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Impulsivity, depression, and suicide in female patients with polycystic ovary syndrome and infertility

Maged A. Gomaa^{1*}, Asmaa A. Desoky¹, Dalal Amer¹, Doaa Alaa² and Mohamed A. Khalil¹

Abstract

Background Polycystic ovary syndrome (PCOS) is a common cause of infertility associated with multiple medical and psychiatric complications. The study compared suicide, impulsivity, and depression in females with PCOS to females with other causes of infertility.

Methods Sixty females with infertility were included in two groups. Group A included 30 females with PCOS and infertility, while group B included 30 females with infertility for other causes than PCOS. The assessment included infertility workup, medical history, hormonal profile, Beck depression inventory (BDI), Short Version of the UPPS-P Impulsive Behavior Scale, and Columbia Suicide Severity Rating Scale.

Results Group A had higher numbers of patients with depression (p-value = 0.04) and higher BDI (p-value = 0.001). Negative urgency, positive urgency, and sensation-seeking were higher in PCOS patients (p-value = 0.001, 0.03, 0.04). A significant positive correlation was found between sensation-seeking, BDI scores (p = 0.01), and LH level (p = 0.03).

Conclusions It was concluded that patients with PCOS have more depression and impulsivity than patients with other causes of infertility. Suicide was not different in both groups.

Keywords PCOS, Impulsivity, Infertility, Suicide, Depression

Background

Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder among females of reproductive age, with a 15–20% prevalence. Clinical findings of PCOS include oligomenorrhea, hirsutism, acne, and obesity. The syndrome is a significant cause of chronic infertility and hyperandrogenism, with the infertility rate up to 70% in females with PCOS [1, 2]. ESHRE/ARM (Rotterdam) Criteria for PCOS diagnosis require two of the following: clinical and/or biochemical

hyperandrogenism, oligoovulation or anovulation, and polycystic ovaries [3, 4].

PCOS symptoms include obesity which is prevalent in 50% of cases, hirsutism, and acne, which result from increased androgen sensitivity even at average androgen level. These symptoms may affect patients psychosocially and lead to depression and anxiety [5]. Indirectly, PCOS can increase depression by causing infertility or pregnancy complications, like diabetes and hypertension [6].

Many psychiatric disorders have been linked to PCOS in females. Schizophrenia, mood disorders, tics, eating disorders, and anxiety disorders have been associated with PCOS [7]. Fifty-seven studies with 172,040 patients included in a meta-analysis found that the risk of mood disorders, obsessive—compulsive disorder, and anxiety disorders are higher in PCOS [8]. The frequency of depression in female patients with PCOS is variable in

magedgomaa@kasralainy.edu.eg

² Gynecology and Obstetrics Department, Kasr Al Ainy Faculty of Medicine, Cairo University, Cairo, Egypt



^{*}Correspondence: Maged A. Gomaa

¹ Psychiatry Department, Kasr Al Ainy Faculty of Medicine, Cairo University, Cairo, Egypt

different studies (28–64%), while anxiety disorders range from 34 to 57%. Psychotic disorders are present in 5.6 to 21.3% of patients [9–11].

Impulsive and aggressive behaviors are associated with the risk of suicide; some researchers have found that 8.1% of women with PCOS are at risk of suicide [12]. The association between females with PCOS and personality disorders, namely borderline personality disorder, has been investigated where both disorders share some common features such as obesity, insulin resistance, and hyperandrogenemia. It has also been found that women with borderline personality disorder had higher androgen levels and a high incidence of PCOS [13]. Anger is increased while anger control is decreased in patients with PCOS regardless of anxiety level. Those patients' anger is related to hyperandrogenemia and high testosterone levels [14].

Other explanation of depression in women with PCOS is the role of inflammation and immune system. Where high estrogen level in PCOS increases interleukin 4 (IL-4), IL-1, IL-6, and interferon g (IFN-g) production having a significant impact on brain monoamines like 5-HT and DA. Cytokines activate the enzyme indoleamine 2,3-dioxygenase, which metabolizes the conversion of tryptophan into kynurenine. This results in lower numbers of 5-HT receptors in the brain and the depletion of tryptophan, the major precursor for 5-HT production; this is added to the role of hyperactive HPA axis due to stress and infertility causing the eruption of depressive symptoms [15].

This study aimed to evaluate suicide, impulsivity, and depression in female patients with PCOS and the association of these domains to the hormonal profile (FSH, LH, thyroid-stimulating hormone, estradiol, and prolactin).

We hypothesize that patients with PCOS have more depressive symptoms, impulsivity, and suicidal tendency than females with other causes of infertility.

Material and methods

Subjects

This observational cross-sectional study included a convenient sample of 30 females with primary infertility (couples who have not become pregnant after at least 1 year of having sex without using birth control methods) due to polycystic ovary syndrome (Group A). Patients were compared to a control group of 30 females with primary infertility due to causes other than ovarian factors (Group B). Suicide, depression, impulsivity, and hormonal disturbances were assessed in both groups.

Patients' age ranged from 18 to 45 years. They were recruited from the Gynecology Clinic (Infertility Clinic) of Faculty of Medicine Hospitals. Data collection lasted 6 months diagnosis of primary infertility due to polycystic ovary was confirmed by at least one gynecology

consultant using Rotterdam criteria [3]. Patients with medical conditions (apart from PCOS complications like type II diabetes, obesity, and metabolic syndrome) or receiving hormonal therapy (apart from clomiphene, a standard treatment for both groups) were excluded. Females with other infertility causes associated with PCOS (e.g., uterine factors, tubal factors) were excluded.

The control group included 30 females with primary infertility due to causes other than ovarian factors. They were matched to the patients regarding age, education, socioeconomic class, and duration of infertility. This group's exclusion criteria included chronic medical conditions, hormonal therapy (apart from clomiphene), and infertility due to other ovarian factors.

Patients with psychiatric disorders—other than personality disorders and depression—or receiving psychotropics were not included in either group.

Procedure

Patients fulfilling inclusion criteria attending the Gynecology Clinic were recruited consecutively after the initial assessment to diagnose the cause of infertility. The gynecological assessment was performed in the gynecology outpatient clinic, including menstrual history and infertility semi-structured interview, medical history, surgical history, weight, height, and history of hirsutism. Speculum examination, abdominal ultrasound, and hormonal profile, including follicular stimulating hormone (FSH), luteinizing hormone (LH), prolactin, estradiol (E2), progesterone, and thyroid-stimulating hormone (TSH) were done.

Psychiatric assessment of both groups included semistructured psychiatric interview, Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM IV-TR) Axis I Disorders (SCID I) [16], Beck depression inventory (BDI), Short Version of the UPPS-P Impulsive Behavior Scale [17], and Columbia Suicide Severity Rating Scale [18].

The semi-structured psychiatric interview included demographic data about the patients and psychiatric, medical, substance, and personal history. Diagnosis of psychiatric disorders was made using SCID I.

The BDI assesses symptoms of depression through a self-rated scale. Twenty-one items are scored from 0=least to 3=most. The total score has a minimum of 0 and a maximum score of 63. An increased score indicates an increase in depression severity. Abdel-Khalek [19] translated and validated the Arabic version.

UPPS-P consists of five subscales (Negative Urgency, Lack of Perseverance, Lack of Premeditation, Sensation Seeking, and Positive Urgency) that assess distinct impulsivity dimensions in a self-report scale. The 20-item questionnaire covers the last 6 months' acts/incidents for each

behavior or attitude. The subject choice ranges from 1 (agree strongly) to 4 (disagree strongly). The French version was translated into Arabic and validated by Bteich, Berbiche [20].

Multi-centers developed the Columbia-Suicide Severity Rating Scale (C-SSRS) to evaluate suicide in detail [18]. In 2012, Food and Drug Administration (FDA) supported C-SSRS as a gold standard for assessing suicide in research. It has been used already in clinical trials throughout the US and worldwide [21]. Several research studies have approved the validity and reliability of C-SSRS in identifying suicide risk [22].

The hormonal assessment included LH/FSH ratio, estradiol, prolactin, and TSH in all women within the last 6 months before the interview. The blood samples were withdrawn on the second day of the menstrual cycle.

The PCOS diagnosis was made using Rotterdam's criteria [3]. Diagnosis is dependent on identifying at least two of the following three features: oligo/anovulation, hyperandrogenism: clinical (hirsutism or male pattern alopecia) or biochemical (raised free androgen index or free testosterone), and polycystic ovaries on ultrasound (when ten small antral follicles are seen in each ovary). Hormonal causes like hyperprolactinemia, thyroid hormone abnormalities, adrenal hormone abnormalities, and Cushing syndrome were excluded.

Ethical considerations

The scientific and ethical committee of the Psychiatry Department approved the research protocol. The approval was further revised and confirmed by the Faculty of Medicine council.

All patients signed the informed consent that the ethical committee approved. The researchers received no funds, and they declared no conflict of interest.

Statistical analysis

The statistical package for Social Sciences (SPSS-version 20) was used to analyze data [23]. Mean and standard deviation presented quantitative data, while frequency (count) and percentage presented the qualitative data. The normality of data was tested using the Shapiro–Wilk test. Quantitative variables were compared using the Mann–Whitney test. Meanwhile, chi-square (x^2) test was used for comparing categorical data. Correlations were done using the Spearman correlation coefficient. Significance was considered when the p-value was less than 0.05.

Results

The mean age of group A was 27.2 ± 6.2 years compared to 29.2 ± 5.7 of the control group (p value=0.19). The mean score of the BMI in group A was 32.24 ± 5.5 , which

was significantly higher than in group B (29.14 ± 4.7) (*p*-value = 0.02) (Table 1).

Depression was more frequent in patients with PCOS, as 53.33% were diagnosed with major depressive disorder (MDD), 13.33% had other diagnoses, and 33.33% had no diagnosis. On the other hand, only 23.33% of patients in group B had MDD, 13.33% had other diagnoses, and 63.33% had no diagnosis (p-value = 0.04). The mean score for the BDI in group A (23.17 ± 8.88) was higher than in group B (13.17 ± 9.35). The difference was statistically significant (p = 0.001) (Table 1).

By applying the UPPS-P impulsive behavior scale, negative urgency was significantly higher in patients of group A (12.6 ± 2.6) than in group B (9.97 ± 2.7) (p-value=0.001). Also, positive urgency was significantly higher in group A (11.7 ± 2.1) than in group B (10.5 ± 2.6) (p-value=0.03). Besides, the sensation-seeking mean score was significantly higher in group A (mean= 9.97 ± 2.15) than in group B (mean= 8.7 ± 2.9) (p-value was 0.04). On the other hand, there were no differences between the two groups regarding lack of premeditation and lack of perseverance scales of the UPPS-P of statistical significance (Table 1).

The mean level of FSH was significantly higher in patients of the PCOS group $(5.20\pm1.12~\text{mIU/ml})$ than that of the control group $(9.82\pm11.61~\text{mIU/ml})$ (p-value < 0.001). Otherwise, there were no statistically significant differences between the two groups regarding LH, TSH, prolactin, and estradiol (Table 1).

The correlation of the PCOS group's clinical and laboratory findings showed that sensation-seeking significantly correlated with BDI scores (p=0.01) and LH level (p=0.03). TSH level significantly correlated with the BDI score (p=0.04) (Table 2).

Discussion

This work aimed to study suicide, depression, and impulsivity in primary infertile females with polycystic ovary syndrome (PCOS). We compared 30 primary infertile females with PCOS to 30 primary infertile females due to causes other than ovarian.

Depression was significantly higher in PCOS patients according to BDI (p<0.001), and diagnosis of MDD was more frequent (p=0.04) in comparison to the control group. Many studies reported that females with PCOS suffer more depression and lower quality of life than other women [24–26]. However, no reported study compared females with PCOS to other females with infertility due to other causes.

Multiple bio-psycho-social factors can explain depression in females with PCOS. Physical and metabolic complications of hyperandrogenism, obesity, and insulin resistance negatively affect mood [27]. Hirsutism and

 Table 1
 Comparison between patients with Polycystic ovaries and the control group

		Patients with PCO ^a	Control group	p
Age (mean ± SD)		27.2 ± 6.2	29.2 ± 5.7	0.19
Level of education N (%)	Illiterate	6 (20%)	9 (30%)	0.58
	Primary	9 (30%)	8 (26.7%)	
	secondary/diploma	12 (40%)	8 (26.7%)	
	University	3 (10%)	5 (16.6%)	
Working status N (%)	Working	4 (13.3%)	2 (6.7%)	0.39
	Not working	26 (86.7%)	28 (93.3%)	
BMI ^b (mean ± SD)		32.24 ± 5.5	29.14±4.7	0.02
Years of infertility (mean ± SD)		5.8 ± 3.4	5.8 ± 3.9	0.97
BDI ^c (mean ± SD)		23.17 ± 8.88	13.17 ± 9.53	< 0.001
Lifetime Suicidal ideations N (%)		13 (43.3%)	11 (36.7%)	0.60
Lifetime Suicidal attempts N (%)		2 (6.7%)	2 (6.7%)	1.00
Lifetime suicidal ideation	No suicidal ideations	17 (56.7%)	19 (63.3%)	0.68
	Wish to be dead	5 (16.7%)	7 (23.3%)	
	Non-specific active suicidal thoughts	2 (6.7%)	0 (0%)	
	Active suicidal ideation with any methods (not plan) without intent to act	2 (6.7%)	1(3.3%)	
	Active suicidal ideation with some intent to act, without specific plan	2 (6.7%)	2 (6.7%)	
	Active suicidal ideation with specific plan and intent	2 (6.7%)	1 (3.3%)	
SCID ^d diagnosis	MDDe	16 (53.33%)	7 (23.33%)	0.04
	Other diagnoses	4 (13.33%)	4 (13.33%)	
	No diagnosis	10 (33.3%)	19 (63.33%)	
UPPS (mean ± SD)	Negative urgency	12.6 ± 2.6	9.97 ± 2.7	0.001
	Positive urgency	11.7 ± 2.1	10.5 ± 2.6	0.03
	Lack of premeditation	8.23 ± 1.7	8.2 ± 2.4	0.79
	Lack of perseverance	7.97 ± 1.93	7.4 ± 2.02	0.36
	Sensation seeking	9.97 ± 2.15	8.7 ± 2.9	0.04
Hormones (mean ± SD)	FSH ^f (mlU/ml)	5.20 ± 1.12	9.82 ± 11.61	< 0.00
	LH ^g (mIU/ml)	6.73 ± 4.74	6.08 ± 4.93	0.57
	LH/FSH ratio	1.33 ± 0.95	0.73 ± 0.29	< 0.00
	TSH ^h (μU/mL)	2.18 ± 1.19	1.87 ± 0.85	0.44
	Prolactin (ng/mL)	12.89±7.33	17.75 ± 11.04	0.05
	Estradiol (pg/mL)	38.16 ± 20.89	33.78 ± 16.26	0.40

^a Polycystic ovaries

acne that affect body image reduce patients' self-esteem and sense of femininity [28]. Moreover, infertility caused by PCOS impacts the patients' marital and social lives [29], especially in the Egyptian community [30].

Patients with PCOS showed higher scores on all UPPS-P scales than the control group, three of these scales were statistically significant (urgency, positive urgency, and

sensation seeking). Positive urgency is related to risky behavior while experiencing extreme positive affect, whereas negative urgency is related to risky behavior while experiencing extreme negative affect [31]. This increase in impulsivity can be attributed to higher androgen levels in patients with PCOS. One study found a significant correlation between total testosterone levels,

^b Body mass index

^c Beck depression inventory

 $^{^{\}rm d}$ Structured clinical interview for DSM IV

^e Major depressive disorder

^f Follicle-stimulating hormone

^g Luteinizing hormone

^h Thyroid-stimulating hormone

Table 2 Correlation between clinical and laboratory findings in patients with polycystic ovaries

N=30		UPPS					BDIa
		Negative urgency	Positive urgency	Lack of premeditation	Lack of perseverance	Sensation seeking	
FSH ^b (mIU/mI)	r	0.05	0.05	0.19	0.15	0.18	0.01
	Р	0.80	0.79	0.32	0.44	0.34	0.99
LH ^c (mIU/mI)	r	0.21	0.19	-0.15	-0.24	0.41	0.23
	Р	0.27	0.31	0.44	0.21	0.03	0.22
LH/FSH	r	0.16	0.16	-0.22	-0.32	0.29	0.21
	р	0.41	0.40	0.25	0.09	0.12	0.27
Estradiol (pg/mL)	r	0.11	0.11	0.11	0.04	-0.02	0.08
	Р	0.56	0.57	0.57	0.84	0.94	0.68
Prolactin (ng/mL)	r	0.11	-0.01	0.27	0.16	-0.04	0.12
	Р	0.56	0.99	0.15	0.41	0.85	0.52
TSH ^d (μU/ml)	r	-0.21	-0.05	-0.17	-0.29	-0.01	-0.37
	Р	0.26	0.77	0.38	0.12	0.96	0.04
BDI	r	0.21	0.05	0.11	-0.09	0.49	
	Р	0.28	0.81	0.55	0.65	0.01	
Age	r	-0.28	-0.12	0.11	0.16	-0.11	0.05
	Р	0.14	0.52	0.55	0.39	0.58	0.81
Years of infertility	r	-0.25	-0.18	-0.04	-0.03	-0.01	-0.01
	Р	0.19	0.33	0.82	0.89	0.98	0.95

^a Beck depression inventory

total impulsiveness scores, motor impulsiveness, and non-planning-related impulsiveness [1]. Sensation seeking, which was significantly higher in the PCOS group, may increase the risk of suicide by increasing depressive symptoms or directly (Lee, Lim, Lee, & Park, 2016).

Lifetime suicidal ideations and lifetime suicidal attempts did not significantly differ between patients with PCOS and the control group. However, active suicidal ideations were twofold higher in PCOS patients (26.7%) than in the control group (13.3%). There was no statistically significant difference between the PCOS patients and controls regarding the number of patients who experienced the whole range of ideations. This can be explained by the relatively small sample size and the low suicidal rates in Egypt. However, the increased percentage of PCOS patients with active suicidal ideations makes them a risk group for suicidal attempts. A higher risk of suicide in the PCOS group was expected due to hyperandrogenism, higher depression, and impulsivity [32].

Forty percent of the group (PCOS patients and controls) had suicidal ideations, and 6.7% of them attempted suicide several times with varying completion levels. These results indicate high suicidality in this group of

infertile patients compared to the results of prevalence of suicide in Egyptian females (1.7 per 100,000) estimated by the World Health Organization (WHO) [33]. This increase in suicide in infertile females is consistent with other studies that found a link between infertility and increased suicidal thoughts [34, 35].

We found no relationship between age or years of infertility to suicide ideations, depression, or depressive symptoms in PCOS patients. Similarly, Ogawa and Takamatsu [36] found no relation between years of infertility and scores of depression in 83 infertile Japanese females.

In PCOS patients, UPPS-P sensation-seeking domain was positively correlated with the severity of depressive symptoms. This replicates Fornaro and his colleagues' results, who reported a positive correlation between depression severity and sensation seeking in patients with major depression [37].

Ortin and Lake [38] reported that sensation seeking was independently associated with depression and suicide. Sensation seeking was also associated with LH levels in PCOS patients in another study. Similar results supported an association between the novelty-seeking dimension, androgen levels, and LH levels in a study conducted on 75 male sex offenders [39].

^b Follicle-stimulating hormone

^c Luteinizing hormone

^d Thyroid-stimulating hormone

Women with PCOS are treated with lifestyle changes as caloric restriction and regular exercise in addition to hormonal contraception, yet the role on insulin sensitizer as pioglitazone and metformin in the management of depressive symptoms in women with PCOS is increasing [15, 40].

This study has some strengths. The control group consisted of primary infertile women with the same infertility duration. We could study the specific effects of having PCOS on suicide, depression, and impulsivity and not merely infertility. We have matched many confounding factors like age, education, and occupation. We have also excluded that the subjects and the controls have any psychotic, medical, or substance history of organic brain disease and not receiving any psychotropic medications.

One of the limitations of this study may be the relatively small number of patients included. Social factors specific to women who may have affected depression or suicide were not explored and controlled, such as traumas, stigma, and social support. Both cases and controls were obtained from patients seeking in vitro fertilization (IVF) for their infertility. There is a possibility that some patients did not disclose their suicidality, as talking openly about suicide might affect their chance of getting the help they needed.

Conclusion

It was concluded that patients with PCOS have more depression and impulsivity than patients with other causes of infertility. Suicide was not different in both groups.

Abbreviations

PCOS	Polycystic ovary syndrome
BDI	Beck depression inventory
FSH	Follicle stimulating hormone
LH	Luteinizing hormone
TSH	Thyroid-stimulating hormone

Estradiol E2

SCID Structured clinical interview for Diagnostic and Statistical Manual

of Mental Disorders, 4th Edition, Text Revision

UPPS Negative urgency, Lack of Premeditation, Lack of Perseverance,

Sensation Seeking

C-SSRS Columbia Suicide Severity Rating Scale FDA Food and Drug Administration SPSS Statistical Package for Social Sciences

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Authors' contributions

Maged Gomaa, MG, Analysis of data, Manuscript preparation and revision, Major contributor in writing the manuscript. Asmaa Desoky, AD, Study design, Psychiatric assessment, Analysis of data, Manuscript preparation and revision. Dalal Amer, DA, Study design, Manuscript preparation and revision. Doaa Alaa, DA, Study design, Gynecological assessment, Manuscript preparation and revision. Mohamed Khalil, MK, Study design, Statistical analysis, Manuscript preparation and revision. All authors. Read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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