Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 8
Open Access

Association Of Hormonal Dysregulation With Pcos In Fertile Women

Misbah Riaz[1], Prof Dr Hasan Ali[2], Dr Khushboo Arif[3], Dr. Zahra Tapal[4], Samina Mohyuddin[5], Faizza Rasheed[6]

[1]Assistant Professor, Biochemistry Bahria University Health Sciences Campus Karachi
[2]Head of Department Biochemistry Bahria University Health Sciences Campus Karachi
[3]Lecturer Physiology Bahria University Health Sciences Campus Karachi
[4]Senior lecturer, Physiology Bahria University Health Sciences Campus Karachi
[5]Assistant professor, Physiology Liaquat college of medicine and dentistry
[6]Lecturer, Biochemistry Shahida Islam medical college

Cite this paper as: Misbah Riaz, Prof Dr Hasan Ali, Dr Khushboo Arif, Dr. Zahra Tapal, Samina Mohyuddin, Faizza Rasheed (2024). Association Of Hormonal Dysregulation With Pcos In Fertile Women. *Frontiers in Health Informatics*, *13 (8) 3236-3245*

ABSTRACT:

OBJECTIVE:

- To investigate the association of hormonal dysregulation with the presence of PCOS in fertile women
- To compare biochemical parameters such as serum FSH, LH, prolactin, testosterone, serum fasting levels, serum insulin levels and HbA1c in PCOS diagnosed group, predisposed group and control group.

STUDY DESIGN: Case Control Study

PLACE AND DURATION OF STUDY: This study was conducted in Obstetrics and gynaecological department of Shifa hospital, Karachi from December 2022 to June 2023.

METHODOLOGY: This case-control study included 105 patients from 3 different groups; PCOS diagnosed group, healthy group, and the predisposed group. Patients assessed in the obstetrics and gynecology outpatient department were sent for lab tests, including FSH, LH, prolactin, testosterone, fasting blood sugar, insulin, and HbA1c. Blood samples were collected during the follicular phase and analyzed at PNS Shifa hospital. One way Anova test was applied for qualitative variables variables. P value < 0.05 was considered statistically significant.

RESULTS: The study included 105 participants with a mean age of 28.21 years. Significant differences were found among study groups for BMI, FSH, LH, LH:FSH ratio, testosterone, prolactin, fasting blood glucose, fasting insulin, and HbA1c levels, indicating notable biochemical variations associated with PCOS status.

CONCLUSIONS: The study concludes a significant association between hormonal imbalances and PCOS in both fertile and infertile women, emphasizing the importance of targeted hormonal assessment and management for all PCOS patients to enhance overall health outcomes.

KEYWORDS: Hormonal Dysregulation, Follicular menstruation, Predisposed group

INTRODUCTION:

Polycystic ovarian syndrome (PCOS) is an endocrine disorder that is described as the numerous small cysts that are formed in the ovaries of most females. PCOS is caused by a deficiency in the process of transcriptional regulation of a genome caused by a polymorphism or even any sequence alteration.[1] The most commonly implicated genes involve androgen receptor proteins, LH receptor proteins, FSH receptor proteins, and Leptin receptor proteins.[2] According to the National Health Services (NHS), common symptoms of PCOS include oily skin, weight gain, complications in conceiving, and irregular periods (NHS, 2021). Additionally, many PCOS patients exhibit irregular hair growth in different areas such as the chest, face, and back.

Past studies have revealed that the main causes or factors that resulted in PCOS prevalence are still unknown. However, differential genetic-dictated hormonal dysfunction is considered to be the underlying cause.[3] Mukherjee (2020) also studied the main features of PCOS and revealed that polycystic ovaries have large sacs in which eggs are matured, but in the case of PCOS patients these sacs are unable to release the eggs.[4]

PCOS is an endocrine disorder that has impacted around 20-30% of women of reproductive age. It is characterized by the presence of multiple ovarian cysts, menstrual irregularities, infertility, excessive hair growth and acne, and a high metabolic disorders risk like obesity and diabetes mellitus.[5] The occurrence of PCOS is notably higher in Pakistan and about 52% of females are encountered as compared to different countries.[6] This high rate indicates the effect of PCOS on the female reproductive system severely.[7]

Hormonal imbalances significantly influence the reproductive system in PCOS, leading to abnormalities such as weight gain, infertility, and excessive hair growth. Women of reproductive age are susceptible to this complex hormonal condition.[8] While irregular periods, high androgen levels, and polycystic ovaries are diagnostic indicators of PCOS in fertile women, the symptoms and available treatments differ from person to person.[9]

The hormonal profiles in PCOS patients typically show altered concentrations of FSH, LH, prolactin, and testosterone compared to healthy females. There is also a potential association between PCOS and fasting blood sugar levels, as women with PCOS are often insulin-resistant. This resistance can lead to inadequate insulin utilization, increasing the risk of elevated fasting blood sugar or type 2 diabetes.[10]

METHODOLOGY

This case-control study was conducted in the Obstetrics and gynecological department of Shifa Hospital, Karachi from December 2022 to June 2023.Approval was obtained from the Institutional Review Board (IRB) under reference number FRC-BUHS-50/2022-512. For the calculation of the sample size, results are calculated from Open Epi, Version 3, open-source calculator—SS Propor is utilized. The required sample size was found to be 105 by using the equation

- Sample size n = [DEFF*Np(1-p)]/ [(d2/Z21-α/2*(N-1)+p*(1-p)]

Sampling was done using a non-probability consecutive sampling technique.

INCLUSION CRITERIA: The inclusion criteria for the study were divided into three groups. The PCOS diagnosed group consisted of women aged 15-45 years with a history of oligomenorrhea and/or anovulation, serum testosterone levels of ≥ 2.5 nmol/L indicating clinical hyperandrogenism, and ultrasonographic evidence of polycystic ovaries. The healthy group included women aged 15-45 years who did not meet the Rotterdam criteria for PCOS. Lastly, the predisposed group comprised women aged 15-45 years with a family history of PCOS.

EXCLUSION CRITERIA: The study excluded women aged <15 and > 45 years, as well as patients currently undergoing treatment for PCOS. Additionally, Patients with 21-hydroxylase deficiency, congenital adrenal hyperplasia, Cushing's syndrome, ovarian tumours, thyroid disease and hyperprolactinaemia were not included. Furthermore, patients taking antidepressants and anxiolytics were excluded from the study

Written informed consent was obtained from the patients prior to their enrollment, ensuring their confidentiality throughout. When the patients attended the outpatient department (Obs and gynae opd) and had been assessed by the consultants, they were sent for their lab tests. The tests included hormonal profile such as FSH, LH, Prolactin, serum

Testosterone levels, fasting blood sugar and fasting insulin and HbA1c. Blood samples for serum FSH, LH, prolactin, and testosterone were collected during the follicular phase (2nd or 3rd day of the menstrual cycle) and sent to the PNS Shifa hospital laboratory. Serum FSH was measured using the Roche FSH Elisa kit (Cat No. 0062576), serum LH with the Roche LH Elisa kit (Cat No. 00621030), serum prolactin with the Roche FSH Elisa kit (Cat No. 00655494), and serum testosterone with the Roche FSH Elisa kit (Cat No. 00688765). Fasting blood sugar was measured using the Roche Elisa kit (Cat No. 625672). Fasting insulin levels were measured using the electrochemiluminescence immunoassay method (Roche Diagnostics GmbH, Mannheim, Germany, Cat No. 682501), and HbA1C was measured using the Roche Elisa kit (Cat No. 708797). The blood reports were assessed. In order to assess BMI, height was measured using measuring tape and weight was determined by means of weighing scale. Transvaginal ultrasound scans of the ovaries were performed using the 5-MHz transvaginal transducer.

Data Analysis was performed by IBM SPSS Statistics version 26. Qualitative variables were presented in terms of frequency. Quantitative variables were presented in term of mean and standard deviation. Mean comparison of quantitative variable was done by one Way ANOVA test. $P \leq 0.05$ was considered as significant.

RESULTS:

A total of 105 participants were included in this study. The mean age of participants was 28.21 years with ages ranging from 16 to 44 years. The descriptive of study population is shown in Table-I.

Table-I: Descriptive Statistics of Study Population (n=105)

		n (%)
Groups	**Case**	35 (33.33%)
	Control	35 (33.33%
	Pre-disposed group	35 (33.33%)
Occurrence of Oligo/Anovulation	**Yes**	35 (33.3%)
	No	70 (66.7%)
Occurrence of Hyperandrogenism	**Yes**	19 (18.1)
	No	86 (81.9)
Occurrence of Hirsutism	**Yes**	30 (28.6%)
	No	75 (71.4%)
Occurrence of Polycystic Ovaries	**Yes**	20 (19%)
	No	85 (81%)
Subjects with family history of PCOS	**Yes**	55 (52.4%)
	No	50 (47.6%)
		Mean (Range)
Age (years)		28.21 (16 - 44)
Height(cm)		143.52 (132 -168)
Weight(kg)		55.42 (36 – 97)
Mass Index(kg/m2)		26.56 (17.90 - 44.28)
FSH (mIU/ml)		6.61 (3.40 - 8.80)
LH (mIU/ml)		10.75 (6.80 - 14.50)
Testosterone (nmol/L)		1.67 (1.10 - 2.49)
Prolactin (µg/L)		1.00 (0.10 -1.90)
LH FSH Ratio		1.67 (1.10 – 2.4)
Fasting Blood Glucose (mmol/L)		5.10 (4.10 – 7.20)
Fasting Insulin Levels (mIU/ml)		8.44 (0.80 -22.80)

HbA1c (%)	5.19 (4.52 -7.00)

Table-II demonstrates the frequency distribution and association of age groups and BMI groups according to study groups. There was insignificant association of study group with age group i-e (p=0.721) while the significant association of obesity (p=0.000) with the study groups was found.

TABLE-II: Association between Age, BMI, and PCOS Status (n=105)

		Study Group			P-VALUE
		Case	**Control**	**Probable**	
Age Groups in Years	<30 years	21(31.8)	21(31.8)	24(36.4)	0.721**
	>30 years	14(35.9)	14(35.9)	11(28.2)	
BMI Groups	Non Obese (<30 kg/m^2)	9(13)	31(44.9)	29(42)	0.000*
	Obese (≥30 kg/m^2)	26(72.2)	4(11.1)	6(16.7)	

Table-III shows mean comparison of biochemical Parameters according to study groups. By applying One Way ANOVA Test, we found significant mean difference for body mass index (p=0.000), serum FSH (p=0.000), serum LH (p=0.009), LH FSH ratio (p=0.000), serum testosterone (p=0.000), prolactin (p=0.000), fasting blood glucose (p=0.000), fasting insulin level (p=0.000), HbA1c (p=0.000).

Table-III: Mean comparison of biochemical parameters according to study groups (n=105)

Biochemical Parameters	**Study Group Mean± Std. Deviation**			**P-Value**
	Case	**Control**	**Probable**	
Age (years)	28.85±6.37	28.17±7.04	25.94±5.47	0.137
Body Mass Index (kg/m^2)	30.91±5.66	22.69±5.07	26.08±7.36	0.000*
S.FSH (mIU/ml)	5.68±1.23	7.59±0.97	6.56±0.80	0.000*
S. LH (mIU/ml)	11.35±1.87	10.19±1.44	10.70±1.22	0.009*
LH FSH Ratio	2.02±0.23	1.34±0.11	1.64±0.18	0.000*
S. Testosterone (nmol/L)	1.20±0.42	0.78±0.45	1.02±0.33	0.000*
Prolactin (µg/L)	24.40±9.50	15.34±3.07	17.93±4.18	0.000*
Fasting Blood Glucose (mmol/L)	5.55±0.91	4.98±0.40	4.76±0.38	0.000*

Fasting Insulin levels (mIU/ml)	11.63±5.65	5.85±2.91	7.85±4.19	0.000*
HbA1c	5.54±0.78	5.09±0.39	4.94±0.31	0.000*

Table-IV illustrates the results of mean comparisons with the detail description of all variables like age, BMI, serum FSH, serum LH, serum Testosterone, serum prolactin, LH: FSH, Fasting blood sugar, Fasting insulin levels and HbA1c. Post hock Tukey HSD test was applied. P<0.05 considered as significant

Table-III: Multiple mean comparisons of biochemical parameters according to study groups (n=105)

Variable	(I) Study Group	(J) Study Group	Mean Difference	P-Value
Age (years)	Case	Control	2.94	0.120
		Probable	4.88*	0.004*
	Control	Case	-2.94	0.120
		Probable	1.94	0.391
	Pre-disposed	Case	-4.88*	0.004*
		Control	-1.94	0.391
Body Mass index (kg/m^2)	Case	Control	8.21*	0.000*
		Pre-disposed	4.82*	0.004*
	Control	Case	-8.21*	0.000*
		Pre-disposed	-3.38	0.058
	Pre-disposed	Case	-4.82*	0.004*
		Control	3.38	0.058
S.FSH (mIU/ml)	Case	Control	-1.90*	0.000*
		Pre-disposed	-0.87*	0.001*
	Control	Case	1.90*	0.000*
		Pre-disposed	1.03*	0.000*
	Pre-disposed	Case	.87*	0.001*
		Control	-1.03*	0.000*

S. LH (mIU/ml)	Case	Control	1.15*	0.006*
		Pre-disposed	0.64	0.191
	Control	Case	-1.15	0.006*
		Pre-disposed	-0.51	0.351
	Pre-disposed	Case	-0.64	0.191
		Control	0.51	0.351
LH FSH ratio	Case	Control	0.68	0.000*
		Pre-disposed	0.38	0.000*
	Control	Case	-0.68	0.000*
		Pre-disposed	-0.29	0.000*
	Pre-disposed	Case	-0.38*	0.000*
		Control	0.29*	0.000*
S.Testosterone (nmol/L)	Case	Control	0.41*	0.000*
		Pre-disposed	0.17	0.191
	Control	Case	-0.41	0.000*
		Pre-disposed	-0.24	0.041*
	Pre-disposed	Case	-0.17	0.191
		Control	0.24	0.041*
Prolactin (µg/L)	Case	Control	9.06	0.000*
		Pre-disposed	6.47	0.000*
	Control	Case	-9.06	0.000*
		Pre-disposed	-2.58	0.200
	Pre-disposed	Case	-6.47	0.000*
		Control	2.58	0.200
Fasting Blood Glucose (nmol/L)	Case	Control	0.57	0.001*
		Pre-disposed	0.78	0.000*
		Case	-0.57	0.001*

	Control	Pre-disposed	0.21	0.333
	Pre-disposed	Case	-0.78	0.000*
		Control	-0.21	0.333
Fasting Insulin levels (Miu/ml)	Case	Control	5.78	0.000*
		Pre-disposed	3.78	0.001*
	Control	Case	-5.78	0.000*
		Pre-disposed	-1.99	0.145
	Pre-disposed	Case	-3.78	0.001*
		Control	1.99	0.145
HbA1c (%)	Case	Control	0.44	0.002*
		Pre-disposed	0.59	0.000*
	Control	Case	-0.44	0.002*
		Pre-disposed	0.15	0.470
	Pre-disposed	Case	-0.59	0.000*
		Control	-0.15	0.470

DISCUSSION

The term polycystic ovary syndrome (PCOS) refers to the endocrine and metabolic disorder that affects 6 to 21% of women of reproductive age, depending on the mean body mass index (BMI), diagnostic criteria, and population used.[11] The researchers in the 1980s reported and explored an association between hyperandrogenism and hyper-insulinemia and revealed the possible aetiologies and complicated reproductive and metabolic conditions with economic and psychosocial consequences across the lifetime.[12] These revolutionary studies identify the relationship of PCOS with various hormones and chemical mediators of the body that contribute to health issues and clinical features. Hormonal changes lead to follicle maturation and ovary deregulation in people with PCOS.

In the present study, out of the included females, case group had a greater mean age as compared to the control group and probable group. Research showed no significant age difference between the groups; hence the age was matched among all the groups. A study conducted by Cakir et al. found that women with PCOS have a higher mean age than controls validating the findings of our study showing a greater mean age in the case group.[13] Carmina et al. found that PCOS severity and metabolic abnormalities increased with age at diagnosis.[14] In contrast, Sousa et al. found no significant difference in mean age between PCOS patients and controls. They found that age may not affect PCOS

development or diagnosis.[15]

Hormonal imbalances play a key role in the development of PCOS, and the levels of Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH) are particularly relevant.[16] FSH and LH imbalances in PCOS women impair ovulation and cause ovarian cysts. The mean serum FSH, LH, and LH/FSH ratios reveal the study participants' hormonal profiles. PCOS and FSH/LH levels are disputed; the altered hypothalamic-pituitary-ovarian feedback system may cause increased FSH levels in PCOS.[17] As a result of this communication breakdown, FSH output rises to compensate for ovulation. However, other studies suggest that FSH levels may not differ between women with PCOS and those without the illness.[18] The LH ratio needs to be reviewed as the normal concentration of testosterone; it is less than 150 ng/dL (≤5.2 nmol/L), this seems effective while reviewing the lower level for PCOS. For example, the specific testosterone values ≤150 ng/dL (≤5.2 nmol/L) show an increase in PCOS, but at the same time if its value is ≥200 ng/dL (≥6.9 nmol/L), which is for a female that might have an ovarian tumor.[19]

PCOS and insulin resistance are linked, hence HbA1c values may be important when discussing PCOS.[20] Polycystic ovarian syndrome (PCOS) is not diabetes, although it increases the risk of insulin resistance and poor glucose metabolism in women. In the present study, PCOS patients had higher fasting insulin levels than controls. The PCOS group had 11.63±5.65 mIU/ml fasting insulin, while the control group had 5.85±2.91 Miu/ml. These findings support PCOS's substantial relationship with insulin resistance. According to Zhang et al., women with PCOS could be more likely to experience insulin resistance, which may result in higher levels of glucose in the blood and could lead to a high HbA1c.[21] However, GÜNGÖR et al. found no significant difference in HbA1C between groups.[22] Despite contradicting findings, PCOS is linked to higher HbA1C levels. In women with PCOS, HbA1C was positively correlated with androgen levels suggesting a link between hormonal dysregulation and glycemic management.[21]

In the current study, PCOS is associated with elevated prolactin levels. PCOS and controls have similar prolactin levels in a study conducted by Mahboobifard et al.[23] Some findings demonstrate that PCOS may not continuously have increased prolactin levels; some authors suggest that BMI and insulin resistance may explain prolactin variations.[24]

Compared to the probable and control groups, the case group had the highest mean serum testosterone level (1.20±0.42 nmol/L). Serum testosterone levels varied significantly between groups (p=0.000). These findings indicate that the case group has the highest testosterone level. Zhang et al. examined serum testosterone levels in PCOS and non-PCOS women. This study found that PCOS patients had greater testosterone levels than controls. PCOS patients' high testosterone levels encourage hyperandrogenism.[25] Sendur et al. reviewed studies on androgen levels in PCOS women and controls. PCOS patients had greater testosterone levels across all Middle Eastern women and Australian women, according to the analysis. These findings support the present study's observation of higher serum testosterone levels in the case group than in the control group.[26]

LIMITATION OF THE STUDY

The study is self-funded and does not receive any research funds from any institute or organization. It is a single-centered study conducted within a specific location or institution. The study has a short duration of six months. The sample size for the study is small.

CONCLUSION

The conclusion of the study indicates that there is a significant association between hormonal imbalances and the presence of PCOS, even in fertile women. The finding suggests that hormonal dysregulation is a key characteristic of PCOS irrespective of fertility status highlighting the need for targeted hormonal assessment and management in all women diagnosed with PCOS to improve overall health outcomes.

CONFLICT OF INTEREST:

None

FUNDING SOURCES

None

ACKNOWLEDGEMENT

We would like to acknowledge all those who participated directly or indirectly in the study.

REFERENCES:

1. Szukiewicz D, Trojanowski S, Kociszewska A, Szewczyk G. Modulation of the inflammatory response in polycystic ovary syndrome (PCOS)—searching for epigenetic factors. International journal of molecular sciences. 2022 Nov 24;23(23):14663. https://doi.org/10.3390/ijms232314663
2. Abraham Gnanadass S, Divakar Prabhu Y, Valsala Gopalakrishnan A. Association of metabolic and inflammatory markers with polycystic ovarian syndrome (PCOS): an update. Archives of Gynecology and Obstetrics. 2021 Mar;303:631-43. https://doi.org/10.1007/s00404-020-05951-2
3. Dou J, Puttabyatappa M, Padmanabhan V, Bakulski KM. Developmental programming: Adipose depot-specific transcriptional regulation by prenatal testosterone excess in a sheep model of PCOS. Molecular and cellular endocrinology. 2021 Mar 1;523:111137. https://doi.org/10.1016/j.mce.2020.111137
4. Mukerjee N. Polycystic Ovary Syndrome (PCOS) symptoms, causes & treatments-a review. International Journal of Science and Research. 2020 Aug;9(7):1949-57. DOI: 10.21275/SR20729004350
5. Zeng LH, Rana S, Hussain L, Asif M, Mehmood MH, Imran I, Younas A, Mahdy A, Al-Joufi FA, Abed SN. Polycystic ovary syndrome: a disorder of reproductive age, its pathogenesis, and a discussion on the emerging role of herbal remedies. Frontiers in Pharmacology. 2022 Jul 18;13:874914. https://doi.org/10.3389/fphar.2022.874914
6. Naz S, Anjum N, Gul I. A community based cross sectional study on prevalence of polycystic ovarian syndrome (PCOS) and health related quality of life in Pakistani females. https://doi.org/10.21203/rs.3.rs-47444/v1
7. Liu Y, Hao H, Lan T, Jia R, Cao M, Zhou L, Zhao Z, Pan W. Physiological and pathological roles of Ang II and Ang-(1-7) in the female reproductive system. Frontiers in Endocrinology. 2022 Dec 23;13:1080285. https://doi.org/10.3389/fendo.2022.1080285
8. Stener-Victorin E, Deng Q. Transmission of polycystic ovary syndrome via epigenetic inheritance. Trends in Molecular Medicine. 2021 Aug 1;27(8):723-4. https://doi.org/10.1016/j.molmed.2021.05.005
9. Zehravi M, Maqbool M, Ara I. Polycystic ovary syndrome and infertility: an update. International journal of adolescent medicine and health. 2022 Apr 18;34(2):1-9. https://doi.org/10.1515/ijamh-2021-0073
10. Pani A, Gironi I, Di Vieste G, Mion E, Bertuzzi F, Pintaudi B. From prediabetes to type 2 diabetes mellitus in women with polycystic ovary syndrome: lifestyle and pharmacological management. International Journal of Endocrinology. 2020 Jun 8;2020. https://doi.org/10.1155/2020/6276187
11. McCartney CR, Marshall JC. Polycystic ovary syndrome. New England Journal of Medicine. 2016 Jul 7;375(1):54-64. **DOI: 10.1056/NEJMcp1514916**
12. Ramanand SJ, Ghongane BB, Ramanand JB, Patwardhan MH, Ghanghas RR, Jain SS. Clinical characteristics of polycystic ovary syndrome in Indian women. Indian journal of endocrinology and metabolism. 2013 Jan 1;17(1):138-45. https://doi.org/10.4103%2F2230-8210.107858
13. Cakir E, Sahin M, Topaloglu O, Colak NB, Karbek B, Gungunes A, Arslan MS, Unsal IO, Tutal E, Ucan B, Delibasi T. The relationship between LH and thyroid volume in patients with PCOS. Journal of ovarian research. 2012 Dec;5:1-6. https://doi.org/10.1186/1757-2215-5-43
14. Carmina E, Campagna AM, Lobo RA. A 20-year follow-up of young women with polycystic ovary syndrome. Obstetrics & Gynecology. 2012 Feb 1;119(2 Part 1):263-9. https://doi.org/10.1097/aog.0b013e31823f7135

15. de Sousa G, Schlüter B, Buschatz D, Menke T, Trowitzsch E, Andler W, Reinehr T. A comparison of polysomnographic variables between obese adolescents with polycystic ovarian syndrome and healthy, normal-weight and obese adolescents. Sleep and Breathing. 2010 Feb;14:33-8. https://doi.org/10.1007/s11325-009-0276-0
16. Mahmud, A.A., Anu, U.H., Foysal, K.A., Hasan, M., Sazib, S.M., Ragib, A.A., Taher, A.B., Hossain, M.S., Islam, M.S., Hossain, M.S. and Emran, T.B., 2022. Elevated serum malondialdehyde (MDA), insulin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and thyroid-stimulating hormone (TSH), and reduced antioxidant vitamins in polycystic ovarian syndrome patients. Narra J, 2(1). https://doi.org/10.52225/narra.v2i1.56
17. Barontini M, García-Rudaz MC, Veldhuis JD. Mechanisms of hypothalamic-pituitary-gonadal disruption in polycystic ovarian syndrome. Archives of medical research. 2001 Nov 1;32(6):544-52. https://doi.org/10.1016/S0188-4409(01)00325-3
18. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, Lizneva D, Natterson-Horowtiz B, Teede HJ, Yildiz BO. Polycystic ovary syndrome. Nature reviews Disease primers. 2016 Aug 11;2(1):1-8. https://doi.org/10.1038/nrdp.2016.57
19. Kadiroğulları P, Demir E, Bahat PY, Kıyak H, Seckin KD. Evaluation of relationship between HbA1c levels and ovarian reserve in patients with type 1 diabetes mellitus. Gynecological Endocrinology. 2020 May 3;36(5):426-30. https://doi.org/10.1080/09513590.2019.1708893
20. Guler I, Himmetoglu O, Turp A, Erdem A, Erdem M, Onan MA, Taskiran C, Taslipinar MY, Guner H. Zinc and homocysteine levels in polycystic ovarian syndrome patients with insulin resistance. Biological trace element research. 2014 Jun;158:297-304. https://doi.org/10.1007/s12011-014-9941-7
21. Zhang B, Wang J, Shen S, Liu J, Sun J, Gu T, Ye X, Zhu D, Bi Y. Association of androgen excess with glucose intolerance in women with polycystic ovary syndrome. BioMed research international. 2018 Mar 8;2018. https://doi.org/10.1155/2018/6869705
22. GÜNGÖR ND, Gürbüz T, OKÇU NT. Correlation between HbA1c and fibrocystic breast disease among polycystic ovary syndrome. Cumhuriyet Medical Journal. 2020 Oct 27;42(3):383-9.
23. Mahboobifard F, Rahmati M, Amiri M, Azizi F, Tehrani FR. To what extent does polycystic ovary syndrome influence the cut-off value of prolactin? Findings of a community-based study. Advances in Medical Sciences. 2022 Mar 1;67(1):79-86. https://doi.org/10.1016/j.advms.2021.12.003
24. Glezer A, Santana MR, Bronstein MD, Donato Jr J, Jallad RS. The interplay between prolactin and cardiovascular disease. Frontiers in Endocrinology. 2023 Jan 10;13:1018090. https://doi.org/10.3389/fendo.2022.1018090
25. Zhang HY, Zhu FF, Xiong J, Shi XB, Fu SX. Characteristics of different phenotypes of polycystic ovary syndrome based on the Rotterdam criteria in a large-scale Chinese population. BJOG: An International Journal of Obstetrics & Gynaecology. 2009 Nov;116(12):1633-9.
26. Sendur SN, Yildiz BO. Influence of ethnicity on different aspects of polycystic ovary syndrome: a systematic review. Reproductive biomedicine online. 2021 Apr 1;42(4):799-818. https://doi.org/10.1016/j.rbmo.2020.12.006