



ASSOCIATION OF POLYCYSTIC OVARY SYNDROME WITH INSULIN RESISTANCE AND GLUCOSE TRANSPORTER GLUT 4.

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ABSTRACT... Objectives: The study was designed to find out the association of PCOS with insulin resistance and GLUT4. **Study Design:** Cross Sectional study. **Setting:** Outdoor Department of Sir Ganga Ram Hospital Lahore. **Period:** March 2016 to December 2016. **Material & Methods:** 37 PCOS women visited Outdoor Department of Sir Ganga Ram Hospital Lahore. Their age range was 25- 36 years. 20 ages matched medical staff of the Sir Ganga Ram Hospital, Lahore with no history of any disease were selected as control. Rotterdam's criteria were used to confirm PCOS. Levels of circulating insulin, GLUT 4 and fasting glucose were estimated. **Results:** Mean age of PCOS patients and of controls was 30.55 and 29.00 years respectively. Values of BMI were insignificantly raised in PCOS in comparison to controls. Levels of circulating GLUT-4, fasting glucose, insulin and resistance of insulin were increased significantly in women with PCOS in comparison to the controls. Decreased ratio of glucose to insulin was seen in PCOS women in comparison to their controls. **Conclusion:** A good association of PCOS was observed with insulin mediated release of glucose transporter GLUT 4 and insulin resistance.

Key words: GLUT 4, Insulin Resistance, PCOS.

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INTRODUCTION

PCOS or polycystic ovary syndrome is a known impaired metabolic pathway disorder. It is caused by interplay between environmental and genetic factors. This may be characterized by insulin resistance in tissues of periphery, helps to increase the vulnerability of cardiovascular problems and type 2 diabetes.¹

Additionally PCOS is linked with metabolic disturbances and malfunctioning of hypothalamic-pituitary-ovarian axis. The syndrome may results in increased levels of hormone androgen, insulin and its resistance. PCOS is also due to imbalance of ratio of FSH and LH, infertility, endometrial dysfunction, obesity and increase risk of cardiovascular problems.^{2,3}

Criteria of diagnosis of PCOS based upon age and increased BMI that may be linked with insulin resistance disturbances in metabolic pathways. The age related variations may effect

on the incidence and complications of PCOS.⁴ A close link between obesity and PCOS may be age dependent and it may be related with reproductive and steroidogenic effects and insulin resistance.⁵ Increased values of BMI may be a factor of malfunctioning of excess amount of androgen and risk of miscarriages.^{6,7}

About 70% of PCOS women have resistance of insulin related with altered function of glucose metabolism in adipose tissue.⁸ It is thought that insulin resistance secondary to diminished glucose uptake via insulin and increased secretion of insulin in PCOS may be a cause of decreased expression of GLUT4 (a glucose transporter).⁹

Additionally, it is proposed that increased expression of micro RNA 93 cause a down regulation of the expression of gene of GLUT in cells of adipose tissue.⁸ Role of micro RNA 93 in pathogenesis of PCOS revealed that over expression of non-coding RNA or micro RNA

in ovarian tissue may be a reason of insulin resistance in PCOS women and also a reason of inhibition of synthesis of GLUT4.¹⁰ It is stated that uptake of blood glucose via insulin is directly dependent on availability of GLUT4.¹¹

GLUT 4 or glucose transporter may take part in the progress of process of insulin resistance in both adipose and muscular tissues of PCOS women.¹² It is measured that role of adipose tissue in uptake of glucose via insulin is only 10 %.¹³

Cross sectional study was designed to find out the association of PCOS with insulin resistance and glucose transporter GLUT 4.

MATERIAL & METHODS

Study was included 37 PCOS women with age range 25-36 years were engaged from Gynae Department of Sir Ganga Ram Hospital Lahore. 20 age matched controls were medical staff of the hospital with no history of any disease. Duration of study was March 2016 to December 2016. Rotterdam's criteria were used to confirm PCOS.¹⁴ Women who have endocrinological disorder like hypo / hyper thyroidism, hyper prolectinemia, with cushing's syndrome and tumor of androgen were not included in the study.

Glucose oxidase method was used to estimate the level of fasting glucose. Level of circulating Insulin and GLUT4 was estimated by technique of ELISA using standard kits. Resistance of insulin and BMI was calculated by standard formula.¹⁵

Data was entered in SPSS 20. Variables were expressed as mean \pm SD. Variation in the values of BMI, levels of serum insulin, GLUT 4, fasting blood sugar and insulin resistance of patients was compared with the normal subjects using student 't' test. Values of P < 0.05 are considered significant.

Study Variables	PCOS women (37)	Normal Subjects or Controls (20)
Age in years	30.55 \pm 2.55	29.00 \pm 2.22
BMI (Kg m ²)	29.77 \pm 4.39	24.60 \pm 1.84
GLUT-4 (arb. Units)	4.77 \pm 4.08	2.24 \pm 0.54
Blood glucose fasting (mg/dl)	120.21 \pm 13.59**	95.0 \pm 9.5
Fasting serum Insulin (IU/ml)	32.54 \pm 14.13**	4.3 \pm 2.9
Glucose insulin ratio	4.52	29.45
(Insulin resistance)	4.46 \pm 2.7**	0.44 \pm 0.6

Table-I. Age, BMI and biochemical parameters in PCOS women and their controls.

**P<0.001 showed significant difference

RESULTS

Mean age of PCOS patients and of controls was 30.55 and 29.00 years respectively. Values of BMI were insignificantly raised in PCOS compared to their controls.

Levels of GLUT-4 were insignificantly raised in PCOS women as in comparison to controls. On the other hand level of circulating fasting glucose and fasting insulin and insulin resistance were increased significantly (P<0.001) in PCOS women in comparison to controls. Decreased glucose insulin ratio was observed in PCOS women in comparison to controls (Table-I).

DISCUSSION

Polycystic ovary syndrome is a known endocrinopathy observed in women during their reproductive period and also recognized to be a psychological and metabolic condition affecting 8 to 13 % women, with a 4-5 fold amplified risk of type 2 diabetes and dyslipdemia.¹⁶

According to our study the mean age of PCOS patients and of controls was 30.55 and 29.00 years respectively. It is stated that there is variation in the phenotype of women having this disease throughout her life and may reorganize with aging.¹⁷ It is demonstrated insulin resistance along with obesity and metabolic disturbances

are main problems in reproductive women with PCOS.⁴ Another study found that physiologic and metabolic dysfunctions of hypothalamic, ovarian, pituitary and adrenal may effect in the reproductive age of PCOS women.¹⁸

In our study values of BMI was insignificantly raised in PCOS in comparison to controls. According to another study, values of BMI were 27.47 Kg/m² and found no significant relationship between occurrence of PCOS, age and BMI.¹⁹ It is proposed that insulin resistance along with steroidogenic and reproductive effects of increased level of serum insulin are the mediating effect of obesity. Production of adipokines via visceral and subcutaneous fat seems to play a role in metabolic function.⁵ A study stated that obesity exacerbates many signs of PCOS. It is thought obesity along with hirsutism and infertility are major problem that may be a cause of stress in patients.²⁰

Our results showed that levels of GLUT-4 were insignificantly raised in PCOS women in comparison to controls. Many study found that insulin mediated increased glucose uptake is directly depend on availability of GLUT4.¹¹ A study observed that inhibition of synthesis of GLUT 4 via micro RNA is targeted by high mobility group A2 and also via sterol regulatory binding protein 1.¹⁰ Another study found that disturbance of the interaction between syntaxin binding protein and MUNC 18c protein in cells of adipose tissue may cause an increase externalization of insulin stimulated GLUT4.²¹ It is reported that this interaction of syntaxin binding protein and MUNC 18c protein mediate the process of exocytosis from beta cells of pancreas and also exocytosis of vesicles of GLUT4 from adipose tissue and skeletal muscle and increase insulin sensitivity.²²

We observed a significant increased in the level of fasting blood glucose and serum insulin along with raised values of insulin resistance. Our study is agreed with no of studies. A study stated that increased level of insulin and luteinizing hormone may be related with risk of insulin resistance in most of the PCOS women. Study found than

increase secretion of ovarian insulin may increase the granulose response of luteinizing hormone, which may increase the production of androgen.²³ The worsening of insulin resistance during the life of reproductive women with PCOS seems to be a cause of obesity.⁴ A study experimentally proved that altered translocation of GLUT 4 to sarcolemma via stimulation of insulin may results insulin resistance.²⁴

We found a decrease ration of glucose to insulin in our PCOS patients. According to a study the insulin sensitivity is related with ratio of blood glucose to serum insulin and a good predictive of insulin sensitivity index. Study found that fasting blood glucose serum insulin ratio < 7.0 is considered as nonstandard and it is < 5.7, it is a prove of insulin resistance. Study concluded that the ratio of fasting blood glucose to serum insulin is a good screening test for insulin resistance.²⁵

CONCLUSION

A good association of polycystic ovary syndrome was observed with insulin mediated release of glucose transporter GLUT 4 and insulin resistance. However, further study is needed on large number of women with reproductive age to reach a better conclusion.

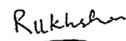
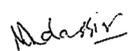
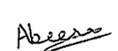
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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Roohi Jabbar	Study design, Data collection, Writing the manuscript.	
2	Rukhshan Khurshid	Formulation of tables reviewed and approved the manuscript.	
3	Uzma Jabbar	Statistical analysis, interpretation of results.	
4	Mudassir Zia	Formulation of tables reviewed and approved the manuscript.	
5	Abeera Mazhar Siddiqui	Statistical analysis, interpretation of results, Reviewed the manuscript.	
6	Farrukh Javaid	Manuscript writing and revising it critically for important intellectual content.	