

# Association of Metabolic Syndrome in Polycystic Ovary Syndrome: Prevalence and Correlation with Infertility - An Overview

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**Abstract:** Background: Polycystic ovarian syndrome (PCOS) is the most common form of anovulatory infertility associated with insulin resistance and obesity. It is a common condition that affects 20% of women of reproductive years. Prevalence of obesity and diabetes mellitus is on the rise owing to urbanization and change in lifestyle. Objective: The aim of the present study was to find out the relationship between PCOS and metabolic syndrome. Materials and Methods: The observational study conducted on 100 women with PCOS (according to Rotterdam criteria) with age of 18 and 35 years and assessed to metabolic syndrome (according to NCEP criteria) and normal pelvic study. Women having diabetes, hypertension, cardiovascular disease, hypothyroidism/ hyperprolactinaemia and secondary causes of androgen excess were excluded from the study. Results: Prevalence of metabolic syndrome is 36%. 63.33% of patients aged 30 – 40 years with fasting hyperglycaemia have metabolic syndrome. Metabolic syndrome (low HDL level) is present in PCOS patient even with normal weight (BMI = 18.5 - 22.99kg/m<sup>2</sup>). The prevalence was higher among obese (91.67%) and morbidly obese (100%). Conclusion: metabolic syndrome manifests at an early age in women with Polycystic ovarian syndrome. PCOS is a sedentary life and obesity related disorder. In PCOS patients diagnosed with metabolic syndrome, progression of syndrome can be altered or retarded by lifestyle modifications.

**Keywords:** Diabetes mellitus, Metabolic Syndrome, Prevalence, Polycystic Ovarian Syndrome.

## 1. Introduction

Polycystic ovarian syndrome (PCOS) is the most common form of anovulatory infertility. PCOS is frequently associated with insulin resistance and obesity<sup>[1]</sup>. It is also one of most common endocrine disorder in women of reproductive age, affecting 5% to 10% of women worldwide<sup>[2]</sup>. The condition is relatively common and affects about 20% of women of reproductive years. The diverse manifestations of PCOS start at an early age when a girl is maturing into a young woman. It is characterized by combination of hyperandrogenism (either clinical or bio-chemical), chronic anovulation and polycystic ovaries<sup>[3]</sup>.

PCOS is characterized by chronic anovulation, oligomenorhea or amenorrhea, hyperandrogenism and polycystic ovary morphology on pelvic ultrasound. The condition is a diagnosis of exclusion and has been a topic of debate and many definitions have evolved over years. Despite insulin resistance in adipose and skeletal muscle, the ovary remains relatively sensitive to insulin. Potentially a gene or series of genes renders the ovaries susceptible to insulin<sup>[4-8]</sup>.

Globally, the prevalence of PCOS ranges from 2.2% to 26%.<sup>[9]</sup> Women with PCOS are also at higher risk for Insulin resistance, Type 2 diabetes mellitus, Obesity, Dyslipidemia, Hypertension, atherosclerotic cardiovascular disease.

In attempting to determine the prevalence of MBS in PCOS, a major variable is the criteria used to define metabolic syndrome<sup>10, 11</sup>. Most widely adapted are the criteria

proposed by the American National Cholesterol Panel (Adult Treatment Panel III (ATP - III)).<sup>[12, 13]</sup> These criteria require the presence of 3 of 5 common CV risk factors (increased waist circumference, blood pressure, elevated fasting blood glucose, low serum high - density lipoprotein (HDL) - cholesterol, and increased triglycerides). Using these criteria, the prevalence in PCOS has been reported to be extremely high, 43–46%<sup>[14, 15]</sup>, primarily on the basis of abnormal lipids and increased waist circumference.

Prevalence of obesity and diabetes mellitus in India is also on the rise owing to urbanization and change in lifestyle. Recent data shows that about one - third of the urban population from large cities of India have the metabolic syndrome. PCOS is one of the major risk factor for metabolic syndrome and the prevalence of metabolic syndrome in PCOS is 40 - 50%<sup>[16]</sup>. The present study was aimed to find out the relationship between PCOS and metabolic syndrome.

## 2. Material and Methods

The observational study was done on 100 women with PCOS (according to Rotterdam criteria) with age of 18 and 35 years and assessed to metabolic syndrome (according to NCEP criteria) and normal pelvic study.

Nature of the study was explained in detail after that informed consent for participating in the study was obtained.

Patients with PCOS were divided into two subgroups according to their particular phenotype: women had

hyperandrogenism and chronic anovulation (classic (C) - PCOS) and hyperandrogenism and polycystic ovaries but normal ovulatory cycles (ovulatory (OV) - PCOS).

**Inclusion Criteria**

- Women with PCOS of age group 18 - 35yr (according to Rotterdam’s criteria).

**Exclusion Criteria**

Women with the following factors were excluded from the study:

- Age >35years.
- Women having Diabetes, hypertension and cardiovascular disease.
- Women more than 40 years of age with irregular periods.
- Females with hypothyroidism/ hyperprolactinaemia.
- Secondary causes of androgen excess.

**Investigations:** Age, weight, waist circumference and blood pressure were recorded.

**Collection of blood samples:** Fasting blood sample of about 6 ml was obtained from the patient for estimation of fasting plasma glucose, high density lipoprotein cholesterol (HDL - c) and triglycerides levels. Plasma glucose was measured by hexokinase/glucose oxidase peroxidase method. HDL - C and triglyceride levels were measured by enzymatic colorimetric method by enzymatic colorimetric method.

**Rotterdams criteria for PCOS [17]:** Two out of three should be present – (1) oligoovulation/ an ovulation (amenorrhea / oligomenorrhea), (2) hyperandrogenism (clinical or bio - chemical) hirsutism, acne, alopecia, elevated level of free or total testosterone and (3) polycystic ovary on USG.

**Criteria for metabolic syndrome [18]:** Three out of five should be present (1) fasting glucose level  $\geq 100$  (2), systolic bp of  $>130$ mmhg and systolic of  $>84$ mmhg (3) waist circumference  $> 35$ inches (4) serum triglyceride  $>150$ mg/dl (5) HDL cholesterol  $< 50$ mg/dl

**3. Results**

Metabolic syndrome was present in 36 (36.0%) cases. Thus, the prevalence of metabolic syndrome is 36%. As the age increases, the prevalence of metabolic syndrome increases i. e. (11/17) 64.70% patients belong to 31 – 40 years.

**Table 1:** Characteristics of Cases

Parameters	No. of cases	Percentage
<b>BMI</b>		
Normal (18.5 - 22.99)	34	34.0
Overweight (23 - 24.99)	16	16.0
Pre - obese (25 - 29.99)	31	31.0
Obese (30 - 39.99)	16	16.0
Morbidity obese (>40)	3	3.0
<b>Parity</b>		
Unmarried	10	10.0
Nulligravida	40	40.0
Primipara	25	25.0
Multipara	25	25.0
<b>Complaints</b>		

Menses disturbances	45	45.0
Primary infertility	40	40.0
Secondary infertility	10	10.0
Hirsutism	5	5.0

**Table 2:** Prevalence of fasting hyperglycemia with age group in metabolic syndrome patients

Age group	No. of patient with metabolic syndrome	Presence of fasting hyperglycemia	Prevalence (%)
<25 yrs	10	4	40.0
26 - 30	15	8	53.0
>30 yrs	11	7	63.33

Metabolic syndrome and hyperglycaemia strongly overlap which ultimately be explained by a common pathogenesis of common clustered conditions. About 63.33% of patients aged 30 – 40 years with fasting hyperglycaemia have metabolic syndrome

**Table 3:** Prevalence of low HDL in different BMI in metabolic syndrome patients

BMI	No. of patient with metabolic syndrome	Presence of Low HDL level	Prevalence (%)
Normal (18.5 - 22.99)	1	1	100
Overweight (23 - 24.99)	4	1	25.0
Pre - obese (25 - 29.99)	17	13	76.47
Obese (30 - 39.99)	12	11	91.67
Morbidity obese (>40)	2	2	100

Metabolic syndrome (low HDL level) is present in PCOS patient even with normal weight. This implies the importance of looking towards the visceral fat rather than subcutaneous fat; out of 12 obese, 11 have low HDL level.

**Table 4:** Prevalence of high triglyceride level in different BMI in metabolic syndrome patients

BMI	No. of patient with metabolic syndrome	Presence high triglyceride level	Prevalence (%)
Normal (18.5 - 22.99)	1	1	100
Overweight (23 - 24.99)	4	2	50.0
Pre - obese (25 - 29.99)	17	12	70.58
Obese (30 - 39.99)	12	11	91.67
Morbidity obese (>40)	2	2	100

The prevalence was higher among obese (91.67%) and morbidly obese (100%).

**4. Discussion**

There are 100 women who are diagnosed to have the polycystic ovarian syndrome, but had different presenting complaints. The prevalence of metabolic syndrome about 36%. Prevalence of IDF defined metabolic syndrome was

29.6% compared to 25.9% using the 2005 ATPIII criteria according to Hildrum et al 2007 study<sup>[19]</sup> which is in accordance with the present study. In our study, the prevalence of metabolic syndrome increases as BMI increases in the PCOS population. In the study conducted by Kalra, et<sup>[20]</sup>, the percentage of pre obese was 44% which is comparable with the present study 47.22%.

In our study, 97.22% were found to have increased FBS, 77.78% have elevated TGL level and 72.22% have low HDL which were comparable to other studies (Table - 5).

**Table 5:** Parameters compared with other studies

Parameters	Our study	Mandrelle et al <sup>[21]</sup> , 2012	Sidra et al <sup>[22]</sup> , 2019	Mehranghiz et al <sup>[23]</sup> , 2015
Elevated S. TGL	77.8%	40.0	19.3%	43.5%
Low S. HDL	72.22%	93.3	80.0%	82.6%
Fasting hyperglycemia	97.22%	25.0	63.2%	13.0%

A waist circumference of 80 cm or above is taken as cut off for metabolic syndrome. The mean waist circumference in metabolic syndrome group is 94.6 cm and in PCOS population without metabolic syndrome it is 83.5 cm with a mean difference of 11.1. Patients not falling into the criteria of metabolic syndrome also had a waist circumference of 80 cm and above. But they didn't have the other parameters to brand them as metabolic syndrome.

In our study most of the cases (40.0%) were belongs to nulligravida followed by multigravida and primigravida each comprises 25.0% of cases. 45.0% of cases presents complaints of disturbances mensus followed by primary infertility which comprises 40.0% of cases. . As PCOS has a linear correlation with metabolic syndrome, it has a galloping rise along with type 2 DM. 80% of an ovulatory infertility is due to PCOS<sup>[24]</sup>. Alaknanda et al<sup>[25]</sup> showed the presence of Primary infertility in 54%. In the study by Joshi et al.<sup>[26]</sup> 46% of patients were married and 43% complained of infertility. Ramanand et al<sup>[27]</sup> in the study on 120 PCOS women, 47 were married and 44.68% of married women complained of infertility.

Metabolic syndrome and hyperglycaemia strongly overlap which ultimately be explained by a common pathogenesis of common clustered conditions. About 63.33% of patients aged 30 – 40 years (Table - 2) with fasting hyperglycaemia have metabolic syndrome, which make it as a strong predictor for long term risk for CHD as well as for diabetes<sup>[28]</sup>

This implies the importance of increasing insulin sensitivity through insulin sensitizers, exercise in the adolescent age group to prevent the increased prevalence of diabetes. Therapeutic carbohydrate restricted diet can prevent or reverse the components of metabolic syndrome and diabetes.

Of the 100, the most common problem for which a PCOS woman attending a hospital visit is menstrual irregularity according to our study (45% had menstrual irregularity in terms of oligomenorrhea and amenorrhea as their presenting complaint). Infertility was the presenting complaint in 40%,

10.0% had secondary infertility and 5.0% came for hirsutism and acne (Table - 1).

Alaknanda et al<sup>[25]</sup> showed the presence of Primary infertility in 54%. In the study by Joshi et al.<sup>[26]</sup> 46% of patients were married and 43% complained of infertility. Ramanand et al<sup>[27]</sup> in the study on 120 PCOS women, 47 were married and 44.68% of married women complained of infertility.

Among the participants in the study, most of them were nulligravida (40.0%), followed by Primi and multigravida each comprises (25.0%) cases and the major complaint was infertility (40%) which is comparable to Ramanand et al<sup>[27]</sup> study.

## 5. Conclusion

It is observed from the present study that metabolic syndrome manifests at an early age in women with Polycystic ovarian syndrome. The present study highlights the need or comprehensive screening or metabolic syndrome in women with PCO attending OPD. PCOS being a common condition prevailing in women with reproductive age group, is the cause of problem for 36 per in 100 patients attending a Gynaecologists. Counseling regarding maintaining normal BMI, with an acceptable waist circumference should be made available to all women especially those diagnosed with PCOS. PCOS is a sedentary life and obesity related disorder. Thus in PCOS patients diagnosed with metabolic syndrome, progression of syndrome can be altered or retarded by lifestyle modifications.

## References

- [1] Legro RS, Kunselman AR, Dodson WC, Duanif A. 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: 165–69.
- [2] Jeengar P, Chauhan M. Association of metabolic syndrome in polycystic ovarian syndrome. *The New Indian Journal of OBGYN.*2017; 3 (2): 90 - 4
- [3] Stein IF, Leventhal ML. Amenorrhoea associated with bilateral polycystic ovaries. *Am J Obstet Gynecol.*1935; 29: 181 - 91
- [4] Crossgnanil PG, Nicolosi AE. Polycystic ovarian disease: Heritability and heterogeneity. *Hum report.*2001; 7: 3 - 7
- [5] Franks S, Gilling - Smith C, Gharani N, McCarthy M. Pathogenesis of polycystic ovary syndrome: evidence for a genetically determined disorder of ovarian androgen production. *Hum Fertil.*2000; 3: 77–9.
- [6] Gharani N, Waterworth DM, Batty S, et al. Association of the steroid synthesis gene CYP11a with polycystic ovary syndrome and hyperandrogenism. *Hum Mol Gen.*1997; 6: 397–402
- [7] Waterworth DM, Bennett ST, Gharani N, et al. Linkage and association of insulin gene VNTR regulatory polymorphism with polycystic ovary syndrome. *Lancet.*1997; 349: 986–90.

- [9] Steppan CM, Bailey ST, Bhat S, et al. The hormone resist in links obesity to diabetes. *Nature*.2001; 409: 307 - 12
- [10] Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of polycystic ovarian syndrome in Indian adolescents. *J Pediatr Adolesc Gynecol*.2011 Aug; 24 (4): 223 - 7. doi: 10.1016/j. jpag.2011.03.002. Epub 2011 May 19. PMID: 21600812.
- [11] Doelle GC. The clinical picture of metabolic syndrome. *Postgraduate Medicine* 2004 116 35–38.
- [12] Prabhakaran D & Anand SS. The metabolic syndrome: an emerging risk state for cardiovascular disease. *Vascular Medicine* 2004 9 55–68.
- [13] Executive Summary of the Third Report of the National Cholesterol Education Program (NECP), Expert Panel on Detection,
- [14] Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *Journal of the American Medical Association* 2001 285 2486–2497.
- [15] Glueck CJ, Papanna R, Wang P, Goldenberg N & Sieve - Smith L. Incidence and treatment of metabolic syndrome in newly referred women with confirmed polycystic ovarian syndrome. *Metabolism* 2003 52 908–915.
- [16] Apridonidze T, Essah P, Iuorno M & Nestler JE. Prevalence and characteristics of metabolic syndrome in women with polycystic ovary syndrome. *Journal of Clinical Endocrinology and Metabolism* 2005 90 1929–1935.
- [17] Harrison's principles of internal medicine, 19 th edition.
- [18] The Rotterdam ESHRE/ASRM - Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long - term health risks related to polycystic ovary syndrome. *Fertil Steril*.2004; 81: 19–25
- [19] Executive Summary of the Third Report of the National Cholesterol Education Program (NECP), Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *Journal of the American Medical Association*.2001; 285: 2486–97.
- [20] Hildrum B, Mykletun A, Hole T, Midthjell K, Dahl AA. Age - specific prevalence of the metabolic syndrome defined by the International Diabetes Federation and the National Cholesterol Education Program: the Norwegian HUNT 2 study. *BMC public health*.2007 Dec; 7 (1): 1 - 9. .
- [21] Kalra A, Nair S, Rai L. Association of obesity and insulin resistance with dyslipidemia in Indian women with polycystic ovarian syndrome. *Indian J Med Sci*.2006; 60: 447 - 53.
- [22] Mandrelle K, Karmath Metabolic syndrome, Bondu DJ, Chandy A, Aleyamma TK, George K. Prevalence of metabolic. Syndrome in women with PCOS attending an infertility clinic in a tertiary care hospital in South India. *J Hum Reprod Sci*.2012; 5: 26 - 31.
- [23] Sidra S, Tariq MH, Farrukh MJ, Mohsin M. Evaluation of clinical manifestations, health risks, and quality of life among women with polycystic ovary syndrome. *PloS one*.2019 Oct 11; 14 (10): e0223329.
- [24] Megranghiz et al. Association of insulin resistance with lipid profile, metabolic syndrome, hormonal aberrations in overweight with PCOS. *J Health population nutrition*, 2015; 33 (1): 157 - 167.
- [25] Ashraf M, Kalra S. PCOS - A metabolic Malady, Mother of all lifestyle disorders in women. *Indian J Endocrinol Metab*.2011; 15 (4): 239 - 241.
- [26] Alaknanda et al. Dr Alakananda, Dr Bishnu Prasad Das, Dr Isha Goel, A Study on Clinical Profile of Patients with Polycystic Ovarian Syndrome Volume 6 Issue 10, October 2017, *International Journal of Science and Research (IJSR)*.
- [27] Joshi AM, Yonzon P, Tandukar S. Clinical Profile of Patients with Polycystic Ovarian Syndrome in Nepal. *Endocrinol Metab Int J*.2017; 4 (2): 83.
- [28] Ramanand SJ, Ghongane BB, Ramanand JB, Patwardhan MH, Ghanghas RR, Jain SS. Clinical characteristics of polycystic ovary syndrome in Indian women. *Indian journal of endocrinology and metabolism*.2013 Jan; 17 (1): 138.
- [29] Alexander CM, Landsman PB, Grundy SM. Metabolic syndrome and hyperglycemia: congruence and divergence. *American Journal of Cardiology*.2006 Oct 1; 98 (7): 982 - 5.