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Original Research

Prevalence of metabolic syndrome in women with polycystic ovary syndrome: Relationship with lifestyle and cardiometabolic biomarkers

Latifa Imen Benharrat[1], Azzeddine Senouci[1], Wassila Benhabib[2], Khedidja Mekki[1,*]

[1] **Laboratory of Clinical and Metabolic Nutrition, University of Oran, Oran 31100, Algeria. Thematic Agency of Research in Health Sciences, Oran, Algeria**
[2] **Department of Epidemiology, University Hospital of Oran, Oran 31037, Algeria**

*Correspondence to: Mekki Khedidja, Laboratory of Clinical and Metabolic Nutrition, Faculty of Natural and Life Science, University of Oran, Thematic Agency of Research in Health Sciences, Oran, Algeria, E-mail: khmekki@hotmail.com, Phone: +213 735023/2130552649929

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Abstract

Background and aims: The objective was to determine the prevalence of metabolic syndrome (MS), its components and their relationship with lifestyle, and cardiometabolic biomarkers among women with polycystic ovary syndrome (PCOS). **Material and methods:** One hundred and two women (30±7 years) were enrolled for the study. Daily energy expenditure (DEE) was assessed by an adapted questionnaire and food intake by a "food frequency questionnaire". We analyzed glycemia, lipid profile, and oxidative stress. **Results:** Among 102 PCOS, 78 (76.4%) were diagnosed with MS. Components of MS included hypertension (56.9%), hyperglycemia (24.5%), hypertriglyceridemia (78.4%), abdominal obesity (94.1%), and low levels of high-density lipoprotein cholesterol (34.3%). In PCOS women with MS compared to PCOS women without MS, DEE was decreased ($p<0.001$) and total energy intake increased ($p<0.001$). A decrease in cooked fruits and vegetable intake ($p<0.001$), whole grains ($p=0.002$), and an increase in the intake of sweetened products and saturated fatty acids ($p<0.001$). TBARS ($p=0.033$) and carbonyls ($p=0.019$) were increased and superoxide dismutase activity ($p<0.001$) and thiols amounts ($p=0.032$) were decreased. **Conclusions:** The prevalence of MS was higher in women with PCOS, characterized by an unhealthy lifestyle and oxidative stress. To prevent type 2 diabetes and cardiovascular disease, the Mediterranean diet and physical activity are the most appropriate support.

Keywords: metabolic syndrome, polycystic ovary syndrome, lifestyle, food intake, energy expenditure, oxidative status.

Background and aims

Polycystic ovary syndrome (PCOS) is considered a complex endocrinopathy in women of reproductive age due to its association with multiple metabolic abnormalities [1, 2]. The prevalence of PCOS among women of childbearing age is estimated to be between 5% and 18% [3]. PCOS is a polygenic multifactorial disorder and its pathogenesis is influenced by both environmental risk factors and genetic susceptibility [4].

Clinicians have listed different criteria for diagnosis, including the National Institutes of Health (NIH; 1990), Rotterdam (2003), and Society Criteria for Excess Androgen and PCOS. The Rotterdam criteria have been found to be more inclusive and are generally preferred [5–6].

Women with PCOS have a higher prevalence of glucose intolerance, obesity, and metabolic syndrome (MS) [7]. Obesity is very common in these patients, with a reported prevalence between 9% and 67% [8].

Insulin resistance and associated metabolic abnormalities appear to be linked to the development and maintenance of PCOS [9]. Hyperinsulinemia in PCOS women contributes to

several problems, including overweight and MS [10–12].

An unhealthy lifestyles like inappropriate diet and sedentary behavior contribute to central adiposity and metabolic co-morbidities that play an important role in the pathogenesis of PCOS [11].

The objective of this study was to estimate the prevalence of metabolic syndrome and its components and their relationship with food intake, energy expenditure, lipids profile, and oxidative status in women with PCOS.

Material and methods

Study design and patients

A cross-sectional survey was conducted among women with PCOS who attended the gynecology department of the Public Health establishment (EPSP) Es Senia, ORAN (Western Algeria), from September 2018 to June 2019.

The exclusion criteria were women who are no longer of childbearing age and pregnant women, and the use of dietary supplements such as vitamins and/or antioxidants. All the steps of the study that was going to be carried out were explained to the patients, and consent was agreed and signed. The experimental protocol was approved by the Committee for Research on Social Sciences and Humanities Subjects of Oran.

One hundred and two women (30±7 years) were included on the basis that they have PCOS (Table 1). Patients were diagnosed according to the Rotterdam Consensus criteria 2003, two of these three are required: Clinical and/or biochemical hyperandrogenism, oligo/amenorrhea, anovulation, and polycystic ovaries appearance on ultrasound [5].

The diagnosis of MS was made according to the criteria of NCEP/ATP III (2001, 2005 revision). The diagnosis was made when three or more components were present: waist circumference (WC) >88 cm, triacylglycerols (TG) ≥1.69 mmol/l, systolic blood pressure (SBP) ≥130 mm Hg and/or diastolic blood pressure (DBP) ≥85 mm Hg, or the use of (anti-hypertensive medication), low concentration of high-density lipoprotein cholesterol (HDL-C ≤1.29 mmol/l, or hyperglycemia (fasting serum glucose ≥6.11 mmol/l or the use of anti-diabetic medication) [13].

Food behavior assessment

Daily energy expenditure (DEE) was measured using an adapted questionnaire. This variable is mainly influenced by lean body mass and the type, duration, and intensity of physical activity. The basal metabolic rate is calculated which represents the largest component of total energy expenditure and is a major contributor to energy expenditure using the formula of Black et al. [14].

To assess food intake, a food frequency questionnaire was developed and adapted to the population. The questionnaire was organized by meal and every meal was structured in the starter, main course, side dish, and dessert. Food groups were used as a basis for meals structure.

Subjects were asked about their usual consumption of the 7 days preceding the interview. A 24-hour "Recall and Record" method was used to validate the food frequency questionnaire. A pilot survey was conducted on a sample of 10 women, and it was used to correct and adapt all questions. We collected information about the quantity consumed and the frequency of consumption of different foods. The conversion of food into nutrients was made using the food table of Souci et al. [15].

Assays

Blood samples were taken by antecubital venipuncture after a 12-hour overnight fast. Samples were collected by low-speed centrifugation at 4000× g at 5° for 20 minutes and stored with sodium heparin (NH).

Glucose and lipid analysis

Blood glucose, triacylglycerols (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) were determined by colorimetric methods (Kits Biolabo, France). Low-density lipoprotein cholesterol (LDL-C) was determined using the Friedwald formula [16].

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Table1: Characteristics of women with polycystic ovary syndrome (n=102).

Characteristic	Value
Age (years)	30±7
Weight (kg)	75.6±7.7
Height (cm)	163.1±4.2
Body mass index (kg/m^2)	28.4±2.4
Place of residence	
Apartment (%)	44 (43.1)
House (%)	57 (55.9)
Other (%)	1 (1.0)
Employment status	
Working (%)	44 (43.1)
Do not work (%)	58 (56.9)
Level of education	
Illiterate (%)	0 (0)
Primary (%)	5 (4.9)
College (%)	13 (12.8)
Secondary (%)	24 (23.5)
University (%)	60 (58.8)
Contraceptive history	
Oral contraception (%)	19 (18.6)
None (%)	83 (81.1)
Hormone treatments	56 (54.9)
PCOS symptoms	
Hirsutism (%)	74 (72.5)
Loss of hair (%)	95 (93.1)
Acne (%)	41 (40.2)
Weight gain (%)	90 (88.2)
Skin hyperpigmentation (%)	75 (73.5)
Diseases	
Dyslipidemia (%)	80 (78.4)
None (%)	12 (11.8)
Biochemical measures	
Urea (mmol/l)	6.60±2.19
Creatinine (mmol/ml)	98±24

Values are given as mean ± SD or number (percentage).

Oxidant and antioxidant status

Serum lipid peroxidation was analyzed by measurement of thiobarbituric acid (TBARS) reagent [17], using malondialdehyde (MDA) as a standard. One milliliter of the diluted sample (protein approximately 2 mg/ml) was added to 2 ml of thiobarbituric acid (final concentration, 0.017 mmol/l) and butylated hydroxytoluene (concentration, 3.36 mmol/l), and incubated for 15 minutes at 100°C. After cooling and centrifugation, the absorbance of the supernatant

was measured at 535 nm. Data were expressed in mmol of TBARS produced/l of serum.

Oxidized proteins were measured by the analysis of carbonyl concentrations [18] using 2,4-dinitrophenylhydrazine. The absorbance of the supernatant was measured between 250 and 300 nm.

Superoxide dismutase (SOD) enzyme activity was determined by a method [19] based on a competition between the oxidation reaction of pyrogallol by $O2^-$ and the dismutation of $O2^-$ by SOD. The product of the auto-oxidation and $O2^-$ both absorb at 325 nm.

Catalase activity assay was performed using spectrophotometric determination of hydrogen peroxide (H_2O_2) [20], which form a stable complex with ammonium molybdate that absorbs at 405 nm.

Thiols were determined by a colorimetric method [21] based on the oxidation reaction of -SH groups with 5,5'-dithiobis-2-nitrobenzoic acid (DTNB), thereby releasing thionitrobenzoic acid (TNB) of yellow color which absorbs at 412 nm.

Statistical analysis

A student's t-test was used to compare two samples when they follow the normal distribution and a Mann-Whitney's U-test was used to compare two samples when they do not follow the normal distribution. Analysis of variance was used to compare three or more samples. Pearson's linear regression was applied for the related numerical variables. $p<0.05$ was considered statistically significant.

Results

Prevalence of MS and its components

This study involved 102 women with PCOS (mean age 30±7 years). Seventy-eight (76.5%) of women were diagnosed with MS. For the various components of MS, 58 (56.9%) patients have hypertension, 25 (24.5%) hyperglycemia, 80 (78.4%) hypertriglyceridemia, 96 (94.1%) have abdominal obesity, and 35 (34.3%) have low levels of HDL-C.

The metabolic characteristics of women with MS compared to those without MS were presented in (Table 2). There was an elevation in blood glucose values (+11.0%, $p<0.001$), TG (+28.6%, $p<0.001$), TC (+11.0%, $p<0.001$) and LDL-C (+33.3%, $p<0.001$), in the MS group compared to women without MS. Moreover, a decrease was noted in HDL-C values (-22.2%, $p<0.001$).

SBP and DBP were elevated ($p<0.001$), in the MS group compared to the group without MS. For the WC an increase was observed (5%, $p<0.05$).

Food behavior

Compared to the group without MS, women with MS have increased total energy intake (TEI) and decreased energy expenditure ($p<0.001$). Total protein intake ($p<0.05$), carbohydrates and fat intake were higher ($p<0.001$) (Table 3). Qualitative analysis of food consumption (Table 3) showed a decrease in animal protein consumption and an increase in vegetable protein ($p<0.001$).

An increase was observed in saturated fatty acids (SFA) intake (+17.9%, $p<0.001$). A reduced intake of monounsaturated fatty acids (MUFA) was noted (-8.1%, $p<0.001$) and polyunsaturated fatty acids (-5.0%, $p<0.01$).

Women with MS have an unbalanced diet; compared with the Mediterranean diet (MD), they had low intakes of MUFA and high intakes of SFA (Table 3).

The consumption of food groups was shown in (Table 4). Women with MS have a high intake of sweet products group by (+28.1%, $p<0.001$), and a decrease in cooked fruits and vegetable intake (-48.1%, $p<0.001$). Cereals group intake was lowered (-34.1%, $p<0.01$), and also dairy products group (-29.2%, $p<0.001$) (Table 4).

In women with MS, we noted an increase in soluble fibers (+14.9%, $p<0.001$), cholesterol (+43.6%, $p<0.001$), and calcium values (+22.1%, $p<0.001$) (Table 5).

Oxidant and antioxidant parameters

In the MS group compared to the group without MS, TBARS concentrations were

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Table 2: Characteristics among women with polycystic ovary syndrome with and without metabolic syndrome (n=102).

Variable	Women without MS (n=27)	Women with MS (n=75)	p-Value
Age (years)	30.8±3.1	30.4±1.7	0.852
Weight (kg)	73.5±5.2	76.3±2.0	0.096
Height (cm)	163.7±4.8	162.9±4.1	0.162
Body mass index (kg/m^2)	27.4±1.7	28.7±0.6	0.182
Waist circumference (cm)	95.2±4.1	100.2±2.0	0.028
Glucose (mmol/l)	4.9±0.5	5.5±0.2	0.015
Triacyglycerols (mmol/l)	1.5±0.1	2.1±0.1	<0.001
Total cholesterol (mmol/l)	4.9±0.3	5.7±0.2	<0.001
HDL-C (mmol/l)	1.8±0.1	1.4±0.1	<0.001
LDL-C (mmol/l)	2.2±0.3	3.3±0.2	<0.001
Systolic blood pressure (mm Hg)	114.0±6.5	128.8±3.1	<0.001
Diastolic blood pressure (mm Hg)	71.8±5.9	82.1±2.4	<0.001

Data are presented as mean±standard error. After analysis of variance, the Student "t"-test was used to compare the means when the values follow the normal distribution and Mann-Whitney's "U"-test when the values do not follow the normal distribution.

increased (+20.2%, p<0.05). Moreover, we noted an elevation in carbonyls concentrations (+25.4%, p<0.05) (Table 6). PCOS women with MS have decreased SOD activity (-20.2%, p<0.001). Thiol values were decreased (-16.8%, p<0.05), No significant difference was noted in Catalase activity.

Correlations analysis

Multiple linear regression analysis showed that the DEE was negatively correlated with triglyceridemia (r= -0.078, p<0.05). TEI was positively correlated with WC (r=0.263; p<0.001) and glycaemia (r=0.272; p<0.001) and LDL-C concentrations (r=0.345, p<0.05).

Discussion

The objective of this study was to assess the prevalence of MS and its components and their relationship with lifestyle and biomarkers in women with PCOS.

We found that MS was prevalent in 73.5% of PCOS women. Literature data reported a prevalence of 22–43% in different populations [7–10]. In this study, the most common individual components were high WC, hypertension and hypertriglyceridemia. It is recognized that each of the MS criteria is associated with an increased risk of developing CVD [22, 24].

PCOS promotes the development of central obesity and insulin resistance, increasing the risk of MS [23, 24]. The higher prevalence of MS is related to unhealthy women's lifestyles.

In our study, women with MS tended to consume more fat and junk food, sugars and refined sugars. Women with PCOS have a greater risk to develop CVD compared to healthy women by worsening metabolic disorders, it is recommended a loss of 5–10% of their body weight in the first year after diagnosis [24]. Reduction in body weight is associated with a decrease in visceral fat leading to decreased insulin resistance and an optimized lipid profile [25]. Adoption of the MD can largely improve symptoms [26–28].

In our study, women with MS had a low intake of MUFA. MUFA are recognized as healthy fats that reduce LDL-C and improve HDL-C levels, which may reduce the risk of CVD. Olive oil is rich in MUFAA is the most common food of MD [27].

Table 3: Energy balance and food intake.

	Women without MS (n=24)	Women with MS (n=78)	p-Value	Mediterranean diet [22]
Daily energy expenditure (MJ)	7.59±0.71	8.57±1.02	<0.001	NA
TEI (MJ)	7.12±0.99	9.22±1.33	<0.001	8
Proportion of TEI (%)	18	16	0.04	10
Animal protein (%)	38	33	<0.001	60
Vegetable protein (%)	62	67	<0.001	40
Total carbohydrates (MJ)	3.13±0.55	4.10±0.62	<0.001	4.4
Proportion of TEI (%)	44	45	<0.001	55
Simple carbohydrates (%)	27	27	<0.001	40
Complex carbohydrates (%)	73	73	<0.001	60
Total lipids (MJ)	2.66±0.39	3.60±0.55	<0.001	2.8
Proportion of TEI (%)	38	39	<0.001	35
Polyunsaturated fatty acids (%)	40	38	0.004	25
Monounsaturated fatty acids (%)	37	34	<0.001	50
Saturated fatty acids (%)	23	28	<0.001	25

NA, not applicable; TEI, total energy intake. Data are presented as mean±standard error. After analysis of variance, the student's "t"-test was used to compare the means when the values follow the normal distribution and Mann-Whitney's "U"-test when the values do not follow the normal distribution.

Table 4: The intake of food groups.

Food groups	Women without MS (n=24)	Women with MS (n=78)	p-Value
Cooked vegetables and fruit (g)	463.5±115.5	240.7±94.0	<0.001
Bread, cereals, rice and pasta (g)	313.7±129.6	207.0±51.8	0.002
Milk and dairy products (g)	173.8±60.9	123.1±15.3	0.001
Meat, poultry and fish (g)	65.1±11.7	74.9±22.8	0.310
Raw vegetables and fruits (g)	99.1±16.9	106.5±26.6	0.225
Fat (g)	67.4±14.1	72.7±19.5	0.513
Sweet products (g)	71.3±16.5	99.1±15.6	<0.001

Data are presented as mean±standard error. After analysis of variance, the student's "t"-test was used to compare the means when the values follow the normal distribution and Mann-Whitney's "U"-test when the values do not follow the normal distribution.

Among the various nutritional strategies, the MD is recognized as a healthy diet for its particular characteristics, including regular consumption of unsaturated fats, low glycemic index carbohydrates, fiber, vitamins, and antioxidants. MD has an anti-oxidant activity through its content in fruits, vegetables, and extra virgin olive oil [27, 29].

Adherence to MD has been shown to be inversely associated with adiposity, insulin resistance, and the risk of diabetes and CVD. It was conceivable that MD could be considered one of the best treatments for women with PCOS [29].

Oxidative stress (OS) is recognized to play a central role in the pathophysiology of many disorders, including PCOS, much research has

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Table 5: Consumption of micronutrients.

Micronutrients	Women without MS (n=24)	Women with MS (n=78)	p-Value[b]
Soluble fibers(g)	14.07±2.28	16.52±2.01	<0.001
Insoluble fibers (g)	4.79±1.03	4.32±1.06	0.139
Cholesterol (mg)	199.46±35.00	353.50±107.35	<0.001
Vitamin A (µg)	3362.56±871.43	2996.28±870.50	0.180
β-carotene (µg)	5717.88±1215.52	5680.56±1112.93	0.759
Vitamin E (mg)	180.23±67.32	182.63±67.77	0.448
Vitamin C (mg)	219.72±58.24	214.34±58.87	0.706
Iron (mg)	26.57±6.28	23.76±6.94	0.235
Calcium (mg)	502.26±88.39	643.96±92.93	<0.001
Selenium (µg)	33.56±6.24	35.99±6.63	0.151
Zinc (mg)	51.24±10.10	45.09±11.43	0.060

Where p-Value represents the results of the statistical analysis and its signification
Data are presented as mean±standard error. After analysis of variance, the student's "t"-test was used to compare the means when the values follow the normal distribution and Mann-Whitney's "U"-test when the values do not follow the normal distribution.

Table 6: Changes in pro and antioxidant parameters in PCOS patients with and without metabolic syndrome.

Micronutrients	Women without MS (n=24)	Women with MS (n=78)	p-Value[b]
TBARS (mmol/l)	21.83±10.78	27.36±10.24	0.033
Carbonyls (mmol/l)	10.73±3.69	14.38±6.16	0.019
SOD (U/ml)	93.44±11.28	74.65±13.98	<0.001
Catalase (KU/l)	3.85±1.59	2.98±1.85	0.104
Thiols (µmol/l)	59.42±19.31	49.45±19.15	0.032

Where p-Value represents the results of the statistical analysis and its signification
Data are presented as mean±standard error. After analysis of variance, the student's "t"-test was used to compare the means when the values follow the normal distribution and Mann-Whitney's "U"-test when the values do not follow the normal distribution.

revealed that circulating oxidative markers are increased in PCOS patients compared to normal and are considered as potential induction of PCOS pathogenesis [30]. Our results showed an increase in OS in women with MS, confirmed by the presence of lipid peroxidation and protein oxidation due to increased levels of TBARS and carbonyls and the decrease in antioxidant defense with decreasing levels of SOD and thiols. This happens when the production of free radicals exceeds the antioxidant capacity of the system. Overproduction of free radicals has been considered a contributing factor in the generation of insulin resistance, diabetes, and CVD [30].

Conclusion

In conclusion, the present study showed that the prevalence of MS and its components was higher in PCOS women. The adoption of a healthy lifestyle based on the principles of the Mediterranean diet, with regular physical activity, seems to be the most appropriate solution to prevent and treat MS in PCOS women.

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