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A STUDY ON PREVALENCE AND PREDICTORS OF RISK FOR METABOLIC SYNDROME IN INDIAN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Objectives were to compare the prevalence of metabolic syndrome (MS) in Indian women with polycystic ovary syndrome (PCOS) using 'International Diabetes Federation (IDF) criteria' and the 'Joint Interim Criteria 2009', and also to assess the metabolic risk factors for associated with this syndrome. This cross sectional study was done on 196 women with PCOS (68 adolescents and 128 adults). Clinical and biochemical tests in each case were done as per recommendations. MS was diagnosed as per the IDF and the Joint Interim 2009 criteria.MS was found in 47.4% (as per IDF criteria) and 59.5% (as per Joint Interim criteria) cases (p= 0.01). Adolescents and adults were equally affected, irrespective of the definition used (p= 0.01 by IDF and p= 0.04 by Joint interim criteria). Prevalence of MS in adolescents utilizing the two definitions, was not significantly different (p= 0.06). Same is also true for adults (p= 0.04). Women with MS, both adolescents and adults, had higher BMI (body mass index) irrespective of the definition used (p= 0.00001). In adults, age of those with MS was significantly higher than those without MS (p= 0.001). Dyslipidemia was more common than elevated fasting blood sugar, using either of the definitions (p= 0.00001). There was no difference in the incidences of elevated blood pressure (systolic and or diastolic) using the two definitions.It remains to be seen by further studies the benefits of identifying more cases of MS in PCOS using the Joint Interim Criteria.

KEY WORDS: **adolescent, joint interim criteria 2009, metabolic syndrome, polycystic ovary syndrome.**

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INTRODUCTION

Metabolic Syndrome (MS) is a group of multiple interrelated risk factors for cardiovascular diseases and type 2 diabetes mellitus, occurring 'more often than by chance alone' [1] due to underlying insulin resistance (IR). Because of the increased risk for morbidity and mortality associated with it, metabolic syndrome has generated much interest among clinicians and research workers. Women with polycystic ovary syndrome (PCOS) are at increased risk of dyslipidaemia[2], diabetes mellitus (DM) / impaired glucose tolerance [3] due to the underlying IR. So these women are at risk of having MS as well.Before evolution of 'joint interim statement', MS in PCOS were defined by various organizations like Adult Treatment Panel-III (ATP-III) [applicable only for adult PCOS cases][4] ,World Health Organization[5], the International Diabetes Federation (IDF)[6].Both WHO and IDF emphasizes on insulin resistance as a clinical risk paradigm. To address the dilemma of clinicians and researchers by various definitions, and to facilitate cross-country comparisons, a new 'joint interim statement' on unanimously agreed specific criteria for the clinical diagnosis of MS, has been issued in 2009. The participating professional organizations were IDF, National Heart, Lung, Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity.[1]In the IDF criteria[6], to diagnose MS waist circumference (WC) should be above 80 cm (cut off value for South Asian woman) with any two of the four additional criteria's mentioned here:(i)Triglyceride (TG) =/>150mg/dl (1.7mmol/litre), (ii) High-density lipoprotein- cholesterol (HDL-C) <50mg/dl (1.3mmol/litre), (iii) systolic blood pressure (SBP)>130mmHg and/or diastolic blood pressure (DBP)>85mmHg, (iv) Fasting plasma glucose (FPG) =/>100mg/dl (5.6mmol/litre).According to the Joint Interim criteria 2009[1], any three or more of the following criteria should be fulfilled:

1. Abdominal obesity: waist circumference >80 cm (cut off value for South Asian women)
2. TG =/> 150 mg/dl (1.7 mmol/l)
3. HDL-C < 50 mg/dl (1.3 mmol/l)
4. Blood Pressure (BP): SBP =/> 130 and or DBP=/>85 mm of Hg
5. FPG = / > 100 mg/dl (5.6mmol/l)

The aim of this study was to find out whether the prevalence rate of MS in women with PCOS differs depending on the criteria used (Joint Interim Criteria 2009 and IDF). The further aim was to assess the importance of dyslipidaemia and fasting glucose abnormalities as risk factors in women with MS.

MATERIALS AND METHODS

A prospective cross sectional study was planned on women with PCOS who were being evaluated in the gynecology clinic of KPC Medical College, a tertiary care hospital from March 2014 to February 2016. Permission was obtained from the ethics committee of the hospital. All women agreed to the investigation protocol. For adolescent girls, one of the parents gave consent to the study. A total of 196 women with PCOS participated, out of whom 68 were adolescents and 128 were adults. These women had detailed clinical and hormonal evaluations for the diagnosis of PCOS according to the Rotterdam 2003 criteria[7] with at least two of the following features: (i) oligo-ovulation or chronic anovulation, (ii) clinical and/or biochemical hyperandrogenism, and (iii) ultrasound appearance of polycystic ovaries. Secondary causes of hyperandrogenism were excluded by appropriate clinical and laboratory tests. Women with history of steroid or oral contraceptive drug intake in the preceding 3 months, and those with previously diagnosed diabetes, were excluded from the study. Oligo-ovulation and / or anovulation was characterized by oligomenorrhoea (intermenstrual intervals of ≥35 days) and amenorrhea (intervals >3 months). Clinical hyperandrogenism was defined as the presence of hirsutism (modified Ferriman-Gallwey score of ≥8) and/or acne. Biochemical hyperandrogenism was present if calculated free testosterone level was more than 2.4%.[8.] Free testosterone level was calculated from estimated total testosterone and sex-hormone-binding-globulin (SHBG) level, assuming the serum albumin level is within physiological limit. Polycystic ovary on ultrasound (Transabdominal) was defined as the presence of at least one ovary 10 cm^3 or more in volume and/or at least one ovary with 12 or more follicles measuring 2-9 mm in diameter. In India, transvaginal USG is not performed on unmarried girls because of social reasons.

Exclusion criteria

1) Women more than 40 years of age with irregular periods
2) Girls with gynecological age less than three years
3) Women who had used oral pills in the preceding three months.
4) Women already diagnosed with diabetes mellitus.
5) Secondary causes of hyperandrogenism.
6) Hypothyroidism, hyperprolactinemia.

Process of evaluation

A standard questionnaire was used to document length of menstrual cycles; personal, medical, and family history of diabetes; hypertension; obesity; and ischemic heart disease. Signs of androgen excess (hirsutism, acne, and alopecia) and insulin resistance (acanthosis) were noted in the physical examination. Anthropometric measurements included waist circumference in centimeters, measured at the narrowest circumference midway between the upper border of iliac crest and the

lower rib margin, and the hip circumference was taken as the widest measurement at the level of the greater trochanters (using a 1cm wide measuring tape). Body mass index (BMI) (kg/m^2) was calculated in each case from height and weight measurements. Height was recorded to the nearest 0.5cm using standard scale. Weight (kg) was taken on a platform type (bathroom scale) machine, the accuracy of which was checked each time before weighing.

Laboratory investigations

Fasting plasma glucose (FPG), plasma high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG) levels were estimated after 12- hour overnight fasting for all patients. Plasma glucose was measured by Glucose oxidase peroxidase method (Roche Diagnostics Gmbh, Mannheim, Germany**.** Impaired glucose tolerance and diabetes was defined in accordance with American Diabetes Association revised definition[9]. HDL-C was measured by direct enzymatic method using surfactant (Roche diagnostics Gmbh, Mannheim, Germany.TG was measured by enzymatic colorimetric method using Glycerol phosphate dehydrogenase. Serum testosterone was measured by electrochemiluminescence Immunoassay. Trans-abdominal ultrasound was performed to study the morphology of ovaries. Ovarian volume measurements were carried out by measuring three perpendicular dimensions (volume for a prolate ellipsoid = 0.5 × length × width × thickness). Follicle numbers were estimated both in longitudinal and antero-posterior cross-sections of the ovaries. Follicles with a mean diameter of 2-9 mm were counted for defining polycystic ovary morphology. Secondary causes of hyperandrogenism like 21-hydroxylase deficiency, Cushing's syndrome, hypothyroidism, hyperprolactinemia, and androgen-secreting tumors were excluded by appropriate clinical and/or laboratory tests. In statistical analysis continuous variables were summarized as mean with standard deviation and analyzed using sample t-test. Categorical variables were expressed as proportions and analyzed by Chi-square test. Univariate analysis was applied to quantify the association between clinical and laboratory variables and the presence of metabolic syndrome.

RESULTS

Out of the 196 women recruited in this study, we found significant difference in prevalence rate of MS as per both the criteria, prevalence rate of metabolic syndrome was 47.4% as per IDF criteria, whereas the prevalence rate as per the Joint Interim criteria 2009 was significantly higher 59.5% (p=0.01)[Table-1]. No significant difference could be found in the prevalence of MS comparing in adult and adolescent population using either of the definitions [Table-2].Mean age is higher in adult PCOS cases diagnosed to have MS [Table-3]. Women diagnosed with MS had higher BMI. There is no significant difference in the mean BMI of patients with MS when compared in adolescents and adults separately using IDF and Joint Interim criteria 2009[Table-3]. The metabolic parameter and blood pressure was compared among the cases diagnosed by the IDF criteria and Joint Interim criteria 2009 and is depicted on table 4.Dyslipidaemia is significantly found in our subjects [98.5% of the cases in IDF criteria and 98.3% in Joint Interim criteria (p=0.0001)]. Elevated fasting plasma glucose level was found in 36.3% (IDF criteria) and 46.4% (Joint Interim criteria) (p=0.00001). It clearly shows dyslipidaemia is far more common than elevated FPG. Elevated BP was found in 50.1% and 52.4% cases respectively (p=0.3).

Table 1
Number of cases diagnosed to have MS

Criteria	Number of cases with MS	%
IDF	94	47.4% *
Joint interim criteria 2009	118	59.5% *

Total number of PCOS cases- 196. *p= 0.0

Table 2
MS in adolescents and adults according to the criteria used [data- number (%)]

Criteria	Adolescents (n=68 cases)	Adults (n=128 cases)
IDF	**30 (47.5)[a]**	**50 (39.1)[a]**
Joint interim criteria	**38 (56.5)[b]**	**78 (60.9)[b]**

[a] p= 0.04, [b] p= 0.01

Table 3
Clinical parameters– data are mean (SD)
Age and BMI

Age	Adolescents		Adults	
Criteria	**With MS Without MS**	**Without MS**	**With MS**	**Without MS**
IDF	**16.8 (1.7)**	**17.2 (1.8)**	**25.7 (2.6)[a]**	**24.1 (3.0)[a]**
Joint interim criteria	**16.9 (1.5)**	**17.3 (1.5)**	**26.3 (3.5)[b]**	**24.8 (3.8)[b]**

[a] p= 0.001 [b] p= 0.02

BMI	Adolescents		Adults	
Criteria	With MS	Without MS	With MS	Without MS
IDF	29.1 (4.0)[c]	23.8 (3.2)[c]	29.5 (4.0)[d]	25.7 (4.2)[d]
Joint interim criteria	28.3 (4.2)[e]	23.4 (3.5)[e]	29.6 (3.8)[f]	27.8 (4.8)[f]

[c, d , e, f] *p= 0.00001*

Table 4
Metabolic parameters and elevated blood pressure

Parameter	IDF criteria (number of cases (%)	Joint interim criteria (number of cases (%)	p value
Dyslipidaemia[a]	68 (98.6)	116 (98.3)	0.3
Elevated fasting plasma glucose[a]	25 (36.2)	55 (46.6)	0.06
Elevated BP	47 (50.1)	62 (52.5)	0.3

[a] *p= 0.00001*

DISCUSSION

Metabolic syndrome is characterized by a group of abnormalities including visceral obesity, hypertension, dyslipidaemia and impaired fasting glucose. It is now recognized that insulin resistance plays a very important role in initiating and perpetuating the pathologic manifestations of MS. The same pathogenic mechanism also occurs in women with PCOS. It is therefore quite obvious that women with PCOS can also have features of MS.In this study the diagnostic criteria proposed by International Diabetic Federation (IDF) and Joint Interim statement were taken into account and the prevalence of the metabolic syndrome among the women with PCOS was compared using the two criteria. From this study, a higher prevalence rate of MS was obtained among the women with PCOS using Joint Interim criteria (59.5%) than using IDF criteria (47.4%)(p=0.01). A similar result was shown by another comparative study in Luxemburg in 2011[10]. According to the mean BMI, results derived from IDF criteria and Joint Interim criteria shows the majority of cases of MS falls under overweight populations. This trend was found in both adult an adolescent population. Snehalatha et al[11] reported that the BMI of normal Indian urban women should be less than 23. In this study the BMI in population with MS is significantly higher than this cut-off level whereas the BMI value of population without MS is close to the referred value. (p=0.00001) We studied two biochemical parameters, dyslipidaemia and fasting blood glucose. Dyslipidemia was found to be far more common than elevated fasting glucose (both as per IDF criteria and Joint Interim criteria). More presence of abnormality of lipid profile over elevated fasting blood glucose emphasizes the importance of screening of lipid profile rather than FPG alone.Women with PCOS often present with cosmetic and/or reproductive symptoms. Attention is generally not paid to assess the future risk of atherosclerosis in these patients. The current study not only shows a very high prevalence of MS in Indian women with PCOS (59.5%), it also clearly outlines the need for evaluation of lipid profile as well. Phenotypic manifestations of PCOS cases are likely to have increased prevalence of atherosclerotic heart disease in this region of the world. The 'joint interim statement' is a new entrant, and its usefulness in clinical practice may only be assessed by worldwide research. Notwithstanding the debate about the usefulness of MS as a marker of future cardiovascular disease, our analysis intends to help facilitate international comparisons in view of the scarce scientific data available on the prevalence of MS among urban Indian women with PCOS. The present study clearly highlights the need for comprehensive screening because of high prevalence of MS. This report will help compare results of different studies across the world.

SUMMARY AND CONCLUSION

Metabolic syndrome is not a disease but simply a clustering of risk factors. Prevalence of MS in PCOS depends on the definition used. Adolescent and adult PCOS patients are equally affected. Dyslipidaemia is more common than elevated fasting glucose level. It remains to be seen by further studies the benefits of identified more cases of MS in PCOS using Joint interim criteria 2009. The intention of identifying the MS was to draw the clinician's and public's attention to the importance of a high quality life style.

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CONFLICT OF INTEREST

Conflict of interest declared none.

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