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Evaluation of Glucose, 8-isoprostane, and some Reproductive Hormones Levels in Women with Obesity, Type 1 Diabetes and Hyperprolactinemia

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ABSTRACT

The world's population is increasingly obese, replacing nutrition and infectious diseases. Cardiovascular disease and diabetes are linked to it. Endocrine disorders like hyperprolactinemia are frequent. It often causes ovulatory problems, menstrual abnormalities, and infertility in women. The autoimmune illness of type 1 diabetes involves abnormal immune responses to β-cell auto antigens. So, this study aimed to the know the effects of obesity, hyper prolactin and type1D in women by estimating some biochemical and hormone parameters. It was conducted on 92 women, ages between (20-40) years, with samples collected from the AL-Sader teaching hospital, Maysan for child and birth hospital, and specialized center for diabetes and endocrinology, from June 2022 to February of 2023. The women divided into four groups: Control group, hyperprolactinemia group (hyper serum prolactin), obesity group (have a body mass index (BMI) over 30 kg/M2), and type 1 diabetes group. The results showed the values of HbA1C and blood glucose in the type1D group increased significantly ($P \leq 0.05$) in comparison with obesity, hyperprolactinemia, and control groups. The values of 8-isoprostance in obesity and hyperprolactinemia groups increased significantly ($P \leq 0.05$) in comparison with other groups The values of follicle stimulating hormone and Latinizing hormone did not differ significantly in all groups. The value of testosterone in obesity group increased significantly ($P \leq 0.05$) in comparison with type1D, hyperprolactinemia and control groups. According to the above results we can conclude the women with obesity showed disorders in the reproductive state by increasing of 8-isoprostance and testosterone values.

Keywords: glucose, 8-isoprostance, hormones, obesity, hyperprolactin.

INTRODUCTION

The prevalence of obesity among people all over the world has increased to the point where it is now overtaking malnutrition and infectious diseases as the leading cause of death and illness. Diseases like diabetes mellitus, heart disease, several types of cancer, and sleep apnea are all linked to fat. A body mass index (weight divided by the square of height) of 30 or higher indicates obesity; however, this definition ignores the risk of disease and early death associated with even mild degrees of overweight and the deleterious effects of abdominal fat (Kopelman, 2000). Common in the endocrine system, hyperprolactinemia may have physiological, pathogenic, or idiopathic causes. Hyperprolactinemia typically causes a reduction in pulsatile gonadotropin releasing hormone (GnRH), a common physiological effect. Different illnesses have different clinical presentations in different age groups and between the sexes. Ovulatory dysfunction, menstrual irregularities, galactorrhea, and infertility are all symptoms of recurrent gonadal dysfunction in women (Majumdar and Mangal, 2015).

Type2 diabetes mellitus (DM) is a metabolic condition characterized by persistently high blood sugar levels. Insulin insufficiency or absence is a hallmark of type1 diabetes (T1DM), an autoimmune illness characterized by abnormal immune responses to particular -cell auto antigens. Organ-specific multiple autoimmunity in the context of autoimmune polyendocrine syndrome (APS) has been reported in children and adolescents with type 1 diabetes (Kakleas *et al*., 2015).

An F2 isoprostane prostaglandin isomer, also known as 8-isoprostane (8-iso- PGF2α). When arachidonic acid in cell membranes is oxidized, it leaks out into the blood and other bodily fluids. It has been established as a reliable and long-lasting biomarker of oxidative stress and lipid peroxidation in a wide range of illnesses (Amirchaghmaghi *et al.,* 2016; Vant Erve *et al.,* 2017). The health in women correlated with many metabolic and endocrine parameters, so that, the current study was designed for the assessment of serum blood glucose, 8-isoprostane and reproductive hormones FSH, LH, and testosterone) in women with obesity, hyperprolactinemia and type1 diabetes.

METHOD

This study was conducted at the AL-Sadder Teaching Hospital, specialist center of endocrine and diabetes, and Maysan for child and birth hospital, from the period of June 2022 to February of 2023. The samples of this study consist of 92 women with an average aged 20-40 years. The women were divided into four groups as follows: Control group (23 healthy women with regular menstrual cycles), obesity group (23) women have a BMI over 30 kg/M^2), hyperprolactinemia group (23 women with hyper serum prolactin), and type1 diabetes group (23 women with type1 diabetes mellitus).

Blood sampling

Venous blood (5) milliliter drowns from fasting women at (9-11 AM). The blood sample was divided into two parts; 2.5 mL of blood was transferred into EDTA tube for HbA1c estimation depend on (Little *et al.,* 1992), and the other part of blood was left for 15 minutes to clot, and then serum was separated by centrifugation at 3000 (rpm) for 5 (min), to measure glucose according to (Freckmann *et al.,* 2014). The remaining serum was transferred into labeled plain tube and stored at -20Ċ° until used for determination of 8-isoprostance follicle stimulating hormone (FSH) and Latinizing hormone (LH) and testosterone (TT) by kits supply from Shanghai yl biotech, China and Roche Cobas, Switzerland, depend on (Wild, 2013; Fung *et al*., 2017).

Statistical analysis

The data was analyzed statistically to determine the significance of the parameters by one way ANOVA (LSD), the differences were considered to be significant at $P \leq 0.05$ the values present as means ± SE (Bryman and Cramer, 2012).

RESULTS

The values of HbA1C in the diabetes type one group (9.8±0.54) increased significantly ($P \leq 0.05$) in comparison with obesity (5.07±0.11), hyperprolactinemia (5.28±0.14), and control groups (4.9±0.11) .No significant differences ($P \leq 0.05$) among obesity, hyperprolactinemia, and control groups in HbA1C values Fig. (1).

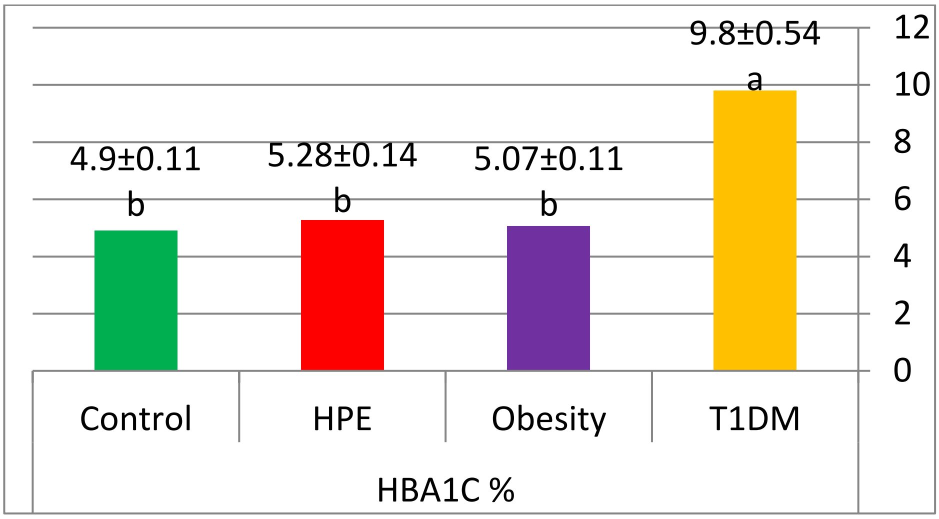

Fig. 1: The HbA1C concentration in control, hyperprolactinemia, obesity and type one diabetes women.

The values of glucose in the diabetes type one group (289.28±24.47 mg/dl) increased significantly ($P \leq 0.05$) in comparison with obesity (98.11±5.55 mg/dl), hyperprolactinemia (94.48±2.78 mg/dl) and control groups (96.54 ±2.63 mg/dl). The results showed no significant differences ($P \leq 0.05$) in glucose value among obesity, hyperprolactinemia and control groups Fig. (2).

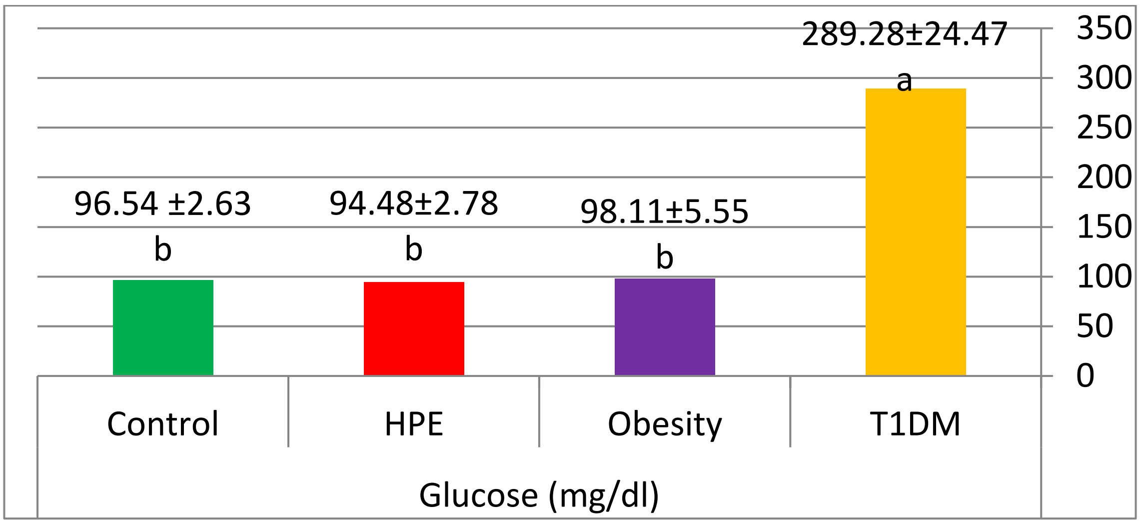

Fig. 2: The glucose concentration in control, hyperprolactinemia, obesity and type one diabetes women.

The concentration of 8-isoprostance in obesity (108.69±4.87 ng/l) and hyperprolactinemia groups (103.42±3.77 ng/l) increased significantly (P≤0.05) compared with diabetes type one (64.15±5.34 ng/l) and control groups (22.68±1.84 ng/l). The concentration of 8-isoprostance in diabetes type one group increased significantly (P≤0.05) compared with control group. While, no significant differences (P≤0.05) in 8-isoprostance between obesity and hyperprolactinemia groups as shown in Fig. (3).

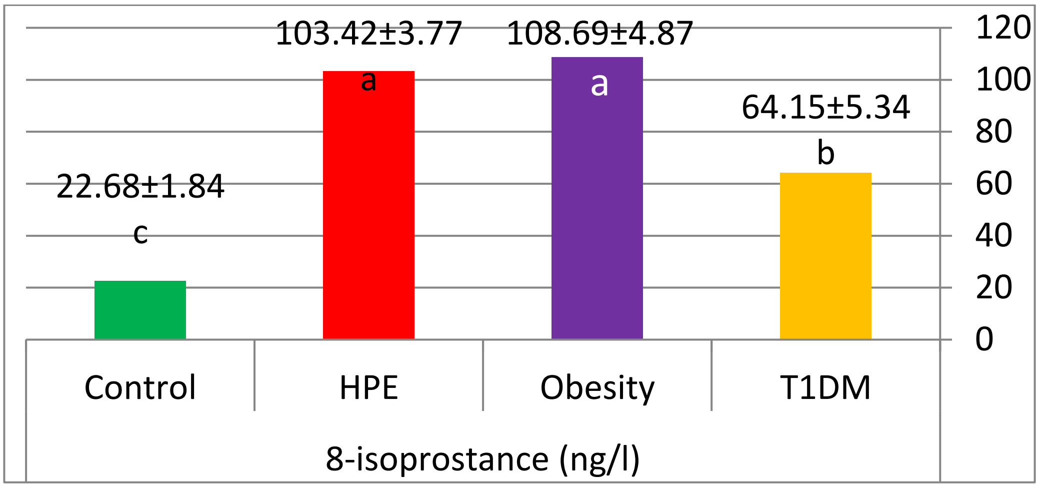

Fig. 3: The 8-isoprostane concentration in control, hyperprolactinemia, obesity and type one diabetes women.

The levels of FSH did not differ significantly (P≤0.05) in the control (6.63±0.34mlu/ml), hyperprolactinemia (6.49±0.34 mlu/ml), obesity (6.25± 0.36 mlu/ml) and type one diabetes groups (6.55±0.36 mlu/ml). Fig. (4).

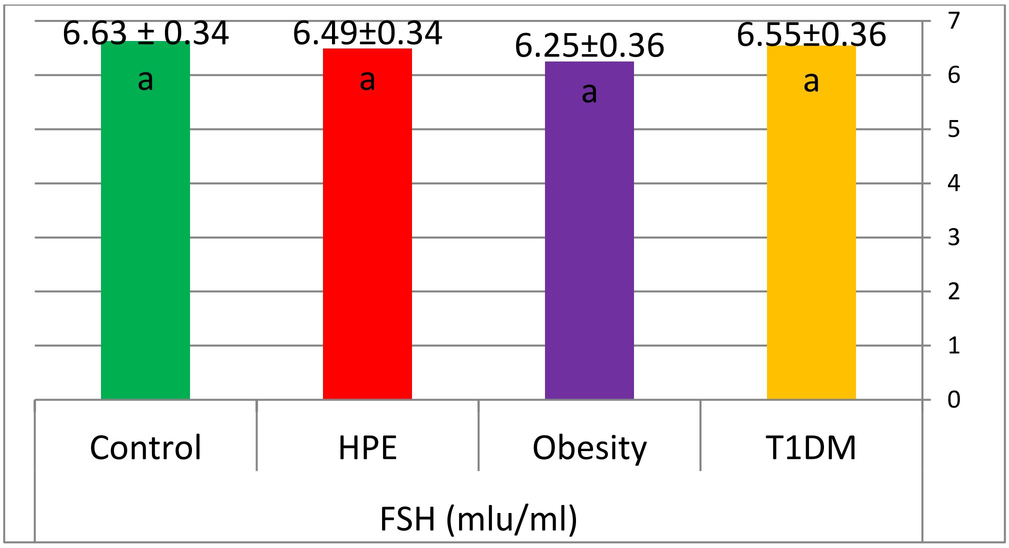

Fig. 4: The FSH concentration in control, Hyperprolactinemia, Obesity and type one diabetes women.

The levels of LH did not differ significantly (P≤0.05) in the control (5.19±0.45 mlu/ml), hyperprolactinema (5.13±0.35 mlu/ml), obesity (4.33±0.37 mlu/ml) and type one diabetes groups (5.00±0.32 mlu/ml) as shown in Fig. (5).

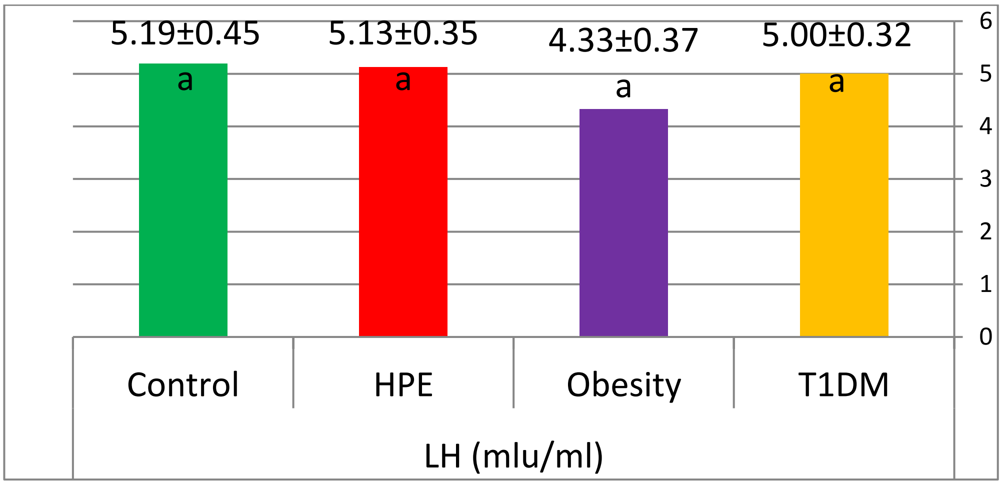

Fig. 5: The LH concentration in control, hyperprolactinemia, obesity and type one diabetes women.

The levels of testosterone in obesity group (0.36±0.03 ng/ml) increased significantly (P≤ 0.05) in comparison with diabetes type one (0.22±0.03 ng/ml), hyperprolactinemia (0.21±0.03 ng/ml) and control groups (0.13 ±0.02 ng/ml). The levels of testosterone in diabetes type one group increased significantly (P≤0.05) compared to the control group. non-significant (P≤0.05) differences in testosterone value between diabetes type one and hyperprolactinemia group. Also, non-significant (P≤0.05) differences between hyperprolactinemia and control groups (0.13±0.09) as shown in Fig. (6).

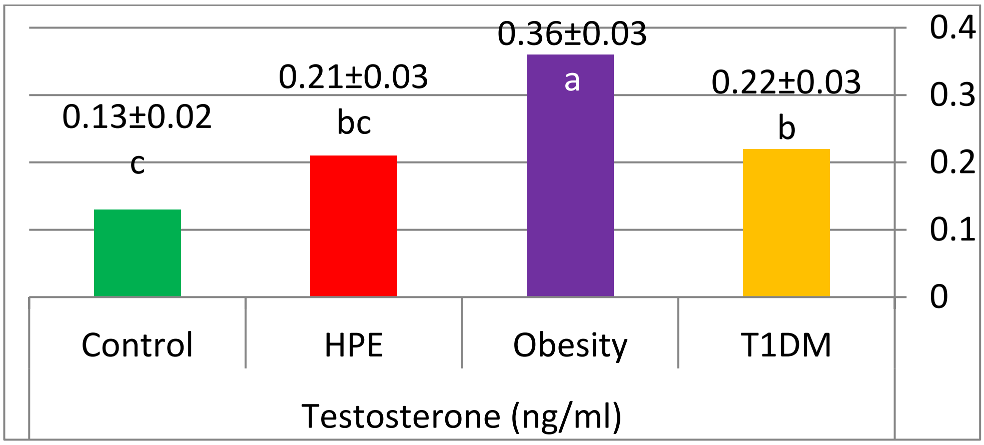

Fig. 6: The testosterone concentration in control, hyperprolactinemia, obesity and type one diabetes women.

DISCUSSION

The values of HbA1C and glucose in the diabetes type one group increased significantly (P≤0.05) compared with obesity, hyperprolactinemia, and control groups. The results in this study may be attributed to the effect of the absence or deficiency of insulin in T1DM patient, insulin decreases blood sugar levels, and in the case of patients with type 1 diabetes, patients suffer from a defect in the beta cells of the pancreas, which work to produce the hormone insulin, which plays a crucial role in the balance of glucose in the blood.

In study by (Posawetz *et al.*, 2021) found no differences between prolactinoma and control groups in fasting glucose, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and HbA1c, and this disagree with our results. Another study found that insulin and HOMA significantly decreased, glucose significantly increased in obese women compared with the control (Arikan and Sagsoz, 2022). Blood glucose was significantly higher in obese and overweight patients in comparison with normal subjects, while there was no difference between obese, and overweight.

Also, HOMA index values, are progressively and significantly higher by going from normal to the overweight and the obese according to study by (Mancini *et al*., 2021).

Significantly higher concentrations of glucose were observed in obese women (metabolic syndrome) MS compared with women without MS (Fatani *et al.,* 2018), this does not agree with our results. Plasma glucose measured was two hours after eating, as well as fasting glucose, and found that they were not associated with obesity among people with diabetes (Azam *et al.*, 2023).

The HOMA, serum insulin, and glucose levels were highest in the class-2 obese (BMI 35.0–39.9) group compared with the class-1 (BMI 30.0–34.9) obese and control groups (Arikan and Sagsoz, 2022), and this does not agree with our results. Previous studies agree with the results of our study regarding the value of glucose, and HBA1C. Alkaabi *et al*., (2022) found that HbA1c was significantly higher among patients with T1DM than controls. In another study, they noted that glucose and average HbA1c increased in T1DM subjects compared to controls (Allwsh and Mohammad, 2013; Kang *et al.*,2021).

The glycemic variability recorded was seven times higher in T1DM than in healthy controls (Valente *et al*., 2021). The glycemic and T2D risk genetic variants contribute to higher FG and FI levels and decreased beta cell function in children, and adolescents. The causal effects of adiposity on increased insulin resistance are detectable from childhood age (Balkhiyarova *et al*.,2022).

Level of 8-isoprostance in obesity, hyperprolactinemia and T1D groups increased significantly ($P \leq 0.05$) in comparison with control groups. In the case of hyperprolactinemia, the reason for the increase in 8-isoprostance may be a hormonal imbalance and its effect on oxidative stress, similar results found 8-isoprostance increase at infertile women had higher prolactin levels than controls (Kani *et al.,* 2019). Increasing in F2-isoprostanes are marker of oxidative stress harmfully; and this rise as a mechanistic link between obesity and cardiovascular risk (Spahis *et al.,* 2016; Otani, 2011; Keaney *et al.,* 2003). Also, the results support the hypothesis that hyper in blood glucose can increase oxidative stress (Ceriello *et al.*, 2007; Esposito *et al*., 2002).

Valente *et al*., (2021) found that no significant differences between the T1D and control groups for gender distribution, in 8-iso-PGF-2α. While, other studies found high levels of 8-isoPGF-2α in T1DM compared to healthy subjects and this agrees with our results (Meng *et al.*, 2022; Altıncık *et al.,* 2016 Wentholt *et al*., 2008). Pękala-Wojciechowska *et al*., (2018) found that 8-isoprostane in the blood of patients with T1DM without complications and T1D with advanced complications were significantly higher compared to the control group, and this agree with our results. While, the concentration of 8-isoprostane in exhaled breath condensate (EBC) was lower in type one diabetic patients have advanced complications, than in patients with T1DM without advanced complications and in the control group.

In study by (Saleem *et al.*, 2023), they noted that BMI was positively correlated with plasma F2-IsoPs and a positive correlation between F2-IsoPs and percent fat. There was an inverse correlation between F2-IsoPs and high-density lipoprotein (HDL-c), while there was a positive correlation between F2-IsoPs and low-density lipoprotein (LDL-c). Less 5-F2t isoprostanes, 15-F2t-isoprostanes, 4-F4t-neuroprostanes, and 10-F4t-neuroprostane were secreted from peri-pancreatic white adipose tissue (pWAT) in obese rats compared to lean animals. Glucose-induced insulin production in the pancreatic islets of Wister rats was also inhibited by 15-F2t isoprostane, but not by 5-F2t-isoprostanes (Laget *et al*., 2022). African Americans have lower levels of systemic F2 -isoprostane levels despite their predisposition to obesity. Type 2D and BMI were inversely correlated with insulin sensitivity in obese women. In addition, they found that plasma F2 -IsoPs levels was significantly associated with reduced insulin sensitivity (Il'yasova *et al.*, 2017). The values of FSH and LH did not differ significantly ($P \leq 0.05$) in all groups. Whereas, the values of testosterone in obesity and diabetes type one increased significantly ($P \leq 0.05$) in comparison with groups control group.

In this study, the differences in the levels of these hormones in the women with hyperprolacteinemia, obesity and T1DM compared to control and compared to each other, probably belonged to the intertwined hormonal interactions. So that, In the hyperprolactinemia group, this may be due to the feedback resulting from the increase in prolactin and its connection with dopamine. Dopamine is the inhibitory factor for prolactin. Dopamine is important in maintaining a healthy level of prolactin. In the event of an increase in prolactin secretion, dopamine flows from the hypothalamus into the circulatory system, and thus leads to a decrease in prolactin secretion and its return to the normal level in the healthy state. Thus, any imbalance in this dopamine balance will affect most of the hormones that have feedback with prolactin (Nappi e*t al*., 2021). In the obese group, the reason may be the outputs of adipose tissue and its effect, Adipose tissue has proven its primary role as an endocrine gland, as it is considered an active and important endocrine tissue. It releases adipocytokines or adipose tissue hormones such as leptin, which has been shown to have an effect on raising the estrogen hormone, especially in women, and therefore the rise in estrogen may lead to a change in the levels of other reproductive hormones (Triantafyllou *et al*., 2016).

While, the differences of the hormones in the T1D group may be due to the absence or decrease of insulin, especially, since all patients in our study are treated with insulin, high insulin levels in women cause testosterone to rise, while, low insulin levels affect in progesterone, therefore may lead to a change in the levels of other reproductive hormones (Melmer *et al*., 2021). The results in this study agree with another study such as (Arslan *et al*., 2022) who noted that prolactin level was significantly higher in the hyperprolactinemia group. No significant differences were detected between the LH levels and FSH in the hyperprolactinemia group compartmented with control. The results of (Elbardisi *et al*., 2021) found in hyperprolactinemia patient a significant increase in LH levels, while, there were no significant differences in the testosterone levels, the prolactin concentration was significantly higher. The value of LH and FSH were no significant difference between women with hyperprolactinemia and women with normal prolactin according to study by (Elnour *et al*., 2021), and this agrees with our results. The levels of FSH and estrogen are lower in females with secondary infertility due to hyperprolactinemia and these results are not consistent with our results (Owiredu *et al*., 2019). Secondary infertility caused by elevated prolactin levels is strongly correlated with FSH levels in the blood. The average amount of FSH was significantly low. Although there was no statistically significant correlation between blood LH levels and the presence or absence of secondary infertility, individuals who experienced secondary infertility had lower LH levels than those who did not (Khan *et al*., 2021). The Women with prolactinoma had significantly higher levels of prolactin this agree with our results, and lower of LH, FSH in women with prolactinoma at premenopausal age 35-45 year (Posawetz *et al*., 20 21). Al-Ttaie *et al.* (2021) observed high level of the prolactin and this agree with our results regarding to the prolactin, LH significantly increased while FSH decreased significantly in the infertility (hyperpolactinemia women) group compared with the controls. E2 decreased glucose uptake by human adipocytes in late postmenopausal women. Since menopause, women's glucose utilization has changed, and this may be due to a decreased ESR1:ESR2 ratio (Ahmed *et al.,* 2022). In study done by (Arikan and Sagsoz, 2022) they noted the mean LH, FSH, AMH did not differ significantly in the class-2 obese (BMI 35.0–39.9), the class-1 obese (BMI 30.0–34.9) and control groups, these results don’t agree with our results.

The overweight or obese in women may have altered endocrine profiles in them such as, high LH, abnormal ratio of FSH and LH in the luteal phase, and low levels of sex hormone-binding globulin (Lash and Armstrong, 2009). A high BMI is associated with decreased estradiol levels in all phases of ovarian cycle and has a negative impact on pregnancy outcomes in obese women (Rehman *et al.,* 2012; Al-Taie and AL-Jawadi, 2019). In obesity women significantly higher concentrations of total testosterone this agree with our results, were observed in subjects with metabolic syndrome (MS) than compared with women without MS (Fatani *et al.,* 2018). Positive correlations between lowering overall testosterone, Sex hormone binding globulin (SHBG) and increased BMI in obesity was noted. As well as, there were no significant changes in levels of free androgens, estradiol and gonadotropins (LH and FSH) (Stárka *et al*., 2020), this does not agree with our results. (Salman and Yser, 2022) showed significant reduction in the concentration of testosterone, LH and AMH hormones, while the concentration of estradiol and leptin hormones were significantly higher in obese women compared with control group, while there was no significant difference for progesterone hormone concentration, this result don't agree with our results. Giviziez *et al*. (2022) noted that overweight increases more than twice the chance of anovulation among infertile women with regular menstrual cycles. Kang *et al*., (2021) they observed that the levels of FSH, LH, and total testosterone levels in young men with T1D were higher than those in the control subjects don't agree with our results, The concentration of the LH, FSH, LH/FSH were similar within obesity, control and T1D subjects according to the study done by (Calcaterra *et al.,* 2021).

Women with type 1 diabetes typically have a shorter reproductive lifespan than their non-diabetic counterparts due to delayed menarche and early onset of menopause. That's why T1D women had an average of 2.5 fewer reproductive years than their non-diabetic counterparts (Yi *et al.,* 2021). The metabolic imbalance plays an important role in reproductive functions, such as the irregularity and duration of the menstrual cycle, the increase in HbA1c increases the duration of the menstrual cycle in women of childbearing age who suffer from type 1 D (Gaete, 2010).

CONCLUSION

According to above results we can conclude, women with type 1 diabetes have elevated levels of HBA1C and glucose, while hyperprolactinemia and obesity levels are normal, and this reflects the functional impact of the diabetic in women with type 1 diabetes. Women with hyperprolactinemia, obesity and type 1 diabetes have elevated levels of 8-isoprostane and this may be due to excessive oxidative stress. The FSH and LH had normal levels in women with hyperprolactinemia, obesity and type 1 diabetes. While, elevated testosterone level in obese women, may be to the ability of adipose tissue to convert other hormones into testosterone.

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تقدير مستويات الجلوكوز، 8- ايزوبروستانز وبعض هرمونات التكاثر عند النساء المصابات بالسمنة، والسكري من النوع الاول وفرط البرولاكتين

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الملخص

اصبحت السمنة شائعة بين سكان العالم وبدأت تحل محل نقص التغذية والامراض المعدية، كما انها ترتبط مع مرض السكري وامراض القلب التاجية، يعد فرط البرولاكتين من اضطرابات الغدد الصم الشائعة عند النساء، كما انه يؤدي الى ضعف وظيفة المناسل مثل اضطرابات التبويض والدورة الشهرية والعقم. يعد السكري من النوع الاول من امراض المناعة الذاتية مع استجابة مناعية الى مستضدات ذاتية متخصصة لخلايا بيتا، لذلك هذه الدراسة تهدف الى معرفة تأثير السمنة وفرط البرولاكتين والسكري من النوع الاول من خلال دراسة بعض المعايير الكيموحيوية والهرمونية، اجريت الدراسة على 92 امرأة، تراوحت اعمارهن بين 20 الى 40 سنة، جمعت العينات من مستشفى الصدر التعليمي، مستشفى الطفل والولادة والمركز التخصصي لأمراض الغدد الصم والسكري في محافظة ميسان خلال الفترة من حزيران 2022 الى شباط 2023، قسمت النساء الى اربع مجاميع، مجموعة السيطرة ومجموعة مصابات بفرط البرولاكتين ومجموعة السمنة ومجموعة المصابات بالسكري النوع الأول، اظهرت النتائج ارتفاع معنوي ($P \leq 0.05$) في مستوى سكر الدم والسكر التراكمي عند النساء المصابات بالسكري من النوع الاول مقارنة مع مجاميع فرط البرولاكتين والسمنة والسيطرة، كما ازدادت قيمة 8 – ايزوبروستانز معنويا ($P \leq 0.05$) عند مجموعتي النساء المصابات بفرط البرولاكتين والسمنة مقارنة بمجموعتي السكري من النوع الاول والسيطرة، لم تختلف قيم هرموني محفز الجريبات واللوتيني معنويا بين المجاميع، بينما ازداد مستوى هرمون التستوستيرون معنويا ($P \leq 0.05$) في مجموعة السمنة مقارنة بباقي المجاميع، من النتائج اعلاه، يمكن الاستنتاج ان النساء البدينات لديهن اضطراب من خلال الارتفاع في قيم 8- ايزوبروستانز التستوستيرون.

الكلمات الدالة: سكر الدم، 8- ايزوبروستانز، الهرمونات، السمنة، فرط البرولاكتين.