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REVEAL OF CERTAIN ADIPOKINES (ADIPONECTIN AND LEPTIN) AND PHYSIOLOGICAL PARAMETERS LEVELS IN WOMEN WITH INFERTILITY

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Abstract: Adipose tissue produces adipokines, and adipocytes have an impact on the reproductive organs through the production of adiponectin and leptin. Therefore, it is essential to evaluate adipokines and sex hormones in order to have a deeper understanding of infertility. Thus, the goal of the current study was to assess adipokines and biochemical markers in infertile patients. In this study, 65 women between the ages of 17 and 40 years old (mean: 27.8±4.08 years) were included. All were consecutively admitted to the clinic at AL-Kut Hospital for Gynecology Obstetrics and Pediatrics (infertility center) at February to May 2024. All women had infertility as diagnosed by the physician. also, this study including 40 healthy women as control group. The results showed that the concentrations of follicle stimulating hormone (7.42±0.13) and luteinising hormone (LH) (7.13±0.25) in serum of infertility women indicated a significant (P <0.05) rise in contrast to healthy women (5.037.42±0.29; 3.657.42±0.16). The levels of MDA (1.93±0.11) demonstrated significant (P <0.05) increase and GSH (0.371±0.027) decreased in infertility women compared with healthy women (1.22±0.09; 0.441±0.014). Adiponectin concentration in serum of infertility patients (4.55±0.19) indicated non-significant (P <0.05) variations in contrast to healthy women (4.61 ± 0.23). the concentration of leptin indicated a significant (P <0.05) rise in infertility women (14.83 ±1.92) in contrast to healthy women (5.48 ±0.41). It is concluded from the study that there was also an imbalance in the case of oxidative stress. On the other hand, it was noted that there is a correlation between leptin levels and infertility in women

Keywords: Adipokines; Infertility; Leptin; Adiponectin; oxidative status

Introduction

A complicated condition, infertility causes serious physical, psychological, and financial issues [1]. According to data from population-based studies, 10–15% of couples worldwide issue with infertility [2]. Primary infertility is characterized by an individual never having given birth, whereas secondary infertility is defined as having at least one pregnancy and not being able to become pregnant again [3]. Apart from the reasons mentioned above, infertility can also arise from a wide range of conditions such as hormone dysregulation, physical disorders, environmental factors, lifestyle decisions, genetic factors, and sexually transmitted diseases (STDs) [4-5]. White adipose tissue stores energy and serves a variety of purposes. It is a crucial endocrine organ that secretes adipokines, which control metabolism and energy homeostasis. Numerous physiological functions, including immunological response, glucose and lipid metabolism, and reproduction, are regulated by these

adipokines. Adipocytes are the primary source of adipokines, which are cytokines [6]. Leptin, adiponectin, resistin, visfatin, omentin, and ghrelin are a few of these adipokines. Adipokines are hormones that act as signaling molecules. When adipokine levels are incorrect, it can lead to inflammation and aberrant cell signaling, which can worsen cell metabolism and function [7]. The most prevalent adipokine, adiponectin, is mostly released by visceral fat cells [8]. Adiponectin is a 30 kDa protein with four domains and 247 amino acids. It contains anti-inflammatory, anti-atherogenic, and insulin-sensitizing properties. Adiponectin also affects the control of glucose and the oxidation of lipid acids, among other metabolic processes [9]. Research conducted both in vitro and in vivo has demonstrated the favorable effects of adiponectin on the reproductive processes, as well as its significant correlation with gonadotropins and other hormones [10]. In white adipose tissues, adipocyte cells release leptin, which is changed in obesity [11]. Furthermore, it can be generated by various reproductive system-related cells in both males and females, including pituitary, hypothalamic, and placental syncytiotrophoblast cells [12]. Research indicates that the female hypothalamic-pituitary-ovarian (HPO) axis has leptin receptors. Consequently, leptin directly regulates every aspect of the HPO axis, as well as every stage of the reproductive process, including puberty, the menstrual cycle, pregnancy, early embryo development, and lactation, in an inhibitory or stimulatory manner depending on its concentration [13–14]. Thus, the goal of the current study was to assess adipokines and biochemical markers in infertile patients.

Methods

Study population

From February to May 2024, this investigation was carried out in the AL-Kut Hospital for Gynecology Obstetrics and Pediatrics (infertility center). 65 infertility women (with polycystic ovary syndrome) between the age range (17-40) years (mean± SD) (27.8±4.08) years provided blood serum samples for the study. Two groups were established from these samples, which are as follows: Control group: During the follicular phase of the menstrual cycle, 40 blood samples from healthy women were taken. Patient group: During the follicular phase, 65 PCOS women had their blood samples taken.

Inclusion criteria

Married women with PCOS who are between the ages of range (17-40) who do not have malignancies in their reproductive systems, urinary tracts, adrenal glands, or pituitaries.

Exclusion criteria

Unmarried women who suffer from other types of infertility causes or who suffer from congenital infertility were not included.

Measurements

- Human Luteinizing Hormone (LH): LH ELISA Kit (SUNLONG, China) used to determining the LH concentration in human serum and plasma using Sandwich-ELISA.
- Follicle-stimulating hormone (FSH): FAH ELISA Kit (SUNLONG, China) used to determining the FAH concentration in plasma using Sandwich-ELISA.
- Reduced Glutathione (GSH) ELISA kit: This ELISA kit uses Sandwich-ELISA as the method (SUNLONG, China, No.: SL0778Hu), and used to determining the GSH levels in plasma.
- Human Malondialdehyde (MDA) ELISA kit: This ELISA kit uses Sandwich-ELISA as the method (SUNLONG, China, No.: SL1135Hu), and to assays MDA levels plasma.

- Adiponectin: ELISA kits from USA Biological Company (My biosource, USA) were used for determining adiponectin.
- Leptin: measuring serum leptin levels with the Leptin (sandwich) Enzyme Immunoassay Kit. This assay is only meant to be used for in vitro diagnosis. This solid phase enzyme-linked immunosorbent assay is based on the sandwich principle (ELISA).

Statistical analysis

The data was coded and input into a computer for statistical analysis using version 18 of the SPSS program (Statistical Package for Social Science). Each data point was arranged according to its frequency, and correlations between variables were examined using the Chi-square test. One considered a p-value of less than 0.05 to be significant [15].

Results and Discussion

Socio-demographic features

Table 1 presented some sociodemographic variables. The largest age group of patients was <20-25 years old, accounting about 41.5% of the total. The Body Mass Index (BMI) of the patients was between 25 and more than 29.9 kg, with a 64.6%. Urban areas made up 67.7% of the patients' residential locations. Patients' smoking status was 53.8% non-smoking.

Table (1): socio-demographic variables of studied groups

Characteristics	Classes	Groups	
		Healthy women	Infertility women
Age	>20-25 years	13 (32.5%)	27(41.5%)
	26-30 years	9(22.5%)	17 (26.2%)
	31-35 years	11 (27.5%)	13 (20.0%)
	36-50 years	7 (17.5%)	8 (12.3%)
	Total	40	65
Body Mass Index (BMI)	< 18.5	15 (37.5%)	4 (6.2%)
	18.5-24.9	19 (47.5%)	19 (29.2%)
	25->29.9	6 (15.0%)	42 (64.6%)
	Total	40	65
Residential Area	Urban	28 (70%)	41 (67.7%)
	Rural	12 (30%)	24 (32.3%)
	Total	40	65
Smoking Status	Yes	2 (5.0%)	9 (13.9%)
	Non	21 (52.5%)	35(53.8%)

	Passive	17 (42.5%)	21 (32.3%)
	Total	40	65

LH and FSH

Table (2) show the concentrations of LH and FSH in infertility women and healthy subjects, where LH concentration in serum of infertility women (7.13±0.25) indicate a (P <0.05) increase compared with healthy women (3.657±0.16), figure (1). The concentration of FSH indicate a significant (P <0.05) reduced in infertility women (7.42±0.13) compared with healthy women (5.037±0.29), figure (2).

Table (1): LH and FSH concentrations in studied groups

Groups / Parameter	Healthy female (no.=40)	infertility female (no.=65)	P-Value
LH (IU/ml)	3.657±0.16	7.13±0.25*	0.001
FSH (IU/ml)	5.037±0.29	7.42±0.13*	0.001

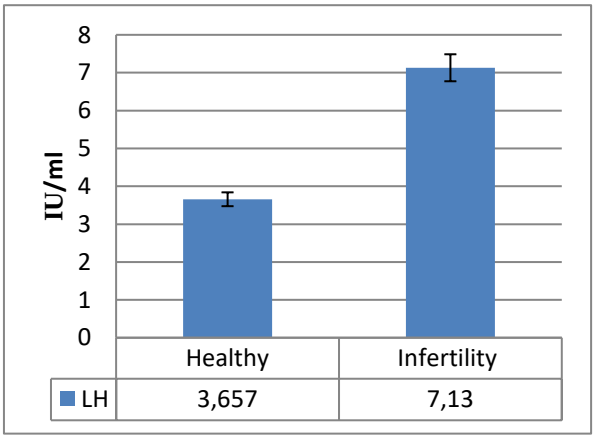

Figure (1): LH concentration in patients and control.

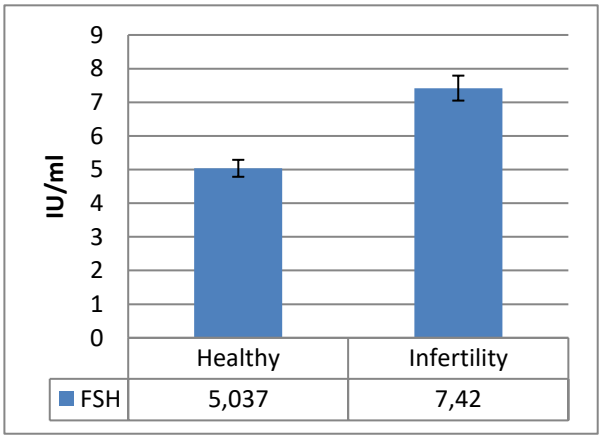

Figure (2): FSH concentration in patients and control.

In obese PCOS patients, we observed a considerable increase in FSH and LH levels. Additionally, there is a weak direct correlation between BMI and levels of LH and a weak inverse correlation between BMI and FSH. According to a study, patients with PCOS had an increased LH/FSH ratio, which was not correlated with age or BMI [16]. Esmaeilzadeh et al.'s study revealed that in women with PCOS, a certain age (≥35 years), a BMI (≥25 kg/m2), and acne were important indications of metabolic problems, including obesity [17]. Research supports the link between LH, weight, and PCOS. For example, Insler et al. found that blood serum levels were significantly higher in PCOS-affected women with normal body weight than in patients with obesity, and Yanira et al. found an inverse relationship between LH and BMI in PCOS-affected women [18–19]. Our findings contradicts a study by Alnakash and Al-Tae'e [20] that found an inverse connection between FSH and BMI in obese women with PCOS. Serum LH levels and the LH/FSH ratio are raised in PCOS due to the abnormal gonadotropin secretion [21]. Our findings concur with those of Ye et al.'s study [22], which reported that the LH mean was (3.8) with no significant outcome. Furthermore, a study conducted by Liu et al. [23] showed that the LH mean was (3.2) and that the result was not significant (P=0.20). In relation to the PCOS group, the mean was larger than the male factor. This is in line with

other research, including one by Lisi et al. [24], which discovered that elevated levels of LH are connected to ovulatory failure and endocrinological disorders. Furthermore, the Jain et al. study [25] found that the mean LH in PCO was (6.95). However, the current study deviates from the research done by Rawdhah et al. [26], who found that there was no significant difference (P=0.429) between PCOS patients and the control group.

Oxidative status

Table (3) indicate the MDA and GSH levels in infertility and healthy women. The levels of MDA (1.93±0.11) indicate a significant (P<0.05) rise and GSH (0.371±0.027) reduced in infertility patients compared with healthy women (1.22±0.09; 0.441±0.014), figures (3 and 4).

Table (1): oxidative status in studied groups

Parameter \ Groups	Healthy female (no.=40)	infertility female (no.=65)	P-Value
MDA (nmol/ml)	1.22±0.09	1.93±0.11*	0.001
GSH (nmol/ml)	0.441±0.014	0.371±0.027*	0.001

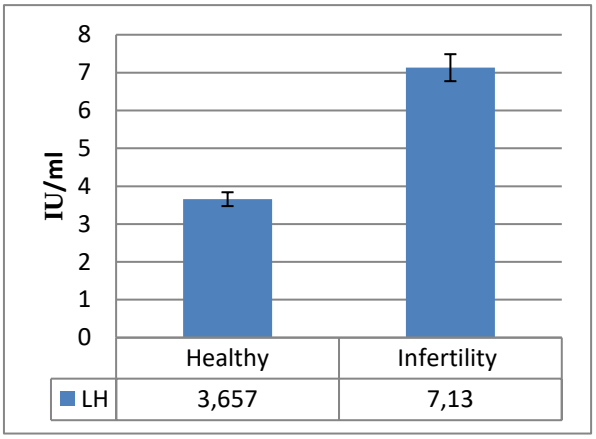

Figure (3): MDA levels in patients and control.

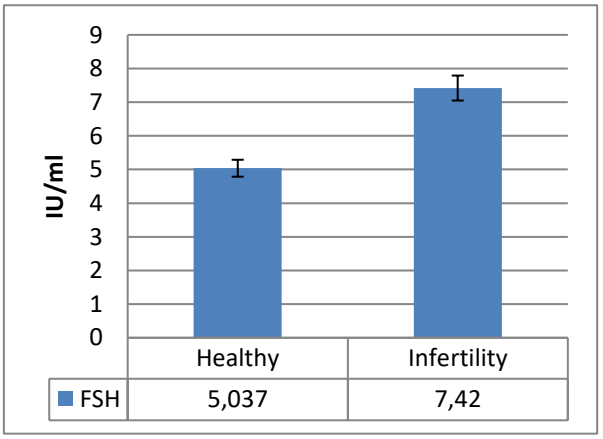

Figure (4): GSH levels in patients and control.

The mechanism of lipid peroxidation of unsaturated fatty acids was found to be significantly increased in a variety of cells, including egg cells. This increase was caused by an increase in the different active forms of nitrogen and oxygen, and it is evident from this increase that a state of oxidative stress was present in the first-type sterile females. MDA is one of the markers of oxidation that occurs within the body as a result of lipid peroxidation of fatty acids [27–28]. Furthermore, sterile women with higher body mass index values showed a statistically significant rise in malondialdehyde (MDA). Fat people (especially those who are morbidly obese) may be the cause of their sleepiness and stress, which increases their need for oxygen to carry out different metabolic functions and create energy, especially through adipose tissue. Researchers have confirmed that there is a high likelihood of lipid peroxidation in obese individuals, particularly when pro-oxidants—which are formed during any muscular stress the body experiences—are available. Additionally, a decrease in various antioxidants can lead to an increase in oxidation, which in turn can increase the concentration of the resulting malondialdehyde. from the various cell sites' fat oxidation process [29]. In line with the findings of the researchers, Table (3) also demonstrated a statistically significant drop in glutathione

levels in infertile women as compared to the control group [30–31].

Adipokines

Table (3) indicate the concentrations of adiponectin and leptin in infertility women and healthy subjects. Adiponectin concentration in serum of infertility patients (4.55±0.19) indicate non-significant (P <0.05) changes in compared with healthy women (4.61 ± 0.23). the concentration of leptin indicates a significant (P <0.05) elevated in infertility patients (14.83 ±1.92) compared with healthy women (5.48 ±0.41).

Table (4): Adiponectin and Leptin in studied groups

Parameter \ Groups	Control (30)	Women with PCOS (50)	P-Value
Adiponectin (µg/ml)	4.61 ± 0.23	4.55±0.19	0.194
Leptin (ng/ml)	5.48 ±0.41	14.83 ±1.92*	0.001

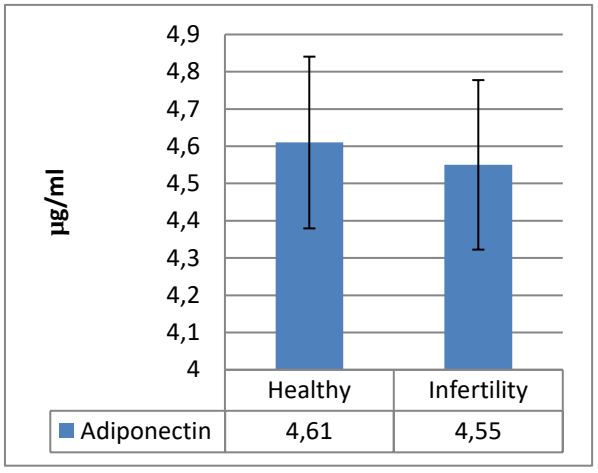

Figure (5): Adiponectin in patients and control.

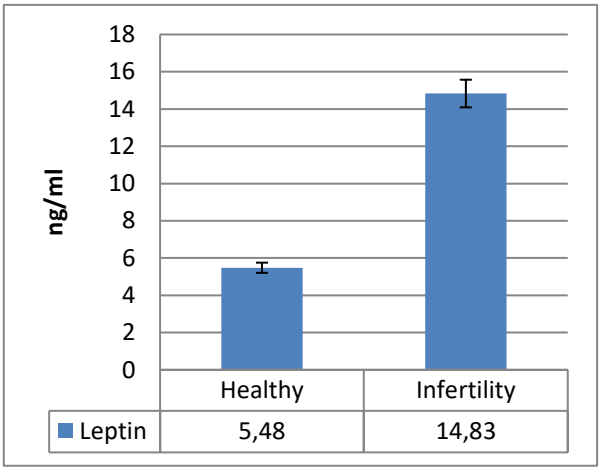

Figure (6): leptin in patients and control.

Specific leptin receptors, which are present in numerous organs, especially the female hypothalamus-pituitary-ovarian axis, are bound and activated by leptin to exhibit biological functions. By inducing the release of gonadotrophins, aromatase enzymes, and gonadotrophin-releasing hormone from the hypothalamus, pituitary gland, and ovaries, respectively, leptin contributes to the activity of the hypothalamus-pituitary axis [32–33]. According to a study by Demir et al. [34], women with infertility that cannot be explained had mean serum leptin levels that were considerably greater than those of patients who were fertile. When normal weight patients were included, the unexplained infertile group's mean serum leptin levels (7.2 (range, 4.3-10.4) versus 3.5 (range, 1.9-6.2) ng/ml) were considerably higher than those of the fertile group. Cyclooxygenase-2, prostaglandin E2, and vascular endothelial growth factor are among the proteins linked to the ovulation process that are induced to express by adiponectin. Steroidogenesis and ovarian gene expression are stimulated by adiponectin in order to preserve ovaries. Additionally, our research revealed no discernible differences between adiponectin cases and controls. Obesity exhibits decreased levels and is a significant factor in the pathophysiology of PCOS [35].

Conclusion

Based on current findings, it is concluded from the study that there was also an imbalance in

the case of oxidative stress. On the other hand, it was noted that there is a correlation between leptin levels and infertility in women

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