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RESEARCH ARTICLE

The effect of obesity indices on fertility markers in overweight women

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ABSTRACT

Background: The precise relationship between obesity and fertility is unknown. It seems that infertility is specifically caused by hyperandrogenism-induced long-term anovulation. **Objective:** The current study aimed to examine many biochemical and reproductive hormone markers in obese women. **Subjects and Methods:** This study included 40 women who suffer from obesity; after drawing 7–10 milliliters of blood, serum was extracted, hormones and biochemical parameters such as cholesterol, triglycerides and gonadotropins were carried out on each female. **Results:** The obtained results showed that both triglycerides and cholesterol levels in patient women (123.46± 9.49; 186.35 ± 5.20 mg/dL), were respectively raised ($p < 0.05$) compared to healthy women (2.63 ± 0.36; 5.27±0.28 mg/dL), respectively. The vitamin D values did not differ significantly ($p < 0.05$) between the healthy (17.03± 1.91 pg/ml) and the unhealthy samples (15.26 ± 3.49 pg/ml). The results of FSH estimation in patients (6.51 ± 0.66 µIU/mL) decreased statistically ($p < 0.05$) in comparison with healthy women (16.96 ± 5.21 µIU/mL). Likewise, the results of LH determination in patients (4.06 ± 0.35 µIU/mL) decreased statistically ($p<0.05$) in comparison with healthy women (15.19 ± 5.66 µIU/mL). **Conclusion:** Our study's findings demonstrated that elevated levels of cholesterol and triglycerides in hyper-androgenized women who have delayed pregnancy and overweight negatively affect gonadotropins with probable infertility.

Keywords: female, infertility, gonadotropins, lipid profile and obesity

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INTRODUCTION

Obesity is a body mass index (BMI) of 30 kg/m2 or more as defined by the World Health Organization (WHO,1997). Lower fertility in women has been associated with obesity in the past, with a longer waiting period to conceive. Several studies have shown the detrimental impact of obesity and being overweight on a woman's ability to conceive. The high prevalence of obesity among infertile women and the established link between obesity and infertility point to the necessity of educational interventions based on the detrimental impacts of obesity and the advantages increase in pregnancy rates by weight loss among infertile subjects, comprising reproductive health (Dag *et al*., 2015; Best & Bhattacharya, 2015). Obesity and infertility have a complicated mode of action that involves hormonal variables, ovulation abnormalities, and menstrual cycle modifications (Mitchell & Fantasia, 2016). Studies are currently being conducted to determine how obesity affects the reproductive processes. Anovulatory cysts and obese women experience more menstrual problems.

Overweight or obese women tend to run a higher risk to their reproductive system. These women have higher rates of conception, miscarriage, and pregnancy problems, as well as an increased risk of subfecundity and infertility (Dag *et al*., 2015). Nevertheless, obesity may also result in a number of other conditions including psychological concerns, endocrine with hormonal disorders, and drug

use including antidepressants and steroids (Pratt & Brody, 2014). According to data from the WHO, 60% of women in the US and most of Europe are overweight (≥ 25 kg/m2), 30% are obese (≥ 30 kg/m2), and 6% (≥ 35 kg/m2) are severely obese (WHO, 1997; Haslam & James, 2005; Norman *et al*., 2004).

Numerous processes such as impeded growth of ovarian follicles, qualitative and quantitative development of oocytes, fertilization, development of embryos, and implantation are among the ways that obesity leads to infertility (Jungheim *et al*., 2013). According to Grodstein *et al*. (1994), patients with a BMI of more than 26.9 kg/m2 who were overweight or obese were more likely to experience ovulatory infertility. Obesity influences the hypothalamus – pituitary – gonadal (HPG) axis by raising circulating free estrogen levels as it increases the conversion of androgens to estrogens in adipose tissue, and this negative feedback loop results in a decrease in gonadotropins (FSH & LH). Hence, anovulatory or irregular cycles are brought on by the disrupted HPG axis (Grodstein *et al*., 1994).

The inability to conceive in women under 35 or after six months in women of 35 and older following a year of therapeutic donor insemination of this age and above is described as infertility (PCASRM, 2013). In poorer nations, infertility is one of the most prevalent diseases of the reproductive system. Even though many obese multiparous women can still become pregnant, the prevalence of infertility is higher in obese women. Anovulate infertility was demonstrated by Grodstein *et al*. (1994) to be more prevalent in overweight and obese patients whose BMI was found to be higher than 26.9 kg/m2. This is because fat tissue converts more androgens to estrogens by α-aromatase, obesity increases free estrogen levels, which affects the HPG axis, and the negative feedback from increased estrogen causes a reduction in gonadotropins. Consequently, irregular or anovulatory cycles are caused by the damaged HPG axis (Grodstein *et al*., 1994). Obesity can alter the endometrium and ovaries, which can disrupt reproductive functioning (Bellver *et al*., 2007). Hormonal and some substrate alterations cause the HPG axis to degrade. In obese women, there is a decrease in high-density lipoprotein (HDL) levels and a rise in triglycerides, insulin, androstenedione, estrone, luteinizing hormone (LH), and very low-density lipoprotein (LDL). These alterations lead to a breakdown in the HPG axis and various gynecological effects (Oyelowo & Johnson, 2017). Consequently, the present work aimed to investigate the relationship between lipid profile and levels of gonadotropins (FSH & LH) in obese women with hyper-androgenized infertility.

SUBJECTS AND METHODS

This study included 40 women, twenty of whom weighed more than 80 kg/each and did not have children over five years old, and the other twenty were healthy women weighing less than 70 kg/each and had children. Searching for conceiving, they visited Al-Sadr Teaching Hospital and some laboratories in the city of Maysan, Iraq. This study was carried out at the College of Science, Science Department Laboratories during the period from November 2022 to April 2023. All women served in this study were subjected to clinical investigation to exclude those who did not clinically have inclusion criteria. Blood samples were carefully collected using a medical syringe to pull out 7-10 milliliters of venous blood for every participant (patients and controls). After allowing the blood sample to clot for 20 minutes at room temperature in a gel tube, the serum was collected and centrifuged for 10 minutes at 300 rpm. Sera were aliquoted in Eppendorf plastic micro-tubes and frozen to the biochemical assays of CHO, TG, Vit.D., FSH, and LH using an ELISA and a Cobas c111 instrument.

Moral Aspects to Take into Account

The Institutional Committee on Health of Al-Sader Teaching Hospital and certain laboratories in Maysan Province granted permission to perform this study, and patient samples were collected under the supervision of qualified medical personnel.

Analytical statistics

The resulting data are shown as mean ± SD. Using the T-test methodology, a statistical analysis of the data was carried out to determine any significant differences by (SPSS) to show the important statistic and significant differences limited on P<0.05 of probability (Al-Rawi & Khalaf Allah, 2000).

RESULTS

In Table 1, the results of triglycerides in patients (123.46 ± 9.49) were significantly increased (p < 0.05) compared to the healthy women (2.63 ± 0.36). Similarly, the results of cholesterol in patients (186.35 ± 5.20) were increased considerably (p < 0.05) compared to the healthy women (5.27±0.28). Additionally, the measures of vitamin D did not differ significantly (p < 0.05) between patients (15.26 ± 3.49 pg/ml) and healthy (17.03± 1.91 pg/ml) women. Measurements of gonadotropins (FSH and LH) in the serum of both healthy and patient women are depicted in Figures (1 and 2). The results of FSH (Figure 1) inpatient women were statistically (p < 0.05) decreased (6.51 ± 0.66) compared to the healthy women (16.96 ± 5.21). Likewise, the results of LH (Figure 2) inpatient women were statistically (p < 0.05) decreased (4.06± 0.35) in comparison with healthy women (15.19 ± 5.66).

DISCUSSION

The findings of the present study are consistent with those of earlier few investigations that examined lipid concentrations, where we noticed an increase in the level of cholesterol and triglycerides in women who did not have a pregnancy. It was previously discovered that alterations in the lipid profile might have a negative impact on pregnancy outcomes by influencing lipoprotein metabolism (Lee *et al*., 2008). Increased free cholesterol and total fat levels in women were linked to lower fertility in a population-based prospective trial including 501 couples (Schisterman *et al*., 2014). When compared to female rats fed a cholesterol-free diet, Shalaby *et al*. (2004) reported that female rats, which were given a diet rich in cholesterol had a considerably lower reproductive rate.

Table 1. Serum concentrations of triglycerides, cholesterol and vitamin D in healthy and patient women

Parameters	Healthy (N=20)	Patients (N=20)
TG (mg/dl)	2.63 b ± 0.36	123.46^{a} ± 9.49
CHO (mg/dl)	5.27^{b} ± 0.28	186.35^{a} ± 5.20
Vit D (pg/ml)	17.03^{a} ± 1.91	15.26^{a} ± 3.49

Data are expressed as means + SD, N is the number of women in each group and SD is standard deviation, TG: Triglyceride, CHO: Cholesterol, Vit.D: Vitamin D. The groups with different symbols are significantly different at P<0.05.

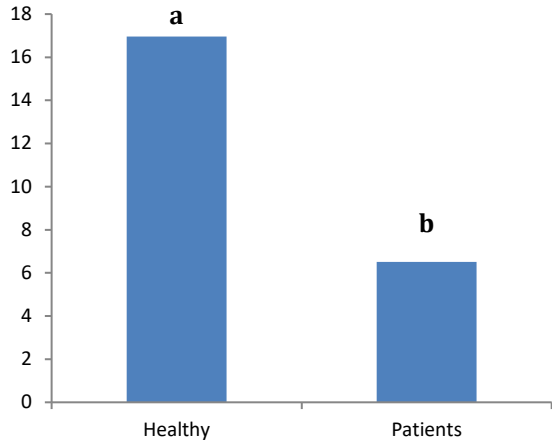

Figure 1. Concentrations of FSH in both healthy and ill women. The values show the mean ± standard deviation. Variations in lettering show that there are substantial differences (P<0.05) between the groups. Comparable letters stand for no discernible differences between the groups.

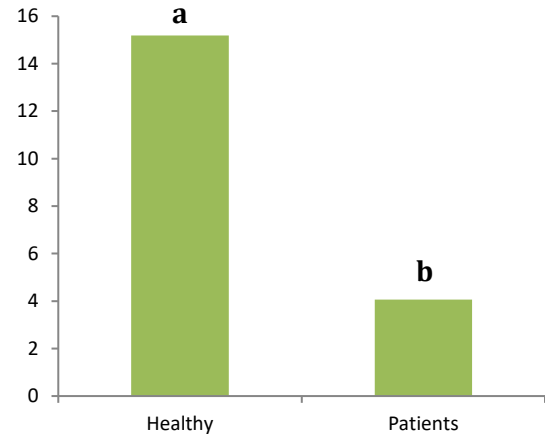

Figure 2. concentrations of LH in both healthy and ill women. The values show the mean ± standard deviation. Variations in lettering show that there are substantial differences (P<0.05) between the groups. Comparable letters stand for no discernible differences between the groups.

However, anti-cholesterol medication would significantly ameliorate this condition. It is thought that lipid abnormalities affect female reproduction. The granulosa cells in reproductive organs are the sites of steroid hormone production, and they use cholesterol as a substrate for steroidogenesis (Miller, 1988). Obesity in fertile women has been associated with fertility issues (Sharma *et al*., 2015); both are crucial in the transportation of cholesterol to ovarian tissue. Early embryo implantation and endometrial receptivity may be hampered by changed endometrial lipid levels (Li *et al*., 2019). The placenta also exhibits widespread lipid infiltration and acute atherosis, which are pathognomonic indicators of possible placental dysfunction (Brosens *et al*., 2020).

Research findings indicate that obesity increases the time that reduces the time needed to obtain a spontaneous pregnancy rate and lowers the likelihood of conception in obese women, including those who ovulate regularly (Gesink *et al*., 2007). Numerous studies revealed as compared to non-obese women that obese women have a threefold higher chance of infertility (Rich-Edwards *et al*., 1994). Additionally, their fertility appears to be compromised in cycles including both spontaneous and aided conception (Zaadstra *et al*., 1993). It has been shown that the chance of getting pregnant drops by 5% for each unit of BMI above 29 kg/m2 (Van Der Steeg *et al*.,2008). Many studies have shown the connection between obesity and lower conception rates as well as the changes to reproductive systems that obesity in early adulthood causes, these women had a higher chance of infertility and menstruation issues (Lake *et al*., 1997).

Our results showed that obese women have lower-than-normal serum FSH and LH that confirm, to a high extent, declining fertility trials. It's interesting to note that obesity does not prevent a woman from becoming subfertile. Additionally, reduced fecundity was observed in eumenorrheic obese women examined by Gesink Law *et al*. (2007) based on data from a sizable Dutch cohort of more than 3,000 women with regular periods and a big American cohort of more than 7,000 women was presented in a study by van der Steeg *et al*. (2008) these cohorts showed that for every BMI point above 29 kg/m2, the chance of spontaneous pregnancy fell linearly.

CONCLUSION

It can be concluded that present findings demonstrated that high levels of cholesterol and triglycerides in women who have delayed pregnancy and excess weight negatively affect female fertility as evidenced by a marked decrease in both FSH and LH.

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CONFLICT OF INTEREST

All authors of this work declared that there was no conflict of interest.

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