Prevalence and Characteristics of Metabolic Syndrome among Polycystic Ovarian Syndrome Patients in Malaysia

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Abstract

Objective: To determine the prevalence of Metabolic Syndrome (MetS) and its characteristics among Polycystic Ovarian Syndrome (PCOS) patients in the north east of Peninsular Malaysia.

Design: This was a cross sectional study conducted among 99 PCOS patients in Obstetrics and Gynaecology Clinics in two tertiary centers in the east coast of Peninsular Malaysia, from May 2008 to May 2010. Socio-demographic data, waist circumference, weight, height and blood pressure were recorded. A fasting blood sample was obtained for serum glucose and lipid profile determination. Metabolic syndrome was defined in accordance with the International Diabetic Federation (IDF) 2005.

Result: The prevalence of Metabolic Syndrome was 43.4% (N=43). Age and a family history of diabetes were significantly associated with MS. (OR=1.11, 95% CI: 1.10, 1.22) and (OR=3.07, 95% CI: 1.22-7.70) respectively.

Conclusion: The prevalence of MetS among PCOS patients was high. Age and a family history of diabetes strongly predicted MetS amongst PCOS patients.

Keywords: Metabolic Syndrome, Polycystic Ovarian Syndrome, prevalence, characteristics

Introduction

Polycystic Ovarian Syndrome (PCOS) is the most common endocrinopathy, affecting 6% of women within a reproductive age group.¹ The overall prevalence of PCOS among women of reproductive ages in the United States (US) was 4%.² While in Spain, the frequency was 6.5% among general reproductive aged women.³ PCOS patients are at a higher risk of developing infertility, dysfunctional uterine bleeding and endometrial carcinoma, and a number of metabolic disorders including insulin resistance, hyperinsulinaemia, Type 2 Diabetes Mellitus, hypertension, dyslipidaemia and cardiovascular disease.⁴ Due to this, early diagnosis of the syndrome should be emphasized.

Metabolic Syndrome (MetS) which is also called insulin resistance syndrome or syndrome 'X', is also responsible for much of the excess cardiovascular disease morbidity among overweight and obese patients and those persons with Type 2 Diabetes Mellitus.⁵ The overall prevalence of MetS appears to be similar between the USA and European countries with reported rates of 23.5% in Spain and 23.9% in Portugal.⁶ A study in Norway showed the occurrence of MetS among the female population to be 30.3% and 25.0% by IDF and Adult Treatment Panel III (ATP III) respectively⁷ while in Chile, the dominance of MetS among women was about the same.⁸ Another study specifically focused among Diabetic Hispanic patients showed only 8% prevalence of MetS (ATP III criteria) and 11% (WHO criteria).⁹ However, the prevalence of Metabolic Syndrome within the Malaysian community using IDF criteria was slightly lower, 22.9%.¹⁰ Prospective studies have established that MetS is associated with a doubling risk of cardiovascular disease.¹¹ Patients with MetS have three times the risk of developing coronary heart disease and strokes as well as an increased risk of cardiovascular mortality compared to those without MetS.¹² The risk of CHD and type 2 Diabetes Mellitus increased significantly with growing amounts of components of MS.¹³

These two syndromes, Metabolic Syndrome and PCOS are inter-related through a condition named Insulin Resistance. Hyperinsulinemic insulin resistance is an almost universal feature of PCOS and occurs both in obese and lean women with the syndrome. Insulin resistance is thought to be the uniting pathogenic factor in the associations between hypertension, glucose intolerance, obesity, lipid abnormalities and coronary artery disease, which together constitutes metabolic syndrome or syndrome 'X'.¹⁴ A few studies conducted worldwide looking for the prevalence of MetS among PCOS patients were within the range of 14.5%¹⁵ to 46.0%¹⁶. However, the prevalence was reported to be as high as 47.3%.¹⁷

PCOS is a reproductive problem and these patients were treated based on this significant aspect. Thus, it is imperative to determine the occurrence of MetS among this high risk community group so that intensive life styles and risk factor management can be practiced in order to reduce the threat of cardio metabolic and the development of Diabetes Mellitus. The purpose of this study is to establish the prevalence of metabolic syndrome and to define the risk factors (characteristics) associated with it among PCOS patients.

Materials and Methods

This cross sectional study involved 99 PCOS patients, aged 18 years and above, who attended a Gynaecology Clinic at two tertiary centers in the north east of peninsular Malaysia (Hospital Universiti Sains Malaysia and Hospital Raja Perempuan Zainab II) from May 2008 till May 2010. Those with Diabetes Mellitus (DM) type 1, thyroid dysfunction, hepatic and renal disease, chronic corticosteroid usage (3 months), pregnant or lactating women and illiterate patients were excluded. A universal sampling method was used in this study due to limited samples. PCOS in this study was diagnosed using the Rotterdam criteria. The Rotterdam criteria indicated that PCOS can be diagnosed by the presence of any two of the three decisive factors¹⁸:

i. Oligo-ovulation and / or anovulation,

ii. Clinical and / or biochemical signs of hyperandrogenism

iii. Polycystic ovaries

The Metabolic Syndrome in this study was diagnosed using the IDF criteria. IDF definition of MetS¹⁹:

i. Central obesity: (Females waist circumference > 80cm) or BMI > 30kg/m2.

Plus any two of the following four factors:

- **Raised TG level**: > 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality.
- **Reduced HDL cholesterol**: < 50mg/dL (1.29mmol/L*) in females, or specific treatment for this lipid abnormality.
- **Raised blood pressure**: systolic BP > 130 or diastolic BP > 85 mm Hg, or treatment of previously diagnosed hypertension.
- **Raised fasting plasma glucose** (FPG) > 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes.

Data Collection

The lists of names of PCOS patients were taken from the diagnostic list in the Gynaecology clinics and they were invited to participate in the study. Sociodemographic data, smoking status, medical history and family history of chronic diseases were assessed using self-rated questionnaires. Measurements such as waist circumference, weight, height and blood pressure readings were recorded. Waist circumference was measured at a point midway between the lowest ribs and the iliac crest using a soft non-stretchable tape and was taken at the end of a normal expiration. Weight in kilogram was weighted while the clothes on using Seca weighing machine. Blood pressure recording were obtained from the right arm of patients at 5 minutes intervals using a mercury column sphygmomanometer after 30 minutes of rest. All the measurements were made by the same person to reduce any bias. Blood investigations such as fasting blood sugar and fasting lipid profiles were taken. Blood samples were sent to a single lab with ISO accreditation (Universiti Sains Malaysia, (USM)). Patients' records were traced and data with regards to PCOS such as clinical manifestations, blood investigations and ultrasound reports were obtained and recorded.

Statistical analysis

The sample size calculations were done for both objectives of the study and the biggest sample size was chosen. Single proportion formula was used for the prevalence objective and Power and Sample Size Calculation software (Dupont and Plummer, 1997) was used for the associated factors objective. Using the power of 80%, the calculated sample size was 104 including 20% dropout rate.

Data entry and statistical analyses were performed using the SPSS version 18. Means and standard deviations for numerical variables and frequency and proportion for categorical variables were reported. Simple logistic regression was used in univariate analysis as a screening in the selection of variables for further analysis. All variables with p value less than 0.25 were selected to be in multiple logistic regressions analysis. A Multiple logistic regression was chosen as the dependent variable of the binary outcome. The level of significance was set at 5% and results were presented with 95% confidence intervals. The independent variables were a mix of numerical and categorical variables. The dependent variable was metabolic syndrome.

The method that was used for variable selection was backward and forward stepwise procedure. Interaction between pairs of variables from all variables in the main effect model was checked. Findings in the final model were presented with an adjusted odds ratio (OR), its 95% confidence interval (CI) and corresponding p value.

Approval by the research and ethics committee

The protocol was approved by the Research and Ethical Committee, School of Medical Sciences, Universiti Sains Malaysia (ref: USMKK/PPP/JEPeM [199.4(2.5)]) and by the National Medical Research and Ethical Committee, Ministry of Health Malaysia (ref:KKM/NIHSEC/08/0804/P09). This study was funded by the short term grant from Universiti Sains Malaysia (USM) (304/PPSP/6131605).

Results

A total of 99 patients were recruited and analyzed. The occurrence of MetS in this study was 43 (43.4%) (according to IDF criteria).

Table 1 reveals the socio-demographic characteristics of PCOS patients with and without metabolic syndrome. All participants were Malays, who had never consumed alcohol and never smoked before. The youngest of the participants was 18 years old and the eldest was 41 years old with mean age of 29.6 year old \pm 4.9.

Table 2 illustrates the clinical manifestation of PCOS among the participants. The most common presentation of PCOS features were menstrual problems. Ultrasonography investigations were carried out in only 89 of the PCOS patients studied.

Table 3 demonstrates the clinical and biochemical characteristics of PCOS patients with and without MetS. For all PCOS patients, the mean value for the clinical and biochemical characteristics was waist circumference (88.7), BMI (32.1), fasting blood glucose (5.7), triglyceride (1.9), systolic blood pressure (127.6), diastolic blood pressure (83.5) and HDL cholesterol (1.3).

Simple logistic regression analysis showed that family history of diabetes mellitus (p=0.01, OR= 0.37, 95%CI: 0.16-0.85), weight (p=0.002, OR= 1.05, 95%CI: 1.02-1.08), and body mass index (p=0.001, OR= 1.16, 95%CI: 1.06-1.27) are the significant associated factors for Metabolic Syndrome.

Table 4 showed the results of multiple logistic regression analysis of potential associated factors for metabolic syndrome among PCOS patients. The result showed that the associated factors for metabolic syndrome were age (OR=1.11, 95% CI: 1.10, 1.22) and a family history of diabetes (OR=3.07, 95% CI: 1.22-7.70).

Discussion

The prevalence of MetS among PCOS patients was higher compared with other Asian studies. In comparison, studies performed in Thailand by Weerakiat et al. in 2007, and Pantasri et al. in 2010, revealed that the prevalence was 35.3% and 24.3% respectively.^{20,21} The possible explanation for this is that the mean BMI in our study was higher compared to the studies in Thailand. Similar findings were observed in a study conducted in Puerto Rico in which MetS was identified in 44% of PCOS patients. Their mean BMI²² was 36 kg/m² which was higher than that demonstrated in our study. This further reflected that the prevalence of MetS was higher in patients with increased BMI.

A few studies looked at the trend of PCOS clinical manifestation, showed quite similar pattern of presentation compared to this study. This finding is expected since those clinical features are the prominent features that characterized the syndrome itself. Oligomenorrhoea was the commonest symptoms, followed by acne and hirsutism.^{2,3,23} Based on the clinical and biochemical profile, most of the PCOS in the current study were overweight or obese, and those with MetS had greater mean for BMI. The same trend was observed in the other parameters such as blood pressure and waist circumference. PCOS patients with MS have pre-hypertension range of blood pressure which put them at more risk of developing the CHD and cerebrovascular disease. Apridonidze et al. in 2005 found that PCOS women with MetS had significantly higher mean BMI, systolic blood pressure, diastolic blood pressure, fasting plasma glucose and TG level but also significantly lower HDL level.¹⁴

The mean weight of PCOS patients with MetS in our study was 82.7kg \pm 11.9 SD. Obesity has been implicated in the pathophysiology of MetS due to its association with hypertension, hyperglycemia and dyslipidemia. Dokras et al. highlighted the factors which determine the increased risk for MetS in PCOS patients. He stated that obesity could increase the probability that PCOS patients would exhibit MetS.¹⁷ A more recent study revealed that prevalence of MS among PCOS increased from 0% in women with BMI <23kg/m² to 54.5% in those with BMI \geq 30kg/m².²⁴

In our study, age was a significant associated factor of MetS which was similar to other studies. We erakiat et al. found that the prevalence of MetS among PCOS patients increased gradually from 22.5% at age <25 years to 53.5% at age >30 years.²⁰ Another study done at the Virginia Commonwealth University Health System also revealed that the prevalence of the MetS increased with age, from 23% in less than 20 year olds to 45% in women aged between 20-29 years, and then to 53% in women aged 30-39 years old. They concluded that age was a significant risk factor affecting the occurrence rate of MetS amid PCOS patients.¹⁴

Age plays a significant role in the prevalence of MetS not only among the PCOS group, but is also illustrated amongst the general population. This is shown from a study which focused on the general population and revealed that based on age, subjects aged 60 years and above exhibited the highest prevalence of MetS (50%) compared to other age groups. Dokras et al. did a comparative study on PCOS and non-PCOS women which revealed a higher frequency of MetS as age increased in both groups.¹⁷ Thus, there was a steady increase in the prevalence of MetS with advancement of age.¹⁰ Another study done in Turkish adults showed that the prevalence of MetS increased with older women, from 9.6% in subjects aged 20-29 years to 74.6% in those aged between 60-69 years old.²⁵ Another study which focused on menopausal women also showed high prevalence of MetS (36.7%). This study showed that previous obstetrics history of HPT, family history of HPT and obesity are associated with increased risk of MetS in this population.²⁶ It would be interesting to see whether the same factors play a major role in the development of MetS in postmenopausal PCOS women. This will remain a question until further study is conducted.

As we age, we either gain weight or find it more difficult to control our weight. In most cases, combination of lesser activity, higher calorie intake and loss of lean muscle are probably making aging women and men gain weight with age. Physiological changes occur with aging leading to increased weight gain; in women, the decline of the estrogen levels and the metabolic rate contributed to weight gain. As we age, the amount and distribution of fat, lean tissues, bone and other structures will change. Fat tissue may increase towards the center of the body, including around the abdominal organ, which will give rise to central obesity. Waist circumference or waist to hip ratio is one of the parameters used in the diagnosis of MetS, thus indirectly it will increase the occurrence of MetS as aging occurs. Abdominal obesity is proven to be an important independent risk factor for diabetes type 2.²⁷

It is a well known fact that within the general population, family history of Diabetes Mellitus is a risk factor for developing Diabetes Mellitus, which is part of a Metabolic Syndrome. From a study conducted in Hong Kong, it is shown that a family history of diabetes mellitus was an independent risk factor for MetS with odds ratio of 4.3(95% CI 1.3-14.1).²⁸

In PCOS women, a family history of diabetes mellitus is also a risk factor for the occurrence of glucose intolerance and diabetes mellitus, thus they are at more risk of developing metabolic syndrome. Ehrmann et al. did a study which looked at the percentage of the glucose tolerance status of PCOS in relation to a family history of diabetes. It showed that a family history of diabetes was present in 44% of PCOS women with diabetes, 39% of PCOS women suffering from Impaired Glucose Tolerance and 21% of PCOS women with normal glucose tolerance. From this, they concluded that PCOS women who had a family history of diabetes were at risk of glucose intolerance compared to those without such a family history.²⁹ The results of our study are in parallel with and support these previous studies.

Conclusion

The prevalence of MetS among PCOS patients (43.4%) was high, thus it can be concluded that PCOS patients belong to the high risk group of developing CHD and CVA. It creates an important issue when dealing with PCOS patients. Focusing out of obstetric and gynecology aspect like routine screening of CVD risk in all PCOS patients should become compulsory in our daily practice. More focus should be emphasized on those PCOS with increasing age and who has family history of DM because they are at more risk to develop MS.

Even though the prevalence of PCOS patients among the general population is quite low, this group of patient is at risk of cardiovascular disease. Focusing this group of patient indirectly will improve the health of women in general. The main focus of the majority of PCOS women who seek treatment at hospital is their reproductive problem ranging from the menstrual to the infertility problem. They might not aware of the risk they carry together with the PCOS diagnosis. Detecting those with metabolic syndrome is very important, so that further treatment and management can be instituted early for them. They need a good follow-up as they are at risk of developing complications.

It was noted from a study that the prevalence of MS among young PCOS was 24%, which was high.¹⁷ As a primary care physician, aggressive screening should be done early and regularly even in those aged less than 30 years old. Before diagnosed to have PCOS, these patients usually present at primary care level for their problems. Those who are as a first liner should be able to detect those at risk of PCOS so that primary prevention could be offered. This includes health education regarding the risk of cardiovascular disease, healthy life style modification and cardiovascular screening. The importance of weight reduction should be emphasized as it carries a significant risk factor for metabolic syndrome.

Similar study focusing on the prevalence of metabolic syndrome among other group at risk of cardiovascular or cerebrovascular disease is very limited. In Malaysia we are lacking of data to compare and review; and due to this, the best option of treatment is not offered to patients as part of their holistic management. Thus, this study recommends further research to be conducted in the area of metabolic syndrome. There might be many more associated factors related to metabolic syndrome that are still not revealed. The current risk factors known could be reflected as a tip of iceberg, there are still more underneath for us to discover.

Limitation

In our study, MetS diagnosis was based on IDF criteria which required the waist circumference as a compulsory feature, which would exclude those PCOS patients with diabetes and hypertension who had normal waist circumference.

This study was done only at two main tertiary centres in north east of Peninsular Malaysia. This may not represent the whole PCOS patients in Malaysia.

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Variable	Non MS n (%)	MS n (%)	
Age	28.82(4.9) ^a	$30.67(4.9)^{a}$	
< 20	3(5.2)	1(2.4)	
21 – 25	10(17.2)	8(19.5)	
26 - 30	26(44.8)	11(26.8)	
31 – 35	11(19.0)	16(39.0)	
36 - 40	5(8.6)	6(14.6)	
> 41	1(1.7)	1(2.4)	
Education level			
Never attended school/	2 (3.6)	3 (7.0)	
Secondary school	27 (48.2)	25 (58.1)	
Tertiary school	27 (48.2)	15 (34.9)	
No income	5 (10.4) 17 (25.4)	1(2.6)	
<u>> 1000</u> 1000-3000	23 (47.9)	18 (47.4)	
\geq 3000	3 (6.3)	3 (7.9)	
Marital status			
Single	13 (23.2)	7 (16.3)	
Married	43 (76.8)	36 (83.7)	

Table 1: Socio-demographic characteristics among PCOS with and without metabolic syndrome patients

Variables	Total n(%)
Oligomenorrhoea	94 (94.9)
Infertility	82 (82.8)
Hirsutism	60 (60.6)
Acne	41 (41.4)
Obesity	87 (87.8)
Hyperpigmentation	11 (11.1)
Ultrasonography (PCO feature)	34 (34.3)

 Table 2: The clinical manifestation of PCOS among study subjects (n=99)

Table 3: The clinical and biochemical characteristics of PCOS patients with and without MS

Variable	Non MS Mean (SD)	MS Mean (SD)	
Waist circumference (cm)	83.3 (12.1)	94.7 (9.2)	
BMI (kg/m ²)	30.4 (5.7)	34.3 (4.3)	
Systolic blood pressure (mmHg)	121.0 (11.4)	136.1 (12.4)	
Diastolic blood pressure (mmHg)	80.3 (10.7)	87.7 (9.0)	
Fasting blood glucose (mmol/L)	5.6 (2.7)	5.9 (2.2)	
Triglyceride (mmol/L)	1.7 (1.3)	2.3 (1.2)	
HDL Cholesterol (mmol/L)	1.4 (0.3)	1.2 (0.3)	

Table 4: The associated factors for metabolic syndrome by multiple logistic
regression

Variable	OR ^a	95% CI°	Wald statistic	df	<i>p</i> value
Age	1.11	1.01-1.23	4.69	1	0.030
Family history of DM	3.07	1.22-7.70	5.70	1	0.017
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^a OR = Odds Ratio

° CI = Confidence Interval