



ANALYSIS OF CLINICAL, HORMONAL AND METABOLIC PARAMETERS OF WOMEN WITH PCOS (POLYCYSTIC OVARY SYNDROME) – A CASE CONTROL STUDY IN KASHMIR

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is one of the most common and heterogeneous endocrine disorders among women of reproductive age. The etiology of PCOS is still unknown and its prevalence varies among population based on genetic and environmental factors. Hyperandrogenism and hyperinsulinemia are the common features of PCOS. It is associated with obesity, insulin resistance and dyslipidemia with an increased risk to diabetes and cardiovascular disease. PCOS receives a considerable attention because of its increasing prevalence, metabolic, reproductive and cardiovascular consequences. **Materials and methods:** A total of 120 women with PCOS and 120 healthy controls were included in the study. Hormonal profile was done by chemiluminescence. Biochemical and lipid profile was evaluated using commercially available diagnostic kits, and insulin levels were measured by enzyme linked immunosorbent assay (ELISA). **Results:** PCOS women had significantly increased weight, waist circumference, BMI, systolic and diastolic blood pressure. LH, LH/FSH ratio and testosterone were also found to be significantly increased in PCOS women compared to healthy controls. Moreover, biochemical parameters including 1hr post glucose, 2hr post glucose, fasting insulin, cholesterol, triglycerides, LDL-Cholesterol, SGPT and uric acid were also found to be significantly increased in PCOS women than healthy controls. HDL-Cholesterol was found to be significantly decreased in PCOS women compared to healthy controls. **Conclusion:** The anthropometric and clinical indices are increased in PCOS women than controls. Moreover women with PCOS have altered hormonal profile, raised glycemic status and lipid profile, and a greater tendency of developing metabolic syndrome in early stages of life. Therefore the evaluation of metabolic status is necessary for better management of women with PCOS.

KEYWORDS: Polycystic ovary syndrome, hyperandrogenism, insulin resistance, metabolic syndrome.

1. INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common heterogeneous endocrinological disorders affecting 5% to 10% of women in reproductive age group. It is characterized by hyperandrogenaemia, chronic oligo/anovulation and polycystic ovarian morphology in ultrasound, and is considered to be the major cause of anovulatory infertility.^[1,2] There are various diagnostic criteria regarding PCOS which are in use like National Institute of Health (NIH), Rotterdam and Androgen Excess Society (AES). The current definition of PCOS is based on Rotterdam criteria which is considered to be more inclusive than the other two criteria, and it defines the syndrome as presence of any two of the following three criteria; 1) Menstrual disturbance;

oligomenorrhoea/anovulation 2) Clinical and/or biochemical signs of hyperandrogenism 3) Ultrasound appearance of polycystic.^[3] The etiopathogenesis of PCOS is multifactorial involving both genetic and environmental factors. Hyperandrogenism is the most observed feature in PCOS women which usually manifests as hirsutism, acne, alopecia and seborrhea. PCOS often exhibits the association of metabolic derangements such as insulin resistance (which accounts for approximately 70% of PCOS cases), impaired glucose tolerance, hypertension, obesity and dyslipidemia.^[4,5] PCOS women are considered to be at high risk for dyslipidemia due to elevated androgen levels and frequent association of this syndrome with obesity.^[6,7] A number of studies have shown that women

with PCOS have higher cholesterol, triglycerides and low density lipoprotein (LDL) levels as well as lower high-density lipoprotein (HDL) levels than age, sex, and weight matched control women.^[8,9] These hormonal and metabolic disturbances are usually present in younger age and chronic disturbances usually predispose PCOS women to the development of vascular disease, diabetes mellitus, atherosclerosis, increased risk of premature clinical presentation of cardiovascular disease and estimated seven fold increased risk of myocardial infarction.^[10,11] A lot of research is being done in the subject of metabolic syndrome and PCOS. Understanding of the pathogenesis of this complex disorder is believed to help in the identification and modification of risk factors in order to improve the health of women with PCOS. In this study, we investigated the clinical, hormonal and biochemical parameters in women with PCOS and normal healthy controls. Further, we made a comparative analysis of all the studied parameters between PCOS women and healthy controls.

2. MATERIALS AND METHODS

Subjects and General Examination: This was a case control study approved by the Institutional ethical committee. This study involves a total of 120 PCOS cases and 120 healthy controls. All the PCOS women were recruited from the Department of Obstetrics and gynecology, Sher-i-kashmir Institute of Medical Sciences (SKIMS), Kashmir. Controls were age matched healthy women with normal menstrual cycles, displaying no evidence of clinical/biochemical hyperandrogenism, having normal ovarian morphology on trans-abdominal ultrasonography and no history of any endocrinological disorder. They were collected from various medical camps organised at various colleges and university of Kashmir. A written informed consent was obtained at the study entry from all subjects. All the women fulfilling the Rotterdam 2003 criteria for diagnosis of PCOS were made to fill a questionnaire involving the details of menstrual history, hirsutism (extent of hair growth), weight gain, acne and family history. Women with hypertension, smoking, pregnancy, hyperprolactinemia, thyroid and adrenal dysfunction, diabetes mellitus and cushings syndrome were excluded from the study. Anthropometric assessment of all PCOS women and healthy controls was done which included measurement of height, weight, waist circumference, hip circumference, waist to hip ratio and detailed systemic examination. Hirsutism assessment was done using modified Ferriman-Gallwey score and a score of 8 out of 36 was taken as significant. Moderate to severe acne was taken as a clinical feature of hyperandrogenemia and all patients were subjected to transabdominal ultrasonography [USG] to measure ovarian morphology and volume.

Hormonal and Biochemical investigations: Venous blood samples were collected from an antecubital vein,

between 08:00 and 09:00 a.m., after an overnight fast for the hormonal and biochemical analysis. The hormonal analysis includes the estimation of Serum LH, FSH, Testosterone, TSH, T4, Prolactin (PRL), 17-OHP and cortisol. Hormonal parameters were determined by chemiluminescent immune assay. The blood sample for hormonal analysis was collected on 2nd to 7th day of the follicular phase of either spontaneous or progesterone induced menstrual cycle.

The biochemical investigations involves the estimation of Oral Glucose tolerance Test, Cholesterol, Triglycerides (TG), HDL-Cholesterol, LDL-Cholesterol, Aspartate transaminase (SGOT), Alanine transaminase (SGPT), Urea, Creatinine and Uric acid. The OGTT was performed using 75 grams of oral anhydrous glucose load dissolved in 300ml of water. All the biochemical parameters were estimated using commercially available diagnostic kits and assays were performed on a semi automated biochemical analyzer [ERBA-Manheim, Germany]. Fasting insulin levels were measured by using ELISA kits.

3. STATISTICAL ANALYSIS

Results were statistically analyzed and data was expressed as mean $\pm$ SD. Data obtained from the study groups were compared by the parametric Student's *t*-test. A P value of <0.05 was used as a criterion for statistical significance. For the analysis, SPSS and INSTAT package were used.

4. RESULTS

Table-1: Baseline and hormonal characteristics in women with PCOS and healthy controls.

Parameters	PCOS women (N=120)	Healthy controls (N=120)
Age (years)	25.61±4.55	25.02±3.46 ^{ns}
Weight (kg)	62.94±10.02	52.84±8.07*
Waist circumference (cm)	84.35±10.30	77.11±6.83*
Waist/hip ratio	0.93±0.08	0.91 ±0.06*
BMI (kg/m ²)	24.80±4.03	20.89±3.77*
Systolic Blood Pressure (mmHg)	125.39±10.07	114.18±10.89*
Diastolic Blood Pressure (mmHg)	77.89±8.09	73.91±7.33*
Ferriman-Gallwey (FG-Score)	14.11±2.57	3.13±1.11*
LH (IU/L)	12.45±3.31	6.48±2.03*
FSH (IU/L)	6.97±1.42	6.27±1.78 ^{ns}
LH/FSH	1.79±0.73	1.03±0.53*
Testosterone (ng/dl)	54.86±14.23	29.03±9.64*

*Significantly different from healthy controls (p<0.05 were considered significant).

^{ns}Non-significant (p>0.05 were considered non-significant).

Table-2: Biochemical and lipid profile of women with PCOS and healthy controls.

Parameters	PCOS women (N=120)	Healthy controls (N=120)
Blood Glucose Fasting (mg/dl)	89.51±10.99	88.54±11.43 ^{ns}
Blood Glucose 1 hr (mg/dl)	137.64±19.74	129.58±18.27*
Blood Glucose 2 hr (mg/dl)	110.52±15.55	97.96±13.27*
Insulin Fasting (μIU/ml)	21.24 ±5.12	10.25±2.92*
Cholesterol (mg/dl)	187.22± 21.65	157.07±19.36*
Triglycerides (mg/dl)	158.84±22.46	106.33±17.32*
HDL (mg/dl)	44.52± 9.62	49.32±13.40*
LDL (mg/dl)	121.29±19.03	90.24±13.53*
SGPT (U/L)	24.05±5.94	16.96±3.49*
SGOT (U/L)	22.74±6.90	21.87±5.60 ^{ns}
Urea (mg/dl)	23.29±5.96	22.29± 4.52 ^{ns}
Creatinine (mg/dl)	0.7675±0.19	0.7592 ±0.17 ^{ns}
Uric acid (mg/dl)	4.10±1.04	2.74± 0.82*

*Significantly different from healthy controls (p<0.05 were considered significant)

^{ns}Non-significant (p>0.05 were considered non-significant)

5. DISCUSSION

PCOS is one of the important endocrine disorders which has heterogenous clinical features and is multifactorial in etiology. Insulin resistance and obesity are the common features which occur frequently in association with PCOS. Increased prevalence of the metabolic syndrome factors such as impaired glucose tolerance or prediabetes, worsened lipid profile, high blood pressure and obesity seem to cluster in women with PCOS compared with general population which increases the risk of PCOS women to type 2 diabetes mellitus and cardiovascular disease.^[12,13]

The present study was conducted to evaluate changes for the basic anthropometric, clinical and hormonal parameters, various biochemical parameters and the lipid profile in PCOS women and normal healthy women. A total of 120 PCOS women and 120 healthy controls were included in this study. The mean age of PCOS women was (25.61±4.55) and that of healthy controls was

(25.02±3.46). In the present study PCOS women presented with increased weight, increased waist circumference, raised systolic BP and increased diastolic BP compared with the healthy controls. Increased waist circumference marked the presence of visceral adiposity in PCOS women as compared to healthy controls. Women with PCOS also presented with increased BMI as compared to healthy women. Our findings corroborate with the visceral adiposity and high BMI that has been reported in women with PCOS.^[14] Hyperandrogenism is considered to be the major underlying factor for PCOS and high testosterone levels have been reported in many women with PCOS. Hyperandrogenism has been reported to be the commonest cause of hirsutism accounting for 90% of cases.^[15] In the present study LH, FSH and testosterone levels were measured in PCOS women and healthy controls. LH and testosterone levels were found to be significantly raised in PCOS women compared with the healthy controls. Recent meta-analysis study of PCOS has reported a number of

reproductive phenotypes of PCOS exist based on the presence and absence of ovulation and hyperandrogenism, and these possible phenotypes show considerable variations in terms of adiposity and insulin resistance.^[4]

Studies have reported that 50-70% of women with PCOS exhibit insulin resistance, which increases the risk of developing type 2 diabetes mellitus.^[16,17] In the present study no significant difference was observed in the fasting Glucose levels in PCOS women and healthy controls. However 1hr Post-glucose levels and 2hr Post-glucose levels were found to be significantly raised in PCOS women compared to healthy controls. Fasting Insulin levels were also observed to be significantly raised in PCOS women in comparison to the healthy controls. Therefore we can say that PCOS is at a risk for developing IGT and type 2 diabetes mellitus compared to healthy controls. Dyslipidemia is a common feature in PCOS, which occurs independent of BMI.^[12,18] The causes of dyslipidemia in PCOS are again multi-factorial and insulin resistance appears to have an important role mediated by stimulation of lipolysis and altered expression of lipoprotein lipase and hepatic lipase.^[19] Approximately 70% of the women with PCOS have disturbances in serum lipid levels with increased levels of triglycerides, LDL and total cholesterol.^[20] In our study, the lipid profile of women with PCOS was found to be significantly higher than normal healthy women. We observed significantly raised Triglycerides, total cholesterol and LDL-cholesterol levels in PCOS women than the normal healthy women. We also observed significantly decreased HDL- cholesterol levels in PCOS women compared with healthy controls. Moreover, PCOS being strongly associated with insulin resistance is a risk factor for the development of fatty liver and renal disease.^[21,22] In the present study PCOS women and healthy controls were also screened for aspartate aminotransferase (SGOT), alanine aminotransferase (SGPT), urea, creatinine and uric acid. Alanine transaminase was found to be significantly raised in PCOS women compared with healthy controls where as similar levels of aspartate transaminase, urea and creatinine were found in both PCOS women and healthy controls. Uric acid levels were also found to be significantly raised in PCOS women compared with healthy controls. Similar reports of uric acid levels in PCOS women were reported by Gozukara et al. (2015).^[23] Uric acid being prooxidant, proinflammatory, and proliferative actions at the endothelial cell level may increase the risk of PCOS women to cardiovascular disease.^[24] Thus, the results of our study show that women with PCOS have increased predisposition to metabolic syndrome when compared with healthy controls as manifested by altered glycemic status and lipid profiles. Therefore, evaluation of the metabolic status in PCOS women is necessary for the global risk assessment of women with PCOS.

CONCLUSIONS

The results of our study showed that women with PCOS have greater waist circumference and BMI indicating the presence of visceral adiposity in PCOS women compared to healthy controls. Further, PCOS women were found to have raised androgen levels, glycemic index, insulin resistance and altered lipid profile with higher cholesterol (both total and LDL), raised triglycerides and lower HDL cholesterol compared with healthy controls. Therefore, the evaluation of the glycemic index and lipid profile in PCOS women may be compulsory for the global cardiovascular risk assessment in women with PCOS.

REFERENCES

1. Fauser BC, Tarlatzis BC, Rebar RW et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertil Steril.*, 2012; 97(1): 28–38.
2. Baird DT, Balen A, Escobar-Morreale HF. Health and fertility in World Health Organization group 2 anovulatory women. *Hum Reprod Update*, 2012; 18(5): 586–99.
3. Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod.*, 2004; 19(1): 41–52.
4. Moran L, Teede H. Metabolic features of the reproductive phenotypes of polycystic ovary syndrome. *Human Reproduction Update*, 2009; 15: 477–88.
5. Nawrocka RJ, Ciećwież S, Marciniak A, Brodowska A, Wiśniewska B, Kotlega D, Starczewski A. Insulin resistance assessment in patients with polycystic ovary syndrome using different diagnostic criteria--impact of metformin treatment. *Ann Agric Environ Med.*, 2013; 20(3): 528–32.
6. Wild RA, Alaupovic P, Parker IJ. Lipid and apolipoprotein abnormalities in hirsute women. *Am J Obstet Gynecol.*, 1992; 166: 1191-97.
7. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. *Endocr Rev.*, 1997; 18(6): 774-00
8. Wild RA. Obesity, lipids, cardiovascular risk, and androgen excess. *Am J Med.*, 1995; 98: 27S-32S.
9. Christian RC, Dumesic DA, Behrenbeck T, Oberg AL, Sheedy PF et al. Prevalence and predictors of coronary artery calcification in women with polycystic ovary syndrome. *J Clin Endocrinol Metab.*, 2003; 88(6): 2562-68.
10. Guzick DS1, Talbott EO, Sutton-Tyrrell K, Herzog HC, Kuller LH, Wolfson SK Jr. Carotid atherosclerosis in women with polycystic ovary syndrome: initial results from a case-control study. *Am J Obstet Gynecol.*, 1996; 174(4): 1224-29.
11. Birdsall MA, Farquhar CM, White HD. Association between polycystic ovaries and extent of coronary

- artery diseases in women having cardiac catheterization. *Ann Intern Med.*, 1997; 126: 32-35.
12. Meyer C, McGrath BP, Teede H. Overweight women with polycystic ovary syndrome have evidence of subclinical cardiovascular disease. *The Journal of Clinical Endocrinology and Metabolism*, 2005; 90: 5711-16
 13. Moran LJ, Misso M, Wild RA, Norman R. Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: A systematic review and meta-analysis. *Human Reproduction Update*, 2010; 16: 347-63.
 14. Ehrmann DA. Polycystic Ovary syndrome. *N Engl J Med.* 2005; 352: 1223-36.
 15. Homburg R. Androgen circle of Polycystic Ovary Syndrome. *Hum Reprod.*, 2009; 24(7): 1548-55.
 16. Sattar N. Reviews: PCOS, insulin resistance and long term risks for Diabetes and vascular disease. *Br J Diabetes vasc Dis.*, 2009; 9: 15-18.
 17. Dabadghao P, Roberts BJ, Wang JX et al. Glucose tolerance abnormalities in Australian women with Polycystic Ovary Syndrome. *MJA.*, 2007; 187(6): 328-31.
 18. Wild RA, Bartholomew MJ. The influence of body weight on lipoprotein lipids in patients with polycystic ovary syndrome. *Am J Obstet Gynecol.*, 1988; 159: 423-27.
 19. Wild RA, Painter PC, Coulson PB, Carruth KB, Ranney GB. Lipoprotein lipid concentrations and cardiovascular risk in women with polycystic ovary syndrome. *J Clin Endocrinol Metab.*, 1985; 61: 946-51.
 20. Gateva A, Kamenov Z. Cardiovascular risk factors in Bulgarian patients with polycystic ovary syndrome and/or obesity. *Obstet Gynecol Int.*, 2012; doi: 10.1155/2012/306347.
 21. Gambarin GM, Kinkhabwala SV, Schiano TD, Bodian C, Yeh HC, Futterweit W. Prevalence of nonalcoholic fatty liver disease in women with polycystic ovary syndrome. *Clin Gastroenterol Hepatol* 2007.
 22. Go AS, Chertow GM, Fan D et al. Chronic kidney disease and the risk of death, cardiovascular events, and hospitalization. *N Engl J Med.*, 2004; 351: 1296-05.
 23. Gozukara IO, Gozukara KH, Kucur SK, Karakılıc EU, Keskin H, Akdeniz D, Aksoy AN, Carlioglu A. Association of glomerular filtration rate with inflammation in polycystic ovary syndrome. *International journal of fertility and sterility*, 2015; 9(2): 176-82
 24. Kanellis J, Kang DH. Uric acid as a mediator of endothelial dysfunction, inflammation, and vascular disease. *Semin Nephrol.*, 2005; 25: 39-42.