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Association between Gonadotrophic Hormones (FSH and LH) and Type 2 Diabetes Mellitus in Adult Iraqi Males: A Case-Control Study

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Abstract

Background: Numerous authors have extensively assessed the correlation between gonadotrophic hormones (FSH and LH) and metabolic disturbances in type 2 diabetes among postmenopausal women. However, there is limited knowledge regarding the connection between metabolic disorders in T2DM and the pituitary-gonadal axis in men. Only a small number of published articles have emphasized noteworthy results in this regard. The objective of this study was to investigate the association between T2DM and serum gonadotrophin levels in men.

Methods: This case-control study was conducted at Al-Ramadi Hospital, Iraq, and included 100 adult males diagnosed with T2DM (case group) and 50 healthy males. The patients were chosen at random among the people attending the Al-Ramadi teaching hospital's diabetes control center. The control group consisted of 50 adult males who were healthcare providers working at the teaching hospital. The study collected various variables, including age, (BMI), serum (FSH), (LH), fasting plasma glucose level, HbA1c%, HOMA-IR, and insulin level.

Results: The mean serum LH was significantly lower in patients with T2DM compared to controls (3.83 ± 1.76 mIU/ml vs. 9.88 ± 1.64 mIU/ml, $p < 0.001$). In addition, the percentage of individuals with low serum LH was significantly high in the patient's group in comparison to that of the control, 95.0 % versus 4.0 %, ($p < 0.001$). The mean serum FSH was also significantly lower in the T2DM group compared to the control group (3.41 ± 1.25 mIU/ml vs. 9.01 ± 1.44 mIU/ml, $p < 0.001$). Furthermore, the proportion of individuals with low serum FSH was significantly higher in the patient group than in the control group (100% vs. 0.0%, $p < 0.001$).

Conclusions: T2DM is associated with significant disruption of the pituitary-gonadal axis, leading to reduced production of FSH and LH in men.

Introduction

Hyperglycemia is a characteristic feature shared by several metabolic disorders, defined as a prolonged increase in blood glucose levels. Diabetes Mellitus (DM) is a heterogeneous medical condition that can affect males and females of any age group [1]. However, DM is associated with endocrine abnormalities, diabetes of the young, and drug-induced hyperglycemia [2]. Type 1 diabetes mellitus is characterized by a significant insulin deficiency, primarily affecting children, adolescents, and young adults. However, it can also occur in older age groups [3].

In DMT2, metabolic abnormalities primarily result from insulin resistance. This means that insulin levels are typically normal or even higher than normal when the illness is in its early stages, known as hyperinsulinemia. The primary abnormality is resistance to insulin action, which is caused by accumulating high amounts of visceral fat due to overweight and obesity [4].

Type 2 disease is a prevalent metabolic disorder (MD) in many communities [5] and worldwide [6]. Risk factors for T2DM include central obesity, a sedentary lifestyle, a high-calorie diet, and a lack of exercise [7]. The major causes of morbidity and death linked with this MD are its long-term effects [8]. The complications of T2DM can be categorized into microvascular complications (e.g., neuropathy, retinopathy, and nephropathy) and macrovascular complications (e.g., strokes and heart attacks) [9].

While many authors have extensively studied the association between metabolic derangements in type 2 diabetes and gonadotrophic hormones (FSH and LH) in women [10], there is limited knowledge about this association in men, and few published reports have focused on significant findings between metabolic derangements in type 2 disease and the pituitary-gonadal axis. The present study's goal is to ascertain if DMT2 and other health conditions are related to serum hormonal levels related to gonadotropins in men.

Methods

A case-control study was conducted in Al-Ramadi, Iraq, involving 100 adult males diagnosed with and 50 healthy control men. Patients were randomly selected from males attending the diabetes control center at the Al-Ramadi teaching hospital. 50 adult males who were healthcare providers working in the same teaching hospital were recruited as the control group. The researchers collected data on several variables, including the participants' age, body mass index (BMI), levels of serum follicle-stimulating hormone (FSH) and (LH), FBG level, HbA1c percentage, HOMA-IR score, and insulin level.

Statistical analysis

The study received ethical approval from the ethics committee of the Anbar Health Directorate, and all participants provided written informed consent. Data were analyzed using SPSS (version 16, IBM, Chicago, USA) and Microsoft Excel 2010. Numeric variables were expressed as mean ± standard deviation (SD) and range, while qualitative variables were expressed as numbers and percentages. The significance level was accepted as 0.05 or less.

Results

Demographic characteristics of DMT2 sufferers and healthy individuals

Table 1 displays the demographic characteristics of the type 2 DM patients and control subjects. The mean age of the DMT2 group was 44.48 ± 8.06 years, which was not significantly different from the control group, with a mean age of 42.85 ± 7.22 years (p = 0.287). However, the mean BMI of the T2DM group was significantly higher than that of the control group (27.12 ± 2.21 kg/m² vs. 24.94 ± 2.59 kg/m², $p < 0.001$). Furthermore, the proportions of overweight (43.0% vs. 16.0%) and obese (33.0% vs. 14.0%) individuals were significantly higher in the T2DM group compared to the control group ($p < 0.001$).

Characteristic	Type 2 DM *n* = 100	Control group *n* = 50	*p* value
Age (years)			
Mean ±SD	44.48 ±8.06	42.85 ±7.22	0.287 I
Range	30 -60	30 -57	NS
BMI (kg/m²)			
Mean ±SD	27.12 ±2.21	24.94 ±2.59	< 0.001 I ***
Range	22.79 -32.14	18.21 -33.03	
Underweight, *n* (%)	1 (1.0 %)	0 (0.0 %)	< 0.001 C ***
Normal weight, *n* (%)	23 (23.0 %)	35 (70.0 %)	
Overweight, *n* (%)	43 (43.0 %)	8 (16.0 %)	
Obese, *n* (%)	33 (33.0 %)	7 (14.0 %)	

Table 1: Demographic characteristics of patients with DMT2 and controls.

Comparison of serum levels of gonadotrophic hormones between patients with diabetes and control group

Table 2 presents a comparison of the serum levels of gonadotrophic hormones (LH and FSH) between the group of patients with type 2 diabetes and the control group. The mean serum LH level was significantly lower in patients with T2DM compared to controls (3.83 ± 1.76 mIU/ml vs. 9.88 ± 1.64 mIU/ml, $p < 0.001$). Moreover, the percentage of individuals with low serum LH levels was (highly significant) in the patient group than in the controls, with values of 95.0% and 4.0%, respectively (p < 0.001).

The mean serum FSH was significantly lower in T2DM patients than in controls (3.41 ± 1.25 IU/L vs. 9.01 ± 1.44 IU/L, $p < 0.001$). Furthermore, the proportion of individuals with low serum FSH was (High Signi. HS) in

the patient group compared to the controls, with 100% versus 0% (p < 0.001).

Characteristic	Type 2 DM *n* = 100	Control group *n* = 50	*P - value*
LH (mIU/ml)			
Mean ±SD	3.83 ±1.76	9.88 ± 1.64	< 0.001 I ***
Range	1 -7.9	7.2 -12.4	
Low	95 (95.0 %)	2 (4.0 %)	< 0.001 C ***
Normal	5 (5.0 %)	48 (96.0 %)	
FSH (IU/L)			
Mean ±SD	3.41 ±1.25	9.01 ±1.44	< 0.001 I ***
Range	1.1 -5.6	6.4 -11.9	
Low	100 (100.0 %)	0 (0.0 %)	< 0.001 C ***
Normal	0 (0.0 %)	50 (100.0 %)	

Table 2: Comparison of serum levels of gonadotrophic hormones (LH and FSH) between patients with diabetes and the control group.

Characteristic	Type 2 DM *n* = 100	Control group *n* = 50	*P - value*
Insulin (ng/ml)			
Mean ±SD	1.73 ±0.30	1.03 ±0.11	< 0.001 I ***
Range	1 -2.3	0.9 -1.3	
Normal	9 (9.0 %)	50 (100.0 %)	< 0.001 C ***
High	91 (91.0 %)	0 (0.0 %)	
HbA1C %			
Mean ±SD	9.64 ±1.34	4.85 ±0.32	< 0.001 I ***
Range	7.3 -13.5	4.3 -5.7	
Normal	0 (0.0 %)	47 (94.0 %)	< 0.001 C ***
High	100 (100.0 %)	3 (6.0 %)	
HOMA-IR			
Mean ±SD	0.77 ±0.18	0.18 ±0.04	< 0.001 I ***
Range	0.4 -1.4	0.1 -0.2	
Normal	0 (0.0 %)	50 (100.0 %)	
High	100 (100.0 %)	0 (0.0 %)	
FBG (mg/dl)			
Mean ±SD	190.15 ±25.37	88.88 ±8.92	< 0.001 I ***
Range	149 -304	75 -110	
Normal	0 (0.0 %)	50 (100.0 %)	< 0.001 C ***
High	100 (100.0 %)	0 (0.0 %)	

Table 3: Glycemic control parameters contrasted between patients with diabetes and the control group.

Glycemic control parameters contrasted between diabetes and controls

The comparison of glycemic control parameters between patients with DMT2 and the controls is presented in Table 3. The mean serum insulin level was (highly significant) in patients with DMT2 compared to the (Healthy), 1.73 ±0.30 ng/ml versus 1.03 ±0.11 ng/ml (p < 0.001). Additionally, the proportion of individuals with high serum insulin was significantly greater in the patient group than in the control group (91.0% vs. 0.0%, $p < 0.001$).

Mean serum HbA1C % was (highly significant) in patients with DMT2 in comparison with the category of controls, 9.64 ±1.34 % versus 4.85 ±0.32 % ($p < 0.001$). In addition, the percentage of individuals with high HbA1c was significantly greater in the patient group compared to the control group (100% vs. 6.0%, $p < 0.001$). Mean serum HOMA-IR was significant high in patients with DMT2 in comparison with the control group, 0.77 ±0.18 versus 0.18 ±0.04, respectively ($p < 0.001$); in addition, the proportion of individuals with high serum HOMA-IR was (HS) in a group in comparison to that of control, 100 % versus 0 %, ($p < 0.001$).

The mean fasting plasma glucose (FPG) was significantly higher in T2DM patients compared to controls (190.15 ± 25.37 mg/dl vs. 88.88 ± 8.92 mg/dl, p < 0.001). In addition, the percentage of individuals with high serum FPG was (highly significant) in patients' groups compared to that of controls, 100 % versus 0 %, ($p < 0.001$).

Discussion

In this study, the mean age of patients with T2DM was 44.48 years (range: 30-60 years). This seems to be the average age of participants in the control group. In other words, some individuals with DMT2 were younger than 45 years old, even though this condition is typically seen in individuals aged 45 or older [11, 12], Instances of DMT2 have been recorded in individuals under the age of 40 and even adolescents [13, 14].

The study found that the average BMI of individuals with DMT2 was (highly significant) than that of the controls, and the number of overweight and obese individuals in the DMT2 group was higher than in the controls. This suggests that obesity is a significant risk factor for DM in the Iraqi population studied. The connection between obesity and DMT2 is highly significant. Obesity is considered a major risk factor for the development of DMT2. Insulin resistance, a hallmark of early-stage T2DM that is usually compensated for by hyperinsulinemia, is primarily caused by obesity. Children who are obese and have high weight, height, and waist circumference are at significant possibility of developing insulin resistance. The early rebound of adiposity at the age of 3 years is a causal element in the rise in weight gain, which leads to an increased BMI in adolescence. The occurrence of DMT2 is linked to the combination of weight gain and insulin deficiency. From the beginning, scientists have associated obesity and peripheral insulin resistance. with a growing number of newly detected cases of DMT2 [15].

This study found that serum levels of both FSH and LH were significantly lower in T2DM patients compared to the control group. The data also showed that LH and FSH levels were positively correlated with BMI and HDL, but negatively correlated with insulin, CRP, HbA1c, HOMA-IR, cholesterol, triglycerides, LDL, and FPG.

In 2006, [16]. a research project that involved 35 males with DMT2 and 35 controls. The study revealed that diabetic men had lower serum FSH and LH concentrations than the controls. The researchers suggested that this could be due to an inadequate response of the pituitary gland to a fall in testosterone, demonstrating a major impact of elevated blood

glucose on how the neurological and endocrine systems interact. Our findings are consistent with a previous study by Maneesh *et al*., who also reported lower serum FSH and LH concentrations in diabetic men [16].

The study's results indicate that the hypothalamus's cells may be responsible for producing LHRH and may not function properly in response to low testosterone levels. The fact that the pituitary gland cannot react as expected to a drop in testosterone suggests that high blood glucose has a major impact on how the neurological and endocrine systems interact. Low serum levels of LH and FSH might be due to decreased secretion and synthesis [17].

Aromatase is an enzyme that is present in fat tissues and converts androgens such as testosterone and androstenedione to estrogens. Therefore, increasing body fat can result in a low serum testosterone level, as more androgens are converted to estrogens [18]. In diabetic men, due to the aromatase enzyme's enhanced activity in adipose tissues, testosterone, and androstenedione are converted to estradiol and estrone at greater rates, respectively, which may contribute to the decrease in testosterone levels. This increased conversion of testosterone and androstenedione to estrogens can have negative feedback and impact the synthesis of LH and FSH. It might be a factor in their reduction. Additionally, the low serum albumin levels observed in diabetic men may be attributed to their nutritional status [19]. By providing the required thiol groups for the antioxidant action known as "chain-breaking," it serves as an antioxidant.

According to [20], The most common type of gonadal dysfunction in diabetic individuals is hypogonadotropic (marked by decreased LH and FSH levels). [21] state that, there is a significant low in serum LH and FSH when comparing diabetic patients of both genders to healthy individuals. [22] studied the association between Total testo., LH, and FSH and showed that those with low testo. had lower levels of both LH and FSH. They also found a (+ve) correlation between (Testo.) and LH/FSH levels. Clinical research has demonstrated 25% of individuals with T2 diabetes have inadequate levels of testosterone and low amounts of LH and FSH [23]. According to research, the occurrence of hypogonadotropic hypogonadism in men with DMT2 is around 30-40%. A 2008 study revealed that younger males with T2DM had a similar prevalence of hypogonadotropic hypogonadism [24].

The analysis revealed that the average levels of serum insulin, HbA1c%, HOMA-IR, and serum fasting blood glucose (FPG) were (highly significant) in diabetics compared to the controls. These outcomes indicate poor glycemic control among the patients, which may be due to non-adherence to diet, exercise, lifestyle modifications, and medication regimens. These findings are consistent with the majority of earlier research that has shown insulin resistance, rather than a decrease in insulin levels, to be the primary cause of DMT2 [25];[26]. As per recent research, the elevated levels of insulin resistance observed in our study are likely attributed to being overweight and obese [27].

Author Contributions

Conceptualization: Bilal Ahmed Thmail, Mohammed Mezher Hussain
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Software: Bilal Ahmed Thmail, Mohammed Mezher Hussain, Amal Rasheed Farhan
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Competing Interest

The authors declare that there is no conflict of interest.

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