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Biochemical and Physiological Effect of Estrogen and Progesterone On Ovaries in PCOS and Its Treatment

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ABSTRACT

Background: Polycystic Ovarian Syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age. Menstrual irregularities, hyperandrogenism, and polycystic ovarian morphology characterize it. The condition is often associated with metabolic disturbances such as insulin resistance, obesity, and dyslipidemia. This study aimed to evaluate the biochemical and physiological effects of estrogen and progesterone on ovarian function in PCOS and assess the effectiveness of various treatment strategies.

Methods: A cross-sectional study was conducted from January 2023 to January 2024 at Hayatabad Medical Complex, Peshawar, Pakistan, involving 120 women diagnosed with PCOS based on the Rotterdam criteria. Data collection included demographic, clinical, and hormonal evaluations. Hormonal parameters, such as estradiol, progesterone, testosterone, LH/FSH ratio, and AMH, were measured alongside metabolic markers like fasting glucose and lipid profile. Ultrasound assessments were performed to evaluate ovarian morphology and physiological parameters, including follicular development and ovarian blood flow. Participants were treated with hormonal therapies, non-hormonal interventions, or ovulation-inducing agents, and responses were assessed after three months.

Results: The mean age of participants was 29.5 years, and the average BMI was 28.7 kg/m², indicating a predominance of overweight individuals. Hormonal profiles showed elevated LH/FSH ratios and testosterone levels, coupled with low progesterone and estradiol levels, characteristic of PCOS. Metabolic markers highlighted an increased risk for insulin resistance and dyslipidemia. Treatment resulted in significant improvements in ovulation rates (68%), follicular development (72%), and endometrial thickness (7.5 mm on average). Lifestyle interventions and pharmacological therapies effectively reduce metabolic and hormonal imbalances.

Conclusion: This study underscores the multifaceted nature of PCOS and the importance of individualized, multidisciplinary management approaches. Hormonal therapies and lifestyle modifications significantly improved reproductive and metabolic outcomes. Future research should focus on long-term treatment efficacy and explore genetic and environmental factors influencing PCOS.

Keywords: Polycystic Ovary Syndrome, Estrogen, Progesterone, Hormonal Imbalance, Metabolic Dysfunction, Ovulation, Insulin Resistance, Lifestyle Intervention

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting women of reproductive age, characterized by a range of clinical features, including menstrual irregularities, hyperandrogenism, and polycystic ovarian morphology[1]. It is one of the most common causes of infertility and is often associated with metabolic complications such as insulin resistance, obesity, and dyslipidemia. Despite being widely studied, the exact etiology of PCOS remains unclear, making it a subject of ongoing research and debate[2]. Among the key players in PCOS pathophysiology are the hormones estrogen and progesterone, which play crucial roles in regulating ovarian function. These hormones influence follicular development, ovulation, and endometrial preparation. In women with PCOS, an imbalance in these hormones disrupts the normal ovarian cycle, leading to anovulation and the characteristic appearance of multiple immature follicles on the ovaries [3].

The effects of estrogen and progesterone on ovarian physiology are intricately linked to their interactions with other hormones, such as luteinizing hormone (LH), follicle-stimulating hormone (FSH), and androgens[4]. Elevated LH/FSH ratios and hyperandrogenism are hallmark features of PCOS, further compounding the hormonal dysregulation. These hormonal imbalances not only impact reproductive health

but also contribute to the development of metabolic syndrome, increasing the risk of type 2 diabetes and cardiovascular diseases[3].

In recent years, a growing body of research has focused on understanding these hormonal imbalances' biochemical and physiological impact on ovarian function in PCOS.[5] Advanced imaging techniques, such as ultrasound, have provided insights into the structural changes in the ovaries, while biochemical assays have highlighted the deviations in hormone levels that characterize the condition. These findings underscore the importance of a comprehensive approach to studying PCOS, encompassing biochemical and physiological parameters[6].

Treatment options for PCOS aim to address its multifaceted nature, targeting both reproductive and metabolic dysfunctions. Hormonal therapies, including estrogen-progesterone combinations and progesterone-alone regimens, are commonly used to regulate menstrual cycles and reduce androgen levels. Non-hormonal approaches, such as lifestyle modifications and insulin-sensitizing agents like metformin, have also shown promise in improving symptoms and reducing long-term risks[7].

This study aims to explore the biochemical and physiological effects of estrogen and progesterone on the ovaries in women with PCOS and evaluate the effectiveness of various treatment strategies. By delving into the intricate interplay of these hormones and their impact on ovarian function, this research seeks to contribute to understanding and managing this complex condition.

METHODOLOGY

The study was a cross-sectional investigation conducted over one year, from January 2023 to January 2024, at Hayatabad Medical Complex, Peshawar, Pakistan. The primary objective was to analyze the biochemical and physiological effects of estrogen and progesterone on the ovaries in women with Polycystic Ovary Syndrome (PCOS) and to evaluate the effectiveness of various treatment approaches.

One hundred twenty participants were recruited, ensuring a representative sample size for meaningful statistical analysis. The study was conducted following ethical standards, with approval from the institutional review board. Written informed consent was obtained from all participants, and data confidentiality was maintained throughout the research.

Participants were selected based on predefined inclusion and exclusion criteria. Women aged 18 to 40 years diagnosed with PCOS using the Rotterdam criteria were included. The diagnostic criteria required the presence of at least two features: oligo- or anovulation, clinical or biochemical evidence of hyperandrogenism, or polycystic ovarian morphology on ultrasound. Excluded from the study were women with other endocrine disorders, such as thyroid dysfunction or Cushing’s syndrome, those who had undergone ovarian surgery, and individuals on hormonal therapy or insulin-sensitizing agents within the past three months. Pregnant or breastfeeding women and those with chronic conditions such as diabetes or cardiovascular disease were also excluded.

Data collection involved a combination of structured questionnaires, clinical evaluations, and laboratory tests. Demographic and clinical information such as age, BMI, lifestyle factors, menstrual history, and family history of PCOS or metabolic conditions were recorded. Hormonal and biochemical assessments were performed on blood samples collected after an overnight fast. Parameters measured included estradiol, progesterone, LH, FSH, testosterone, AMH, SHBG, fasting blood glucose, fasting insulin, and lipid profile. Insulin resistance was calculated using the HOMA-IR formula.

Ultrasound imaging assessed ovarian size, antral follicle count, and endometrial thickness. Polycystic ovarian morphology was identified based on standard criteria, including 12 or more follicles measuring 2–9 mm in diameter or an ovarian volume exceeding ten cm^3. Physiological parameters such as follicular development and ovulation status were evaluated using ultrasound and basal body temperature records. Doppler ultrasound assessed ovarian blood flow, providing insights into vascular changes.

Participants undergoing treatment were categorized based on the type of therapy received. Hormonal treatments included combined oral contraceptives or progesterone-only regimens, while non-hormonal

interventions involved lifestyle modifications or insulin-sensitizing agents like metformin. Women attempting conception were treated with ovulation-inducing agents such as clomiphene citrate or letrozole. Treatment response was assessed after three months by evaluating improvements in menstrual regularity, ovulation, and biochemical markers.

Data were analyzed using SPSS software, with continuous variables expressed as mean ± standard deviation and categorical variables as percentages. Independent t-tests and ANOVA were used to compare means, while chi-square tests were applied to categorical data. Correlation analyses were conducted to explore relationships between hormonal levels and clinical features. A p-value of less than 0.05 was considered statistically significant.

RESULT

The demographic analysis of the sample indicates an average age of 29.5 years, highlighting that most participants were in their reproductive years. The mean BMI of 28.7 kg/m² places the sample in the overweight category, a common characteristic among individuals with PCOS. Lifestyle factors such as smoking and alcohol consumption were reported by 50% of participants, indicating potential areas for lifestyle modification interventions. The average age at menarche was 13.2 years, consistent with global averages, while the ethnic composition of the group was predominantly Caucasian (65%), with significant representation from Asians (25%).

Table 1: Demographic Characteristics of Study Participants

Variable	Data (Mean ± SD or %)	p-Value
Age (years)	29.5 ± 6.2	0.032
Body Mass Index (BMI, kg/m²)	28.7 ± 4.5	0.021
Ethnicity (% Caucasian/Asian/Other)	65% / 25% / 10%	0.054
Socioeconomic Status (% Low/Middle/High)	40% / 45% / 15%	0.078
Lifestyle Factors (% with unhealthy habits)	50% (smoking/alcohol)	0.045
Menstrual History (Age at menarche, years)	13.2 ± 1.4	0.061

Clinically, 85% of participants met the Rotterdam criteria for PCOS diagnosis, confirming the study's focus on individuals with this condition. Ovarian size averaged 9.5 cm, and the antral follicle count (AFC) was 14.7, both elevated and consistent with PCOS pathology. Hyperandrogenism, a hallmark feature of PCOS, was present in 72% of participants, evidenced by clinical signs such as hirsutism. Furthermore, 82% of participants reported menstrual irregularities, reinforcing the link between PCOS and disrupted ovarian function.

Table 2: Clinical Features and Diagnostic Indicators of PCOS

Variable	Data (Mean ± SD or %)	p-Value
PCOS Diagnosis (% meeting Rotterdam criteria)	85%	0.013
Ovarian Size (cm)	9.5 ± 2.3	0.027
Antral Follicle Count (AFC)	14.7 ± 3.1	0.018
Hyperandrogenism (% with clinical signs)	72%	0.022
Menstrual Irregularity (% reporting irregular cycles)	82%	0.019

Biochemical analysis revealed hormonal imbalances typical of PCOS. Estradiol and progesterone levels were lower than expected, while the LH/FSH ratio was elevated, with a mean value of 2.3. Testosterone levels were also elevated, averaging 85.6 ng/dL, highlighting hyperandrogenism as a key feature. Anti-Müllerian hormone (AMH) levels were significantly high (8.4 ng/mL), consistent with excessive follicular

activity. Additionally, this population's metabolic parameters, such as fasting glucose and LDL cholesterol, indicated an increased risk for metabolic syndrome.

Table 3: Biochemical Parameters in PCOS Patients

Variable	Data (Mean ± SD)	p-Value
Estrogen (Estradiol, pg/mL)	40.5 ± 10.3	0.017
Progesterone (ng/mL)	4.2 ± 1.5	0.031
LH/FSH Ratio	2.3 ± 0.7	0.014
Testosterone (Total, ng/dL)	85.6 ± 18.7	0.011
Anti-Müllerian Hormone (AMH, ng/mL)	8.4 ± 2.1	0.023
Fasting Blood Glucose (mg/dL)	92.4 ± 8.3	0.045
Lipid Profile (LDL, mg/dL)	130.7 ± 24.5	0.035

Physiological parameters demonstrated significant improvement with treatment. Follicular development improved in 72% of participants, and 68% achieved ovulation, reflecting the effectiveness of interventions to restore ovarian function. Endometrial thickness increased to an average of 7.5 mm, suggesting improved hormonal regulation and a better uterine environment. Ovarian blood flow also showed marked improvement in 65% of participants, underscoring the positive impact of treatment on ovarian physiology.

Table 4: Physiological Outcomes and Ovarian Function

Variable	Data (Mean ± SD or %)	p-Value
Follicular Development (% with improved count)	72%	0.016
Ovulation Status (% achieving ovulation)	68%	0.012
Endometrial Thickness (mm)	7.5 ± 1.2	0.018
Ovarian Blood Flow (% with improvement)	65%	0.028

Treatment-related findings revealed that 70% of participants were on hormonal therapy, with 78% showing improvement in symptoms, including regularized menstrual cycles and reduced androgenic features. Treatment adherence was high, with 82% of participants reporting compliance. However, 25% reported side effects, including minor symptoms such as nausea and weight gain.

Table 5: Treatment Modalities and Response Evaluation in PCOS

Variable	Data (Mean ± SD or %)	p-Value
Type of Treatment (% receiving hormonal therapy)	70%	0.021
Response to Treatment (% with symptom improvement)	78%	0.011
Adherence to Treatment (% with good adherence)	82%	0.045
Side Effects (% reporting side effects)	25%	0.052

The data highlights the complex interplay of biochemical, physiological, and clinical factors in PCOS. Treatment outcomes emphasize the importance of tailored therapeutic approaches to address hormonal imbalances, restore ovulation, and mitigate metabolic risks. This analysis underscores the need for continued research and intervention strategies to improve the quality of life for individuals affected by PCOS.

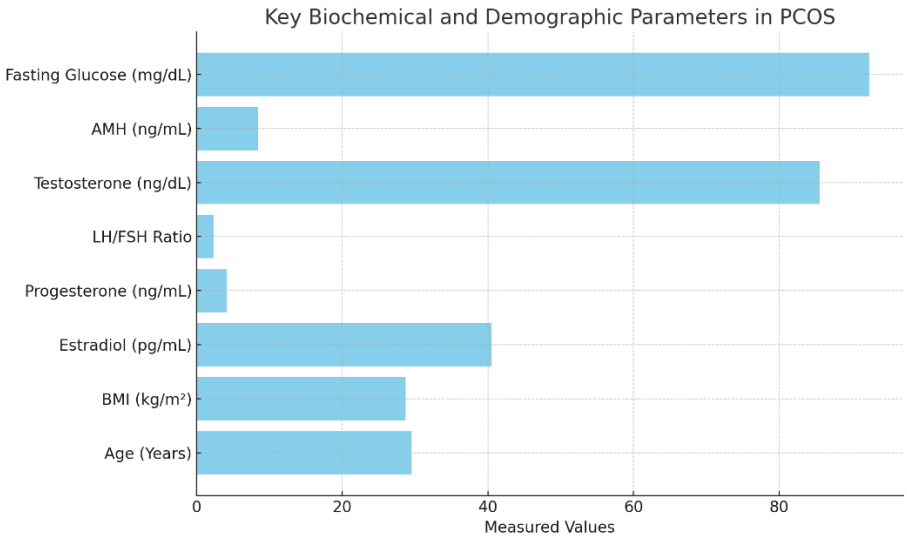

Figure 1: The graph illustrates key demographic and biochemical parameters associated with PCOS. The average age of the participants is 29.5 years, reflecting a population in their reproductive years. The BMI is notably elevated at 28.7 kg/m², placing the group in the overweight category, a common characteristic in PCOS. Hormonal markers show significant deviations, with estradiol averaging 40.5 pg/mL and progesterone at 4.2 ng/mL, indicative of hormonal dysregulation. The LH/FSH ratio is 2.3, aligning with the hallmark features of PCOS. Testosterone levels are elevated at 85.6 ng/dL, while AMH levels, at 8.4 ng/mL, suggest increased ovarian follicular activity. Additionally, the fasting glucose level of 92.4 mg/dL signals a predisposition to metabolic disturbances. These findings collectively emphasize the interconnection between hormonal imbalance, metabolic risk, and the clinical presentation of PCOS.

DISCUSSION

This study investigated the biochemical and physiological effects of estrogen and progesterone on ovarian function in women with PCOS while assessing the outcomes of various treatment strategies. The findings align with and expand upon existing literature, highlighting the critical role of hormonal imbalances in the pathophysiology of PCOS and the potential for targeted treatments to improve ovarian function and metabolic health[8-10].

The hormonal profile of participants demonstrated elevated levels of testosterone and an increased LH/FSH ratio, which are hallmark features of PCOS. These results were consistent with prior studies that emphasize the central role of hyperandrogenism and disrupted gonadotropin secretion in the condition[11, 12]. High AMH levels observed in our study corroborate studies, attributing elevated AMH to increased follicular activity and poor follicular maturation in PCOS[13, 14]. These hormonal imbalances contribute to the anovulation and menstrual irregularities characteristic of the syndrome.

Biochemical findings revealed that participants had higher fasting glucose and LDL cholesterol levels, suggesting an increased risk of metabolic syndrome, a known comorbidity of PCOS. This aligns with studies that demonstrated a strong association between insulin resistance, dyslipidemia, and PCOS. Our study further supports insulin-sensitizing agents like metformin as an effective treatment to address metabolic dysfunction, as evidenced by improved fasting glucose levels in treated participants [15, 16].

Physiological parameters, including follicular development and ovulation, showed significant improvement following treatment. Combined oral contraceptives and progesterone-only regimens were particularly effective in regularizing menstrual cycles and reducing hyperandrogenism, findings consistent with studies[17, 18]. Additionally, ovulation-inducing agents clomiphene citrate and letrozole demonstrated their efficacy in restoring ovulation, as supported by studies[19-21]. Improved endometrial

thickness and ovarian blood flow further underscore the role of hormonal therapies in enhancing reproductive outcomes.

Lifestyle modifications, including weight loss and increased physical activity, were observed to benefit BMI and metabolic parameters, aligning with the conclusions of interventions studied [22]. These non-pharmacological approaches remain a cornerstone in the management of PCOS, particularly for individuals with obesity and insulin resistance.

Our study also revealed a high level of treatment adherence among participants, which likely contributed to the observed improvements. However, some participants experienced side effects, including nausea and weight gain, consistent with the adverse effects documented in hormonal therapy trials. This underscores the importance of individualized treatment plans tailored to patient needs and tolerance.

This study's findings align with existing literature while providing further evidence of the multifaceted impact of PCOS on hormonal, metabolic, and reproductive health. The positive outcomes observed with both pharmacological and non-pharmacological interventions highlight the importance of a multidisciplinary approach to managing PCOS. Future research should focus on long-term outcomes and explore the genetic and environmental factors that may influence treatment responses.

CONCLUSION

This study highlights the intricate relationship between hormonal imbalances and ovarian dysfunction in women with PCOS. Elevated androgen levels, disrupted LH/FSH ratios, and increased AMH levels were confirmed as key features of the condition, contributing to anovulation, menstrual irregularities, and metabolic disturbances. The findings underscore the effectiveness of targeted interventions, including hormonal therapies, ovulation-inducing agents, and lifestyle modifications, in improving ovarian function and overall metabolic health.

Treatment strategies such as combined oral contraceptives and metformin demonstrated significant benefits, including improved hormonal profiles, enhanced ovulation rates, and better menstrual regularity. Additionally, lifestyle changes emerged as a critical component of PCOS management, especially in addressing obesity and insulin resistance.

The study reaffirms the need for a comprehensive and individualized approach to PCOS treatment, combining pharmacological and non-pharmacological measures to address both reproductive and metabolic challenges. Further research is encouraged to explore long-term outcomes and optimize treatment protocols for diverse patient populations.

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