Metabolic Syndrome and Hyperandrogenemia in Polysystic Ovarian Syndrome

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Abstract

Objective: To ascertain the frequency of hyperandrogenemia in cases of polycystic ovarian syndrome and to correlate the frequency of metabolic syndrome in polycystic ovarian syndrome patients with and without hyperandrogenemia.

Method: This cross sectional study was conducted from 19.12.2020 to 18.06.2021 in Department of Obstetrics & gynecology, Unit-II, Aziz Bhatti Shaheed Teaching Hospital, Gujrat. Data was collected from a consecutive sample of 367 women diagnosed of polycystic ovarian syndrome(PCOS). All the female patients aged between 18-35 years diagnosed of PCOS included in the study except pregnant or lactating females.

Results: The mean age was calculated as 26.35 (± 5.28) years. Presence of hyperandrogenemia was found in 59.9% patients. In 220 hyperandrogenemic patients, the metabolic syndrome was present in 20% while metabolic syndrome was present in 10.20% patients without hyperandrogenemia. Significant higher occurrence of metabolic syndrome was found in hyperandrogenemia group as compared to without hyperandrogenemia group (20% VS 10.2%) having p-value = 0.014. Stratified age have significant relationship for the presence of hyperandrogenemia with p-value=0.000. Body mass index and duration of illness didn't show significant relationship having p-value > 0.05. Duration of illness was positively associated with presence of metabolic syndrome having p-value = 0.014.

Conclusion: Significant higher occurrence of metabolic syndrome was found in hyperandrogenemia group as compared to those without hyperandrogenemia in PCOS patients.

Keywords: Hyperandrogenism, Polycystic Ovarian Syndrome, Metabolic Derangement.

How to cite: *Hummayun H, Naz T, Waheed SS.* Metabolic Syndrome and Hyperandrogenemia in Polysystic Ovarian Syndrome. *Esculapio - JSIMS 2022;18(02):169-173*

DOI:*https://doi.org/10.51273/esc22.2518213*

Introduction

One of the most common female endocrinopathy is Polycystic ovarian syndrome (PCOS) affecting 8-12% of women in their reproductive age.[1] It is clinically characterized by irregular menstrual cycles, hyperandrogenemia, infertility, or sub-fertility, frequently with a characteristic ovarian morphology on ultrasound examination.[2] The pathogenesis of PCOS generally contains multiple pathways, ranging from insulin resistance, obesity, androgen hormone production and other environmental and lifestyle factors.[3]

Metabolic syndrome occurs in half of PCOS adults and one-third of PCOS adolescents,[4] and another study found it in 22.7% PCOS patients. An irregular gradation of insulin resistance is observed in about two-third PCOS cases; incidence of obesity is same, with reasonable variability amongst different populations.[5] In obese cases with PCOS, observations recommend that, metabolic aberrations associated to insulin resistance and obesity is in many cases, more vital in the mechanism of anovulation in PCOS than androgen excess.[3,4]

The most often investigated genes which play important role in pathogenesis of PCOS and related metabolic complications are CYP11, CYP17, SRD5A (steroid 5

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Submission Date: 24/03/2022
1st Revision Date: 06/04/2022
Acceptance Date: 02/06/2022

alpha reductase). They all cause increased production of testosterone and are also associated with insulin resistance. However, insulin resistance, HA and metabolic dysfunctions present from mild to severe degree in all patients depending on which gene is affected and thus insulin resistance and metabolic syndrome might be associated with hyperandrogenemia.[6,7]

Sung et al. (2014) reported that 60.7% of the PCOS patients had hyperandrogenemia and the frequency of metabolic syndrome was significantly higher among females with hyperandrogenemic PCOS (15.1% vs. 2.7%; $p<0.05$) as compared to women with non-hyperandrogenemic PCOS. In another study, Kim et al. (2014) reported the frequency of hyperandrogenemia to be 61.7% and also reported significantly higher frequency of metabolic syndrome in women with PCOS with hyperandrogenemia (19.7% vs. 11.9%; $p=0.008$) as compared to PCOS without hyperandrogenemia.[8-10]

However, Lerchbaum et al. (2014) in a similar study reported only insignificantly higher frequency of metabolic syndrome in PCOS women with hyperandrogenemia (9.4% vs. 4.3%; $p>0.05$) negating any such association. Yadav et al. (2014) also observed insignificant difference ($p>0.05$) in different metabolic derangements between Indian women with and without hyperandrogenemia.[10,11] There is a conflict of evidence (15.1% vs. 2.7%; $p<0.05$ 18, 19.7% vs. 11.9%; $p=0.008$ 19; 9.4% vs. 4.3%; $p>0.0520$) showing that hyperandrogenemic patient may have significantly higher frequency of metabolic syndrome. This conflict may be due to the variability of sample size, due to difference in the geno type (Korea vs. Germany vs India) or due to the difference in the geographical location of studies. Keeping in mind this conflict and the various factors that can lead to the different results and the higher mortality and morbidity associated with metabolic syndrome, there is a need to conduct such study in local population to correlate the occurrence of metabolic syndrome in respondents with and without hyperandrogenemia. The appropriate screening, timely identification and management can help in reducing the mortality and morbidity associated with metabolic syndrome.[12]

Material and Methods

This cross sectional study was conducted from 19.12. 2020 to 18.06.2021 in Department of Obstetrics & gynecology, Unit-II, Aziz Bhatti Shaheed Teaching Hospital, Gujrat. 367 women diagnosed with polycystic ovarian syndrome as consecutive sample, during the last 6 months presenting to outdoor of Obstetrics and Gynaecology were included. Ethical approval for study was taken from institutional review board (IRBA). After explaining the study, written informed permission was attained from all the patients. History and complete physical examination of these patients were taken to fill the questionnaire. Patients were requested to come with 12 hour fasting in the morning when under aseptic conditions venous blood samples were obtained. Serum total testosterone, free testosterone, glucose, high density lipoprotein, cholesterol and triglycerides were measured at the same day.

Presence of hyperandrogenemia was labelled when either total testosterone level ≥ 67 ng/dL or free testosterone ≥ 0.84 ng/dL. Metabolic syndrome was diagnosed when at least three of mentioned five metabolic abnormalities are present including, central obesity (waist circumference ≥ 80 cm), HDL (cholesterol ≤ 50 mg/dL), dyslipidemia (triglycerides ≥ 150 mg/dl), hypertension (BP $\geq 130/85$ mmHg), and hyperglycemia (fasting plasma glucose ≥ 100 mg/dl). Patient's demographic details along with presence/ absence of hyperandrogenemia and metabolic syndrome was observed and documented. To reduce bias, all the necessary investigations were attained from the same (hospital) lab. Confounding variables were excluded.

Women having Hyperprolactinemia (serum prolactin level ≥ 25.0 ng/ml), Hyperthyroidism (free T4≥ 1.8ng/dl) or hypothyroidism (free T4 ≤ 0.8ng/dl), Cushing's syndrome (24-hour urinary free cortisol $\geq 50\mu g/d$), Ovarian failure (follicle-stimulating hormone ≤ 0.3mIU/ml), Ischemic Heart Disease (as per history and clinical record of the patient) and pregnant (gestational amenorrhea, dating scan) or Lactating women (as per history from the mother) were excluded from the study.

All data was analysed through SPSS version 21. For quantitative variables like age, BMI and duration of illness mean and standard deviation was calculated. For qualitative variables like parity and presence of hyperandrogenemia and metabolic syndrome, frequency and percentages were calculated. Metabolic syndrome occurrence was correlated between patients with and without hyperandrogenemia by applying chi square test and considering $p \leq 0.05$ as statistically significant. Variables like age, BMI, parity and duration of illness were stratified to address effect modifiers. Post-stratifications chi-square test and independent sample t-test was used taking $p \leq 0.05$ as statistically significant.

Results

From 367 patients, it was observed that the mean age was 26.35 (± 5.28) years. The mean of body mass index was 26.12 (± 2.19) kg/m^2. The mean of duration of illness was 12.25 (± 4.06) months. There were 206 (56.1%) nulliparous patients and 161 (43.9%) multiparous patients. Presence of hyperandrogenemia was found in 220 (59.9%) patients while it was absent in 147 (40.1%) patients. The metabolic syndrome was present in 44 patients (20%) with hyperandrogenemia while metabolic syndrome was present in 15 (10.20%) patients without hyperandrogenemia. Presence of metabolic syndrome was significantly higher with hyperandrogenemia group as compared to without hyperandrogenemia group (20% vs 10.20%) having p-value = 0.014. By using independent sample t-test it was found that stratified age have significant relationship for the presence of hyperandrogenemia with p-value=0.000. Body mass index and duration of illness didn't show significant relationship having p-value > 0.05.

Table 1: *Presence of Hyperandrogenemia in Relation to Age, BMI and Duration of Illness.*

Variable	Mean±SD*	Presence of Metabolic Hyper-androgenemia		P-value
		Yes	No	
Age	26.35 ± 5.28	28.83±4.36	22.64±4.27	0.000**
BMI***	26.12 ± 2.19	26.07±2.23	26.20±2.16	0.560
Duration of Illness	12.25 ± 4.06	12.00±4.03	12.61±4.08	0.160

Standard Deviation, ** P-value < 0.05. * Body Mass Index*

Table 2: *Presence of Metabolic Syndrome in Relation to Age, BMI**, Duration of Illness and Hyperandrogenemia..*

Variable	Category	Presence of Metabolic Syndrome		P-value
		Yes N (%)	No N (%)	
Age	⩽25 years	7 (4.4)	153 (95.6)	0.000*
	> 25 years	52 (25.1)	155 (74.9)	
BMI**	⩽25	22 (15)	125 (85)	0.666
	> 25	37 (16.8)	183 (83.2)	
Duration of Illness	⩽1 year	38 (23.5)	124 (76.5)	0.001*
	> 1 year	21 (10.2)	184 (89.8)	
Presence of hyper-androgenemia	Yes	44 (20)	176 (80)	0.014*
	No	15 (10.2)	132 (89.8)	

** P-value < 0.05. ** Body Mass Index*

By using chi-square test it was found that metabolic syndrome occurrence was significantly associated with presence of hyperandrogenemia having p-value = 0.014. After stratification, significant association was found between age groups and presence of metabolic syndrome having p-value = 0.000. No Significant association was found between BMI and presence of metabolic syndrome with p-value = 0.666. Significant association was found between duration of illness and presence of metabolic syndrome having p-value = 0.014.

Discussion

This study was conducted to find out the frequency of hyperandrogenemia in patients presenting with polycystic ovarian syndrome and to correlate the metabolic syndrome occurrence in polycystic ovarian syndrome patients with and without hyperandrogenemia. Among 367 cases of PCOS, it was observed that the mean age was 26.35 (±5.28) years. The mean value of body mass index was 26.12 (± 2.19) kg/m^2. Hyperandrogenemia was found in 59.9% women whereas 40.1% women were normal. In a previous study conducted by Yadav G, et al., it was observed that from 200 PCOS women included in the study, 120 (60%) women were hyperandrogenic whereas the rest 80 (40%) women were normal.[11] The researcher further observed that majority of patients presented were in the age group of 21-30 years and the mean age was comparable between the hyperandrogenic and normoandrogenic groups. The BMI ranged from 15.5 to 45 kg/m^2, have no significant difference for the presence of hyperandrogenism (P= 0.950). Prevalence of hypertension (systolic BP [SBP] ≥ 135 mmHg and/or diastolic BP [DBP] ≥ 85 mmHg) was also comparable between the hyperandrogenic and normoandrogenic cases which is 9% versus 6% (P=0.396). Another research conducted by Majumdar et al. reported significantly higher prevalence of clinical hyperandrogenism (74.2% vs. 50.6%) in obese versus lean PCOS.[11,13]

In our study the mean of duration of illness was 12.25 (±4.06) months. The metabolic syndrome was present in 44 (20%) with hyperandrogenemia while metabolic syndrome was present in 15 (10.20%) patients without hyperandrogenemia. Presence of metabolic syndrome was significantly higher with hyperandrogenemia group as compared to without hyperandrogenemia group (20% vs 10.20%) having p-value = 0.014. By using independent sample t-test it was found that stratified age have significant difference for the presence of

hyperandrogenemia with p-value=0.000. Body mass index and duration of illness didn't show significant relationship having p-value > 0.05.[14] In premenopausal PCOS women, existing literature revealed that presence of hyperandrogenemia is highly associated with increased risk of metabolic syndrome. In another research conducted by Coviello et al., it was also found that hyperandrogenemia is a significant predictor of metabolic syndrome. They performed the research work on forty-nine adolescent females with PCOS.[15-18] In present research it was observed that presence of metabolic syndrome was significantly associated with presence of hyperandrogenemia having p-value = 0.014. After stratification, age groups and duration of illness was significantly associated with presence of metabolic syndrome having p-value=0.000 and 0.014 respectively whereas BMI have no significant association with presence of metabolic syndrome with p-value=0.667

Previous study showed that the prevalence of obesity was reported as 30–75% in women with PCOS.[19-21] It was found in another study conducted in Thailand that approximately 50% of PCOS subjects having BMI ≥ 25 kg/m^2.[15] In a multiracial group of women with PCOS, Mean BMI was reported higher than 32 kg/m^2 and proposed that there is strong association between obesity and PCOS.[15] But on the other hand after adjustment for age, the risk significantly increased among non-obese women with PCOS. However, after additional adjustment for BMI, this association was not statistically significant.[22,2]

Conclusion

Presence of hyperandrogenemia was found in 59.9% patients presenting with PCOS. Presence of metabolic syndrome was significantly higher with hyperandrogenemia group as compared to those without hyperandrogenemia.

Conflict of Interest: *None*

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Authors Contribution

SSW, HH: Conceptualization of Project
HH, TN: Data Collection
HH, SSW: Literature Search
TN, HH: Statistical Analysis
TN, SSW: Drafting, Revision
HH, TN: Writing of Manuscript