

THE PREVALENCE OF METABOLIC SYNDROME IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Background:The metabolic syndrome (syndrome X) , also called "insulin resistance syndrome" is a cluster of cardiovascular risk factors associated with excess fat. the metabolic syndrome is more common among women with PCOS than in normal women), particularly in those with hyperinsulinaemia and obesity

Objective: The Aim of the study was to determine the prevalence of metabolic syndrome, and it's main determinants in women with PCOS.

Methods: Two –hundred twenty women , 105 patients with polycystic ovary syndrome (PCOS) and 115 control , were included in this study to determine the prevalence of the metabolic syndrome & its main determinants among women with PCOS .

Results: The study revealed that 82.1% of women with PCOS were nulliparae compared to 8.91% of controls ($P < 0.001$) . Blood pressure $> 130/ 85$ mm.Hg and waist circumference > 88 cm were found among 37.14% and 60% of patients with PCOS respectively in comparison to 12.17% and 25.2% of control women respectively ($P < 0.001$). Over weight and obesity were observed among 48.6% and 40% of PCOS women respectively compared to 25.2% and 12.2% of controls respectively ($P < 0.001$) . Only 3.3% of patients with PCOS were fertile , 73.9% with primary infertility and 22.8% with secondary infertility . The comparative figures among controls were 82.3% , 4.2% and 13.5% ($P < 0.001$) . The main menstrual disorder associated with PCOS was oligomenorrhoea , observed in 72.4 of patients , compared to 3.5% in control women ($P < 0.001$) . Hirsutism was found among 62.9% of PCOS patients in comparison to 5.2% of controls ($P < 0.001$) . Women with PCOS showed significantly higher FBG , TC, TG and LDL-C levels ($P < 0.001$) and significantly lower HDL-C levels ($P < 0.01$) compared to control women .

The frequency of metabolic syndrome in PCOS was 34.3% compared to 6.1% in control women ($P < 0.001$) .

Conclusion : the prevalence of metabolic syndrome in PCOS is nearly 6 times higher than in controls . Women with PCOS share multiple cardiovascular risk factors , and thereby , more prone to cardiovascular events .

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies, affecting approximately 4% to 7% of women of reproductive age ⁽¹⁾. PCOS is associated with a broad range of clinical presentations including hirsutism, menstrual irregularities, and infertility. Most women with PCOS have hyperandrogenemia, elevated luteinizing hormone (LH), and normal or decreased follicle-stimulating hormone (FSH). Metabolic abnormalities and sequelae of PCOS resemble those of syndrome X. PCOS is characterized by insulin resistance and compensatory hyperinsulinemia ⁽²⁾. Women with PCOS are often obese, usually because of excessive central fat accumulation. PCOS is associated with Dyslipidemia, systolic hypertension and hyperfibrinogenemia ⁽³⁻⁵⁾. Such women are at an increased risk of type 2 diabetes mellitus, atherosclerosis and coronary artery disease including myocardial infarction ⁽⁶⁾. The metabolic syndrome (syndrome X), also called "insulin resistance syndrome" is a cluster of cardiovascular risk factors associated with excess fat. A commonly used definition defines the syndrome as the coexistence of three or more of the following five abnormalities: high blood pressure, impaired glucose tolerance, dyslipidaemia (high levels of TC, TG, LDL) or (low level of HDL) and abdominal obesity. The metabolic syndrome is associated with a high risk for atherosclerosis, cardiovascular disease, thrombotic events, and mortality ^(1,2). Several investigators studied the relationship between PCOS and the metabolic syndrome, they found that the metabolic syndrome is more common among women with PCOS than in normal

women ⁽⁷⁻⁹⁾, particularly in those with hyperinsulinaemia and obesity ⁽¹⁰⁾. The Aim of the study was to determine the prevalence of metabolic syndrome, and its main determinants in women with PCOS.

Subjects & Methods :

In this study, conducted at Basrah Maternity and Child Hospital, from January, 2005 throughout June, 2006. A total of 220 women, 17-40 years of age were included. They were outpatients attendant at the infertility centre and the gynaecological out-patient clinic in the hospital. Among these women, 105 were diagnosed as polycystic ovary syndrome (PCOS) by clinical, and ultrasonographic methods, while the remaining 115 (in whom PCOS was excluded) were considered as a control group. Detailed history was taken from every participant including menstrual history, history of infertility and obstetric history. In addition thorough physical examination was carried out beside measuring blood pressure, waist circumference and body mass index (BMI). All the studied women were subjected to pelvic ultrasonography as well as measurement of lipid profile: TC, TG, HDL-C, and LDL-C, and fasting blood glucose (FBG) level. Statistical analysis was carried out using Chi-square (χ^2) test. $P < 0.05$ was considered to be statistically significant.

RESULTS

Table 1 presents the age distribution, marriage and parity among patients and controls, where age distribution was comparable in the two groups and the vast majority of women in the age range of 20-40 years (88.6% in patients with PCOS compared to 88% in controls). In addition, 90.5% of patients were married compared to

87.8% of the control group . On the other hand , the vast majority of women with PCOS (82.1%) were nulliparae compared to 8.91% only among controls , where as 17.9% of PCOS women were with parity of 1-5 compared to 86.14% in the control group ($P < 0.001$) no grandmultiparae found among patients (0%) with PCOS compared to 4.95% among control women . As shown in Table 2, (37.14%) of PCOS women have blood pressure of $> 130/85$ mm. Hg compared to only 12.17% of control women $P < 0.001$. Concerning waist circumference, (60%) of women with PCOS were with a circumference of > 88 cm compared to (25.2%) of controls $P < 0.001$. On the otherhand overweight and obesity were found among 48.6% and 40% respectively of PCOS women, $P < 0.001$ compared to (25.2%) and (12.2%) respectively of control women . Normal BMI was observed among 8.6% only of patients compared to 58.3% of control group , $P < 0.001$. Table 3 presents the clinical presentation among the study groups . Only (3.3%) of patients with PCOS were fertile , (73.9%) with primary infertility and (22.8%) with secondary infertility , unlike the control group , where the majority of women were fertile (82.3%) , (13.5%) with secondary infertility and (4.2%) with primary infertility , $P < 0.001$. Concerning menstrual disorders, (72.4%) of PCOS women have oligomenorrhoea, (5.7%) with menorrhagia, (7.6%) with secondary amenorrhoea and only (14.3%) of normal menstrual cycle , unlike control women, were only (3.5%) with oligomenorrhoea, (10.4%) with menorrhagia , (3.5%) with secondary amenorrhoea and the majority (82.6%) with normal cycles , $P < 0.001$) . In addition , about two-third of women with PCOS (62.9%) have hirsutism compared to only (5.2%) of control women

($P < 0.001$) . As shown in Table 4 , serum levels of TC, TG , LDL-C and FBG ($P < 0.001$) were significantly higher, and serum HDL-C level ($P < 0.01$) was significantly lower among women with PCOS compared with controls . Table 5 present the frequency of metabolic syndrome among the studied women . Metabolic syndrome was found among 34.3% of patients compared to 6.1% of controls ($P < 0.01$) .

DISCUSSION

The clinical features of patients with PCOS overlap some of the chief complaints already discussed— amenorrhoea and abnormal bleeding . However , additional problems of infertility, hirsutism , and insulin resistance implicate pathogenetic factors different from those so far emphasized ⁽¹¹⁾. The pathophysiology of PCOS includes anovulation , elevated but not surging LH, elevated androgen production in addition to follicular atresia without maturation. In PCOS, the following pathophysiological abnormalities have been described: an increased pulsatile GnRH secretion^(18,19), disordered ovarian , and sometimes, adrenal androgen secretion^(14,15), ovarian cystic changes and hyperinsulinaemia⁽¹⁶⁾ . It was suggested that excess insulin levels can cause or aggravate ovarian androgen production⁽¹⁶⁻¹⁸⁾. Hyperinsulinaemia and insulin resistance are essential components of PCOS, and may also be associated with hypertension , dyslipidaemia and an increased risk of cardiovascular disease, and hence , the name " metabolic syndrome " ^(11,19). PCOS has a huge burden on fertility, with the vast majority of married women with PCOS (82.1%) were nulliparae (Table 1) .This finding supported by the observation that 96.7% of the studied PCOS women were infertile (

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Table 4) . Infertility or reduced fertility is an important intrinsic feature of PCOS . We found that 37.1% of PCOS women had a blood pressure more than 130/ 85 mm. Hg. This figure is different from that of others ⁽²⁰⁾ , whereas higher than a figure of 21% observed by Ehrmann et al⁽²⁷⁾ . As an elevated blood pressure is an essential component of the metabolic Syndrome^(1,2) . The present study revealed that 60% of women with PCOS were with a waist circumference of more than 88 cm, 48.6% were over weight and 40% were obese (Table 2) . Several studies reported higher waist circumference in association with PCOS ^(6,21) . Folia et al ⁽²²⁾ , observed that 50% of patient with PCOS were obese , while Azziz⁽²³⁾ reported a figure of an increased BMI in 72.3% of PCOS patients. Obesity is an important pathophysiological factor in PCOS affecting other disordered clinical and biochemical parameters . It has been suggested that hyperinsulinaemia , dyslipidaemia and hypertension in PCOS is related to obesity⁽³⁾ . Menstrual abnormalities (particularly oligomenorrhoea) , and hirsutism are consistent finding in association with PCOS. We found oligomenorrhoea in 72.4% , and hirsutism in 62.9% of women with PCOS, Table3. These findings are due to hyperandrogenism present in PCOS patients. Elevated ovarian androgen secretion tends to block the growth of a dominant ovarian follicle . Excessive androgens stimulate the growth of terminal hair in a male- pattern distribution⁽²⁴⁾ . PCOS is associated with significant adverse changes in FBG and lipid parameters , as presented in Table 4 . These significant alterations in lipid profile and blood sugar , though still within the normal limits yet , however , having substantial adverse influences on the cardiovascular risk particularly when

associated with other cardiovascular risk factors already existing among patients with PCOS, notably, obesity, hypertension, hyperinsulinaemia and insulin resistance . Dyslipidaemia in association with PCOS is a consistent observation in several studies^(6,20,21,23,25,26) . PCOS patients exhibit an abnormal lipid profile with reduced HDL-C levels , an increased TG levels and slightly elevated LDL-C concentrations . However , normal LDL-C level may be misleading as LDL particles shows variations in size and atherogenicity , with smaller dense LDL particles are harmful and more atherogenic , and high concentrations often occurs in association with hypertriglyceridaemia , with frequently normal LDL-C , increased hepatic lipase activity and insulin resistance ⁽²⁷⁾ . We found that 34.3% of women with fulfill the criteria of metabolic syndrome, Table 6. Such figure indicates that the risk of metabolic syndrome is increased nearly 6-fold in women with PCOS than in control women . Most of published studies reported an increased risk of metabolic syndrome in PCOS^(20,21,25,28) , reaching up to 11-fold increased risk of metabolic syndrome compared to control women ^(9,23) . PCOS is the most common cause of increased cardiovascular risk in young adult women ⁽²⁹⁾ . In conclusion, women with PCOS are , undoubtedly, at greater risk of metabolic syndrome than normal women , and thus , at more risk of cardiovascular disease & would be more prone to cardiovascular events. We recommend that all obese and overweight women with PCOS should be screened for metabolic syndrome and, when the syndrome is not found, the screening should be repeated every 2 or 3 years. Treatment consists in lifestyle intervention. Pharmacological therapies

should be used only when lifestyle fails to normalize cardiovascular risk factors .

Table 1 : Age distribution, marriage and parity

Age (year)		PCOs		Controls	
		No.	%	No.	%
< 20		12	11.4	14	12.2
20-40		93	88.6	101	87.8
> 40		0	0	0	0
Total		105	100.0	115	100.0
Marriage	Yes	95	90.5	101	87.8
	No	10	9.5	14	12.2
	Total	105	100.0	115	100.0
Parity ***	0	78	82.1	9	8.91
	<5	17	17.9	87	86.14
	≥5	0	0	5	4.95
	Total	95*	100.0	101**	100.0

* unmarried among PCOs women = 10

** unmarried among controls = 14

*** parity : $X^2 = 101.7$

P < 0.001

Table 2 : Clinical characteristics

Parameter		PCOs		Control	
		No.	%	No.	%
Blood pressure (mmHg)*	≤ 130/85	66	62.86	101	87.83
	> 130/85	39	37.14	14	12.17
	Total	105	100.0	115	100.0
Waist circumference (cm)**	≤ 88	42	40	86	74.8
	> 88	63	60	29	25.2
	Total	105	100.0	115	100.0
BMI (kg/m ²) ***	< 19	3	2.8	5	4.3
	19-25	9	8.6	67	58.3
	> 25-30	51	48.6	29	25.2
	> 30	42	40	14	12.2
	Total	105	100.0	115	100.0

* Blood pressure : $X^2 = 18.7$, P < 0.001

** Waist circumference : $X^2 = 27.31$, P < 0.001

*** BMI : $X^2 = 64.48$, P < 0.001

Table 3 : Clinical presentation

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Clinical parameter		PCOs		Control	
		No.	%	No.	%
Fertility *	Fertile	3	3.3	79	82.3
	Primary infertility	68	73.9	4	4.2
	Secondary infertility	21	22.8	13	13.5
	Total	92 ⁽¹⁾	100.0	96 ⁽²⁾	100.0
Menstrual disorder **	Menorrhagia	6	5.7	12	10.4
	Secondary amenorrhoea	8	7.6	4	3.5
	Oligomenorrhoea	76	72.4	4	3.5
	No abnormality	15	14.3	95	82.6
	Total	105	100.0	115	100.0
Hirsutism ***	Present	66	62.9	6	5.2
	Absent	39	37.1	109	94.8
	Total	105	100.0	115	100.0

* Among married women

(1) : Among PCOs = unmarried = 10 married since < 1 year = 3 i.e. total = 105-13=92

(2) : Among control = unmarried = 14 married since < 1 year = 5 total = 115-19 = 96

* : Fertility : $X^2 = 129.21$, $P < 0.001$

** : Menstrual disorders $X^2 = 126.11$, $P < 0.001$

*** Hirsutism : $X^2 = 82.84$, $P < 0.001$

Table 4 : Biochemical Parameters

Parameter (mg/dl)	PCOS (n=105)	Controls (n=115)	t-value	P- value
TC	202.6 (35.8)	187.5 (30.2)	3.38	$P < 0.001$
TG	153.1 (45.4)	134.9 (30.2)	3.53	$P < 0.001$
LDL-C	115.3 (36.4)	97.2 (30.7)	3.99	$P < 0.001$
HDL-C	52.3 (14.8)	57.6 (14.9)	2.64	$P < 0.01$
FBG	108.1 (21.8)	98.6 (15.5)	3.75	$P < 0.001$

Values are given in \bar{x} (SD) .

Table 5 : The metabolic syndrome

The metabolic syndrome	PCOs		Controls	
	No.	%	No.	%
Present	36	34.3	7	6.1
Absent	69	65.7	108	93.9
Total	105	100.0	115	100.0

$X^2 = 27.83$, $P < 0.001$

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تحديد إنتشار حدوث متلازمة الأيض (X) بين النساء اللواتي لديهن متلازمة التكريس المبيضي المتعدد

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الخلاصة:

المقدمة:

تضمنت هذه الدراسة المستقبلية التي أجريت في مستشفى البصرة للولادة والأطفال ٢٢٠ امرأة منهم ١٠٥ امرأة لديهن متلازمة التكريس المبيضي المتعدد (الحالات) و ١١٥ امرأة لا توجد لديهن أي علامات متلازمة التكريس المبيضي المتعدد (الحالات الضابطة).

هدف الدراسة:

كان هدف الدراسة هو لتحديد إنتشار حدوث متلازمة الأيض (X) بين النساء اللواتي لديهن متلازمة التكريس المبيضي المتعدد وأيضاً لتحديد العوامل الرئيسية المؤثرة على حدوثه مع دراسة بعض المتغيرات السريرية والخصائص الكيميائية للنساء المصابات بهذه المتلازمة ومتلازمة التكريس المبيضي المتعدد.

النتائج:

أظهرت الدراسة بأن ٨٢,١% من النساء المصابات بمتلازمة التكريس المبيضي المتعدد كن ممن ليس لديهن أطفال بالمقارنة مع ٨,٩١% من الحالات الضابطة مع وجود فرق معنوي ($P<0.001$) إرتفاع ضغط الدم أكثر من ٨٥/١٣٠ ملم زئبق ومحيط الخصر أكثر من ٨٨ سم كان موجوداً في ٣٤,١٤% و ٦٠% من الحالات بالتتابع بالمقارنة مع ١٢,١٧% و ٢٥,٢% في الحالات الضابطة بالتتابع. لوحظ زيادة الوزن والسمنة بين ٤٨,٦% و ٤٠% من الحالات بالتتابع بالمقارنة مع ٢٥,٢% و ١٢,٢% من الحالات الضابطة بالتتابع.

كان هناك ٣,٣% من الحالات لديهن خصوبة طبيعية، ٧٣,٩% لديهن عقم أولي و ٢٢,٨% لديهن عقم ثانوي مقارنة مقارنة بالحالات الضابطة، حيث كانت الأرقام ٨٢,٣%، ٤,٢% و ١٣,٥% مع وجود فرق معنوي واضح ($P<0.001$).

إضطراب الدورة في مجموعة الحالات كانت مقسمة كالتالي: شحة الدورة في ٧٢,٤% بالمقارنة ٣,٥% في مجموعة الحالات الضابطة ($P<0.001$)، ظهور الشعر كان موجوداً في ٦٢,٩% من الحالات بالمقارنة مع ٥,٢% من المجموعة الضابطة ($P<0.001$).

أظهرت الفحوصات المخبرية وجود زيادة في نسبة السكر في الدم، الكوليسترول، الترايكلسيريد مع LDL-C ($P<0.001$) مع نقصان واضح في مستوى HDL-C ($P<0.01$) مقارنة بالحالات الضابطة. تبين أن تكرار حدوث متلازمة الأيض في مجموعة الحالات كان ٣٤,٣% مقارنة مع ٦,١% في الحالات الضابطة وبفرق معنوي ($P<0.001$).

الخلاصة

إن إنتشار متلازمة الأيض في النساء اللواتي لديهن متلازمة التكريس المبيضي المتعدد هي ٦ مرات أكثر من الحالات الضابطة.

إن النساء المصابات بالتكريس المبيضي المتعدد لديهن خصائص سريرية وكيميائية مختلفة مثل: إرتفاع ضغط الدم، السمنة، إرتفاع نسبة السكر في الدم وإضطراب في مستويات الدهون، لذلك هؤلاء النساء لديهن عوامل كثيرة لزيادة الخطورة على القلب والأوعية الدموية ويكون أكثر عرضة لإصابات القلب.