
Age groups (year)	13 – 21	36 (60)	22(63)	0.783 (X2)
	No. (%) 22 – 30	24 (40)	13(37)	
Height (cm)	Male	152.76± 6.4	164.78± 2.9	0.001*
	Mean ± SD Female	149.71± 7.7	162.94± 2	0.001*
Weight (kg)	Male	47.52± 9.4	65.39± 10.01	0.001*
	Mean ± SD Female	46.19± 9	63.29± 9.3	0.001*
BMI	Mean ± SD	19.97± 2.7	23.91± 3.1	0.001*
BMI groups	<18.5	28 (46.67)	1(2.9)	0.001†*
	No. (%) 18.5-24.99	32 (53.34)	22(62.9)	
	25-29.99	--	9 (25.7)	
	≥30	--	3 (8.5)	
Splenectomy	Yes	45 (75)	--	0.001(X2)*
	No. (%) No	15 (25)	35(100)	
Other endocrine disease				0.082 (X2)
	No. (%) Present	6 (10)	--	
	Absent	54 (90)	35(100)	

BMI; body mass index (calculated based on (NCD Risk Factor Collaboration, 2016, page 35).

(a)Statistical testing using chi-square test(X<sup>2</sup>),Fisher’s exact test (†) or independent sample t test.

(\*) Difference is significant at the 0.05 level (2-tailed).

**Table (2). Distribution of study sample according to hemoglobin level, transfusion regimen and iron status.**

Variables	Cases (n=60)	Controls (n=35)	P-Value <sup>a</sup>
Blood hemoglobin (g/dl) [Mean ± SD]			
Males	7.64 ±0.87	14.14 ±0.48	0.001*
Females	7.48 ±0.86	12.18 ±0.47	0.001*
Blood hemoglobin categories			0.001 (X <sup>2</sup> )*
6-7.49	29(48.33%)	--	
7.5-8.99	27(45%)	--	
9≥	4(6.67%)	35(100%)	
Blood transfusion regimen per year			
12 Blood transfusions	12(20%)	---	
16 Blood transfusion	20(33.33%)		
24 Blood transfusion	28(46.67%)		

Variables	Cases (n=60)	Controls (n=35)	P-Value <sup>a</sup>
Age of using ICT			
Before 10 years old	40(66.7%)		
After 10 years old	20(33.3%)		
Compliance to ICT regimen			
Excellent Compliance	13(21.7%)		
Good Compliance	15(25%)		
poor Compliance	32(53.3%)		

(a)Statistical testing using chi-square test( $X^2$ ), or independent sample t test.

(\*)Difference is significant at the 0.05 level (2-tailed).

**Table (3). Medical characteristics of patients and control groups**

Variables		Cases (n=60)	Controls (n=35)	P-Value <sup>a</sup>
		Mean $\pm$ SD	Mean $\pm$ SD	
Ferritin (ng/ml)	Females	7007 $\pm$ 92895	106 $\pm$ 29	0.001*
	Males	6381 $\pm$ 2813	170 $\pm$ 25	0.001*
ALT(IU/l)		82.68 $\pm$ 38.9	24.71 $\pm$ 5.4	0.001*
AST(IU/l)		76.5 $\pm$ 41.4	24.63 $\pm$ 6.3	0.001*
ALP (U/l)		355.4 $\pm$ 109	220.1 $\pm$ 209	0.001*
T. Protein(g/dl)		6.29 $\pm$ 0.6	7.44 $\pm$ 0.5	0.001*
Albumin (g/dl)		3.87 $\pm$ 0.5	4.11 $\pm$ 0.2	0.001*
D. bilirubin (mg/dl)		0.61 $\pm$ 0.3	0.1397 $\pm$ 0.04	0.001*
T. bilirubin (mg/dl)		2.13 $\pm$ 1.4	0.72 $\pm$ 0.1	0.001*
INR		1.25 $\pm$ 0.1	0.93 $\pm$ 0.1	0.001*
LH (mIU/ml)	Female	2.70 $\pm$ 2.7	6.15 $\pm$ 1.2	0.005*
	Male	1.87 $\pm$ 1.8	6.27 $\pm$ 0.8	0.001*
FSH (mIU/ml)	Female	3.46 $\pm$ 3	5.42 $\pm$ 1.2	0.010*
	Male	2.11 $\pm$ 1.9	5.62 $\pm$ 0.7	0.001*
Estrogen in females (Pg/ml)		28.07 $\pm$ 21.9	67.22 $\pm$ 27.5	0.001*
Total testosterone in males (ng/dl)		168.62 $\pm$ 174	486 $\pm$ 118.1	0.001*

(a)Statistical testing using independent t-Test.

(\*) Difference is significant at the 0.05 level (2-tailed).

**Table (4). Detailed estimates from logistic regression models for determination risk factors for hypogonadism .**

Predictor	Regression coefficient(B)	Wald	P-Value <sup>a</sup>	Odds ratio
Gender(1)	-3.501	3.175	0.075	0.030
Age	-0.171	0.933	0.334	0.843
BMI	-0.543	2.712	.1000	.5810
Hb	-3.912	7.524	.006*0	.0200
Ferritin	0.001	5.644	0.018*	1.001
Blood transfusion per year				
12- transfusions per year	-8.626	7.184	0.007*	0.000
16- transfusions per year	-4.485	3.517	0.061	0.011
Age of using ICT	-0.377	2.613	0.106	0.686
ICTcompliance				
ICTcompliance(1) (poor)	3.356	10.303	.001*0	28.678
ICTcompliance(2)(good)	0.855	.9170	0.338	2.352

(\*)Statistical significant for individual predictor at the 0.05 level.

**Table (5). Relationship between hypogonadism and medical characteristics.**

Variable	Categories	Hypogonadism(n=45)	Non-Hypogonadism(n=15)	p-value <sup>a</sup>
Splenectomy	Yes	34 (75.56)	11 (24.44)	0.556 <sup>†</sup>
	No	11 (73.33)	4 (26.67)	
Other endocrine disorder	Present	6 (100)	0 (0)	0.321 <sup>†</sup>
	Absent	39 (72.22)	15 (27.78)	
ALT	Mean ± SD	87.2 ± 39.60	69 ± 34	0.11
AST	Mean ± SD	80.6 ± 42.80	64.1 ± 35.4	0.18
ALP	Mean ± SD	366.91 ± 117.82	320.93 ± 68.72	0.073

(a)Statistical testing using chi-square test(X<sup>2</sup>), Fisher’s exact test (†) or independent sample t test.

(\*)Difference is significant at the 0.05 level (2-tailed).

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## مدى انتشار قصور الغدد التناسلية في مرضى التلاسيميا العظمى ( $\beta$ ) في قطاع غزة

أمين توفيق حمد<sup>1</sup>، محمد زغبير<sup>2</sup>، إلهام أحمد شاهين<sup>3</sup>

1 أستاذ مشارك في علم الأدوية ، كلية الصيدلة - جامعة الأزهر، غزة - فلسطين.

2 أستاذ مشارك في أمراض الغدد الصماء، كلية الطب - جامعة الأزهر، غزة - فلسطين.

3 ماجستير في العلوم الصيدلانية ، مستشفى الشيخ حمد بن خليفة آل ثاني للتأهيل والأطراف الصناعية ، غزة- فلسطين .

### ملخص

أجريت هذه الدراسة لتحديد مدى انتشار قصور الغدد التناسلية بين المراهقين من مرضى التلاسيميا العظمى ( $\beta$ )، ودور أدوية إزالة الحديد في الوقاية منه. تم جمع البيانات من (60) من مرضى التلاسيميا العظمى ( $\beta$ ) و (35) شخصاً سليماً تتراوح أعمارهم بين 13 و 30 عاماً من خلال الاستبانة ومراجعته السجلات الطبية لجمع الخصائص الاجتماعية والديمغرافية ، نظام نقل الدم، تاريخ البدء باستخدام أدوية إزالة الحديد ومدى الانتظام بأخذها وحالة البلوغ. كذلك تم إجراء العديد من التحاليل التي شملت تحليل الدم الكامل، تركيز الفريتين في الدم واختبارات وظائف الغدة النخامية و الغدد التناسلية بحيث تمت جميعها في الصباح الساعة (08.00- 9.00 صباحاً) بعد ليلة من الصيام ، و أسبوع إلى أسبوعين من نقل الدم. تحليل البيانات تم باستخدام تحليل الانحدار اللوجستي ،اختبار (ت) للعينات المستقلة واختبار كاي المربع. أظهرت النتائج أن معدل انتشار قصور الغدد التناسلية لدى مرضى التلاسيميا العظمى ( $\beta$ ) في قطاع غزة يصل إلى 75 % ، وقد كان تركيز الفريتين لدى المرضى حوالي  $6704.83 \pm 2849$  جم/مل وكان جميعهم لهم تركيز الفريتين أعلى من 2000 جم/مل مما يشير إلى زيادة شديدة في الحديد لديهم. ومن خلال تحليل الانحدار اللوجستي تبين أن انخفاض مستوى الهيموغلوبين ( $p = 0.006$ ) ، وارتفاع مستوى الفريتين ( $p = 0.018$ ) ، وارتفاع نقل الدم سنوياً (24 عمليات نقل دم) ( $p = 0.007$ ) ، وسوء الالتزام بأدوية إزالة الحديد ( $p = 0.001$ ) هي من أهم العوامل المسببة لقصور الغدد التناسلية وتخلص هذه الدراسة إلى أن قصور الغدد التناسلية منتشر بشكل كبير بين مرضى التلاسيميا العظمى ( $\beta$ ) في قطاع غزة، ويرتبط وجودها بانخفاض قيم الهيموجلوبين، زيادة تركيز الحديد في الدم، ارتفاع معدل نقل الدم وانخفاض الالتزام باستخدام أدوية إزالة الحديد.

**الكلمات الدالة:** التلاسيميا العظمى ( $\beta$ )، قصور الغدد التناسلية، الزيادة في مستويات الحديد، أدوية إزالة الحديد، قطاع غزة.

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