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Original Research Article

Oxidative Stress and Cardiovascular Risk Factors among Women with Polycystic Ovary Syndrome

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Abstract

The endocrine disorder known as polycystic ovarian syndrome (PCOS) is linked to issues with the metabolism and the cardiovascular system. About 6–14 percent of women who are childbearing age are affected ^[1]. The two main characteristics of PCOS are hyperinsulinemia and hyperandrogenemia^[2]. Although PCOS is a polygenic trait with multiple underlying genetic interactions and predispositions, environmental factors such as nutrition, exercise, pollution, and stress have a substantial role in the development of the illness ^[3].

As a result of an excessive amount of LH being produced by the pituitary gland or, if the ovaries are insulin-sensitive, due to hyperinsulinemia, it is characterised by an excess of ovarian androgen hormones, particularly testosterone. Infertility, indicators of androgen excess such hirsutism, virilization, acne, alopecia, and monthly irregularities like amenorrhea and dysfunctional bleeding are common symptoms seen in women with PCOS^[4]. Additionally, comorbidities like dyslipidemia, obesity, metabolic syndrome, type 2 diabetes, and hypertension are more common in women with PCOS. In addition to other characteristics including endothelial dysfunction and a chronic low-grade inflammatory state, PCOS increases the risk of cardiovascular disease^[5].

PCOS is a heterogenous syndrome that manifests through changes in the metabolic balance in which mitochondrial dysfunctions have been shown to facilitate the progression and occurrence of various complications of this disease ^[6]. Oxidative stress (OS) is linked to PCOS in obese women as well as CVD. Oxidative stress affects the female reproductive system and causes infertility, contributing to the pathophysiology of infertility ^[7].

Because of their increased androgen levels, frequent obesity, hyperinsulinemia, and insulin resistance, women with PCOS usually have dyslipidemia. Insulin levels more so than

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androgen levels are best at predicting lipid problems. Treatment of hyperandrogenism had little effect on PCOS's lipid profiles. Atherogenesis and cardiovascular disease appear to share similar characteristics. Hypertriglyceridemia is brought on by increased very lowdensity lipoprotein (VLDL) production, which is induced by elevated plasma insulin levels. Low-density and intermediate-density lipoproteins, both of which are atherogenic, are created as the lipid and apolipoproteins are excreted from the VLDL particle ^[8-11].

Objectives

This study was planned to determine dyslipidemia and whether oxidative stress is associated with increased risk of cardiovascular disease in women with PCOS.

Materials and Methods

This case control study was conducted among 50 PCOS patient and 50 controls among age group of 18-40 years after getting approval from Institutional Ethics committee.

Inclusion criteria: PCOS was defined as having less than six menstrual cycles in the previous year, oligomenorrhea, hirsutism (Ferriman-Gallwey score of 7), LH/FSH ratios of 3.0, hyperandrogenemia, and numerous subcapsular follicles by transvaginal ultrasound examination^[12]. Exclusion criteria: Infections, use of medications known to affect insulin secretion or action, lipoprotein metabolism, hypertension, smoking, cardiovascular disease in the family, endocrinopathies such as diabetes, Cushing syndrome, or tumours that secrete androgen, late-onset 21 hydroxylase deficiency, thyroid dysfunction, and hyperprolactinemia. Data collection: After a 10-hour fast, blood samples were collected and serum glucose, total cholesterol, TG, HDL, and very-low-density lipoprotein (VLDL) levels were determined using commercially available diagnostic kits. Friedewald's formula was used to calculate LDL levels ^[13]. The BMI was calculated by dividing the weight in kilogrammes by the height in metres squared. Before beginning the study, informed consent was obtained.

Data analysis: The mean ± SD were compared using 't'-test from MS Excel. The p value of <0.05 is considered statistically significant.

Result

The average age of people with PCOS was 24.2 ± 3.5 years, compared to 24.85 ± 2.78 years for controls. In PCOS and Controls, the observed BMI was 30.2 ± 4.6 and 27.15 ± 2.79 , respectively.

| | PCOS (n-50) | Control (n-50) |
|--------------------------|----------------|----------------|
| Age (in years) | 24.2 ± 3.5 | 24.85 ± 2.78 |
| BMI (Kg/m ³) | 30.2 ± 4.6 | 27.15 ± 2.79 |

| Characteristics in obese | PCOS | Control | P Value |
|--------------------------|--------------|-------------|---------|
| Cholesterol (mg/dl) | 275.08±20.2 | 192.96±13.2 | <0.001 |
| Triglyceride (mg/dl) | 167.03±36.74 | 130.70±32.8 | <0.001 |
| HDL (mg/dl) | 20.70±5.4 | 31.92±7.5 | <0.001 |
| LDL (mg/dl) | 141.51±26.8 | 26.05±6.51 | <0.001 |
| MDA (nmol/mL) | 7.14±0.54 | 3.96±0.42 | <0.001 |

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Serum cholesterol was higher in obese PCOS group compared to obese Control group however statistically significant difference was found. Statistical difference was seen in the levels of triglyceride, HDL, LDL and MDA among obese PCOS and obese control group

| Characteristics in non-obese | PCOS | Control | P Value |
|------------------------------|--------------|------------|---------|
| Cholesterol (mg/dl) | 163.64±30.1 | 149.34±15 | <0.001 |
| Triglyceride (mg/dl) | 131.12±36.71 | 92.74±30 | <0.001 |
| HDL (mg/dl) | 28.80±8.45 | 37.02±7.5 | <0.001 |
| LDL (mg/dl) | 127.97±24.96 | 26.23±6.02 | <0.001 |
| MDA (nmol/mL) | 5.54±0.32 | 1.91±0.40 | <0.001 |

 Table 3: Comparison of Characteristics of non-obese women in PCOS and controls

Serum cholesterol was higher in non-obese PCOS group compared to non-obese Control group however statistically significant difference was found. Statistical difference was seen in the levels of triglyceride, HDL, LDL and MDA among non-obese PCOS and non-obese control group.

Although there was a statistically significant difference between the obese PCOS group and the obese Control group, serum cholesterol was greater in the obese PCOS group. Triglyceride, HDL, LDL, and MDA levels were statistically different between the obese PCOS group and the obese control group. Although there was a statistically significant difference between the non-obese PCOS group and the non-obese Control group, serum cholesterol was greater in the PCOS group. Triglyceride, HDL, LDL, and MDA levels between the non-obese PCOS group and the non-obese control group, serum cholesterol was greater in the PCOS group. Triglyceride, HDL, LDL, and MDA levels between the non-obese PCOS group and the non-obese control group were statistically different.

Discussion

The most frequent metabolic aberration in PCOS is dyslipidemia. Approximately 70% of PCOS women have borderline or high lipid levels, according to recommendations from the National Cholesterol Education Program ^[12]. The most prevalent types of dyslipidemia seen in conditions of insulin resistance include high levels of total cholesterol, small dense LDL, and low levels of HDL. Another independent risk factor for cardiovascular events is lower HDL levels ^[13-17] In contrast to their controls, PCOS women were shown to have dyslipidemia. PCOS obese women had deranged lipid levels as compared to non-obese. Other studies made similar findings ^[18-21].

The pathological condition known as oxidative stress occurs when the ratio of oxidant generation to detoxification tips in favour of a prooxidant state, overwhelming an antioxidant defense and resulting in an accumulation of reactive oxygen species (ROS). COS patients experience oxidative stress as a result of hyperglycemia, IR, and chronic inflammation, which causes an overproduction of ROS. Tumor necrosis factor (TNF) is produced by hyperglycemia from multinuclear cells (MNC), which contributes to inflammation.

Malondialdehyde (MDA) levels, a marker of lipid peroxidation, and superoxide dismutase (SOD) activity rose, whereas erythrocyte reduced glutathione (GSH) levels fell in PCOS women, according to a recent study. PCOS had considerably higher serum levels of MDA, the byproduct of lipid peroxidation. PCOS obese women had deranged MDA level as compared to non-obese. Numerous more investigations came to the same conclusions ^[19, 20] There has been an increase in coronary heart disease risk factors in PCOS-afflicted women over the past years, according to several studies ^[22-24], and some of these studies suggested a

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link between hyperinsulinemia, a side effect of insulin resistance, and a higher risk of cardiovascular disease in PCOS^[25-26].

Conclusion

Our study reveals that, in addition to the known risk factors for cardiovascular disease, such as insulin resistance, hypertension, central obesity, and dyslipidemia, increased oxidative stress and lower antioxidant capacity may increase the risk of cardiovascular disease in women with PCOS. Therefore, PCOS women should have their lipid profiles and oxidative stress assessed. They should also be given antioxidant supplements, which can help to prevent coronary vascular disorders. This study can increase our understanding of the critical impact that dietary changes and pharmacological therapies for metabolic disorders play in reducing the cardiovascular risk in PCOS women. Inflammatory marker detection can improve PCOS outcome and lower overall morbidity.

References

- 1. Knochenhauer ES, Key TJ, Kahsar-Miller M, et al. Prevalence of the polycystic ovary syndrome in unselected black and white women of the south eastern United States: a prospective study. J Clin Endocrinol Metab 1998;83:3078–82.
- 2. Wild RA, Grubb B, Hartz A, et al. Clinical signs of androgen excess as risk factors for coronary artery disease. FertilSteril 1990;54:255–9.
- 3. McKittrick M. Diet and polycystic ovary syndrome. Nutr Today 2002;37: 63–9.
- Dumesic DA, Oberfield SE, Stener-Victorin E, Marshall JC, Laven JS, Legro RS. Scientific Statement on the Diagnostic Criteria, Epidemiology, Pathophysiology, and Molecular Genetics of Polycystic Ovary Syndrome.Endocrine Rev (2015) 36:487–525. doi: 10.1210/er.2015-1018
- 5. Rojas J, Chavez M, Olivar L, Rojas M, Morillo J, Mejias J, et al. Polycystic Ovary Syndrome, Insulin Resistance, and Obesity: Navigating the Pathophysiologic Labyrinth. Int J Reprod Med (2014) 2014:719050. doi: 10.1155/2014/719050
- 6. Zhang J, Bao Y, Zhou X, Zheng L. Polycystic ovary syndrome and mitochondrial dysfunction. Reprod Biol Endocrinol (2019) 17:67. doi: 10.1186/s12958-019-0509-4
- 7. Tehrani FR, Rashidi H, Khomami MB, Tohidi M, Azizi F. The prevalence of metabolic disorders in various phenotypes of polycystic ovary syndrome: a community based study in Southwest of Iran. Reproductive biology and endocrinology. 2014;12(89):1-6.
- 8. Kitzinger C, Willmott J. 'The thief of womanhood': women's experience of polycystic ovarian syndrome. Social science and medicine. 2002; 54(3):349-361.
- 9. Castro AV, Kolka CM, Kim SP, Bergman RN. Obesity, insulin resistance and comorbidities? Mechanisms of association. Arquivosbrasileiros de endocrinologia e metabologia. 2014;58(6):600-609.
- 10. Velez LM & Motta AB. Association between polycystic ovary syndrome and metabolic syndrome. Current medicinal chemistry. 2014; 21(35): 3999-4012.
- DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care. 1991; 14(3):173-194.
- 12. Bannigida DM, Nayak SB. Coronary Risk Factors and Oxidative Stress in Women with PCOS. Indian J Med Biochem 2019;23(2):267-269.
- Slowinska-Srzednicka J, Zgliczynski S, Wierzbicki M, Srzednicki M, Stopinska-Gluszak U, Zgliczynski W, et al. The role of hyperinsulinemia in the development of lipid disturbances in nonobese and obese women with the polycystic ovary syndrome. J Endocrinol Invest 1991; 14:569–75.

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- 14. Writing Group for the PEPI Trial. Effects of estrogen or estrogen/ progestin regimens on heart disease risk factors in postmenopausal women. The postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. JAMA 1995;273:199–208.
- 15. Hulley S, Grady D, Bush T, Furberg C, Herrington D, Riggs B, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/ progestin Replacement Study (HERS) Research Group. JAMA 1998; 280:605–13.
- 16. Lieberman EH, Gerhard MD, Uehata A, Walsh BW, Selwyn AP, Ganz P, et al. Estrogen improves endothelium-dependent, flow-mediated vasodilation in post-menopausal women. Ann Intern Med 1994;121: 936–41.
- 17. Wild RA, Grubb BG, Hartz A, VanNort JJ, Bachman W, Bartholomew M. Clinical signs of androgen excess as risk factors for coronary artery disease. FertilSteril 1990;54:255–9.
- 18. Zuo T, Zhu M, Xu W. Roles of Oxidative Stress in Polycystic Ovary Syndrome and Cancers. Oxidative Medicine and Cellular Longevity. 2016;1:1-15.
- 19. Desai V, Prasad NR, Manohar SM, Sachan A, Lakshmi Narasimha SRP, Bitla ARR. Oxidative Stress in Non-Obese Women with Polycystic Ovarian Syndrome. Journal of Clinical and Diagnostic Research. 2014; 8(7): 1-3.
- 20. Karabulut AB, Cakmak M, Kiran RT, Sahin I. Oxidative Stress Status, Metabolic Profile and Cardiovascular Risk Factors in Patients with Polycystic Ovary Syndrome. Medicine Science. 2012;1(1):27-34.
- Valkenburg TO, Regine PM, Theunissen S, Huberdina PM, Smedts, Dallinga-Thie GM et al. A More Atherogenic Serum Lipoprotein Profile Is Present in Women with Polycystic Ovary syndrome: A Case-Control Study. J Clin Endocrinol Metab. February 2008; 93(2):470-476.
- 22. Talbott E, Guzick D, Clerici A, Berga S, Detre K, Weimer K, et al. Coronary heart disease risk factors in women with polycystic ovary syndrome. ArteriosclerThrombVasc Biol 1995;15:821–6.
- 23. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev 1997;18:774–800.
- 24. Birdsall MA, Farquhar CM, White HD. Association between polycystic ovaries and extent of coronary artery disease in women having cardiac catheterization. Ann Intern Med 1997;126:32–5.
- 25. Conway GS, Agrawal R, Betteridge DJ, Jacobs HS. Risk factors for coronary artery disease in lean and obese women with the polycystic ovary syndrome. Clin Endocrinol (Oxf) 1992;37:119–25.
- 26. Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes Care 1999;22:141–6.