A Comparative Case Control Study of Serum Lipid Profile and Insulin Resistance in Polycystic Ovary Syndrome (PCOS) and Non PCOS Patients

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ABSTRACT

BACKGROUND

Polycystic Ovary Syndrome (PCOS) is a spectrum of disorders that causes many negative effects involving a variety of systems in the body such as the endocrine, metabolic, and reproductive systems. Metabolic problems may include insulin resistance, metabolic syndrome, impaired glucose tolerance (abnormal glucose metabolism), diabetes mellitus, and potentially cardiovascular disease. This study is aimed at comparing the lipid parameters and insulin resistance in overweight PCOS patients with those of overweight non PCOS females and investigate the association between lipid parameters and insulin resistance with respect to PCOS after nullifying the effect of increased Body Mass Index (BMI).

METHODS

This is a comparative case control study conducted among 100 females of reproductive age group with BMI > 25, attending the outpatient department of a tertiary care hospital. Out of these 100 women, 50 were PCOS (cases) and rest 50 were non PCOS (controls) matched for age, sex and BMI.

RESULTS

Distribution of age between the two groups was not identical (p value < 0.001). 26 % patients in non PCOS group had total cholesterol > 200 compared to 10 % patients in PCOS group. This difference is statistically significant (p value = 0.037). Non PCOS group has higher low-density lipoprotein > 130, but difference is not statistically significant. The PCOS group has higher triglyceride > 150, but the difference is not statistically significant. Regarding the high-density lipoprotein value, there was no significant difference between the groups. Fasting Plasma Insulin is higher in overweight PCOS group (72 %) in comparison with overweight non PCOS group (58 %). However, it is not statistically significant. Insulin resistance is higher in overweight PCOS group in comparison with overweight non PCOS group (50 %), but it is not statistically significant.

CONCLUSIONS

PCOS may be an independent risk factor for increased fasting plasma insulin, insulin resistance, and increased TG. Non PCOS group had higher total cholesterol (TC) and LDL in comparison to PCOS group. The TC difference between the two groups is statistically significant. There was no significant difference in abnormal HDL value in both groups.

KEYWORDS

Polycystic Ovary Syndrome, Dyslipidemia, Insulin Resistance

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BACKGROUND

PCOS is a heterogeneous collection of signs and symptoms that, gathered together, forms a spectrum of a disorders ranging from mild presentation in some to severe disturbance of reproductive, endocrine and metabolic function in others. It is the commonest endocrine condition to affect women with an estimated prevalence of 10 – 15 % (depending on the population studied and the diagnostic criteria used). In 2003, the European Society for Human Reproduction and Embryology (ESHRE) and the American Society of Reproductive Medicine (ASRM) held a consensus meeting in Rotterdam and proposed that a diagnosis of PCOS should be made if two out of three criteria are met: the presence of clinical or biochemical features of hyperandrogenism, oligo-ovulation or anovulation (i.e. menstrual cycle disturbance) and/or polycystic ovaries on ultrasound, once appropriate investigations have been performed to exclude other causes of menstrual disturbance and androgen excess.[1]

The diagnosis requires the exclusion of specific underlying diseases of the adrenal or pituitary glands (e.g. hyperprolactinemia, acromegaly, congenital adrenal hyperplasia, Cushing's syndrome and androgen-secreting tumours of the ovary or adrenal gland). The presence of insulin resistance, central obesity, and dyslipidaemia appears to place women with PCOS at higher risk of developing diabetes and cardiovascular disease.

Women who are obese, and also many slim women with PCOS will have insulin resistance and elevated serum concentrations of insulin. Insulin resistance is defined as a reduced glucose response to a given amount of insulin and may occur secondary to resistance at the insulin receptor, decreased hepatic clearance of insulin and / or increased pancreatic sensitivity. Both obese and non - obese women with PCOS are more insulin resistant than age - and weight - matched women with normal ovaries. Thus, there appear to be factors in women with PCOS that promote insulin resistance and that are independent of obesity. Women with PCOS who are oligomenorrheic are also more likely to be insulin resistant than are those with regular cycles, irrespective of their body mass index (BMI).

The hyperinsulinemia seen in PCOS most likely results from Increased secretion of basal insulin, decreased hepatic insulin clearance or due to the defect in the insulin receptors in which the receptors are unable to adequately carry out phosphorylation of the substrate.[2] Women with PCOS are at higher risk for dyslipidaemia.[3,4] The reasons are not very clear but maybe because of Increased androgen levels[5] which decreases lipoprotein lipase (LPL) activity in abdominal fat cells that leads to central obesity. It may also be due to Insulin resistance and hyperinsulinemia - In women with obesity there is an increased production of FFA (stimulation of lipolysis) and decreased activity of LPL, Hepatic lipase as a result of IR.[2,6] Genetic and environmental factors[3] may also play a role leading to dyslipidaemia.

This study is aimed at comparing the lipid parameters and insulin resistance in overweight PCOS patients with those in overweight non PCOS females and to investigate the association between lipid parameters and insulin resistance with respect to PCOS after nullifying the effect of increased Body mass index (BMI).

METHODS

This is a comparative case control study of females of reproductive age group who attended the outpatient department of a tertiary care hospital. Data was collected from overweight PCOS and non PCOS women and was compared to find an association of abnormal lipid profile and insulin resistance in PCOS females after nullifying the effect of increased body mass index (BMI). The sample included 100 reproductive age group women with BMI> 25. Out of these 100 women, 50 PCOS (cases) and rest 50 non PCOS (controls) matched for age, sex and BMI. PCOS cases were selected as per the Rotterdam criteria (2003) for selecting PCOS cases. Women with known case of any heart disease, hypertension, diabetes, liver disorder, renal disorder, hypothyroidism, and hyperlipidaemia were excluded from the study. Blood investigations done were Fasting Lipid profile (total cholesterol, LDL, HDL, TG), Fasting serum insulin level, and Fasting glucose level. HOMA IR (Homeostatic model assessment) was calculated by using the formula: Fasting insulin (Mu / ml) x Fasting glucose (mg / dl) / 405. Measurements – BMI (Weight in Kg / Height in m^2) and Waist circumference were also done. Parametric data association between the groups was tested using independent t-test. Non - parametric data compared between the groups using Mann Whitney U test. Categorical variable was tested using Chi square/Fisher`s exact test. For all test p value<0.05 is considered as statistically significant.

RESULTS

	PCOS	Non PCOS
Mean	28.30	34.28
Median	27.50	36.00
Std. Deviation	5.704	6.068
Minimum	20	20
Maximum	40	40
Table 1. Age		
p value<0.001		

A total of 100 patients was recruited for the study. They were distributed between 20 years and 40 years. Mean age in PCOS group was 28.30 with a standard deviation (SD) of 5.704. Mean age in non PCOS group was 34.28 with a standard deviation (SD) 6.068. Distribution of age between the two groups was not identical (p value<0.001) (statistically significant).

BMI	PCOS	Non PCOS
Mean	30.42	31.9
Median	28.47	29.43
Std. Deviation	5.53	6.8
Minimum	25	25.25
Maximum	50.90	54.16
Table 2. Body Mass Index (BMI)		
p value 0.235, BMI was comparable between the groups		

TC	Group		Total
	PCOS	Non - PCOS	
<200	45 (90 %)	37 (74 %)	82 (82 %)
>200	5 (10 %)	13 (26 %)	18 (18 %)
Total	**50 %**	**50 %**	**100 %**

Table 3. Total Cholesterol (TC)

26% non PCOS group has TC>200 while 10% PCOS group has TC > 200. This difference is statistically significant (p value 0.037). Mean value in PCOS group is 173.76 with a standard deviation (SD) 24.5. Mean value in non PCOS group is 181.52 with a standard deviation (SD) 35.4.

	Group		Total
	PCOS	Non PCOS	
< 130	41 (82 %)	33 (66 %)	74 (74 %)
> = 130	9 (18 %)	17 (34 %)	26 (26 %)
Total	**50 %**	**50 %**	**100 %**

Table 4. Low Density Lipoprotein (LDL)

34 % non PCOS group has LDL>130 while 18 % PCOS group has LDL>130. This difference is not statistically significant (p value 0.068). Mean value in PCOS group is 111.43 with a standard deviation (SD) 19.38. Mean value in non PCOS group is 114.84 with a standard deviation (SD) 27.73.

TG	Group		Total
	PCOS	Non - PCOS	
< 150	40 (80 %)	42 (84 %)	82 (82 %)
> = 150	10 (20%)	8 (16 %)	18 (18 %)
Total	**50 %**	**50 %**	**100 %**

Table 5. Triglycerides (TG)

20 % PCOS group has TG>150 while 16 % non PCOS group has LDL>150. This difference is not statistically significant (p value 0.603). Mean value in PCOS group is 98.94 with a standard deviation (SD) 46.84. Mean value in non PCOS group is 104.32 with a standard deviation (SD) 53.68.

	Group		Total
	PCOS	Non PCOS	
> 60	5 (10 %)	4 (8 %)	9 (9 %)
< = 60	45 (90 %)	46 (92 %)	91 (91 %)
Total	**50 %**	**50 %**	**100 %**

Table 6. High Density Lipoprotein (HDL)

90% PCOS group has HDL<60 while 92 % non PCOS group has HDL<60. This difference is not statistically significant (P value>0.99). Mean value in PCOS group is 43.55 with a standard deviation (SD) 10.64. Mean value in non PCOS group is 45.48 with a standard deviation (SD) 9.46.

FPI	Group		Total
	PCOS	Non - PCOS	
< 10	14 (28 %)	21 (42 %)	35(35 %)
> 10	36 (72 %)	29 (58 %)	65 (65 %)
Total	**50 %**	**50 %**	**100 %**

Table 7. Fasting Plasma Insulin and PCOS

Fasting Plasma Insulin is higher in overweight PCOS group (72 %) in comparison with overweight non PCOS group (58 %). However, it is not statistically significant (p value 0.208).

Insulin resistance is higher in overweight PCOS group (66%) in comparison with overweight non PCOS group (50%). However, it is not statistically significant (p value 0.156).

IR	Group		Total
	PCOS	Non - PCOS	
<2.5	17 (34 %)	25 (50%)	42(42%)
>2.5	33 (66%)	25 (50%)	58(58%)
Total	**50%**	**50%**	**100%**

Table 8. IR and PCOS

DISCUSSION

A retrospective study conducted by Cristian Ioan Iuhas et al[7] showed that both total cholesterol and LDL cholesterol were positively associated with PCOS but not with HDL cholesterol (beta = 0.3, p = 0.01 for total cholesterol, beta = 0.44, p<0.001 for LDL cholesterol). In our study Serum Total cholesterol and LDL is higher in overweight non PCOS group) than PCOS group (26 % vs. 10 %, p 0.037) and (34 % vs. 18 %, p 0.068. This may be due to confounding effect of age, higher age group women being included in non PCOS group. Serum HDL level is comparable between two groups with no significant difference.

The Study conducted by Robert A. Wild et al[8] with 29 patients with PCOS and 30 normal women had lipoprotein lipid and androgen profiles compared after a 12 hr fast. PCOS patients had higher mean serum TG (122 +/- 11 vs. 63 +/- 3 mg % dl) and VLDL (24 +/- 2 Vs 13 +/- 1 mg % dl), but lower HDL (43 +/- 2 Vs 58 +/- 2 mg % dl, p<0.05). Hence concluded, that hyperandrogenemia in women may result in male pattern of lipoprotein lipid concentrations. Another cross-sectional study conducted by Mehranghiz Ebrahimi Mamaghani et al[9] showed associations of insulin resistance (IR) with endocrino-metabolic parameters in PCOS. In our study Serum TG level is higher in overweight PCOS group (20% vs 16 %). Mean value of serum TG in PCOS group is 98.94 while in non PCOS group it is 104.32. However, it is not statistically significant (p value 0.603). The reason for statistically not significant may be due to the small sample size as well as the significant age difference between two groups. Hence it is difficult to draw definitive conclusion. A prospective study conducted by Anuradha Kalka et al[10] on 65 women with PCOS - insulin resistant and insulin sensitive concluded that insulin resistance is associated with dyslipidemia in women with PCOS, independent of obesity. The difference between the two groups for total cholesterol (p = 0.002), TG (p = <0.001) and HDL (p = <0.001) was statistically significant but for LDL (p = 0.07) was not statistically significant. Case control study conducted by C. Meyer et al[4] on 100 overweight women with PCOS and 20 subjects of similar body mass index and age concluded that subjects with PCOS had elevated fasting insulin(19.6 +/- 1.4 Vs 6.8 +/- 0.8 µU / ml) and HOMA IR (4.1 +/- 0.3 Vs 1.3 +/- 0.2). In addition, those with PCOS had elevated cholesterol (5.1 +/- 0.1 Vs 4.6 +/- 0.2 mmol/l) and TG (1.4 +/- 0.1 Vs 0.9 +/- 0.1 mmol/l). In our study PCO group had higher fasting plasma insulin and insulin resistance than non PCOS group (72 % vs 58 %) and (66 % vs 50 %) respectively. Hence PCOS may be an independent risk factor for increased fasting plasma insulin and insulin resistance.

CONCLUSIONS

PCOS may be an independent risk factor for increased fasting plasma insulin, insulin resistance and increased TG. Non PCOS group had higher TC and LDL in comparison to PCOS group. TC difference between 2 groups is statistically significant. There was no significant difference in abnormal HDL value in both groups.

Limitations

Selection bias - PCOS women were selected from a younger age group while non PCOS were selected from a higher age group. Small sample size - As our analysis is relatively small, our results have less statistical power.

Financial or Other Competing Interests: None.

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