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Role of luteinizing and follicle-stimulating hormones in women diagnosed with polycystic ovary syndrome

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ABSTRACT

The aim of this study was to investigate the relationship between luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels in women diagnosed with polycystic ovary syndrome (PCOS) in Saudi Arabia and to compare obesity levels. In this case-control study, 101 PCOS women and 54 control subjects were enrolled in King Khalid University Hospital. Based on Rotterdam criteria, PCOS women were enrolled. Anthropometric measurements were collected between PCOS and control women. ANOVA analysis was performed in PCOS women to measure the PCOS variables. The study results demonstrate that LH levels are significantly associated with PCOS women (p=0.06). ANOVA analysis indicated that age (p=0.001) and LH (p=0.05) were significantly related among the age groups. The weight, height, and BMI were significantly associated in PCOS women among PCOS subjects with obesity (p<0.05). This study concludes as LH and FSH levels were high in PCOS women with different forms of obesity and LH is correlated (p=0.06) between PCOS and control women. Additionally, elevated BMI levels were not associated with LH and FSH levels.

1. Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrine clinical condition in women, affecting 15-20% of women of reproductive age. According to Rotterdam diagnostic criteria, PCOS affects 83% of women with anovulatory infertility and 89% of hyperandrogenic women (Aboeldalyl et al., 2021), which is characterized by Acne, frontal alopecia, hair loss, hirsutism, multiple cysts in the ovaries, and eventual metabolic repercussions like obesity, IR, T2DM, and cardiovascular disease are recognized as psychosocial problems (Prabhu et al., 2021). PCOS was first identified by Stein and Leventhal (1935) as a condition characterized by oligomenorrhea and polycystic ovaries, as well as varied frequencies of acne, obesity, and hirsutism. PCOS development is linked to multifactorial inheritance, with multiple combinations of metabolic, endocrine, genetic, and elevated body mass index contributing to PCOS development (Fulghesu et al., 2021). Since Burghen et al. (1980) studies first indicated that insulin resistance (IR) was implicated in the pathophysiological process of PCOS in 1980, research on PCOS-IR has been deepened. The interaction between IR and hyperinsulinemia is essential in the etiology of PCOS, which is attributed to long-term complications (Burghen et al., 1980, Hu et al., 2014). PCOS is a heterogeneous disorder with a wide range of symptoms and an underlying cause that has yet to be determined. In approximately 50% of the incidence, PCOS is transmitted from mother to daughter in the autosomal dominant manner. PCOS is associated with obesity and insulin resistance, which in turn leads to type 2 diabetes (T2D). There is genetic evidence that chronic disease in one or both parents might affect a child's womb and increase the likelihood that the child would develop PCOS (Bogari, 2020). Women will not notice PCOS as a potential risk factor for infertility due to a lack of ovulation until they are unable to conceive. The ovaries' menstrual cycle and other processes are regulated by hormones. The hormone levels are constantly disrupted in women who suffer from this, causing the ovaries to malfunction and an ovarian cyst to form. Despite the fact that certain cysts can cause serious issues including discomfort, rupture, or bleeding, most are not harmful. As a result of these cysts, some women experience menstrual problems such as anovulation or amenorrhea (Abraham Gnanadass et al., 2021). The anterior

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pituitary gland's gonadotropic cells produce luteinizing hormone (LH). In response to gonadotropin-releasing hormone from the hypothalamus, the anterior pituitary secretes follicle-stimulating hormone (FSH). In both males and females, FSH has an important function in the development and reproduction of sex. FSH affects human growth, maturation, sexual development, and reproduction (Abood and Hathal, 2021). Increased LH levels and abnormalities in the LH/ FSH ratio are common in women with PCOS, and these could be signs of gonadotropin-releasing hormone secretion dysfunction (Daghestani, 2018). Although an overall altered hormonal milieu is responsible for defective ovarian maturation, FSH remains one of the most important hormonal regulators (de Castro et al., 2003). This study was meticulously designed to investigate the role of LH and FSH levels in both PCOS and control women. The aim of this study was to investigate the relationship between LH and FSH levels in women diagnosed with PCOS in Saudi Arabia and to compare obesity levels.

2. Materials and methods

2.1. Sample recruitment

This study has obtained an ethical grant from the Institutional Review Board at King Saud University (KSU). Saudi women who participated in this study have signed the informed consent form. In this case-control study, 155 Saudi women were enrolled in the Department of Obstetrics and Gynecology at King Khalid University Hospital (KKUH). The 155 samples were collected between January 2021 to November 2021 on the hospital premises. The 155 samples were categorized into 101 women diagnosed with PCOS and the remaining 54 samples as non-PCOS or control subjects. The inclusion criteria of PCOS women were categorized based on Rotterdam criteria which involve (i) oligo or anovulation, (ii) Biochemical and clinical hyperandrogenism, and (iii) polycystic ovaries. The women who don't fall under Rotterdam criteria were excluded from this study. The Saudi women with normal ovulation are considered as inclusion criteria of controls and women with fertility, ovarian lesions, endometriosis and other family histories including PCOS will be excluded from this study.

2.2. Sample collection

In this study, 3ml of the coagulant blood sample was collected from 155 women who were involved in this study. Non-fasting peripheral blood was collected in a coagulant tube and used to extract the serum. The extracted serum separated after the centrifugation and it was used to measure the LH and FSH levels in 155 women. LH and FSH levels were analyzed using serum samples obtained in a red vacutainer tube, which is designed to collect coagulant blood. Hormonal assays were carried out using automatic COBAS analyzer machines, which are used to measure the lipid profile (biochemical) parameters of the chemiluminescence method (Alharbi et al., 2014). LH and FSH levels were measured in the chemistry laboratory on KKUH premises.

2.3. Obesity levels

Body mass index (BMI), which is determined using weight (kgs) and height, was used to determine the obesity ranges of the recruited women (cms). The normal BMI range is 25kg/m2, and overweight is defined as 25.0-29.9kg/m2. When the BMI exceeds 30kg/m2, it is classified as obesity (Class-I Obesity), which is defined as 30-34.9kg/m2, Class-II obesity is defined as 35.0-39.9kg/m2, and Class-III obesity is defined as 40kg/m2 and above (Alshammary and Khan, 2021). BMI levels were measured in all of the women who participated in this study.

2.4. Statistical analysis

T-tests were used to calculate the mean of PCOS women and controls. The mean and standard deviation were calculated in Excel, and one-way ANOVA analysis was performed in results section (Khan et al., 2019).

3. Results

In this hospital-based case-control study, 155 women were enrolled and categorized into 101 as PCOS women and 54 as fertile women. The mean age of PCOS and control women in this study were found to be 32.03+5.33 and 33.12±4.98 years. The BMI of both the women groups was found to be similar (p=0.32) including weight (p=0.33) and height (p=0.62). None of the women who participated in this study had a family history of PCOS. The PCOS women had FSH levels of 6.90±2.79 and 6.25±2.81 in controls (p=0.17). The LH levels were elevated in PCOS women (7.56±4.69) when compared to control subjects (6.14±3.76) and showed a significant association (p=0.06). The anthropometric details were recorded in Table 1.

Table 1: Anthropometric measurements between PCOS and control women

Anthropometric measurements	PCOS (n=101)	Controls (n=54)	P-value
Age (Years)	32.03 ±5.33	33.12±4.98	0.21
Weight (Kgs)	74.49±14.14	72.15±14.83	0.33
Height (cms)	158.11±10.75	157.32±10.65	0.62
BMI (kg/m^2)	28.97±4.85	28.18±4.67	0.32
FSH (IU/mL)	6.90±2.79	6.25±2.81	0.17
LH	7.56±4.69	6.14±3.76	0.06
Family History	00 (0%)	00 (0%)	NA

Table 2 defines the PCOS women categorized into three variation groups such as (i) group-I is defined as between 20-29 years of age and 31.7% women were involved, (ii) group-II is categorized as 59.4% of PCOS women included between the age range of 30-39 years and (iii) group-III is categorized as 40-49 years of women with the involvement of 8.9%. The mean age of group-I (25.81±2.02), group-II (33.95±2.72), and group-III (41.44±1.74) showed a significant association (p=0.001). Obesity details such as height (158.88±4.07), weight (79.72±10.07), and BMI (31.37±4.26) were found to be high in group-III women as they age (41.44±1.74) were found to be high among the three groups with non-significant association (p<0.05). The LH (8.81±4.72) and FSH (7.36±3.23) levels were found to be high in the group-I women. ANOVA analysis revealed a positive association only in age (p=0.001) and LH (p=0.05) levels.

Table 2: ANOVA analysis performed as per categorization of age in PCOS women

Anthropometric measurements	[20-29 Years] (n=32)	[30-39 Years] (n=60)	[40-49] (n=09)	P-value
Age (Year)	25.81±2.02	33.95±2.72	41.44±1.74	0.001
Weight (Kg)	70.89±11.17	75.62±15.72	79.72±10.07	0.15
Height (cm)	158.69±5.72	157.68±13.27	158.88±4.07	0.89
BMI (kg/m²)	28.06±4.71	29.09±4.94	31.37±4.26	0.18
FSH (IU/mL)	7.36±3.23	6.71±2.71	6.52±1.29	0.52
LH	8.81±4.72	7.32±4.71	4.68±3.09	0.05

In Table 3, obesity cases were categorized into five groups (i) underweight-19.8%, (ii) overweight-39.6%, (iii) Class-I obesity=31.7%, (iv) Obesity class-II-6.9%, and (v) Obesity Class-III-1.9%. The LH levels (8.33±5.03) were found to be high among the categorized underweight groups (p=0.48). Height (159.39±4.89) and FSH (7.09±3.01) levels were found to be highly expressed among the overweight subjects. Age (36.0±5.38), weight (101.0±0.00), and BMI (42.1±0.00) were recorded highly among Class obese (IIandIII) groups (p<0.05). The obesity details such as weight, height, and BMI were strongly associated in PCOS women (p<0.00±1).

Table 3: Classification of BMI levels in PCOS women

	Underweight (n=20)	Overweight (n=40)	Obesity Class-I (n=32)	Obesity Class-II (n=07)	Obesity Class-III (n=02)	P-value
Age (Years)	30.3±3.68	31.9±5.91	32.4±5.30	36.0±5.38	32.5±0.70	0.18
Weight (Kgs)	65.01±22.96	70.69±6.19	79.64±6.72	92.11±6.88	101±0.00	0.0003
Height (cms)	157.2±22.33	159.39±4.89	157.27±5.33	158.1±5.14	155±0.00	0.0009
BMI (kg/m²)	22.26±2.26	27.64±1.50	32.39±1.51	36.8±0.84	42.1±0.00	<0.0001
FSH (IU/mL)	6.81±2.55	7.09±3.01	6.77±2.91	6.75±2.41	6.50±1.83	0.98
LH	8.33±5.03	7.98±4.54	7.25±5.04	5.11±1.72	4.99±5.38	0.48

4. Discussion

This is a hospital-based case-control study that was conducted at KSU hospital on 101 PCOS women and 54 healthy women controls (fertile/non-PCOS women). The aim of this study was to investigate the obesity, LH, and FSH levels in PCOS women in the Saudi population. When compared to control subjects, this case-control study demonstrates that LH levels are significantly associated with PCOS women (p=0.06). ANOVA analysis indicated that age (p=0.001) and LH (p=0.05) were significantly related among the age groups. In Table 3, weight, height, and BMI were significantly associated with PCOS women among obese PCOS subjects (p<0.05). The current study results confirmed the mean elevated FH levels in PCOS women with young Saudi women diagnosed with PCOS. This study was found to be consistent with the findings of previous study results in global wide studies (Abood and Hathal, 2021; Balen et al., 2003; Haller et al., 2008). This may be happening due to the autoantibodies (Anti-FSH and Anti-LH) first arising prior to the onset of hormonal or clinical abnormalities, which is most likely since most hereditary diseases manifest themselves during adolescence. The results of this study did not correlate with the FSH levels (6.90±2.79 vs 4.9±5.9) found in a Saudi Arabian study (Al-Mulhim et al., 2013). One of the predictions could be a small sample size in PCOS participants since control subjects had similar values (6.25±2.81 vs 6.6±1.6), which is owing to the equivalent number of controls (n=50) chosen in both studies. Similar results were found in other studies also (Saadia, 2020; Schmidt et al., 2011). Lal et al. (2017) studies were not in association with the current study results (Lal et al., 2017). In this study, the PCOS women were selected based on Rotterdam criteria rather than ESHRE or ASRM, or NIH criteria.

Obesity and PCOS have a well-defined association. Obesity has been identified as one of the risk factors for PCOS, which is a common factor between endocrine and reproductive disorders. The etiology of PCOS has not been identified as of the end of the first trimester of 2022, but it is predicted to be a combination of reproductive and metabolic abnormalities, which leads to hormonal imbalance in the form of high estrogen and androgen levels (AlSinan and Shaman, 2017). Further, PCOS is associated with a slew of metabolic abnormalities, including hyperinsulinemia, peripheral insulin resistance, and an increase in blood glucose levels unrelated to weight gain. Defects in insulin action and secretion have been shown to increase the risk of metabolic diseases and obesity (Šimková et al., 2020). Co-morbid disorders of PCOS, such as overweight and obesity are thought to have a significant part in the etiology of PCOS. According to a preliminary study, a high LH/FSH ratio is associated with metabolic characteristics of PCOS, such as obesity, among a subset of women with this condition. There is a lack of data on the LH/FSH ratio and its connection to obesity and other postmenopausal disorders. Pre and perimenopausal women's gonadotropins (FSH and LH) levels fluctuate often, making it difficult to accurately measure the LH/FSH ratio in postmenopausal women (Beydoun et al., 2012). Increased ovarian androgen production and other adverse effects are caused by an altered LH-FSH ratio. Hyperandrogenemia reduces estrogen's negative feedback to the hypothalamus, resulting in an increase in LH pulse frequency. PCOS is associated with numerous clinical symptoms, including hyperandrogenism (Morshed et al., 2021).

In this study, the BMI levels were found to be in the range of overweight i.e., 28.97±4.85 in PCOS women and 28.18±4.67 in control subjects. Furthermore, BMI was categorized into five categories as described in Table 3. Both FSH and LH levels were not associated with sub-categories of BMI levels in PCOS women. This study was also similar to the previous studies (Alnakash and Al-Tae e, 2007; Kiddy et al., 1990; Saadia, 2020). One of the strengths of this study is defined as Saudi women confirmed with PCOS were involved in this study from a single hospital and the main limitation of this study was the limited sample size and the longitudinal study was designed.

5. Conclusion

This study concludes as LH and FSH levels were high in PCOS women with different forms of obesity and LH is correlated (p=0.06) between PCOS and control women. Additionally, elevated BMI levels were not associated with LH and FSH levels. Future studies should be carried out within the large population.

Compliance with ethical standards

Ethical consideration

This study has obtained an ethical grant from the Institutional Review Board at King Saud University (KSU). Saudi women who participated in this study have signed the informed consent form.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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