European Science Methodical Journal
ISSN (E): 2938-3641
Volume 2, Issue 1, January, 2024

Studying the Effect of Sex Hormones and Their Relationship with Thyroid Hormones in Some Women Suffering from Secondary Infertility and Obesity in Baghdad Governorate

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Abstract:
The current study was conducted on 80 women aged between 25-40 years who attended outpatient clinics in Baghdad Governorate for the period from (October to the end of November) of the year 2023 after recording their information, and the samples were divided into two groups:
• Patients group: It included (40) blood samples from women suffering from secondary infertility and obesity.
• Healthy group: It included (40) blood samples from healthy women (as a control group).
After that, blood was collected from a group of patients and healthy people and was separated by a centrifuge. Then the biochemical variables were measured, which included (FSH, LH, Testo, TSH, T3, T4, Insulin, and glucose). The results of the current research showed a significant increase in each of the levels (LH, Testo, TSH, Insulin, and glucose) in the blood serum of patients with secondary infertility and obesity compared to the control group, with a significant decrease in the level of (FSH, T4) with no differences. Significant at the level (T3) in both groups and at the level of probability $P \leq 0.05$.

Keywords: Secondary Infertility, Obesity, Insulin, Sex hormones, Thyroid hormones.

Introduction

Infertility is one of the complex diseases that affect the reproductive system, which is defined as the failure to become pregnant despite regular, unprotected intercourse. Infertility has a psychological and social impact on women and men [(1)]. It is also known as a disorder that occurs in women due to many causes that may be known or unknown [(2)].
Secondary infertility is considered one of the types of infertility, which is defined as the failure to obtain pregnancy after a previous pregnancy has been completed within a period of childbearing. Therefore, women whose pregnancy leads to the birth of a stillborn fetus or who are subjected to repeated spontaneous miscarriages and do not obtain pregnancy despite having frequent and inappropriate sexual intercourse. Protected women suffer from secondary

infertility, and almost in general (10-15%) of couples suffer from infertility, which affects more than 80 million people around the world, and then secondary infertility outnumbers primary infertility [3,4].

The excess weight found in most obese women greatly affects reproductive function, and the hormonal changes that occur in most obese women are not sterile. However, excess weight and its negative impact on fertility are well documented, as excess weight harms fertility. Through its role in controlling the ovulation process, egg development, fetal growth, and improving the uterine lining, as well as influencing the progress and quality of fertilization, overweight women are more than twice as likely to suffer from infertility than women of normal weight [5].

Obesity and insulin resistance are linked for women with PCOS, as it must be noted that the fat that causes obesity is visceral fat and not subcutaneous fat, meaning that obesity is concentrated in the abdominal area and not the entire body [6].

Insulin resistance is a disease condition in which insulin-dependent cells, such as skeletal muscle and adipocytes, do not respond properly to normal levels of insulin. It is often described as the main cause of type 2 diabetes. Among the causes of insulin resistance are high levels of plasma fats due to excessive food intake and stress. Obesity-induced endoplasmic reticulum affects insulin formation, as it tends to disrupt the formation or distortion of insulin receptors, leading to weak insulin signaling [7].

Insulin resistance is exacerbated by obesity, as females with PCOS are more susceptible to insulin resistance, which may lead to abnormal catabolism of glucose and fats. Moreover, increased insulin reduces the circulating amount of globulin linked to sex hormones and enhances free androgens that restrict folliculogenesis, leading to insufficiency Irregular menstruation and impotence [8]. This condition constitutes more than 50% of women with anovulation, as it is more apparent in women with chronic anovulation than in women with normal ovulation, despite the fact that insulin resistance occurs in almost all women with polycystic ovary syndrome [9].

Secondary infertility related to obesity has several drug treatments, such as (metformin pills, Clomiphene citrate pills, or hormone-regulating needles), and there are some cases that require surgical intervention such as cyst removal or cauterization [10,11].

A well-functioning thyroid is crucial during pregnancy, and undergoes physiological changes to maintain fetal growth. There is a noticeable increase in the size of the thyroid gland during pregnancy, by 10% in women who have good iodine intake and by 20-40% in those who suffer from iodine deficiency. Thyroid function also changes through an increase in thyroxine binding globulin (TBG). Due to the level of estradiol, or through the stimulating effects of human chorionic gonadotropin (hCG), with a reflection on the hypothalamic-pituitary-thyroid axis [12].

The thyroid gland is closely linked to a woman's fertility, as pregnancy has a major impact on the thyroid gland, and disorders in the thyroid gland have been linked to infertility in most women who suffer from obesity, with good birth and fetal outcomes proven [13,14].

Thyroid hormones regulate hormone receptors and endometrial receptivity, a phase in which all actors, including thyroid hormones, cooperate to prepare and allow the blastocyst implantation window, with constant changes throughout the menstrual cycle [15,16]. Changes in thyroid hormones can also have harmful effects on the placenta, and may cause miscarriage. However, the molecular mechanisms involved are not yet fully understood [17]. Through the increase in thyroid hormones and sex hormones, the current research aims to study the effect of sex hormones and their relationship with thyroid hormones in some women suffering from secondary infertility and obesity in Baghdad Governorate.

Collection of Specimens

The current study was conducted on 80 women aged between (25-40) years who visited outpatient clinics in Baghdad Governorate for the period from (October to the end of November) of the year 2023 after recording their information, and the samples were divided into two groups:

• Patients group: It included (40) blood samples from women suffering from secondary infertility and obesity.

• Healthy group: It included (40) blood samples from healthy women (as a control group).

After that, blood was collected from a group of patients and healthy people and was separated by a centrifuge. Then the biochemical variables were measured, which included (Sex hormones, Thyroid hormones, Insulin, and Glucose).

Estimating the levels of Sexual and Thyroid hormones for both groups of patients and healthy people:

Concentrations of sex and thyroid hormones were measured by following the steps indicated in the Minividas hormone testing device using a specialized measuring kit that varies from one device to another and according to its manufacturer. The Minividas hormone assay is an automated screening system based on the principles of enzyme-linked fluorescence (ELISA) assays [18].

Estimating the Insulin level for both groups of patients and healthy people:

The level of insulin in blood serum was estimated using a measuring kit for the hormone insulin and the ELISA test method, according to the manufacturer, Monobind Inc, USA.

Estimating the glucose level for both groups of patients and healthy people:

The concentration of glucose in the blood serum for all samples was estimated using the enzymatic calorimetric method, using a ready-made kit manufactured by the Italian company AMS [19].

Statistical Analysis

The SPSS statistical program was used to find the mean and the value of the standard deviation (SD±), and the averages were also determined for the group of patients with secondary

European Science Methodical Journal
ISSN (E): 2938-3641
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infertility and obesity compared to the control group (healthy people) using the T-test and at the probability level ($P \leq 0.05$).

Results:

• Measuring the levels of biochemical variables for the samples studied in both groups:

The table below shows the mean ± standard deviation of the biochemical variables for the samples studied in both groups

Groups / Parameter	Mean ± SD		P-Value
	Control n=40	Patients n=40	
LH (µIU/ml)	8.76±1.72	30.01±1.12	P ≤ 0.05
FSH (µIU/ml)	18.067±2.64	6.96±0.29	P ≤ 0.05
Testo (µIU/ml)	0.76±0.09	7.79±0.84	P ≤ 0.05
TSH (µIU/ml)	1.72±0.13	23.37±3.28	P ≤ 0.05
T4 (µg/dl)	9.03±0.73	3.91±0.45	P ≤ 0.05
T3 (pg/ml)	1.26±0.07	1.37±0.38	P ≤ 0.05
Insulin (µU/L)	21.54±2.85	42.79±3.07	P ≤ 0.05
Glucose (mg/ml)	106.81±122.61	165.11±14.81	P ≤ 0.05

The results of the current research showed a significant increase in each of the levels (LH, Testo, TSH, Insulin, and Glucose) in the blood serum of patients with secondary infertility and obesity compared to the control group, with a significant decrease in the level of (FSH, T4) with no differences. Significant at the level (T3) in both groups and at its level, probability $P \leq 0.05$. As shown in the figures below:

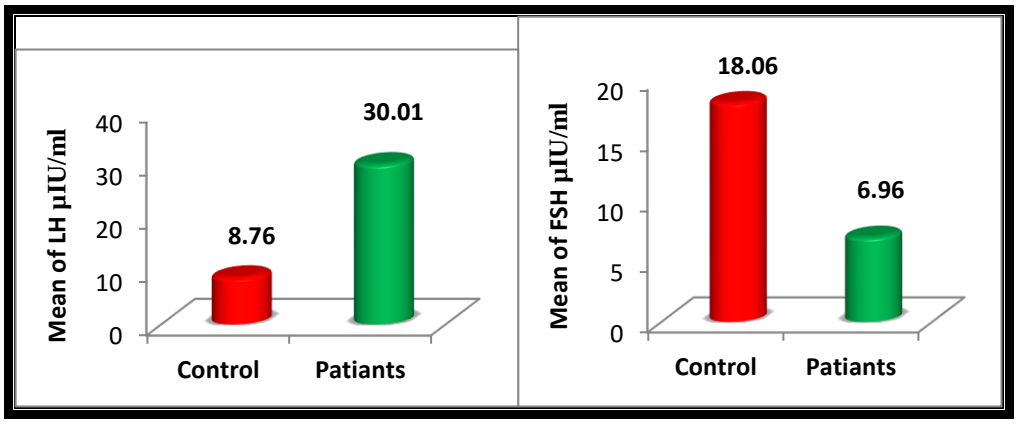

Figure (1): FSH level in the two studied groups

Figure (2): LH level in the two studied groups

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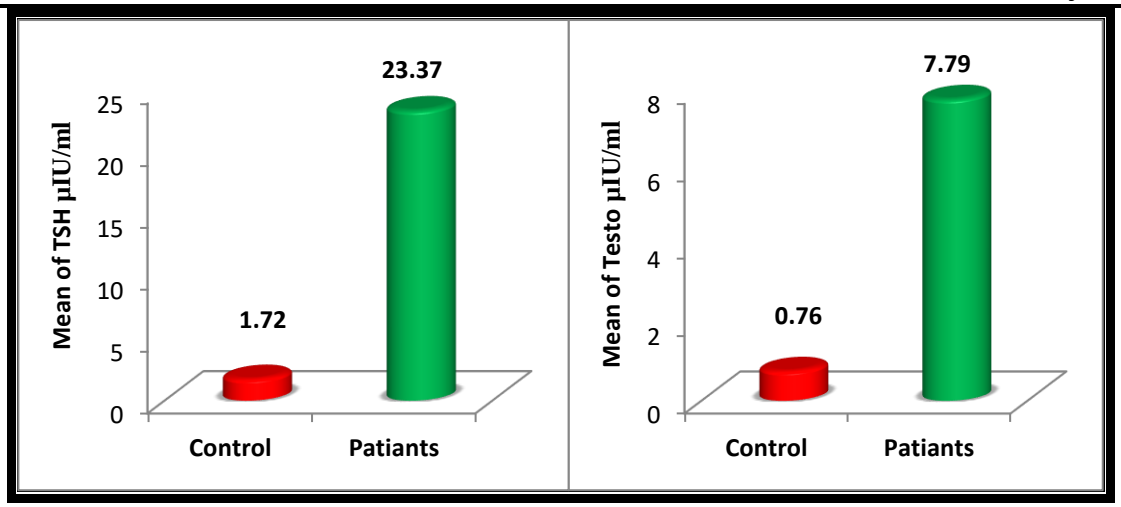

Figure (3): Testo level in the two studied groups

Figure (4): TSH level in the two studied groups

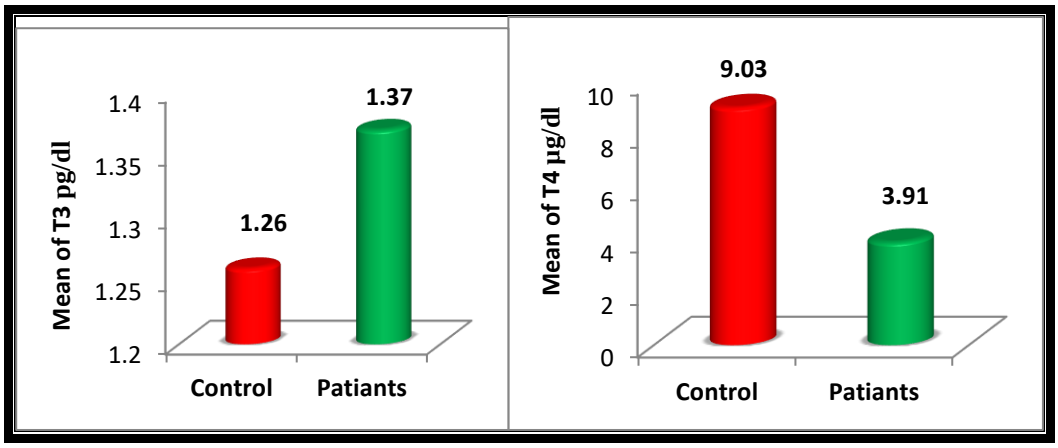

Figure (5): T4 level in the two studied groups

Figure (6): T3 level in the two studied groups

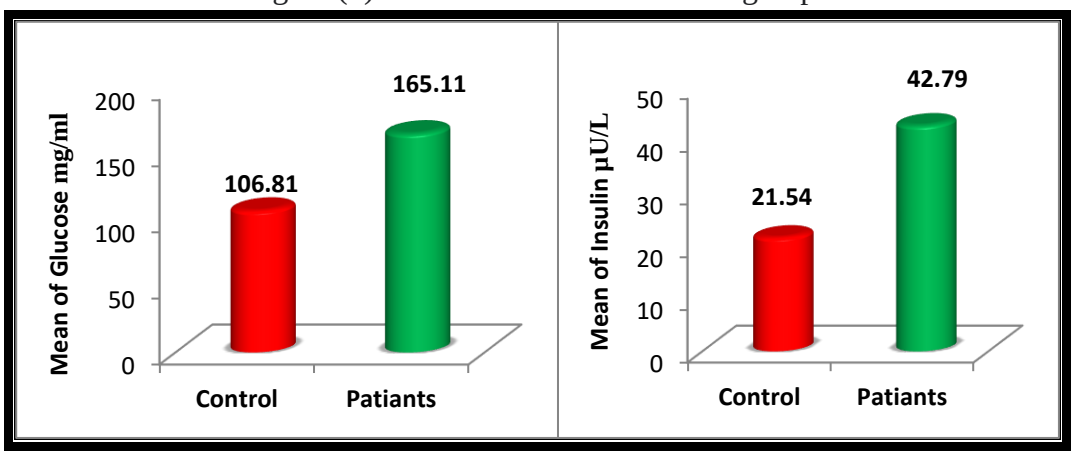

Figure (7): Insulin level in the two studied groups

Figure (8): Glucose level in the two studied groups

Discussion:

Childlessness has a significant impact on millions of people during marriage around the world, as hormonal changes in males and females contribute to this condition in a similar way (20-30%), and the endocrine system plays an important role in this condition, among other factors. Diseases of these endocrine glands include thyroid disorders, which lead to infertility in women, with evidence of infertility in men, as continuous treatment for such cases is immediate and likely to improve the chances of success and the occurrence of pregnancies [20].

The results of the current study agree with the results of S. Alhassa and his group [21] and (E. Khashchen) and his group [22], who in their study showed a significant increase in the levels of both LH and Testo in patients with secondary infertility and obesity compared to the control group (healthy women). The reason for the increase in sex hormones is due to menstrual disorders in women suffering from infertility and obesity, in addition to the effect of the hormone prolactin, which directly affects the FSH hormone and thus its effect on the formation of the egg in the early stages of its release, which causes an imbalance in the ovulation process or ovulation [23]. The reason for the high level of luteinizing hormone in the group of patients suffering from secondary infertility and obesity may also be due to the increased sensitivity of the pituitary gland to the gonadotropin-releasing hormone luteinizing hormone, and this leads to an increase in the concentration of GnRH or to changes in its secretion patterns [24].

In addition to the increase in the level of the hormone estradiol. And a decrease in the level of the hormone (FSH) [25]. The reason for the decrease is due to the production of adrenaline from the adrenal gland, which has a direct effect on the concentration of the hormone (FSH) through the secretion of androgens [26]. Increased levels of testosterone indicate androgen excess, and abnormal ovarian or adrenal gland function leads to increased formation of androgens [27].It is worth noting that any difference in the percentage of testosterone, that is, if the percentage of its free fraction increases, this leads to many disorders, the most important of which are irregular menstruation and the appearance of excess hair. Likewise, increasing its concentration in the blood leads to a decrease in the secretion of the LH hormone from the pituitary gland [28].

Thyroid hormones are of great importance to the reproductive process and play a pivotal role in multiple aspects of female reproductive function, starting from the beginning of embryo implantation and follicle formation until the placenta [29]. Given that thyroid function is complexly and regulated through the hypothalamic-pituitary axis, disturbances in thyroid function can have significant effects on reproductive processes [30].

The results of our study agree with the results of both (A AL-Azzawy) and his group [31] and (Frayyeh) and his group [32], who in their study showed an increase in the levels of thyroid hormones in patients with secondary infertility compared to the control group (healthy people). The reason for this is an increase in the TSH hormone, which indirectly affects FSH receptors, as an abnormal TSH level is linked to a decrease in the clinical pregnancy rate, and a high level of TSH is the most sensitive indicator for evaluating thyroid function, as TSH receptors are expressed on a wide range of levels. It is widespread in egg cells and the granulosa cells of the

ovary. TSH can also enhance the LH receptors on the surface of the granulosa cells, as there is a close relationship between the granulosa cells in the follicles and the eggs [33].

Thyroid hormones are essential for the proper functioning of the female reproductive system because they act directly on the tissues of the ovary, uterus, and placenta via nuclear receptors. Therefore, increased thyroid secretion leads to poor fertility or infertility [34]. Maternal thyroid hormones such as free thyroxine (FT4) are involved in metabolic exchange mechanisms in preimplantation embryos [35].

. Thyroid-stimulating hormone (TSH) may also affect reproductive outcomes directly, since TSH receptors are found in granulosa cells and in the ovarian stroma, as well as in the human endometrium, especially during folliculogenesis [36].

In addition, the hormones insulin and glucose showed a significant increase in the group of women suffering from secondary infertility and obesity compared to the control group. The results of our current study agree with the results of (C.L.Mulder) and his group [37]. Increased insulin secretion negatively affects the formation of ovarian follicles and ovulation, in addition to Insulin resistance, which is considered the main factor causing the link between obesity and fertility-related disorders, is directly responsible for increasing the rates of androgen production from the ovaries by inhibiting the liver's synthesis of sex hormone-related globulin and insulin-like growth factor-binding protein. Androgen excess, in turn, represents one of the main factors that It leads to changes in ovarian physiology, ovulatory disorders, and infertility [38,39].

High blood sugar levels also reduce antioxidants and increase lipid peroxidation, which in turn leads to polycystic ovary syndrome, which is characterized by anovulation, which ultimately leads to infertility [40]. Also, increased glucose secretion in the serum of infertile patients indicates a defect in the secretion of the hormone insulin, and this is an indication of the presence of insulin resistance, which is directly related to a high level of glucose in the blood. It was also found that a defect in insulin action in women suffering from secondary infertility has a limited effect on the process Metabolism of glucose in the blood [41].

Conclusions:

It was concluded from the current research:

1- There was a significant increase in each of the levels (LH, Testo, TSH, insulin, and glucose) in the blood serums of patients suffering from secondary infertility and obesity compared to the control group, at the level of probability $P \leq 0.05$.

2- There was a significant decrease in the level of (FSH and T4) in the blood serum of patients suffering from secondary infertility and obesity compared to the control group, at its level, probability $P \leq 0.05$.

3- There are no significant differences in the level of (T3) in both groups when its level has a probability of $P \leq 0.05$.

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