Original Research Paper

Volume-9 | Issue-4 | April-2019 | PRINT ISSN No 2249-555X

Biochemistry

EARLY SCREENING OF IMPAIRED GLUCOSE TOLERANCE IN POLYCYSTIC OVARY SYNDROME WOMEN TO PREVENT DEVELOPMENT OF TYPE -2 DIABETIC MELLITUS & IT'S COMPLICATIONS.

Dr Meghatai Bhise

Department of biochemistry, Lokmanya Tilak Municipal General Hospital and Lokmanya Tilak Municipal Medical College, Sion Mumbai

ABSTRACT Polycystic ovary syndrome (PCOS) is Commonest endocrine disorder that affects almost 6 -10% woman in reproductive age group. A cross sectional study is carried out to evaluate risk of development of impaired glucose tolerance in women with polycystic ovarian syndrome characterized by oligo- or anovulation, biochemical or clinical hyperandrogenism, and polycystic ovarian morphology on ultrasonography. 2 hour oral glucose tolerance test carried out in women with PCOS and women without PCOS. The prevalence of Impaired glucose tolerance and type 2 diabetic mellitus in women with PCOS is substantially higher than expected when compared with age- and weight-matched populations of women without PCOS. There is highly significant rise in the fasting plasma glucose & 2 hr glucose level in polycystic ovary syndrome women. However to conclude oral glucose tolerance test was a more reliable for predictor of impaired glucose metabolism and periodic screening with oral glucose tolerance test useful in early diagnosis and prevention of development diabetic mellitus and its complications in PCOS women.

KEYWORDS : Polycystic Ovarian Syndrome, Oral Glucose Tolerance Test, Diabetic Mellitus, Impaired Glucose Tolerance.

Introduction

Polycystic ovary syndrome (PCOS) is one of the common endocrine disorder that affects 6 -10% of woman in reproductive age.[1,2,3] It was first described in 1935 by American gynecologists Irving F. Stein Sr. and Michael L. Leventhal thus for decades it was termed as Stein-Leventhal syndrome. It is a disorder of women which is characterized by an elevated level of male hormones (androgen) and infrequent or absent ovulation (anovulation). It is also characterized by the presence of polycystic ovaries, oligomenorrhea/amenorrhea.[4]

Material and method:

A cross sectional study and has been carried out in our institute during the period of February 2014 - August 2015. All the study subjects were examined & investigated according to predefined Performa. The study protocol was approved by the Ethical Committee of the Institute. Informed written consent was obtained from all the study subjects enrolled in the study.

Group A Consists of 60 clinically diagnosed and biochemically confirmed cases of polycystic ovarian syndrome. These were selected from patients attending the outpatient department of Obstetrics and Gynaecology. Group B Consist of 60 age and sex matched normal individuals were studied as controls were enrolled in the present study
All the calculations were done by using Microsoft Office Excel 2007 and statistical analysis was done using the SPSS software, Version 11.5. All statistical data was analysed by, Levene's test for Equality of Variances, t-test for Equality of Means. Mann-Whitney test. P-value less than 0.05 ($P < 0.05$) was considered to be statistically significant (S). P value of less than 0.001 ($P < 0.001$) was considered to be statistically highly significant (HS). P-value more than 0.05 ($P > 0.05$) was considered to be statistically non-significant (NS)

Discussion

Insulin resistance clinically defined as the inability of known quantities of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population.

Insulin resistance is characterized by an impaired glucose response to a specific amount of insulin more severe form of insulin resistance in PCOS range from impaired glucose tolerance to frank NIDDM.

PCOS is a heterogeneous disorder of uncertain cause.[9] but there is strong evidence that it is a genetic disease. The genetic component appears to be inherited in an autosomal dominant fashion with high genetic penetrance but variable expressivity in females.

Polycystic ovaries develop when the ovaries are stimulated to produce excessive amounts of male hormones (androgens), in particular testosterone, by either one or a combination of the following

1. The release of excessive luteinizing hormone (LH) by the anterior pituitary gland.
2. High levels of insulin in the blood (hyperinsulinaemia) in women whose ovaries are sensitive to this stimulus[5]

The syndrome most widely termed as polycystic due to the common sign on ultrasound examination of multiple (poly) ovarian cysts. These "cysts" are actually immature follicles, which are developed from primordial follicles, but the development has stopped ("arrested") at an early antral stage due to the disturbed ovarian function. The follicles may be oriented along the ovarian periphery, appearing as a 'string of pearls' on ultrasound examination.

A majority of people with PCOS have insulin resistance are obese. Their elevated insulin levels contribute to or cause the abnormalities seen in the hypothalamic-pituitary-ovarian axis that lead to PCOS. Hyperinsulinemia increases GnRH pulse frequency, LH over FSH dominance, increased ovarian androgen production decreased follicular maturation, and decreased SHBG binding; all these factors contribute to the development of PCOS, Insulin resistance is a common finding among women with a normal weight as well as overweight women.[6]

PCOS may be associated with chronic inflammation, with several investigators correlating inflammatory mediators with anovulation and other PCOS symptoms. Similarly, there seems to be a relation between PCOS and increased level of oxidative stress.[7]

PCOS is not only a reproductive endocrinopathy but also a metabolic disorder. PCOS is associated with hyperinsulinemia, glucose intolerance, obesity. Women with PCOS have an approximately sevenfold increased risk of developing type 2 diabetes mellitus (DM), compared to that of unaffected women.

Insulin resistance is frequently observed in both lean and obese women. More sever degree of insulin resistance or impaired glucose tolerance, however, are common in obese women with PCOS.

The association of hyperandrogenism and Carbohydrate metabolism was first described by Achard and Thiers in 1921 as “la diabete des femmes a barbe” (diabetes of bearded women).

Beta cell dysfunction is demonstrable in women with PCOS before the onset of glucose intolerance. The age of onset of diabetes appears to be earlier in the third or fourth decade of life. IR and pancreatic β-cell dysfunction are recognized as major factors in developing T2DM23
Glucose intolerance is associated with

1) Decreased first phase insulin secretion,
2) Decreased glucose deposition index,
3) Increased hepatic glucose production.

These metabolic abnormalities are precursors of type 2 DM (as manifested by the significant impairment of the β-cell function) which compensates for severe peripheral IR and elevated hepatic glucose production in women with impaired glucose tolerance.

Disturbances in insulin action are particularly related to PCOS pathogenesis. In women with PCOS, basal insulin secretion is increased and hepatic insulin clearance is reduced, resulting in

hyperinsulinemia. Insulin-stimulated glucose utilization is decreased by 35 to 40 percent in women with PCOS, independent of obesity, a decrease similar in magnitude to that seen in type 2 DM Obesity and PCOS have a synergistic negative impact on insulin sensitivity, so that hepatic insulin resistance is found only in PCOS women who are obese.

Under normal circumstances, insulin secretion increases as insulin sensitivity decreases, in order to maintain glucose homeostasis. This relationship of insulin sensitivity and insulin secretion, known as the disposition index, is described by a hyperbolic curve19 In both non obese and obese PCOS women, insulin secretion is inappropriately low for their degree of insulin resistance, suggesting the presence of pancreatic beta-cell dysfunction in these patients.

Women with PCOS share many features in common with the metabolic syndrome in particular. Dyslipidemia is likely to be the major risk factors for CVD in women with PCOS. The reason for the increase in the risk is not yet clear; hyperandrogenism has not yet been recognized as a risk factor for cardiovascular disease and studies on pre- menopausal women do not show a clear association between hyperandrogenism and the risk of future cardiovascular events. Insulin resistance and dyslipidemia seem to have an important role on the risk of cardiovascular pathology in women with PCOS. It is still not known to what degree dyslipidemia contributes to this risk.

In PCOS women's early screening of modifiable cardiovascular risk factors may help in preventing the development of cardiovascular disease.

Insulin is the chief regulator of glucose metabolism in the body. Its actions are mediated via the insulin receptor (IR) which is widely distributed in both non-insulin sensitive tissues. It acts to maintain glucose homeostasis in both the fed and fasting state in skeletal muscle and adipose tissue, insulin controls glucose uptake via enhanced translocation, docking and fusion of glucose transporter-4 (GLUT4) into plasma membranes This step is considered the rate-limiting step for glucose utilization and glycogenolysis.[8,9]

In relation to glucose metabolism, it is well recognized that under normal physiological conditions, insulin suppresses glucose production in the post-prandial state while eliciting glycogenolysis and gluconeogenesis in the absorptive state. This ensures sufficient levels of glucose are available as an energy substrate for tissues, particularly the brain and red blood cells, under all physiological states while maintaining euglycaemia in obesity, there is diminished insulin-induced suppression of glucose production, probably as a result of elevated glucose- 6-phophatase activity. The latter is likely to occur due to increased hepatic FFA influx that stimulates β-oxidation leading to the generation of acetyl-CoA, citrate and glucose-6-phosphate, substrates that down regulate insulin-induced inhibition of gluconeogenesis and glycogenolysis in the liver In obesity, there is defects in insulin's glucose regulatory functions that result in disruption of the above metabolic processes leading to hyperglycaemia, hyperinsulinaemia and insulin resistance.[10]

About one third of lean women with PCOS have raised insulin levels. Raised insulin concentrations have a side effect in the body of stimulating the ovary to produce more androgens. Androgens also contribute in alterations of glucose metabolism by inhibiting peripheral and hepatic insulin action. That leads to glucose accumulation and results into hyperglycemia in lean PCOS patient.

Chart 1: Showing FBS distribution in study groups.

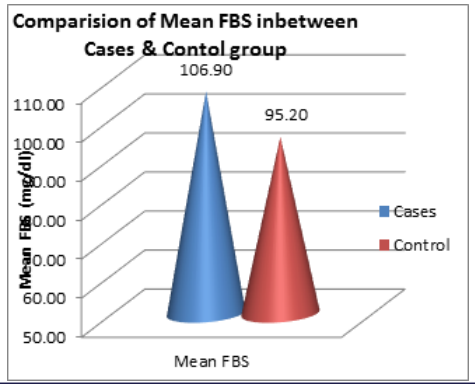

Chart 2: Showing 2hr OGTT distribution in study groups.

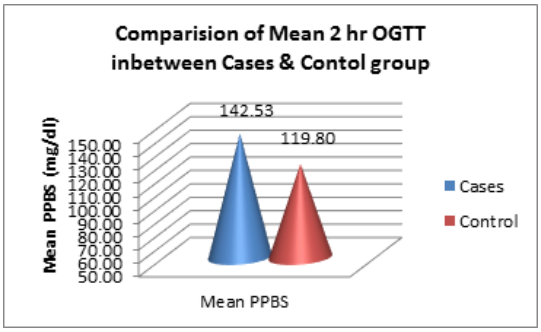

Table 1. : Comparison of Fasting Plasma glucose (FPG) in study groups

Parameter	Group A (n=60) (mean ± SD)	Group B (n=60) (mean ± SD)	P value
FPG	106.90±19.5	95.20±13.11	<0.001 (HS)

HS (P < 0.001) = highly significant.

In this study, we found highly significant (0.001) rise in the FPG in group A as compared to group B. Group A had mean of fasting plasma glucose level 106.90 ± 19.5 as compared to mean of fasting plasma glucose level 95.20 ± 13.11 group B.

Table 2: Comparison of 2 hr OGTT in study groups

Parameter	Group A (n=60) (mean ± SD)	Group B (n=60) (mean ± SD)	P value
2 hr OGTT	142.53±31.24	119.80±16.64	<0.001 (HS)

HS (P < 0.001) = highly significant.

In this study, we found highly significant (0.001) rise 2 hr glucose level in group A as compared to group B. Group A has mean of 2 hr glucose level after giving 75 gms of glucose 142.53 ± 31.24 as compared to group B who had mean of glucose level after giving 75 gms oral glucose 119.80 ± 16.64.

Conclusion

From the present study it can be concluded that OGTT was a more reliable for predictor of impaired glucose metabolism and periodic screening with OGTT useful in early diagnosis and prevention of development diabetic mellitus and its complications in PCOS women.

REFERENCES

1) Diamanti-Kandarakis E, Kouli CR, Bergiele AT, Filandra FA, Tsianateli TC, Spina GG, Zapanti ED, BartIzis M (1999). A survey of the polycystic ovary syndrome in the Greek island of Lesbos: hormonal and metabolic profile : J Clin Endocrinol Metab 84, 4006-4011.
2) Asuncion M, CalvoRM,San Milla´n JL, Sancho J, Avila S, Escobar- Morreale HF.(2000). A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain: J Clin Endocrinol Metab 85, 2434-2438.
3) Azziz R,WoodsKS, 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 Metab 89, 2745-2749.
4) Stein IF, Leventhal ML.(1935). Amenorrhea associated with bilateral polycystic ovaries : Am J Obstet Gynecol. 29,181-191.
5) Kiddy, D S, Sharp, PS, White. (1999). Differences in clinical endocrine features between obese and non-obese subjects with polycystic ovary syndrome an analysis of 263 consecutive cases: Clin. EndocnnoL, 32, 213-220.
6) Lithell, H, Nilhu, SJ., Bergh, T and Sebnus I. (1987). Metabolic profile in obese women with the polycystic ovary syndrome: Int J Obesity, 11, 1-8.
7) Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK. (1999). Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome: Diabetes Care. 22, 141-146
8) Rosenbaum D, Haber RS, Dunaif A. (1993). Insulin resistance in polycystic ovary syndrome: decreased expression of GLUT-4 glucose transporters in adipocytes : Am J Physiol, 264, 197–202
9) Dunaif A, Xia J, Book C-B. (1995). Excessive insulin receptor serine phosphorylation in cultured fibroblasts and in skeletal muscle: A potential mechanism for insulin resistance in the polycystic ovary syndrome: J Clin Invest, 96, 801.
10) Dunaif A, Graf M, Mandeli J, Laumas V, Dobrjansky A. (1987). Characterization of groups of hyperandrogenic women with acanthosis nigricans, impaired glucose tolerance and/or hyperinsulinemia: J Clin Endocrinol Metab, 65, 499–507.