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Hyperandrogenism and Its Correlation with Metabolic Syndrome in Patients of PCOS

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Abstract

Introduction: Polycystic ovary syndrome (PCOS) represents the most prevalent endocrine disorder affecting women of reproductive age globally. The primary clinical feature of polycystic ovary syndrome (PCOS) is hyperandrogenism. Hence; the present study was conducted for assessing the correlation of hyperandrogenism with metabolic syndrome (MetS) in patients of PCOS.

Materials & methods: A total of 100 PCOS patients were evaluated. Complete demographic and clinical details of all the patients was obtained. A Performa was made and complete medical history was recorded. Anthropometric variables were evaluated. Blood samples were obtained from all the patients and serum hormonal and biochemical profile was evaluated. All the PCOS patients were divided into two study groups; PCOS without hyperandrogenism and hyperandrogenism PCOS patients. Occurrence of MetS was assessed among PCOS patients. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

Results: A total of 100 PCOS patients were evaluated. Among them, 50 were of PCOS without hyperandrogenism while the remaining 50 were of hyperandrogenism PCOS. Metabolic syndrome was seen in 2 percent of the patients without hyperandrogenic PCOS while it was seen in 18 percent of the patients with Hyperandrogenism PCOS. A significant correlation

was seen in between Hyperandrogenism and metabolic syndrome in PCOS patients.

Conclusion: PCOS is a common condition affecting significant proportion of female population. There exists a significant linear correlation between hyperandrogenism with metabolic syndrome in PCOS patients.

Keywords: Polycystic Ovarian Syndrome, Hyperandrogenism, Metabolic Syndrome

Introduction

Polycystic ovary syndrome (PCOS) represents the most prevalent endocrine disorder affecting women of reproductive age globally. Its prevalence is estimated to be as high as 2.2%-26% globally contingent upon the diagnostic criteria utilized. Specialty society guidelines widely endorse that the diagnosis of PCOS should be established based on the presence of at least two out of the following three criteria: chronic anovulation, hyperandrogenism (either clinical or biochemical), and the presence of polycystic ovaries.[1- 3] The diagnosis is one of exclusion, necessitating the elimination of other disorders that may present with similar clinical manifestations. Such disorders include thyroid dysfunction, hyperprolactinemia, and non-classical congenital adrenal hyperplasia. In certain cases, a more comprehensive evaluation may be warranted if clinical signs indicate alternative etiologies. Despite its significant prevalence, PCOS remains frequently underdiagnosed, often requiring multiple consultations or visits to different healthcare providers for proper identification, typically spanning over a year.[4, 5]

The primary clinical feature of polycystic ovary syndrome (PCOS) is hyperandrogenism. Elevated androgen levels significantly disrupt granulosa cell functionality and follicular maturation through intricate pathways that contribute to obesity and insulin resistance. A majority of PCOS patients exhibiting hyperandrogenism experience defects in steroid secretion, which lead to irregular folliculogenesis and inadequate selection of dominant follicles.[6] The presence of hyperandrogenism is associated with symptoms such as obesity, hirsutism, acne, and androgenetic alopecia, all of which can impose considerable psychological distress on affected women. Therapeutic interventions, including combined oral contraceptive pills, metformin, pioglitazone, and low-dose spironolactone, have been shown to enhance pregnancy outcomes by reducing androgen levels in the body.[7] It is important to recognize that PCOS is a heterogeneous condition, and hyperandrogenism is not the sole contributing factor. The interplay of obesity and insulin resistance exacerbates the manifestations of hyperandrogenism, creating a detrimental cycle that facilitates the progression of PCOS. Despite extensive research efforts, the precise pathogenic mechanisms underlying PCOS remain elusive.[8, 9] Hence; the present study was conducted for assessing the correlation of hyperandrogenism with metabolic syndrome in patients of PCOS.

Materials & methods

The present study was conducted among 100 patients attending the OBSTETRICS and GYNAECOLOGY OPD at ACHARAYA SHRI CHANDER COLLEGE OF MEDICAL SCIENCES AND HOSPITAL for assessing the correlation of hyperandrogenism with metabolic syndrome in patients of PCOS over a period of one year from july 2023 to june 2024. Complete demographic and clinical details of all the patients was obtained. A Performa was made and complete medical history was recorded. Anthropometric variables were evaluated.

Blood samples were obtained from all the patients and serum hormonal and biochemical profile was evaluated. All the PCOS patients were divided into two study groups; PCOS patients without hyperandrogenism and hyperandrogenism PCOS patients. MetS was present if any three of the following criteria was fulfilled according to International Diabetes Federation consensus statement[10]: (1) waist circumference ≥80 cm, (2) Elevated blood pressure (≥130/85 mmHg), (3) Raised fasting blood glucose ≥5.6 mmol/L, (4) Decreased HDL cholesterol (<1.3 mmol/L), and (5) Increased triglyceride levels (≥1.7 mmol/L). Occurrence of MetS was assessed among PCOS patients. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software. Chi-square test and student t test were used for evaluation of level of significance.

Results

A total of 100 PCOS patients were evaluated. Among them, 50 were of without hyperandrogenic PCOS while the remaining 50 were of hyperandrogenism PCOS. Mean age of the PCOS without hyperandrogenism and hyperandrogenism PCOS was 29.6 years and 28.1 years respectively. Mean weight and mean BMI of the hyperandrogenism PCOS patients was significantly higher in comparison to PCOS patients without hyperandrogenism. Mean testosterone levels were significantly higher in Hyperandrogenism PCOS patients in comparison to PCOS patients without hyperandrogenism. Metabolic syndrome was seen in 2 percent of the patients without hyperandrogenic PCOS while it was seen in 18 percent of the patients with Hyperandrogenism PCOS. A significant correlation was seen in between Hyperandrogenism and metabolic syndrome in PCOS patients.

Table 1: Distribution of PCOS patients according to study groups

Variable	PCOS without hyperandrogenism	Hyperandrogenism PCOS	Total
Number	50	50	100

Table 2: Comparison of demographic data

Variable	PCOS without hyperandrogenism	Hyperandrogenism PCOS	p-value
Mean age (years)	29.6	28.1	0.23
Mean weight (Kg)	73.6	83.3	0.00*
Mean BMI (Kg/m^2)	24.9	29.4	0.00*

*: Significant

Table 3: Comparison of testosterone levels

Testosterone levels	PCOS without hyperandrogenism	Hyperandrogenism PCOS	p-value
Total (nmol/L)	1.86	3.95	0.00*
Free (nmol/L)	0.032	0.079	0.00*

*: Significant

Table 4: Comparison of hormone levels

Hormone levels	PCOS without hyperandrogenism	Hyperandrogenism PCOS	p-value
FSH (IU/L)	5.96	5.51	0.94
LH (IU/L)	9.32	12.75	0.01*
Prolactin levels (mIU/L)	223.7	239.4	0.56

*: Significant

Table 5: Correlation between metabolic syndrome and Hyperandrogenism

Metabolic syndrome	PCOS without hyperandrogenism	Hyperandrogenism PCOS	p-value
Present	1 (2%)	9 (18%)	0.00*
Absent	49 (98%)	41 (82%)	
Total	50 (100%)	50 (100%)	

*: Significant

Discussion

PCOS is characterized by a complex etiology that encompasses both genetic factors and environmental influences. It is recognized as the most prevalent endocrine disorder among women, affecting approximately 2.2–26% of those of reproductive age. A hallmark of PCOS is the presence of elevated androgen levels, particularly testosterone (T), which are associated with adverse outcomes such as abdominal adiposity, glucose intolerance, insulin resistance, and disruptions in ovulation. Both androstenedione and testosterone play significant roles in the overall androgenic profile.[11- 13] A comprehensive cohort study indicated that women with PCOS exhibiting elevated free testosterone levels face a heightened metabolic risk compared to those with solely increased androstenedione levels. In contrast, normoandrogenic women with oligo- or anovulation and polycystic ovaries tend to display a metabolic profile that is less severe and more akin to that of healthy controls. The clinical assessment of hyperandrogenism, as measured by the Ferriman Gallwey (FG) score, is influenced by factors such as ethnicity, the sensitivity of hair follicles to androgens, and the biochemical levels of circulating androgens. Consequently, the FG score shows only a modest correlation with total serum testosterone levels. Additionally, hyperandrogenemia, rather than hirsutism, has been identified as an independent predictor of metabolic syndrome (MetS) in women with PCOS. Given that women with PCOS often present with an unfavorable metabolic profile early in adulthood, it is essential to stratify these patients based on metabolic risk outcomes, independent of the various phenotypes of PCOS.[13- 15] Hence; the present study was conducted for assessing the correlation of hyperandrogenism with metabolic syndrome in patients of PCOS.

A total of 100 PCOS patients were evaluated. Among them, 50 were of without hyperandrogenic PCOS while the remaining 50 were of hyperandrogenism PCOS. Mean age of the normal PCOS and hyperandrogenism PCOS was 29.6 years and 28.1 years respectively. Mean weight and mean BMI of the hyperandrogenism PCOS patients was significantly higher in comparison to normal PCOS patients. Mean testosterone levels were significantly higher in Hyperandrogenism PCOS patients in comparison to normal PCOS patients. Several studies have also reported other potential mechanisms of

hyperandrogenism-induced PCOS, such as dihydrotestosterone (DHT), which could contribute to mitochondrial fission in granulosa cells of PCOS patients, and excess androgens induce ER stress, which may damage oocyte quality. Besides, Wang et al. found that hyperandrogenism may contribute to chronic low-grade inflammation in ovary and granulosa cells of PCOS by generating NLRP3 inflammasome, which further promotes granulosa cells pyroptotic death and ovarian fibrosis. Therefore, hyperandrogenism plays a complicated role in PCOS.[16, 17] In a similar study conducted by Yang R et al, authors evaluated the effect of hyperandrogenism (HA) in polycystic ovary syndrome (PCOS) on metabolic parameters. They searched PubMed, EMBASE, Cochrane, Web of Science, Chinese Biomedical Database (CBM), China National Knowledge Infrastructure (CNKI), WanFang data and VIP for clinical observational studies. The study evaluated PCOS patients with or without HA on metabolic parameters was included. Prevalence of metabolic syndrome, indexes of insulin resistance (IR) including homeostasis model assessment IR index (HOMA-IR), incidence of IR, biomarkers of serum lipid metabolism such as total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), and low density lipoprotein (LDL). Of 4457 identified trials, 32 observational studies were included for the final analysis comprising 9556 female with PCOS. 6482 cases were having HA, and the others were negative. There were significant differences in the incidence of metabolic syndrome, HOMA-IR, rate of IR, TC level and HDL level between PCOS patients with or without HA, except for LDL level. No significant publication bias was found as P value of Egger's test was 0.82. HA play an important role in metabolic disorders in PCOS patients. The incidence of metabolic syndrome, IR indexes, and most biomarkers of serum lipid metabolism were significantly different between patients with and without HA.[18]

Metabolic syndrome was seen in 2 percent of the patients with normal PCOS while it was seen in 18 percent of the patients with Hyperandrogenism PCOS. A significant correlation was seen in between Hyperandrogenism and metabolic syndrome in PCOS patients. As described in previous literature, the increased levels of testosterone feeds back on the hypothalamus, decreasing the ability of estradiol and progesterone to slow down GnRH pulse frequency. The ovaries do not appear to be the primary abnormality in PCOS since they have the ability of responding promptly to changes in gonadotropin secretion; ovulation occurs in response to the surge in secretion of FSH stimulated by clomiphene citrate. Furthermore, weight reduction in obese patients reduces estrone and insulin levels, normalizes gonadotropin secretion, and regulates menstrual cycles in women with PCOS.[19, 20] Burghen GA et al evaluated basal plasma total immunoreactive insulin (insulin), androstenedione, and testosterone in 14 obesewomen: 8 with polycystic ovarian disease (PCOD) and 6 obese controls. All 3 hormones were significantly elevated ($P < 0.02$ to $P < 0.001$) in PCOD patients. A significant correlation amon basal levels of plasma insulin, androstenedione, and testosterone was demonstrated. The PCOD group had significantly higher levels of glucose at 1, 2, and 3 h, with similar significant increases in plasma insulin levels at 0, 2, and 3 h. A significant correlation was found between plasma insulin response areas and plasma testosterone ($P < 0.001$) in the control and PCOD patients. These studies demonstrate

that hyperandrogenism correlates with hyperinsulinism.[21]

Conclusion

PCOS is a common condition affecting significant proportion of female population. There exists a significant linear correlation between hyperandrogenism with metabolic syndrome in PCOS patients.

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