Full Length Research Article
Advancements in Life Sciences – International Quarterly Journal of Biological Sciences

ARTICLE INFO

Date Received: 18/06/2023;
Date Revised: 30/07/2023;
Date Published Online: 20/10/2023;

Authors' Affiliation:
1. Department of Public Health, Anbar Health Department, Al-Ramadi - Iraq
2. College of Health and Medical Techniques, Middle Technical University, Baghdad - Iraq
3. Middle Technical Institute, Middle Technical University, Al – Mansour - Iraq
Nursing College. Al-esraa University, Baghdad - Iraq

***Corresponding Author:**
Bilal Ahmed Thmail
Email:
bilal.ahmed.th@gmail.com

How to Cite:
Thmail BA, Hussain MM, Farhan AR (2023). Association between gonadotrophic hormones (FSH and LH) and Type 2 diabetes mellitus in Adult Iraqi Males: a case-control Study. Adv. Life Sci. 10S(1): 25-29.

Keywords:
Gonadotrophic hormones; DMT2

Open Access

Association between gonadotrophic hormones (FSH and LH) and Type 2 diabetes mellitus in Adult Iraqi Males: a case-control Study

Bilal Ahmed Thmail*[1], Mohammed Mezher Hussain[2], Amal Rasheed Farhan[3]

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; On the other hand, there is limited knowledge regarding the connection between metabolic disorders in DMT2 and the pituitary-gonadal axis for men. Only a small number of published articles have emphasized noteworthy results in this regard. The current study has labeled an objective of how DMT2 is linked to serum hormonal levels concerning gonadotrophins.

Methods: Iraq, Al-Ramadi Hospital served as the site of case-control research, involving 100 adult males diagnosed with DMT2 and 50 healthy male people as a control group. 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: Mean serum LH was significant lower in patients with DMT2 Compared to controls, 3.83 ±1.76 mIU/ml versus 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 %, ($p < 0.001$). Mean serum FSH was significant lower in patients with DMT2 in comparison with the category of controls, 3.41 ±1.25 mIU/ml versus 9.01 ±1.44 mIU/ml, ($p < 0.001$); Moreover, the percentage of people with low serum FSH was significantly higher in patients' group in comparison to that of control, 100 % versus 0.0 %, ($p < 0.001$).

Conclusions: DMT2 is linked with a significant effect on the pituitary-gonadal axis leading to reduced production of FSH and LH hormones in men.

Introduction

Hyperglycemia is a characteristic feature shared by several metabolic disorders, defined as a prolonged increase in blood glucose levels. DM is a heterogeneous medical that qualifies as this condition category and 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]. DMT2 risk factors include the following. include central obesity, a sedentary lifestyle, a diet high in calories, 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 DMT2 can be broadly categorized into microvascular complications (MC), include neuropathy, retinopathy, and renal impairment, and MC, such as both strokes and heart attacks [9].

Many authors have extensively studied the association between metabolic derangements in type 2 diabetes and gonadotrophic hormones, (FSH) and (LH), in women [10] However, there is limited knowledge about such an 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. The study was conducted in a hospital setting, with patients randomly selected from male people visiting the diabetes control center at the 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 committee gave the study its approval on ethical aspects related to the health directorate, and All participants gave their signed approval. The software SPSS and Exc.2010 (version 16, IBM, USA, Chicago) was used to analyze obtained data. The expression of numeric variables and qualitative variables was done as mean, standard deviation, and range and as number and percentage, respectively. 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 DMT2 group was (highly significant) than that of the control group, with values of 27.12 ± 2.21 kg/m2 and 24.94 ± 2.59 kg/m2 (p < 0.001). Furthermore, the percentage of overweight and obese individuals in the DMT2 group was higher than that in the control group, with 43% and 33%, respectively, and 11 (14.7%) versus 16% and 14%, respectively. These differences in proportions were also significant (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 NS
Range	30 -60	30 -57	
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 DMT2 compared to the controls, with values of 3.83 ±1.76 mIU/ml and 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 average serum FSH was Signi. lower in patients with DMT2 compared to the controls (healthy), at 3.41 ± 1.25 mIU/ml versus 9.01 ± 1.44 mIU/ml (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 (HS) in the patients than in the controls, 91.0% versus 0.0%, respectively (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 serum HbA1C % was (HS) in patients into that of control, 100% versus 5 % (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).

Mean serum fasting blood glucose (FPG) was significant high in patients with DM disease in comparison with the category of controls, 190.15 ±25.37 mg/dl versus 88.88 ±8.92 mg/dl, (p < 0.001); in addition, the percentage of individuals with high serum FPG was (highly significant) in patients' group in compared to that of controls, 100 % versus 0 %, (p < 0.001).

Discussion

The average age of DMT2 in the study was 44.48 years, ranging from 30-60 yrs. 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 DMT2 and usually compensates for 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].

The research revealed that both FSH and LH (were Significantly lower) in DMT2 patients compared to the control group. Moreover, LH had a positive (+ve) correlation with BMI and HDL, but negative (-ve) correlations with insulin, CRP, HbA1c, HOMA-IR, cholesterol, triglyceride, LDL, and FPG. Similarly, FSH had a (+ve) correlation with BMI and HDL, but (-ve) correlations with insulin, CRP, HbA1c, HOMA-IR, cholesterol, triglyceride, 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. We agree with [16]. It is good to see that your findings align with the previous study by Maneesh et al. and that you also agree with their explanation for the observed decrease in LH and FSH levels in diabetics. Building on existing research is an important aspect of scientific inquiry, and your study adds to the body of knowledge on this topic.

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 T2 disease had a similar hyperproliferation of (HH.) [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 suggest poor glycemic control, which is likely caused by diabetic patients' non-adherence to weight loss, lifestyle modifications, exercise, and medication. 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
Data Curation: Bilal Ahmed Thmail , Amal Rasheed Farhan
Formal Analysis: Bilal Ahmed Thmail, Mohammed Mezher Hussain, Amal Rasheed Farhan
Funding Acquisition: Mohammed Mezher Hussain
Investigation: Bilal Ahmed Thmail, Mohammed Mezher Hussain, Amal Rasheed Farhan
Methodology: Bilal Ahmed Thmail, Mohammed Mezher Hussain, Amal Rasheed Farhan
Project Administration: Bilal Ahmed Thmail
Resources: Bilal Ahmed Thmail, Mohammed Mezher Hussain, Amal Rasheed Farhan
Software: Bilal Ahmed Thmail, Mohammed Mezher Hussain, Amal Rasheed Farhan
Supervision: Mohammed Mezher Hussain, Amal Rasheed Farhan
Validation: Bilal Ahmed Thmail, Mohammed Mezher Hussain
Visualization: Bilal Ahmed Thmail, Mohammed Mezher Hussain, Amal Rasheed Farhan
Writing – Original Draft Preparation: Bilal Ahmed Thmail, Amal Rasheed Farhan
Writing – Review & Editing: Bilal Ahmed Thmail, Mohammed Mezher Hussain, Amal Rasheed Farhan

Competing Interest

The authors declare that there is no conflict of interest.

References

1. Banday M, Sameer S, Nissar S. Pathophysiology of diabetes: An overview. Avicenna journal of medicine, (2020); 10(4), 174–188.
2. Kharroubi T, Darwish H. Diabetes mellitus: The epidemic of the century. World journal of diabetes, (2015); 6(6), 850–867.
3. DiMeglio A, Evans-Molina C, Oram A. Type 1 diabetes; Lancet (London, England), (2018); 391(10138): 2449–2462.
4. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe B, Ostolaza H, Martín C. Pathophysiology of

Type 2 Diabetes Mellitus. International journal of molecular sciences, (2020); 21(17): 6275.
5. Abusaib M, Ahmed M, Nwayyir H, Alidrisi H, Al-Abbood M, Al-Bayati A, Al-Ibrahimi S, Al-Kharasani A, Al-Rubaye H, Mahwi T, Ashor A, Howlett H, Shakir M, Al-Naqshbandi M, Mansour A. Iraqi Experts Consensus on the Management of Type 2 Diabetes/Prediabetes in Adults. Clinical medicine insights. Endocrinology and diabetes, (2020); 13, 1179551420942232.
6. Khan B, Hashim J, King K, Govender D, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes - Global Burden of Disease and Forecasted Trends. Journal of epidemiology and global health, (2020); 10(1), 107–111.
7. Ismail L, Materwala H, Al Kaabi J. Association of risk factors with type 2 diabetes. A systematic review. Computational and structural biotechnology journal, (2021); 19, 1759–1785.
8. Deshpande D, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Physical therapy, (2008); 88(11), 1254–1264.
9. Farmaki P, Damaskos C, Garmpis N, Garmpi A, Savvanis S, Diamantis E. Complications of Type 2 Diabetes Mellitus. Current cardiology reviews, (2020); 16(4), 249–251.
10. Stefanska A, Cembrowska P, Kubacka J, Kuligowska-Prusinska M, Sypniewska G. Gonadotropins and Their Association with the Risk of Prediabetes and Type 2 Diabetes in Middle-Aged Postmenopausal Women. Disease markers, (2019); 2384069.
11. Olokoba B, Obateru A, Olokoba B. Type 2 diabetes mellitus: a review of current trends. Oman Medical Journal, (2012); 27(4), 269–273.
12. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. International Journal Medicine Science, (2014); 11(11):1185-1200.
13. Temneanu R, Trandafir M, Purcarea R. Type 2 diabetes mellitus in children and adolescents: a relatively new clinical problem within pediatric practice. Journal Medicine Life, (2016); 9(3): 235-239.
14. Xu H, Verre C. Type 2 Diabetes Mellitus in Children. American Family Physician, (2018); 2018 Nov 1; 98(9): 590-594.
15. Chobot A, Górowska-Kowolik K, Sokołowska M, Jarosz-Chobot P. Obesity and diabetes-Not only a simple link between two epidemics. Diabetes Metabolism Research and Reviews, (2018); 34(7): e3042
16. Maneesh M, Jayalakshmi H, Singh A, Chakrabarti A. Impaired hypothalamic-pituitary-gonadal axis function in men with diabetes mellitus. Indian journal of clinical biochemistry, (2006); 21(1), 165–168.
17. Emanuele A, Emanuele V. Alcohol's effects on male reproduction. Alcohol health and research world, (2001); 22(3), 195–201.
18. Prichard J, Despres P, Gagnon J, Tchernof A, Nadeaci A, Tremblag A, Bouchard C. Journal of Clinical Endocrinology and Metabolisms. (1998); 83 (9), 3277-3284.
19. Das K, Nayak P, Vasudevan M. Biochemical markers of alcohol consumption. Indian journal of clinical Biochemistry, (2003); 18 (2), 111- 118.
20. Ali R, Alameri N, AL Rumaidh S, Ethaib S. Correlation between reproductive hormones levels and semen quality in patients with diabetes. Journal of Medicine and life, (2022); 15(12), 1507–1510.
21. Hussein Z, Al-Qatsi J. Effect of diabetes mellitus Type 2 on Pituitary Gland Hormones (FSH, LH) in men and Women in Iraq. Journal of Al-Nahrain University Science, (2012); 15, 75-79.
22. Zheng R, Cao L, Cao W, Chu X, Hu Y, Zhang H, Xu J, Sun H, Bao W, Liu K, Liu C. Risk Factors for Hypogonadism in Male Patients with Type 2 Diabetes. Journal of diabetes research, (2016); 5162167.
23. Basu K, Singhania P, Bandyopadhyay R, Biswas K. Late-onset hypogonadism in type 2 diabetic and nondiabetic male: a comparative study. Journal of Indian Medical Association, (2012); 110(8), 573-575.
24. Chandel A, Dhindsa S, Topiwala S, Chaudhuri A, Dandona P. Testosterone concentration in young patients with diabetes. Diabetes care, (2008); 31(10), 2013–2017.
25. Ndisang JF, Vannacci A, Rastogi S. Insulin Resistance, Type 1 and Type 2 Diabetes, and Related Complications 2017. Journal of Diabetes Research, (2017); 2017: 1478294.
26. Sampath Kumar A, Maiya AG, Shastry BA, Vaishali K, Ravishankar N, Hazari A, Gundmi S, Jadhav R. Exercise and insulin resistance in type 2 diabetes mellitus: A systematic review and meta-analysis. Annals of Physical and Rehabilitation Medicine, (2019); Mar; 62(2): 98-103.
27. Czech MP. Insulin action and resistance in obesity and type 2 diabetes. National of Medicine, (2017); 23(7): 804-814.