

## **A REVIEW ON POLYCYSTIC OVARIAN SYNDROME AND ITS RELATION WITH THE METABOLIC SYNDROME**

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### **ABSTRACT**

Polycystic ovary syndrome (PCOS) is a common endocrine disorder seen in every 1 in 15 women worldwide and 5-10% of childbearing women (20-40 years). The objective of this review is to update the current clinical manifestations of PCOS and its close relation with the metabolic syndrome. PCOS is characterised by obesity, hyperandrogenism and insulin resistance associated with type 2 diabetes mellitus. Obesity is a main cause of adverse pregnancy outcomes and increases the risk of pregnancy complication within PCOS. Insulin resistance can be a link between glucose intolerance and the increase in cardiovascular risk. Insulin resistance also plays a pathogenic role as the metabolic syndrome in cardiovascular disease and PCOS. Cardiovascular risk factors in the PCOS cases are an increase in mean BMI, waist-to-hip ratio, total cholesterol, HDL cholesterol, insulin, triglyceride levels and systolic blood pressure. The risk factors of the PCOS are associated with an adverse lipid profile and high blood pressure. Carotid artery wall thicknesses are associated with lipids, waist-to-hip ratio and with obesity. PCOS not only exhibits metabolic risks but also produce complications during pregnancy which includes gestational diabetes, pregnancy-induced hypertension and delivery by caesarean section, premature deliveries and perinatal mortality. From this review, it may be concluded that there is a close relationship between PCOS and the metabolic syndrome with common characteristics and obesity in many cases, was found to exacerbate cardiovascular risk factors. Hence, encouraging weight reduction in the obese patients may reduce the risks of PCOS.

**Key words:** PCOS, insulin resistance, obesity, metabolic syndrome, cardiovascular risks.

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## INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder, categorized by chronic anovulation and hyperandrogenism seen in every 1 in 15 women worldwide and 5 to 10% of childbearing women (20-40 years), mainly in premenopausal women<sup>1-5</sup>. The incidence of PCOS varies according to the analytical criteria used. According to NIH and Rotterdam criteria, it ranges from 9% and up to 18% in women of reproductive age respectively<sup>6-9</sup>. Cysts are immature follicles that have developed from primordial follicles but the growth has stopped at an antral stage due to the troubled ovarian function. On ultrasound scan, the follicle appears like “string of beads” along the ovarian periphery. PCOS is defined as the presence of two of the following criteria: hyperandrogenism, ovulatory dysfunction, and polycystic ovaries on ultrasound (12 or more follicles, 2-9 mm in diameter, and/ or increased ovarian volume >10 ml). Clinical presentation of PCOS include hirsutism, acne, alopecia, irregular menstrual cycles, oligomenorrhea, amenorrhea, ovulatory dysfunction and infertility increased risk for type 2 diabetes, dyslipidemia, hypertension etc.

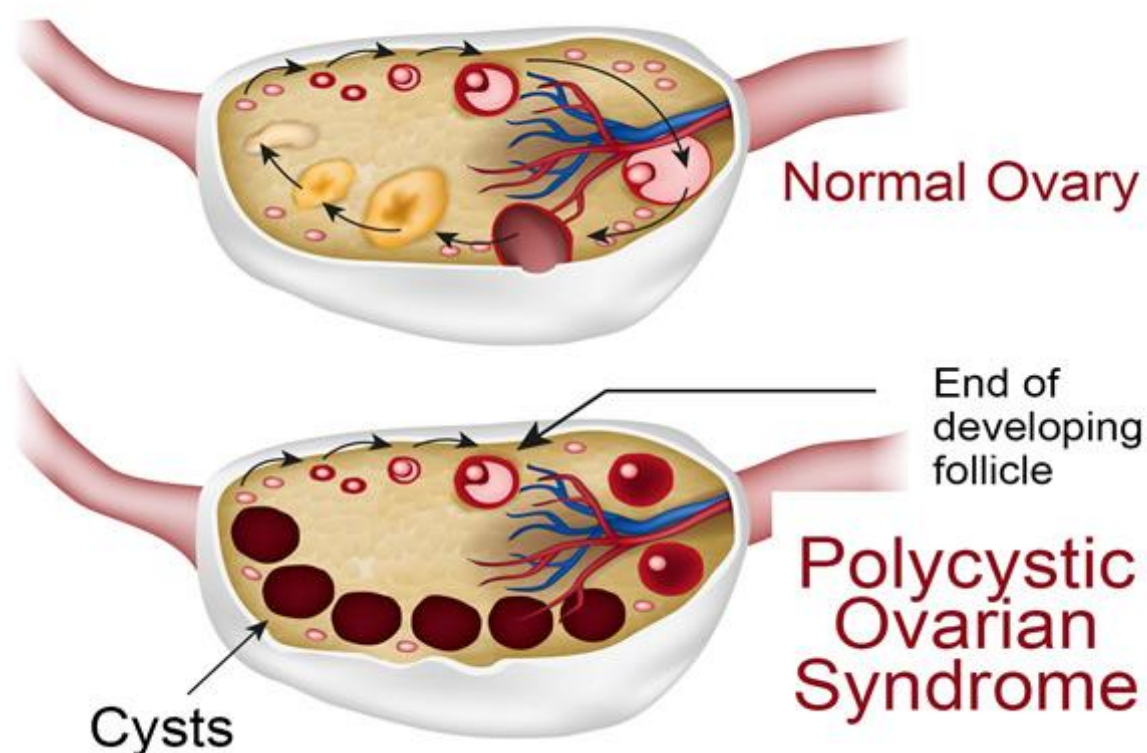


Fig 1: Comparison between normal ovary and polycystic ovarian syndrome<sup>10</sup>

The National Cholesterol Education Program's Adult Treatment Panel III (NCEPATP III) in 2001<sup>11</sup> defines metabolic syndrome (MBS) as the presence of at least three of the following five criteria. Abdominal/central obesity (waist circumference >88cms), Serum triglycerides 150mg/dl or greater, Serum HDL cholesterol less than 50 mg/dl, BP 130/85 or greater and Fasting blood sugar (FBS) 110mg/dl or more. The fundamental causes of the syndrome are genetic and environmental: overweight, obesity, and physical immobility, which guide to

insulin resistance, hyperinsulinemia, endothelial dysfunction and inflammation<sup>12</sup>. The main etiological factor is the insulin resistance and it contributes to overall hyperandrogenemia, leading to hirsutism, menstrual problems and anovulation. This is also the main accountable factor connecting PCOS with hypertension, dyslipidaemia, impaired glucose tolerance and type 2 diabetes mellitus (DM), central obesity and sub clinical carotid atherosclerosis<sup>13-14</sup>.

Middle-aged women with PCOS have been found to have a greater prevalence of carotid artery atherosclerosis and coronary artery disease than women without PCOS<sup>14-15</sup>. Sex hormone-binding globulin (SHBG), the blood transport protein for testosterone and estradiol<sup>16</sup> which is first and foremost derived from the liver was found to be lower in women with PCOS compared with those without PCOS. A low SHBG level was strongly associated with the incidence of the metabolic syndrome. Both low SHBG levels and the metabolic syndrome were reported to indicate a severe degree of insulin resistance<sup>17-18</sup>. Women with PCOS and metabolic syndromes were more obese and older than women with PCOS without metabolic syndrome.

## **RELATIONSHIP OF PCOS WITH OTHER DISEASE CONDITIONS**

### **Inter-relationship between PCOS and metabolic syndrome on the basis of Coronary artery disease**

Women with PCOS shows an amplified risk of coronary artery diseases which includes decreased HDL cholesterol, elevated LDL cholesterol and triglycerides, increased hypertension and insulin resistance. These risk factors are similar in case of metabolic syndrome which in turn forms the coronary artery disease<sup>19-21</sup>. Patients with PCOS exhibit decreased nitric oxide production which results in the damage of flow mediated dilatation of branchial artery, after all results in certain features like type 2 diabetes mellitus, insulin resistance, hypertension and obesity<sup>22-23</sup>. Surrogate markers of coronary atherosclerosis like increased carotid IMT, impaired elasticity of carotid and brachial artery walls paves way for the accumulation of calcium in coronary artery. Patients with PCOS illustrate more deposits of calcium in their coronary artery<sup>24</sup>.

### **Inter-relationship between PCOS and metabolic syndrome on the basis of Dyslipidaemia**

Dyslipidaemia may represent the most common metabolic abnormality in PCOS. Dyslipidaemia usually includes low high-density lipoprotein (HDL)-cholesterol, elevated triglyceride concentrations and less often increased low-density lipoproteins (LDL) and total cholesterol levels<sup>25</sup>. The elevation in triglyceride levels may represent the main contributor for the production of small, dense LDL: these particles are usually formed by the action of hepatic lipase from lipoprotein precursors enriched in triglycerides<sup>26</sup>. There is presence of milder forms of atherogenic dyslipidaemia in PCOS and these were connected to the degree of insulin resistance.

### **Inter-relationship between PCOS and metabolic syndrome on the basis of Diabetes mellitus**

It is well known that hyperinsulinemia and obesity are common features of PCOS. These alterations can lead to glucose metabolism disorders and increased risk of developing diabetes mellitus. Insulin resistance (and compensatory hyperinsulinemia) is an important factor in maintaining hyperandrogenemia by acting directly on theca cells inducing excess androgen production. Insulin also acts as a co-gonadotropin, increasing the effect of LH on ovarian androgen secretion. In consequence, both insulin and androgens act on the liver

inhibiting SHBG secretion, leading to increased free and bioactive androgen circulating levels and making clinical hyperandrogenism worse. In addition, insulin resistance plays a central role on the pathophysiology of metabolic syndrome and on the cardiovascular risk in PCOS women. The consequences of the above are metabolic syndrome. Various risk factors for developing GDM have been described, including obesity and hyperinsulinemia, which are also associated with increased insulin resistance in women with PCOS. These patients present increased adiposity, particularly abdominal, associated with hyperandrogenemia. Previous reports suggest that the increased incidence of GDM is largely explained by obesity and less by PCOS<sup>27-30</sup>. By the age of 40 years, up to 40% of all women with PCOS will have developed type II diabetes or impaired glucose tolerance (in the United States)<sup>31</sup>. Because women with PCOS have an incidence of insulin resistance of 25–70%, they would appear to be at increased risk of developing gestational diabetic complications<sup>4</sup>. The ‘Barker hypothesis’ of fetal programming *in utero* suggests that the fetal nutrition and endocrine environment (e.g. hyperinsulinaemia) may effect neuroendocrine systems regulating body weight, food intake and metabolism, with consequences for long-term health in the offspring<sup>32</sup>.

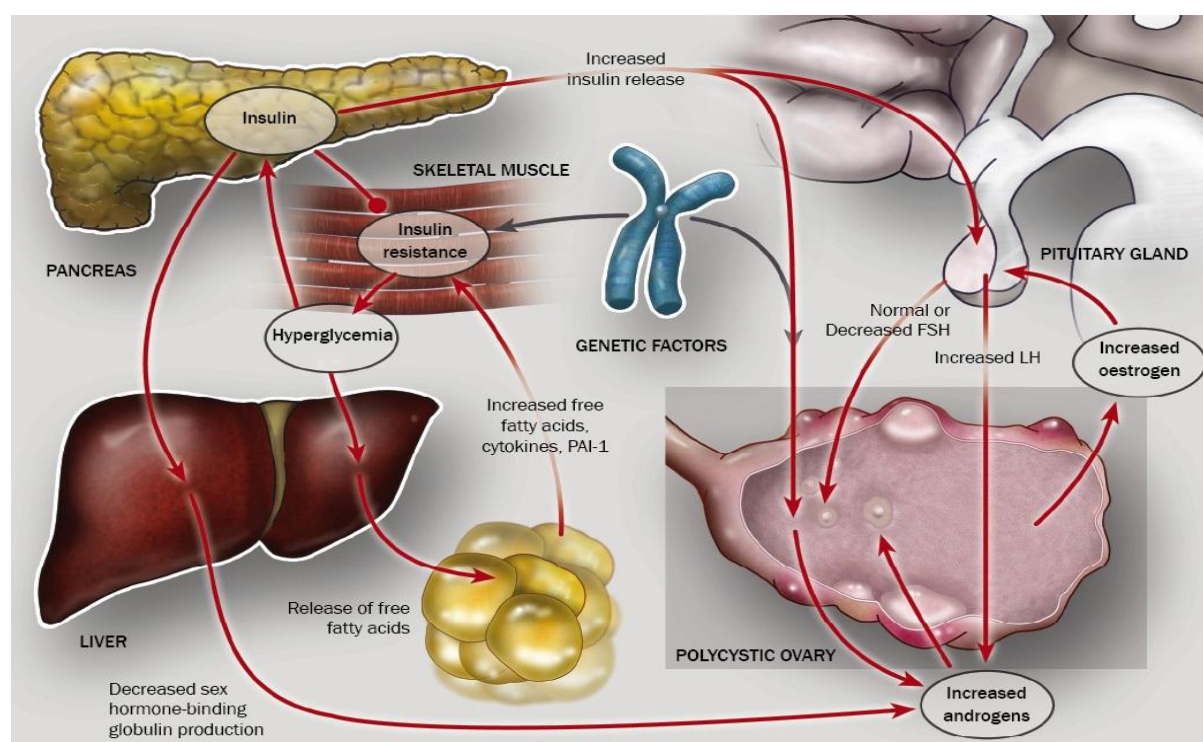


Fig 2: Relation of PCOS with other metabolic syndromes<sup>33</sup>

## CONCLUSION

It is seen that there is a close relationship between the PCOS and the metabolic syndrome through various similar characteristics like insulin resistance, hyperlipidemia, obesity, type 2 diabetes mellitus, glucose intolerance, increased waist-to-hip ratio and hypertension. As obesity exacerbates cardiovascular risk factors, hence encouraging weight reduction in the obese patients can reduce the risks of PCOS.

## REFERENCES

- [1] A.Dunaif,. Insulin resistance and the polycystic ovary syndrome: mechanism andimplications for pathogenesis, *Endoc Rev.*, vol.18, pp.774-800, 1997.
- [2] G.M.Reaven, Role of insulin resistance in human disease, *Diabetes.*,vol.37, pp.1595-1607, 1988.
- [3] T.Tanbo, P.O.Dale,andO.Lunde, Obstetric outcome in singleton pregnancies after assisted reproduction, *Obstet Gynecol.*, vol.86, pp.188–192, 1995.
- [4] R.S.Legro, V.D.Castracane and R.P.Kauffman, Detecting insulin resistance in polycystic ovary syndrome: purposes and pitfalls,*ObstetGynecolSurv.*, Vol.59,pp.141–154, 2004.
- [5] E.S.Knochenhauser, T.J.Key, and M.Kahsar-Miller,Prevalence of the polycystic ovary syndrome in unselected black and white women of south-eastern United States: a prospective study,*JClinEndocrinolMetab.*, Vol.83, pp.3078-3082, 1998.
- [6] R.Azziz, R.S.Woods, R.Reyna, The prevalence and features of the polycystic ovary syndrome in an unselected population,*J Clin EndocrinolMetab.*, vol.89, pp.2745-2749,2004.
- [7] M.Asuncion, R.M.Calvo, J.L.SanMillan, J.Sancho, S.Avila and H.F.Escobar- Morreale, A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain,*J Clin Endocrinol Metab.*,vol.85, pp.2434-2238, 2000.
- [8] W.A.March, V.M.Moore, K.J.Willson, D.I.Phillips, R.J.Norman and M.J.Davies, The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria,*HumReprod.*, vol.25,pp.544-551, 2010.
- [9] L.Haakova, D.Cibula, K.Rezabek,M.Hill and M.Fanta, Pregnancy outcome in women with PCOS and in controls matched by age and weight,*HumReprod.*, vol.18, pp.1438-1441, 2003.
- [10] Polycystic ovarian syndrome. Infertility guidance website <http://www.ivfgurus.com>. Updated March 8, 2016. Accessed April 20, 2017.
- [11] Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report,*Circulation.*, vol.106,pp.3143–3421.
- [12] P.M.Ridker, J.E.Buring, N.R.Cookand N.Rifai, C-reactive protein,the metabolic syndrome, and risk of incident cardiovascular events:an 8-year follow-up of 14719 initially healthy American women,*Circulation.*,vol.107, pp.391–397, 2003.
- [13] R.S.Legro, A.R.KunselmanandW.C.Dodson, Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective controlled study in 254 affected women, *J Clin EndocrinolMetab.*, vol.84, pp.165–169,1999.

- [14] E.O.Talbott, D.S.Guzick and K.Sutton-Tyrrell, Evidence for association between polycystic ovary syndrome and premature carotid atherosclerosis in middle-aged women, *ArteriosclerThrombVasc Biol.*, vol.20, pp.2414–2421, 2000.
- [15] R.C.Christian, D.A.Dumesic, T.Behrenbeck, A.L.Oberg and P.F.Sheedy, Prevalence and predictors of coronary artery calcification in women with polycystic ovary syndrome, *J Clin Endocrinol Metab.*, vol.88, pp.2562–2568, 2003.
- [16] P.H.Petra, The plasma sex steroid binding protein (SBP or SHBG): A critical review of recent developments on the structure, molecular biology and function, *J Steroid BiochemMol Biol.*, vol.40, pp.735–753, 1991.
- [17] S.M.Kahn, D.J.DHryb, A.M.Nakhla, N.A.Romas and W.Rosner, Sex hormone-binding globulin is synthesized in target cells, *J Endocrinol.*, vol.175, pp.113–120, 2002.
- [18] A.S.Cikim, N.Ozbey, E.Sencer, S.Molvalilar and Y.Orhan, Associations among sex hormone binding globulin concentrations and characteristics of the metabolic syndrome in obese women, *DiabetesNutrMetab.*, vol.17, pp.290–295, 2004.
- [19] L.Mattson, G.Culberg, L.Hamberger, G.Samsioe and G.Silfverstolpe, Lipid metabolism in women with polycystic ovary syndrome: possible implications for an increased risk of coronary heart disease, *FertilSteril.*, vol.42, pp.579 –584, 1984.
- [20] R.Wild, P.Painter, P.Coulson, K.Carruth and G.Ranney, Lipoprotein lipid concentrations and cardiovascular risk in women with polycystic ovary syndrome, *J Clin EndocrinolMetab.*, vol.61, pp.946 –951, 1985.
- [21] R.J.Chang, R.Nakamura, H.Judd and S.Kaplan, Insulin resistance in non-obese patients with polycystic ovarian disease, *J Clin EndocrinolMetab.*, vol.51, pp.356 –359, 1983.
- [22] G.Paradisi, H.O.Steinberg, A.Hempfling, J.Cronin, G.Hook, M.K.Shepard and A.D.Baron, Polycystic ovary syndrome is associated with endothelial dysfunction, *Circulation.*, vol.103, pp.1410–1415, 2001.
- [23] F.Orio F, S.Palomba, T.Cascella, B.De Simone, S.DiBiase, T.Russo, D.Labella, F.Zullo, G.Lombardi and A.Colao, Early impairment of endothelial structure and function in young normal-weight women with polycystic ovary syndrome, *J Clin EndocrinolMetab.*, vol.89, pp.4588–4593, 2004.
- [24] R.C.Christian, D.A.Dumesic, T.Behrenbeck, A.L.Oberg, P.F.Sheedy PF and L.A.Fitzpatrick, Prevalence and predictors of coronary artery calcification in women with polycystic ovary syndrome, *J ClinEndocrinolMetab.*, vol.88, pp.2562–2568, 2003.
- [25] A.J.Cussons, B.G.Stuckey and G.F.Watts, Cardiovascular disease in the polycystic ovary syndrome: new insights and perspectives, *Atherosclerosis.*, vol.185, pp.227–239, 2006.
- [26] K.Berneis, M.Rizzo, F.Fruzzetti, V.Lazzarini and E.Carmina, Atherogenic lipoprotein phenotype and LDL size and subclasses in women with polycystic ovary syndrome, *J Clin EndocrinolMetab.*, vol.92, pp.186–189, 2007.

- [27] L1.Haakova, D.Cibula, K.Rezabek, M.Hill and M.Fanta, Pregnancy outcome in women with PCOS and in controls matched by age and weight, *Hum Reprod.*, vol.18, pp.1438-1441, 2003.
- [28] C.M.Boomsma, M.J.Eijkemans, E.G.Hughes, G.H.Visser and B.C.Fauser, A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome, *Hum Reprod Update.*, vol.12, pp.673-683, 2006.
- [29] E.Reyes-Muñoz, G.Castellanos-Barroso, B.Y.Ramírez-Eugenio, C.Ortega-González and A.Parra, The risk of gestational diabetes mellitus among Mexican women with a history of infertility and polycystic ovary syndrome, *FertilSteril.*, vol.97, pp.1467-1471, 2012.
- [30] C.M.Boomsma, B.C.Fauser, N.S.Macklon, Pregnancy complications in women with polycystic ovary syndrome, *SeminReprod Med.*, vol.26, pp.72-84, 2008.
- [31] A.Dunaif, Hyperandrogenic anovulation (PCOS): a unique disorder of insulin action associated with an increased risk of non-insulin-dependent diabetes mellitus, *Am J Med.*, vol.98, pp.33–39, 1995.
- [32] D.J.Barker, Fetal programming of coronary heart disease, *Trends EndocrinolMetab.*, vol.13, pp.364–368, 2002.
- [33] J.E.Nestler, Polycystic ovarian syndrome, *NEJM.*, vol.358: pp.47-54, 2008.