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THE IMPACT OF HBA1C LEVEL ON FSH AND LH CHANGES DURING MENOPAUSAL TRANSITION IN DIABETES WOMEN

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ABSTRACT

Diabetes mellitus (DM) is a prevalent endocrine disorder characterized by prolonged elevation of blood glucose levels. Haemoglobin A1c (HbA1c) serves as a critical metric for assessing mean glycaemic control in individuals with diabetes. In this study, we aimed to explore the impact of diabetic control, measured by HbA1c levels, on pituitary gonadotropins (FSH and LH) in Iraqi women with Type 2 diabetes during the menopausal transition. A cross-sectional study involving one hundred diabetic menopausal women aged between 45 and 60 years was conducted from November 2023 to March 2024. Participants were categorized into groups based on HbA1c values indicating good or poor glycaemic control. Data on various variables including age, height, weight, BMI, fasting blood sugar, HbA1c, FSH, and LH were collected and analysed. Our findings revealed no significant difference in LH or FSH levels among diabetic women with varying degrees of HbA1c control. Spearman's rho correlation coefficients showed weak negative correlations between HbA1c and both LH and FSH levels. These results underscore the complex interplay between glycaemic control, hormonal regulation, and metabolic factors in diabetic women during the menopausal transition.

KEYWORDS: Diabetes mellitus; Menopausal transition; HbA1C; FSH; LH

INTRODUCTION

Diabetes mellitus, commonly referred to as diabetes, encompasses a cluster of prevalent endocrine disorders marked by prolonged elevation of blood glucose levels (hyperglycaemia) [1,2]. This condition arises from either inadequate insulin production by the pancreas or diminished responsiveness of the body's cells to insulin's actions [3]. The primary classifications of diabetes include type 1 and type 2, alongside additional variants. Type 2 diabetes (T2D), previously termed adult-onset diabetes, manifests with elevated blood sugar levels, insulin resistance, and a relative insufficiency of insulin [1,2]

Type 2 diabetes accounts for approximately 90% of all diabetes cases, while the remaining 10% are primarily attributed to type 1 diabetes and gestational diabetes [4]. Type 1 diabetes is characterized by a reduced overall production of insulin, stemming from an autoimmune-mediated destruction of insulin-producing beta cells in the pancreas [5]. Diagnosis of diabetes is typically confirmed through

blood tests, including fasting plasma glucose, oral glucose tolerance test, or measurement of glycated haemoglobin (A1C) [6].

Haemoglobin A1c (HbA1c) stands as the prevailing metric for assessing mean glycaemic control. It reflects the proportion of hemoglobin molecules bound to glucose. Elevated HbA1c levels indicate higher glucose concentrations over the preceding 2-3 months. Consequently, an HbA1c test is crucial for monitoring the average glucose levels in individuals with diabetes and, when elevated, aids in diagnosing the condition [7].

Per the guidelines of the American Diabetes Association (ADA), the diagnosis of Type 2 Diabetes Mellitus (T2DM) relies on specific plasma glucose criteria. This includes fasting plasma glucose (FPG ≥ 126 mg/dL), or the 2-hour postprandial plasma glucose level during a 75-gram oral glucose tolerance test (2 h-PPG ≥ 200 mg/dL), or alternatively, the measurement of glycated hemoglobin (HbA1c ≥ 6.5%; ≥48 mmol/mol) [8].

Luteinizing hormone (LH), also referred to as luteinising hormone or lutropin, and follicle-stimulating hormone (FSH), are both a glycoprotein polypeptide hormone, and are both produced by gonadotropic cells within the anterior pituitary gland [9]. Their secretion is regulated by gonadotropin-releasing hormone (GnRH) originating from the hypothalamus [9]. FSH plays a pivotal role in governing the development, growth, pubertal maturation, and reproductive processes within the body, while FSH and LH collaborate within the reproductive system [10].

In females the acute surge of LH, known as the LH surge, initiates ovulation and the formation of the corpus luteum [11]. In males, where LH was formerly termed interstitial cell–stimulating hormone (ICSH), and it stimulates Leydig cell production of testosterone and acting synergistically with FSH [11].

Type 2 diabetes has been associated with hypogonadism due to impaired secretion of gonadotrophins, including FSH and LH, by the pituitary gland [12]. This impairment may stem from insulin resistance or associated underlying mechanisms [12]. Hypogonadism's high prevalence in Type 2 diabetes patients has been linked to factors such as hyperglycaemia, insulin resistance, and inflammatory mediators like interleukins and tumour necrosis factor [13]. Hypogonadism has also been identified as a risk factor for diabetes onset, while diabetes itself is a risk factor for hypogonadism development [14].

The menopausal transition typically spans from the initiation of irregular menstrual cycles until menopause occurs. Menopause is determined retrospectively and is recognized when menstrual activity halts for a minimum of 12 consecutive months, with no other identifiable physiological or pathological reasons [15].

The age at which menopause occurs is affected by various factors, including dietary habits, levels of physical activity, smoking habits, socioeconomic status, body mass index (BMI), ethnicity, cultural norms, and concurrent medical or gynaecological conditions [16].

The hormonal changes that occur during the menopausal transition are intricate, leading to significant fluctuations in serum levels of oestradiol, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) during its initial phases [17].

Research findings revealed that menopausal diabetics exhibited significantly decreased serum levels of FSH and LH, alongside elevated oestradiol (E2) levels, compared to the control group [18].

Body Mass Index (BMI) serves as a practical guideline for roughly classifying individuals according to their tissue mass (including muscle, fat, and bone) relative to their height. The main categories for adults based on BMI include underweight (below 18.5 kg/m2), normal weight (18.5 to 24.9), overweight (25 to 29.9), and obese (30 or higher) [19].

This study aims to explore the impact of diabetic control on pituitary gonadotrophins (FSH and LH) in Iraqi women with Type 2 diabetes during menopausal Transition.

MATERIALS AND METHODS

A cross-sectional study conducted from November 2023 to March 2024 involved one hundred diabetic menopausal women aged between 45 and 60 years, and they grouped into two grouped according to HbA1c values, a Good glycaemic control < 8% and a Poor glycaemic control > 8% [20]. Selected from the National Diabetes Center at Al Mustansiriyah University, Data collection encompassed variables such as age, height, weight, body mass index (BMI), fasting blood sugar, HbA1c, follicle-stimulating hormone (FSH), and luteinizing hormone (LH).

Sample Collection and Biochemical Analysis

In a sterile environment, venous blood samples were obtained from each participant after an overnight fast, employing a sterile disposable syringe. Approximately 3ml of blood was allocated to a regular sample tube, while 2ml was transferred to an EDTA sample tube for the evaluation of FSH, LH, fasting blood glucose, and HbA1c, respectively.

The blood samples stored in regular tubes were frozen at -20ºC until the assessment of pituitary gonadotrophins (FSH & LH) using Elecsys FSH and Elecsys LH immunoassays, facilitating the quantitative determination of FSH and LH in human serum, respectively.

All samples underwent fasting blood glucose analysis utilizing the GLUC2 kit from Germany in the Cobas C1 Device.

HbA1c determination was carried out via turbidimetric inhibition immunoassay (TINIA) on hemolyzed whole blood.

Statistical Analysis

The data collected in the study was conducted using IBM SPSS Statistics 26.0. Mann-Whitney U and Spearman's rho correlation coefficients were employed for data interpretation.

Ethical approval

All research involving human participants adhered to ethical guidelines established by the relevant institutional or national review board, ensuring compliance with the principles outlined in the 1964 Declaration of Helsinki and any subsequent revisions or comparable ethical standards.

RESULT

In this study, 100 postmenopausal women were assessed. And according to the Mann-Whitney U test findings, there is no significant difference detected in LH or FSH levels among diabetic women with varying degrees of HbA1C control (table 1).

Table 1 *(Test Statistics (Mann-Whitney U))*

Test Statistics (Mann-Whitney U)			
	Good Controlled (median, Min and max)	Poor Controlled median (min and max)	Asymp. Sig. (2-tailed)
LH	29 (6.98 – 69.9)	27.5 (3.24 – 59.56)	0.209
FSH	60.3 (10.43 – 118.7)	52.25 (5.27 – 116.7)	0.216

The Mann-Whitney U test resulted in a corresponding p-value of 0.209 for LH and p-value of 0.216 for FSH Therefore, we fail to reject the null hypothesis, indicating no significant difference in LH and FSH levels between the groups based on HbA1C control.

In the "Good Controlled" group, the median LH level is 29, ranging from 6.98 to 69.9, and the median FSH level is 60.3, ranging from 10.43 to 118.7.

In contrast, in the "Poor Controlled" group, the median LH level is 27.5, with a range from 3.24 to 59.56, and the median FSH level is 52.25, with a range from 5.27 to 116.7.

Table 2 *(displays the Spearman's rho correlation coefficients among different variables.)*

Variable	**BMI**	**FBS**	**FSH**	**LH**	**HbA1C**	**Age**	**Weight**	**Height**
BMI	1	0.054	-0.225*	-0.238*	-0.135	0.068	0.878**	-0.295**
FBS	0.054	1	-0.071	-0.17	0.613**	-0.102	0.096	0.111
FSH	-0.225*	-0.071	1	0.721**	-0.186	0.156	-0.236*	-0.04
LH	-0.238*	-0.17	0.721**	1	-0.165	0.124	-0.230*	-0.086
HbA1C	-0.135	0.613**	-0.186	-0.165	1	-0.211*	-0.043	0.236*
Age	0.068	-0.102	0.156	0.124	-0.211*	1	-0.073	-0.293**
Weight	0.878**	0.096	-0.236*	-0.230*	-0.043	-0.073	1	0.139
Height	-0.295**	0.111	-0.04	-0.086	0.236*	-0.293**	0.139	1
* Correlation is significant at the 0.05 level (2-tailed). ** Correlation is significant at the 0.01 level (2-tailed).								

BMI (Body Mass Index) has a strong positive correlation with weight (0.878**), and BMI also has a moderate negative correlation with height (-0.295**). FBS has a moderate positive correlation with HbA1C (0.613**) and a weak positive correlation with weight (0.096). FSH and LH have a strong positive correlation (0.721**). Age has a weak positive correlation with FSH (0.156) and LH (0.124). HbA1C has a moderate positive correlation with FBS (0.613**) and a weak positive correlation with

height (0.236*). Weight has a moderate negative correlation with height (-0.295**). Height has a weak positive correlation with HbA1C (0.236*).

There is a weak negative correlation between HbA1C and LH (-0.165). And there is a weak negative correlation between HbA1C and FSH (-0.186). Overall, these results suggest that there is a weak negative association between HbA1C and both LH and FSH levels. Additionally, there is a strong positive correlation between LH and FSH levels.

DISCUSSION

The study aimed to explore the impact of HbA1C levels on Gonadotropins hormones change during the menopausal transition in diabetic women. The results revealed no significant difference in LH or FSH levels among diabetic women with varying degrees of HbA1C control, as indicated by the Mann-Whitney U test. Similarly, Spearman's rho correlation coefficients showed weak negative correlations between HbA1C and both LH and FSH levels.

These findings align with previous research conducted by Rawnaq J. Kadhim and Salman A. Ahmed [21], who conducted a study comparing gonadotropin levels in diabetes mellitus females, contributing to the understanding of hormonal imbalances in diabetic individuals. Additionally, Lateef et al. [22] estimated the prolactin level in Iraqi diabetic women of menopause, providing further insights into hormonal dynamics in this population. Moreover, Şahin et al. [23] examined the impact of the type of menopause and menopausal duration on the development of pre-diabetes mellitus and diabetes mellitus in postmenopausal women, shedding light on the relationship between menopausal factors and diabetes risk. Furthermore, Wang et al. [24] conducted a 10-year prospective study involving 300,000 women in China, revealing insights into the association between menopausal status, age at natural menopause, and the risk of diabetes. This study underscores the importance of considering hormonal changes in postmenopausal women when examining diabetes risk factors.

CONCLUSION

In conclusion, while this study did not identify significant differences in LH and FSH levels based on HbA1C control among postmenopausal Iraqi women with diabetes, it did underscore the complex interplay between glycemic control, hormonal regulation, and metabolic factors. These findings highlight the need for comprehensive management strategies that consider the diverse influences on hormone levels and metabolic health in diabetic individuals.

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CONFLICTS OF INTEREST

The author declares no conflict of interest.

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