Study of the Effect of Type 2 Diabetes Mellitus on Fertility in Some patients in Misan Province

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Abstract

The aim of the present study was attempted to assess the levels of total testosterone, follicular-stimulating hormone, luteinizing hormone, prolactin and estradiol in type 2 diabetes mellitus men. The current study included forty-five with diabetes type 2 and fifteen health's individuals as control. The diabetes patients divided into 3 groups according to ages first (30-39 year), second (40-49) and third group (50-59). As well as divided into 3 group according to period of injury first (1-5 year), second (6-10 year) and third group (11-15 year). The results of current study showed the following: fasting Blood Glucose (F.B.G) and Hemoglobin A1C (HbA1C) showed increased significantly ($P<0.05$) in all groups diabetes compared to control. Follicular stimulating hormone (FSH), luteinizing hormone (LH) and Total testosterone (TT) decreased significantly ($P<0.05$) in all groups of diabetes compared to control. While Prolactin (PRL) and Estradiol (E2) increased significantly ($P<0.05$) in all groups of diabetes compared to control according to age and duration. According to the results of the present study concluded decreased levels of TT, FSH and LH in type 2 diabetes mellitus men.

Keywords: FSH, LH, Diabetes, Men, Misan.

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دراسة تأثير داء السكري من النوع الثاني على الخصوبة لدى بعض مرضى محافظة ميسان

حسين حميدي جليب الكعبي و زينب عبد الجبار رضا العلي

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الخلاصة

هدفت الدراسة لتقييم مستويات هرمون التستوستيرون الكلي، الهرمون المحفز للجريبات، هرمون اللوتيني بالإضافة إلى البرولاكتين والإستراديول عند الرجال المصابين بداء السكري من النوع الثاني. اشتملت الدراسة الحالية على خمسة أربعين مصابًا بمرض السكري من النوع الثاني وخمسة عشر من الذكور الاصحاء، حيث تم تقسيم المرضى حسب العمر ومدة الإصابة، وتم تقسيم العمر إلى ثلاث مجموعات، الأولى (30-39)، والثانية (40-49)، والمجموعة الثالثة (50-59) عام. بينما تنقسم المدة أيضا إلى ثلاث مجموعات، الأولى (1-5) والثانية (6-10) والمجموعة الثالثة (11-15) سنة. اظهرت نتائج الدراسه الحالية زياده معنوية في كل من سكر الدم والسكر التراكمي في جميع مجاميع السكري مقارنة بمجموعة السيطرة، بينما انخفض هورمون المحفز للجريبات وهورمون اللوتيني والتيستسرون الكلي معنويا في جميع المجاميع السكري (العمر والمدة) مقارنه بمجموعة السيطرة، بينما ارتفع هورمون البرولاكتين والاستراديول معنويا في جميع مجاميع السكري (العمر والمدة) مقارنه بمجموعة السيطرة. استنتج من الدراسة الحالية انخفاض في مستويات الهرمونات التكاثرية عند الرجال المصابين بمرض السكري من النوع الثاني في محافظة ميسان .

الكلمات المفتاحية: هورمون المحفز للجريبات، وهورمون اللوتيني، داء السكري، الرجال، ميسان.

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Introduction

Diabetes mellitus (DM) is a major challenge for global public health, and it comprises a heterogeneous etiology of diseases characterized by elevated blood glucose [1]. Type I diabetes is caused by autoimmune destruction of insulin - producing pancreatic β cells, culminating insulinopenia with resultant hyperglycemia. It is diagnosed during infancy and requiring exogenous insulin for survival [2].

Type II diabetes is a complex disorder characterized by imbalance between insulin resistance and insulin secretion that induce liver glucose output by preventing glycogen formation and stimulating glycogenolysis and gluconeogenesis [3].

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Type II associated with hypothalamic-pituitary-gonadal (HPG) axis suppression, where decrease in testosterone and other sex hormone [4].

DM may affect male reproductive function at many levels as a result of its effects on the control of spermatogenesis, or by decreased penile erection and ejaculation [5]. DM causes effect of the epididymis, with a negative impact on spermatozoon transit [5]. Varied mechanism makes a case for the spermatozoon harm discovered in diabetes patients, these comprise endocrine disorder, neuropathy and increased aerobic stress [39]. Several authors recommend that DM alter serum androgen levels, this is often related to a steroid genetic defect in Leydig cells [6]. The present study was aimed to study effect type 2 DM on some hormonal parameters in men of Misan province.

Material and methods

Subject

This study was carried out at the AL-sadder Teaching Hospital and center for Endocrinology and diabetes specialist in Al-amraa City, Missan. The study population comprised of 60 men aged 30-60 years of whom 45 pateint with type II diabeteic and a group of 15 healthy men as control group from February 2018 to November 2018.

Blood sampling

Blood vein was obtained from fasting individuals at (8-10 AM) then divided into two transferred into EDTA tube for HbA1C determination and other part was transferred into plane tube for glucose and hormonal study.

1- Biochemical Parameters

Determination the level of glucose in serum

The serum glucose was determined by enzymatic colorimetric (GOD-PAP) method, using kit supplied by Spin react, Spain [7].

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Determination of the level HbA1c

The method principle according to instrument Bio Rad, France which dependent by ion – exchange high –performance liquid chromatographic (HPLC) [8].

2- Determination the level of hormonal change

Vidas (FSH, LH and PRL) in human serum employed on the VIDAS family tools for the quantitative, using ELFA technique (enzyme Linked Fluorescent Assay), The method is used according to Biomerieux Kit procedure of Vidas FSH, LH and PRL [9,10].

Testosterone

Procedure

Vidas testosterone (T) is an automated quantitative examination of total testosterone in human serum employed on the VIDAS family tools, using ELFA technique (Enzyme Linked Fluorescent Assay), the method is used according to Biomerieux Kit procedure [11].

Estradiol II (E2)

Procedure

Vidas Estradiol (E2) is an automated quantitative examination of total 17β – estradiol in human serum employed on the VIDAS family tools for the quantitative, using ELFA technique (Enzyme Linked Fluorescent assay), the methods are used according to Biomerieux Kit procedure [12].

Results

Biochemical parameters (According to age)

Fasting Blood Glucose (F.B.G) and HbA1C levels

The result was showed significant difference (P< 0.05) in F.B.G for all group as compared to the control, also no any significant differences (P< 0.05) between first and second group, while significant differences (P< 0.05) between second and third group. HbA1C showed significant

difference (P< 0.05) in all group as compared to the control, on any significant difference between first and third group, table 1.

Table 1: The values of F.B.G and HbA1c in control and patient with DM T2 (According to age)

Groups	F.B.G (mg/dl)	HbA1C (%)
First group (30-39) year	ab 285.46±17.15	a 9.97±0.50
Second group (40-49) year	b 253.53±13.46	ab 11.75±0.55
Third group (50-59) year	a 315.07±35.0.9	a 9.06±0.48
Control	c 93.20±2.13	c 5.00±0.15
LSD	58.60	1.28

Mean ± SE

The different letters refer to significant difference among group at level of (P<0.05).
The same letters refer to non-significant difference among group.

Hormonal parameters

Follicular stimulating hormone (FSH)

The FSH level in the first (3.03±0.41), the second (2.66±0.24) and the third groups (3.63±0.34) were significantly decrease (P <0.05) in comparison with control group (7.03±0.55). Also, all three groups did not differ significantly (P<0.05) among them, table 2.

Luteinizing hormone (LH)

Non-significant variation was recorded in the level of LH among first, second and third (2.62 ± 0.36, 2.20 ± 0.17 and 2.93 ± 0.31) respectably. But all three groups which significantly decreased (P < 0.05) compared to control (4.60 ± 0.36) group, table 2.

Total Testosterone (TT)

Total testosterone (TT) level in the first group (2.60 ± 0.25), the second (2.27 ± 0.17) and the third groups (2.73 ± 0.17) were significantly decrease (P < 0.05) than the control group (4.51 ± 0.23). Also, all three groups did not differ significantly (P< 0.05) among them, table 2.

Estradiol (E2)

Estradiol (E2) level did not differ significantly (P < 0.05) in first (30.61 ± 2.85), second (31.24 ± 1.95) and third groups (25.28 ± 2.11). The first and second groups which increased significantly (P < 0.05) compared to control. While there is non-significant difference (P<0.05) between control and third group, table 2.

Prolactin (PRL)

Prolactin (PRL) in the first (13.83 ± 1.70) second group (15.89 ± 1.22) increased significantly (P < 0.05) in comparison with the control group (9.77 ± 0.75ng / ml), third group (10.78 ± 1.52) did not differ significantly (P < 0.05) in comparison with control group, no any significant difference between first and second group, while second group increase significantly compared with third group, table 2.

Table 2: The values of hormonal in serum control and patients with DMT2 (According to age)

Groups	FSH (mlU/ml)	LH (mlU/ml)	TT (ng/ml)	E2 (pg/ml)	PRL (ng/ml)
First group (30-39) year	b 3.03±0.41	a 2.62±0.36	b 2.60±0.25	a 30.61±2.85	ab 13.83±1.70
Second group (40-49) year	b 2.66±0.24	b 2.20±0.17	b 2.27±0.17	a 31.24±1.95	a 15.89±1.22
Third group (50-59) year	b 3.63±0.34	b 2.93±0.31	b 2.73±0.17	ab 25.28±2.11	b 10.78±1.52
Control	a 7.03±0.55	a 4.60±0.36	a 4.51±0.23	b 20.28±2.01	b 9.77±0.92
LSD	1.15	0.89	0.60	6.41	3.92

Mean ± SE.

The different letters refer to significant difference among group at level of (P<0.05).
The same letters refer to non-significant difference among group.

Biochemical parameters (according to duration)

Fasting Blood Glucose (F.B.G) and HbA1C levels

The result was showed significant difference (P < 0.05) in F.B.G for all group as compared to the control, also no any significant differences (P < 0.05) between first and second group, as

well as second and third group while significant differences (P < 0.05) between first and third group. Same result with regard to HbA1C, table 3.

Table 3: The values of F.B.G and HbA1c in control and patient with DM T2 (According to duration of injury DM)

Groups	F.B.G (mg / dl)	HbA1C (%)
First group (1-5) year	b 266.21±19.46	b 9.37±0.46
Second group (6-10) year	ab 280.26±34.73	ab 10.86±0.37
Third group (11-15) year	a 333.72±19.11	a 11.20±0.80
Control	c 93.20±2.13	c 5.00±0.15
LSD	59.10	1.52

Mean ± SE.

The different letters refer to significant difference among group at level of (P < 0.05).

The same letters refer to non-significant difference among group.

Hormones parameters

Follicular stimulating hormone (FSH)

The FSH values in the first (2.92 ± 0.26), second (2.97 ± 0.46) and the third (3.63 ± 0.41) group were significantly decrease (P < 0.05) than the control (7.03 ± 0.55) group. While no significant variation was recorded in the level of FSH among first, second and third groups, table 4.

Luteinizing hormone (LH)

The values of LH values in the first (2.29 ± 0.20), second (2.88 ± 0.33) and third (3.05 ± 0.39) groups were significantly decrease (P < 0.05) than the control (4.60 ± 0.36) group. While no significant variation was recorded in the level of LH among first, second and third groups, table 4.

Total Testosterone (TT)

The values of testosterone (TT) values in the first (2.50 ± 0.14), second (2.33 ± 0.28) and the third (2.68 ± 0.23) group were significantly decrease (P < 0.05) than the control (4.51 ± 0.23)

group. While no significant variation was recorded in the level of (T) among first, second and third groups, table 4.

Estradiol (E2)

The values of Estradiol (E2) values which increased significantly ($P < 0.05$) in the first (28.25 ± 1.88), second (28.05 ± 2.97) and third (28.66 ± 3.04) groups compared to control (20.28 ± 2.01). While no significant variation was recorded in the level of (E2) among first, second and third groups, table 4.

Prolactin (PRL)

The values of Prolactin (PRL) values which increased significantly ($P < 0.05$) in the first (15.37 ± 1.27), second (13.12 ± 1.45) and third (13.19 ± 1.63) groups compared to control (9.77 ± 0.95). While no significant variation was recorded in the level of prolactin among first, second and third groups, table 4.

Table 4: The values of hormonal in serum control and patients with DMT2 (According to duration of injury DMT2)

Groups	FSH (mlU / ml)	LH (mlU / ml)	TT (ng / ml)	E2 (pg / ml)	PRL (ng / ml)
First group (1-5) year	b 2.90 ± 0.26	b 2.29 ± 0.20	b 2.50 ± 0.14	a 28.25 ± 1.88	a 15.37 ± 1.27
Second group (6-10) year	b 2.97 ± 0.46	b 2.88 ± 0.33	b 2.33 ± 0.28	a 28.05 ± 2.97	a 13.12 ± 1.45
Third group (11-15) year	b 3.63 ± 0.41	b 3.03 ± 0.59	b 2.68 ± 0.23	a 28.66 ± 3.04	a 13.19±1.63
Control	a 7.03±0.55	a 4.60 ± 0.36	a 4.51 ± 0.23	b 20.28 ± 2.01	b 9.77 ± 0.95
LSD	1.16	0.86	0.61	6.65	3.83

Mean ± SE.

The different letters refer to significant difference among group at level of ($P < 0.05$).

The same letters refer to non-significant difference among group.

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Discussion

Biochemical parameters (According to Age)

The DM is a group of metabolic disorders characterized by hyperglycemia, the elevation in FBG level may be resulting from defection in insulin secretion, insulin action or both. Blood glucose is controlled by two processes: first insulin secretion by pancreatic B cell in response to a nutrient challenge and second by insulin action on target organ i. e liver and adipose tissue [13]. Our results are in agreement with study that which demonstrated T2DM is often associated with result from insufficient insulin production, insulin secretion and insulin resistance [14 and 15]. The result of the present study showed that the diabetic patients had significantly high concentration of FBG and HbA1C ($P < 0.05$) than control group.

According to the American Diabetes Association (ADA) guidelines (2007), the value of HbA1c should be kept below 7% in all diabetics [16]. However, the patients under study are poorly controlled because HbA1c of the patient's group ≥ 9.9% and this result is previously reported in other reports and correlated with different complications of DM in patients with elevated levels of HbA1c in T2DM [17]. In comparison with a study by [18], found that HbA1c in a diabetic group was $6.7 \pm 0.1\%$

In our study show decrease significantly in testosterone, FSH, LH and e significant increase in PRL and E2 in T2DM comparison with control group.

Study by [19] observed decreased significantly in T while increased significantly in LH and FSH in men.

The presence of low free testosterone level suggests that insufficient testosterone may be a risk factor in these patients [20 and 21].

The testosterone level was significantly decreased in men compared to controls. Also, LH and FSH were significantly increased in men, these results are in agreement with the study of [19

and 22]. The presence of low free testosterone levels suggests that testosterone insufficiency may be a risk factor for type 2 diabetic

The result of carried out study by [4], noted that TT decreased and E2 be increased in diabetic patients with type II when compared with control.

Men with diabetic have decrease testosterone concentration than control, may be due to trans (TT) into estradiol (E2) by the action aromatase in adipose tissue therefore, a reduce of (TT) with increase aromatase, which is a result of high number adipocyte in diabetic men [23].

Type 2 diabetic is associated with decrease testosterone and increase estradiol high estradiol / testosterone ratio associated with abdominal and subcutaneous fat and cause more aromatization of testosterone to estradiol [4].

La vignera. [6], referred to DM decrease TT, this associated with steriogentic defect in lyding cell Dhindsa *et al*., [24], demonstrated that 33% of men with type 2 diabetes had significantly lower levels of free testosterone.

Ota *et al*. [25], show that low testosterone associated with insulin resistance diabetic men.

Pitteloudet *et al.* [26], observed the leydig cell population and testosterone metabolites were reduced, which was inversely related to the increase of insulin resistance.

Ding *et al*., [27] were indicated that endogenous sex hormones may differentially modulate glycemic status and risk of type 2 diabetes in men & women. Hussein and Al-Qaisi [15] observed a significant reduction in FSH and LH levels diabetic men when compared with control.

AL-Shammaa, *et al.* [28] found low FSH, LH, T may be due to Leydig and Sertoli cell which decrease with insulin deficiency which was referred to as a cause of impotence in diabetics, also defects in insulin secretion may change testicular and accessory sexual glands function.

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Also, Al-Fartosy and mohammed [29] carried out in may san, Iraq show reduced luteinizing hormone and follicle stimulating hormone to response to gonadotropin-releasing hormone in diabetic men indicated a decreased acute releasable pool of pituitary gonadotropins.

In other hand study by, [4], didn't agreement with our result, study carried on 40 patients with T2DM observed high level FSH, LH compared with control, because leydig cell and follicle cell more resistance to gonadotropin hormone.

Study by [30], showed in Nigeria on 175 men where high level of prolactin level diabetes mellitus type 2 with compared with control, and high level of prolactin cause hypothalamic pituitary dysfunction and can suppress gonadal function direct. The cause of the elevated mean serum PRL level and occasionally observed hyper prolactinaemia in diabetics is not clear. Differences in dietary habits would be one possible explanation since diet is known to influence serum PRL levels [31].

Page *et al*. [32] reported that glucose administration in the rat suppresses the firing of central dopamine neurons; hence it is tempting to speculate that chronically elevated blood glucose in diabetics could raise serum PRL level by suppressing dopaminergic neuronal activity.

Biochemical parameters (According to Duration of DM)

Our result agreement with study by verma *et al*. [33] which observed a significantly increase in FBG and HbA1C values in male and female diabetic patients with time progressing. study prove that the amount of carbohydrate attached to the HbA1c increases with increasing duration of the disease [34]. Our study shows decreases significantly in testosterone, FSH, LH and in decrease significantly in PRL and E2 in T2DM comparison with control group with time progressing.

Study was done with male patients. Found decrease of testosterone when compared to control with time progressing [24 and 35].

The cause of decline in T is likely a combination of testicular and pituitary/hypothalamic defects

The study was done formale patients with type 2 diabetes referred to the center for management of diabetes, found decrease of FSH and LH when compared to control, because of hypogonadism in these patients could be decreased gonadotropin secretion [24].

Ballester, observed a significant reduction in FSH and LH in rat induce diabetes, may be due to absence of stimulating affect of insulin on leyding cell which result decrease in FSH and LH levels [36]. Our results show increase a significant of prolactin compared with control study by [37] carried out on 157 men with diabetes mellitus, where found increase significantly compared with control. High level of prolactin cause of infertility in male and female mammals, elevated prolactin may impact reproduction through an action on the GnRH neurons of the hypothalamus and / or on the pituitary gland to affect secretion of the gonadotropins, LH, and FSH [38].

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