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ORIGINAL ARTICLE

ASSOCIATION OF DYSLIPIDEMIA WITH ANXIETY AND DEPRESSION IN PATIENTS OF POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

OBJECTIVE: To find-out the association of dyslipidemia with anxiety and depression in patients with polycystic ovarian syndrome (PCOS).

METHODS: This descriptive cross-sectional study was conducted at Mardan Medical Complex, Mardan, Pakistan from December-2019 to March-2020. One hundred & forty diagnosed cases of PCOS, ranging in age from 20-40 years, were selected through purposive sampling. Anxiety and depression were calculated using hospital anxiety and depression scale (HADS) score. Total cholesterol (TC), triglycerides, low-density-lipoproteins (LDL), high-density-lipoproteins (HDL) and testosterone were tested through fasting blood samples.

RESULTS: Anxiety and depression were documented in 102 (72.9%) & 99 (70.7%) cases respectively. Primary infertility, oligomenorrhoea, Hirsutism & acne were present in 69 (49.3%), 111 (73.5%), 81 (57.9%) and 55 (39.3%) patients respectively. Twenty-two (15.7%) patients were overweight/obese. All patients had raised testosterone levels and polycystic ovaries on ultrasound. Raised triglyceride levels (≥150 mg/dl), Low levels of HDL (< 60mg/dl), raised levels of LDL (≥130 mg/dl), raised cholesterol levels (≥200 mg/dl) were reported in 71/99 (71.7%), 56/99 (56.6%), 38/99 (38.4%) & 10/99 (10.2%) cases with depression as compared to 27/41 (65.9%), 13/41 (31.7%), 21/41 (51.2%) & 14/41(34.1%) non-depressed patients respectively. Similarly raised triglyceride levels, low levels of HDL, raised levels of LDL, raised cholesterol levels were reported in 73/102 (71.6%), 58/102 (56.9%), 40/102 (39.2%) & 12/102 (11.76%) cases with anxiety as compared to 25/38 (65.8%), 11/38 (28.9%), 19/38 (50%) and 12/38 (31.6%) patients without anxiety respectively.

CONCLUSION: Dyslipidemia, anxiety and depression are very common in PCOS. Dyslipidemia is associated with anxiety and depression in PCOS patients.

KEY WORDS: Polycystic Ovary Syndrome (MeSH); Anxiety (MeSH); Depression (MeSH); Dyslipidemias (MeSH); Triglycerides (MeSH); Cholesterol (MeSH); Lipids (MeSH); Hospital Anxiety and Depression Score (Non-MeSH); Hirsutism (MeSH); Obesity (MeSH).

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INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a heterogenic endocrine disorder presenting with menstrual irregularities, infertility and features of hyperandrogenism i.e., acne, hirsutism and alopecia and metabolic syndrome.[1] PCOS affects 6-18% of women in reproductive age group. This syndrome is primarily considered as a reproductive and metabolic disorder, but these patients also show higher rates of psychological morbidities.[2]

Cinar et al, has reported depression rates between 14 and 64 % in PCOS patients.[3] Such a wide range of prevalence might be due to reasons like different socio-cultural populations, ethnic differences and variations in methodologies for depression screening.[3] PCOS women also show increased prevalence of anxiety than in general population (3457% versus 18%).[3] The main factors responsible for such high rates of anxiety disorders may be acne, hirsutism and obesity.[3] PCOS patients have 30-40 % risk of developing insulin resistance, impaired glucose tolerance and Type 2 diabetes mellitus.[3] Other risk factors for cardiovascular disease (CVD) such as hypertension, dyslipidemia, atherosclerosis and endothelial dysfunction are also reported to be associated with PCOS.[3] In US, 70% of PCOS women have dyslipidemia showing different patterns. High triglycerides (TG) and low high-density lipoproteins (HDL) are common in PCOS women while high values of low-density lipoproteins (LDL) may be related to hyperandrogenism.[4]

There is scarce available data (both local and international) on association of dyslipidemia with anxiety and depression in PCOS patients. So, the present study was conducted to find out frequency of anxiety and depression in PCOS patients and to look for association of dyslipidemia with anxiety and depression in these patients in our local setup. We hope that general practitioners and gynecologists shall focus attention on psychological assessment and lipid measurement in this group of patients, in order to categorize them for optimal management.

METHODS

This descriptive cross-sectional study was done on young women of reproductive age coming to outpatient Department of Gynecology and Obstetrics at Mardan Medical Complex, Mardan, Khyber Pakhtunkhwa- Pakistan. Sample size was calculated using the following formula, $n=\frac{z^2(p \times q)}{e^2}$ Where prevalence of PCOS is taken as 10 in 100. Inclusion criteria were women, both married and unmarried, with age of 20-40 years having polycystic ovarian syndrome of any duration while pregnant

TABLE I: DEMOGRAPHIC AND CLINICAL CHARACTERISTIC OF STUDY POPULATION (N=140)

Variables	Characteristic	Frequency	Percentage
Marital status	Married	104	74.3
	Un-married	36	25.7
Menstrual irregularities	Oligomenorrhoea	111	79.3
	Polymenorrhoea	25	17.9
	Normal cycle	4	2.9
Clinical Hyper-Androgenism	Hirsutism	81	57.9
	Acne	55	39.3
Biochemical Hyper - Androgenism	Raised Serum testosterone	140	100%
Infertility	Primary	69	49.3
	Secondary	33	23.6
Body Mass Index (BMI)	Under-weight	36	25.7%
	Normal	82	58.6%
	Overweight/Obese	22	15.7%
Pelvic Ultrasound	Right ovary cystic	42	30.0
	Left ovary cystic	50	35.7
	Both ovaries cystic	48	34.3
Psychological stress	Anxiety	102	72.9
	Depression	99	70.7
Triglycerides	Desirable (<150 mg/dl)	42	30
	Borderline risk (150-199 mg/dl)	37	26.4
	High-risk (≥200 mg/dl)	61	43.6
High Density Lipoproteins (HDL)	Desirable (>60 mg /dl)	71	50.7
	Borderline risk (35-59 mg/dl)	57	40.7
	High risk (<35 mg/dl)	12	8.6
Low Density Lipoproteins (LDL)	Desirable (60-129 mg/dl)	81	57.9
	Borderline risk (130-159 mg/dl)	56	40.0
	High risk (≥160 mg/dl)	3	2.1
Total Cholesterol	Desirable (<200 mg/dl)	116	82.9
	Borderline risk (200-239 mg/dl)	19	13.6
	High risk (≥240 mg/dl)	5	3.6

women, patients with known endocrine disorders like Cushing syndrome, hyper-prolactinemia, diabetes and hypertension and those taking oral contraceptive pills were excluded from the study.

Patients were diagnosed as PCOS according to Rotterdam criteria[5] applied on suspected cases using purposive sampling technique. Rotterdam criteria for the diagnosis of PCOS is the presence of at least two out of following three features:

1. Oligo-ovulation or anovulation on the basis of history of oligomenorrhoea/ polymenorrhoea
2. Clinical hyperandrogenism on the basis of acne, hirsutism and alopecia or biochemical hyperandrogenism on the basis of raised free testosterone levels
3. Polycystic ovaries on the basis of ultrasonic findings of 10 or more antral follicles in each ovary.

After taking informed consent, relevant demographic, anthropometric, clinical and PCOS related data were collected and entered on a specially designed proforma which included information like name, age, weight, height, marital status, menstrual history, present and past medical history and drug history. Body mass index (BMI) was calculated as weight in kg divided by height per square meter (kg/m^2) with a cut off value of ≥24 considered as overweight or obese.[6] Clinical examination findings like blood pressure, any systemic illness, presence of acne, hirsutism and male pattern alopecia and ultrasound findings of ovarian antral follicles were also noted.

Hospital Anxiety and Depression Scale (HADS) score for each patient was calculated for determination of anxiety and depression. HADS is a 14 items questionnaire; seven are related to anxiety and seven to depression symptoms. Each question has marks of 0 1, 2 and 3. Score for each category can range from 0 to 21. A score of 7 or below shows no anxiety and depression while a score of 8 and above indicates the presence of anxiety and depression.[7] A validated Urdu version was utilized in the study.[8]

All patients were tested for fasting serum lipid profile and free testosterone levels. Different componenets of fasting lipids were checked by using the following principles; Total cholesterol level (TC) was determined after enzymatic hydrolysis and oxidation. Determination of TG after enzymatic splitting with lipoprotien lipase was done. HDL, which remain in the supernatant after centrifugation was enzymatically determined by the DIALAB cholestrol CHOD-PAP reagent. LDL was measured from measured values of TC, TG and HDL according to following relationship among them; LDL = TC HDL (TG/5).[9] Values of TC, LDL and TG below which they were considerd normal were taken as; 200 mg/dl, 130 mg/dl and 150 mg/dl respectively while cut off value for HDL above which it was considered normal was taken as 60 mg/dl.[10]

Testosterone was measured by the Testosterone Chemiluminescence Immunoassay.[11] It is based on the principle of competitive binding between testosterone in the test specimen and testosterone-HRP conjugate for a constant amount of rabbit anti-testosterone. Cutoff value of total testosterone was taken as 0.9 ηg/ml. All the collected data was entered into the proforma. Thereafter the data was recorded and analyzed using Statistical Package for Social Sciences (SPSS) version 23.

For both anxiety and depression separately, patients were divided into two sets of two groups each; that is PCOS women with anxiety and without anxiety and PCOS women with depression and without depression. Association was assessed by comparing the two groups in each set for presence of all four components of dyslipidemia by using chi-square test (χ^2) with a p value of <0.05 considered as statistically significant. Analyzed Data is presented in the form of tables and charts.

RESULTS

Out of 140 women, 104 (74.3%) were married. All patients were ranging in age from 20-40 years with menarche at the age of 12-15 years. Primary infertility was present in 69 (49.3%) and oligomenorrhoea in 111 (73.5%).

TABLE II:COMPARISON OF LIPID PROFILE IN POLYCYSTIC OVARIAN SYNDROME PATIENTS WITH AND WITHOUT DEPRESSION

		Depression			Chi Square
		Present (n=99)	Not present (n=41)	Total (n=140)	
Triglycerides	Desirable (<150mg/dl)	28 (28.3%)	14 (34.1%)	42 (30%)	0.078
	Borderline risk (150-199 mg/dl)	27 (27.3%)	10 (24.4%)	37 (26.4%)	
	High-risk (≥200 mg/dl)	44 (44.4%)	17 (41.9%)	61 (43.6%)	
High Density Lipoproteins (HDL)	Desirable (>60 mg /dl)	43 (43.4%)	28 (68.3%)	71 (50.7%)	0.010*
	Borderline risk (35-59mg/dl)	51 (51.5%)	6 (14.6%)	57 (40.7%)	
	High risk (<35mg/dl)	5 (5.1%)	7 (17.1%)	12 (8.6%)	
Low Density Lipoproteins (LDL)	Desirable (60-129mg/dl)	61 (61.89%)	20 (48.8%)	81 (57.9%)	0.143
	Borderline risk (130-159mg/dl)	35 (35.4%)	21 (51.2%)	56 (40.0%)	
	High risk ≥160mg/dl)	3 (3.09%)	0 (0%)	3 (2.1%)	
Total Cholesterol	Desirable (<200mg/dl)	89 (89.8%)	27 (65.9%)	116 (82.9%)	0.010*
	Borderline risk (200-239mg/dl)	5 (5.1%)	14 (34.1%)	19 (13.6%)	
	High risk (≥240mg/dl)	5 (5.1%)	0 (0%)	5 (3.6%)	

* p<0.05

Hirsutism was present in 81 (57.9%) while 55 (39.3%) patients had acne. Twenty-two (15.7%) patients were overweight/obese. All patients had raised total testosterone levels and had polycystic ovaries on ultrasound.

Anxiety was present in 102 (72.9%) while depression in 99 (70.7%). Out of 140 patients with PCOS, desirable levels of Triglycerides (<150 mg/dl), HDL (>60 mg /dl), LDL <130mg/dl) & Total Cholesterol (<200mg/dl) were observed in 42 (30%), 71 (50.7%), 81 (57.9%) and 116 (82.9%) cases respectively. Cholesterol was raised in 25 (17.2%), LDL was raised in 59 (42.1%), HDL was decreased in 69 (49.3%) and TG was raised in 98 (70%) patients (Table I).

Comparison of lipid profile in PCOS patients with and without depression is given in Table II. Raised triglyceride levels (≥150 mg/dl) were observed in 71/99 (71.7%) of depressed patients as compared to 27/41 (65.9%) patients without depression (p>0.05). Low levels of HDL (<60mg/dl) were found in 56/99 (56.6%) depressed patients and 13/41 (31.7%) non-depressed patients (p<0.05). Raised levels of LDL (≥130 mg/dl) were found in 38/99 (38.4%) patients with depression as compared to 21/41 (51.2%) non-depressed patients. Raised cholesterol levels (≥200 mg/dl) were found in 10/99 (10.2%) of depressed patients and 14/41(34.1%) non-depressed patients (p<0.05).

Comparison of lipid profile in PCOS patients with and without anxiety is given in Table III. Raised triglyceride levels (≥150 mg/dl) were present in 73/102 (71.6%) patients having anxiety as compared to 25/38 (65.8%) patients without anxiety (p>0.05). Low levels of HDL (< 60mg/dl) were found in 58/102 (56.9%) patients having anxiety and 11/38 (28.9%) patients having no anxiety (p<0.05). Raised levels of LDL (≥130 mg/dl) were found in 40/102 (39.2%) patients having anxiety as compared to 19/38 (50%) patients having no anxiety (P>0.05). Raised total cholesterol levels (≥200 mg/dl) were found in 12/102 (11.76%) patients having anxiety and 12/38 (31.6%) patients having no anxiety (p<0.05).

DISCUSSION

This study was conducted to determine the frequency of depression and anxiety in PCOS patients and the association of anxiety and depression with dyslipidemia. A total of 140 patients were selected on the basis of clinical and biochemical confirmation of PCOS. Anxiety and depression were very common finding among these patients. The causes of anxiety and depression were menstrual irregularities, hirsutism, infertility and obesity. Dyslipidemia was associated with Anxiety and depression in PCOS patients. Raised levels of testosterone were present in all patients with PCOS.

Zehra S et al, conducted a cross sectional study in Pakistan. Their study stated that anxiety and depression scores were high in PCOS patients compared to control. In their study, anxiety was present in 42.6% while depression was present in 31.1 % and 20% of the study group had both anxiety and depression. They stated that anxiety and depression levels were more prevalent in PCOS patients and are related with acne, hirsutism, obesity, menstrual irregularities, infertility, and dyslipidemia and insulin resistance. Their findings supported our findings of anxiety and depression and their association with dyslipidemia in PCOS patients.[12]

In another cross-sectional study performed by Enjezab et al, 64.5% of the PCOS patients were found to have depression, similar to our study. They found no correlation of depression with BMI, IR and total testosterone levels. In our study we also did not find correlation between anxiety, depression, BMI and IR but our study show that all the patients have raised testosterone level which is responsible androgenic features of PCOS.[13] In another cross-sectional study performed by Xiaoli Chen et al, BMI levels of PCOS patients were compared with controls. According to WHO, generally Asian have higher body fat than white population of the same age, sex and BMI. They stated that waist hip ratio, serum insulin and TG were positively correlated with BMI in PCOS patients. With increasing BMI, the prevalence of fasting insulin, central obesity and dyslipidemia also increases. They found increased levels of TG, fasting insulin and fasting glucose in the study group. Thus, the risk of having metabolic syndrome is higher in PCOS patients compared with control. They also showed that insulin levels were positively correlated with BMI. And BMI is correlated positively with TG and negatively with HDL.[14] Our study shows that 15.7% of the selected patients had raised BMI (obese/overweight) which may because of small sample size and

TABLE III: COMPARISON OF LIPID PROFILE IN POLYCYSTIC OVARIAN SYNDROME PATIENTS WITH AND WITHOUT ANXIETY

Parameters		Anxiety			Chi square
		Present (n=102)	Not Present (n=38)	Total (n=140)	
Triglycerides	Desirable (<150mg/dl)	29 (28.4%)	13 (34.2%)	42 (30%)	0.075
	Borderline risk (150-199mg/dl)	27 (26.5%)	10 (26.3%)	37 (26.4%)	
	High-risk (≥200 mg/dl)	46 (45.1%)	15 (39.5%)	61 (43.6%)	
High Density Lipoproteins (HDL)	Desirable (>60 mg /dl)	44 (43.1%)	27 (71.1%)	71 (50.7%)	0.011*
	Borderline risk (35 - 59mg/dl)	51 (50%)	6 (15.8%)	57 (40.7%)	
	High risk (<35mg /dl)	7 (6.9%	5 (13.2%)	12 (8.6%)	
Low Density Lipoproteins (LDL)	Desirable (60-129mg/dl)	62 (60.8%)	19 (50%)	81 (57.9%)	0.051
	Borderline risk (130-159mg/dl)	38 (37.3%)	18 (47.4%)	56 (40%)	
	High risk (≥160mg/dl)	2 (2%)	1 (2%)	3 (2.1%)	
Total Cholesterol	Desirable (<200mg/dl)	90 (88.2%)	26 (68.4%)	116 (82.9%)	0.019*
	Borderline risk (200-239mg/dl)	9 (8.8%)	10 (26.3%)	19 (13.6%)	
	High risk (≥240mg/dl)	3 (2.9%)	2 (5.3%)	5 (3.5%)	

* p<0.05

random selection, variability in ethnicity and other socio demographic variations.

Moreover, in our study correlation of BMI and dyslipidemia was not determined. A classic lipid profile with significantly elevated TG, raised cholesterol, raised LDL and decreased serum HDL levels was noted in the study by Bilal et al.[15] Same pattern of dyslipidemia was noted in our study. Hence, in PCOS patients, to assess cardiovascular risk factors, lipid profile should be essential part of investigation. These findings were supported by other studies on national and international level. Nesecinar et al, also showed significant correlation between anxiety, depression and metabolic parameters including dyslipidemia.[3]

The AE-PCOS society created a panel which suggested that weight loss was associated with improvement in dyslipidemia and depression.[16]

CONCLUSION

This study showed that dyslipidemia including high cholesterol, LDL, low HDL and raised TG levels are common in PCOS patients. Anxiety and depression are also very common and present in almost two third of patients with PCOS. There is a strong relationship of dyslipidemia with anxiety and depression in these patients. Further research is recommended to explore the relationship of dyslipidemia with anxiety and depression in patients with PCOS.

RECOMMENDATIONS

PCOS should be diagnosed as early as possible. Psychological assessment along with dyslipidemia screening of all the patients with PCOS should be conducted for their timely management to prevent CVD. Awareness and educational programs may be arranged for young adult females at school and college levels to educate them about the squeal associated with PCOS. Dyslipidemia associated with PCOS is an important risk factor for cardiovascular diseases and addressing these risks by lifestyle modification, psychiatric counseling and medication will improve the cardiovascular outcomes in PCOS patients.

LIMITATIONS

This was a cross-sectional study where limited number of patients were selected. There was no control group. Other CVD risk factors were not taken into consideration. A prospective cohort study will give a more in-depth view and knowledge of CVD risk factors and their association with anxiety and depression in PCOS patients.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

RH: Conception and study design, acquisition, analysis and interpretation of data, drafting the manuscript, critical review, approval of final version to be published

SUR: Conception and study design, critical review, approval of final version to be published

TZ: Acquisition of data, critical review, approval of final version to be published

MT: Acquisition of data, drafting the manuscript, approval of final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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