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Increased Risk of Infertility, Marital Maladjustment and Psychological Morbidity in PCOS Patients of Southern Punjab, Pakistan

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ABSTRACT

The clinical manifestations of polycystic ovarian syndrome (PCOS) have been linked with psychotic morbidity and infertility in the women of fertile age. Considering limited research data available about the psychological aspects in these patients, we conducted current study to assess psychotic distress and infertility in PCOS patients of southern Punjab, Pakistan. In this study 204 PCOS women and 150 controls were enrolled. Data of recruited patients was collected from different hospitals of South Punjab. A standardized questionnaire was used for obtaining formal consent and ethical approval. Our findings revealed that psychological morbidity was most common among infertile PCOS patients. The prevalence of anxiety (61.8% vs. 18.7%), depression (56.9% vs.15.3%), sleep apnea (35.3% vs. 6.7%), eating disorders (18.1% vs. 1.3%), marital maladjustment (27.5% vs. 5.3%), poor quality of life (35.3% vs. 3.3%) and migraine (55.4% vs. 10.7%) was significantly high in PCOS women as compared to controls ($p<0.001$). Infertility was significantly linked to psychotic implications and PCOS female ($p<0.001$). So, infertile PCOS patients were more depressed and anxious as compared to fertile. Infertility, especially primary infertility represents a major risk factor for psychological implications in Pakistani PCOS women of southern Punjab. Psychological disturbance was found to be more prevalent in married females as compared to unmarried females.

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Key words
Polycystic ovarian syndrome, Psychotic morbidity, Anxiety/ Depression, Sleep apnea, Marital maladjustment

INTRODUCTION

In human females of fertile age, the most prevalent endocrine disorder was foremost revealed by Stein and Leventhal in 1935 and is known as "Polycystic Ovarian Syndrome (PCOS)" (Stein and Leventhal, 1935; Asuncion *et al*., 2000). Its prevalence ranges between 4-25% (Nasiri *et al*., 2013) and World Health Organization (WHO) has calculated approximately 116 million women worldwide (3.4% of the population) affected by PCOS (Mohan, 2010). In Pakistan approximately 5-10% women were affected by this disorder (Azziz *et al*., 2009) and this disease is characterized by numerous phenotypes such as hirsutism, acne, obesity, problems in weight loss and maintaining BMI, decreased ratio of follicle stimulating hormone (FSH) to lentinizing hormone (LH) and pelvic pain (Goswami *et al*., 2012). Elevated ratio of LH to FSH among females of reproductive age is thought to be most frequent hormonal disorder and one of the main etiology of subfertility (Boomsma *et al*., 2008; Teede *et al*., 2010) and menstrual irregularity such as anovulation, menorrhagia, oligomenorrhea and infertility as well (Ovesen *et al*., 1998). This disorder leads to high cholesterol level, type 2 diabetes, obesity, endometriosis and increased risk of miscarriages (Speroff and Fritz, 2005). The precise and specific cause of this disease is still unclear, numerous factors such as high insulin level and its resistance, obesity, genetic predisposition, chemical contamination and environmental hazards (Nasiri *et al*., 2013) involved in PCOS. Goswami and coworkers reported stress, contraceptive pills usage, hormonal imbalance, overstimulation and secretions of the adrenal glands during infancy have contributed in the progress of this disorder (Goswami *et al*., 2012). All psychogenic complications appeared due to clinical manifestation such as hirsutism, acne, obesity and infertility. These patients not only experience depression and anxiety due to concerns about their femininity but also have a poor and lower self-esteem and image (Masuleh, 2018; Shahbazi *et al*., 2017; Amini

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et al., 2012; Ciplaka-Gaffin *et al*., 2012; Shakerardekani *et al*., 2011). Arshad *et al.* (2012) reported that PCOS causes negative impact on various aspects of quality of life and affect their activities, physical performance and mental health. Furthermore, approximately 40% of such patients experience depression to some extent and obesity was observed to be major causative agent of depression. So, negative moods and depression reduced the quality of life (QoL) and self-efficacy of these patients (Deeks *et al*., 2010). This syndrome also affects the marital adjustment of such patients as well as various psychological consequences including sexual dysfunction and social maladjustment (Drosdzol *et al*., 2007; Hahn *et al*., 2005). Whereas marital maladjustment causes depressing impact on couple's QoL and also decreases the intensity of happiness among individuals (Darvizeh and Kahaki, 2008). PCOS is recognized to be the risk factor for anxiety (Roy-Byrne *et al*., 2008) and depression (Brydon *et al*., 2006). In PCOS the frequency of depression ranged between 27.9-64% (Bhattacharya and Jha, 2010; Deeks *et al*., 2010) which is higher than taht of normal human females (7.2-8%) (Gwynn *et al*., 2008). Anxiety is highly prevalent in PCOS patients ranging from 34% (Deeks *et al*., 2010) to 58% (Benson *et al*., 2009) as compared to 18% in normal females (Gwynn *et al*., 2008). The depression in PCOS patients has been reported to be 40% and incidence of suicide elevated up to 7 times (Kerchner *et al*., 2009; Mansson *et al*., 2008). Although different ethnicities, geographical and racial factors might be involved in its prevalence, but increased anxiety and depression in such patients seen to be majorly responsible (Eggers and Kirchengast, 2001; Bishop *et al*., 2009). However, acne (Benson *et al*., 2009), hirsutism and BMI (Hahn *et al*., 2005) have been associated with elevated psychotic distresses while no association has been reported by others (Kerchner *et al*., 2009). Various psychological distresses have impact on body image, and self confidence. The fear of infertility leads to loss of femininity, worries about less attractive body, depression and anxiety (Podfigurna-Stopa *et al*., 2015; Spritzer *et al*., 2019). These factors proved to be threat to decrease the QoL of the patients (Morshedi *et al*., 2021). Poor QoL in such patients is associated with anxiety, depression, aggression, sexual dis-satisfaction, even life dis-satisfaction, body pain, weight gain, menstrual dysfunction, infertility and reduced interpersonal relationships (Kitzinger and Willmott, 2002; Trent *et al*., 2002, 2003, 2005; Elsenbruch *et al*., 2003).

This study was undertaken due to limited research data available related to psychological dimensions of PCOS in Pakistan, particularly southern Punjab.

MATERIALS AND METHODS

The study population consisted of 354 (post and premenopausal) women from Southern Punjab, Pakistan (204 diagnosed as PCOS and 150 controls), between the ages of 15-60 years. Data of recruited patients was collected from different hospitals of South Punjab (Bakhtawar Amin Memorial hospital Multan, Nishtar hospital Multan, DHQ Muzaffargarh, THQ Jatoi, Muzaffargarh and Indus hospital Muzaffargarh). Patients were diagnosed on the basis of Rotterdam criteria, fulfilling any two of the given three conditions (i) biochemical or clinical manifestation due to hyperandrogenism, (ii) an-ovulation and (iii) polycystic ovaries (The Rotterdam ESHRE/ASRM-sponsored PCOS Consensus Workshop Group, 2004). All these respondents who suffered due to androgen secreting from tumors, cushing's syndrome, thyroid malfunctioning, adrenal hyperplasia, hyperprolactinaemia, pregnant or lactating women and those who received prior hormonal therapy were excluded from present study. Only those females were included in this study who fulfilled the inclusion criteria (Rotterdam criterian) of PCOS. A standardized questionnaire was administered in order to collect the data after obtaining ethical approval from University Research Ethics Committee (UREC) via letter No: WUM/UREC/0008. All participants were informed about the norms and objectives of this study and clearly stated written consent was obtained from each participant. Therefore, each individual underwent physical examination and anthropometric measurement.

Psychological estimation of anxiety and depression was assessed by the "Hospital Anxiety and Depression Scale (HADS)". The maximum score for depression and anxiety is 21 for each. Bjelland *et al*. (2002) considered cut-off point of 8/21 by following numerous studies which identified cut-off value of 8/21 for depression as well as anxiety. Specificity for anxiety (HADS-A) and depression (HADS-D) is 0.78 and 0.79 respectively and sensitivity for both is 0.9 and 0.82, respectively.

The data was analyzed by using SPSS (v. 20), categorical data was analyzed by Chi-square test and association between different variables was determined by Pearson Correlation coefficient. For all results "p" value less than or equal to 0.05 was observed to be statistically significant.

RESULTS

In current study, depression, anxiety, sleep apnea, eating disorders, reduced quality of life, marital maladjustment and migraine were found to be highly significant in PCOS versus controls. PCOS patients

showed high frequency of depression (56.9% vs. 15.3%; p<0.001), anxiety (61.8% vs. 18.7%; p<0.001), sleep apnea (35.3% vs. 6.7%; p<0.001), eating disorders (18.1% vs. 1.3%; p<0.001), reduced quality of life (35.3% vs. 3.3%; p<0.001), marital maladjustment (27.5% vs. 5.3%; p<0.001) and migraine (55.4% vs. 10.7%; p-value <0.001), as compared to healthy controls (Table I).

Table I. Prevalence of Psychological abnormalities in PCOS and controls.

Parameters	Controls (n=150)	PCOS (n=204)	Chi-square	OR (95%CI)
Depression	23 (15.3%)	116*** (56.9%)	62.52[a]	7.28 (4.31-12.29)
Anxiety	28 (18.7%)	126*** (61.8%)	65.33[a]	7.04 (4.28-11.59)
Sleep apnea	10 (6.7%)	72*** (35.3%)	39.80[a]	7.64 (3.78-15.42)
Eating disorders	2 (1.3%)	37 *** (18.1%)	24.90[a]	16.40 (3.89-69.20)
Reduced quality of life	5 (3.3%)	72*** (35.3%)	51.88[a]	15.82 (6.20-40.36)
Marital maladjustment	8 (5.3%)	56*** (27.5%)		
Migraine	16 (10.7%)	113*** (55.4%)	74.66[a]	10.40 (5.78-18.71)

*$p \leq 0.05$= significant; **$p \leq 0.01$=highly significant; ***$p \leq 0.001$= very highly significant; OR, odds ratio; CI, confidence interval; "n" in parenthesis indicates "number of subjects"; [a] for Chi square test.

Demographic characteristics like marital status, educational status and socioeconomic status and locality, were compared in PCOS and healthy control subjects. Married PCOS patients were significantly affected (63.7% vs. 40.7%, χ^2=18.5, p<0.001) as compared to married controls. This disease was more prevalent in urban than rural area with statistically significant association (55.9% vs. 44.1%, χ^2= 64.27[a], p<0.001) (Table II).

Results revealed that the most common factor of psychological distress was infertility followed by PCOS. Infertility is significantly high in PCOS cases as compared to controls and found to be significantly associated with PCOS (62.3% vs. 21.3%, χ^2= 27.919[a], p<0.001) (Table-III).

Non-significant difference was observed in primary and secondary infertility of PCOS and controls (χ^2=0.71[a], p=0.4). However primary infertility in PCOS patients was more frequent as compared to secondary infertility (56.8% vs. 43.2%) and the percentage of PCOS patients in 0.50-5.49 years duration of infertility was high than controls (χ^2= 4.3[a], p=0.37) but result was non-significant (Table IV).

Table II. Demographic features of PCOS and controls.

Parameters	Controls (n=150)	PCOS (n=204)	Chi-square	p value
Marital status				
Unmarried	89 (59.3%)	74 (36.3%)	18.5[a]	<0.001***
Married	61 (40.7%)	130 (63.7%)		
Educational status				
Illiterate	56 (37.3%)	74 (36.3%)	6.709[a]	0.243
Middle	15 (10.0%)	31 (15.2%)		
High	23 (15.3%)	43 (21.1%)		
Intermediate	33 (22.0%)	34 (16.7%)		
Graduate	4 (2.7%)	6 (2.9%)		
Postgraduate	19 (12.7%)	16 (7.8%)		
Socioeconomic status				
Lower	40 (26.7%)	66 (32.4%)	1.332[a]	0.248
Middle	110 (73.3%)	138 (67.6%)		
Locality				
Rural	129 (86.0%)	90 (44.1%)	64.27[a]	<0.001***
Urban	21 (14.0%)	114 (55.9%)		

For statistical details see Table I.

Table III. Prevalence of infertility in PCOS and controls.

Parameters	PCOS (n=130)	Controls (n=61)	Chi-square	OR (95%CI)	p value
Infertility					
Yes	81 (62.3%)	13 (21.3%)	27.919[a]	0.164 (0.081-0.333)	<0.001***
No	49 (37.7%)	48 (78.7%)			

For statistical details and abbreviations see Table I.

Psychological morbidities like depression (r=0.145, p=0.03), anxiety (r=0.137, p=0.05), sleep apnea (r=0.345, p<0.001), reduced quality of life (r=0.172, p=0.01) and marital maladjustment (r=0.611, p<0.001) were statistically significantly linked with infertility. Infertility was non-significantly associated with eating disorders (r= 0.125, p= 0.075), while negatively linked with migraine (r= -0.015, p= 0.833) (Table V).

Table IV. Prevalence of type of infertility and its duration in PCOS and controls.

Parameters	PCOS (n=81)	Controls (n=13)	Chi square	p value
Type of infertility				
Primary infertility	46(56.8%)	9(69.2%)	0.71[a]	0.4
Secondary infertility	35(43.2%)	4(30.8%)		
Duration of infertility				
0.50-5.49 years	40(49.4%)	4 (30.8%)	4.3[a]	0.37
5.50-10.49 years	26(32.1%)	4 (30.8%)		
10.50-15.49 years	9(11.1%)	2 (15.4%)		
15.50-20.49 years	3(3.7%)	2 (15.4%)		
20.50-25.49 years	3(3.7%)	1 (7.7%)		

For statistical details see Table I.

Table V. Association of infertility to psychological implications.

Parameters	r-value	p-value
Depression	0.145	0.03**
Anxiety	0.137	0.05*
Sleep apnea	0.345	<0.001***
Eating disorders	0.125	0.075
Reduced quality of life	0.172	0.01**
Marital maladjustment	0.611	<0.001***
Migraine	-0.015	0.833

For statistical details see Table I.

Table VI. Prevalence of psychological abnormalities in married and unmarried PCOS patients.

Parameters	Unmarried (n=74)	Married (n=130)	Chi square	OR (95% CI)
Depression	29 (39.2%)	87*** (66.9%)	14.787	3.14 (1.74-5.68)
Anxiety	29 (39.2%)	91*** (70.0%)	18.482	3.62 (1.99-6.59)
Sleep apnea	11 (14.9%)	61*** (46.9%)	21.222	5.06 (2.45-10.48)
Eating disorders	7 (9.5%)	30* (23.1%)	5.890	2.87 (1.19-6.92)
Reduced quality of life	13 (17.6%)	59*** (45.4%)	15.978	3.90 (1.95-7.78)
Migraine	40 (54.1%)	73 (56.2%)	0.084	1.09 (0.61-1.93)

For statistical details see Table I.

All psychological abnormalities observed were highly significant in married PCOS women as compared to unmarried cases. Married females showed highly significant level of depression (66.9% vs. 39.2%; p<0.001), anxiety (70.0% vs. 39.2%; p<0.001), sleep apnea (46.9% vs. 14.9%; p<0.001), eating disorders (23.1% vs. 9.5%; p=0.015), reduced quality of life (45.4% vs. 17.6%; p<0.001) and migraine (56.2% vs. 54.1%; p=0.772), as compared to unmarried cases (Table VI).

Table VII. Prevalence of psychological abnormalities in urban and rural PCOS patients.

Parameters	Urban (n=114)	Rural (n=90)	Chi square	OR (95% CI)	p value
Depression	68 (59.6%)	48 (53.3%)	0.818[a]	1.29 (0.74-2.26)	0.366
Anxiety	69 (60.5%)	51 (56.7%)	0.309[a]	1.17 (0.67-2.06)	0.578
Sleep apnea	43 (37.7%)	29 (32.2%)	0.665[a]	1.27 (0.71-2.28)	0.415
Eating disorders	23 (20.2%)	14 (15.6%)	0.723[a]	1.37 (0.66-2.85)	0.395
Reduced quality of life	39 (34.2%)	33 (36.7%)	0.133[a]	0.90 (0.50-1.60)	0.715
Marital maladjustment	32 (28.1%)	2 (26.7%)			
Migraine	63 (55.3%)	50 (55.6%)	0.002[a]	0.99 (0.57-1.72)	0.967

For statistical details and abbreviations see Table I.

DISCUSSION

The major objective of current study was to explore the frequency/prevalence of infertility, marital maladjustment and psychotic implications and well beings in PCOS women of Pakistan. Our results showed significantly elevated incidence of anxiety, depression, sleep apnea, eating disorders, poor quality of life, marital maladjustment and migraine among patients with PCOS than that of the controls, with p<0.001. Various studies indicated higher frequency of psychological distress mostly anxiety, depressive and bipolar disorders among PCOS patients (Rasgon *et al.*, 2003; Klipstein and Goldberg, 2006; Bazarganipour *et al.*, 2013). Similarly, in 2019, a study reported 61.8% depression among young married PCOS patients in Pakistan. They observed that depression not only deteriorate psychological wellbeing but cause drastic impact on physical health of patients (Sidra *et al.*, 2019).

Numerous studies had reported same findings that anxiety and depression were most common distress

problems in PCOS patients (Mansson *et al*., 2008; Rassi *et al*., 2010; Cinar *et al*., 2011; Tan *et al*., 2017). These findings were found to be significantly increased incidence of social phobia in such cases and elevated incidence of anxiety disorder (Mansson *et al*., 2008). The findings of Sulaiman *et al*. (2017) are also in agreement with our study as they reported that the elevated risk of psychological burden is linked with this disease. Several other studies revealed that such patients tend to exhibit elevated risk of emotional distress (Teede *et al*., 2010; Barry *et al*., 2011; Veltman-Verhulst *et al*., 2012; Blay *et al*., 2016; Cooney *et al*., 2017). Our findings were in accordance with the findings exhibited by Bhattacharya and Jha (2010) who observed higher frequency of depression in cases as compared to controls. Asdaq and Yasmin (2020) also reported that anxiety, depression and stress were more frequent in cases as compared to control in Riyadh, Saudi Arabia (Asdaq and Yasmin, 2020). The current study also indicated that PCOS, anxiety, sleep apnea, eating disorders, poor QoL, marital maladjustment and migraine as risk factor for depression in Pakistani women. Several researchers had reported that hirsutism (Sonino *et al*., 1993) and acne (Mallon *et al*., 1999) are associated with anxiety, however other findings did not observe such association (Kerchner *et al*., 2009). Infertility became very common and troubling health threat facing married PCOS women. Our study also indicated that infertility is also a major risk factor for psychological implications, poor quality of life and marital maladjustment. Various studies had also confirmed that psychological disorders among PCOS patients might be associated with infertility (Cwikel *et al*., 2004). Many findings also indicated that infertile women felt greater pressure, irrespective of whether they are responsible for infertility (Zhang *et al*., 2009). However, as a result of after effects of infertility, Chinese PCOS women experienced pressure from within their married life, family and even society (Tan *et al*., 2017; Wang *et al*., 2016). Due to infertility, majority of PCOS women felt helpless and guilty (Zhang *et al*., 2009). Disturbed stress attitude and increased pressure (Benson *et al*., 2008) results in higher risk of decreased quality of life and psychiatric implications. Tan *et al*. (2017) reported that infertile PCOS patients were more likely anxious and depressed as compared to normal without fertility requirements. Our findings revealed that PCOS patients had more prevalent primary infertility versus secondary infertility. The results described by Eleawi *et al*. (2015) are in agreement with our findings, they also reported high prevalence of primary infertility in cases (Eleawi *et al*., 2015). Furthermore, our study revealed that such patients also showed high risk for the development of sleep disorders. Nandalike and coworkers reported that the frequency of "obstructive sleep apnea" (OSA) was higher in PCOS patients (Nandalike *et al*., 2012). In this study significantly high frequency rate of migraine was among women with PCOS ($p<0.001$), whereas Pourabolghasem and coworkers were not agreed and reported that migraine is not more frequent in PCOS affected women ($p=0.13$) (Pourabolghasem *et al*., 2009).

CONCLUSIONS

In conclusion, patients with PCOS are at increased risk of infertility, marital maladjustment which leads to psychological implications (anxiety, depression, sleep apnea), eating disorders, poor quality of life and migraine. All psychological variables were also highly prevalent in married as compared to unmarried PCOS patients.

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Statement of conflict of interest

The authors have declared no conflict of interest.

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