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ASSESSMENT OF REPRODUCTIVE HEALTH, METABOLIC AND CARDIOVASCULAR RISK PROFILE IN FIRST-DEGREE RELATIVES OF WOMEN WITH POLYCYSTIC OVARIAN SYNDROME: A HOSPITAL-BASED STUDY IN MAHARASHTRA, INDIA

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is an endocrine and metabolic disorder in women with attributes of substantial genetic predisposition and potentially varied, but not yet blatantly identified, triggers. Moreover, it has clinical repercussions across the lifespan and is pertinent to related family members. In addition to the increased heritability of reproductive hallmarks of PCOS, first degree relatives (FDR) of these women have great potential of developing endocrine and metabolic co-morbidities of PCOS particularly obesity, insulin resistance, dyslipidaemia and metabolic syndrome. The purpose of current research was to explore reproductive health, glucose tolerance status and cardiovascular risk profile in first-degree relatives of women with PCOS. **Materials and Methods:** This case-control study included FDR of PCOS women (fathers, mothers, brothers and sisters) compared with equivalent number of age-matched FDR of non-PCOS control women. Primary outcome measures were prevalence of PCOS and isolated PCOS features (hirsutism, menstrual irregularities and ovarian morphological changes), impaired glucose tolerance, type 2 diabetes mellitus and dyslipidaemia. Mean differences in body mass index, waist-hip ratio, fasting and 2-hr blood glucose, lipoprotein components were assessed in all participants. **Result:** Prevalence of PCOS diagnosis (29.4%) and isolated PCOS attributes was notably higher in female FDR of PCOS probands than in control FDR. The mothers (21.7%) and fathers (18.1%) of PCOS women had increased prevalence of T2DM than controls parents. Frequency of systemic hypertension (25%), central obesity (55.9%) and dyslipidaemia (28.9%) was significantly raised in FDR of PCOS probands than of control FDR. Male FDR of PCOS patients appeared to have a higher risk of premature baldness than did control FDR. **Conclusion:** Our study indicates that seemingly healthy first-degree relatives of PCOS probands encountered reproductive and cardiometabolic dysregulations. There is clustering of glucose intolerance and classical cardiovascular risk elements in this population. Accordingly, FDR of PCOS women exhibit an increased risk of diabetes and cardiovascular disease, as do PCOS probands. Further emphasis should be conferred to this population with well-timed and regular screening in such a way that preventive strategies could be constituted to circumvent ensuing cardiometabolic aberrations.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is amongst the most frequent endocrinological and metabolic disorders observed in pre-menopausal women with a prevalence varying around 6% to 20%, according to the diagnostic guidelines used.[1,2] It is a chronic disorder alongside psychological and reproductive manifestations typically commencing in adolescence later transitioning to include infertility and advancing

metabolic complications over time.[3] Besides reproductive traits, in particular chronic anovulation, hyperandrogenism and polycystic ovaries, this disorder has manifested an increased prevalence of various cardiometabolic risk factors inclusive of central obesity, insulin resistance (IR), hyperinsulinemia, impaired glucose tolerance (IGT), hypertension and dyslipidaemia.[4] Hyperandrogenism along with adiposity induced cardiometabolic dysfunction and chronic, low-grade systemic inflammation has been implicated as risk element towards endothelial dysfunction, atherosclerosis and cardiovascular diseases (CVD) in PCOS women.[2,5] PCOS is regarded as an isolated risk factor for type 2 diabetes mellitus (T2DM) and for rapid evolution from impaired glucose tolerance to full-blown diabetes. Moreover, T2DM occurs well before in PCOS and 50% of these women will become affected within 10 years of diagnosis. Consequently, women with PCOS need to be screened earlier and more often than general population for development of CVD and type 2 diabetes.[6]

Even when the pathophysiology of PCOS continues to be elusive up till now, familial clustering in consistence with genetic susceptivity has been a recurrent decimal in various epidemiological studies exploring PCOS.[6] Foregoing family studies of PCOS have reported increased frequency of this syndrome, its phenotypes and associated metabolic abnormalities in first-degree relatives (FDR) of the affected.[7] Familial clustering studies have elicited that a substantial proportion of PCOS women have an affected family member, typically a mother or sister.[8] What is more, a phenotypic male equivalent of PCOS, presenting with high probability of premature male pattern baldness (PMPB) i.e., alopecia developing before 30 years of age and increased hairiness, have been described.[8]

In addition to the high inheritability of reproductive attributes of PCOS, several studies have demonstrated an increased prevalence of cardiometabolic aberrations in first-degree relatives of PCOS females.[9] FDR of PCOS (male as well as females) are at high risk of developing endocrine along with metabolic derangements of PCOS in particular obesity, IR and impaired insulin sensitivity, glucose intolerance, hyperlipidemia and metabolic syndrome.[10] Former studies have demonstrated that fathers of PCOS women had increased 10-year risk for CVD and higher prevalence of heart attacks and strokes in comparison with the reference population. Besides, cardiovascular incidents ensued at an early age in mothers of PCOS women.[11] It is obscure whether disturbances in lipoprotein metabolism are too inherited in families of these women.[12] It is also possible that PCOS corresponds to an intricate multifaceted trait, inherited in the same manner as type 2 diabetes and a considerable proportion of PCOS FDR might potentially have raised insulin levels and greater risk of glucose intolerance.[13,14]

Therefore, we postulated that together with add-on history of PCOS in offspring, the parents of women suffering from PCOS are susceptible to increased risk of CVD and T2DM as well. This exploratory study was proposed to compare reproductive well-being, metabolic and cardiovascular risk profiles among first degree relatives of PCOS and control group women. Moreover, we analyzed prevalence of PCOS and its associated features, hypertension, dyslipidaemia and various pertinent surrogate markers such as fasting and 2-hour glucose levels, IGT and T2DM between parents and siblings of PCOS and non-PCOS women. Well-timed recognition of these high-risk individuals could possibly reduce the risk of metabolic and cardiovascular complications in future. Great plausibility for preventive health care exists and might alleviate these cardiometabolic risks. Furthermore, our research will set forth a comprehensive overview of different biomarker profiles to enlighten the complex etiopathogenesis of PCOS.

MATERIALS AND METHODS

We carried out the present case-control study in a tertiary care, teaching hospital situated in West India by convenient sampling technique. We enrolled 48 women with a confirmed PCOS diagnosis (age group 18–40 years) attending the gynaecology clinic of hospital. 40 age-matched healthy females without any recent or also former history of PCOS were recruited from society volunteers to serve as control group. None of the control subject had any first-degree relative with known diagnosis of PCOS, or characteristic features of PCOS, based upon the interview.

Women suffering from PCOS are designated as PCOS probands. Subsequent to the consent from PCOS probands, an attempt was made to approach their first-degree relatives. Mothers, fathers, sisters and brothers of PCOS probands (referred to subsequently as Mothers PCOS, Fathers PCOS, Sisters PCOS and Brothers PCOS) were enrolled. A total of 100 PCOS FDR who fulfilled the selection criteria were studied. 100 first degree relatives of control group women were also included to form four age-matched control subgroups, denoted as Mothers Control, Fathers Control, Sisters Control and Brothers Control.

Diagnosis of PCOS was made in accordance with guidelines specified by Rotterdam 2003 ESHRE/ASRM PCOS Consensus Workshop Group diagnostic criteria, when at least two of the following three criteria were fulfilled:[5,16] (1) ovulatory dysfunction resulting in oligomenorrhea (mean bleeding interval of 35–182 days during last six menstrual bleeds) or anovulation, and/or amenorrhea (absence of menstrual bleeding for >182 days), (2) clinical (hirsutism) and/or biochemical signs of hyperandrogenism, (3) polycystic ovarian

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morphology on ultrasound (>12 follicles measuring 2–9 mm in diameter or ovarian volume >10 ml in at least one ovary).

FDR with diabetes mellitus, coronary artery disease, hepatic or renal dysfunction, thyroid disorders, pregnant and lactating women were excluded from this study. Subjects with current or previous use (within 3 months) of glucocorticoids, oral contraceptives, hormonal replacement therapy, drugs modifying carbohydrate and lipid metabolism were also excluded from the study.

Study protocol was approved by the Institutional Ethical Committee. Informed, written consents were obtained from women with PCOS and non-PCOS as well as from their FDRs, after detailed explanation of purpose and nature of the study. All the procedures were performed in line with the relevant guidelines and regulations.

For parents of PCOS women, comparable age for controls was stated as > 40 years, while for siblings, comparable age for controls was 18-40 yrs. A thorough clinical evaluation was conducted in all participants and socio-demographic details, anthropometric variables which include weight, height, waist circumference (WC), hip circumference (HC) and blood pressure were documented by using a pre-designed questionnaire. Body mass index (BMI) was computed as per the formula [weight(kg)/[height(m)^2] to assess the obesity degree. Waist-to-hip ratio (WHR) was also measured. Male relatives of PCOS and control women were evaluated for degree and time of onset of balding. Premature baldness was defined as significant frontoparietal hair loss (type IV or V of the Hamilton score) before age of 30 years.[17]

Fasting venous blood samples were collected from all participants and analyzed for biochemical parameters such as glucose and lipid profile, followed by an oral glucose tolerance test (OGTT) with 75-g anhydrous glucose. Glucose tolerance state was evaluated using American Diabetes Association (ADA) criteria.[14]

Statistical Analysis

Data collected based on the research objectives were analyzed using GraphPad Prism, version 7.0 software system. Descriptive statistical methods such as mean and standard deviation were employed to summarize continuous variables. Frequencies and percentages were used for categorical data. Student's unpaired t-test was applied to compare biochemical variables between the groups. Analysis of frequency difference between groups was evaluated by chi-square (χ^2) test. Statistical significance was set at $p < 0.05$.

RESULTS

Total 100 first degree relatives of 48 PCOS women [Mothers PCOS (32), Fathers PCOS (20), Sisters PCOS (29) and Brothers PCOS (19)] were studied. These were compared with 100 age-matched FDR of 40 control women [Mothers Control (26), Fathers Control (28), Sisters Control (22) and Brothers Control (24)].

[Table 1], compares the prevalence of PCOS diagnosis rate, hirsutism, menstrual irregularities and ovarian morphological changes together with impaired glucose tolerance, T2DM and dyslipidaemia between first degree relatives of PCOS and control women.

PCOS was diagnosed in 29.4% (18.5% mothers and 32.3% sisters) of female FDR of PCOS women, while in 4.1% of control FDR. This proportion was more in Sisters PCOS when compared with that in Sisters Control. However, no significant difference was noticed between Mothers PCOS and Mothers Control group. Frequency of isolated PCOS symptoms namely hirsutism, menstrual irregularities and ovarian morphological changes was 17.9%, 29.3% and 15.2% respectively that was significantly increased in female FDR of PCOS women than in control FDR. [Table 1]

The proportion of impaired glucose tolerance was 35% in FDR of PCOS in our study as compared to 14% in control FDR. It was 26.1% in Mothers PCOS, 32.7% in Fathers PCOS, 16% in Sisters PCOS and 12% Brothers PCOS. 27.8% of FDR of PCOS women were diagnosed with T2DM as opposed to 5.7% of control FDR. Mothers (21.7%) and fathers (18.1%) of PCOS group had statistically significant higher prevalence of diabetes than controls parents. The proportion of T2DM was higher in sisters and brothers of PCOS than siblings of control group women; however, neither of this difference was statistically significant. [Table 1]

Amongst cardiovascular risk evaluation parameters, frequency of systemic hypertension (25% vs 11.4%), abdominal obesity (55.9% vs 21.2%) and dyslipidaemia (28.9% vs 9.2%) were comparable in FDR of PCOS and control women respectively and the difference was statistically significant. [Table 1]

The prevalence of individual lipoprotein components was TC >200 mg/dL (32.1% vs. 17.5%), TG >150 mg/dL (27.4% vs. 19%), HDL < 50 mg/dL (33.9% vs. 20.6%), LDL >130 mg/dL (29.7% vs. 14.2%) respectively in PCOS and control FDRs.

In male FDR of PCOS women, the altogether proportion of premature baldness was 21.7% whilst it was 10.5% in FDR of controls. It was observed in 38.6% of Brothers PCOS and 13.7% of Brothers Control. Fathers of PCOS group women also seemed to have increased risk of premature baldness than did control fathers. The differences were of statistical power. [Table 1]

Subgroup evaluation was carried out for the demographic and biochemical characteristics among Mothers PCOS and Mothers Control, Fathers PCOS and Fathers Control, Sisters PCOS and Sisters Control, Brothers PCOS and Brothers Control groups and represented in Tables II, III, IV and V respectively.

The parents and sisters of PCOS women had increased WHR, when compared with those of control group women. The parents of PCOS group

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had raised systolic-diastolic BP than control parents. No significant difference in blood pressure was noticed between siblings of PCOS and control women. The fasting and 2-hour plasma glucose, TC, TG and LDL cholesterol were higher while HDL was lower in FDR of PCOS patients than control FDR.

Table 1: Comparison of Prevalence of reproductive and metabolic parameters among First Degree Relatives of PCOS and Control Women

Sr. No.	Clinical Parameters	FDR of PCOS women (100)	FDR of non-PCOS women (100)	'P' value
1.	PCOS Diagnosis Rate	29.4%	4.1%	< 0.05
2.	Hirsutism	17.9%	6.8%	< 0.05
3.	Menstrual Irregularities	29.3%	12.1%	< 0.05
4.	Ovarian Morphological Changes	15.2%	3.5%	-
5.	PMPB	21.7%	10.5%	< 0.05
6.	Impaired Glucose Tolerance	35%	14%	< 0.05
7.	Type 2 Diabetes Mellitus	27.8%	5.7%	< 0.05
8.	Abdominal Obesity	55.9%	21.2%	< 0.05
9.	Hypertension	25%	11.4%	-
10.	Dyslipidaemia	28.9%	9.2%	< 0.05

Table 2: Comparison of Demographic and Biochemical Parameters among Mothers PCOS and Mothers Control Groups (Student's unpaired 't' test)

Sr. No.	Clinical Parameters	Mothers PCOS Group (32)	Mothers Control Group (26)	'P' value
1.	Age (years)	53.41 ± 6.92	48.12 ± 8.1	-
2.	BMI (kg/m2)	32.82 ± 5.47	27.21 ± 3.77	< 0.05
3.	W/H Ratio	0.93 ± 0.07	0.82 ± 0.03	< 0.05
4.	Systolic Blood Pressure (mm Hg)	134.95 ± 10.32	115.24 ± 6.5	< 0.05
5.	Diastolic Blood Pressure (mm Hg)	82.12 ± 7.86	74.59 ± 4.41	< 0.05
6.	Fasting Glucose (mg/dl) (70-100)	122.5 ± 16.93	98.21 ± 12.7	< 0.05
7.	2-hour Plasma Glucose (mg/dl) (<140)	176.5 ± 21.8	137.5 ± 15.72	< 0.05
8.	TC (mg/dl) (Upto 200)	218.59 ± 36.13	169.42 ± 18.25	< 0.05
9.	TG (mg/dl) (Upto 150)	139.79 ± 31.95	124.72 ± 17.29	-
10.	HDL (mg/dl) (40 –60)	39.76 ± 8.95	52.74 ± 10.45	< 0.05
11.	LDL (mg/dl) (Upto 100)	130.61 ± 18.32	93.27 ± 14.7	< 0.05

Table 3: Comparison of Demographic and Biochemical Parameters in Fathers PCOS and Fathers Control Groups (Student's unpaired 't' test)

Sr. No.	Clinical Parameters	Fathers PCOS Group (20)	Fathers Control Group (28)	'P' value
1.	Age (years)	57.23 ± 49.21	53.6 ± 9.12	-
2.	BMI (kg/m2)	33.17 ± 5.42	28.3 ± 3.5	-
3.	W/H Ratio	1.0 ± 0.15	0.9 ± 0.09	< 0.05
4.	Systolic Blood Pressure (mm Hg)	130.61 ± 7.16	119 ± 10.27	< 0.05
5.	Diastolic Blood Pressure (mm Hg)	87.19 ± 6.57	80.2 ± 8.63	< 0.05
6.	Fasting Glucose (mg/dl) (70-100)	105.16 ± 19.43	92.4 ± 13.06	< 0.05
7.	2-hour Plasma Glucose (mg/dl) (<140)	157.9 ± 28.13	130.47 ± 20.05	< 0.05
8.	TC (mg/dl) (Upto 200)	217.35 ± 26.19	162.78 ± 22.86	< 0.05
9.	TG (mg/dl) (Upto 150)	161.28 ± 19.52	117.04 ± 21.7	-
10.	HDL (mg/dl) (40 –60)	37.32 ± 9.08	50.64 ± 12.35	< 0.05
11.	LDL (mg/dl) (Upto 100)	132.69 ± 26.52	92.47 ± 25.81	-

Table 4: Comparison of Demographic and Biochemical Parameters in Sisters PCOS and Sisters Control Groups (Student's unpaired 't' test)

Sr. No.	Clinical Parameters	Sisters PCOS Group (29)	Sisters Control Group (22)	'P' value
1.	Age (years)	30.52 ± 8.29	27.43 ± 5.1	-
2.	BMI (kg/m2)	27.35 ± 5.12	25.83 ± 3.95	< 0.05
3.	W/H Ratio	0.85 ± 0.09	0.79 ± 0.05	< 0.05
4.	Systolic Blood Pressure (mm Hg)	116.7 ± 10.43	110 ± 7.35	-
5.	Diastolic Blood Pressure (mm Hg)	76.32 ± 12.47	72.52 ± 7.91	-
6.	Fasting Glucose (mg/dl) (70-100)	105.05 ± 17.95	93.2 ± 10.81	-
7.	2-hour Plasma Glucose (mg/dl) (<140)	148.3 ± 30.71	129.17 ± 23.65	-
8.	TC (mg/dl) (Upto 200)	187.94 ± 29.72	169.87 ± 23.51	< 0.05
9.	TG (mg/dl) (Upto 150)	138.19 ± 28.14	125.64 ± 23.17	-
10.	HDL (mg/dl) (40 –60)	42.37 ± 9.35	51.63 ± 10.24	< 0.05
11.	LDL (mg/dl) (Upto 100)	127.92 ± 20.56	98.42 ± 17.28	< 0.05

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Table 5: Comparison of Demographic and Biochemical Parameters in Brothers PCOS and Brothers Control Groups (Student's unpaired 't' test)

Sr. No.	Clinical Parameters	Brothers PCOS Group (19)	Brothers Control Group (24)	'P' value
1.	Age (years)	29.37 ± 9.58	25.93 ± 5.71	-
2.	BMI (kg/m2)	26.92 ± 4.23	24.59 ± 5.81	-
3.	W/H Ratio	0.94 ± 0.08	0.80 ± 0.05	-
4.	Systolic Blood Pressure (mm Hg)	118.54 ± 11.79	119.4 ± 5.85	-
5.	Diastolic Blood Pressure (mm Hg)	76.34 ± 5.82	73.29 ± 6.19	-
6.	Fasting Glucose (mg/dl) (70-100)	97.38 ± 14.47	86.47 ± 9.10	< 0.05
7.	2-hour Plasma Glucose (mg/dl) (<140)	128.27 ± 19.1	120.6 ± 25.84	< 0.05
8.	TC (mg/dl) (Upto 200)	218.79 ± 20.38	189.64 ± 15.98	< 0.05
9.	TG (mg/dl) (Upto 150)	132.61 ± 18.94	129.76 ± 19.5	-
10.	HDL (mg/dl) (40 –60)	45.11 ± 8.2	50.76 ± 10.43	< 0.05
11.	LDL (mg/dl) (Upto 100)	119.37 ± 21.92	108.74 ± 18.32	< 0.05

DISCUSSION

PCOS is a systemic endocrine and metabolic condition having manifestations throughout the lifespan and represents the crucial public health and economic burden.[3] As research on PCOS is expeditiously advancing, it is essential that research evidence is translated to knowledge and action amongst PCOS women, healthcare specialists as well as policy makers.[1] Familial clustering of PCOS in consistence with genetic susceptibility had been well-established in literature.[14] Our study addressed the reproductive health, cardiovascular and metabolic risk profile in first degree relatives of women suffering from PCOS.

PCOS was more frequently diagnosed in female FDR of PCOS women and they revealed high prevalence of isolated PCOS features than Control FDR, proposing the heritable component and high degree of familial clustering tendency of this disorder. Increased androgen levels are thought to be one of the contributors to suboptimal uterine conditions in mothers of PCOS patients. Hyper exposure to androgens in the intrauterine environment might possibly reprogram the genes concerned with ovarian follicular development, ovarian steroidogenesis and insulin metabolism which may finally bring about PCOS development in offspring.[1] In one of the studies by Ahmad T et al, prevalence of PCOS was 26% in PCOS FDR while 5.4% in Control FDR.[7] Melissa D et al, found that prevalence of PCOS was 24% and 32% in mothers and sisters of PCOS probands respectively while it was 4% in controls.[18] In study by L Agnieszka et al, diagnosis of PCOS was made in 18.2% sisters.[19] Findings by these researchers are in accordance with the outcomes of our study.

The male FDR of PCOS in our study manifested hyperandrogenism in the form of premature balding and the prevalence was more as compared to controls. This premature male pattern baldness has been designated as the phenotypic male counterpart of PCOS.[14] Similar results were noted by Ahmad T et al,[7] and L Agnieszka et al.[19]

This study has displayed statistically significantly increased proportion of glucose intolerance and T2DM in FDR of PCOS probands regardless of the degree of obesity when compared with FDR of controls. Studies have demonstrated the heritable component of β-cell dysfunction in families of PCOS women. Accordingly, it would be reasonable to anticipate higher prevalence of glucose intolerance status in FDR of women with PCOS.[9] Comparable findings were reported by BuLent O Yildiz et al,[13] and V Putthussery et al.[11]

PCOS by itself has been established as significant risk element for developing type 2 diabetes and as stated by ADA guidelines, history of PCOS is counted as criteria for screening of T2DM.[2] As reported by Developmental Origins of Health and Disease theory, unfavourable intrauterine conditions in mothers of PCOS women might lead to adaptations in their offspring which could bring about metabolic and endocrinological disorders later in life.[1] This might potentially explain high degree of glucose intolerance in PCOS FDR observed in our study.

In this study, we assessed the cardiovascular disease risk in FDR of women with POCS using traditional risk factors such as obesity, hypertension and dyslipidaemia. FDR of PCOS have significantly increased prevalence of systemic hypertension, central adiposity and dyslipidaemia as compared to control FDR. In addition, TC, TG and LDL cholesterol concentrations were higher while HDL level was lower in PCOS FDR than in Controls. Similar results were obtained by Iram Shabir et al,[14] Akbarzadeh M et al [20] and Murat Yılmaz et al.[15] These findings imply that first‑degree relatives of PCOS women are predisposed to hypertension and dyslipidaemia which increases the risk of CVD.

Dyslipidaemia, a well-recognised risk factor for CVD could be the most prevailing metabolic aberration in PCOS women. Even though different kinds of lipid profile parameters were deranged, dyslipidaemia was observed in all PCOS FDR groups. Hence, first-degree relatives of PCOS subjects should have a complete lipoprotein evaluation as part of their cardiovascular risk assessment and be treated with therapeutic interventions and lifestyle modifications.

PCOS women have increased peripheral insulin resistance, which triggers ovarian and adipose tissue androgen production and impairs sex hormone binding globulin (SHBG) synthesis in liver through hyperinsulinemia.[9] Studies have presented parallel outcomes in FDR of PCOS women as well. This early

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decline in SHBG may partially explain the potential abnormalities in glucose and lipid metabolism in PCOS FDR commencing at a relatively young age, considering the role of SHBG in metabolic disorders.[1]

The strength of our study was a well-defined homogenous cohort of cases which were compared with age-matched controls ensuring the uniformity of data. However, sample size was relatively small and this was a single center study and all women were infertile PCOS. Hence, our results may not reflect the true picture of entire PCOS population. Further community based; longitudinal studies are needed to delineate the cardiometabolic risk among family members of PCOS women.

CONCLUSION

This study provides evidence of reproductive and metabolic dysregulations in first degree relatives of PCOS women. PCOS and its associated features in the probands have implications for FDR and both male and female relatives are affected. Thus, there may be a genetic component to the reproductive and metabolic abnormalities in PCOS probands and their FDR. This eventually elucidates familial risk of the disorder and its associated sequalae like diabetes and cardiovascular diseases. Consequently, in the absence of molecular diagnostic biomarkers, positive family history of PCOS seems to be highly informative risk factor. Thereupon, families of PCOS women represents a high-risk group and should be screened routinely for cardiometabolic dysregulations. This will facilitate to pick out the candidates for timely therapeutic intervention which would be beneficial, as long-term complications could be delayed or prevented. Management of PCOS FDR should be aimed towards the support, education, addressing psychological issues and encouraging healthy lifestyle with targeted medical therapy as required. In the interim, comprehensive evidence-based guidelines are necessary to direct consumers and clinicians in optimal PCOS management.

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