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ASSESSMENT OF GONADOTROPIN-RELEASING HORMONE LEVELS IN OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Gonadotropin-releasing hormone (GnRH) is one of the major hormones affecting the reproductive system, and when elevated, it leads to polycystic ovarian syndrome. Obesity is a main cause of GnRH elevation. A current study was conducted from October to December 2024 and included 100 samples from Iraqi women diagnosed with polycystic ovary syndrome (PCOS), collected from the Infertility Center at Al-Sadder Medical City and Al-Zahraa Teaching Hospital, alongside 100 samples from healthy women. The concentration of GnRH was measured using an enzyme-linked immunosorbent assay (ELISA) kit to evaluate variations in this biochemical parameter between healthy individuals and PCOS patients. Statistical analysis was performed using a P-value test ($P < 0.05$) to assess the significance of the study results. GnRH concentrations were elevated in PCOS patients compared to the control group. Significant differences ($P < 0.05$) were observed between the two groups, with a P-value of 0.0001. In conclusion, GnRH levels were elevated in PCOS patients when compared with healthy individuals, so GnRH highly associated with the occurrence of PCOS and contribute to hormonal disorders.

KEYWORDS: Gonadotropin Releasing Hormone, Polycystic Ovary Syndrome, Obesity.

INTRODUCTION

Gonadotropin-releasing hormone (GnRH) is a decapeptide hypothalamic hormone that plays a pivotal role in the regulation of the hypothalamic-pituitary-gonadal (HPG) axis [1]. Synthesized and secreted by GnRH neurons, this hormone is essential for the control of reproductive function across all vertebrates, including humans, non-human primates, and pigs. GnRH serves as the primary regulator of gonadotropin synthesis and release, thereby orchestrating key processes in reproduction and fertility [2]. The gene encoding the GnRH precursor is located on chromosome8[3]. The prehormone consists of 89 amino acids, and upon processing, the active form of GnRH is secreted at the median eminence into the hypophyseal portal circulation, where it is transported to the anterior pituitary to regulate

gonadotropin release [4]. In women with polycystic ovary syndrome (PCOS), the frequency of GnRH pulses increases by approximately 40%, representing a hallmark feature of the condition. This heightened GnRH activity drives an increase in luteinizing hormone (LH) secretion from the adenohypophysis, which subsequently stimulates ovarian overproduction of androgens. The frequency of GnRH pulses is a critical determinant of gonadotropin secretion, with rapid pulses preferentially promoting LH synthesis and release, while slower pulses favor the production and secretion of follicle-stimulating hormone (FSH) by the pituitary gland [5,6]. Studies using animal models suggest that the phenotype of polycystic ovary syndrome (PCOS) may arise from androgen exposure that primarily influences central neural mechanisms rather than direct ovarian effects [7]. Notably, GnRH neurons lack receptors for both androgens and progesterone, indicating that sex steroids likely exert their effects through presynaptic regulatory pathways [8]. Polycystic ovarian syndrome is a prevalent endocrine disorder affecting women of reproductive age and is closely associated with the global rise in obesity [9]. Obesity impacts approximately 38–88% of women with PCOS, exacerbating its clinical manifestations. PCOS can be classified into four distinct phenotypes: insulin-resistant, adrenal, inflammatory, and post-pill [10]. The prevalence of polycystic ovarian syndrome is estimated to be 21–22% among randomly selected women [11]. A defining feature of PCOS is hyperandrogenism, often accompanied by anovulation or ovulatory dysfunction and the presence of polycystic ovarian morphology [12]. In most cases, PCOS is also associated with metabolic dysfunction, characterized by insulin resistance and compensatory hyperinsulinemia [13]. Luteinizing hormone (LH) hypersecretion occurs in over 60% of patients with polycystic ovarian syndrome. Evidence indicates that elevated LH levels disrupt oocyte maturation, leading to reduced pregnancy rates and an increased risk of miscarriage [14,15]. Luteinizing hormone plays a critical role in stimulating the production of ovarian steroids. Additionally, LH regulates the timing and coordination of the menstrual cycle by facilitating ovulation and supporting the implantation of the zygote in the uterus [16]. Follicle-stimulating hormone (FSH) is a gonadotropin and polypeptide hormone synthesized and secreted by gonadotropic cells in the adenohypophysis. In females, FSH promotes oocyte growth by stimulating granulosa cells. Its secretion is regulated through feedback mechanisms involving estrogen produced by the ovary via the hypothalamic-pituitary-gonadal (HPG) axis [17]. The luteinizing hormone to follicle-stimulating hormone (LH/FSH) ratio is elevated in patients with polycystic ovarian syndrome (PCOS) compared to healthy women, contributing to anovulation [18].

MATERIALS AND METHODS

Samples Collection

This study was conducted from October to December 2024 and included 100 women with polycystic ovary syndrome (PCOS) and 100 healthy women. All samples were collected from the Infertility Center at Al-Sadder Medical City and Al-Zahraa Teaching Hospital. All patients had irregular menstrual cycles and were between 18 and 35 years of age. None of the participants were using medication or oral contraceptives at the time of the study. Blood samples were collected during the follicular phase (days 3, 4, or 5 of the menstrual cycle).

Statistical Analysis:

A statistical study was conducted using the Statistical Package for Social Sciences (SPSS version 26, Inc., Chicago, IL, USA) and Microsoft Excel. The results and examples of the current study were analyzed. Statistical significance was determined with a p-value less than 0.05 ($P < 0.05$) [19].

Ethical approval:

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The study protocol, participant information, and consent form were reviewed and approved by the local ethics committee at the College of Biotechnology, Al-Qassim Green University.

RESULTS

Biochemical results:

Gonadotropin-releasing hormone levels were measured in the blood serum of women with PCOS and healthy individuals. The results showed that GnRH levels were significantly elevated in PCOS patients compared to healthy individuals, with a P-value of 0.0001. These findings are presented in Table 1.

The mean serum concentration of GnRH among PCOS patients was 345.85 ± 72.2B ng/L, compared to 177.23 ± 5.12A ng/L in healthy women.

Table 1 *(Comparison of GnRH Levels Between PCOS Patients and Healthy Controls.)*

Groups	GnRH (ng\l)
Control	177.23±5.12A
Patients	345.85±72.2B
T test	17.88
P value	<0.0001*

Different letters between any two means vertically denote to the significant difference at P<0.05.

DISCUSSION

The results of this study are consistent with those of Constantin et al. (2022), who demonstrated that GnRH secretion from the hypothalamus stimulates the synthesis and secretion of LH and FSH from the anterior pituitary [19].

Oduwole et al. (2021) illustrated that luteinizing hormone stimulates theca cells to synthesize androstenedione from cholesterol through the action of desmolase. FSH-stimulated granulosa cells then undergo changes in androgenic sex hormones, with aromatase converting androstenedione to estrogen, which is subsequently secreted by the granulosa cells [20].

Wang and Li. (2023) demonstrated that the activation of elevated luteinizing hormone secretion stimulates the maturation of premature oocytes, leading to fertilization defects and potentially increasing the risk of miscarriage in cases of polycystic ovary syndrome [21].

A previous study by Thualfiqar and Jumana (2024) demonstrated that the elevation of leptin hormone in obese women leads to the hypersecretion of GnRH from the hypothalamus, ultimately contributing to the development of polycystic ovary syndrome (PCOS) [8].

CONCLUSION

The elevated levels of GnRH observed in polycystic ovary syndrome are primarily associated with obesity, which is a major contributor to this increase. The expansion of fat tissue mass leads to an increase in leptin hormone levels, and the elevated leptin subsequently stimulates the increased secretion of GnRH.

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