BODY MASS INDEX AND WAIST: HIP RATIO IN PATIENTS OF POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Objective: *The purpose of checking Body Mass Index was to find out if obesity is present in Polycystic ovary syndrome or not as obesity is a major contributor to hormonal imbalance and also causes insulin resistance which is thought to be present in polycystic ovary syndrome.*

Materials and Methods: *This was a cross-sectional (comparative) study conducted at Jinnahabad Medical Centre, which is a private hospital in Abbottabad from 1st January 2013 to 31st July 2013 over six months. We took 40 cases of PCOS and 40 controls of infertility without PCOS. History was made and general physical examination was done. Body Mass Index was calculated, and the waist/hip ratio was determined. Hirsutism was checked, and each patient underwent an ultrasound scan for checking the presence of a polycystic ovary. Data were analyzed with SPSS software.*

Results: *Patients with PCOS had raised BMI and waist: hip ratio, whereas the infertile non-PCOS group had an increased waist/hip ratio.*

Conclusion: *Central obesity is a cardinal feature of PCOS and infertility without PCOS.*

Keywords: *Polycystic Ovary Syndrome, Infertility, Waist, Hip ratio, Body Mass Index, Hirsutism.*

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine, metabolic disorder of reproductive age group women, which affects 6-10% of pre-menopausal women.[1] These patients are frequently obese, infertile, have irregular menses, are hirsute, and have a polycystic ovary on ultrasound. In PCOS patients there are increased levels of Total Testosterone, increased levels of luteinizing hormone (LH), increased ratio of luteinizing hormone to follicle-stimulating hormone (normal 1:1 but in polycystic ovary syndrome it is 2:1 or more), elevated prolactin, hyperinsulinemia, deranged oral glucose tolerance test(OGTT) and altered lipid profile.[2]

To diagnose a patient as having PCOS the Rotterdam 2003 Criteria is used, which states that a patient must have two of the following:

1. Evidence of hyperandrogenism (clinical or biochemical),
2. Anovulation or Oligo-ovulation in the form of amenorrhoea or oligomenorrhoea,

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3. The appearance of Polycystic ovary on ultrasound.[3]

PCOS has complex pathophysiology involving the interaction of genes, environmental factors, and altered endocrine pathways. All these pathways cause the altered function of an enzyme cytochrome P450c17α in the ovary. It is a bifunctional enzyme that first converts progesterone to 17-alpha hydroxyprogesterone via 17alpha hydroxylase activity and then converts 17alpha hydroxyprogesterone to androstenedione via 17-20 lyase activity. In normal menstruating females, the androstenedione is converted to estradiol by FSH dependent aromatase enzyme in the granulosa cells of the ovary. In PCOS due to abnormal endocrine pathways, the FSH levels are low, and LH levels are high, so this androstenedione not only gets accumulated in the ovary[4] but is also converted to testosterone by 17 beta reductase present in the thecal cells of the ovary and released into the blood.[5] Androstenedione causes growth of the follicles in the early stages, but the persistence of its high levels retard the further growth of follicles into mature ones.[6] Hence ovulation does not occur, and the ovary becomes polycystic in appearance.[7] As there is no ovulation so cyclic menstruation is scanty or none at all, and infertility becomes a problem if the patient is desirous of pregnancy. Increased levels of androgens in blood cause clinical signs of hyperandrogenism like Hirsutism, acne and androgenic alopecia etc.[8]

Only 1% of the total androgens produced in the female body are free in the plasma. The rest is transported by being bound mostly to sex hormone-binding globulin (SHBG), which is produced by the liver. Reduction in the plasma levels of SHBG causes an increase in the number of free androgens in the blood which then cause clinical or biochemical hyperandrogenism.[8]

Patients with PCOS have insulin resistance, which is thought to be a post-receptor binding defect causing higher than normal levels of insulin to produce a similar response resulting in hyperinsulinemia.[9,10] Insulin stimulates LH receptors in ovarian theca cells which augments androgen production from the ovary.[11]

Increased insulin levels also cause decreased production of SHBG from the liver, which in turn increases free androgens in the blood.[12] Metformin, a biguanide, increases insulin sensitivity and improves metabolic, ovarian, and androgen status in PCOS. This also shows that insulin resistance may be the cause of PCOS.[13]

About 60% of females with PCOS have raised BMI mostly occurring in the overweight or obese range,[14] and 70% are insulin resistant.[15] Despite insulin resistance, the ovaries are sensitive to insulin actions which increases the thecal androgen production by augmenting cytochrome P450 c17α activity.[16]

PCOS starts at the time of onset of puberty. During puberty, there is hyperinsulinemia and insulin resistance, which is physiological and completely reversible. However, in some adolescent girls, there is the persistence of hyperinsulinemia resulting in adolescent PCOS.[17] In adolescent girls who are genetically susceptible to PCOS, there is some form of abnormal feedback pathways of the endocrine system which continue to prevail beyond six months to two years which is the normal time required for the feedback pathways to return to normal.[16]

Obesity is present in most of the patients with PCOS, along with insulin resistance. The reason for this is nutrient toxicity. Excess of nutrition, especially high fat intake, cause hindrance in glucose transport into the cells by increasing competition for its uptake by cells. This causes an increase in blood glucose levels and leads to insulin resistance and hyperinsulinemia.[18]

Treatment of PCOS includes treating menstrual irregularity by combined oral contraceptive pills and treating hyperinsulinemia and insulin resistance with metformin. Hirsutism is treated cosmetically by laser, waxing, bleaching, shaving, and with drugs like cyproterone acetate, which is an anti-androgen. Treating infertility by induction of ovulation with drugs like clomiphene citrate or other infertility treatments. Changes in lifestyle which includes diet restriction, exercise etc.[18]

MATERIALS AND METHODS

The research was conducted on patients visiting the gynecology clinic at Jinnahabad Medical Center, which is a private hospital in Abbottabad (Khyber Pakhtunkhwa) over six months.

Ethical approval was granted by the Advanced Studies Research Board (ASRB) of Khyber Medical University. Ethical approval and NOC were also

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taken from the administration of Jinnahabad Medical Centre. Written informed consent was taken from all the participants.

Study Design: This was a Cross-Sectional Study (Comparative).

We selected 40 cases of Polycystic Ovary Syndrome. We also selected 40 controls of infertility without Polycystic Ovary Syndrome.

Criteria for selection of patients:

Inclusion Criteria for Cases;- In the PCOS group, we took females age 20-45 years who met the Rotterdam Criteria for diagnosis of PCOS according to which a patient should have two of the following three to be diagnosed with PCOS.

4. Menstrual disturbances in the form of oligomenorrhoea or amenorrhoea,
5. Evidence of hyperandrogenism (clinical features and biochemical elevation of testosterone) and
6. Polycystic ovary on ultrasound.3

Exclusion Criteria for Cases;-Patients with a documented history of other co-morbidities like diabetes and hypertension or the use of hormones, smoking/drug abuse, were excluded.

Inclusion Criteria for Controls: Control group included females of reproductive age group (20-45 years), suffering from primary infertility or secondary infertility as per WHO guidelines. According to WHO, infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse." If a woman has never before given a live birth, then its primary infertility and secondary infertility is "the inability to get pregnant or give live birth after previously getting pregnant and giving a live birth" (www.who.int/reproductive-health/topics/infertility/definitions).

Exclusion Criteria for Controls

Patients who were pregnant or using medicines, especially hormones or were infertile and had PCOS or a documented history of diabetes, hypertension, smoking, and drug abuse.

History was taken from all the subjects with special emphasis on menstrual history, history of weight gain, abnormal hair distribution, etc. All the participants were subjected to an ultrasound scan to check for polycystic ovaries. The ovary is described as polycystic if there are ten or more cysts (2-8 mm in diameter) present peripherally, a dense stroma, and an enlarged ovary size > 10 cm3 (http://radiopaedia.org/articles/polycystic-ovarian-syndrome 8/12/2015).

A detailed physical examination was carried out, including a general physical examination and examination of the reproductive system. The Ferriman–Gallwey score was used for assessing the degree of Hirsutism in the patients. Nine areas of the body were examined to see the extent of hair growth. These included upper lip, chin, chest, upper back, lower back, upper abdomen, lower abdomen, upper arms, and thighs. Hair growth was scored from 0 (no or zero growth of terminal hair) to 4 (excessive hair growth) in each of the nine body areas. A patient's score could thus vary from a minimum of 0 to a maximum of 36. A score of 8 or more was taken as an indicator of hyperandrogenism.19

Body Mass Index (BMI) was calculated by dividing the weight in kilogram by the height in meter square:-

$$BMI = \frac{\text{weight in kilogram}}{(\text{height in meter})^2}$$

BMI of less than or equal to 18.4 was classified as underweight, BMI of 18.5-24.9 kg/m2 is an ideal weight, BMI of 25-29.9 kg/m2 were overweight, and a BMI of 30-39.9 kg/m2 were obese whereas a BMI of over 40 kg/m2 were grouped as very obese as per WHO guidelines.20

Waist/hip ratio was calculated according to WHO guidelines, which say that waist circumference is to be measured halfway between the lower margin of the rib cage and the upper margin of the iliac crest usually a little above the umbilicus. The hip circumference is measured at the widest part of the buttocks with a non-stretchable tape (http://en.wikipedia.org). Waist: Hip ratio above 0.82 is considered obese.

Blood samples were taken in the early follicular phase of the menstrual cycle from all the patients included in the study; however, these are beyond the scope of this paper.

Statistical Analysis

SPSS software was used for statistical analysis

of the results. Students-test was used to compare the BMI and Waist/hip ratio. P-value < 0.05 was taken as statistically significant.

RESULTS

In the PCOS group, 29 out of 40 patients were centrally obese with a waist/hip ratio above 0.82, and in the infertile group without PCOS, 28 out of 40 patients were centrally obese. After applying t-test, we found that there was no statistically significant difference between the waist: the hip ratio of patients with PCOS and Infertile group, shown below.

The values of the body mass index for the patients with PCOS and the infertile group without PCOS were compared. Using a t-test, we got a p-value < 0.05, which meant that there is a significant difference. The BMI of subjects with PCOS was higher than the BMI of the infertile group without PCOS.

Correlations:-Applying Pearson's correlate, we found out that the BMI and waist/hip ratio of the cases of PCOS were positively correlated. (r = .335, p-value < 0.05).

DISCUSSION

In this study, we compared patients with PCOS with those of infertility without PCOS. We wanted to check for differences between these patients.

Obesity, which was measured by calculating BMI, was present in the majority of patients with PCOS. The BMI of patients with PCOS was significantly greater than the BMI of infertile patients without PCOS (p-value less than 0.05).

Waist: The hip ratio of above 0.82 is considered as centrally obese. Central obesity was present in the majority of patients with PCOS, as well as the infertile group without PCOS. Thus central obesity has a vital role to play in causing infertility in both groups.

Central obesity is a cardinal feature of metabolic syndrome. In patients with PCOS, there is metabolic syndrome like disturbances such as hyperinsulinemia, increased intra-abdominal fat, dyslipidemia. Increased insulin is thought to act on the liver and cause decreased production of SHBG. In experiments done on animals, it was shown that excess of nutrients like glucose and fructose suppressed the action of SHBG promoter gene and thus caused decreased production of SHBG which in turn increased free testosterone in blood.[21]

Table 1: Comparison of Waist/Hip ratio and Hirsutism among the two groups

	PCOS	INFERTILITY
Waist/Hip ratio above 0.82	29/40 (72.5 %)	28/40 (70 %)
Hirsutism present	31/40 (77.5%)	4/40 (10%)

Table 2: Comparison of BMI between the two groups

	PCOS (kg/m2)	Infertility (kg/m2)
Below 18.4(underweight)	0	5(12.5%)
18.5-24.9(ideal weight)	9(22.5%)	19(47.5)
25-29.9(overweight)	7(17.5%)	13(32.5%)
30-39.9(obese)	23(57.5%)	3(7.5%)
Over 40(very obese)	1(2.5%)	0

Table 3: Comparison of BMI and Waist/Hip ratio among the two groups

	PCOS Mean ±1SD	INFERTILITY Mean ±1SD	SIGNIFICANCE
BMI	29.36±5.49	23.36±4.06	<0.05
Waist/Hip ratio	0.86±0.07	0.85±0.062	>0.05

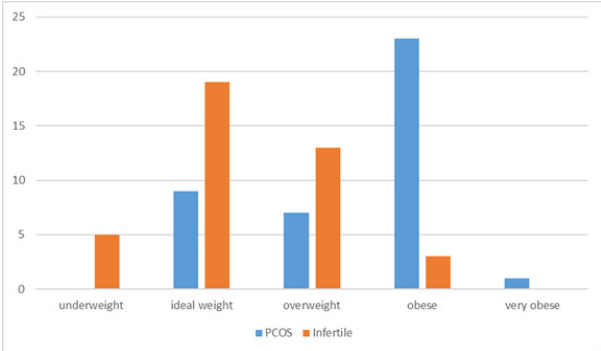

Fig 1: Frequency of IOTN Health component

There is a lot of evidence that infertility and a higher risk of obstetric complications are both because of obesity, even in patients without PCOS. Losing weight has a positive effect on decreasing menstrual irregularities and Hirsutism. Weight loss should not be achieved only with diet restriction but should be combined with lifestyle changes, including increased exercise. Exercise cause uptake of glucose in the skeletal muscles without the requirement of insulin.[22] Women who are grossly obese and overweight have two-fold higher odds of menstrual

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irregularity as compared to healthy controls.[23]

Obesity, especially central obesity, was present in both the groups in this study. Nutrient toxicity causes hyperinsulinemia which increases ovarian androgen biosynthesis[18] and increased activity of cytochrome P450c17alpha.[24]

Increased levels of androgens occurs due to increased peripheral conversion of fat in adipose tissue to androgens,[25] decreased production of SHBG resulting in increased bioavailability of free testosterone.[26]

The adipose tissue release a lot of protein like hormones called adipokines. Adipokines are thought to play a role in insulin resistance leading to infertility. These are leptin, adiponectin, and resistin. Leptin is a satiety hormone that causes satiety, but in PCOS, there is leptin resistance, so leptin levels increase in the blood, causing Hyperleptinemia.[27] There is also decreased production of adiponectin from the adipose tissue which is potent insulin-sensitizing agent.[28] There is an increase in resistin levels which is another adipokine or hormone-like protein secreted by the adipose tissue which impairs insulin action and increases insulin resistance.[29]

CONCLUSION

Patients with PCOS have increased BMI as compared to the infertile group without PCOS. Central obesity was a prominent feature of both the PCOS group and the infertile group without PCOS, thereby suggesting that this might be the leading cause of infertility in both the groups.

REFERENCES

1. Hart R, Hickey M, Franks S (2004). Definitions, prevalence, and symptoms of polycystic ovaries and polycystic ovarian syndrome. Best Pract Res Clin Obstet Gynaecol. 18 (5):671-683.
2. Lenarcik.A, Bidzińska-Speichert.B, Tworowska-Bardzińska.U, Krępuła.K (2011). Hormonal abnormalities in first-degree relatives of women with polycystic ovary syndrome (PCOS).Endokrynologia Polska 62(2):129-133.
3. Kauffman RP, Baker TE, Baker VM, DiMarino P, CastracaneVD (2008). Endocrine and metabolic disturbances among phenotypic expressions of polycystic ovary syndrome according to the 2003 Rotterdam consensus criteria. Am J Obstet Gynaecol. 198(6):670-677.
4. Blank SK, McCartney CR, Marshall JC (2006). The origins and sequelae of abnormal neuroendocrine function in polycystic ovary syndrome. Hum Reprod.12 (4):351-361.
5. Catherine G.Baptiste, Marie-Claude Battista, Andreanne Trottier, and Jean-Claude Baillargeon (2010). Insulin and hyperandrogenism in women with polycystic ovary syndrome. J Steroid Biochem Mol Biol. 122(1-3):1016-1026.
6. Jie Qiao and Huai L. Feng (2011). Extra- and intra-ovarian factors in polycystic ovary syndrome: impact on oocyte maturation and embryo developmental competence. Hum Reprod Update. 17 (1):17-33.
7. Rosenfield Robert L, Bordini Brian (2010). Evidence that obesity and androgens have independent and opposing effects on gonadotropin production from puberty to maturity. Brain Res. 1364: 186–197.
8. Goudas VT, Dumesic DA (1997). Polycystic ovary syndrome. Endocrinol Metab Clin North Am. 26 (4):893-912.
9. Ehrmann DA, Kasza K, Azziz R, Legro RS, Ghazzi MN (2005). Effects of race and family history of type 2 diabetes on the metabolic status of women with polycystic ovary syndrome. J Clin Endocrinol Metab. 90(1):66-71.
10. Lakkakula Bhaskar Venkata Kameswara Subrahmanya, Thangavelu Maheswari, GodlaUsha Rani (2013). Genetic variants associated with insulin signaling and glucose homeostasis in the pathogenesis of insulin resistance in polycystic ovary syndrome: a systematic review. J Assist Reprod Genet. 30 (7):883-895.
11. Marshall John C, Dunaif, Andrea (2012). All Women With PCOS Should Be Treated For Insulin Resistance. Fertil Steril. 97(1):18-22.
12. Nestler JE, Powers LP, Matt DW (1991). A direct effect of hyperinsulinemia on serum sex hormone-binding globulin levels in obese women with polycystic ovary syndrome. J Clin Endocrinol Metab. 72(1):83-89.
13. Maruthini D, Harris S.E, Barth J.H, Balen A.H, Campbell B.K, H.M. Picton (2013). The effect of metformin treatment in vivo on acute and long-term energy metabolism and progesterone production in vitro by granulosa cells from women with polycystic ovary syndrome. Hum Reprod . 29(10):2302–2316.
14. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO (2004). The prevalence and features of the polycystic ovary syndrome in an unselected population.J Clin Endocrinol. 89(6):2745-2749.
15. Carmina E, Lobo RA (2004). Use of fasting blood to assess the prevalence of insulin resistance in women with polycystic ovary syndrome. Fertil Steril. 82(3):661–665.
16. Munir I, Yen HW, Geller DH (2004). Insulin augmentation of 17alpha-hydroxylase activity is mediated by phosphatidyl inositol 3-kinase but not extracellular signal-regulated kinase-1/2 in human ovarian theca cells.

Endocrinology. 145(1):175-183.

17. Moran A, Jacobs DR Jr, Steinberger J, Cohen P, Hong CP, Prineas R, Sinaiko AR (2002). Association between the insulin resistance of puberty and the insulin-like growth factor-I/growth hormone axis. J Clin Endocrinol Metab. 87(10):4817-4820.
18. Proietto J (2005). Mechanisms of insulin resistance caused by nutrient toxicity. Hepatol Res. 33(2):87-91.
19. Yildiz BO, Bolour S, Woods K, Moore A, Azziz R (2010). Visually scoring Hirsutism. Hum Reprod Update. 16(1):51-64.
20. Xuemei Sui, Michael J LaMonte, James N Laditka, James W Hardin, Nancy Chase, Steven P Hooker, Steven N Blair (2007). Cardiorespiratory Fitness and Adiposity as Mortality Predictors in Older Adults. JAMA. 298(21):2507-2516.
21. Selva DM, Hogeveen KN, Innis SM, Hammond GL (2007). Monosaccharide-induced lipogenesis regulates the human hepatic sex hormone-binding globulin gene. 117(12):3979-3987.S
22. Hoeger KM, Kochman L, Wixom N, Craig K, Miller RK, Guzick DS (2004). A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. Fertil Steril. 82(2):421-429.
23. Wei S, Schmidt MD, Dwyer T, Norman RJ, Venn AJ (2009). Obesity and menstrual irregularity: associations with SHBG, testosterone, and insulin. Obesity(silver spring). 17(5):1070-1076.
24. Marshall John C, Dunaif, Andrea (2012). All Women With PCOS Should Be Treated For Insulin Resistance. Fertil Steril. 97(1):18-22.
25. Poretsky L, Cataldo NA, Rosenwaks Z, Giudice LC (1999). The insulin-related ovarian regulatory system in health and disease. Endocr Rev. 20(4):535-582.
26. Hogeveen KN, Cousin P, Pugeat M, Dewailly D, Soudan B, Hammond GL (2002). Human sex hormone-binding globulin variants associated with hyperandrogenism and ovarian dysfunction. J Clin Invest. 109(7):973-981.
27. Jeon YE, Lee KE, Jung JA, Yim SY, Kim H, Seo SK, Cho S, Choi YS, Lee BS (2013). Kisspeptin, leptin, and retinol-binding protein 4 in women with polycystic ovary syndrome. Gynecol Obstet Invest. 75(4):268-74.
28. Pangaribuan B, Yusuf I, Mansyur M, Wijaya A (2011). Serum adiponectin and resistin in relation to insulin resistance and markers of hyperandrogenism in lean and obese women with polycystic ovary syndrome. Ther Adv Endocrinol Metab. 2(6):235-245.
29. Baranova Ancha, Tran Thuy Phuong, Afendy Arian, Wang Lei, Shamsaddini Amirhossein, Mehta Rohini, Chandhoke Vikas, Birerdinc Aybike, Younossi Zobair M (2013). Molecular signature of adipose tissue in patients with both Non-Alcoholic Fatty Liver Disease (NAFLD) and Polycystic Ovarian Syndrome (PCOS). J Transl Med. 11(1):133-137.