Original Research Article **Biochemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

STUDY OF INSULIN RESISTANCE IN PREGNANCY WITH IMPAIRED GLUCOSE TOLERANCE

B.JYOTHIRMAYI*[1] AND M.VASANTHA[2]

[1]Department of Biochemistry, SRM Medical College Hospital ,SRM University,Kattankulathur,Kancheepuram district,Tamilnadu, India.
[2]Department of Biochemistry,SRM Medical College Hospital,SRM University

ABSTRACT

Pregnancy is a diabetogenic state which alters carbohydrate metabolism, influences insulin production and its regulation resulting in insulin resistance state. Decreased insulin sensitivity and associated risk factors like obesity can lead to development of diabetes over a period of time if not monitored regularly. Two groups of women were studied: pregnant women with normal glucose tolerance (n =30) as control and pregnant women with impaired glucose tolerance (n=30) as subjects Insulin levels were significantly high in subjects compared to controls. (14.55±5.5 7.25±5.0 P< 0.001).Insulin resistance was calculated using HOMAIR (2.9±1.7 1.45±0.0.87).Our study suggests that pregnant women with impaired glucose tolerance display a state of insulin resistance.

KEY WORDS: Insulin, Insulin resistance, pregnancy and impaired glucose tolerance.

B.JYOTHIRMAYI
Department of Biochemistry,SRM Medical College Hospital ,SRM University,Kattankulathur,Kancheepuram district,Tamilnadu, India

INTRODUCTION

Pregnancy alters the normal balances of carbohydrate metabolism and insulin requirements, which is often referred to as 'diabetogenic' state. Pregnancy results in a state of insulin resistance (Dahlgren,2006)[1].[1] Insulin resistance is defined as a decrease of biological action of insulin (catalano,2010;Robert 1995) [2] and presents as hyperinsulinemia or decreased ability of insulin to regulate glucose utilisation. (Kim etal.,1996)[3]. The resistance to insulin can be due to prereceptor (insulin antibodies), receptor deficiency on cell surface or decreased number of receptors [or] defects in intracellular insulin signalling pathway. (Catalano, 2010)[4]. During pregnancy insulin resistance is counteracted by increasing their insulin secretion and when it is not enough to meet the insulin resistance, glucose intolerance develops and leads to gestational diabetes.(kuhl etal1985)[5].Gestational diabetes is usually diagnosed during second or third trimester of pregnancy. GDM over the period of time develops into type 2 diabetes. According to WHO GDM is defined as diabetes in pregnancy when fasting blood glucose levels are >140 mg/dl or >198 mg/dl after 75g of glucose load.(Shalayal etal.,2010)[6] ,During the course of gestation,maternal insulin increases in response to glucose and other stimuli. IGT designed glucose tolerance results intermediate between normal glucose homeostasis and overt diabetes.(kahnetal., 2005; Bilous and Donnelly,2010; Burch,1994)[7]. It is diagnosed if fasting glucose > 108 mg/dl but < 140 mg/dl. Or 2hr glucose > 140mg/dl and< 200mg/dl.(shalayel etal.,2010; Hope etal.,1993)[8]. Insulin resistance is defined as normal or elevated insulin level produces an attenuated biological response and this refers to impaired sensitivity to insulin mediated glucose disposal.(Wilcox,2005) [9] .The aim of our study is to understand about insulin levels and insulin resistance that occurs during pregnancy and to create awareness among women during pregnancy to prevent diabetes and its associated complications in both mother and offspring.

MATERIALS AND METHODS

Thirty pregnant women with impaired glucose tolerance as subjects and thirty pregnant women with normal glucose tolerance were selected for the study who attended Obstetrics and Gynaec O.P SRM Medical college Hospital and research centre, Kattankulathur. INCLUSION CRITERIA: We have included pregnant women with family H/o diabetes, H/o big baby in previous pregnancy are included in the study. EXCLUSION CRITERIA: women with gestational diabetes were excluded from the study. Informed consent and institutional ethical committee approval was obtained. Ethical Clearance Number: 222/ IEC/2012.

Parameter analysis

Fasting blood sample was collected to assess blood glucose by Glucose- peroxidase method in Auto analyser (Beckmann Coulter) and insulin levels by Flouro Enzymatic Immunometric. Analysis (FEIA) method using TOSOH hormone analyser.

Statistical analysis

Data was expressed as mean, standard deviation and 'p' value was calculated using students 't' test. Calculations were performed using Statistical Packages for Social Sciences (SPSS) programme. Insulin resistance was calculated using HOMAIR formula.

RESULTS

Blood glucose, both fasting and post prandial levels were significantly high in Subjects when compared to controls. Fasting insulin levels was also significantly high in subjects compared to controls (P<0.001).

Table (1)

Shows blood glucose levels both in fasting and post prandial state and Insulin in fasting state in normal glucose tolerant pregnant women (controls) and in impaired glucose tolerant subjects

Parameters	Controls	Subjects	P value.
FBS	88.85±11.0	108±12.2	P<0.001
PBS	102.7±15.5	116± 25	P< 0.001
INSULIN	7.25±5.0	14.55±5.5	P< 0.001

FBS- Fasting blood glucose PBS – Post prandial blood glucose

Table (2)

Shows Insulin resistance in controls and subjects

Parameter	Controls	Subjects
HOMA IR	1.45 ± 0.87	2.9 ± 1.7

DISCUSSION

From the study we observed that insulin resistance is high in pregnant women with impaired glucose tolerance compared to normal glucose tolerant pregnant women. Several studies have demonstrated similar results in normal human pregnancy..Gestational diabetes has become more common in pregnant women which can be attributed to the life style modifications, dietary habits and genetic inheritance. Several studies has shown that insulin resistance and gestational diabetes can be due to maternal and placental hormonal changes which occur during pregnancy such as estrogen, progesterone, human placental lactogen, cortisol and prolactin. These changes can also alter carbohydrate metabolism.(Brudnell,1993)[10]. Presence of insulin resistance can be demonstrated in pregnancy by the

presence of hyperinsulinemia and euglycemia a circumstance that fulfils Berson and Yalows definition of insulin resistance i.e.," a state in which greater than normal amounts of insulin is required to elicit a normal response"[11] .The insulin resistance of pregnancy appear to be peripheral or target tissue resistance to insulin. Insulin action in insulin target cells consists of complex sequence of events. Insulin resistance can be subdivided into abnormalities of insulin sensitivity and abnormalities of insulin responsivity. Decreased insulin response or increased resistance shows defect in the action of insulin at target level. In pregnancy the defect could be at target tissues[12.] Pregnancy can alter insulin levels, which in turn influences or alters carbohydrate metabolism. The narrow line of balances involved in insulin production, regulation and action changes in a dynamic way throughout the gestation. In Normal women compensatory increase in insulin production occurs to overcome the resistance. During pregnancy there will be progressive increase in post prandial blood sugar levels secondary to increase in insulin resistance, which was also observed in our study .The metabolic syndrome of pregnancy includes an increased risk of hypertensive, metabolic disturbances of nutrient metabolism and inflammation. Although these pregnancy- related conditions are most likely to clinically resolve once the woman is delivered, these individuals still have the sub clinical underlying metabolic disorder, and are at increased risk for the metabolic syndrome in later life, particularly if there is increased postpartum weight gain.(Villamor & Cnattingius 2006)[13.]Genetic factors also play a role in the development of diabetes (Brudenell,1993)[14.] .Several studies suggest that GDM is inherited and usually NIDDM. The common feature of both is that both results due to insulin deficiency and insulin resistance which can be due to beta cell dysfunction .These studies also suggest the incidence of first degree family history of diabetes was significantly high in GDM and IGT groups in our study out of 30 subjects we got 3 subjects with a family history of diabetes. Pregnant women with H/o of big babies in previous delivery were also present in our study. All these factors can lead to development of diabetes in later life and certainly regular monitoring of blood glucose levels is needed.

CONCLUSION

The observation of our present study shows that women with impaired glucose tolerance has high insulin levels and increased insulin resistance and a decrease in maximum insulin responsitivity and are at risk of developing gestational diabetes in later life. Several risk factors like age, family history, obesity, history of big babies in previous pregnancies can lead to development of impaired glucose tolerance and gestational diabetes in mother, cesarian delivery in mother and neonatal hypoglycaemia, macrosomia and insulinemia in neonate at birth are observed in several studies.

ACKNOWLEDGEMENT

We thank department of Obstetrics and Gynaecology for their assistance in selecting subjects and controls for our study without whom the study could not be possible. We thank all the participants for their cooperation.

REFERENCES

1. Dahlgren J. Pregnancy and insulin resistance. Metabolic syndrome and related disorders. American Diabetes Association. 2006 June; 4(2):149-52.
2. Catalano PM. Obesity, insulin resistance and pregnancy outcome. Reproduction. 2010 Sep; 140(3): 365–71.
3. Kim JK, Wi JK, Young JH. Plasma free fatty acids decrease insulin – stimulated skeletal muscle glucose uptake by suppressing glycolysis in conscious rats. Diabetes.1996 Apr; 45(4): 446-53.
4. Catalano PM. Obesity, insulin resistance and pregnancy outcome. Reproduction. 2010 Sep; 140(3): 365–71.
5. Kuhl C, Anderson O. Etiology and pathology of gestational diabetes mellitus. Diabetes. 1985 Jun; 34 (suppl 2):66-70.
6. Shalayel MH, Elrobh MS, Idris SA, Mohammed MS, Ahmed SA. Prolactin and insulin estimates in pregnancy with glucose intolerance. Pak J Med Sci. 2010 Jan; 26(1): 102-6.
7. Kahn CR, Weir GC, King GL, Joslin's Diabetes Mellitus. In: Mirsolav Radenkovic, Teodora Smiljanic editors. Lipincott Williams and Wilkins. 14th ed. USA. Academic press; 2011. P. 332- 6.
8. Shalayel, Elrobh MS, Idris SA, Mohammed MS, Ahmed SA. Prolactin and insulin estimates in pregnancy with glucose intolerance. Pak J Med Sci. 2010 Jan; 26(1):102-6.
9. Wilcox G. Insulin and Insulin Resistance. Clin Biochem Rev. 2005 May; 26 (2): 19-39.
10. Brudnell M. Gestational Diabetes. In: Turnbull SA, Chamberlain editors. Diabetic Pregnancy in Obstetrics 2nd ed. Churchill Livingstone, Edinburgh, London, Melbourne and Newyork. 2011.p. 585- 602.
11. Berson SA, Yalow RS. Antagonists and insulin resistance. In: Ellenberg M, Rifkin H, editors. Diabetes Mellitus: Theory and Practice. 2nd ed. New York: McGraw-Hill; 1970.p. 388–423.
12. Kolterman OG, Insel J, Saekow M, Olefsky,JM. Mechanisms of insulin resistance in human obesity. J Clin Invest. 1980 Jun; 65(6):1272-84.
13. Villamor E, Cnattingius S. Inter pregnancy weight change and risk of adverse pregnancy outcomes: a population based study. Lancet. 2006 Mar; 368(9542)1164-70.
14. Brudnell M. Gestational Diabetes. In: Turnbull SA, Chamberlain editors. Diabetes pregnancy in Obstetrics. 2nd ed. Churchill Livingstone, Edinburgh, London, Melbourne and Newyork. 2011. p.585-602.