

Association of Hypertension and BMI in Polycystic Ovary Syndrome in Non Obese Asian Women

Tanzeela Akram¹, Ambreen Tauseef², Qurratulann Afza Gardner³, Mehwish Qamar⁴, Sahar Javed⁵, Syeda Abeer Fatima⁴

¹Professor & Head, Department of Physiology, CMH, Lahore Medical College & Institute of Dentistry, Lahore, Punjab, Pakistan.

²Associate Professor, Department of Physiology, CMH, Lahore Medical College & Institute of Dentistry, Lahore, Punjab, Pakistan.

³Associate Professor, School of Biological Sciences, University of the Punjab, Lahore, Punjab, Pakistan.

⁴Assistant Professor, Department of Physiology, Islam Medical and Dental College, Sialkot, Punjab, Pakistan.

⁵Assistant Professor, Department of Biochemistry, CMH, Lahore Medical College & Institute of Dentistry, Lahore, Punjab, Pakistan.

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS), is a disorder affecting 6 – 8% of women of reproductive age. The objective of this study was to evaluate the association of hypertension and BMI with PCOS in women of reproductive age. Since ethnicity, socioeconomic status and life style are known to effect a predisposition to various metabolic disorders, the objective of this study was to determine hypertension in PCOS and its relationship with BMI in premenopausal women with PCOS in a sample of local population. **Methods:** The present study was performed on 50 women with PCOS and 30 age-matched healthy women (controls). Patients were selected by history, estimation of fasting glucose, plasma insulin levels and transvaginal ultrasound. The subjects underwent a detailed medical history, general physical examination, systolic (SBP) and diastolic blood pressures (DBP). Fasting blood samples were analyzed for glucose and insulin. **Results:** MAP, serum insulin and HOMA-IR were significantly higher in subjects with PCOS (P value < 0.05). However, no significant difference in fasting glucose levels and BMI was observed. **Conclusion:** The present data on premenopausal subjects indicate that women with PCOS are at risk of developing hypertension. Furthermore, insulin resistance in subjects with PCOS is markedly higher as compared to normal subjects leading to an increased insulin secretion which at this stage is adequate to maintain glucose levels within the normal range.

Keywords: non-obese, hypertension, PCOS, BMI.

INTRODUCTION

PCOS is one of the most common endocrine disease which affects 6 – 8% of women of reproductive age.^[1,2] The most common characteristics of PCOS are anovulation, oligoovulation, hyperandrogenism, metabolic disturbances and large ovaries with multiple cysts.^[3,4] The symptoms and their severity varies between women and the condition is believed to be a genetic disorder,^[5] LH and insulin are believed to be out of balance in PCOS.^[6]

Common symptoms of PCOS include menstrual irregularity, excess hair growth on face, chest or abdomen, obesity and insulin resistance.^[7] Excessive hair growth on face is due to increased production of androgens. Women with PCOS are also at risk for type II diabetes mellitus (T2DM) and hyperestrogen-related cancers.^[8] High risk of spontaneous abortion has also been observed in PCOS.^[9]

The diagnosis of PCOS is usually made on the basis of clinical, biochemical and ultrasonographic

criteria. A polycystic ovary is enlarged and rounded, having a tough, white, thick outer covering with a mean volume of 12 cm³. Polycystic ovary is 2 – 5 times larger than the normal ovaries.^[10] The cysts present in the ovaries are follicles containing eggs that have failed to ovulate.

As far as etiology of PCOS is concerned, it is still unclear although genetic factors have been implicated.^[12] Ovaries produce excessive androgens in PCOS.^[13] In addition, insulin acts with LH and stimulates ovarian androgen production which results in suppression of sex-hormone binding globulin (SHBG) by the liver. SHBG binds both testosterone and estradiol, therefore, there is an increase in the level of both the hormones.

A high prevalence of insulin resistance and hyperinsulinemia in PCOS has been reported previously.^[11] Acanthosis nigricans is often associated with insulin resistance.

Over the past decade, it has been reported that women with PCOS demonstrate an increase in body mass index (BMI), systolic blood pressure (SBP) and insulin levels.^[12,13] The present study was undertaken with the aim of determining hypertension in PCOS and its relationship with BMI in premenopausal women with PCOS.

Name & Address of Corresponding Author

Dr. Ambreen Tauseef,
Associate Professor,
Department of Physiology,
CMH, Lahore Medical College & Institute of Dentistry,
Lahore, Punjab, Pakistan
Email:ambertauseef@hotmail.com

MATERIALS AND METHODS

This case-control study included 50 patients with PCOS and 30 age-matched controls. All subjects were divided into two groups: Group 1: fifty women with PCOS (20 – 39 years) and group 2: thirty healthy subjects (20 – 39 years). Informed consent was obtained from each subject. The protocol of the study was approved by Ethical Review Committee, University of Health Sciences, Lahore.

A complete physical examination was performed on all subjects including heart rate, systolic (SBP) and diastolic (DBP) blood pressure by mercury sphygmomanometer. The mean arterial pressure (MAP) was calculated by the formula: $BP + 1/3$ pulse pressure. Height and weight were determined with a portable scale and portable stadiometer. Body mass index (BMI) was calculated as weight in kg / height in square meters.

Five ml fasting blood samples were collected and centrifuged at 3000 rpm for 10-15 minutes to obtain serum. Serum samples were aliquoted and glucose levels were measured. The remaining serum was stored at – 80 degrees until analyzed.

Serum insulin levels were determined by ELIZA.^[14] Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated by the following formula: $HOMA-IR = \text{Fasting insulin (Uu/ml)} \times \text{Fasting glucose (mmol/l)}$.^[15]

All the participants with pregnancy, Cushing's syndrome, hypothyroidism, hyperprolactinemia, use of oral contraceptives, glucocorticoids, ovulation induction drugs, antiobesity drugs, anti-hypertensive drugs or history of any neoplasia were excluded. All these factors were ruled out by using an appropriate questionnaire, status record and physical examination.

Statistical analysis:

Data was entered and analyzed by SPSS version 22, applying student's t test for the significance of differences between two groups. P value ≤ 0.05 was considered statistically significant.

RESULTS

Out of fifty women with PCOS, 54% had oligo- or amenorrhea, 54% had hirsutism and 58% had hyperandrogenism. In addition, 38 patients had primary infertility, 12 had secondary infertility and Acanthosis nigricans in only eight patients.

Physical parameters:

The mean BMI values were not significantly different among patients and controls [Figure 1]. MAP was significantly higher ($P < 0.001$) in subjects with PCOS [Figure 2]. There were no significant differences in fasting glucose levels [Figure 3], whereas, PCOS patients had significantly higher insulin levels [Figure 4] as compared to their age matched controls.

HOMA-IR was significantly higher in patients with PCOS [Figure 5] as compared to respective controls.

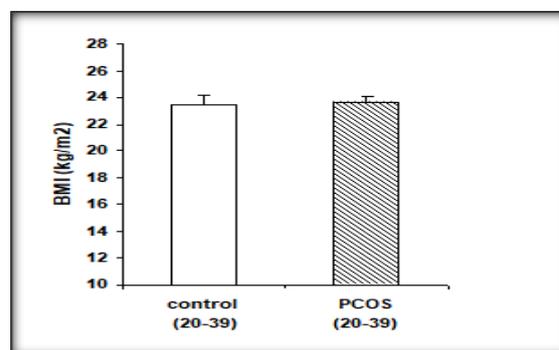


Figure 1: No significant difference between the two age groups.

The MAP, on the other hand, was significantly higher ($P < 0.001$) in subjects with PCOS as compared to their age matched controls.

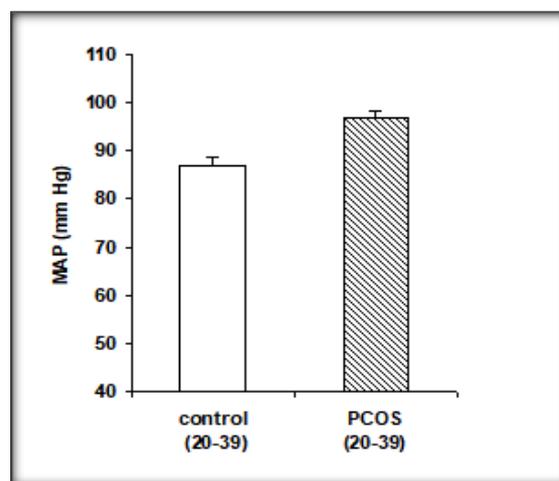


Figure 2. Significant difference ($P < 0.001$) between controls and PCOS patients of corresponding age group.

Fasting glucose levels: No significant differences in fasting glucose levels were observed between PCOS patients and controls.

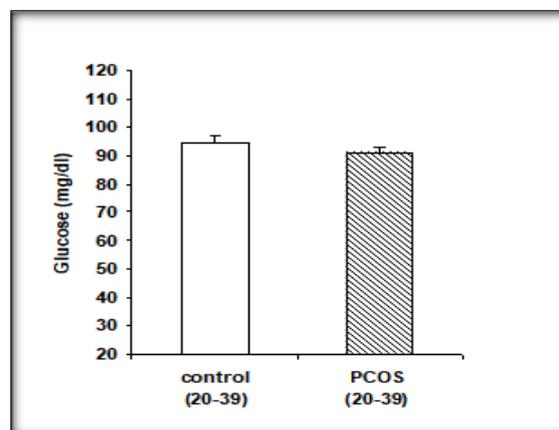


Figure 3. No significant difference in serum glucose in subjects with PCOS and normal subjects.

Serum Insulin

PCOS patients had significantly higher ($P < 0.05$) fasting insulin levels as compared to their age matched controls.

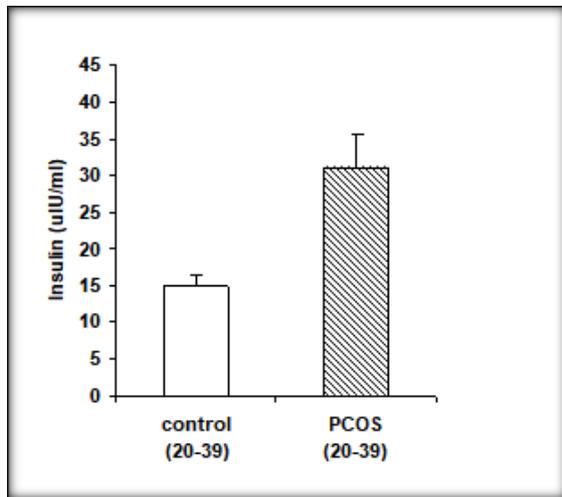


Figure 4. Significant difference between controls and PCOS patients of corresponding age groups.

HOMA-IR

Insulin resistance as assessed by HOMA-IR was significantly higher ($P < 0.05$) in patients with PCOS as compared to respective controls in both the age groups and when the two age groups were combined together. However, no significant difference was noted between younger and older groups.

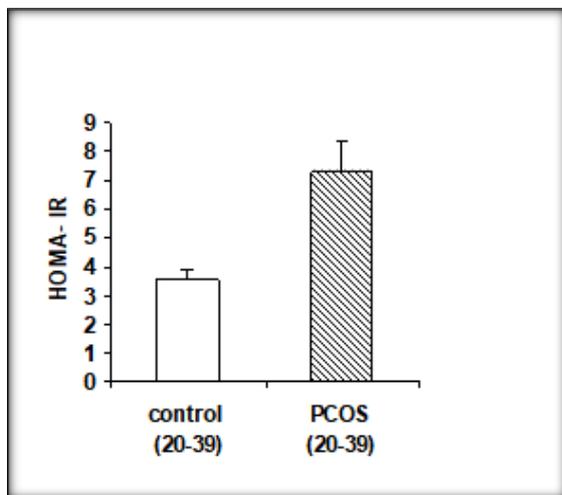


Figure 5. Significant difference between controls and PCOS patients of corresponding age groups.

DISCUSSION

Insulin resistance was supposed to be strongly correlated with obesity, but in our study, it was also more frequently encountered in non-obese patients with PCOS than in non-obese controls. This suggested that the pathophysiological change may not only be a result of obesity but also an intrinsic

etiologic basis for PCOS regardless of obesity. Relative genes variations, defect of the certain signaling pathways, and the vicious circle between the two with hyperandrogenism are proposed as possible underlying mechanisms.

The prevalence of hypertension was higher in women with PCOS as compared to controls. We show a trend towards an association between PCOS and hypertension and a clear association between BMI, T2DM, and hypertension. It is hypothesized that hyperandrogenism seen in women with PCOS may be associated with hypertension.

In our study fasting insulin levels of PCOS patients in both age groups were significantly higher than their age matched controls^[16] Previously, based on observation that obese women with PCOS developed greater degree of insulin resistance has been interpreted as due to an increase in body mass. This possibility was ruled out in the present study by including non-obese PCOS and their age matched controls. Hyperinsulinemia stimulates ovarian cytochrome P450c17 α activity in non-obese women with PCOS, thereby increasing serum androgen concentrations and as a consequence, decreasing serum sex hormone-binding globulin (HSBG) concentration.^[17] Hyperinsulinemia has also been reported to stimulate adrenal P450c17 α activity of some affected women. In this study, fasting glucose levels in PCOS patients and controls were within the normal range but insulin levels were significantly raised in women with PCOS. These observations indicate a tendency towards insulin resistance that is compensated by an increased secretion of insulin sufficient to keep glucose levels in the normal range in these patients.

In a previous study, androgen levels were significantly and positively correlated with both systolic and diastolic BP in women with PCOS independent of insulin resistance. It is demonstrated by our study showing that hyperandrogenism seen in women with PCOS may be associated with hypertension.

The present study therefore, supports the view of hyperinsulinemia and insulin sensitivity as salient features of the syndrome even in the absence of obesity. The PCOS may itself confer insulin resistance and degree of hyperinsulinemia correlated significantly with cardiovascular risks in PCOS, independent of BMI.^[18]

Our data demonstrates that PCOS is independently associated with major cardiovascular risk factors such as hypertension, dyslipidemia and diabetes mellitus. These results support and extend the previous investigations regarding an association between PCOS and cardiovascular risk factors that are independent of age and BMI in a selected population of premenopausal women.

It is suggested that early screening and intervention should be extended to this subset of patients. Future study should be focused on elucidating the underlying

mechanism and finding the optimal time point for screening. The present data warrants further studies on a much larger sample size to determine the precised relationships between PCOS and metabolic dysfunction leading to a predisposition to cardiovascular risks and for appropriate counseling of this section of population.

Table 1: Mean \pm SEM levels of parameters in subjects with PCOS and controls of 20-39 year age group.

| Parameters | Controls | PCOS |
|--------------------------------|-----------------|-------------------|
| BMI (kg/m ²) | 23.5 \pm 0.71 | 23.6 \pm 0.50 |
| MAP (mm Hg) | 87.1 \pm 1.4 | 97 \pm 1.23 * |
| Fasting glucose (mg/dl) | 94.8 \pm 2.3 | 91.2 \pm 2.11 |
| Fasting insulin (μ IU/ml) | 14.9 \pm 1.4 | 31 \pm 4.5 * |
| HOMA-IR | 3.54 \pm 0.37 | 7.27 \pm 1.08 * |

* Significantly different from the control group; P<0.05 (Student's t test).

CONCLUSION

In this study, we noted an increased prevalence of hypertension in young women reporting PCOS. The mean BMI values of the patients with PCOS and controls were not significantly different in the two age matched groups. Yet in women with PCOS, hypertension appeared to not be associated with BMI, akin to observations on diabetes risk in PCOS, suggesting that metabolic abnormalities in PCOS may be independent of BMI.

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