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Original Research Article

ANALYSIS OF HYPERANDROGENBISM AND REPRODUCTIVE LOSS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Abstract: *The present study aimed to analyze the level of androgen (testosterone) hormone among PCOS females during reproductive age. Hyperandrogenism is an endocrine disorder characterized by high levels of androgen hormones and is associated with reproductive problems predominantly in women. Blood samples of ten normal and fifty PCOS females were taken from Gujrat, Punjab, Pakistan. Information including age, height, weight, cholesterol, glucose, BMI, and any previous medical record was obtained with the patient's consent. The samples of control and PCOS patients were analyzed through Chemiluminescent Immunoassay (CLIA) for the quantitative determination of testosterone in human serum. The levels of testosterone (mean ± SEM: 2.617 ± 0.1411), glucose (mean ± SEM: 171.5 ± 4.814), cholesterol (mean ± SEM: 209.9 ± 3.674) and BMI (mean ± SEM: ±29.26 ± 1.026) in PCOS was significantly (P<0.0001) high than control subjects (testosterone: mean ± SEM: 1.278 ± 0.1556), (glucose: mean ± SEM: 87.00 ± 6.675), (cholesterol: ± SEM: 96.50 ± 5.480), (BMI: mean ± SEM: 16.21 ± 0.5638) respectively. We conclude that hyperandrogenism may be the cause of infertility in PCOS patients. Hormone replacement therapies may prove to be effective in retrieving the complications induced by hyperandrogenism.*

Keywords: Hyperandrogenism, Polycystic Ovarian Syndrome, Infertility

Introduction

PCOS is a common disease in young females. Patients with this disease may suffer from many complications related to hormonal disturbance, hirsutism, infertility, and lipid profile; many small cysts are formed in the ovary, which fails to regularize the release of eggs (Chang & Dumesic, 2019). Hyperandrogenism is a primary cause of polycystic ovary syndrome at the reproductive age and oligo-anovulation and is often associated with infertility and metabolic disorders. Premenopausal women secreting excess androgens and persons who have metabolic diseases are at high risk for developing polycystic ovary syndrome (Ortiz-Flores et al., 2019). PCOS is a multifarious disease that can influence the fertility rate of the complete physical and mental state of women, although it is mainly found in those females whose menstrual cycle is disturbed. Common symptoms include facial hairs, enlarged ovaries, obesity, and metabolic syndrome. (Ganie et al., 2019). The widespread presence of polycystic ovary disease is more significant in those women who are overweight and have sleep disorders, and this disease depends on several factors, especially genetic and environmental factors (Simon et al., 2020).

Polycystic ovary syndrome is caused by the high prevalence of adrenal hyperandrogenism and a man-made version of chemicals known as a steroid that is made naturally in the human body. They are also known as corticosteroids (Rosenfield & Ehrmann, 2016) Levels of different hormones in PCOS patients.

Excess follicle-stimulating hormone (FSH) concentration is found in the menstrual cycle, and less concentration of anti-Mullerian hormone (AMH) is found in women. The levels of interleukin-6 and interleukin-8 are reduced by the use of three three-month treatments, both the combination of metformin with pioglitazone; also reduced the chances of polycystic ovary disease in females of reproductive age (Shah et al., 2019). Clomiphene citrate is used to increase the rate of fertilization in suspected women of polycystic ovary disease. These women have been treated with laparoscopic ovarian drilling for the irregular menstrual cycle or which has no period at all (Sinha et al, 2019). Usually, the testosterone level is high in women with PCOS (Huang et al, 2019, Zhou et al, 2020). High levels of Chemerin have also been found in patients with polycystic ovary syndrome.

According to the clinical determination, hirsutism and infertility are most common along with many other metabolic disorders that appear in women with polycystic ovary disease (Polyzos et al., 2018). The adrenal and thyroid disorders and diabetes I and II are closely associated with polycystic ovary disease (Zhou et al., 2020).

The main symptoms of this disease are irregular menstrual periods during childbearing age (Akram & Roohi, 2015). In Karachi, the number of women with PCOS along with defects of metabolism is approximately 35.6%. Different parameters of PCOS such as body mass index, diabetes, cardiovascular disease, and dyslipidemia, show more

difference between PCOS and those without PCOS. The incidence of non-fertile women with PCOS in Pakistan is 38.5%, and for women with inflammation in the uterus, fallopian tube, reproductive system, and pelvic inflammation is around 44% (Arain et al., 2015). Approximately 75% of women who are childless have suffered from PCOS because fertilization does not occur in PCOS (Costello et al., 2019).

The diagnostic criteria of PCOS in the clinical presentation have a differential diagnosis. Which is present in 10% of women, which can help in the diagnosis of PCOS (Yamany et al., 2020). PCOS is an endocrine disorder. It can be confirmed by taking an individual's history, such as failure of menses to occur by age 16. Our objective was to analyze hyperandrogenism in women with polycystic ovary syndrome and to find the effects of polycystic ovary syndrome on fertility in women.

Methodology

The study included fifty human females with PCOS and ten healthy normal females. The females were selected based on reproductive age, ranging from 18 to 40. Polycystic ovary syndrome female patients were selected showing all the definite symptoms of hyperandrogenism disease. The symptoms recorded were hirsutism, infertility, obesity, and irregular menstrual cycle (Chang & Dumesic, 2019).

Weight, height, body mass index (BMI), and any previous medical record i.e. demographics and history were recorded. BMI was calculated by taking weight in pounds and height by BMI calculator. According to WHO (2004), a person is considered normal weight if she has a BMI equal to 18.5-24.9 kg/m2, underweight if a BMI is less than 18.5 kg/m2, overweight if she has a BMI equal to 25-29.95 kg/m2 and BMI of 30 kg/m2 or greater is considered to be obese. All females were residents of Gujrat City, Punjab. Any female patient that has signs of cancer or any familial history of fatal disease, i.e., Hepatitis, AIDs, or any genetic disease, was excluded from the study. Informed written consent was obtained from all patients. Female patients with all clinical signs of PCOS having a reproductive age group of 18-45 were included in the study.

The blood samples analysis for testosterone was done at Genomic Lab Rawalpindi, Punjab, Pakistan. Blood samples (2 ml) were taken from healthy women with PCOS. Blood samples were then transferred to the EDTA-coated tubes for further processing. Until centrifugation, they were stored in the refrigerator at 4-6 C. Centrifugation was done within 4 hours of blood collection at 3000rpm at 28 oC for 15 minutes. Serum of blood was isolated in the Eppendorf vials (1.5 ml capacity) and stored at 2-8 C and for longer periods at -10 C until further hormonal analysis. Hormonal testosterone analysis was done using the CL-series TESTO assay (Cat# TESTO112) on a chemiluminescence immunoassay analyzer (CL 900i, Mindray, Gurgaon, India). The analyzer automatically calculated the testosterone concentration of each sample on the master calibration curve from the barcode and 4-parameter logistic curve fitting (4 PLC) with the relative light units (RLUs) generated from three-level calibrators of defined concentration values. The results were shown in the unit of ng/mL. Graph Pad Prism 5 (Graph et al., USA) statistically analyzed androgen serum concentration changes.

Results

The present study revealed a significant increase in testosterone levels during reproductive age (18 – 40 years). The levels of testosterone in PCOS (mean ± SEM: 2.617 ± 0.1411) were significantly (P<0.0001) higher than those control subjects (mean ± SEM: 1.278 ± 0.1556). Similarly, glucose in PCOS (mean ± SEM: 171.5 ± 4.814) was significantly (P<0.0001) higher than control subjects (mean ± SEM: 87.00 ± 6.675), and cholesterol in PCOS (mean ± SEM: 209.9 ± 3.674) was also found significantly (P<0.0001) higher than control subjects (mean ± SEM: 96.50 ± 5.480). The BMI of PCOS was (mean ± SEM: ±29.26 ± 1.026) found higher than control subjects (mean ± SEM: 16.21 ± 0.5638). The age of PCOS was (mean ± SEM: 25.92 ± 0.7300), whereas that of control subjects was (mean ± SEM: 25.20 ± 0.6289).

The current study found that the testosterone level increased in PCOS but not in the control group as shown in Figure

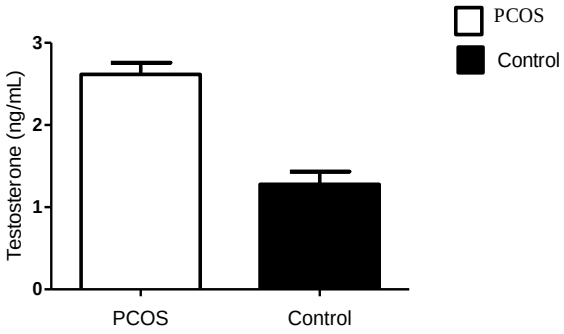

Figure 1 Changes in the Serum Testosterone Levels of Normal and PCOS.

(*The levels of testosterone in PCOS (mean ± SEM: 2.617 ± 0.1411) were significantly (P<0.0001) high than control subjects (mean ± SEM: 1.278 ± 0.1556)*

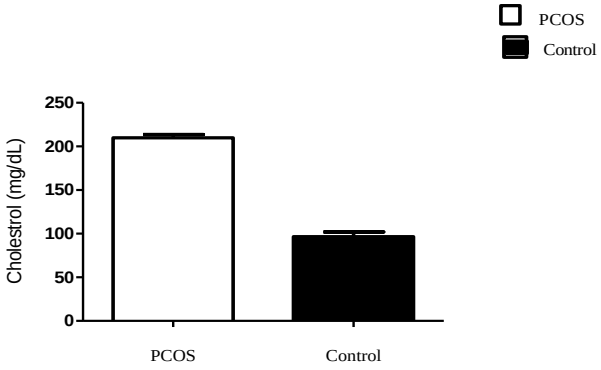

Figure 2 Comparison of Cholesterol Levels between Normal and PCOS.

Cholesterol in PCOS (mean ± SEM: 209.9 ± 3.674) was also found significantly (P<0.0001) higher than in control subjects (mean ± SEM: 96.50 ± 5.480).

A previous study supported our results that testosterone was slightly higher in PCOS patients. They find the correlation between hyperandrogenism, phenotypic features of hyperandrogenism, and hirsutism in women with PCOS.

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Our study showed a strong relationship between higher testosterone levels and BMI. Out of 50, only 35 (71%) participants had a BMI greater than 25 (overweight), and 15 (26%) had 18-25 (normal) BMI, which shows a resemblance with Pasquali, R studies (Pasquali, R. 2006).
Our study clearly showed that the cholesterol of PCOS was up to 220 mg/dL, as the reference value indicated. In contrast, the cholesterol in the non-polycystic ovarian syndrome group was lower and under normal ranges up to (100 mg/dL). A significant ($P \leq 0.05$) increase existed in the PCOS group as shown in Figure 2.
Our result showed similarity with the previous results of Rocha et al., who reported a high cholesterol level in PCOS compared to the control group. So, we agree with the previous findings which reported that an abnormal amount of lipids (210 mg/dL) were found in Korean women with PCOS. Their results align with our studies because our study showed cholesterol levels ranging between 200 and 220 mg/dL, as shown in Figure 4.2 (Rocha et al., 2011).
Our study showed that the glucose level in women with PCOS they have more than 150 mg/dL, while in ordinary women, the glucose level is up to 100 mg/dL. There is a significant ($P \leq 0.05$) increase in the PCOS group as shown in Figure 3.

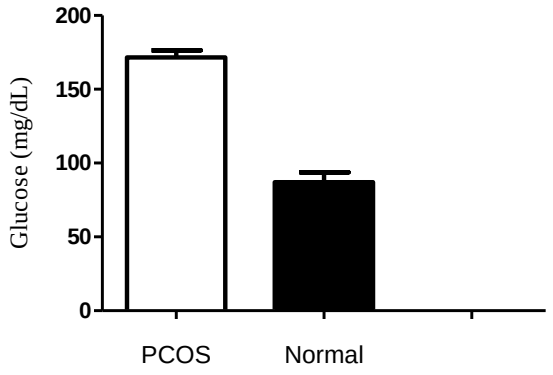

Figure 3. Comparison of Glucose Levels between Normal and PCOS Patients.
Glucose in PCOS (mean ± SEM: 171.5 ± 4.814) was significantly (P<0.0001) higher than in control subjects (mean ± SEM: 87.00 ± 6.675).
It means the results of our thesis showed more similarities with their study (Bu, Kuok, 2012).

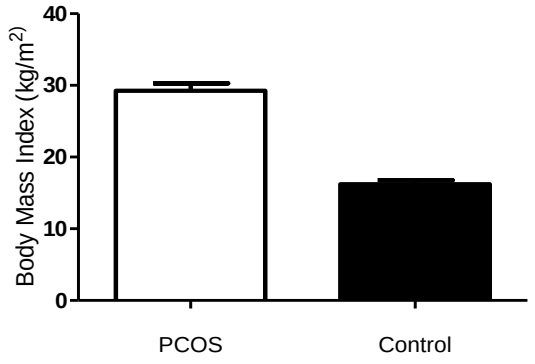

Figure 4 Comparison of BMI between Normal and PCOS Patients.
BMI of PCOS was (mean ± SEM: ±29.26 ± 1.026) found higher than control subjects (mean ± SEM: 16.21 ± 0.5638).

The androgen hormone influences the reproductive status of the female. In the end, we recommend antiandrogen replacement therapies or related medicines to overcome high levels of androgen in the body. As high testosterone level in women leads to infertility, it is suggested to lower androgen in women with PCOS to get relief from the infertility and symptoms of PCOS.

Conclusion

The study indicates that women with PCOS have higher levels of testosterone, glucose, and cholesterol compared to those without the condition. These results highlight the hormonal and metabolic implications of PCOS. The findings are consistent with prior research that suggests a link between hyperandrogenism, BMI, and PCOS symptoms. The study recommends antiandrogen therapies as potential interventions to address high androgen levels and improve reproductive outcomes for those with PCOS. These findings provide a deeper understanding of the complexities of the condition, which can guide future research and targeted treatments. The study emphasizes the importance of addressing hormonal and metabolic imbalances in PCOS for better reproductive health.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department Concerned.
Consent for publication
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Conflict of interest

The authors declared absence of conflict of interest.

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Data entry and Data analysis, drafting article
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