

Obesity and Insulin Resistance Among Infertile Women With Polycystic Ovarian Syndrome

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ABSTRACT

Objective To find out the frequency of obesity and insulin resistance among infertile women with polycystic ovarian syndrome (PCOS).

Study design Descriptive case series.

Place & Duration of study Baqai Institute of Reproduction & Developmental Sciences (BIRDS), from July 2012 to June 2013.

Methodology Women who had PCOS were selected on the basis of Rotterdam criteria between the ages of 16 to 40 years. Detailed history, physical examination, transvaginal ultrasound and hormone profile were done. Women who had other endocrinological problems like thyroid disorder, hyperprolactinemia, diabetes mellitus, Cushing syndrome and androgens producing tumours were excluded from the study.

Results A total of 318 (35.49%) infertile women were diagnosed as PCOS out of 896 women who visited BIRDS during the study period. Majority (n=178 - 55.97%) of the women were between 21-30 years of age. Oligomenorrhea was the commonest menstrual irregularity found in 203 (63.83%) women. Mild hirsutism was noted in 204 (64.15%) women. On transvaginal scan PCO were observed in 298 (93.71%) women. Class I obesity was observed in 64 (20.12%), while 8.49% (n=27) had class II obesity. Class III obesity was found in 2(0.62%) women only. The number of overweight women was 132(41.50%). High LH/FSH ratio was found in 185 (58.17%) women. Insulin resistance was observed in 201(63.20%) women.

Conclusion All manifestations of PCOS were more frequent and severe in obese patients.

Key words Polycystic ovarian syndrome, Obesity, Insulin resistance.

INTRODUCTION:

Polycystic ovarian syndrome was first described by Stein and Leventhal in 1935 in women with oligo-anovulation, obesity, hirsutism and enlarged polycystic ovaries.¹ The cause of PCOS is multifactorial and complex. The disease has genetic basis that is affected by environmental factors. Hyperandrogenism, ovulatory dysfunction (manifesting as a menstrual disturbance), insulin resistance, obesity, luteinizing hormone (LH)

hypersecretion, metabolic syndrome, and polycystic ovarian morphology are common characteristics found in women with PCOS, yet not all women with PCOS manifest each of these conditions.²

PCOS is defined by different criteria. National Institute of Health (NIH, 1991) defines PCOS as the condition having; (1) hyperandrogenism and / or hyperandrogenemia (2) oligo-anovulation and (3) exclusion of related disorders.³ Rotterdam criteria defines PCOS after excluding other relevant problems by two of three characteristics; (1) oligo-anovulation (2) clinical and or biochemical evidence of excess androgen production (3) polycystic ovaries on ultrasound.^{3,4}

Obesity is an important risk factor for PCOS.

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Literature review shows that 30-70% of PCOS females are obese, though disease is also seen in women of normal weight but with less frequency.⁵⁻⁷ About 40% of females with PCOS have insulin resistance which increases up to 70% in presence of obesity.⁶ Anovulation in PCOS leads to unopposed estrogen secretion which is a risk factor for endometrial hyperplasia and carcinoma. Detection of insulin resistance in PCOS may assist in planning optimal treatment for anovulatory infertility and hyperandrogenemia.⁸ Obesity is strongly associated with PCOS, but it is not always necessary for its development. The present research is focused to find out the frequency of obesity and insulin resistance among infertile women with PCOS.

METHODOLOGY:

This descriptive case study included a total 318 infertile women between the ages of 16-40 years who were selected from the outpatient department of Baqai Institute of Reproduction & Developmental Sciences over a period of one year from July 2012 to June 2013. The PCOS was diagnosed on the basis of Rotterdam criteria. All women who had other endocrinological problems were excluded.

Detailed history and physical examination were carried out. Variables noted were current age, age of menarche, age of onset of menstrual irregularity and infertility, clinical features of hyperandrogenism (hirsutism, acne) etc. Secondary amenorrhoea was defined as cessation of menstruation for six months in reproductive age group which was not due to pregnancy. Oligomenorrhoea meant menses at intervals of more than 35 days.⁹

Obesity was defined using World Health Organization (WHO) and National Institute of Health (NIH) criteria; underweight as body mass index (BMI) < 18.5, normal weight as BMI between 18.5-24.9, overweight as BMI between 25-29.9 and obesity as a BMI of 30 or greater.^{10,11} Obesity was further divided into class I (BMI 30-34.9), class II (BMI 35-39.9) and class III (BMI > 40). BMI was calculated using formula; $BMI = \text{Weight (Kg)} / \text{Height(m)}^2$

Hirsutism which is excessive hair growth with male pattern of distribution in a female was graded using index of Ferriman and Gallwey (IFG) which scores presence of hairs on 11 body areas (upper lip, chin, chest, upper and lower abdomen, thighs, upper and lower back, arm, forearm, buttocks).¹² A score of 4-8 was considered as mild, 8-44 as moderate and > 44 the most severe.

Women were advised for fasting blood sugar, serum prolactin and serum TSH levels to exclude other

endocrine disorders. Hormone profile included serum fasting insulin level, day 2 or 3 serum LH /FSH levels. Insulin up to 10 microIU / ml was considered normal. Normal range of FSH in early follicular phase of menstrual cycle was taken as 3.2 -10 mIU /ml and for LH 1.2 -10 mIU/ml. Ratio of LH /FSH was considered high if found >2:1. Ovaries were evaluated by transvaginal ultrasound and defined as polycystic if they had 10 or more follicles measuring 2 – 10 mm in diameter per ovary with increased density of the stroma.

RESULTS:

A total of 896 women visited BIRDS during study period of whom 318 (35.49%) infertile women were diagnosed as having PCOS. Most (n=178, 55.97%) of the women were between 21-30 years of age. A total of 267 (83.96%) women had primary infertility. Oligomenorrhoea was the commonest menstrual irregularity found in 203 (63.83%) women with PCOS. Secondary amenorrhoea was found in 18 (5.66%) women.

Hirsutism was noted in 238 women. Mild hirsutism was found in 204 (64.15%), while severe observed in 6 (1.88%) women. Acne was found in 106 (33.33%) women. On transvaginal scan PCO were observed in 298 (93.71%) women. Class I obesity was found in 64 (20.12%), while 27 (8.49%) had class II Obesity. Class III Obesity was found only in 2 (0.62%) women. 132 (41.50%) women were overweight. High LH/FSH ratio was found in 185 (58.17%) women. Insulin resistance was found in 201(63.20%) women.

DISCUSSION:

PCOS is a heterogeneous disorder and the liberalized Rotterdam criteria may have expanded the prevalence of this disease in the reproductive age female population by as much as 50% according to some estimates.¹³ In our study frequency of PCOS was 35.49%. In present cohort most of the females (55.97%) were in younger age group (21-30 years). Another study showed the higher incidence (57.81%) among the same age group.¹⁴

Major characteristic of PCOS is chronic anovulation, which in our study was reflected by oligomenorrhoea in 63.83%. Other study showed oligomenorrhoea as 79.68% and secondary amenorrhoea 20.13%.¹⁴ In Italian women population Crosignani and Nicolosi also reported higher percentage of oligomenorrhoeic PCOS women (54%).¹⁵

In our study hirsutism was found in 238 women among those 64.15% had mild while only

1.88% had severe hirsutism. In two large studies, the prevalence of hirsutism in PCOS varied from 56% in normal weight women to 70% among obese women with PCOS.¹⁶ In Saudi females 46% versus 15% cases had hirsutism in obese and nonobese females respectively.¹⁷

Diagnosis of PCOS does not always require presence of PCO on ultrasound. In our study PCO on transvaginal ultrasound were found in 93.71% while Khan MI reports that 80-100% of women with PCOS had polycystic ovaries.¹⁸ Ultrasound evidence of PCO was found in 39 (60.93%) women in another study.¹⁴

In our study 41.50% women were overweight and 20.12% were in class I obesity. Joan et al review revealed that Asians PCOS women had a lowest prevalence of obesity whereas blacks and Hispanics had the highest.¹⁹ The prevalence of overweight and obesity varies between 40-70% in different studies.^{8,20} High prevalence of overweight and obesity was found in Saudi females (68.8%).¹⁷

Multiple etiological factors for insulin resistance have been suggested. It is also important to note that not all women with insulin resistance develop PCOS. In our study 63.20% women had insulin levels greater than 10 mIU/ml indicating mild to moderate insulin resistance which is similar to results found in other studies. Wijeyaratne et al observed that fasting insulin levels were higher in South Asian PCOS women than in Caucasian PCOS women.²¹ Kayman et al reported that Mexican American women with PCOS were significantly more insulin resistant than their white counter parts.²² Raised LH / FSH ratio was found in 45.4% - 94% of women with PCOS.²³ In this study 58.17% women had LH/FSH ratio >2:1.

CONCLUSION:

There is a close relation between obesity, insulin resistance and symptoms severity in women with PCOS.

REFERENCES:

1. Stein I, Leventhal M. Amenorrhea associated with bilateral polycystic ovaries. *Am J Obstet Gynecol.* 1935;29:181-91.
2. Franks S. Controversy in clinical endocrinology: diagnosis of polycystic ovarian syndrome: In defense of the Rotterdam criteria. *J Clin Endocrinol Metab.* 2006;91:786-9.

3. Azziz R. Diagnosis of polycystic ovarian syndrome: The Rotterdam criteria are premature. *J Clin Endocrinol Metab.* 2005;3:781-5.
4. Welt CK. Discrete subsets of weight on phenotype and metabolic features. *J Clin Endocrinol Metab.* 2006;12:4842-8.
5. Vrbikova J, Hainer V. Obesity and polycystic ovary syndrome. *Obeste Facts.* 2009;2:26-35.
6. Venkatesan AM, Dunaif A, Corbould A. Insulin resistance in polycystic ovarian syndrome: Progress and paradoxes: Recent *Prog Horm Res.* 2001;56:295-308.
7. Grundy SM, Brewer HB Jr, Cleeman, JI, Smith SC Jr, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation.* 2004;109:433-8.
8. Norman RJ, Wu R, Stanziewicz MT. Polycystic ovary syndrome. *Med J Aust.* 2004; 180:132-7.
9. Campbell S, Monga A. Disorders of menstrual cycle. *Gynaecology by Ten Teachers.* 17th edition. 2000:47- 63.
10. World Health Organization, Obesity; Preventing and Managing the Global Epidemic, Report of the WHO Consultation on Obesity. Geneva: World Health Organization; 3-5 June 1997.
11. National Institute of Health. Clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults: the evidence based report. Bethesda, MD: National Institute of Health, US Department of Health and Human Services; 1998.
12. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. *J Clin Endocrinol Metab.* 1961;21:1440-8.
13. Broekmans FJ, Knauff EA, Valkenburg O, Laven JS, Eijkemans MJ, Fauser BC. PCOS according to the Rotterdam consensus criteria: Change in prevalence among WHO-II anovulation and association with metabolic

- factors. *Br J Obstet Gynaecol.* 2006;113:1210-7.
14. Adil F, Ansar H, Munir A. Polycystic ovarian syndrome and hyperinsulinaemia *J Liaquat Uni Med Health Sci.* 2005;4:89-93.
 15. Crosnani PG, Nicolosi AE .Polycystic ovarian disease : heritability and heterogeneity. *Hum Reprod.* 2001;7:3-7.
 16. Seli E, Duleba AJ. Optimizing ovulation induction in women with PCOS. *Curr Opin Obstet Gynecol.* 2002;14:245-53.
 17. Meher-un-Nisa. Impact of obesity on frequency and pattern of disease in polycystic ovarian syndrome (PCOS). *Ann King Edward Med Uni.* 2010;16:75-81.
 18. Khan MI, David MK. Polycystic ovarian syndrome. 2003 [Internet] Available at: <http://www.emedicine.com>.
 19. Lo JC, Feigenbaum SL, Yang J, Pressman AR, Selby JV, Go AS. Epidemiology and adverse cardiovascular risk profile of diagnosed polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2006;91:1357-63.
 20. Polycystic ovary syndrome. [Internet] Available at: [http:// www.infertilityphysician.com/androgen/pcos.html](http://www.infertilityphysician.com/androgen/pcos.html).
 21. Wajeyarantne CN , Balen AH Barth JA, Berichetz PE. Clinical manifestations and insulin resistance in polycystic ovary syndrome (PCOS) among south Asians and Caucasians: is there a difference ? *Clin Endocrinol.* 2002;57:343-50.
 22. Kauffman RP, Baker M, Dimarino P, Castracane VD. Hyperinsulinemia and circulating dehydroepiandrosterone sulfate in white and Mexican American women with polycystic ovary syndrome. *Fertil Steril.* 2006;85:1010-6.
 23. Banaszewska B, Spaczynski RZ, Pawel PM. Incidence of elevated LH/FSH ratio in polycystic ovary syndrome women with normo and hyperinsulinaemia. *Ann Academiae Medicae Biostatocensis.* 2003;48:131-4.