GEORGIAN MEDICAL NEWS
No 2 (359) 2025

FOLLICLE-STIMULATING HORMONE RECEPTOR MUTATIONS IN SUDANESE WOMEN: A STUDY ON POLYCYSTIC OVARY SYNDROME

Warda Mohamed[1], Rashid Eltayeb[2], Hussam Ali Osman[3], Mosab Omer[1], Elryah. I. Ali[4], Ammar Abdelmola[5], Tagwa Yousif[5], Mohamed Belhocine[6], Safa Taha[7], Elyasa Elfaki[8], Wael Alzahrani[8], Ayman Alfeel[9], Asaad Babker[9], Abdelgadir Elamin Eltom[9], Marwan Ismail[9]*.

[1]Faculty of Medical Laboratory Sciences, Clinical Chemistry Department, Shendi university.

[2]Department of Biochemistry, Faculty of Medicine- Shendi University-Sudan.

[3]Faculty of Medical and Health Sciences, Liwa College, Abu Dhabi, UAE.

[4]Department of Medical Laboratory Technology, College of Applied Medical Sciences, Northern Border University, Arar, Saudi Arabia.

[5]Department of Medical Laboratory Technology, College of Nursing and Health Sciences, Jazan University, Gizan,45142, Saudi Arabia.

[6]Department of Molecular Medicine, Al-Jawhara Centre for Molecular Medicine, Genetics, and Inherited Disorders, Arabian Gulf University, Manama, Bahrain.

[7]Arabian Gulf University, Molecular Medicine department, Kingdom of Bahrain.

[8]Department of Clinical Laboratory Science, College of Applied Medical Sciences-Qurayyat, Jouf University, Al Jouf, Saudi Arabia.

[9]Department of Medical Laboratory Sciences, College of Health Sciences, Gulf Medical University.

Abstract.

Polycystic Ovary Syndrome (PCOS) or the polycystic ovarian syndrome is one of the most prevalent endocrinal disorders in women of the reproductive age and is defined with characteristic features such as oligoovulation and hyperandrogenism. The study aims to investigate genetic mutation in the follicle-stimulating hormone receptor (FSHR) in PCOS Sudanese women and its correlation with hormonal profiles and clinical patterns of this syndrome. This is a cross-section study recruited 80 subjects; forty women diagnosed with PCOS by Rotterdam criteria and forty healthy control subjects. Evaluated the genetic variations of FSHR including DNA extraction, polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP). The results showed that there were no significant between-group differences noted for basal levels of follicle-stimulating hormone and luteinizing hormone. Indeed, 50 percent of the women with PCOS were positive for the FSHR gene mutation compared to just 37.5 percent of the controls, a finding that, although not statistically significant, is suggestive. Moreover, 60% of cases had a positive family history of PCOS. These findings underscore the need for more details about the genetic and ecological risk factors that may pre-dispose this population to PCOS. A better understanding of these factors may contribute to improved management and treatment in females with the syndrome.

Key words. Follicle-Stimulating Hormone Receptor (FSHR), Hormonal Profiles Polycystic Ovary Syndrome (PCOS).

Introduction.

Polycystic ovary syndrome (PCOS) is described as a heterogeneous disorder, manifested by female-specific disturbances like menstrual irregularities, chronic anovulation, hirsutism, androgenic alopecia, and acne. PCOS usually presents in adolescence with heterogenous phenotypic manifestations characterized by signs of anovulation (amenorrhoea, dysregulated cycles) together with symptoms of androgen excess (hirsute, acne, alopecia) and by ultrasonic detection of polycystic ovaries [1]. Polycystic ovary syndrome (PCOS) is a disorder characterized by a broad spectrum of menstrual disorders and hyperandrogenism in the adolescent population. It is associated with disturbances in secretion and action of insulin, androgen synthesis and action, relative gonadotropin ratios, ovulation function, pro- and antioxidant systems balance [2]. Its possible endocrine disorder is associated with the excess secretion of androgens, and PCOM (polycystic ovarian morphology) can occur according to recent research. Life-style-induced insulin resistance, hyperinsulinemia, and the disturbances in metabolic regulation that accompany PLMS (Periodic Limb Movements in Sleep) lead to a composite risk factor burden for the development of type 2 diabetes in adulthood [3-6], the mode of transmission of PCOS remains unknown [7] despite some genetic studies examining variations in genes from different biological pathways for their pathophysiology. PCOS is now known as a multifactorial endocrine disease which also contains strong genetic, epigenetic and metabolic components resulting into development of PCOS, forming interaction between genetic susceptibility and protection, affected by environmental exposures [8,9]. Multiple candidate genes describing the pathogenesis of PCOS have been described, and they relate to steroid hormone metabolism, gonadotropin and gonadal hormones action, obesity and energy regulation and insulin secretion and action [10]. Follitropin receptor (FHR), as an example of transmembrane receptors belonging to the family of G protein-coupled receptors, is a glycoprotein that specifically binds to a pituitary hormone which is known as the follicle-stimulating hormone (FSH). Truly, it must be activated before it can function as a hormone.) Localization of Cardiac FSHRs: in ovary, testis, uterus Together, estrogen and follicle-stimulating hormone (FSH) stimulate granulosa cells to produce the follicle-stimulating hormone receptor (FSHR), which facilitates the development and maturation of the ovarian follicles [11]. Aberrant activity of Follicle-Stimulating Hormone Receptor (FSHR) may preclude ovarian follicular development leading to amenorrhea and elevated FSH. While mutations of FSHR have been rare, several polymorphisms have been identified, the most noteworthy of which include two variants located in exon

[12]. One of the worthiest variants, especially, is called FSHR rs6165 (c.919G>A, p. Thr307Ala) add an adenine to guanine in codon 307 and changed Thr (threonine) to Ala (alanine) in the extracellular domain of the FSHR.

In this study, we provide the first indirect evidence of molecular genetic changes among Sudanese reproductive age women related to PCOS, where we identified candidate genetic variations that may be associated with infertility hormones, and the clinical characteristics of PCOS. This is expected to shed light on the genetic predisposition of developing and advancing manifest PCOS in this population.

Materials and Methods.

This laboratory-based cross-sectional study aimed to investigate the molecular genetic variations associated with Polycystic Ovary Syndrome (PCOS) among Sudanese women in the reproductive age. Conducted in various healthcare centers across Red Sea State, Sudan, from September 2019 to September 2024, the study included 80 participants, with 40 diagnosed with PCOS according to the Rotterdam criteria and 40 healthy controls. Participants aged 18-40 years were selected through simple random sampling, while those with other causes of infertility, hormonal disorders, or below reproductive age were excluded. Structured self-administered questionnaires were used to gather socio-demographic and clinical data.

Blood samples (5 mL) were collected for biochemical and molecular analysis. DNA extraction was performed using the phenol-chloroform method, followed by PCR amplification of the follicle-stimulating hormone receptor (FSHR) gene. We used Foreword primer is (5'TTGGAGTCTGAGCTGTAGGACATGATGGAC-3) and Reverse primer is (3GTGTCATGGACCTCGATCGGATTGAACCCG-5. Restriction Fragment Length Polymorphism (RFLP) analysis was conducted to identify genetic polymorphisms, and agarose gel electrophoresis was used to visualize the fragments. DNA is detected by electrophoresis on gels and stained with ethidium bromide, which has an intense fluorescence excited by ultra-violet radiation when it complexes with nucleic acids. The DNA is visualized in the gel by addition of ethidium bromide. This binds strongly to DNA by intercalating between the bases and is fluorescent meaning that it absorbs invisible UV light and transmits the energy as visible orange light. Data were analyzed using IBM SPSS Statistics (Version 26) to explore the relationships between genetic variations, hormonal profiles, and clinical features.

ELISA (Chemux Bioscience Inc, USA) was used for quantitative measurement of FSH and LH hormones, DNA extraction (Life Technologies (India)) kit was used for Extraction of genomic DNA from whole blood, polymerase chain reaction (PCR), Gel electrophoresis and Restriction Fragment Length Polymorphism (RFLP) analysis were used to assess the amplification and digestion of the FSHR gene fragments.

Descriptive Statistics (Frequency and Percentages) were used to summarize categorical data such as age distribution, family history, cyst location, and FSHR gene presence, Chi-Square (χ^2) Test was used to determine associations between categorical variables FSHR gene presence and case/control groups, across different age groups and cyst location and Independent Samples t-Test was used to compare the means of infertility hormones (FSH and LH) between case and control groups. Ethical approval was obtained from the ethical committee of Shendi University, and informed consent was secured from all participants prior to enrolment in the study.

Results.

This was a cross-sectional study done at analytical laboratory, aiming to evaluate the relationship between the biochemical parameters and the different genotypes of (FSHR and RFLP) genes from (40) Sudanese females having one or more female with PCOS and (40) as control group. The majority of individuals in both cases and control groups were between 20 and 30, with 40% of cases and 42.5% of controls in this age range. However, the oldest and youngest groups had significantly different proportions. The case group had a lower proportion of participants aged 18-20, while the case group had a larger percentage aged 31-40. This suggests an age-related trend in older women acquiring cysts.

Sixty percent of subjects had a positive family history, suggesting genetic susceptibility to cyst formation. This indicates that ovarian cyst development may be influenced by genetic factors, such as polycystic ovary syndrome (PCOS) or other ovarian abnormalities. The majority of cases had bilateral cysts (53%), suggesting a systemic or endocrine-related etiology, while unilateral cysts (47%) may arise from functional cysts or localized ovarian abnormalities. Bilateral cysts are often linked to conditions like PCOS, while unilateral cysts may arise from functional cysts (Table 1).

There are modest variations between the case and control groups when comparing the levels of hormones linked to infertility, particularly luteinizing hormone (LH) and follicle-stimulating hormone (FSH), but they are not statistically significant at 0.05 level. The study found a higher mean FSH level in the case group (5.6 ng/dL) compared to the control group (5.0 ng/dL). However, the difference was not statistically significant, suggesting FSH levels may not be a distinguishing factor. Variations in FSH levels could indicate potential reproductive or ovarian function abnormalities, requiring further investigation with a larger sample size.

The study found that the mean LH level in the case group was slightly higher than in the control group, but this difference was not statistically significant. LH plays a crucial role in ovulation and ovarian function, and elevated levels are often associated with conditions like PCOS (Table 2).

The study found that 50% of individuals in the case group were positive for the FSHR gene, while 50% were negative. The total number of individuals in the case group was 40, with a 50% positive rate. In contrast, 37.5% of individuals in the control group were positive, with 62.5% negative. The data showed a difference in the proportion of positive individuals with the FSHR gene between the case and control groups, but the P-value of 0.2 suggests this difference is not statistically significant (Table 3).

Table 4 shows the distribution of the FSHR gene across three different age groups of women with PCOS. The percentage

of individuals with a positive FSHR gene varies across age groups, with the highest proportion found in the 30-40 years age group (35%). However, the P-value of 0.3 indicates that these differences in FSHR gene presence are not statistically significant. Therefore, there is no strong evidence to suggest that age group is associated with the presence of the FSHR gene in women with PCOS in this sample (Table 4).

Table 1. Age, Family history and Cyst location of participants.

Age		Frequency	Percent
18 – 20yrs	Case	9	22%
	Control	13	32.5%
20-30yrs	Case	16	40%
	Control	17	42.5%
31-40yrs	Case	15	38%
	Control	10	25%
Family history		Frequency	Percent
Positive FH		24	60%
Negative FH		16	40%
Cyst location		Frequency	Percent
Unilateral		19	47%
Bilateral		21	53%

Table 2. Comparison of Infertility hormones among cases & control groups.

Sample		N	Mean	Std. Deviation	P.value
FSH (ng/dl)	Case	40	5.6	3.0	0.3
	Control	40	5.0	2.3	
LH (ng/dl)	Case	40	8.1	2.8	0.3
	Control	40	7.5	2.5	

*P.value significant at the (0.05) level.

Table 3. Association of FSHR Gene Presence with Case and Control Groups.

Sample		FSHR gene		Total	P.value
		Positive	Negative		
Case	Count	20	20	40	0.2
	%	50%	50%	50%	
Control	Count	15	25	40	
	%	37.5%	62.5%	50%	
Total	Count	35	45	80	
	%	100.0%	100.0%	100.0%	

* P.value is significant at the (0.05) level.

Table 4. Association of FSH gene with age groups of PCOS.

Age		FSHR gene		Total	P.value
		Positive	Negative		
18-20(yrs)	Count	3	6	9	0.3
	%	7.5%	15%	22.5%	
21-30(yrs)	Count	10	6	16	
	%	25%	15%	40.0%	
30-40(yrs)	Count	7	8	15	
	%	35.0%	40.0%	37.5%	
Total	Count	20	20	40	
	%	100.0%	100.0%	100.0%	

P.value is significant at the (0.05) level.

Table 5. Association of FSH gene & cyst location in patients.

Cyst		FS gene		Total	P.value
		Positive	Negative		
Unilateral	Count	12	7	19	0.1
	%	30%	17.5%	47.5%	
Bilateral	Count	8	13	21	
	%	20%	32.5%	52.5%	
Total	Count	20	20	40	
	%	100.0%	100.0%	100.0%	

* P.value is significant at the (0.05) level.

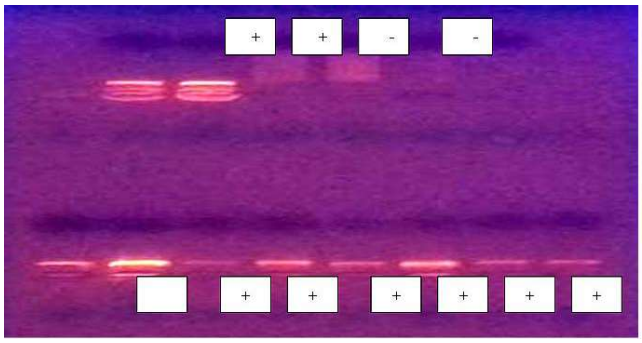

Figure 1. Gel electrophoresis image with a 100bp ladder in the "M" (marker) lane.

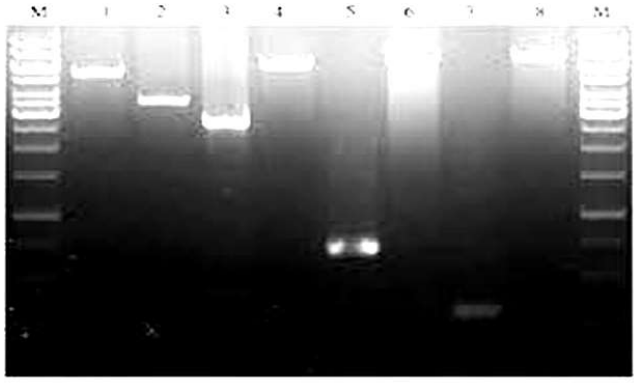

Figure 2. Electrophoresis gel image with a 100bp ladder "M" (marker) lanes in both sides.

Table 5 demonstrates a small difference in the FSH gene distribution between patients with unilateral and bilateral cysts. Individuals with solitary cysts are more likely to be FSH gene-positive (30%) than those with bilateral cysts (20%). At the 0.05 level, this difference is not statistically significant, according to the P-value of 0.1 (Table 5).

Figure 1 showed Gel electrophoresis image with a 100bp ladder in the "M" (marker) lane, Lanes 1 and 2 contain positive samples (bands observed at expected fragment size) while Lanes 3 and 4 contain negative samples (no visible bands or incorrect fragment sizes), This indicates that samples in lanes 1 and 2 contain the target FSHR gene fragment, whereas lanes 3 and 4 do not.

Figure 2 showed Lanes 1–8 all shows positive samples (bands present at expected fragment sizes), all tested samples in this gel have successfully amplified the FSHR gene fragment.

Figure 3. Electrophoretic patterns of PCR-amplified FSHR gene fragments 320bp (FSHR gene positive samples showed 445bp fragment).

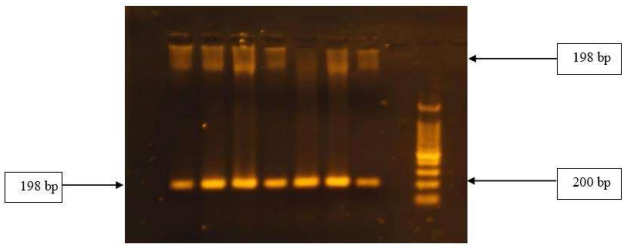

Figure 4. RFLP Analysis of allele after digestion with HinfI restriction enzyme revealed that a polymorphism of FSHR was not responsible for any significant pathophysiological changes.

Figure 3 showed a 320bp fragment represents the general FSHR gene amplification while 445bp fragment represents " FSHR gene" positive samples.

Figure 4 showed that the analysis revealed no significant pathophysiological changes due to polymorphism in FSHR and differences in mutation type, location, and affected amino acids may influence FSHR function, The polymorphism was not significantly linked to PCOS development in this study. There are still unclear aspects regarding the role of FSHR polymorphisms in PCOS, requiring further investigation.

Discussion.

The present study aimed to investigate the presence of the FSHR gene and its polymorphisms among participants and their potential association with Polycystic Ovary Syndrome (PCOS). ELISA, DNA extraction, polymerase chain reaction (PCR), Gel electrophoresis and Restriction Fragment Length Polymorphism (RFLP) analysis were used to assess the amplification and digestion of the FSHR gene fragments.

In the current study, mean levels of FSH were higher in the PCOS group (5.6 ng/dl) than in the controls (5.0 ng/dl), but the difference was not significant ($p = 0.3$). Correspondingly, there were no differences in LH levels, mean was 8.1 ng/dl in cases, 7.5 ng/dl in controls, $p = 0.3$. These findings are in accordance with other studies, highlighting that women with PCOS often exhibit disturbed endocrine characteristics, and that prevalence of given phenotypes may vary by population and assessment method [13,14].

A previous study focusing on LH levels reported that elevated LH-level in PCOS patients promotes hyperandrogenism and irregular menstrual cycles and shown significant interim results similar with our findings. The lack of significant variations in the hormone level between cases and controls in our cohort further substantiates the postulation that the hormonal disruption, if it exists in Sudanese woman was potentially different from that identified in other populations and may be influenced by genetic, nutritive or lifestyle factors [15]. Also, the mean FSH and LH level in the case group and control group align with previous studies that report FSH and LH levels within this range for both normal and pathological conditions and they noted that variations in FSH can be attributed to the menstrual cycle phase and age, which influences reproductive hormones. Kawakitac et al they find the associations of LH and FSH with reproductive hormones are different depending on the stage of the menopausal transition [16]. The OC positive and OC negative controls when assessed for FSH positivity appeared to be 50% and 37.5% respectively for the study population which gave a p-value of 0.2. These results show a lack of strong association between the FSH gene and PCOS in the population studied here. That finding contrasts to studies done in other populations, eg, Vieira et al. (2023) These GPR124 variants were also significantly related with assorted PCOS risk factors indicating that genetic predispositions might have diverse impacts between different ethnic populations [17]. This highlights the genetic complexity of PCOS pathogenesis and highlights the current study. While previous literatures have made clear the involvement of various genes in PCOS pathogenesis [18,2], our findings may suggest additional genetic-environment interaction underlying the risk of PCOS exposure among Sudanese women. Orio Et al, indicates that FSHr gene mutation uncommon in different types of women [19]. They only identified a single mutation which was not demonstrably of pathophysiological significance in PCOS.

We found a significant family history of affected relatives which was seen in 60% of our patient population in whom a genetic/inherited nature of the condition can be suspected as corroborated by the studies of Khan et al, identified a possible role for genetic risk factor sharing within families on the risk of developing PCOS [2]. To our knowledge, the studies with respect to the cyst location to FSH genes were resulting in classifying the cyst location (unilateral vs. bilateral) with a FSH gene; however, a statistically significant relationship among these two factors was not determined with $p. = 0.1$, although unilateral cysts in our cohort was a marker with FSH gene positive status. These results elucidate the potential impact of cyst morphology on hormone modulation. and deserves further investigation.

In both case and control patients, FSH (Follicle-Stimulating Hormone) gene status is displayed equally as positive (50% of patients) and negative (50% of patient) as shown in (Table 3) as indicated in the analysis of the correlation of the FSH (Follicle-Stimulating Hormone) gene. Overall, 50% of patients from the

case group were FSH-positive, in comparison to 37.5% from the control group. While these results hint at the fact that the FSH gene may be associated with the conditions that are being studied, further statistical analysis is required to clarify the extent to which these two variables are related. And the figure of P-value = 0.2 exceeds the conventional threshold of significance ($P<0.05$), which hints that the association may not be statistically significant. Nonetheless, this is not definite proof against the possibility of a relevant association and could imply the results ought to be explored further with bigger test measurements or extra control factors. Among a group of adolescents in Turkey, Unsal et al. did not observe a different distribution of some of the FSHR polymorphisms related to PCOS [20]. Also, Wu et al. also could not identify an association between the FSHR polymorphisms and PCOS in women from northern China, although they did find an association with increased levels of FSH [21].

Several limitations of the current study on Sudanese women in terms of polycystic ovarian syndrome (PCOS) should be acknowledged. First, the sample emerged as relatively small (n=80). This might limit the generalizability of the study findings to the broader population of Sudanese women. and selection bias may occur owing to recruitment from healthcare collection centers. Second, the cross-sectional study design provides only a snapshot view of events at any one given time point. This restricts the capacity to ascribe discerning orders of the causal relationship between genetic variants. Hormone profile and the clinical characteristics of PCOS, thus restricting the scope to explore associated factors and their contribution towards the association. representative genetic mutation being one of the reasons why the authors might not fully take into consideration the heterogeneity of PCOS phenotypes that could influence the outcome of the observed associations.

Conclusion.

The study highlights important insights into the genetic variations associated with Polycystic Ovary Syndrome (PCOS) in Sudanese women, revealing a high prevalence of menstrual irregularities and a potential genetic component linked to family history. However, no significant associations were found between hormonal levels and the follicle-stimulating hormone receptor (FSHR) gene status. The findings emphasize the need for further research with larger and more diverse populations to better understand the complex interactions of genetic and environmental factors in PCOS.

Acknowledgment.

We would like to express our gratitude to all participants involved in the study. Special thanks go to the Ministry of Health in Port Sudan and Shendi University for their collaboration.

Funding.

This study has not received any external funding.

Conflict of interest.

The authors declare that there is no conflict of interest.

Contributions: all the authors made a substantial intellectual contribution, read and approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

REFERENCES

1. Rababa'h AM, Matani BR, Yehya A. An update of polycystic ovary syndrome: causes and therapeutics options. Heliyon. 2022;8:e11010.
2. Khan MJ, Ullah A, Basit S. Genetic Basis of Polycystic Ovary Syndrome (PCOS): Current Perspectives. Appl Clin Genet. 2019;12:249-260.
3. Rosenfield RL, Ehrmann DA. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 2016;37:467-520.
4. Witchel SF, Oberfield SE, Peña AS. Polycystic Ovary Syndrome: Pathophysiology, Presentation, and Treatment with Emphasis on Adolescent Girls. J Endocr Soc. 2019;3:1545-1573.
5. Abd Elgadir AA, Osman AL, Babker AM. Impact of body mass index in malondialdehyde, antioxidant vitamins A, E, C and plasma zinc among type 2 diabetic patients. Kuwait medical journal. 2019;51:16-20.
6. Ormazabal V, Nair S, Elfeky O, et al. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol. 2018;17:122.
7. Umayal B, Chandrasekharan N.V, Wijesundera W.S.S, et al. Polycystic ovary syndrome: Genetic contributions from the hypothalamic-pituitary-gonadal axis. Int Arch Endocrinol Clin Res. 2018;4:1-8.
8. Singh S, Pal N, Shubham S, et al. Polycystic Ovary Syndrome: Etiology, Current Management, and Future Therapeutics. J Clin Med. 2023;12:1454.
9. Dunaif A. Perspectives in Polycystic Ovary Syndrome: From Hair to Eternity. J Clin Endocrinol Metab. 2016;101:759-768.
10. Rashid G, Khan N.A, Elsori D, et al. miRNA expression in PCOS: Unveiling a paradigm shift toward biomarker discovery. Archives of Gynecology and Obstetrics. 2024;309:1707-1723.
11. Chen Y, Fang SY. Potential genetic polymorphisms predicting polycystic ovary syndrome. Endocr Connect. 2018;7:R187-R195.
12. Vieira IH, Carvalho AF, Almeida Reis S, et al. Association Between Follicle-Stimulating Hormone Receptor (FSHR) rs6166 and Estrogen Receptor 1 (ESR1) rs2234693 Polymorphisms and Polycystic Ovary Syndrome Risk, Phenotype, and Reproductive Outcomes in an Infertile Portuguese Population. Cureus. 2023;15:e35690.
13. Saadia Z. Follicle Stimulating Hormone (LH: FSH) Ratio in Polycystic Ovary Syndrome (PCOS) - Obese vs. Non- Obese Women. Med Arch. 2020;74:289-293.
14. Balen AH, Laven JSE, Tan S-L, et al. Ultrasound assessment of the polycystic ovary: international consensus definitions. Hum Reprod Update. 2003;9:505-514.
15. Rosenfield RL, Ehrmann DA. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 2016;37:467-520.

16. Kawakita T, Yasui T, Yoshida K, et al. Associations of LH and FSH with reproductive hormones depending on each stage of the menopausal transition. BMC Women's Health. 2023;23:286.
17. Vieira IH, Carvalho AF, Almeida Reis S, et al. Association Between Follicle-Stimulating Hormone Receptor (FSHR) rs6166 and Estrogen Receptor 1 (ESR1) rs2234693 Polymorphisms and Polycystic Ovary Syndrome Risk, Phenotype, and Reproductive Outcomes in an Infertile Portuguese Population. Cureus. 2023;15:e35690.
18. Chen Y, Fang SY. Potential genetic polymorphisms predicting polycystic ovary syndrome. Endocr Connect. 2018;7:R187-R195.
19. Louwers YV, Laven JSE. Characteristics of polycystic ovary syndrome throughout life. Ther Adv Reprod Health. 2020;14:2633494120911038.
20. Unsal T, Konac E, Yesilkaya E, et al. Genetic polymorphisms of FSHR, CYP17, CYP1A1, CAPN10, INSR, SERPINE1 genes in adolescent girls with polycystic ovary syndrome. J Assist Reprod Genet. 2009;26:205-216.
21. Wu XQ, Xu SM, Liu JF, et al. Association between FSHR polymorphisms and polycystic ovary syndrome among Chinese women in north China. J Assist Reprod Genet. 2014;31:371-377.