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Betalipotropin, subfatin and number of hormonal and biochemical variables in infertile women

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ABSTRACT
Background: Many modern and different hormonal tests are often performed for infertility patients because of its importance and wide spread in society.
Methods: This study was conducted in the Medical City Hospital and some outpatient clinics in the city of Baghdad for the period from 10/23/2023 to 12/23/2023, and data were collected on gender, age, body mass index (BMI) and family history of the disease in 90 sample and the hormones were measured, subfatin, β-Lipotropin, FSH, LH and GNRH and Statistical analyzes, were measured via ELISA kit then were performed using analysis of variance (T-test).
Results: The results of the study showed a significant increase at the level ($P \leq 0.05$) in the concentrations of hormones, subfatin, β-Lipotropin, FSH and LH in sterile women compared to the group of healthy women. GNRH hormone showed a significant decrease in sterile women compared to the group of healthy women.
Conclusion: This study confirms that the subfatin hormone has a clear effect on infertility through its close association with obesity, which is a major cause of infertility. This study also proved the association of β-Lipotropin with psychological infertility through its direct effect on mood and behavior, which in turn causes amenorrhea and other major causes of infertility.
Keywords: Infertile women, β-Lipotropin, Subfatin.

Introduction

Infertility or sub-fertility is the failure to conceive after one year of regular sexual intercourse without the use of contraception [1]. Approximately one-third of couples' infertility cases are primarily attributed to the woman, one-third to the man, and one-third to interaction Between of theme, 20% of cases are unexplained infertility [2],and approximately 15% of couples are infertile [3]. Infertility may be primary or secondary, primary infertility referring to the infertility of a couple who were never able to conceive, while secondary infertility is the failure to conceive after a previous pregnancy in the absence of contraception, breastfeeding, or postpartum amenorrhea Primary infertility is more common than secondary infertility [4].

Female infertility may occur due to Polycystic ovary syndrome, Hormonal disorders, Premature ovarian failure, Genital infections, Endometriosis, Fallopian tube obstruction, Congenital uterine abnormalities, Uterine adhesion, or Immunological causes, Prolonged use of oral contraceptives Which in turn may lead to a disruption of the balance of the microbiota in the vagina, causing cervical injuries, Socio-cultural factors, or other medical complications [5-8]. The psychological causes of infertility are of great importance, as it was found that the psychological factors that affect the woman and lead to the failure of sexual intercourse or affect the hormonal balance and the contractions and relaxations of the uterine muscles, tubes, etc., and thus the inability to produce the egg [9]. Infertility may be caused by the woman, the man, or both, or is unexplained [10,11], and that 30-40% of infertility cases are unexplained, and unexplained infertility usually refers to couples who were unable to conceive despite all tests such as ovulation and ductal obstruction fallopian tubes tests and their semen analysis are normal [12].

Subfatin, also called Meteorin or METRNL, represents the newly discovered adipokine [13]. It is secreted by adipose tissue, brain, and skeletal muscle and has insulin-sensitizing and anti-inflammatory activity [14]. Beta-lipotropine is a single-chain peptide secreted by the pituitary gland and was first isolated from bovine pituitary glands [15]. It has many physiological functions including stimulating lipolysis and melanogenesis. It also acts as an essential precursor hormone for Beta-Melanotroin and Beta- Endorphin hormone [16]. Gonadotropin releasing hormone (GNRH) is secreted from the hypothalamus, and has an effect on the secretion and manufacture of reproductive hormones secreted by the ovaries and testicles [17]. GNRH stimulates the secretion of the hormones LH and FSH from the anterior lobe of the pituitary gland [18].

Luteinizing hormone (LH) is secreted by the pituitary gland in response to GNRH. It is present in both sexes and contributes to the maturation of primary germ cells, stimulates estrogen secretion from the ovaries [19], and helps regulate the menstrual cycle in females by playing roles in both ovulation and implantation of the egg in the uterus [20], Follicle stimulating hormone (FSH) is secreted response to GNRH, and plays a role in sexual development and reproduction [21].

Sample

The samples was collected from the infertility outpatient clinics in Baghdad city. The total members of infertile women was 60 as a study group and 30 healthy fertile women were consider as control group.

Blood collection

Blood samples were obtained from a vein of 5 ml from each woman, using a Disposable Syringe, and placing the blood in plastic tubes free of anticoagulant until conducting hormonal tests, and separating the blood after coagulation using a centrifuge at a speed of 4000 cycles/min for 10 minutes, then the clear blood serum was withdrawn by means of a micropipette. Each form was numbered, and the patient's name and the date of drawing the sample were written for each patient. Then the serum was stored in Eppendorf tubes at a temperature of -20 °C until the required examinations are performed.

Hormonal analysis

The concentrations of hormones include β-Lipotropin, Subfatin, Lutenizing hormone, Follicular Stimulating Hormone, LH/FSH ratio and Gonadotropin releasing hormone were measured via enzyme linked immune sorbent assay (ELISA) by using the commercial kits (ELISA kit, Human, MyBiosourse, USA) and procedures was followed as given in the kits catalogs.

Statistical analysis

All values expressed as mean± S.D data analyzed done by using analysis of variance (T-test).

Result

The results shows significant increase β-Lipotropin, Subfatin, Lutenizing hormone, Follicular stimulating hormone, LH/FSH ratio levels and significant decrease in Gonadotropin releasing hormone levels in infertile women group compare with control group.

Table 1. Mean serum values of variables in patients compared to controls.

Group	Subfatin	β-Lipotropin	Lutenizing hormone	Follicular Stimulating hormone	Gonadotropin releasing hormone
Control	**2.25±0.40**	**75.14±14.13**	**11.03±1.92**	**7.09±1.84**	**343.12±43.04**
Patient	**3.98±0.78**	**114.93±18.75**	**23.46±5.05**	**11.87±2.74**	**120.35±43.91**

Discussion

The increase in the level came as a result of the serum subfatin level being significantly linked to the lipid profile, glucose profile, and insulin resistance, as there was a correlation between subfatin and BMI. It has been proven that subfatin levels have increased in individuals suffering from obesity and are closely related to body mass index [14,22], also reported a higher level of subfatin in fat cells in obese children compared to lean children. Therefore, obesity contributes to an increased risk of fertility disorders and limits the ovulation process because obesity is a known cause of menstrual and ovulation disorders, decreased egg quality and quantity, and infertility [23].

The increase in the level of β-Lipotropin came as a result of the profound effect of the opioid β-endorphin (which is derived from β-Lipotropin) on the mood, psychological state, and behavior, It is secreted with ACTH in response to stress and plays an important role in the balance of the central nervous system [24]. Bad mood and psychological distress are factors that contribute to infertility, as psychological distress has been found to be high in infertile couples, and psychological menopause is more common in infertile women [25]. Stress and anxiety are among the psychological effects that increase the ability to eat, especially foods which naturally activates the neurotransmitters that stimulate the happiness hormones endorphins, serotonin, oxytocin, and dopamine (DOSE), enhancing their flow and making eating sweets and fast food more enjoyable and exciting. This is one of the most important causes of belly fat, which is one of the clinical indicators of polycystic ovary syndrome (PCOS) [26]. β-Lipotropin stimulates the synthesis of corticosteroids such as cortisol, which controls the metabolism of fats and proteins, and the formation of anti-inflammatory drugs by preventing the release of phospholipids, and hydrocortisone is involved in a wide range of physiological processes, including the response to psychological stress, the immune reaction, and the control of inflammation, carbohydrate metabolism, and protein catabolism [27]. The effect of β-Lipotropin is mediated by the ACTH receptor that stimulates the activity of the adrenal cortex and the secretion of corticosteroid hormones by it, The anterior pituitary gland influences the metabolism of Through a number of hormones, including growth hormone, ACTH, and the hormone β-Lipotropin, whose function is to break down fats into amino acids, glycerol, and other hormones [28].

An increase in the level of LH may affect the synthesis of ovarian follicles (Ovarian Folliculogensis), which results abnormally from the function of the follicular atresia cells [29]. The disturbance in the secretion of the LH hormone is attributed to a dysfunction in the pituitary gland or a disturbance in the response of the secreted steroid hormones from the gonads [30]. The high concentration of LH in female patients may be the result of low levels of estrogen and progesterone, as LH is inhibited in normal cases when the levels of estradiol 2 and progesterone rise through a negative feedback mechanism [31]. A study conducted by others [32] indicated that the high concentration of the LH hormone in sterile females may be due to a large percentage of infertile women suffering from PCOS syndrome, as the results in a number of studies show an imbalance in the ratio in the secretion of the hormone LH and FSH (LH FSH ratio) in females. Infertile women and those with PCOS syndrome reach 2:1, and this imbalance makes the ovaries unable to secrete hormones in the correct way [33,34].

The high concentration of follicle-stimulating hormone (FSH) in this group of patients may be an indication of ovarian dysfunction, and since FSH is one of the most important hormones controlling the maturation and development of eggs, any decrease or increase in its concentration causes an imbalance in the ovulation process and loss of the feedback mechanism and may be a sign of infertility or Approaching menopause, and it may also occur as a result of psychological stress or nutritional imbalance, and the clear rise in FSH concentration is a clear indication of a decrease in the concentration of estrogen and progesterone and the lack of a feedback mechanism [35], and it has been pointed out that aging has a role in the rise The level of FSH, or its elevation, may be due to several other reasons, including autoimmune disorders, thyroid diseases, adrenergic gland dysfunction,

chromosomal defects, damage resulting from pelvic surgery, abortion, and pelvic inflammatory diseases, as well as chemotherapy and radiotherapy [36].

The relative increase in FSH/LH occurs as a result of a disturbance in GNRH resulting from a defect in the hypothalamus, pituitary, ovary, or adrenal glands [37]. This occurs due to abnormal negative feedback by the hormone estrogen, which results in an increase in the release of LH, and the relative increase in GNRH leads to the regulation of transcription of the LH beta subunit through the FSH beta subunit, which leads to an increase in the level of FSH/LH in patients with polycystic ovary syndrome. In a study conducted by others [38], it showed an increase in the levels of FSH/LH and prolactin in infertile women. According to the results of others [39] in which it was found that PCOS combined with hypothyroidism showed a significant increase in the LH/FSH ratio, and this was proven by the study of [40] as they found that the level of LH/FSH showed increase in women suffering from infertility resulting from hypothyroidism compared to healthy women because the altered hormonal status of the GNRH hormone is responsible for the irregular menstrual cycle and predisposes women with hypothyroidism to PCOS syndrome and thus to infertility. Recent studies indicated that women with infertility resulting from PCOS showed a relatively high level of LH/FSH [41,42].

Stimulation of increased GNRH secretion leads to elevated serum levels and results in excessive secretion of LH, which stimulates the synthesis of steroidal hormones (androgens and estrogens) by ovarian cells, thus contributing to hyperandrogenism associated with PCOS [43]. Also, high levels of GNRH lead to an increase in the secretion of the follicle-stimulating hormone (FSH), thus stimulating the ovaries to produce multiple heterogeneous follicles and impeding the regulated follicular growth and thus the lack or absence of follicles that reach the stage of maturity and appropriate size [44], and inhibition of secretion leads to GNRH indicates an imbalance in the secretion of pituitary hormones and, consequently, an imbalance in the gonadal hormones. The menstrual cycle and the fertilization process depend on a hormonal system called the hypothalamic-pituitary-gonadal (HPG) axis, and the occurrence of any form of disturbance in it directly affects the Women's menstrual cycle and fertility [45] . Also, hyperprolactin inhibits GNRH and thus inhibits LH and FSH hormones. Functional hypothalamic amenorrhea (FHA) due to chronic anovulation without identifiable organic causes is directly related to decreased GNRH function or cessation of secretion of GNRH, leading to insufficient ovarian function. In addition, these factors within the ovary could explain Also the reason for the low GNRH [46].

Conclusion

This study confirms that the subfatin hormone has a clear effect on infertility through its close association with obesity, which is a major cause of infertility. This study also proved the association of β-Lipotropin with psychological infertility through its direct effect on mood and behavior, which in turn causes amenorrhea and other major causes of infertility.

ETHICAL APPROVAL

The research protocol was approved by the Ethical Committee of College of Applied Sciences, Samarra University, Samarra, Iraq.

CONSENT TO PARTICIPATE:

Informed consent was taken from each subject before their enrolment in the study.

HUMAN AND ANIMAL RIGHTS

The study conducted in adherence with Helsinki Ethical standards.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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