

## Prevalence of cardiovascular risk factors among patients with polycystic ovarian syndrome (PCOS) in Erbil city

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### Abstract

**Background:** Polycystic ovarian syndrome is a common endocrine disorder of women during reproductive age, associated with increased risk of cardiometabolic diseases.

**Objective:** To assess the prevalence of cardiovascular risk factors in patients with the polycystic ovarian syndrome in comparison to age-matched control.

**Patients and Methods:** This cross-sectional study is conducted in Erbil city from September 2020 to January 2021. It included 40 cases of polycystic ovarian syndrome and 40 cases of healthy controls. Participants underwent detailed history, physical examination. Laboratory investigations (blood sugar, lipid profile, serum testosterone and serum prolactin) and pelvic ultrasound were done for them. Data analysis was performed by Statistical Package for Social Sciences (SPSS) version 25.

**Results:** Women with the polycystic ovarian syndrome have a higher proportion to obesity, abnormal blood sugar, and dyslipidemia, they have higher rate of menstrual irregularity, hyperandrogenic state and hirsutism, than age-matched control. The risk for hypertension remains the same for both PCOS and the control group.

**Conclusion:** The proportion of obesity, diabetes, and dyslipidemia is higher in Polycystic ovarian syndrome than the control group.

**Keywords:** Polycystic ovarian syndrome, obesity, diabetes mellitus, heart disease

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### Introduction

Polycystic ovary syndrome (PCOS) is a common disorder in women of reproductive age, with a prevalence of 5–16% under different diagnostic criteria and across several ethnic groups, with exact pathogenesis still unclear [1].

Ovarian dysfunction continues to be the main feature that makes this syndrome the major cause of anovulatory associated with infertility [2].

It has different clinical presentations, which are: hirsutism and male pattern balding consistent with hyperandrogenism, Irregular or absent menstrual cycles, subfertility or infertility, psychological symptoms (anxiety, depression, psychosexual dysfunction, eating disorders), metabolic features (obesity, dyslipidemia, and diabetes)[3].

General agreement exists now among the community of endocrinologists and gynecologists that the diagnosis of PCOS should be based on the Rotterdam criteria, which include two of the following three features: oligo-/amenorrhea, hyperandrogenism (clinical or biochemical), and polycystic ovaries on ultrasound, after exclusion of other endocrinopathies[1].

There is growing evidence that women with PCOS have increased risk for cardiovascular disease, as they have increased risk for dyslipidemia, T2DM, and obesity. Our aim is to study significant risk factors of cardiovascular disease among PCOS patients compared to age-matched women without PCOS.

## Patients and Methods

### Study design

This is a case-control study, conducted in a Maternity teaching hospital (consultation department and IVF center) and Hawler teaching hospital (Endocrine and Internal medicine consultation departments). In addition to private clinic of obstetrics and gynecology –Erbil-Iraq.

Case collection was done from September 2020 to January 2021. Forty cases of PCOS

and 40 cases of age-matched controls have been recruited.

### Inclusion criteria

Females of reproductive age with any of the following features have been included (virilization and hirsutism, menstrual irregularities, or Ultrasound evidence of PCOS).

### Exclusion criteria

Patients with known ischemic heart disease, pregnancy, or other causes of ovarian cyst or hyperandrogenism were excluded from the study.

### Data collection

Participants (cases and control) were interviewed in the consultation room, a detailed history was taken from them regarding features of hyperandrogenism (acne, temporal balding, hirsutism), their menstrual cycle (regular, irregular; amenorrhea, polymenorrhea or oligomenorrhea), also family history, past medical history and drug history were taken.

Participants underwent general physical examination including blood pressure and pulse rate. their weight, height, and calculated body mass index have been estimated. We used American Heart Association (AHA)[4] categories for blood pressure characteristics, which are:

Normal blood pressure (SBP <120, DBP<80), Elevated blood pressure (SBP 120-129, DBP <80), Hypertension stage 1 (SBP 130-139, DBP 80-89), Hypertension stage 2 (SBP >140, DBP >90).

According to their body mass index, we divided them into 3 categories:

Normal BMI (18.5-24.9), Overweight (25-29.9) & Obese (>30).

Blood samples from each participant were taken for measurement of lipid profile, blood sugar, serum prolactin, serum testosterone, and a pregnancy test.

Normal and abnormal ranges of blood sugar are determined according to ADA (American Diabetic Association)[5]. Normal blood sugar is <140mg/dl, prediabetes range is 140-199mg/dl, while diabetes diagnosed when blood sugar is >200mg/dl.

Pelvic ultrasound has been performed for all participants to find ultra-sonographic features of PCOS. The Ferriman-Gallwey scale used to assess their hirsutism, in which a score of 1 to 4 is given for nine areas of the body, a total score less than 8 is considered normal, a score of 8 to 15 indicates mild hirsutism, and a score greater than 15 indicates moderate or severe hirsutism. A score of zero indicates an absence of terminal hair[6]. (American family physician).

### Statistical analysis

The data were recorded on a specially designed questionnaire, collected and entered in the computer via Microsoft Excel worksheet (Excel 2010) and then analyzed using an appropriate data system which is called Statistical Package for Social Sciences (SPSS) version 25 and the results were compared between patients with different variables, with a statistical significance level of  $\leq 0.05$ . The results were presented as rates, ratios, frequencies, percentages in tables and

figures and analyzed using t-test and Chi-square tests.

### Results

Demographic and Clinical characteristics of PCOS group are Table (1): Participants of age group (15-24) years old are (10) (25%), while those of age groups (25-34) & (>35) years are 20 (50%) each. According to their marital status (10(25%) single *versus* 30(75%) married).

Participants who have abnormal body weight are 32(80%), (15 (37.5%) overweight, 17(42.5%) obese).

With regard to AHA (American Heart Association) definition and staging of hypertension, 12 (30%) are hypertensive.

Normal blood sugar was found among 30 (75%), but 10(25%) have prediabetes.

Most of the PCOS group have an abnormal menstrual cycle, of which 35(87.5%) have oligomenorrhea, 4(10%) have polymenorrhea, only one of them have a regular cycle. All of PCOS group have hirsutism and ultra-sonographic features of PCOS.

Table (2) shows the lipid profile, serum prolactin and serum free testosterone of the PCOS group. The mean triglyceride level is 160.24 (SD 94.04), mean cholesterol level is 156.47 (SD 44.71), mean LDL level is 80.76 (SD 28.88) and mean HDL level is 49.96 (17.74). The mean Serum prolactin is 20.72 (SD 9.30), while for free testosterone is 0.81 (SD 0.56).

**Table (1):**Demographic and clinical characteristics of PCOS group

Character	Frequency	Percent (%)
Age groups		
15-24 years	10	25
25-34 years	20	50
>35 years	10	25
Marital status		
Single	10	25
Married	30	75
BMI		
Normal	8	20
Overweight	15	37.5
Obese	17	42.5
Blood pressure		
Normal	27	67.5
Elevated	1	2.5
Hypertension stage 1	8	20
Hypertension stage 2	4	10
Blood sugar		
Normal	30	75
Prediabetes	10	25
Menstrual cycle		
Regular	1	2.5
Oligomenorrhea	35	87.5
Polymenorrhea	4	10
Hirsutism		
Present	40	100

\* PCOS, polycystic ovarian syndrome

**Table (2):** Laboratory findings (lipid profile, serum prolactin and free testosterone) of PCOS group

	N	Range	Minimum	Maximum	Mean	Standard deviation
Triglyceride	40	604	74	678	160.24	94.04
Cholesterol	40	182	98	280	156.47	44.71
LDL	40	126.2	40.8	167	80.76	28.88
HDL	40	119	25	144	49.96	17.74
Prolactin	40	42.99	7.01	50	20.72	9.30
Testosterone	40	2.55	0.05	2.6	0.81	0.56

\* LDL, low density lipoprotein; HDL, high density lipoprotein

Demographic and Clinical characteristics of participants in PCOS and Control group Table (3): We had 40 cases of PCOS and 40 cases of age-matched controls, most of the participants are of age group (25-35 years), 20(50.0%) in the PCOS group and 19(47.5%)

in the control group, the total is (39,48.8%). While participants in age group (>35 years) comprise about 22(27.5%) of the study, 10(25.0%) among cases and 12(30.0%) among controls. Those aged 15- 24 years are 10(25%) in the PCOS group and 9(22.5%) in the control group. Total is 19(23.8%) P-value is 0.878. With

regard to participant`s Body Mass Index(BMI), twenty-six (32.5%) of participants have normal weight (cases;8,20.0% vs controls 18,45.0%). While 15(37.5%) in PCOS and 17(42.5%)in control group are overweight. Obesity found among 17(42.5%) cases *versus* 5(12.5%) controls.

P-value is 0.005.

Normal blood pressure is found among (27(67.5%) cases Vs 30(75%)controls). Elevated blood pressure was found in one participant (2.5%) in each group. Hypertension (stage I), have the same incidence among both groups (8(20%) participants). Four (10%) participants in the PCOS group and one (2.5%) in the control group are hypertensive.

P-value is 0.690.

Random blood sugar below 140 mg/dl, found among (30(75%) cases Vs 38(95%) controls). Ten (25%) participants in PCOS group had prediabetes in comparison to 1(2.5%) in the control group. None of the cases had diabetes but only one control was diabetic.

P-value 0.007.

Regarding the menstrual cycle, all participants in the control group have a regular cycle (40 (100%)), while those in the PCOS group have oligomenorrhea 35(87.5%), polymenorrhea 4(10%), regular cycle 1(2.5%).

P-value 0.005

None of participants in the control group has hirsutism, but all of PCOS group has hirsutism (40(100%)). P-value 0.005

**Table (3):** Demographic and clinical features of participants of PCOS and control group

Character	Case	Control	P-value
Age groups			0.878
15-24 years	10 (25%)	9 (22.5%)	
25-34 years	20 (50%)	19 (47.5%)	
>35 years	10 (25%)	12 (30%)	
Marital status			0.617
Single	10 (25%)	12 (30%)	
Married	30 (75%)	28 (70%)	
BMI			0.005
Normal	8 (20%)	18 (45%)	
Over-weight	15 (37.5%)	17 (42.5%)	
Obese	17 (42.5%)	5 (12.5%)	
Blood pressure			0.690
Normal	27 (67.5%)	30 (75%)	
Elevated	1 (2.5%)	1 (2.5%)	
Hypertension stage 1	8 (20%)	8 (20%)	
Hypertension stage 2	4 (10%)	1 (2.5%)	
Blood sugar			0.007
Normal	30 (75%)	38 (95%)	
Prediabetes	10 (25%)	1 (2.5%)	
Diabetes	0	1 (2.5%)	
Menstrual cycle			0.005
Regular	1 (2.5%)	40 (100%)	
Oligomenorrhea	35 (87.5%)	0	
Polymenorrhea	4 (10%)	0	
Hirsutism			0.005
Present	40 (100%)	0	
Absent	0	40 (100%)	

Table (4) shows lipid profile, serum testosterone and free testosterone of the PCOS group and the control group.

Mean triglyceride was (160.24 cases versus 133.50 control. P-value 0.093.

Mean cholesterol was (156.47 cases versus 137.89 controls. P-value 0.051.

Mean LDL was (80.76 cases versus 58.14 controls. P- value 0.001

Mean HDL was (49.96 cases versus 53.19 controls. P-value 0.295).

**Table (3):** laboratory finding (lipid profile, serum prolactin and serum free testosterone) of PCOS and control group

Variable	Study group	N	Mean	Std. Dev	P
Triglyceride	Case	40	160.24	94.04	0.093
	Control	40	133.50	29.17	
Cholesterol	Case	40	156.47	44.71	0.051
	Control	40	137.89	39.08	
LDL	Case	40	80.76	28.88	0.001
	Control	40	58.14	22.55	
HDL	Case	40	49.96	17.74	0.295
	Control	40	53.19	7.78	
Prolactin	Case	40	20.72	9.30	0.001
	Control	40	14.92	2.20	
Testosterone	Case	40	0.81	0.56	0.001
	Control	40	0.27	0.35	

## Discussion

In this study, there is no significant difference in age between PCOS and the control group, they are matched, in order to assess their cardiovascular risk more clearly. This study shows significant differences between both groups in regard to the risk of obesity.

Obesity is a common finding in women with PCOS, between 40–80% of women with this condition are reported to be overweight or obese. The consistent association between PCOS and obesity suggests a biological basis for this observation [2]. The polycystic ovarian syndrome will have increased resistance to insulin, which may be increased by physical inactivity and high calories intake, which all leads to central obesity.

Obesity has major adverse effects on health. Obesity is associated with an increase

in mortality, with a 50-100% increased risk of death from all causes compared to normal weight individuals, mostly due to cardiovascular causes [7].

Large, high-quality longitudinal or prospective studies have confirmed that obesity is a significant risk factor for and contributor to increased morbidity and mortality, primarily from cardiovascular diseases and diabetes, but also from cancer and other acute and chronic diseases, including osteoarthritis, liver and kidney disease, sleep apnea, and depression, for the majority of these comorbid conditions, weight loss can result in a significant reduction in risk [8]. These results support previous studies that they observed an association between PCOS and Obesity, as (Joan C. Lo *et al*) [9], which is a large cohort

study, involving 12,734 PCOS patients, demonstrated that PCOS is independently associated with a higher proportion of major cardiovascular risk factors such as abnormal blood sugar, hypertension, dyslipidemia, and obesity. On the other hand, our results differ from other studies, (ABickerton *et al*)[10] and (Fahimeh Ramezani Tehrani *et al*)[11], in which they have no significant difference in obesity between PCOS and Control group, this may be due to their small size study participants, different classification and characteristics of participants, or duration of their study.

This study shows no significant difference between PCOS and control group in risk of hypertension. One explanation for that is, most of the participants of both groups are young age group of (15-34). It's rare to have essential hypertension in this age groups. Same findings were found in other trials as (Ramezani Tehrani *et al*) [11] and (Akram *et al*) [12]. while significant findings found in (Lo *et al*) [9], this may be due to their large number of participants and part of them have diagnosed hypertension, coronary heart disease, cerebrovascular disease or peripheral vascular disease. However, several studies demonstrated an association between PCOS and hypertension, but did not adjust for an elevated BMI. A Dutch study of PCOS women demonstrated a higher prevalence of hypertension among premenopausal women with PCOS compared to women without PCOS; however, the PCOS population was significantly more obese and the obesity could be responsible for the greater prevalence of hypertension in this population [13]. Wild *et al.* conducted a retrospective examination of women with PCOS diagnosed

an average of 31 years previously and found an increased prevalence of hypertension compared to a cohort of control women [13].

Another significant difference present between both groups is their blood sugar level and proportion of prediabetes or diabetes. Twenty-five percent (25%) of the PCOS group have prediabetes. in contrast, 5% of the control group have abnormal blood sugar. Being obese especially central obesity, leads to increased insulin resistance, together with genetic predisposition, high blood sugar and free fatty acids, all cause progressive loss of beta cells of the pancreas and impaired glucose tolerance or diabetes.

It has been shown that insulin resistance and increased insulin secretion play a pivotal role in the pathogenesis of PCOS by stimulating the ovarian production of androgens[14].

Insulin resistance may result from several mechanisms in PCOS women: decreased insulin secretion and/or hepatic clearance, defected gluconeogenesis in the liver and impaired signaling pathways or receptors of insulin. Insulin resistance could promote cardiovascular diseases directly through sympathetic overactivity, endothelial dysfunction, and vascular reactivity pathologies; and/or indirectly via damaging fibrinolysis, impairing lipolysis suppression, and inducing hypertension [10]. According to prospective studies, women with PCOS present abnormal glucose tolerance and diabetes mellitus in 31%-35% and 7.5%-10%, respectively [14].

Same findings were found in (Bilal *et al*) [15], (JLo *et al*) [9], and (Bickerton *et al*) [10]. While (Tanzeela Akram *et al*)[12] have no significant finding regarding abnormal

blood sugar between both groups, this may be explained by the fact that all of their participants are not obese, although participants of PCOS group have higher insulin level that may be sign of future development of insulin resistance, this hyperinsulinemia may be sufficient to keep their blood sugar in normal range. In (Ramezani Tehrani *et al*) [11], also there is no significant difference in regard to blood sugar, although PCOS women have a higher level of insulin and insulin resistance this faded away over time as they followed up by twelve years, may be due to disappearance of PCOS effect in the older age groups.

LDL level is significantly higher among patients in the PCOS group than in the control group. This is important as LDL is one of the modifiable risk factors for ischemic heart disease.

Dyslipidemia in PCOS is similar to that seen in metabolic syndrome, characterized by low levels of HDL, the small particle size of low-density lipoprotein cholesterol (LDL), and high triglyceride cholesterol levels. This pattern is more often seen in obese than in lean PCOS, likely secondary to the presence of greater insulin resistance in obesity [13]. Findings of several other trails are same, as (Lo *et al*) [9], (Akram *et al*) [12] and (Bilal *et al*) [15]. No significant difference between PCOS and control group was found in these studies, (Bickerton *et al*) [10], as it has a small sample size. Ramezani Tehrani *et al* [11] also has no significant difference in regard to LDL, They have a large sample size, followed up their participants every three year and different characteristics and subgroups of participants.

This study shows a significant difference in menstrual cycle abnormality, (97%) of PCOS group have an abnormal menstrual cycle in the form of oligomenorrhea mainly, this attributed to their chronic anovulation.

There is a significant difference in serum free testosterone and prolactin level in the PCOS group in comparison to the control group. Participants of the PCOS group have hirsutism, which is absent among those in the control group this indicates a hyperandrogenic state, which is the main underlying pathophysiology of polycystic ovarian syndrome.

#### **Limitation of the study**

The main limitation of this study is the small number of participants, because of coronavirus pandemic, which made difficult in finding and selection of participants.

#### **Conclusions**

The proportion of obesity, diabetes and dyslipidemia is higher in Polycystic ovarian syndrome than than control group.

#### **Recommendations**

We recommend a better clinical and laboratory evaluation of patients who have Polycystic Ovarian Syndrome, for early identification of cardiovascular risk factors and subsequent management. Further studies are needed to include a larger number of participants, and more extensive laboratory and imaging techniques, to identify more specifically the subgroups of PCOS with a higher risk of cardiovascular disease.

**Source of funding:** Nill.

**Ethical clearance:** This study was submitted to the Ethics and Scientific committees of community medicine of the Kurdistan Board of Medical Specialties for



scientific and ethical approval. This study was explained for each patient and verbal consent was obtained from each patient or his/her guardian. Confidentiality and anonymity of data were ensured.

**Conflict of interest:** Nill

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