Hormonal Profile in PCOD patients: A Case-Control Study at a Tertiary Care Center

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Abstract:
Background: Polycystic ovarian syndrome (PCOS) is commonest endocrine disorder among females of reproductive globally. Stein and Leventhal 1st described PCOS in 1935. The prevalence of PCOS ranged between 5% to 15% based on the diagnostic criteria. Existing literature on the hormonal profile is PCOS is less. Hence the current study was undertaken. The objective of this study to is know the hormonal profile in PCOS patients when compared to normal or healthy controls.
Materials and Methods: This case-control study was done at a tertiary care center among 100 subjects in the department of Biochemistry at Kurnool Medical College, Andhra Pradesh, from July 2022 to December 2022. Group C includes 50 female controls or normal subjects. Group P includes 50 females diagnosed with PCOS. All subjects were aged above 18 years. Hormonal levels between two groups of patients were assessed and compared.
Results: There is no significant difference in the mean age of patients in both groups. There is a significant difference in thyroid-stimulatinghormone (TSH), prolactin, luteinizinghormone (LH), Follicle stimulating hormone (FSH), and testosteronelevels between cases and controls.All these levels were more in cases compared to controls. LH/FSH ratio is also significantly more in cases compared to controls.The incidence of hirsutism is significantly more in cases compared to controls.
Conclusion:We found that PCOS is associated with abnormal thyroid profile and reproductive hormones. This implies the significance of early correction of thyroid disorders in managing fertility issues associated with PCOS. All women with PCOS should have their thyroid function tests and hormonal tests monitored regularly.
Key Words:Hormonal profile, Polycystic ovarian syndrome, Prolactin, Case-control study, Thyroid profile, Obesity

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I. Introduction

Polycystic ovarian syndrome (PCOS) is commonest endocrine disorder among females of reproductive globally. Stein and Leventhal 1st described PCOS in 1935. The prevalence of PCOS ranged between 5% to 15% based on the diagnostic criteria. Diagnosis of PCOS is based on the presence of a minimum of two of the following criteria:

- Chronic anovulation
- Hyperandrogenism and
- Polycystic ovaries.

Environment playsa vital role in the expression of triggering genes and the progression of the disease.[1-3]PCOS is commonly underdiagnosed and takes ≥ 1 visitor and these commonly occur in more than a 1-year timeframe. A delay in diagnosis can cause the progression of various comorbidities, making it challenging to implement lifestyle interventions, which is critical for improving the quality of life. Comorbidities include metabolic syndrome, infertility, obesity, impaired glucose tolerance, type 2 diabetes, depression, endometrial cancer, obstructive sleep apnea and non-alcoholic fatty liver disease.

Differential diagnoses of PCOS include thyroid disease, congenital adrenal hyperplasia and hyperprolactinemia. All PCOS patients need more extensive workup if clinical features suggest other causes.[4-6] There is more chance to have abnormal thyroid profile, serum prolactin, follicle-stimulating hormone (FSH), Luteinizing hormone (LH), oestrogen and testosterone levels in patients with PCOS. Existing literature on the hormonal profile is PCOS is less. Hence the current study was undertaken.

Objective: The objective of this study to is know the hormonal profile in PCOS patients when compared to normal or healthy controls.

II. Materials And Methods

Source of data and type of study: This observative case-control study was done on patients who came to outpatient unit of a tertiary care center named Kurnool medical college and general hospital.

Study Design: Observational, case-control study

Study Location: This study was done at a tertiary care teaching hospitalin the Department of Biochemistry at Kurnool Medical College and General Hospital, Kurnool, Andhra Pradesh.

Study Duration: The study was done for 6 months from July 2022 to December 2022.

Sample size: 100 patients

Sample size calculation:

In India, the prevalence of PCOS ranges from 5.5 to 22.5%[7-8] based on diagnostic criteria used. Considering the prevalence as 22.5%, the sample size is estimated as follows:

$$N=Z^2PQ/E^2$$
$$N=\text{Sample size}$$
$$P=\text{Prevalence}$$
$$Q=1-P$$
$$N=93$$
$$\text{Confidence levels -75\%(power)}$$
$$\text{Error-5\%}$$

93 is the minimum sample size. So, we included 100 patients in our study, considering few losses to follow-up and incomplete data.

Subjects and selection method: Group P: 50 patients diagnosed to have PCOS.

Group C: 50 patients who were normal or healthy controls, who came with patients (accompanying persons).

Inclusion criteria:
* Females aged above 18 years
* Patients who provided informed consent to participate in the study
* Cases: Patients diagnosed with PCOS as per Androgen excess PCOS society
* Controls: Normal regular menstruating women

Exclusion criteria:
* Patients with hypothyroidism
* Patients with diabetes, congenital adrenal hyperplasia
* Patients with hypertension
* Patients with hyperprolactinemia
* Patients with androgen-secreting tumors
* Smokers
* Pregnant and lactating women
* Patients with cardiovascular disorders
* Patients using hormonal contraceptives

Parameters assessed:
* Age
* TSH(Thyroid-stimulating hormone) levels
* FSH
* LH
* Prolactin
* Testosterone levels
* LH/FSH ratio
* Incidence of hirsutism

Normal levels:

Normal levels of FSH: 3-20 mIU/ml

Normal levels of LH< 7mIU/ml

Normal levels of TSH 0.4-4 uIU/ml

Normal levels of prolactin< 24 ng/ml on the third day of menses.

Normal levels of testosterone in women: 15 to 70 ng/dl.

Sample collection: After overnight fasting, samples were collected in the morning on 3rd day of menses. The samples were left for 1hour and then, the serum was separated by centrifugationat 3000 rotations per minute for 10 minutes. The samples were analyzed by Chemiluminescence immunoassay (CLIA) process using fully automated analyzer.

Ethical considerations: Ethical committee approval was taken before conducting the study. The informed consent form was taken from every parent of infants who participated in the study.

Statistical analysis:

Data analysis was done using Epi Info software version 7.2.5. The results were expressed as mean ± S.D, percentages, and all numerical parameters were compared between two groups using students'T-test. Comparison of proportions or categorical parameters was done using the chi-square test. P value < 0.05 was considered significant.

III. Results

Age: The mean age of subjects in group C was 22.4±2.3 years and the mean age of subjects in group P was 24.9±2.0 years. There is no significant difference in age between both groups as per T-test.

Table 1 illustrates the mean age of subjects in each group

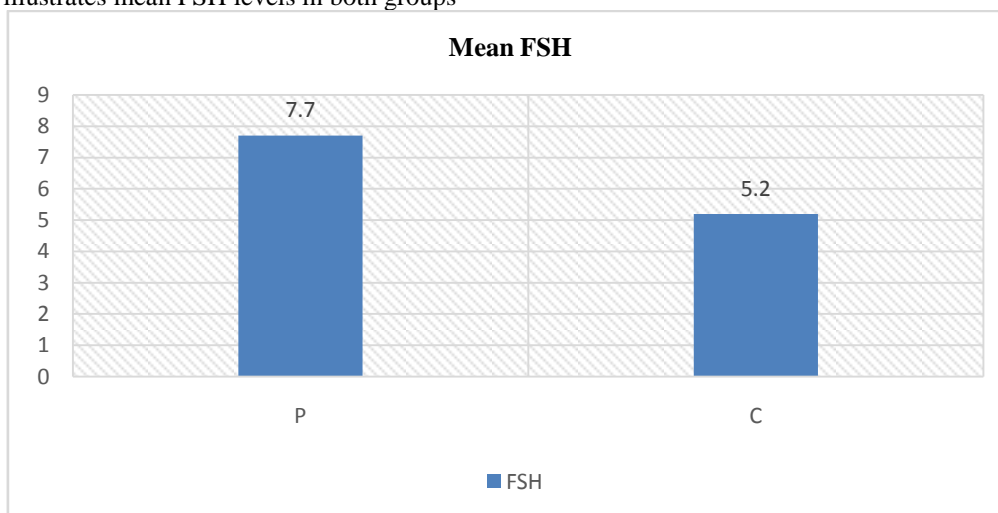| Groups	Mean age	P value
Group P	24.9±2.0	0.27 T value: 1.08
Group C	24.4±2.3	

TSH levels: There is a significant difference in TSH levels in both groups, as per T-test(p=0.0001).

Table 2 illustrates mean TSH levelsin both groups.

Groups	Mean weight	P value
Group P	6.12±1.3	0.0001 T value:14.67
Group C	2.6±1.09	

FSH levels: There is a significant difference in FSH levels in both groups, as per T-test(p=0.0001). FSH levels are within normal range in both groups.

Graph 1 illustrates mean FSH levels in both groups

LH levels:

There is a significant difference in LH levels between two groups. It was significantly more in the case group compared to controls.
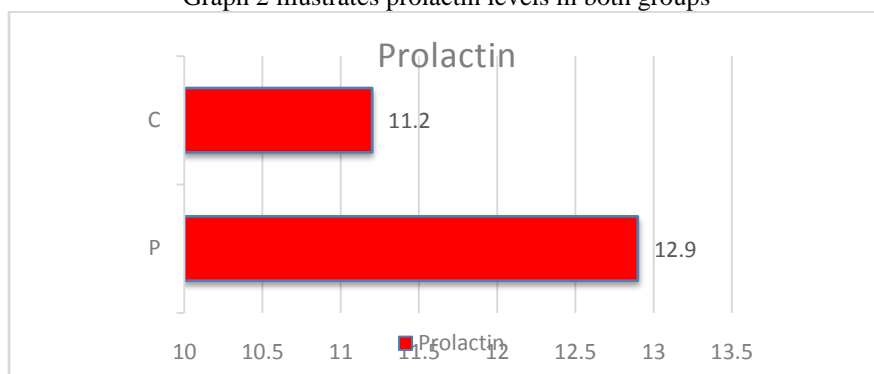
Table 3 illustrates the mean LH levels in both groups

Groups	Mean LH levels	P value
Group P	15.4±6.8	P =0.0001 T=10.41
Group C	5.2±1.3	

Prolactin levels:

There is no significant difference in prolactin levels between the two groups. (p=0.08). Prolactin levels were normal in both groups.

Graph 2 illustrates prolactin levels in both groups

Testosterone levels:

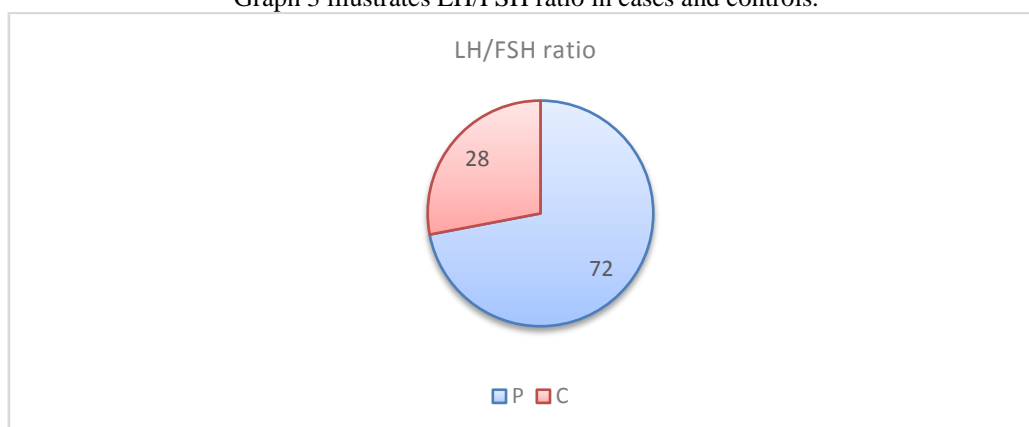There is a significant difference in mean testosterone levels between the two groups of subjects(p=0.001).

Table 4: Mean testosterone levels in both groups

Groups	Mean duration of cry	P value
Group P	74.3±12.1	P =0.0001 T=26.11
Group C	22.3±7.2	

LH/FSH ratio:

This ratio was significantly more in PCOS patients compared to controls. (72% in cases vs 28% in controls), as per chi-square analysis(p=0.0001).
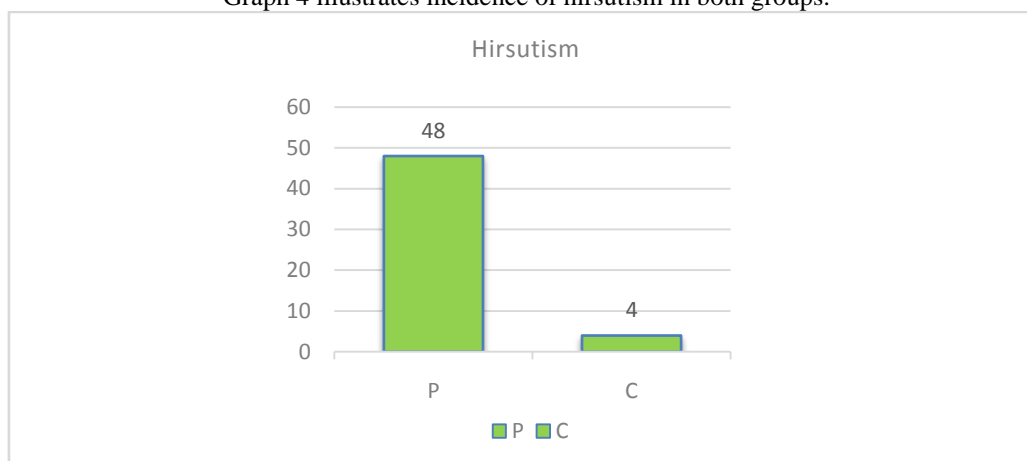
Graph 3 illustrates LH/FSH ratio in cases and controls.

Incidence of hirsutism:

Hirsutism was seen in 48%of cases and 4% of controls. There was a significant difference in the incidence of hirsutism between cases and controls. (p=0.0001).

Graph 4 illustrates incidence of hirsutism in both groups.

IV. Discussion

The current study included 100 subjects. There is no significant difference in the mean age of subjects between both groups. Hence the comparison is justifiable between groups with no age bias. Our study assessed the hormonal profile of PCOS patients compared to normal controls. It was found that all hormonal levels were more among PCOS patients except for prolactin.

There was no significant difference in the mean age between cases and controls.

In the study of **Kiran Dahiya et al.**[9]Among 50 patients, 20 patients were aged 18-25 years, 20 patients were aged 26-30 years. The mean age of PCOS cases was 27.48 ± 4.22 years and mean age of controls was 28.28 ± 3.55 years. There was no significant difference in the mean age, similar to our study.

Our study results showed high LH/FSH ratio, high prevalence of hirsutism and high levels of testosterone among PCOS cases.In the clinical trial done by **Janssen et al.**[10] in 2004, 343 patients with PCOS were included. PCOS patients were found to have more LH/FSH ratio, increased testosterone and a high prevalence of hirsutism, similar to our study results.

LH/FSH ratio is our study was 72% among PCOS patients.

Sinha et al.[11] also identified high LH/FSH ratio in PCOS patients, which is 55%.**Anlakash et al.**[12]reported this to be 64%

Hypothyroidism can cause PCOS-like ovaries and worsening of PCOS and Insulin resistance.[13-14]

In our study, the mean TSH levels were more among PCOS cases compared to controls. This implies that PCOS patients have more chance of hypothyroidism. In the study done by **Tagliaferri et al.**[15]242 PCOS patients were included. Subclinical hypothyroidism was found in 14.28% of PCOS women vs 1.14 % of controls.

Singh J et al.[16] found a significant relationship between the incidence of PCOS and thyroiditis.

In the study of **Jie Cai et al**.[17]TSH level is more in PCOS patients compared to controls, which is 2.29 vs. 1.86 mu/L. TSH level is positively correlated with serum triglycerides, apoB, and negatively associated with apoA levels.

Hefler et al.[18] found a significant elevation in levels ofanti-histone and anti-DNA antibodies among PCOS cases. Also, there is a significant correlation between serum antinuclear antibodies and TSH levels.

The strength of this study was we provided data on abnormal hormonal profiles among PCOS patients. This information helps to take appropriate measures for PCOS patients, which in turn helps to provide better clinical outcomes.

The main limitation of our study is small sample size.

We recommend studies on the assessment of thyroid-specific antibodies and serological markers of autoimmunity in PCOS patients compared to controls.

V. Conclusion

In the current study, we tested the hormonal profile of PCOS patients and compared it with normal subjects.We found that PCOS is associated with abnormal thyroid profiles and reproductive hormones. This implies the significance of early correction of thyroid disorders in managing fertility issues associated with PCOS. All women with PCOS should have their thyroid function tests and hormonal tests monitored regularly.

There were no conflicts of interest.

The study is self-sponsored.

References

[1]. Goyal A, Ganie MA. Idiopathic Hyperprolactinemia Presenting as Polycystic Ovary Syndrome in Identical Twin Sisters: A Case Report and Literature Review. Cureus. 2018 Jul 19;10(7): e3004. [PMC free article] [PubMed]

[2]. Albu D, Albu A. The relationship between anti-Müllerian hormone serum level and body mass index in a large cohort of infertile patients. Endocrine. 2019 Jan;63(1):157-163. [PubMed]

[3]. Spinedi E, Cardinali DP. The Polycystic Ovary Syndrome and the Metabolic Syndrome: A Possible Chronobiotic-Cytoprotective Adjuvant Therapy. Int J Endocrinol. 2018; 2018:1349868. [PMC free article] [PubMed]

[4]. Ding DC, Chen W, Wang JH, Lin SZ. Association between polycystic ovarian syndrome and endometrial, ovarian, and breast cancer: A population-based cohort study in Taiwan. Medicine (Baltimore). 2018 Sep;97(39): e12608. [PMC free article] [PubMed]

[5]. Zhang C, Ma J, Wang W, Sun Y, Sun K. Lysyl oxidase blockade ameliorates anovulation in polycystic ovary syndrome. Hum Reprod. 2018 Nov 01;33(11):2096-2106. [PubMed]

[6]. Norman RJ, Teede HJ. A new evidence-based guideline for assessment and management of polycystic ovary syndrome. Med J Aust. 2018 Sep 01;209(7):299-300. [PubMed]

[7]. Gupta M SD, Toppo M, Priya A, Sethia S, Gupta P. A cross sectional study of polycystic ovarian syndrome among young women in Bhopal, Central India. Int J Community Med Public Health2018; 5:95-100.

[8]. Joshi B, Mukherjee S, Patil A, Purandare A, Chauhan S, Vaidya R. A cross-sectional study of polycystic ovarian syndrome among adolescent and young girls in Mumbai, India. Indian J Endocrinol Metab 2014; 18:317-24.

[9]. Dahiya K, Sachdeva A, Singh V, Dahiya P, Singh R, Dhankhar R, et al. Reproductive Hormone And Thyroid Hormone Profile In Polycystic Ovarian Syndrome. 2012 [cited 2023 Jan 31]; Available from: https://www.webmedcentral.com/article_view/3455

[10]. High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Janssen OE, Mehlmauer N, Hahn S, Offner AH, Gärtner R. Eur J Endocrinol. 2004; 150:363–369. [PubMed] [Google Scholar] [Ref list]

[11]. Sinha U, Sinharay K, Saha S, Longkumer TA, Baul SN, Pal SK. Thyroid disorders in polycystic ovarian syndrome subjects: A tertiary hospital-based cross-sectional study from Eastern India. Indian J Endocrinol Metab. 2013;17(2):304-9

[12]. Anlakash AH. Polycystic ovarian syndrome - The correlation between LH/FSH ratio and disease manifestation. Middle East Fertil Soc J. 2007;12(1):35-40

[13]. Yildiz BO, Bolour S, Woods K, Moore A, Azziz R. Visually scoring hirsutism. Hum Reprod Update. 2010;16(1):51-64.

[14]. Garelli S, Masiero S, Plebani M, Chen S, Furmaniak J, Armanini D, et al. High prevalence of chronic thyroiditis in patients with polycystic ovary syndrome. Eur J ObstetGynecolReprod Biol. 2013;169(2):248-51

[15]. Tagliaferri V, Romualdi D, Guido M, Mancini A, De Cicco S, et al. The link between metabolic features and TSH levels in polycystic ovary syndrome is modulated by the body weight: an euglycaemic-hyperinsulinaemic clamp study. Eur J Endocrinol. 2016 Nov;175(5):433-41. doi: 10.1530/EJE-16-0358. Epub 2016 Aug 10. PMID: 27511825.

[16]. Singh J, Wong H, Ahluwalia N, Go RM, Guerrero-Go MA. Metabolic, Hormonal, Immunologic, and Genetic Factors Associated With the Incidence of Thyroid Disorders in Polycystic Ovarian Syndrome Patients. Cureus. 2020 Nov 24;12(11):e11681. doi: 10.7759/cureus.11681. PMID: 33391917; PMCID: PMC7769736.

[17]. Cai J, Zhang Y, Wang Y, Li S, Wang L, Zheng J, et al. High thyroid stimulating hormone level is associated with hyperandrogenism in euthyroid polycystic ovary syndrome (PCOS) women, independent of age, BMI, and thyroid autoimmunity: A cross-sectional analysis. Front Endocrinol (Lausanne) [Internet]. 2019; 10:222. Available from: http://dx.doi.org/10.3389/fendo.2019.00222

[18]. Hefler-Frischmuth K, Walch K, Huebl W, Baumuehlner K, Tempfer C, Hefler L. Serologic markers of autoimmunity in women with polycystic ovary syndrome. FertilSteril. 2010 May 1;93(7):2291-4. doi: 10.1016/j.fertnstert.2009.01.056. Epub 2009 Mar 17. PMID: 19296936.