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STUDY THE EFFECT OF TYPE 2 DIABETES MELLITUS ON LEVEL OF REPRODUCTIVE HORMONES IN A SAMPLE OF IRAQI WOMEN

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ABSTRACT
The present study was aimed to investigate the effects of type 2 diabetes mellitus (T2DM) on the levels of HbA1c, reproductive hormones (progesterone and estradiol), FSH, LH and prolactin on in sample of Iraqi women. Sixty diabetic female patients and 30 apparently healthy controls were involved in the study during their attendance at Specialist Center for Endocrine and Diabetes Diseases in Baghdad from November 2016 to April 2017. The age of women ranged 30-45 years. The results of FBG showed highly significant (P <0.01) increase (206.83 ±9.57 mg/dl) in diabetic groups in comparison with control group (98.93 ±3.57 mg / dl), also the HbA_{1c} showed highly significant (P <0.01) increase in diabetic groups (8.43 ±0.21%) in comparison with control group (5.34 ±0.08%). BMI was highly significant (P<0.01) increase in women with diabetes (34.15 ±0.62 kg/m2) compared to control (24.41 ±0.60 kg/m2). Progesterone level showed highly significant (P <0.01) decrease in T2DM group (4.55 ±0.52 ng/ml) when compared with control group (7.03 ±0.96 ng/ml). Estradiol level showed highly significant (P <0.01) decrease in diabetic group (47.84 ±4.60 pg/ml) in comparison with control group (77.58 ±6.44 pg/ml). FSH level showed highly significant (P <0.01) increase in T2DM group (8.11 ± 0.20 mIU/ml) when compared with control (5.56 ±0.51 mIU/ml). LH level was highly significant (P <0.01) increase in T2DM group (6.83 ±0.16 mIU/ml) in comparison with control group (3.58 ±0.30 mIU/ml), highly significant (P <0.01) increase in T2DM group (15.16 ±0.60 ng/ml) in comparison with control group (13.96 ±0.60 ng/ml).

KEY WORDS: type 2 diabetes, reproductive hormones, Iraqi women, HbA1c.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders described by a chronic hyperglycemic condition causing from defects in insulin secret insulin action or both[1]. That chronic hyperglycemic condition due to insufficient production of insulin (type 1 diabetes) or the insufficiency of cells to use insulin properly (type 2 diabetes)[2]. HbA_{1c} is a form of hemoglobin that is measured primarily to identify the three-month average plasma glucose concentration; the test is limited to a three-month average because the lifespan of a red blood cell is four months (120 days)[3]. During premenopausal period insulin resistance become more prevalent and many women notice that their blood sugar levels increase, due to sex hormones effect; also, they notice that when woman reaches menopause the body becomes more sensitive to insulin like it was prior to premenopausal period, and the levels of estrogen and progesterone decline [4].

One of the complications of type 2 (T2DM) is the disturbance of sexual and reproductive diabetes mellitus, many studies have been shown that T2DM causing low level estrogen and progesterone, Lower metabolism that results in weight gain and obesity is the main cause of type II diabetes in women[5]. Progesterone is an endogenous steroid and progestogen sex hormone involved in the menstrual cycle, pregnancy, and embryogenesis of humans and other species. It belongs to a group of steroid hormones called the progestogens and is the major progestogen in the body[6]. Progesterone is sometimes called the "hormone of pregnancy[7]. While Estrogen is the primary female sex hormone as well as a medication, it is responsible for the development and regulation of the female reproductive system and they promote the development of female secondary sexual characteristics, such as breasts, and are also involved in the thickening of the endometrium and other aspects of regulating the menstrual cycle. In males, estrogen regulates certain functions of the reproductive system important to the maturation of sperm. Estrogen may also refer to any substance, natural or synthetic, that mimics the effects of the natural hormone [8].

MATERIALS & METHODS

Sixty female patients with diabetes type 2 and 30 healthy were involved in this study during their attendance at the National Diabetes Center (AL Mustansiriya University). The diagnosed of patients as having diabetes type 2 were based on the history, anthropometric measurements and clinical examination. Measurement of anthropometric variables in all participants was done according to standard methods.

Blood samples collection

Blood samples were collected from each patient on the following basis: Fasting test (10-14 h before breakfast). In each stage, ten milliliters of venous blood were withdrawn from each obese patient .The samples were dropped into clean disposable tubes, left at room temperature for 15 minutes for clot formation and then centrifuged for 10

minutes at 3000 run per minute. The serum was separated and FBG progesterone, Estradiol, FSH, LH and Prolactin were measured by using Enzyme Linked Fluorescent Assay using minividas (Biomerieux) and whole blood (HbA_{1c}) by a sandwich immunodetection method by using ichroma.

Statistical Analysis

The Statistical Analysis System- SAS (2012) program was used to achieve of difference factors in study parameters T-Test was used to significant compare between means.

RESULTS & DISCUSSION

The increasing in the level of FBG in diabetic patients was in agreement with many researchers [13-16, 4]. During perimenopause many women find that their blood sugar levels increase, during this time the body becomes more resistant to insulin which causes this increase in blood sugar levels[17]. That chronic diabetes is a group of metabolic diseases considered by hyperglycemia, the elevation in FBG level may be resulting from defects in insulin secretion, insulin action or both[18]. The FBG test is directly proportional to the severity of the diabetes mellitus[19, 20]. So the increase in the level of FBG in this study was also in agreement with that reported by[21] that stated FBG level 126 mg/dl, in diabetic patients groups showed high level of FBG when compared with the control group. This study showed a significant raise of HbA1c in diabetic female compared to control and this is similar to the findings in a group of patients studied by other researchers[22-24].The International Diabetes Federation (IDF) recommend HbA_{1c} values below 6.5% while American Diabetes Association (ADA) recommend that the HbA1c be below 7% for most patients to indicate good glycemic control [25]. The rises in the level of HbA_{1c} was associated with the increasing level of FBG in diabetic groups, that testing HbA_{1c} is appealing as measures chronic glycaemia in diabetic patients.

TABLE 1: shows the level of FBG and HbA1c in the study groups (Mean ± SE)

The Groups	No.	Mean ±SE	
		FBG (mg/dl)	HbA_{1c} (%)
Control	30	98.93 ± 3.57	5.34 ± 0.08
Patients	60	206.83 ± 9.57	8.43 ± 0.21
T-Test	---	27.453 **	0.601 **

* (P<0.05) ** (P<0.01), NS: Non-Significant.

It has been used as an objecting marker of average glycemic control in the monitoring of patients with diabetes[26].That the major consequences of hyperglycemia are excessive non-enzymatic glycosylation of various body proteins like hemoglobin, albumin. So the elevation of HbA_{1c} levels in this study indicates reduced control of blood glucose levels[27]. The serum glucose is unstable in patients with DM and one effective way to monitor it by measured HbA1c, which give the average blood glucose level of preceding 2-3 months. The HbA_{1c} will be a valuable adjunct to blood glucose determinations in epidemiological studies [15]. Another study, which included 500 people with type 2 diabetes, found that HbA_{1c} was more than 8%, and there was a significant relationship with increased duration of diabetes [28].

TABLE 2: shows the levels of FSH, LH, Prolactin , Progesterone and Estradiol in the study groups (Mean ± SE)

Groups	No.	Mean ± SE					
		FSH (mIU/ml)	LH (mIU/m)	prolactin (ng/ml)	Progesterone (ng/ml)	Estradiol (pg/ml)	BMI
Control	30	5.56 ±0.51	3.58 ±0.30	13.96 ±0.60	7.03 ± 0.96	77.58± 6.44	24.4±0.60
Patients	60	8.11 ±0.20	6.83 ±0.16	15.16 ±0.60	4.55 ± 0.52	47.84± 4.60	34.1±0.62
T-Test	---	0.918 **	0.621 **	2.186 *	1.990**	15.806 **	1.928 **

* (P<0.05), ** (P<0.01), NS: Non-Significant

The study showed a decrease in estradiol and progesterone levels in the patients group compared with control group. 14 in another study showed the data revealed an inverse correlation between serum estradiol level and BMI[29]. Suggested two hypotheses to prove the inverse correlation between BMI and estradiol level. First, a high BMI may be associated with ovulatory insufficiency beyond its known role in increasing ovulatory cycles. The hypothesis is also supported by epidemiological data suggesting that a BMI as low as 24 kg/m^2 is associated with an increased risk of an ovulatory infertility. A second hypothesis may be through an indirect regulation by sex hormone binding globulin (SHBG). As SHBG declines, free estradiol should increase. Therefore, in response to decreased SHBG, may decrease to lower total estradiol production by the ovaries, thus keeping free estradiol relatively constant. Additionally, the molecular clearance rate of estradiol is positively associated with weight, also potentially reducing total estradiol levels [30, 14]. Higher BMI may be associated with lower estradiol levels. Premenopausal obese women have lower serum estradiol than their normal weight counterparts. However, postmenopausal obese women have significantly higher estradiol than normal-weight women[31]. This relationship in postmenopausal women was also noted in another study, which in addition found further increases in estradiol levels with the metabolic syndrome [32].

The positive association of BMI and estradiol in postmenopausal obese women is consistent with the well-recognized changes in estrogen metabolism that occurs with ovarian senescence, when the contribution of estradiol from fat becomes dominant and obese women

have higher estradiol levels than non-obese women [33-35] while there is a negative association between estradiol and BMI in premenopausal women [36,33,37] the mechanisms for this association remain unclear. Possibly the low levels of sex hormone-binding globulin (SHBG) in obese premenopausal women, which are positively correlated with estradiol levels [38, 39] result in greater clearance and consequentially lower levels of estradiol. It is hypothesized that the association between obesity and hormones is related to insulin resistance or to other adipose-derived substances such as adiponectin or leptin [40, 41]. However, measures of insulin sensitivity did not refer to reproductive hormones in obese women in the menopausal transition, suggesting that BMI may influence reproductive hormones apart from its relationship with the metabolic syndrome[34]. As in the Estradiol the level of progesterone was inversely correlated with BMI[29], thus decreasing progesterone levels in obese women with type 2 diabetes. In another study [42] where it has been noted that the optimal weight before pregnancy may be useful in regulating the level of progesterone in the blood, and that the reduction of progesterone linked to obesity. Even so, [43] studied the differences in serum sex hormones and lipid levels in Caucasian and African-American premenopausal women and concluded that race is an important determinant of plasma triglycerides and sex hormone levels, even after adjustment for differences in body size. Another study also showed that progesterone, similar to estradiol, appears to decrease with increasing BMI. Levels of progesterone are lower in obese perimenopausal women than in women with normal BMI [44] a similar result was found in obese premenopausal women with normal cycles [45].

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