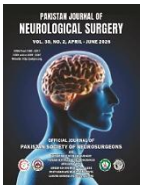

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Original Research

Correlation Between Polycystic Ovary Syndrome and Neuropsychiatric Manifestations: Clinical and Hormonal Perspectives

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ABSTRACT

Objective: Polycystic Ovary Syndrome is a prevalent endocrine illness in women of reproductive age, and it is becoming increasingly linked to neuropsychiatric disturbances. Hormonal imbalance, insulin resistance and chronic inflammation are possible contributors to psychological morbidity among the affected women. The study aimed to establish the relationship between Polycystic Ovary Syndrome and neuropsychiatric manifestations, both in clinical and hormonal aspects.

Materials & Methods: This is an analytical cross-sectional study that was done within Lady Reading Hospital. Three hundred women aged from 18 to 40 years were recruited, 150 of whom were diagnosed with Polycystic Ovary Syndrome who met the Rotterdam criteria, and 150 healthy women were age-matched. Clinical and anthropometric parameters, hormonal status, metabolic parameters and inflammatory markers were measured. Psychological scales were used in measuring depression and anxiety.

Results: Females with PCOS had significantly higher BMI, serum levels of T, fasting insulin levels and HOMA IR value compared to the controls. Moderate to severe depressive symptoms were found in 46 percent, and clinically significant anxiety symptoms were found in 52 percent. The score of depression and anxiety was positively correlated with total testosterone and insulin resistance. The mild yet significant association between C-reactive protein and anxiety symptoms was also found.

Conclusion: Polycystic Ovary Syndrome has a strong correlation with the neuropsychiatric symptoms. The imbalance in hormones and dysfunction of the metabolism seem to be a significant factor in psychological distress. It is important to perform an endocrine and mental health evaluation as part of the management.

Keywords: PCOS, Hyperandrogenism, Insulin resistance, Depression and Anxiety, Neuropsychiatric manifestation, Inflammation and Hormonal imbalance.

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INTRODUCTION

This condition may pose challenges for women, more than just physical. Many go through mood swings, anxiety and depression. These feelings may occur due to the hormonal shifts within the body, but also because of noticeable physical changes such as excess body weight, acne or unwanted hair growth. Such physical changes can impact a woman's self-confidence and self-esteem.[1]

Also, the metabolism of sugar and energy is important. In most women who suffer from this, insulin is poorly utilized, and it can cause fatigue and weight gain. This imbalance can also impact the brain and mood and cause the person to feel low, stressed or mentally exhausted. These issues can add up over time and become more challenging to live with.[2]

This condition may also cause emotional problems, as it can cause changes in menstrual cycles and fertility. This can add to the stress and pressure women face in many cultures, such as our own. For this reason, mental health is as crucial as physical health when discussing the treatment. With the right support, counselling, and awareness, the females will be better able to take care of their physical and emotional health.[3]

The past 20 years have seen the growing interest in the neuropsychiatric aspect of PCOS. The women who have this condition often complain of mood swings, anxiety, low self-esteem, cognitive impairment, sleep disorders and poor quality of life. The weight of these manifestations can be as many or more than the reproductive and metabolic complications. Women with PCOS are reported to have a very high rate of depression and anxiety disorders as compared to their age-matched controls. Some emerging associations with bipolar spectrum disorders, attention deficit symptoms, eating disorders and even changes in patterns of stress reactivity are also noted. The results show that PCOS may be a gynecologic disorder, but a disorder of the neuroendocrine system with widespread psychological ramification.[4]

A pathophysiology between PCOS and neuropsychiatric manifestations is multifactorial and includes complicated hormonal, metabolic, inflammatory, and psychosocial processes. Hyperandrogenism – a feature of PCOS – is at the heart of the situation. Circulating high levels of androgens may influence brain structure and brain functioning through changes in several neurotransmitter circuits such as serotonin, dopamine and gamma aminobutyric acid. The limbic structures, such as the amygdala and hippocampus, which are important in emotional regulation, interact with androgens. Overexposure to androgens has been theorized to shift stress responsiveness and regulation of mood processes, which may predispose women who experience it to anxiety and depressive symptoms.[5]

Another cardinal characteristic of PCOS, which also adds to neuropsychiatric vulnerability, is insulin resistance. Hyperinsulinemia disrupts the signals in the central nervous system and may alter neurotransmitter balance. The receptors of insulin are spread widely in the brain, especially in areas of the brain that deal with cognition and mood. Chronic insulin resistance has been linked to cognitive dysfunction and depression in diabetic and non-diabetic subjects. Metabolic dysregulation in direct neurochemical pathways and systemic inflammation contribute to psychological distress in women with PCOS.[6]

Low-grade chronic inflammation has also been linked with the pathogenesis of PCOS. Levels of other inflammatory cytokines, such as interleukin-6 and tumour necrosis factor alpha, are very common and tend to be elevated. These inflammatory mediators are capable of getting through the blood-brain barrier and affecting neurotransmitter metabolism, neuroplasticity and the activity of the hypothalamic pituitary adrenal axis6. There may be changes in the pattern of cortisol secretion as a result of hypothalamic pituitary adrenal axis dysfunction, which can result

in stress sensitivity and mood disorders. Thus, the endocrine dysfunction/neuropsychiatric dysfunction relationship might be an inflammatory environment associated with PCOS.[7]

Clinically speaking, those overt signs of PCOS do have a considerable impact on psychological well-being. Hirsutism, acne, obesity and irregular periods can be responsible for body image dissatisfaction, social withdrawal and low self-confidence.[8] Infertility is one of the most common consequences of chronic anovulation and can contribute to emotional distress and lead to depressive episodes, particularly in societies where the social identity of a person is tied closely to their fertility. All of this combined usually leads to a lesser quality of life and psychological ill health (morbidity).[8]

The neuroimaging research has been initiated on structural and functional brain alterations in the female population with PCOS. The volume of the gray matter in the prefrontal cortex and limbic areas has been reported to change. According to functional imaging, there are variations in the emotional processing and reward-related circuits. While the cause of PCOS is not yet fully understood, these data suggest that hormone dysregulation in PCOS may be measurable in alterations to neural architecture and connectivity.[9]

Young people with PCOS are a highly susceptible population. The developmental psychosocial adaptation can be impaired because of the appearance of the symptoms at a significant stage of development. Exposure to hyperandrogenism and metabolic malformations in early childhood can have an impact on neurodevelopmental pathways. Research suggests a prevalence of depressive symptoms and anxiety among adolescents with PCOS compared to healthy adolescents. Early detection and a combined approach are hence necessary to avoid the psychological impacts in the long term.[10]

The other factor is the interdependent link between PCOS and mental health. Hormonal imbalance can be worsened by psychological stress due to the stimulation of the hypothalamic pituitary adrenal axis. The insulin resistance and weight gain resulting from chronic stress aggravate the metabolic characteristics of PCOS. This is a cycle, which emphasizes the importance of considering the whole person (endocrine and psychological).[11]

Therapies for PCOS, such as lifestyle modifications, insulin sensitizers (such as metformin) and hormonal birth control, may have an impact on mental health. Better quality of life and mood are associated with weight loss and better control of mood. However, the psychological side effects of some hormonal therapies are unpredictable and change from person to person, and can only be controlled on a case-by-case basis. Regular psychological screening and counselling for PCOS is increasingly recommended.[12]

Although there have been reports of psychological disturbances in patients with PCOS, few studies in low and middle-income countries have studied the interplay among the clinical, hormonal, metabolic and neuropsychiatric parameters. However, most studies performed to date have addressed a reproductive or psychological dimension separately and have neglected to discuss the interaction between them, especially among the local population. There is a lack of sufficient information to develop a comprehensive management strategy specific to regional health settings. Hence, this study aimed to assess the relationship between PCOS and neuropsychiatric symptoms by correlating clinical parameters, hormonal profile, metabolic parameters and inflammatory markers with depression and anxiety outcomes among PCOS women visiting a tertiary diagnosis centre.

MATERIAL AND METHODS

Study Design and Setting

The current study was conducted in a large hospital where many women visit for the treatment of hormonal and reproductive issues. Through the

participation of various specialists, including gynecologists, endocrinologists and mental health workers, the study was able to examine both the physical and emotional side of the condition. This helped in a better understanding of how the body was impacted by PCOS, as well as the mind.

Before starting the study, proper approval was taken from the hospital's ethical committee (IRB Ref No: 274/LRH/MTI) to ensure that all procedures were safe and followed medical guidelines. All participants were briefed on the purpose of the study in simple terms, and they expressed consent before being included. They were respected, and their personal information was kept confidential and only used for research purposes.

The number of participants that were part of the study was carefully determined to ensure that the results obtained were accurate and meaningful. The researchers accounted for a sufficient number of women in both the affected and healthy populations to allow for appropriate comparisons between the two. This helped in making sure that the differences seen in mental health and hormone levels were reliable and not due to chance.

Study Population

In this study, women between the ages of 18 and 40 who visited the outpatient clinics of Lady Reading Hospital were included. They were divided into two groups. The first group included women who had Polycystic Ovary Syndrome (PCOS), which was diagnosed using standard medical guidelines. The second group included women of similar age who were healthy, had regular menstrual cycles, and showed normal ovaries on ultrasound.

Each group had 150 women, making a total of 300 participants. The researchers selected participants as they came to the clinic one after another, instead of choosing them randomly. This approach helped include a steady flow of patients, although it may not perfectly represent all women in the general population.

Inclusion Criteria

This study included women aged 18 to 40 years because this is the time in life when Polycystic Ovary Syndrome (PCOS) is most commonly seen and when women are in their reproductive years. Only those women who agreed to take part were included, and each participant was permitted after the study was explained to them.

Patients were deemed to have Polycystic Ovary Syndrome if they had irregular or absent periods, evidence of elevated male hormone levels (such as excess hair growth or blood elevation of male hormones) and ultrasound results of several small cysts in the ovary. All three features were rigorously scrutinized for confirmation of diagnosis.

The control group consisted of healthy women who had normal menstrual cycles, did not exhibit excess male hormones and had normal ultrasound reports. These women provided an appreciation for baseline information, which allowed the differences to be appreciated with the condition present. All participants had to agree to full clinical, hormonal and psychological testing to participate in the study.

Exclusion Criteria

Women who were pregnant or lactating were not taken into consideration. Participants who had psychiatric diagnoses at a time before PCOS diagnosis were not considered. The women who had any psychotropic medications, hormonal therapy, insulin sensitizers, or corticosteroids in the past three months were not included. Illnesses that were excluded to reduce the likelihood of confounding factors were those involving thyroid

disorders, hyperprolactinemia, Cushing syndrome, congenital adrenal hyperplasia, diabetes mellitus, chronic systemic illness, neurological disorders or substance abuse.

Anthropometric Assessment/Clinical

Clinical assessment was done extensively on all participants. A structured questionnaire was used in collecting demographic information. Body mass index, height and weight were assessed, and waist circumference was measured. The modified Ferriman Gallwey was used to measure clinical manifestations of hyperandrogenism, including hirsutism. The history of menstruation and blood pressure was observed.

Hormone and Biochemical Assessment

All participants had their blood samples collected in a laboratory environment within a safe and standardized environment. Blood was collected from a vein, typically in the arm, with proper sterile techniques to maintain the safety and accuracy of the procedure. All the samples were carefully taken in the laboratory to obtain satisfactory results.

Different hormone and blood sugar tests were performed on these samples. They contained significant female and male hormones like luteinizing hormone, follicle-stimulating hormone, total and free testosterone, prolactin and thyroid hormone. Blood sugar and insulin were also tested to get a sense of the body's sugar metabolism.

Insulin resistance has been calculated using a special formula to assess insulin resistance – the body's response to insulin. A blood test (C-reactive protein) to determine whether there was any inflammation (swelling or irritation) in the body was also performed. The tests assisted in comprehending hormonal equilibrium and the total health of the body.

Neuropsychiatric Assessment

The participants' mental health was assessed using standard questionnaires to check for depression, anxiety, and overall quality of life. These assessments were carried out by trained staff who did not know the participants' lab or hormone results, so their evaluations remained fair and unbiased.

Statistical Analysis

The data collected were all fed into a computer program known as SPSS (Statistical Package for Social Sciences) version 26. Doctors often use this software to store and process health-related information in an easy-to-understand and logical manner.

The information was then presented in a condensed and simple manner. For instance, average numbers such as age were presented, and percentages for group-based information, such as the presence or absence of symptoms. This helped in clearly understanding the differences between the two groups.

Different statistical tests were employed for comparing the results between groups, depending on the nature of the data. Some tests were used to compare averages, while others were used to compare percentages. Special types of correlation were also utilized to examine the relationships among the hormones and mental health symptoms. A value referred to as a p-value was used to determine the meaningfulness of the results, and p-values below 0.05 were interpreted as being statistically significant.

RESULTS

Baseline Demographic and Clinical Parameters:

The study involved 300 women, 150 of whom were diagnosed with polycystic ovary syndrome (PCOS) and 150 who were not. The results are tabulated and interpreted below.

Baseline demographic and clinical parameters of both groups are presented in Table 1. The mean

ages were not significantly different between the two groups. But women with P.O.S had a significantly greater BMI and waist circumference. Body mass index was 29.4 ± 4.2 kg/m² in the Polycystic Ovary Syndrome group compared to 24.8 ± 3.7 kg/m² in controls ($p < 0.001$). Similarly, waist circumference was greater in cases (92.6 ± 8.3 cm vs 81.4 ± 7.5 cm, $p < 0.001$). There were also significantly more women in the Polycystic Ovary Syndrome group who had hirsutism and menstrual irregularities.

Table 1: *Baseline Demographic and Clinical Characteristics.*

Variable	PCOS Group (n = 150)	Control Group (n = 150)	p value
Mean Age (years)	26.8 ± 4.9	27.3 ± 5.1	0.412
Body Mass Index (kg/m²)	29.4 ± 4.2	24.8 ± 3.7	< 0.001
Waist Circumference (cm)	92.6 ± 8.3	81.4 ± 7.5	< 0.001
Menstrual Irregularity	117 (78%)	0 (0%)	< 0.001
Hirsutism	96 (64%)	12 (8%)	< 0.001

Table 2 presents the comparison of hormonal profiles between the two groups. Women with Polycystic Ovary Syndrome had significantly higher levels of serum total testosterone, luteinizing hormone, and LH/FSH ratio compared to controls. Total testosterone levels were significantly elevated in the Polycystic Ovary Syndrome group (0.92 ± 0.31 ng/ml vs 0.41 ± 0.18 ng/ml, $p < 0.001$). There was no statistically significant difference in follicle-stimulating hormone and prolactin levels between the two groups.

Table 2: *Hormonal Profile Comparison.*

Parameter	PCOS Group (Mean ± SD)	Control Group (Mean ± SD)	p value
Total Testosterone (ng/ml)	0.92 ± 0.31	0.41 ± 0.18	< 0.001
LH (IU/L)	11.8 ± 4.5	6.4 ± 2.3	< 0.001
FSH (IU/L)	5.9 ± 1.8	6.1 ± 1.7	0.328
LH/FSH Ratio	2.0 ± 0.7	1.0 ± 0.4	< 0.001
Prolactin (ng/ml)	14.2 ± 5.1	13.6 ± 4.7	0.287

Table 3 presents the metabolic and inflammatory parameters of the two groups. Fasting glucose, fasting insulin, and HOMA-IR values were significantly higher in the Polycystic Ovary Syndrome group, indicating increased insulin resistance. Fasting insulin levels were 18.7 ± 6.4 µIU/ml in the Polycystic Ovary Syndrome group compared to 9.6 ± 3.1 µIU/ml in controls ($p < 0.001$). Similarly, HOMA-IR was significantly elevated (4.7 ± 1.8 vs 2.1 ± 0.9, $p < 0.001$). C-reactive protein levels were also significantly higher in the Polycystic Ovary Syndrome group, reflecting increased inflammatory activity.

Table 3: Metabolic and Inflammatory Parameters

Parameter	PCOS Group (Mean ± SD)	Control Group (Mean ± SD)	p value
Fasting Glucose (mg/dl)	101.5 ± 12.4	92.3 ± 10.6	< 0.001
Fasting Insulin (µIU/ml)	18.7 ± 6.4	9.6 ± 3.1	< 0.001
HOMA IR	4.7 ± 1.8	2.1 ± 0.9	< 0.001
C Reactive Protein (mg/L)	5.2 ± 2.3	2.8 ± 1.4	< 0.001

Table 4 presents the neuropsychiatric outcomes of the two groups. Women with Polycystic Ovary Syndrome had significantly higher

Table 4: *Neuropsychiatric Assessment.*

Assessment Tool	PCOS Group (Mean ± SD)	Control Group (Mean ± SD)	p value
Beck Depression Score	19.6 ± 8.3	11.2 ± 6.1	< 0.001
Moderate to Severe Depression	69 (46%)	27 (18%)	< 0.001
Hamilton Anxiety Score	17.9 ± 7.5	9.8 ± 5.4	< 0.001
Clinically Significant Anxiety	78 (52%)	32 (21%)	< 0.001
MoCA Score	25.8 ± 2.1	27.1 ± 1.9	0.003

depression and anxiety scores compared to controls. Depression scores were 19.6 ± 8.3 in the Polycystic Ovary Syndrome group versus 11.2 ± 6.1 in controls ($p < 0.001$), with 46% of participants exhibiting moderate to severe depressive symptoms. Anxiety scores were also significantly higher (17.9 ± 7.5 vs 9.8 ± 5.4, $p < 0.001$), with 52% showing clinically significant anxiety. Cognitive scores were slightly lower in the Polycystic Ovary Syndrome group, although they remained largely within normal limits.

Table 5 presents the correlation analysis within the Polycystic Ovary Syndrome group. Total testosterone, fasting insulin, and HOMA-IR demonstrated significant positive correlations with both depression and anxiety scores. HOMA-IR showed the strongest correlation with depression ($r = 0.47$, $p < 0.001$), followed by fasting insulin and total testosterone. C-reactive protein showed a weaker but statistically significant association with anxiety symptoms.

Table 5: *Correlation Between Hormonal Parameters and Neuropsychiatric Scores in PCOS Group.*

Variable	Depression Score (r)	Anxiety Score (r)	p value
Total Testosterone	0.41	0.38	< 0.001
Fasting Insulin	0.44	0.36	< 0.001
HOMA IR	0.47	0.39	< 0.001
C Reactive Protein	0.29	0.31	0.002

Overall, the findings indicate that women with Polycystic Ovary Syndrome demonstrated significantly higher neuropsychiatric symptom burden compared to healthy controls. Hormonal imbalance, insulin resistance, and inflammatory markers showed meaningful correlations with psychological distress, suggesting a strong endocrine–psychiatric interaction in this population.

DISCUSSION

The study focused on women with Polycystic Ovary Syndrome (PCOS) visiting a hospital and compared them with normal women to explore the relationship between PCOS and mental health issues. The results showed that women with PCOS were much more likely to suffer from depression and anxiety compared to women without the condition. Almost half (46%) of women with PCOS reported moderate to severe symptoms of depression, and approximately 52% reported significant levels of anxiety. This is a clear indicator that PCOS is not just a physical or reproductive issue, but it also has a great impact on the mental health and emotional well-being of a woman's day-to-day life.[13]

Additionally, the study discovered these psychological issues were correlated with modifications in the body. Women with PCOS who had higher levels of male-type hormones (such as testosterone) were more likely to feel depressed and anxious. This can lead to hormone imbalance, having a direct impact on mood and emotions. In addition, many women with PCOS also had issues with insulin resistance, or the body's inability to utilize sugar. It was also found that these women had elevated insulin levels, which were also associated with greater mental health symptoms. Therefore, there appears to be a relationship between both hormone issues and metabolic issues, in relation to emotional distress.[14]

One of the other key discoveries was the function of inflammation in the body. Low-level, long-term inflammation was observed in women with PCOS, as indicated by elevated blood markers of inflammation (CRP). This kind of inflammation can have an impact on brain function and stress response. This means that women may be more vulnerable to stress and be at increased risk for mood disorders such as anxiety and depression. This indicates that shifts within the body can affect the person's mental state.[15]

The study also elaborated that PCOS impacts women on more than one level. It may cause changes in self-confidence, body image and social life as well as physical and hormonal changes.

These emotional and social challenges may aggravate psychological issues. All of these indicate a complex condition that involves the whole body and mind, so treatment needs to take into account both sides of the coin.[16]

The other significant thing to consider is that mental health can have an impact on PCOS as well. Stress, anxiety and depression are all factors of PCOS, but these can worsen the physical symptoms and the imbalance in hormones. This can lead to an ever-worsening downward spiral between physical and mental issues, making it increasingly difficult to deal with over time.[17]

Given these results, studies indicate the need to routinely assess mental health in PCOS women's hospital and clinic settings. Early detection of depression and anxiety symptoms can facilitate treatment and improve quality of life. In addition to treating physical symptoms, doctors must be psychologically supportive if necessary.[22]

Lastly, this study provides valuable information; however, it does have some limitations. It doesn't clearly establish that one thing directly causes another, and it is based on a single moment in time. Some answers also rely on participants' own words regarding their emotions, which may not be accurate. However, the study indicates that a comprehensive treatment strategy that integrates physical, hormonal and mental health care is crucial to achieve a better outcome in the treatment of PCOS.

CONCLUSION

The results of this study showed a clear correlation between PCOS and the neuropsychiatric burden, with depression, anxiety, and hyperandrogenism showing high correlation with insulin resistance and inflammatory activity. The results reveal that metabolic and hormonal disturbances are not only important to the physical symptoms of the disease but also play a significant role in psychological morbidity. Regular psychiatric and/or mental health screening and integrated endocrine–psychiatric management may help to enhance overall patient outcomes. More detailed and longitudinal research is needed to confirm causal links and develop interventions.

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AUTHORS CONTRIBUTIONS

Serial Number	Author's Full Name	Intellectual Contribution to the Paper in Terms of
1.	Surraya Israr	Study design and methodology.
2.	Sundus Rahman	Paper writing.
3.	Devi Kumari	Data collection and calculations.
4.	Romaisa Zeb	Analysis of data and interpretation of results.
5.	Hunniya Ayyaz	Literature review.
6.	Maira Batool Rizvi	Data collection.
7.	Iqra Sajjad	Referencing.
8.	Iftikhar Saleem	Data collection.