

# Polycystic Ovarian Syndrome: An Unsolved Women's Health Disorder

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## ABSTRACT

Hyperandrogenism commonly known as PCOS and perpetual anovulation is a standout amongst the most widely recognized endocrine issue. The clinical and biochemical components are heterogeneous, and there has been much verbal confrontation with reference to whether it speaks to a solitary issue or a few. As of late, it has gotten to be obvious that the polycystic ovary disorder not just is the most regular reason for anovulation and of hirsutism, but at the same time is connected with a trademark metabolic unsettling influence (imperviousness to the activity of insulin) that may have critical ramifications for long haul wellbeing.

## INTRODUCTION

Polycystic Ovary Syndrome (PCOS), present in 6-10% of conceptive matured ladies, is the most widely recognized endocrinopathy in this population and adds to increased infertility [1-4], dyslipidaemia [5,6], and especially expanded danger of type 2 diabetes [7,8]. It is presently comprehended that around 75% of these patients are insulin resistant and/or hyperinsulinemic [9], and are considerably more Insulin resistant than BMI-coordinated non-PCOS controls [10]. High insulin focuses are considered to assume a noteworthy part in the pathophysiology of PCOS, adding to both hyperandrogenism and oligomenorrhea/infertility [10]. Raised insulin focuses add to hirsutism and anovulation by enlarging LH discharge by the pituitary organ [11], diminishing blend of SHBG by the liver [12], and acting synergistically with LH on ovarian theca cells to fortify testosterone combination [1]. Hyperinsulinemia and insulin resistance additionally potentiate the maladaptive cardiovascular danger profile [13] that happens in PCOS, including fasting and postprandial hypertriglyceridemia [14], diminished high thickness lipoprotein cholesterol (HDL-C) [14], expanded plasma plasminogen activator inhibitor [9], diminished fibrinolytic limit [15], second rate systemic irritation [16], endothelial brokenness [17], and expanded danger for atherosclerotic illness [18]. In this way, bringing down encompassing insulin fixations in ladies with PCOS may have various useful impacts.

Polycystic ovary disorder (PCOS), a standout amongst the most widely recognized reasons for ovulatory infertility, influences 4-7% of ladies. In spite of the fact that it was viewed as that PCOS may have some hereditary segment and that clinical components of this issue may change for the duration of an existence range, beginning from immaturity to postmenopausal age, no exertion has been made to characterize contrasts in the phenotype and clinical presentation as indicated by age. For sure, it has been broadly perceived in the most recent decade that few components of metabolic disorder, especially insulin resistance and hyperinsulinemia, are conflictly present in the lion's share of ladies with PCOS. This speaks to a vital variable in the assessment of PCOS all through life, which infers that PCOS independent from anyone else may not be a hyper androgenic turmoil only identified with youthful and rich matured ladies, however may likewise have some wellbeing suggestions sometime down the road [19-27].

In young ladies with PCOS, hyperandrogenism, menses anomalies, and insulin resistance may happen together, stressing the pathophysiological part of abundance androgen and insulin on PCOS. Hyperandrogenism and barrenness speak to the real grumbings of PCOS in grown-up ripe age. Also, weight and MS may influence more than a large portion of these ladies [27-37]. Further down the road, it turns out to be clear that the relationship of weight (especially the stomach phenotype) and PCOS renders influenced ladies more powerless to create type 2 diabetes mellitus (T2DM), with some distinction in the commonness rates among nations, recommending that natural elements are essential in deciding individual weakness. Little is thought about ovarian morphology and

androgen generation in ladies with PCOS after menopause [38-42]. A few studies found that morphological ultrasonographic highlights steady with polycystic ovaries are extremely basic in postmenopausal ladies, and that these components are connected with higher than typical testosterone levels and metabolic changes. There is an undeniable requirement for further research here. Distinguishing proof of real objections and elements of PCOS amid the diverse ages of an influenced lady may help, truth is told, to arrange singular remedial methodologies, and, conceivably, forestall long haul incessant metabolic sicknesses [43-57].

### TREATMENT

Bringing down insulin grades with metformin [58,59], thiazolidinedione's [60,61], and dietary weight reduction [62] have been connected with diminished androgen fixations, expanded ovulation and pregnancy, and diminished plasma triglycerides in insulin safe ladies with PCOS. While metformin is as often as possible used to treat PCOS, it is not a genuine insulin sensitizer, and thiazolidinedione's, while viable in diminishing insulin resistance and encompassing insulin focuses [63], cause weight addition, may expand danger of cardiovascular occasions [64], potentiate osteoporosis [65], liquid maintenance [66], and are not affirmed for use in pregnancy. Dietary weight reduction, the principal line intercession, is sheltered and can lessen encompassing insulin focuses by 30% [67], however is occasionally managed [68], and in this manner long haul advantages are once in a while figured it out.

### MANIFESTATIONS IN THE INITIAL STAGES

PCOS is connected to changes in hormone levels that make it harder for the ovaries to discharge completely developed (full grown) eggs. The purposes behind these progressions are misty. The hormones influenced are:

- Estrogen and progesterone, the female hormones that help a lady's ovaries discharge eggs.
- Androgen, a male hormone that is found in little sums in ladies.

Ordinarily, one or more eggs are discharged amid a lady's cycle. This is known as ovulation. By and large, this arrival of eggs happens around 2 weeks after the begin of a menstrual period.

In PCOS, full grown eggs are not discharged. Rather, they stay in the ovaries with a little measure of liquid around them. There can be a large portion of these. Be that as it may, not all ladies with the condition will have ovaries with this appearance. These issues with the arrival of eggs can add to fertility. Alternate manifestations of this issue are because of the hormone uneven characters.

More often than not, PCOS is analysed in ladies in their 20s or 30s. In any case, it might likewise influence young ladies. The side effects regularly start when a young lady's periods begin. Ladies with this issue frequently have a mother or sister who has comparable side effects.

- Not getting a period after you have had one or more typical ones amid pubescence (auxiliary amenorrhea)
- Irregular periods that may travel every which way, and be light to substantial

Side Effects of PCOS:

- Extra body hair that develops on the mid-section, gut, face, and around the areolas
- Acne on the face, mid-section, or back
- Skin changes, for example, dull or tough skin markings and wrinkles around the armpits, crotch, neck, and bosoms

The advancement of male attributes is not run of the mill of PCOS and may demonstrate another issue. The accompanying changes may show another issue separated from PCOS:

- Thinning hair on the head at the sanctuaries, called male example sparseness.
- Enlargement of the clitoris
- Deepening of the voice
- Decrease in bosom size

Certain way of life changes, for example, eating regimen and activity are viewed as first-line treatment for juvenile young ladies and ladies with polycystic ovarian disorder (PCOS). Pharmacologic medicines are saved for purported metabolic disturbances, for example, anovulation, hirsutism, and menstrual inconsistencies [69-72]. Mean platelet volume is a marker connected with unfavourable cardiovascular occasions, and ladies with recently analysed PCOS seem to have essentially raised MPV levels. Kabil Kucur et al reported that utilization of ethinyl estradiol/cyproterone acetic acid derivation or metformin for the treatment of ladies with PCOS appeared to have comparative valuable impacts in decreasing MPV [73-78].

Consultation with an endocrinologist is important for playing out an adrenocorticotrophic hormone (ACTH) incitement test or for different reasons for menstrual anomaly, for example, thyroid malady or pituitary adenoma. A conceptive endocrinologist ought to be counselled if the patient is barren and wishes pregnancy [78-82]. Most doctors would concur that polycystic ovary disorder (PCOS) can be analysed clinically in the lady giving hirsutism, sporadic menstrual cycles, weight, and an exemplary ovarian morphology; in any case, impressive contention remains in regards to the demonstrative criteria for PCOS in ladies who present with less of the great side effects [83-88]. After extensive level headed discussion at a 1990 National Institutes of Health Conference on PCOS, three insignificant criteria were proposed [88-100].

### CONCLUSION

PCOS is an intricate condition in ladies with indications over the lifespan and mirrors a noteworthy wellbeing and monetary weight in numerous nations. Treatment ought to target both short and long-term regenerative, metabolic and mental angles. Given the aetiological part of insulin resistance and the effect of heftiness on both hyperinsulinaemia and hyperandrogenism. Misfortune in body weight of around 5% to 10% has been appeared to enhance large portions of the side effects of PCOS. Administration of PCOS ought to concentrate on restorative treatment alongside bolster, training, tending to mental needs and empowering sound way of life. Checking and administration of long haul metabolic confusions is likewise a vital piece of routine clinical consideration. Screening high-chance relatives for metabolic issue ought to likewise be made a need.

### REFERENCES

1. Jafarian T, et al. Are beta2-Adrenergic Receptor Gene Single-Nucleotide Polymorphisms Associated with Polycystic Ovary Syndrome? A Pharmacogenetic Study. *Gynecol Obstet (Sunnyvale)*. 2015;5:343.
2. Zemer VS, et al. Sotos Syndrome with Co-Morbid Polycystic Kidney Disease: A Case Report. *J Clin Case Rep*. 2015;5:612.
3. Mbamara SU, et al. Successful Pregnancy in a Woman with Chronic Kidney Disease Due to Autosomal Polycystic Disease-A Case Report. *Gynecol Obstet (Sunnyvale)*. 2015;5:338.
4. Dalia P, et al. Substituting Poly and Mono-unsaturated Fat for Dietary Carbohydrate Reduces Hyperinsulinemia in Women with Polycystic Ovary Syndrome. *J Nutr Food Sci*. 2015;5:429.
5. Sharma TR. Polycystic Ovarian Syndrome and Borderline Personality Disorder: 3 Case Reports and Scientific Review of Literature. *J Psychiatry*. 2015;pp:336.
6. Mariusz N, et al. Liver Cysts in Autosomal Dominant Polycystic Kidney Disease. *J Kidney*. 2015;1:i101.
7. Kabel MA. Polycystic Ovarian Syndrome: Insights into Pathogenesis, Diagnosis, Prognosis, Pharmacological and Non-Pharmacological Treatment. *J Pharma Reports*. 2016;1:103.
8. Mahendru R and Bansal S. Lifestyle Modifications as the first line therapy in Polycystic Ovary Syndrome. *J Preg Child Health*. 2016;e128.
9. Junfen L, et al. Bone Morphogenetic Proteins are Significantly Reduced in the Follicular Fluid of Han Chinese Polycystic Ovary Syndrome Patients. *Reprod Syst Sex Disord*. 2016;5:160.
10. Elise C, et al. Polycystic Ovarian Syndrome and Eating Disorder Quality of Life: A Pilot Study. *JFIV Reprod Med Genet*. 2016;4:171.
11. Werner TWR. Adult Dominant Polycystic Kidney Disease (ADPKD). *J Med Surg Pathol*. 2016;1:104.

12. Chhabra S and Taori A (2016) Polycystic Ovarian Syndrome in Perimenopausal Women: A Pilot Study. *Reprod Syst Sex Disord*. 2015;5:157.
13. Mohamed SA. Renal Stem Cells Transplantation in Autosomal Recessive Polycystic Kidney Disease; a Visible Science Fiction. *Gen Med (Los Angeles)*. 2016;257.
14. Iljazovic E. Polycystic Ovarian Syndrome in Perimenopausal Women:A Pilot Study- Observation Regarding Study Approach. *Reprod Syst Sex Disord*. 2016;5:177.
15. Kansra AR and Marquart K. Comparison of Clinical and Biochemical Parameters in Adolescent Girls with Polycystic Ovary Syndrome in Different Clinical Settings. *J Women's Health Care*. 2016;5:310.
16. Neoklis AG, et al. Polycystic Ovarian Morphology is Associated with Hyperandrogenemia and Insulin Resistance in Women with Polycystic Ovary Syndrome (PCOS). *J Steroids Horm Sci*. 2016;7:169.
17. Abiad F, et al. Bariatric Surgery in the Management of Adolescent and Adult Obese Patients with Polycystic Ovarian Syndrome. *J Obes Weight Loss Ther*. 2016;6:303.
18. Ciriza PC and Varo N. Serum Osteoprotegerin is Diminished in the Polycystic Ovary Syndrome and Associated with Insulin Resistance. *Biochem Anal Biochem*. 2016;5:247.
19. Sur D and Chakravorty R. Genetic Polymorphism in the Vitamin D Receptor Gene and 25-Hydroxyvitamin D Serum Levels in East Indian Women with Polycystic Ovary Syndrome. *J Mol Biomark Diagn*. 2015;6:247.
20. Singh V. Polycystic Kidney Disease: A Paradigm in Major Kidney Disorders. *Biochem Physiol*. 2015;4:161.
21. Xianqin Q and Madeleine O. Successful Treatment of Polycystic Ovarian Syndrome, Nonalcoholic Fatty Liver Disease and Infertility with Chinese Herbal Medicine:A Case Report. *Endocrinol Metab Syndr*. 2015;4:183.
22. Xianqin Q. Natural Approach to Coexisting Non-alcoholic Fatty Liver Disease and Polycystic Ovarian Syndrome. *Endocrinol Metab Syndr*. 2015;4:182.
23. Sandhu H and Kuburas R. Insulin Resistance in Women with Polycystic Ovary Syndrome: Optimising treatment by Implementing an in vitro Insulin Resistance Organ Culture Model. *Clinics Mother Child Health*, 2015.
24. Jennifer LP, et al. Low Starch/Low Dairy Diet Results in Successful Treatment of Obesity and Co-Morbidities Linked to Polycystic Ovary Syndrome (PCOS). *J Obes Weight Loss Ther*. 2015;5:259.
25. Frøssing S, et al. The LIPT-Study: On Risk Markers of Vascular Thrombosis in Polycystic Ovary Syndrome. A Randomized, Double-Blind, Placebo-Controlled Study of the Effect of Liraglutide. *J Obes*

- Weight Loss Ther. 2015;5:254.
26. Shuchi Jain, et al. Genetic Polymorphism of CYP1A1 (T6235C) Gene as a Risk Factor for Polycystic Ovary Syndrome. *Andrology (Los Angel)*. 2015;4:129.
  27. Abdelmegeed A, et al. A Comparative Study between GnRH Antagonist and Long Agonist Protocols in Patients with Polycystic Ovarian Syndrome (PCOS) undergoing in vitro Fertilization. *JFIV Reprod Med Genet*. 2015;3:137.
  28. Asma E and Elmahaishi MS (2015) Does the Use of Highly Purified Human Menopausal Gonadotrophin (HP-HMG) avoid Ovarian Hyperstimulation Syndrome (OHSS) in Polycystic Ovary (PCO) Patients in Assisted Reproduction (IVF/ICSI)? *Gynecol Obstet (Sunnyvale)*. 2015;5:273.
  29. Liern JM, et al. Use of Rapamycin in Pediatric Patients with Autosomal Dominant Polycystic Kidney Disease. *Gen Med (Los Angel)*. 2015;1:160.
  30. Jain M, et al. Genetic polymorphism of CYP1A1 (T6235C) Gene as a Risk Factor for Polycystic Ovary Syndrome. *Gynecol Obstet (Sunnyvale)*. 2015;5:263.
  31. Patel JN, et al. Congenital Hepatic Fibrosis Associated with Polycystic Kidney Disease. *J Liver*. 2015;4:171.
  32. Singh AK, et al. Do Aromatase Inhibitors Offer Better Choice Than Selective Estrogen Receptor Modulators For Management Of Polycystic Ovarian Syndrome? *Medical and Health Sciences*.
  33. Tan M and Kim SH. Does Polycystic Ovarian Syndrome Increase Insulin Resistance Above and Beyond Obesity? *Endocrinol Metab Syndr*. 2014;3:142.
  34. Unfer V, et al. Polycystic Ovary Syndrome: Features, Diagnostic Criteria and Treatments. *Endocrinol Metab Syndr*. 2014;3:136.
  35. Zahid N. Role of Anti-Mullerian Hormone (AMH) in Polycystic Ovary Syndrome (PCOS)? A Mini Review. *Reprod Syst Sex Disord*. 2014;3:143.
  36. Huang D, et al. Low Frequency Electro-Acupuncture and Physical Exercise Induces Menstruation in A Young Woman with Amenorrhea Related to Polycystic Ovary Syndrome: A Case Report. *Altern Integ Med*. 2014;3:166.
  37. Nagesh AK, et al. Past, Present and Future of Insulin Gene and Its Related Genes In Relation To Polycystic Ovary Syndrome. *J Mol Genet Med*. 2014;8:107.
  38. Vine DF, et al. Insulin and Testosterone are Associated with Elevated Intestinal Secretion of Lipids and Lipoproteins in a Rodent Model of the Metabolic and Polycystic Ovary Syndrome. *J Diabetes*

- Metab. 2014;5:391.
39. Sahin AE, et al. Positive Effects of Acupuncture on Menstrual Irregularity and Infertility in a Patient with Polycystic Ovary Syndrome. *Fam Med Med Sci Res.* 2014;3:121.
  40. Neves E, et al. Polycystic Ovary Syndrome: Correlation between Phenotypes and Metabolic Syndrome. *J Steroids Horm Sci.* 2013. 2014;5:132.
  41. Julia VL, et al. Prevalence of Gestational Diabetes Mellitus in Patients with Polycystic Ovary Syndrome. *J Diabetes Metab.* 2014;5:354.
  42. Cnossen WR and Drenth JPH. Somatic Hits in Polycystic Liver Diseases. *J Carcinog Mutagen.* 2014;5:154.
  43. Antonio SL and Alfonsa P. Know your Enemy: The Rationale of Using Inositol in the Treatment of Polycystic Ovary Syndrome. *Endocrinol Metab Syndr.* 2013;2:e121.
  44. Ayla U, et al. The Fluctuation in the Heart Rate Variability Throughout Ovulation Induction Cycle: Is the Case Different in Polycystic Ovary Syndrome? *Gynecol Obstet (Sunnyvale).* 2013;3:172.
  45. Orakpo N and Swan J. Zumba: An Antidote for Uncontrolled Weight Gain Associated with Polycystic Ovarian Syndrome with Subclinical Hypothyroidism? *J Gerontol Geriatric Res.* 2013;2:132.
  46. Elsayed MA. Agnucaston and Clomiphen Citrate in Infertile Patients with Polycystic Ovaries. *J IVF Reprod Med Genet.* 2013;1:108.
  47. El-Hafez HAA, et al. Thyroid Function and Volume are Associated with Anthropometric Measurements and Insulin Resistance in Egyptian Women with Polycystic Ovary Syndrome. *J Diabetes Metab.* 2013;4:288.
  48. Mohan SK and Priya VV. Lipid peroxidation, glutathione, ascorbic acid, vitamin E, antioxidant enzyme and serum homocysteine status in patients with polycystic ovary syndrome. *Biology and medicine,* 2009.
  49. Baris Ata, et al. Effect of Body Mass Index on In Vitro Maturation Treatment Outcomes in Women without Polycystic Ovarian Syndrome. *J IVF Reprod Med Genet.* 2013;1:104.
  50. Karaca I, et al. Treatment of Premenstrual Syndrome with Progesterone in Women with Polycystic Ovary Syndrome. *Gynecol Obstet (Sunnyvale).* 2013;3:151.
  51. Wetzka B, et al. An h-OGLT is an Appropriate Approach for the Determination of Glucose and Insulin Dynamics in Female Functional Androgenization (Including ?Polycystic Ovary Syndrome?). *Endocrinol Metab Syndr.* 2013;S1:011.

52. Denaday F. Polycystic Ovary Syndrome (PCOS). *J Fertiliz In Vitro*. 2012;2:117.
53. Nasr AAM, et al. A Modified Technique of Laparoscopic Ovarian Drilling for Polycystic Ovary Syndrome Using Harmonic Scalpel. *J Diabetes Metab*. 2013;S6:008.
54. Hamid Akbari, et al. The First Report of Clinical and Pathological Studies of Polycystic Kidney Disease in a Herrik Lamb in the Middle East. *J Bacteriol Parasitol*. 2012;3:139.
55. Tomic V and Tomic J. Infertility Treatment in Patients with Polycystic Ovary Syndrome (PCOS). *J Fertiliz In Vitro*. 2012;2:e113.
56. Krishna VV. Chronic Disease and Polycystic Ovary Syndrome: Are they Related? *J Women's Health Care*. 2012;1:101e.
57. Polycystic Ovary Syndrome and Insulin Resistance. *J Diabetes Metab*. 2012;S2:005.
58. Yiqiang Cai. Role of Animal Models in the Study of Human Genetic Polycystic Kidney Disease. *Hereditary Genet*. 2012;1:e102.
59. Gattone VH and Bacallao. Novel Therapies for Polycystic Kidney Disease. *J Genet Syndr Gene Ther*. 2011;S4:001.
60. Mohamed SS, et al. Hypertension in Black Africans with Autosomal Polycystic Kidney Disease. *J Nephrol Ther*. 2011;1:102.
61. Stephen F. Polycystic ovary syndrome. *N Engl J Med*. 1995;333:853-861.
62. David AE. Polycystic ovary syndrome. *N Engl J Med*. 2005;352:1223-1236.
63. Robert NJ. Polycystic ovary syndrome. *The Lancet*. 2007;370:685-697.
64. David GS. Polycystic ovary syndrome. *Obstet Gynecol*. 2004;103:181-193.
65. Homburg R. Polycystic ovary syndrome. *Best Pract Res Clin Obstet Gynaecol*. 2008;22:261-274.
66. Goudas VT and Dumesic DA. Polycystic ovary syndrome. *Endocrinol Metab Clin North Am*. 1997;26:893-912.
67. Pasquali R and Gambineri A. Polycystic ovary syndrome. *Ann N Y Acad Sci*. 2006;1092:158-174.
68. Taylor AE. Polycystic ovary syndrome. *Endocrinol Metab Clin*. 1998;27:877-902.
69. King J. Polycystic ovary syndrome. *J Midwifery Womens Health*. 2006;51:415-422.



70. Franks S. Polycystic ovary syndrome. *Arch Dis Child*. 1997;77:89-90.
71. Cheung AP and Chang RJ. Polycystic ovary syndrome. *Clin Obstet Gynecol*. 1990;33:655-657.
72. Nandi A, et al. Polycystic ovary syndrome. *Endocrinol Metab Clin North Am*. 2014;43:123-147.
73. Chen ZJ and Shi Y. Polycystic ovary syndrome. *Front Med*. 2010;4:280-284.
74. Eshre TR and Group ASPCW. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril*. 2004;81:19-25.
75. Ginsburg J and Havard CW. Polycystic ovary syndrome. *BMJ*. 1976;2:737.
76. Macut D, et al. *Polycystic Ovary Syndrome*. Karger Medical and Scientific Publishers, 2012.
77. Chang RJ. *Polycystic ovary syndrome*. Springer Science & Business Media, 2012.
78. Legro RS, et al. 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 Endocrinol Metab* 1999;84:165-169.
79. Azziz R, et al. The prevalence and features of the polycystic ovary syndrome in an unselected population. *J Clin Endocrinol Metab*. 2004;89:2745-2749.
80. Dunaif A, et al. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. *Diabetes*. 1989;38:1165-1174.
81. Knochenhauer ES, et al. Prevalence of the Polycystic Ovary Syndrome in unselected black and white Women of the Southeastern United States: A prospective study. *J Clin Endocrinol Metab* 1998;83:3078-3082.
82. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis 1. *Endocr Rev* 1997;18:774-800.
83. Shelley DR and Dunaif A. Polycystic ovary syndrome. *Comprehensive therapy*. 1990;16:26-34.
84. Dewailly D. Polycystic ovary syndrome. *J Gynecol Obstet Biol Reprod*. 2000;29:298-301.
85. Velazquez EM, et al. Metformin therapy in polycystic ovary syndrome reduces hyperinsulinemia, insulin resistance, hyperandrogenemia, and systolic blood pressure, while facilitating normal menses and pregnancy. *Metabolism*. 1994;43:647-654.
86. Kiddy DS, et al. Improvement in endocrine and ovarian function during dietary treatment of obese women with polycystic ovary syndrome. *Clin endocrinol*. 1992;36:105-111.



87. Asunción M, et al. A prospective study of the prevalence of the polycystic ovary syndrome in unselected caucasian women from spain. *J Clin Endocrinol Metabol.* 2000;85:2434-2438.
88. Dahlgren E, et al. Women with polycystic ovary syndrome wedge resected in 1956 to 1965: a long-term follow-up focusing on natural history and circulating hormones. *Fertility and sterility.* 1992;57:505-513.
89. Gilling-Smith C and Franks S. Polycystic ovary syndrome. *Reprod Med Rev.* 1993;2:15-32.
90. Ehrmann DA, et al. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. *Diabetes care.* 1999;22:141-146.
91. Azziz R, et al. Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an androgen excess society guideline. *J Clin Endocrinol Metabol.* 2006;91:4237-4245.
92. Diamanti-Kandarakis E, et al. A survey of the polycystic ovary syndrome in the Greek island of Lesbos: hormonal and metabolic profile. *J. Clin. Endocrinol. Metab* 1999;84:4006-4011.
93. Franks S. Polycystic ovary syndrome. *Trends Endocrinol Metab,*1989;1:60-63.
94. Lord JM, et al. Metformin in polycystic ovary syndrome: systematic review and meta-analysis. *BMJ.* 2003;327:951.
95. Khan KA, et al. Polycystic ovarian syndrome. *J Cardiometab Syndr.* 2006;1:125-132.
96. Yen SSC. Review article: the polycystic ovary syndrome. *Clin Endocrinol.* 1980;12:177-208.
97. Carmina E, et al. Does ethnicity influence the prevalence of adrenal hyperandrogenism and insulin resistance in polycystic ovary syndrome? *Am J Obstet Gynecol.* 1992;167:1807-1812.
98. Balen AH, et al. Andrology: Polycystic ovary syndrome: the spectrum of the disorder in 1741 patients. *Human Reproduction.* 1995;10:2107-2111.
99. Legro RS, et al. A Fasting Glucose to Insulin Ratio Is a Useful Measure of Insulin Sensitivity in Women with Polycystic Ovary Syndrome. *J Clin Endocrinol Metabol.* 1998;83:2694-2698.
100. Apridonidze T, et al. Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome. *J Clin Endocrin & Metabol.* 2005;90:1929-1935.