Metabolic syndrome in women with polycystic ovary syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is the most common form of chronic anovulation associated with androgen excess; it occurs in about 5 – 10% 0f reproductive age women. Metabolic syndrome is characterized by insulin resistance, hypertension, obesity, abnormalities of blood clotting and dyslipidemia.
Adult women with PCOS have an increased prevalence of the metabolic syndrome(MBS).
Objectives: To detect the prevalence of metabolic syndrome in women with proved PCOS, attending the Specialized Center for Endocrinology and Diabetes, in Baghdad.
Materials and methods : A total number of 40 women with proved PCOS were included in this study which was conducted in the Specialized Center for Endocrinology and Diabetes-Baghdad, over a period of 5 months(from April till September 2005).In addition to measuring waist circumference and body mass index(BMI),all patients were tested for the levels of C-peptide, Fasting plasma glucose(FPG), Serum luteinizing hormone(LH), Follicle st – imulating hormone(FSH), Prolactin(PRL), Progesterone, estradiol(E2), testosterone,T3,T4 and TSH .
Also lipid profile, glycated hemoglobin(HbA1c) were estimated to all patients. Glucose tolerance test(GTT) using 75 gm of glucose was performed on all patients.
Results: Out of 40 women with PCOS,eleven patients(27.5%) have impaired GTT. Twenty patients (50%) out of 40 fulfil the criteria of the International Diabetes Fideration(IDF)
Consensus Definition of the metabolic syndrome(MBS)-2005.
Thirty-Seven patients(92.5%) have a waist circumference more than 80 cm.
Thirty-two patients(80%) have secondary amenorrhea.
Hirsuitism and increased BMI(body mass index) were present in 33 patients(82.5%)
The mean C-peptide level was higher in those patients who had impaired GTT(11 patients),meaning that GTT can be used to detect insulin resistance specially in Labs. where measurements of insulin levels are not available.
Conclusions :

1. Metabolic syndrome is present in 50% of our patients,using the IDF Consensus Definition of the metabolic syndrome-2005.
2. Glucose tolerance test can be used to detect the presence of insulin resistance specially in Labs. where measurements of insulin levels are not available.
3. Insulin resistance is present in 27.5% in women with PCOS who were included in our study.

Keywords : Polycystic ovary syndrome (PCOS), metabolic syndrome(MBS),Fasting plasma glucose (FPG)

Al - Kindy Col Med J 2011 ; Vol .7 No. (1) p: 4-10

Introduction:

Polycystic ovary syndrome (PCOS) is the most common form of chronic anovulation associated with androgen excess,occurring in 5-10% of reproductive age women(1). It is also the most common endocrine abnormality in premenopausal women (2). It typically presents with amenorrhoea ,oligomenorrhoea ,hirsuitism and acne, and commonly occurs at mid-twenties of age (3-5).
In 1935 ,Stein and Leventhal published their findings in seven women with amenorrhoea , hirsuitism, obesity, and a characteristic polycystic appearance to their ovaries, which was one of the first descriptions of this complex phenotype today known as the PCOS (6,7).
A precise and uniform definition of the syndrome is lacking. An international consensus group(8) proposed that the syndrome can be diagnosed after the exclusion of other medical conditions that cause irregular menstrual cycles and androgen excess, and the determination that at least two of the following are present :
Oligoovulation or anovulation(usually manifested as oligomenorrhoea or amenorrhoea), elevated levels of circulating androgens(hyperandrogenemia) or clinical manifestations of androgen excess(hyperandrogenism), and polycystic ovaries as defined by ultrasonography(9).
These criteria acknowledge the condition as functional : polycystic ovaries need not be present to make a diagnosis of the PCOS(10), and conversely, their presence alone does not establish the diagnosis (11,12).
Women with PCOS almost always have some aberration in gonadotropin secretion as compared with women who have normal menstrual cycles (13).

While insulin resistance is not part of the diagnostic criteria for PCOS, its importance in the pathogenesis of PCOS cannot be denied. PCOS is associated with insulin resistance independent of total or fat-free body mass. Post-receptor defects in the action of insulin have been described in PCOS which are similar to those found in obesity and type 2 Diabetes (14).

Treatment with insulin sensitizers, metformin and thiazolidinediones, improve both metabolic and abnormal patterns and also improve ovulation in PCOS (15-18).

Adult women with PCOS have an increased prevalence of the metabolic syndrome(MBS). The prevalence of MBS is also increasing in adolescents(19).This is not surprising, since both the PCOS and the MBS share insulin resistance as a central pathogenetic feature(20).

It has been shown that treatment to reduce insulin levels and resistance improve the symptoms of PCOS such as high levels of androgens but the exact cause of the insulin resistance is not entirely clear. The result of this unclear pathogenesis place the focus of treatment on the symptoms of insulin resistance (21) .

Women with PCOS have a four to five fold increased risk for development of complications of coronary and cerebrovascular atherosclerosis(22-24).Metabolic syndrome(MBS) is a constellation of metabolic disorders that all results from the primary disorder of insulin resistance, and all the metabolic abnormalities associated with this syndrome can lead to cardiovascular disorders, and when present as a group, the risk for cardiovascular disease and premature death are very high (25,26).

The characteristic disorders present in this syndrome include : insulin resistance, hypertension, abnormalities of blood clotting, and dyslipidemia, in addition to obesity.

More than 22% of people in the united states meet three or more of these criteria (27).

The International Diabetes Federation(IDF) Consensus Definition of the MBS(April-2005) is as follows :

1. Central obesity : waist circumference≥ 94cm for men, and ≥80cm for women.

2. Plus any two of the following 4 factors :

a. Raised serum triglyceride ; ≥150mg/100m/ (1.7mmol/l)

b. Reduced HDL-C , ＜40mg/100m/ (1.03mmol/l) in male, ＜50mg/100m/ (1.29mmol/l) in female, or a history of treatment for dyslipidemia.

c. Raised blood pressure : ≥130/≥85 mm Hg or treatment of previously diagnosed hypertension.

d. Raised Fasting plasma glucose , ≥100mg/100m/(5.6mmol/l) or previously iagnosed type2 diabetes mellitus.

Methods:

This study was performed on 40 women with proved PCOS, attending the Specialized Center for Endocrinology and Diabetes in Baghdad, from April till September 2005.

Glucose tolerance test, using 75gm glucose was performed on all patients.

Other aspects of the MBS were taken into consideration, such as obesity, hypertension, and dyslipidemia.

The C-peptide level was estimated for all patients, also the levels of a number of other hormones were tested, as part of the investigations for menstrual disturbances, hirsuitism, or infertility, and these included: LH,FSH,PRL ,Progesterone,E2, testosterone,T3,T4,and TSH. Other biochemical tests included in the study were, FPG, Lipid profile, and glycated hemoglobin (HbA1C).

Measurement of waist circumference, in addition to BMI(body mass index) was done to all patients. We applied the IDF Consensus Definition of the MBS-2005, on our patients. T-test for statistical analysis was used.

Results:

From table(1) it appears that the most common prevalence of PCOS falls in the age group 15 – 35 . Table(2) shows the material status with details of fertility state.

Twenty-nine patients(72.5%) have increased weight with hirsuitism (Table3). Thirty-seven patients(92.5%) have a waist circumference more than 80cm ($P<0.05$) (Table4). Table(5) shows that 32 patients(80%) have secondary amenorrhoea ($P<0.001$). Table(6) shows the blood pressure status in which 22 patients(55%) are hypertensive compared to 18 normotensive patients(45%).

Mean C-peptide level in those with positive post-challenge test was 3.536 ng/ml (N 1.07-3.51 ng/ml), while its mean in the remaining 29 patients was 3.012ng/ml.Also HbA1c is higher in those with impaired GTT compared with those without(5.89%vs5.0%)($P<0.05$) (Tables 7,8).

Out of 40 women with PCOS, eleven patients showed a positive post-challenge test (27.5%), using 75gm glucose, five of them(45.45%) are fulfilling the criteria of the IDF Consensus Definition of the MBS-2005, while the total number of those who fulfil these criteria are 20 out of 40(50%) (Table 9).

From table(10) we can see the details of blood pressure, FPG, s.Triglycerides, HDL-C, with their relation to each other in patients with MBS.

The mean levels of s.prolactine and serum testosterone are shown in table(11), while table(12) shows the mean values of s.progesterone and s.testosterone in those women with and without hirsuitism ($P<0.001$).The relation between waist circumference and serum triglyceride levels, in those with waist circumference more than 80cm is shown in table(13) which shows that 50% of patients have increased s.TG and waist circumference ＞80cm. ($P<0.05$)

Table 1 : age, duration & F.H. of P.C.O.S.

Age	No.(%)	Duration	No.(%)	F.H	
15-25	18(45%)	< 5 y	14(35%)	yes	no
26-35	18(45%)	6-10 y	20(50%)		
36-45	4(10%)	> 10 y	6(15%)	29(72.5%)	11(27.5%)
Total	40(100%)		40(100%)		

FH = Family history
PCOS = Polycystic ovary syndrome.

Table 2 : The marital & fertility status

Single	Married	infertile	fertile	Prim.infert.	Second infert.
15(37.5%)	25(62.5%)	22(88%)	3(12%)	14(63.6%)	8(36.4%)

Table 3 : the presentation & Duration

	≤ 5 y	> 5	Total
Increase wt+ hirsuit.	29(72.5%)	4(10%)	33(82.5%)
Increase wt. only	4(10%)	3(7.5%)	7(17.5%)
P value T test 3.779 df = 1, P-Value = 0.052			

wt. = weight
hirsuit. = hirsuitism

Table 4 : the mean waist circum. & BMI

	Waist.circum	BMI Mean ±SD	No.
With MBS	94.42cm	31.74±2.56	20(50%)
Without MBS	91.30cm	29.85±1.98	20(50%)
Total no. with waist circumference	93.7cm	30.32	37(92.5%)
P value T test 2.6117 df = 38 P value= 0.0128			

MBS = Metabolic syndrome
Circum. = circumference
BMI = Body mass index

Table 5 : the state of menstruation

Sec.amenorrhoea	oligomenorrhoea	regul.menses	Total
32 (80%)	6 (15%)	2 (5%)	40 (100%)
X^2=19.601 DF = 2, P-Value = 0.000			

Table 6 : the B.P status

HT	normotensive	Total
22(55%)	18(45%)	40(100%)
P value T test	0.201 DF = 1, P-Value = 0.654	

B.P = Blood Pressure
HT = Hypertensive

Table 7 : the results of post-challenge 75gm glucose test

Impaired GTT	normal GTT	Total
11(27.5%)	29(72.5%)	40(100%)
P value T test	4.266 DF = 1, P-Value = 0.039	

Table 8 : the mean FPG, 2-hour post-challenge Glucose, C-peptide,& HbA1c levels

	FPG mmol Mean SD	2-hPCG Mean SD	C-pept. (ng/ml) Mean SD	HbA1c Mean SD
Impaired GTT (11)	5.03 (1.46)	8.48 (2.05)	3.536 (0.92)	5.89(1.88)
Normal GTT (29)	4.17(1.82) (75.06)	5.40(2.08) (97.2)	3.012(1.02)	5.00(2.01)
P value T test	0.1691	0.0002	0.1451	0.2113

GTT = Glucose tolerance test
FPG = Fasting plasma glucose
2-hPCG = two hour post-challenge glucose
C-pept. = C-peptide . (N.1-3.51)

Table 9 : the No. of patients with MBS according to IDF Consensus Definition 2005

Patients	MBS
Impaired GTT(11)	5(45.45%) – (12.5% of total)
Normal GTT(29)	15(51.72%) – (37.5% of total)
Total(40)	20(50% of total)

MBS = Metabolic syndrome
IDF = International Diabetes Federation
GTT = Glucose tolerance test .

Table 10 : the details of those with MBS(IDF 2005)

Inc.B.P+inc.TG	Inc.B.P+inc.FPG	inc.B.P+dec.HDL	inc.TG+dec.HDL	Total
8(8/20)	1(1/20)	3(3/20)	8(8/20)	20
40%	5%	15%	40%	100%

BP = Blood pressure
FPG = Fasting plasma glucose
HDL = High density Lipoprotein
Inc. = increased
dec. = decreased

Table 11 : the mean values of s.PRL & s.Testo. in patients with and without MBS

	.PRL Mean ±SD	Testo. Mean ±SD
MBS(20)	*19.3±3.15	*1.56±0.79
Without MBS(20)	*17.0±2.48	*1.48±0.90
Impaired GTT(11)	25.45±3.43	0.9±0.82
P value T test	*0.0144	*0.7668
	(S)	(NS)

MBS = Metabolic syndrome
s.PRL = serum prolactin (N,1.3-25miu/ml)
s.Testo. = serum testosterone (N, 0.1-0.9miu/ml)
GTT = Glucose tolerance test .

Table 12 : the mean values of s.Prog.,& Testo. in those patients with and without hirsuitism

	Prog. miu/ml Mean ±SD	Testo. miu/ml Mean ±SD
Hirsuitism (29)	3.6 ±1.43	1.6 ±0.68
Without Hirsuitism (11)	0.85±0.66	1.06±0.82
P value T test	0.0001	0.0806

Prog. = Progesterone (N. 0.12 – 6.22)
Testo. = Testosterone (N. 0.4 – 0.9)

Table 13 : the relation between waist circumference and TG level

↑waist circumference(＞80cm) + ↑TG	normal waist + normal TG	↑waist circumference + normal TG	Total
20 patients (50%)	3 patients (7.5%)	17 patients (42.5%)	40 patients (100%)
P value T test 8.025 DF = 2, P-Value = 0.018			

TG = Triglyceride

Discussion:

Family history was positive for PCOS in 29 patients(72.5%)(Table1) which stresses that an effort should be spent on detecting and managing these cases . Among the married 25 women(62.5%), 22 0f them(88%) are infertile(table2). It is said that PCOS is one of the most common causes of infertility in females (28) .

Hirsuitism and increased BMI were present in 33 patients(82.5%) which goes with the international percentage of hirsuitism among women with PCOS, which is around 80% (Table 3) (29) . Thirty-seven patients(92.5%) have increased waist circumference much above the accepted levels in the IDF Consensus Definition of the MBS with details shown in table(4). This high percentage (92.5%) needs to be compared with other studies, not present in the available references. Fifty percent of our patients are obese(BMI $\geqslant$30kg/m2) which goes with the international percentage of 50 , (30) . Thirty-two(80%) of these 40 women have secondary amenorrhoea (table5). Hypertension was present in 22 patients(55%) while 18 patients(45%) were normotensive and this is one of the criteria for MBS (Table 6) .From these data we can see that among these 40 women with PCOS, eleven (27.5%) have impaired GTT, using 75gm glucose, with a mean C-peptide level of 3.536 ng/ml, while the mean C-peptide level in those with normal GTT was 3.012 ng/ml (Normal 1.07-3.51 ng/ml), indicating that those patients with impaired GTT have definite insulin resistance, when compared with those who have normal GTT, and this gives us an indication that impaired GTT can be used as an indicator for the presence of insulin resistance, specially in laboratories where C-peptide estimation is not available, tables (7,8) .

This percentage of 27.5 is among the international range of 20-40 % among patients with PCOS, which is approximately seven-fold higher than the rates in age and weight-matched women (31,32) .Twenty patients(50%) fulfil the criteria of the IDF Consensus Definition of the MBS-2005, which is in agreement with another study done by Anuja Dokras, et al, where the percentage was 47.3% compared to 4.3% in the control group(30), while the prevalence of MBS among adolescent girls with PCOS was 37% in anther study done by Andrea D.coviella (Table 9) (19) .There was a strong association between hypertension and increased serum triglyceride level in 40% of those with MBS and also an increased s.TG with decreased sHDL.C in 40% of cases(table10). It is said that serum TG/HDL-C $>$3.2 has a high sensitivity and specificity for the detection of MBS in women with PCOS (33) .The mean serum prolactin and serum testosterone levels were higher among women with MBS than those without (table11), while table(12) shows the mean values of serum progesterone and testosterone in those with and without hirsuitism. Thirty-six patients(90%) fall in the age group of 15-35 which is the child-bearing age (table1). This is in agreement with other studies (33) .Table(13) shows that 20 patients(50%) out of 40 have waist circumference more than 80cm in addition to increased serum triglyceride level, and this is an important association between waist circumference and serum triglyceride level, although larger studies are needed to evaluate this association, and also the association between PCOS and BMI and its effect in the development of MBS (33) .

Conclusions:

1. Among 40 women with PCOS who were included in this study, eleven patients(27.5%) have impaired GTT, using 75gm glucose, with a mean C-peptide level of 3.536 ng/ml which is higher than the upper normal limit of 3.51 ng/ml, and also higher than its level in women with normal GTT who were included in this study, which supports the importance of post-challenge test as a predictor of insulin resistance, specially in those laboratories where insulin levels are not available .
2. Twenty patients(50%) fulfil the criteria of the International Diabetes Federation Consensus Definition of the Metabolic Syndrome-2005,putting in mind the importance of waist circumference in the diagnosis of MBS, as it is considered the main denominator when looking for the criteria of the syndrome. Thirty-seven patients(92.5%) out of the 40 who were included in this study have a Waist circumference more than 80cm .

Recommendations:

1. It is important to test every woman with PCOS for all the aspects of the metabolic syndrome and to manage them accordingly ..
2. We have to stress to all our collegues who are dealing with these cases to explain to women with PCOS that management of this syndrome is not only important for fertility or menstrual problems but also for the health of the woman herself .

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