

Relationship between Clinico-Socio-Demographic Factors and Psychology of Women Diagnosed with Polycystic Ovary Syndrome

Anu Bansal¹, Jasobanta Sethi^{2,*}, Raju K Parasher³, Manisha Tomar⁴

¹PhD Scholar, Department of Physiotherapy, Amity Institute of Health Allied Sciences, Amity University, Uttar Pradesh, 201313, India

²Director, Department of Physiotherapy, Amity Institute of Health Allied Sciences, Amity University, Uttar Pradesh, 201313, India

³Director, Amar Jyoti Institute of Physiotherapy, University of Delhi, New Delhi 110092, India

⁴Consultant Gynaecologist, Motherhood Hospital, Noida, Uttar Pradesh, India

Received December 3, 2022; Revised February 8, 2023; Accepted March 12, 2023

Cite This Paper in the Following Citation Styles

(a): [1] Anu Bansal, Jasobanta Sethi, Raju K Parasher, Manisha Tomar, "Relationship between Clinico-Socio-Demographic Factors and Psychology of Women Diagnosed with Polycystic Ovary Syndrome," *Universal Journal of Public Health*, Vol. 11, No. 2, pp. 205 - 213, 2023. DOI: 10.13189/ujph.2023.110202.

(b): Anu Bansal, Jasobanta Sethi, Raju K Parasher, Manisha Tomar (2023). Relationship between Clinico-Socio-Demographic Factors and Psychology of Women Diagnosed with Polycystic Ovary Syndrome. *Universal Journal of Public Health*, 11(2), 205 - 213. DOI: 10.13189/ujph.2023.110202.

Copyright©2023 by authors, all rights reserved. Authors agree that this article remains permanently open access under the terms of the Creative Commons Attribution License 4.0 International License

Abstract Background: Polycystic Ovary Syndrome (PCOS) is an endocrine disorder affecting up to 22.5% of women of reproductive age. Women with PCOS experience high rates of depression and anxiety. **Settings and Design:** Cross sectional study design. **Objective:** Primary objective of study was to estimate the prevalence of depression, anxiety and stress among women with PCOS. Secondary objective was to analyze association of psychological factors (depression, anxiety and stress) with sociodemographic factors and clinical aspects among Indian women with PCOS. **Methods:** One hundred and four women in the reproductive age group (18–45 years) diagnosed with PCOS as per Rotterdam criteria, without any pre-existing psychiatric illness were interviewed for depression, anxiety and stress using DASS21 scale. **Result:** Out of 104 women with PCOS 46.16% suffered from mild to moderate levels of depression, 64.42% experienced (mild to extremely severe) anxiety while 53.85% reported varying degrees of stress. Women with higher BMI (overweight and obese), hirsutism scores and having acne were more susceptible to being depressed. The odds ratio for women experiencing depression were as follows: hirsutism scores was 1.113, being overweight, 5.023 (1.359 to 18.566), being obese was 3.298 (1.167 to 9.314), and having acne was 3.29 (1.267 to 8.541). **Conclusion:** It is observed a large percentage of women with PCOS suffer

from psychological factors such as depression, anxiety and stress. Also, BMI, hirsutism and acne were found to be significant contributors to depression among women with PCOS. It is suggested that clinicians and healthcare practitioners develop and utilize a comprehensive approach in the management of PCOS based on biopsychosocial model of health.

Keywords Demography, Social Factors, PCOS, Depression, Anxiety, Stress, Clinical Factors

1. Introduction

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age [1]. In India, the prevalence of Polycystic Ovary syndrome was reported to be between 3.7% - 22.5%, [2] and is characterized, as per the Rotterdam criteria, by presence of any two features of the following: irregular menstruation, signs of biochemical hyperandrogenism and /or polycystic ovarian morphology on ultrasound [3]. Apart from the typical clinical presentation such women also experience a wide range of symptoms such as infertility, presence of excessive thick, coarse hair in a male-like pattern at various

sites - face, neck, chest and back, excessive weight gain in a short span of time, acne, male pattern baldness with gradual disappearance of hair from areas of scalp as well as disturbed mental health [4].

A few studies have reported that women with PCOS experience high rates of depression and anxiety compared to women without PCOS [5]. In addition, studies have also reported a prevalence of anxiety ranging from 28% to 39% and a prevalence of depression ranging from 11% to 25.7% respectively among women with PCOS [1,6,7].

A recent study indicated that there were many interconnected and mutually reinforcing pathways that put women with PCOS at risk for depression and includes disturbances in the endocrine axes which lead to an increase in Luteinizing Hormone, hyperandrogenism and its clinical manifestations, alterations in the metabolic pathways, and menstrual abnormalities [8-10]. A meta-analysis concluded that even though there is a high prevalence of anxiety and depression among women with PCOS, no conclusive evidence with regard to the underlying mechanisms has been examined and/or proposed [11].

Thus, the primary objective(s) of this study was firstly, to estimate the prevalence of depression, anxiety, and stress among women with PCOS. Secondly, to analyze the association of depression, anxiety, and stress with sociodemographic factors such as age, BMI, employment status, and clinical factors such as menstrual irregularities, hirsutism, acne, etc. in Indian women with PCOS.

2. Materials and Methods

2.1. Study Design and Setting

Ethical clearance was obtained from Institutional Ethical Committee (AUUP/IEC/2018/08). The design of the study was cross sectional. The study was carried out from May 2018 to February 2020. Convenience sampling method was used.

2.2. Participants

Women diagnosed with PCOS by gynecologist/physician were recruited from polyclinics/clinics and healthcare institutions in Delhi and/or NCR.

2.3. Sampling Method and Sample Size

The prevalence of PCOS in India has varied from 3.7% to 22.5% across Indian studies [2]. Prevalence of anxiety and depression has been reported to be 38.6% and 25.7% respectively [12]. Taking this value as reference, the minimum required sample size with 10% margin of error and 5% level of significance was calculated to be 92 patients. To reduce the margin of error, a total sample of 104 was taken.

Formula used to calculate sample size was: $n \geq \{p(1-p)\}/(ME/z_{\alpha})^2$ where Z_{α} is value of Z at two-sided alpha

error of 5%, ME is margin of error and p is the prevalence of anxiety or depression.

2.4. Eligibility Criteria

The study sample consisted of women of reproductive age (18-40 years old) living in Delhi and NCR diagnosed with PCOS by a gynecologist/physician based on the Rotterdam criteria for PCOS [13]. Women with PCOS who were willing to participate in the study and could read and write English were recruited for the study. Women with a history of cardiopulmonary, endocrine disorders other than PCOS, neurological disease, musculoskeletal conditions, and those with pre-existing clinical psychological problems, were excluded from the study.

2.5. Data Collection

Participants were briefed with regard to the study and the research objectives. Following informed consent, participants were administered an evidence based clinical checklist that was developed based on a comprehensive literature review. The checklist included sociodemographic measures such as age, BMI and employment status and clinical aspects such as menstrual irregularities, hirsutism, acne, and the wish to conceive. Standardized tests were used to measure parameters as needed.

Height was measured to 0.5 cm using calibrated stadiometer. Body mass was measured using calibrated clinical scale to the nearest 0.01 kg. BMI was calculated as the ratio of body weight in kilograms to the square of the height in meters. Employment status was taken as employed/ student or homemaker. Data on menstrual cyclicity, the wish to conceive and acne were as self-reported by participants. Hirsutism was assessed on a modified Ferriman Gallwey measure [14].

Psychological status of each patient was determined using DASS 21 scale which was developed by Lovibond and Lovibond [15]. It assesses the presence and intensity of depression, anxiety, and stress on a 4-point Likert scale. Each scale has seven items and a higher score indicates a higher participant symptomatology.

2.6. Data Analysis

Data collected were recorded in a spreadsheet and analyzed using the Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0.

The presentation of the Categorical variables was done in the form of frequencies and percentages (%) and the quantitative data were presented as the means \pm SD and as median with 25th and 75th percentiles (interquartile range) as indicated. Univariate and multivariate logistic regression was used to determine significant predictors (risk factors) associated with depression, anxiety and stress.

A p value of less than 0.05, was considered as statistically significant.

3. Results

A total of 104 women diagnosed with PCOS were recruited for the study. Seventy five percent (75%) of the women belonged to age group (18-25yrs) and twenty five percent (25%) were in the age group (26-34 yrs). Eighty four percent (83.6%) of the women included in study were employed and/or were students while sixteen percent (16.3%) were homemakers. Interestingly, 2.88% women had BMI category <18.5kg/m², 26.9% women had normal BMI (18.5 – 22.9 kg/m²), 16.3% women were overweight (23-24.9 kg/m²), and 53.8% were obese (>=25kg/m²). Forty two percent (42.3%) of the women complained of hirsutism and twenty two percent (22.1%) expressed a desire to conceive.

Factors associated with the psychological status of women with PCOS were further analyzed by sociodemographic factors such as age, BMI and occupation and clinical aspects such as menstrual irregularity, hirsutism, acne and willing to conceive.

3.1. Prevalence of Depression, Anxiety and Stress

Depression

As seen in Table 1 and Figure 1, it was observed that

forty six percent (46.16%) of the cohort suffered from mild to severe levels of depression while fifty four percent (53.85%) had normal levels. Twenty two percent (22.12%) experienced mild levels, twenty two percent (22.12%) had moderate levels of depression and only two percent (1.92%) had severe levels. Mean value of depression was 9.15 ± 6.2, with median (25th-75th percentile) of 8 (range 4-12).

Anxiety

Sixty four percent (64.42%) of the women with PCOS suffered from mild to extremely severe degrees of anxiety, while thirty six percent (35.58%) had no anxiety. Thirteen percent (12.5%) reported mild anxiety levels, thirty six percent (35.58%) had moderate levels of anxiety of patients, thirteen percent (13.46%) suffered from severe anxiety, while only three percent (2.88%) suffered from extreme anxiety. Mean value of anxiety scores was 9.13 ± 5.07 with a median (25th-75th percentile) of 10 (range 6-12) (Refer to Table 1 & Figure 1).

Stress

Fifty four percent (53.85%) of women were stressed, while forty six percent (46.15%) had normal stress levels. Thirty nine percent (39.42%) had mild levels of stress and fourteen percent (14.42%) had moderate levels of stress.

Mean value of stress was 12.23 ± 6.2, with a median (25th-75th percentile) of 12 (range 8-16) (Refer to Table 1 & Figure 1).

Table 1. Frequency distribution and central tendencies of depression, anxiety and stress scores in women with PCOS

Depression, anxiety and stress	Frequency	Mean ±SD	Percentage
Depression			
0-9 {Normal}	56		53.85%
10-12 {Mild}	23		22.12%
13-20 {Moderate}	23		22.12%
21-27 {Severe}	2		1.92%
Mean ±SD		9.15 ± 6.2	
Median (25th-75th percentile)		8(4-12)	
Range		0-24	
Anxiety			
0-6 {Normal}	37		35.58%
7-9 {Mild}	13		12.50%
10-14 {Moderate}	37		35.58%
15-19 {Severe}	14		13.46%
20-42 {Extremely severe}	3		2.88%
Mean ±SD		9.13 ± 5.07	
Median (25th-75th percentile)		10(6-12)	
Range		0-20	
Stress			
0-10 {Normal}	48		46.15%
11-18 {Mild}	41		39.42%
19-26 {Moderate}	15		14.42%
Mean ±SD		12.23 ± 6.2	
Median(25th-75th percentile)		12(8-16)	
Range		0-26	

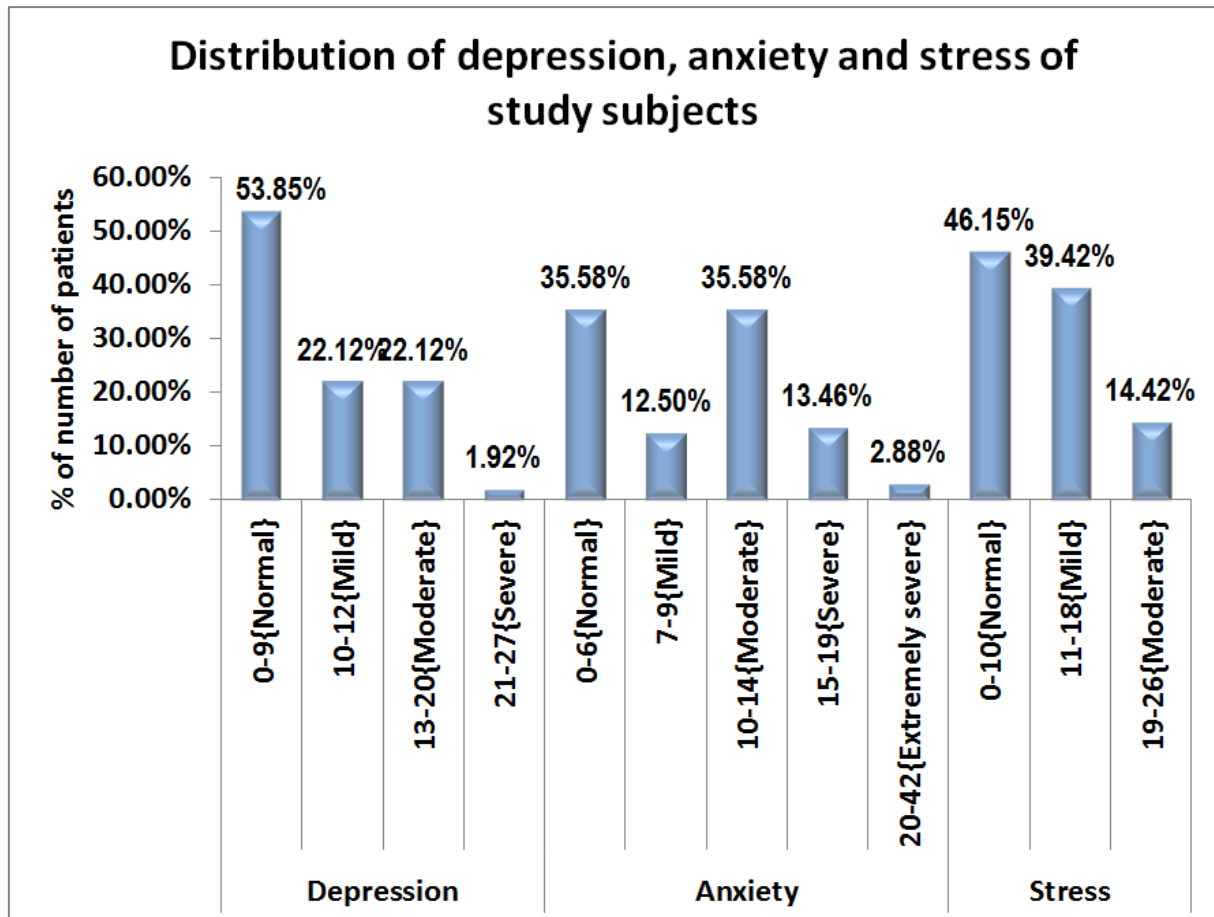


Figure 1. Frequency distributions of depression, anxiety and stress scores in women with PCOS

3.2. Association of Clinico-socio-demographic Risk Factors with Depression among PCOS Women

Hirsutism, body mass index (kg/m^2): 23 to 24.99 kg/m^2 {Overweight}, $\geq 25 \text{ kg/m}^2$ {Obese}, acne were significant risk factors of depression on performing univariate regression analysis as observed in Table 2.

Table 2. Logistic regression table highlighting association of clinico-socio-demographic risk factors depression (* $p < 0.05$)

Depression	Beta coefficient	Standard error	P value	Odds ratio	Odds ratio Lower bound (95%)	Odds ratio Upper bound (95%)
Age (years)	-0.062	0.054	0.252	0.940	0.844	1.045
Hirsutism	0.107	0.038	0.005*	1.113	1.033	1.199
Body mass index (kg/m^2)						
18.5 to 22.99 kg/m^2 {Normal BMI}				1.000		
<18.5 kg/m^2 {Underweight}	1.754	1.292	0.175	5.776	0.459	72.691
23 to 24.99 kg/m^2 {Overweight}	1.614	0.667	0.016*	5.023	1.359	18.566
$\geq 25 \text{ kg/m}^2$ {Obese}	1.193	0.530	0.024*	3.298	1.167	9.314
Employment status	-0.586	0.537	0.275	0.556	0.194	1.595
Menstrual Irregularity	3.067	3.580	0.392	21.485	0.019	23957.452
Acne	1.191	0.487	0.014*	3.290	1.267	8.541
Willing to conceive	-0.367	0.481	0.446	0.693	0.270	1.780

As seen in Table 2, it was observed that there was a significant increase in depression experienced by women with PCOS with an increase in hirsutism, acne, and obesity. The risk of depression significantly increased with an odds ratio of 1.113 (range 1.033 to 1.199). Additionally, patients who were overweight increased their risk of depression by 5.023 (range 1.359 to 18.566), and if obese risk increased by 3.298 (range 1.167 to 9.314). Women who developed acne increased their risk by 3.29 (range 1.267 to 8.541).

3.3. Association of Clinico-socio-demographic Risk Factors with Anxiety among PCOS Women

Interestingly, even though 64% of the women with PCOS reported mild to extremely severe anxiety but none of the sociodemographic variables such as age, BMI,

unemployment or clinical manifestations such as hirsutism score, menstrual irregularity, acne and wish to conceive were found to be a significant risk factor of anxiety on performing univariate regression (p value >0.05) as depicted in Table 3.

3.4. Association of Clinico-socio-demographic Risk Factors with Stress among PCOS Women

Logistic regression analysis of the clinico-socio-demographic factors such as age, BMI, employment status as well as clinical manifestations such as hirsutism score, menstrual irregularity, acne and wish to conceive failed to reveal any significant predictors in women with PCOS experiencing stress (p value >0.05) as seen in Table 4.

Table 3. Logistic regression table highlighting association of clinico-socio-demographic risk factors with anxiety (*p<0.05)

Anxiety	Beta coefficient	Standard error	P value	Odds ratio	Odds ratio Lower bound (95%)	Odds ratio Upper bound (95%)
Age (years)	-0.043	0.055	0.433	0.958	0.860	1.067
Hirsutism	0.071	0.040	0.074	1.074	0.993	1.161
Body mass index (kg/m²)						
18.5 to 22.99 kg/m ² {Normal BMI}				1.000		
<18.5 kg/m ² {Underweight}	2.026	1.808	0.263	7.584	0.219	262.557
23 to 24.99 kg/m ² {Overweight}	0.960	0.652	0.141	2.612	0.727	9.379
>=25 kg/m ² {Obese}	0.734	0.482	0.128	2.084	0.810	5.363
Employment status	-0.327	0.574	0.570	0.721	0.234	2.224
Menstrual Irregularity	0.598	1.429	0.676	1.818	0.110	29.943
Acne	0.203	0.487	0.676	1.225	0.472	3.181
Willing to conceive	0.019	0.494	0.970	1.019	0.387	2.681

Table 4. Logistic regression table highlighting association of clinico-socio-demographic risk factors with stress (*p<0.05)

Stress	Beta coefficient	Standard error	P value	Odds ratio	Odds ratio Lower bound (95%)	Odds ratio Upper bound (95%)
Age (years)	0.010	0.053	0.852	1.010	0.910	1.121
Hirsutism	0.066	0.036	0.067	1.068	0.995	1.147
Body mass index (kg/m²)						
18.5 to 22.99 kg/m ² {Normal BMI}				1.000		
<18.5 kg/m ² {Underweight}	2.233	1.970	0.257	9.331	0.196	443.274
23 to 24.99 kg/m ² {Overweight}	0.505	0.624	0.418	1.657	0.488	5.625
>=25 kg/m ² {Obese}	0.044	0.473	0.926	1.045	0.413	2.642
Employment status	-0.536	0.551	0.330	0.585	0.199	1.721
Menstrual Irregularity	0.156	1.428	0.913	1.168	0.071	19.196
Acne	0.329	0.466	0.480	1.390	0.558	3.465
Willing to conceive	-0.086	0.473	0.856	0.918	0.363	2.320

4. Discussion

In the present study, in a representative sample of young women with PCOS of reproductive age, it was observed that a large number suffered from depression 46.16%, anxiety 64.42% and stress 53.85%. These psychological deficits, particularly depression have been attributed to a number of pathophysiological deviations and /or clinico-socio-demographic risk factors. Similar to results found in this study, several studies have reported an increased risk of depression with obesity in women with PCOS [16,17]. Body image related factors such as BMI and waist circumference have been identified with the occurrence of depression like behaviors among PCOS women [17]. Also, in adolescents with PCOS, obesity is considered as one of the major factors causing depression [18]. However, others have reported the risk for depression can be independent of BMI in women with PCOS [19]. Abdominal obesity is characterized by hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis. Hyperactivity of opioid system in obese women results in hyperactivity of hypothalamic-pituitary-adrenal axis which increases cortisol levels that results in fat accumulation and weight gain due to conversion of premature adipocytes to adipocytes. In addition, change in setpoint of HPA axis leads to an altered regulation of adrenocorticotrophic hormone (ACTH) and cortisol secretory activity which have been suggested to cause depression. Even increased production and secretion of corticotropin releasing hormone and impaired corticosteroid receptor signaling in various brain regions have been proposed to cause depression [20-25]. Similar to other studies [16,17], in this study it was observed that the risk for depression increased as a function of increase in BMI. Thus, overweight, and obese women with PCOS were more prone to depression.

Overall, depression can also result from social factor such as unemployment. It has been reported that there is a higher prevalence of depressive symptoms and major depressive disorder in unemployed individuals of both genders [26]. However, no such association was found between the prevalence of depression in women with PCOS and their work profile. Additionally, it was expected that older women suffering from PCOS would report being more depressed than younger women but no such trend was found. It has been observed and reported that typical abnormal features of PCOS become ameliorated with the increase in age and clinical features of PCOS affecting self-confidence tend to easily frustrate younger PCOS patients than middle aged women [27-29].

In the present study, clinical features such as hirsutism and acne were identified as risk factors associated with depression. Women with hirsutism have expressed body image dissatisfaction [30,31] and the degree of dissatisfaction was found to be associated with the severity of depressive symptoms [32]. However, there was a lack of relationship between extent of hirsutism and level of depression [33]. Similarly, acne has been found to be

associated with depression, although no association was observed between severity of acne and the degree of depression among women with PCOS [34].

A possible mechanism explaining depression among PCOS women is the disturbance in Luteinizing Hormone pulsatility observed in PCOS women which affects all levels of the Hypothalamic Pituitary Ovarian axis. In women with PCOS, a disruption in the feedback to the HPO axis from elevated estrogen levels in the follicular phase causes LH dysregulation. Several studies have reported major depressive disorders in women that are associated with disruption of LH pulsatility in the follicular phase of the menstrual cycle [35,36].

Women with PCOS as observed in this study as well, experience substantial anxiety linked to a number of clinico-socio-demographic factors. Body image related factors such as BMI and hirsutism among fertile and infertile women have been shown to be positively correlated with anxiety like behavior, however, even though women with PCOS reported high levels of anxiety, the increased odds ratio of these factors, did not achieve statistical significance in the present study [17]. Evidence suggests that women with PCOS face fertility related issues after marriage and, additionally distress due to social and family pressure [37] along with unsuccessful infertility treatment [38] which contributes to anxiety in these women. Interestingly, the wish to conceive did not achieve statistical significance as an associated risk factor for anxiety among women with PCOS in the present study.

Clinico-socio-demographic manifestations such as work status, age, menstrual irregularity, acne and hirsutism, in contrast to their impact on depression did not contribute significantly to an increase in level of anxiety in present study. In contrast others have noted that these factors negatively impact self-image, self-esteem, and body image, that is an individual's psychological experience of his/her body appearance and function. Importantly, these deficits have been shown to correlate significantly with levels of anxiety [39-42]. Overall, hyperandrogenemia, hyperinsulinemia and aberrant ghrelin levels have been suggested as an explanation for abnormal anxiety levels in women with PCOS, however, its etiology is still unclear [40,43].

Clinical and demographic factors associated with PCOS such as age, work status, menstrual irregularity, hirsutism, acne as well as high BMI were not found to be significantly linked to a stress as risk factors in women with PCOS, similar to those reported in adolescents [44]. However, several studies have reported strong associations between menstrual dysfunction, hirsutism, seborrhea and hair loss to psychological distress while acne did not [45,46].

Genetic, developmental, and environmental factors enhance metabolic stress [47]. High stress levels especially in women facing infertility consequently results in additional health issues, emotional distress, marital problems, and aggravated stress [48-50].

5. Conclusions

A large number of women with PCOS experience various levels of depression, anxiety and stress as a result of their condition. Furthermore, it is important to note that several sociodemographic and clinical factors were linked to psychological distress experienced by them. Specifically with regard to depression, it was found that BMI, hirsutism, and acne significantly increased the risk of depression. It is suggested that these findings can be used by clinicians and healthcare practitioners to develop a comprehensive approach for the management of women with PCOS using biopsychosocial model of health [51,52].

6. Clinical Implications and Recommendations

Clinically, it is imperative women suffering from PCOS should be screened for depression, anxiety and stress including the associated clinico-socio-demographic risk factors. Screening should be incorporated on an ongoing regular basis, as its manifestation may change positively, and/or negatively during its course of treatment. Measures should be taken by including a wellness program, including mindfulness, yoga etc., as well as by encouraging the patient to adopt an active lifestyle. Women suffering from hirsutism, acne and more mood alterations due to aberrant hormonal profiles should receive psychological counselling in addition to their medical management. It is also suggested that future studies include an assessment of the patient's hormonal and personality profiles as well as other psychological parameters such as self-esteem, self-confidence, body image etc.

Financial Support and Sponsorship

Nil.

Conflicts of Interest

There are no conflicts of interest.

REFERENCES

- [1] Conte F, Banting L, Teede HJ, Stepto NK, "Mental health and physical activity in women with polycystic ovary syndrome: a brief review," *Sports Med.*, 45(4), 497-504, 2015. doi: 10.1007/s40279-014-0291-6. PMID: 25430602; PMCID: PMC4382527.
- [2] Malik S, Jain K, Talwar P, Prasad S, Dhorepatil B, Gouri Devi, "Management of polycystic ovary syndrome in India," *Fertil Sci Res.*, 1,23-43,2014.
- [3] Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R et al., "Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group," *Fertil Steril.*, 97(1), 28-38.e25, 2012. doi: 10.1016/j.fertnstert.2011.09.024. Epub 2011 Dec 6. PMID: 22153789.
- [4] Malik-Aslam A, Reaney MD, Speight J, "The suitability of polycystic ovary syndrome-specific questionnaires for measuring the impact of PCOS on quality of life in clinical trials," *Value Health*, 13(4), 440-6, 2010. doi: 10.1111/j.1524-4733.2010.00696. x. Epub 2010 Mar 10. PMID: 20230548.
- [5] Månsson M, Holte J, Landin-Wilhelmsen K, Dahlgren E, Johansson A, Landén M, "Women with polycystic ovary syndrome are often depressed or anxious--a case control study." *Psychoneuroendocrinology*, 33(8), 1132-8, 2008. doi: 10.1016/j.psyneuen.2008.06.003. Epub 2008 Jul 30. PMID: 18672334.
- [6] Hussain A, Chandel RK, Ganie MA, Dar MA, Rather YH, Wani ZA et al., "Prevalence of psychiatric disorders in patients with a diagnosis of polycystic ovary syndrome in Kashmir." *Indian J Psychol Med.*, 37(1),66-70, 2015. doi: 10.4103/0253-7176.150822. PMID: 25722515; PMCID: PMC4341314.
- [7] Upadhyaya SK, Sharma A, Agrawal A, "Prevalence of anxiety and depression in polycystic ovarian syndrome," *Int J Med Sci Public Health*, 5,681-3, 2016.
- [8] Gnawali A, Patel V, Cuello-Ramírez A, Al Kaabi AS, Noor A, Rashid MY et al., "Why are Women with Polycystic Ovary Syndrome at Increased Risk of Depression? Exploring the Etiological Maze," *Cureus* 22, 13(2), e13489, 2021. doi: 10.7759/cureus.13489. PMID: 33777576; PMCID: PMC7990040.
- [9] Yen SS, "The polycystic ovary syndrome," *Clin Endocrinol (Oxf)*, 12(2), 177-207, 1980. doi: 10.1111/j.1365-2265.1980.tb02132. x. PMID: 6772357.
- [10] McKenna TJ, "Pathogenesis and treatment of polycystic ovary syndrome," *N Engl J Med.*, 318(9), 558-62, 1988. doi: 10.1056/NEJM198803033180906. PMID: 3277057.
- [11] Wang Y, Ni Z, Li K, "The prevalence of anxiety and depression of different severity in women with polycystic ovary syndrome: a meta-analysis," *Gynecol Endocrinol.*, 37(12), 1072-1078, 2021. doi: 10.1080/09513590.2021.1942452. Epub 2021 Jun 24. PMID: 34165386.
- [12] Chaudhari AP, Mazumdar K, Mehta PD, "Anxiety, Depression, and Quality of Life in Women with Polycystic Ovarian Syndrome." *Indian J Psychol Med.* 40(3), 239-246, 2018. doi: 10.4103/IJPSYM.IJPSYM_561_17. PMID: 29875531; PMCID: PMC5968645.
- [13] Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril.*, 81(1), 19-25, 2004. doi: 10.1016/j.fertnstert.2003.10.004. PMID: 14711538.
- [14] Ferriman D, Gallwey JD, "Clinical assessment of body hair growth in women," *J Clin Endocrinol Metab.*, 21, 1440-7, 1961. doi: 10.1210/jcem-21-11-1440. PMID: 13892577.
- [15] Lovibond PF, Lovibond SH, "The structure of negative

- emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories," *Behav Res Ther.*, 33(3), 335-43, 1995. doi: 10.1016/0005-7967(94)00075-u. PMID: 7726811.
- [16] Mirghafourvand M, Charandabi SM, Lak TB, Aliasghari F, "Predictors of Depression in Iranian Women with Polycystic Ovarian Syndrome," *Community Ment Health J.*, 54(8), 1274-1283, 2018. doi: 10.1007/s10597-017-0188-6. Epub 2017 Nov 14. PMID: 29138958.
- [17] Lin H, Liu M, Zhong D, Ng EHY, Liu J, Li J, Shi Y, Zhang C, Wen X, Mai Z, Ou M, Ma H, "The Prevalence and Factors Associated With Anxiety-Like and Depression-Like Behaviors in Women With Polycystic Ovary Syndrome," *Front Psychiatry*, 12, 709674, 2021. doi: 10.3389/fpsy.2021.709674. PMID: 34744814; PMCID: PMC8563587.
- [18] Arslanian SA, Lewy VD, Danadian K, "Glucose intolerance in obese adolescents with polycystic ovary syndrome: roles of insulin resistance and beta-cell dysfunction and risk of cardiovascular disease," *J Clin Endocrinol Metab.*, 86(1), 66-71, 2001. doi: 10.1210/jcem.86.1.7123. PMID: 11231980.
- [19] Dokras A, Clifton S, Futterweit W, Wild R, "Increased risk for abnormal depression scores in women with polycystic ovary syndrome: a systematic review and meta-analysis," *Obstet Gynecol.*, 117(1), 145-152, 2011. doi: 10.1097/AOG.0b013e318202b0a4. PMID: 21173657.
- [20] Pasquali R, Vicennati V, "Activity of the hypothalamic-pituitary-adrenal axis in different obesity phenotypes," *Int J Obes Relat Metab Disord.*, 24 Suppl 2, S47-9, 2000. PMID: 10997608.
- [21] Walker BR, "Activation of the hypothalamic-pituitary-adrenal axis in obesity: cause or consequence?" *Growth Horm IGF Res.*, 11 Suppl A, S91-5, 2001. doi: 10.1016/s1096-6374(01)80015-0. PMID: 11527096.
- [22] Belanoff JK, Kalehzan M, Sund B, Fleming Ficek SK, Schatzberg AF, "Cortisol activity and cognitive changes in psychotic major depression," *Am J Psychiatry*, 158(10), 1612-6, 2001. doi: 10.1176/appi.ajp.158.10.1612. PMID: 11578992.
- [23] Holsboer F, "The corticosteroid receptor hypothesis of depression," *Neuropsychopharmacology*, 23(5), 477-501, 2000. doi: 10.1016/S0893-133X(00)00159-7. PMID: 11027914.
- [24] Angela C. Incollingo Rodriguez, Elissa S. Epel, Megan L. White, Erin C. Standen, Jonathan R. Seckl, A. Janet Tomiyama, "Hypothalamic-pituitary-adrenal axis dysregulation and cortisol activity in obesity: A systematic review," *Psychoneuroendocrinology* 62, 301-318, 2015.
- [25] Maurizio Guido, Mario Ciampelli, Anna Maria Fulghesu, Virginia Pavone, Angela Barini, Laura De Marinis, Rosa Cento, Alessandro Caruso, and Antonio Lanzone, "Influence of body mass on the hypothalamic-pituitary-adrenal-axis response to naloxone in patients with polycystic ovary syndrome," *Fertility and Sterility*, 71(3), 1999.
- [26] Amiri S, "Unemployment associated with major depression disorder and depressive symptoms: a systematic review and meta-analysis," *Int J Occup Saf Ergon.*, 5, 1-13, 2021. doi: 10.1080/10803548.2021.1954793. Epub ahead of print. PMID: 34259616.
- [27] Harnod T, Chen W, Wang JH, Lin SZ, Ding DC, "Association between depression risk and polycystic ovarian syndrome in young women: a retrospective nationwide population-based cohort study (1998-2013)," *Hum Reprod.*, 34(9), 1830-1837, 2019. doi: 10.1093/humrep/dez081. PMID: 31407777.
- [28] Farrell K, Antoni MH, "Insulin resistance, obesity, inflammation, and depression in polycystic ovary syndrome: biobehavioral mechanisms and interventions," *Fertil Steril.*, 94(5), 1565-74, 2010. doi: 10.1016/j.fertnstert.2010.03.081. Epub 2010 May 14. PMID: 20471009; PMCID: PMC2941530.
- [29] McCartney CR, Marshall JC, "CLINICAL PRACTICE. Polycystic Ovary Syndrome," *N Engl J Med.*, 375(1), 54-64, 2016. doi: 10.1056/NEJMcpl514916. PMID: 27406348; PMCID: PMC5301909.
- [30] Keegan A, Liao LM, Boyle M, Keegan A, Liao L-M, Boyle M, "Hirsutism: a psychological analysis," *Journal of Health Psychology*, 8(3), 327-45, 2005.
- [31] Barth JH, Catalan J, Cherry CA, Day A, "Psychological morbidity in women referred for treatment of hirsutism," *J Psychosom Res.* 37(6), 615-9, 1993;.
- [32] Lisa M. Pastore, James T. Patrie, Wendy L. Morris, Parchayi Dalal, and Megan J Bray, "Depression Symptoms and Body Dissatisfaction Association Among Polycystic Ovary Syndrome," *Women J Psychosom Res.*, 71(4), 270-276, 2011. doi: 10.1016/j.jpsychores.2011.02.005.
- [33] Shulman LH, DeRogatis L, Spielvogel R, Miller JL & Rose LI, "Serum androgens and depression in women with facial hirsutism," *Journal of the American Academy of Dermatology*, 27, 178-181, 1992.
- [34] Rasgon NL, Rao RC, Hwang S, Altshuler LL, Elman S, Zuckerbrow-Miller J, Korenman SG, Rasgon NL, Rao RC, Hwang S, Altshuler LL, Elman S, Zuckerbrow-Miller J, Korenman SG, "Depression in women with polycystic ovary syndrome: clinical and biochemical correlates," *J Affect Disord.* 74(3), 299-304, 2003 [PubMed: 12738050]
- [35] Grambsch P, Young EA, Meller WH, "Pulsatile luteinizing hormone disruption in depression," *Psychoneuroendocrinology*, 29(7), 825-9, 2004. doi: 10.1016/S0306-4530(03)00146-X. PMID: 15177697.
- [36] Hernández-Hernández OT, Martínez-Mota L, Herrera-Pérez JJ, Jiménez-Rubio G, "Role of Estradiol in the Expression of Genes Involved in Serotonin Neurotransmission: Implications for Female Depression," *Curr Neuropharmacol.* 17(5), 459-471, 2019. doi: 10.2174/1570159X16666180628165107. PMID: 29956632; PMCID: PMC6520586.
- [37] Aqınaz G, Albayrak E, Acımaz B, Başer M, Soyak M, Zararsız G, İpek M, Üderris I, "Level of anxiety, depression, self-esteem, social anxiety, and quality of life among the women with polycystic ovary syndrome," *Scientific World Journal*, 2013, 851815, 2013. doi: 10.1155/2013/851815. PMID: 23935436; PMCID: PMC3725786.
- [38] S. Benson, S. Hahn, S. Tan, K. Mann, O.E. Janssen, M. Schedlowski, and S. Elsenbruch, "Prevalence and implications of anxiety in polycystic ovary syndrome:

results of an internet-based survey in Germany,” *Human Reproduction*, 24(6), 1446–1451, 2009

- [39] M. Azizi and F. Elyasi, “Psychosomatic aspects of polycystic ovarian syndrome: a review,” *Iranian Journal of Psychiatry and Behavioral Sciences*, 11(2), 21–30, 2017.
- [40] Alur-Gupta S, Chemerinski A, Liu C, Lipson J, Allison K, Sammel MD, Dokras A, “Body-image distress is increased in women with polycystic ovary syndrome and mediates depression and anxiety,” *Fertil Steril.*, 112(5), 930-938.e1, 2019. doi: 10.1016/j.fertnstert.2019.06.018. Epub 2019 Aug 5. PMID: 31395311; PMCID: PMC6858949.
- [41] Deeks AA, Gibson-Helm ME, Paul E, Teede HJ, “Is having polycystic ovary syndrome a predictor of poor psychological function including anxiety and depression?” *Hum Reprod.*, 26(6), 1399-407, 2011. doi: 10.1093/humrep/der071. Epub 2011 Mar 23. PMID: 21436137.
- [42] Friedman KE, Reichmann SK, Costanzo PR, Musante GJ, “Body image partially mediates the relationship between obesity and psychological distress,” *Obes Res.*, 10(1), 33-41, 2002. doi: 10.1038/oby.2002.5. PMID: 11786599.
- [43] Komarowska H, Stangierski A, Warmuz-Stangierska I, Lodyga M, Ochmanska K, Wasko R, Wanic-Kossowska M, Ruchala M, “Differences in the psychological and hormonal presentation of lean and obese patients with polycystic ovary syndrome,” *Neuro Endocrinol Lett.*, 34(7), 669-74, 2013. PMID: 24464003.
- [44] Khafagy G, El Sayed I, Abbas S, Soliman S, “Perceived Stress Scale Among Adolescents with Polycystic Ovary Syndrome,” *Int J Womens Health*, 12, 1253-1258, 2020. doi: 10.2147/IJWH.S279245. PMID: 33402850; PMCID: PMC7778675.
- [45] Eggers S, Kirchengast S, “The polycystic ovary syndrome--a medical condition but also an important psychosocial problem,” *Coll Antropol.*, 25(2), 673-85, 2001. PMID: 11811299.
- [46] Kitzinger C, Willmott J, “The thief of womanhood: women's experience of polycystic ovarian syndrome,” *Soc Sci Med.*, 54(3), 349-61. 2002. doi: 10.1016/s0277-9536(01)00034-x. PMID: 11824912.
- [47] Papalou O, Diamanti-Kandarakis E, “The role of stress in PCOS,” *Expert Rev Endocrinol Metab.*, 12(1), 87-95, 2017. doi: 10.1080/17446651.2017.1266250. Epub 2016 Dec 7. PMID: 30058880.
- [48] Ozkan M, Baysal B, “Emotional distress of infertile women in Turkey,” *Clin Exp Obstet Gynecol.*, 33(1), 44-6, 2006. PMID: 16761539.
- [49] Soltani M, Shairi MR, Roshan R, Rahimi CR, “The impact of emotionally focused therapy on emotional distress in infertile couples,” *Int J Fertil Steril.*, 7(4), 337-44, 2014. Epub 2013 Dec 22. PMID: 24520504; PMCID: PMC3901179.
- [50] Katole A, Saoji AV, “Prevalence of Primary Infertility and its Associated Risk Factors in Urban Population of Central India: A Community-Based Cross-Sectional Study,” *Indian J Community Med.*, 44(4), 337-341. 2019. doi: 10.4103/ijcm.IJCM_7_19. PMID: 31802796; PMCID: PMC6881900.
- [51] Engel G. The need for a new medical model: a challenge for biomedicine. *Science* 1977, 196: 129-136, DOI: <http://dx.doi.org/10.3109/13561828909043606>
- [52] Bansal A, Sethi J, Parasher RK, Tomar, “Supervised Structured Exercise Program on Adolescents with Polycystic Ovary Syndrome: Two Case Reports,” *J Clin of Diagn Res.*, 16(2),2022. QD01-QD03.