ORIGINAL ARTICLE

LIPID PROFILE AND SERUM INSULIN LEVELS IN GESTATIONAL DIABETES

Rubina Aziz[1], Tabassum Mahboob[2]

ABSTRACT

Objectives: To evaluate the glucose intolerance, insulin, and lipid profile in women who developed gestational Diabetes, compared to healthy pregnancy.

Design: Observational study

Patients and Methods: One hundred pregnant women, 50 healthy as control group and 50 already diagnosed gestational diabetic women as study group were selected. Plasma fasting (FBS) and post prandial glucose (RBS), serum insulin and serum lipid profile (total lipids, cholesterol, triglycerides, HDL-cholesterol and LDL- cholesterol) of both were monitored. Mean values were compared using t-test.

Results: Mean FBS [124.76±4.22 vs. 90.06±1.20 mg/dl], mean RBS [221.38±6.68 vs. 120.32±1.97 mg/dl], insulin [32.10±0.83 vs. 17.88±0.54 μIU/ml], mean cholesterol [216.60±5.87 vs. 166.38±3.19 mg/dl], mean triglycerides [189.36±6.76 vs. 106.28±2.85 mg/dl], LDL-cholesterol [131.08±4.73 vs. 102.48±2.18 mg/dl] and total lipids [825.24±16.92 vs. 653.96±15.40 mg/dl] were higher in GDM groups as compared to normal controls ($p<0.01$). Mean HDL-cholesterol [41.24±0.65 vs. 48.34±0.66 mg/dl] showed significantly lower concentration in GDM group as compared to controls ($p<0.01$).

Conclusion: Mean insulin and lipid levels, except HDL-cholesterol, were significantly higher in gestational diabetics compared to controls.

Keywords: Gestational diabetes, hyperlipidemia, insulin resistance, hypertriglyceridemia, high density lipoproteins, low density lipoproteins.

INTRODUCTION

Gestational Diabetes is defined as glucose intolerance that is first diagnosed during pregnancy.[1] The incidence of Gestational Diabetes Mellitus (GDM) has doubled over the last 6–8 years. GDM carries long-term implications for the subsequent development of type 2 diabetes in the mother and increased risk of obesity and glucose intolerance in the offspring.[2] Normal pregnancy has been characterized as a "diabetogenic state" because of the progressive increase in post prandial glucose and insulin response in late gestation.[3,4] Gestational diabetes is a complication of pregnancy associated with an increase in maternal and perinatal morbidity.[4] Women with gestational Diabetes mellitus are at an increased risk of the development of diabetes (usually type 2) after pregnancy.[5] The underlying pathophysiology of gestational diabetes is a function of decreased maternal insulin sensitivity or increased insulin resistance. Insulin resistance is defined as the inability of a defined concentration of insulin to affect a predictable biological response of nutrient metabolism at the level of the target tissue. Significant alterations in glucose metabolism

1. Medical Technologist Department of Biochemistry, Federal Govt Urdu University for Arts, Sciences, and Technology. Karachi, Pakistan.
2. Professor Department of Biochemistry, University of Karachi, Pakistan.
Correspondence: Dr. Rubina Aziz, Medical Technologist Department of Biochemistry, Federal Govt Urdu University for Arts, Sciences, And Technology. Karachi, Pakistan.
E-mail: rubinaaziz67@hotmail.com
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occur in women who develop gestational diabetes relative to pregnant woman with normal glucose tolerance. Decreased insulin response to a glucose challenge was also demonstrated in women with gestational diabetes in late gestation.[6] Pregnancy and diabetes have an additive effect on the development of an atherogenic lipid profile. Importantly, this is exaggerated earlier in pregnancy in gestational diabetes.[7] The hallmarks of insulin resistance syndrome are glucose intolerance; hyperinsulinemia, a characteristic dyslipidemia, obesity, (in particular with central fat distribution) and hypertension.[8]

In the view of above findings the present study was designed to evaluate the status of blood glucose and insulin levels and lipid profile in women who had developed gestational Diabetes compared to those who did not.

PATIENTS AND METHODS

This study was carried out on a total of 100 pregnant women (50 normal pregnant women and 50 gestational diabetic women) of same age in third trimester of pregnancy, selected from Obstetrics and Gynaecology wards and outpatients departments of Holy Family Hospital, Civil Hospital, Jinnah Post Graduate Medical Center and Godhra Muslim Medical Center, Karachi from December 2004 to February 2005.

Inclusion criteria for Group I (control group) were normal pregnant women without family history of Diabetes or other endocrine disorders, or history of taking any hypoglycemic or hyperglycemic medicines.

Group II (gestational diabetic) included diabetic women, where the diagnosis was made using the criteria after performing a fasting 3-h, 100-g oral glucose tolerance test (OGTT) with a screening test (50-g oral glucose challenge) showing a 1-h glucose value < 140 mg/dl (7.8 mmol/l).[5]

All pregnancies with hypertension, metabolic disorder or fetal abnormalities were excluded from the study.

Fasting plasma glucose, serum insulin and lipid profile (total cholesterol, triglycerides, HDL- cholesterol, LDL-cholesterol and total lipids) samples were obtained in fasting state. Post prandial glucose samples were taken 2 hours after of breakfast. Plasma glucose (mg/dl) were determined after enzymatic oxidation in the presence of glucose oxidase. The hydrogen peroxide formed reacts, under catalysis of peroxidase, with phenol and 4-aminophenazone to form a red-violet quinoneimine dye as indicator.[9] Serum insulin (µlU/ml) were measured by an enzyme immunometric assay on the Immulite analyzer.[10,11]

Serum total cholesterol (mg/dl) was determined after enzymatic hydrolysis and oxidation.Indicator quinoneimine was formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase11 by standard kit methods.[12]

Serum triglycerides (mg/dl) were determined after enzymatic hydrolysis with lipases. The indicator was a quinoneimine formed from hydrogen peroxide, (4-aminophenazone and 4-cholorophenol under the catalytic influence of peroxidase) by standard kit methods.[13, 12] Chylomicrons, very low density lipoproteins and low density lipoproteins were precipitated by addition of phosphotungstic acid and magnesium ions to the sample. The cholesterol content of the supernatant was determined enzymatically) by standard kit methods.[13,12] LDL was precipitated by addition polyvinyl sulphate to the sample and the concentration was calculated from the difference between the serum total cholesterol and the cholesterol in the supernatant after centrifugation), by standard kit methods.[12] Total lipids in mg/dl were estimated by standard kit method.[14] Body Mass Index (BMI) was calculated by dividing body weight (kg) by the square of height (meters).Verbaly informed consent was obtained from all women.

The Data was analyzed using SPSS (Ver.15) soft wear. The descriptive statistics was shown as mean ± SEM. The indepent two-samples "t" test was employed to compare the two groups. The P –Value less then 0.01 was assumed as asignificant difference.

RESULTS

Clinical and laboratory parameters are given in Tables-1 and 2 respectively.

Mean age [23.66±0.35 vs. 23.62±0.41 years], mean gravid status [2.00±0.15 vs. 2.22±0.18], mean gestational

ages [31.42±0.14 vs. 31.98±0.21weekly] and mean BMI [27.92±0.47 vs. 27.62±0.25] of the gestational diabetic group and control group were not significantly different as shown in table 1.

The mean plasma fasting glucose [124.76±4.22 vs. 90.06±1.20 mg/dl] and mean postprandial glucose [221.38±6.68 vs. 120.32±1.97 mg/dl] concentration in GDM group were significantly higher than normal pregnant women ($p<0.01$). Mean serum insulin [32.10±0.83 vs. 17.88±0.54 µIU/ml] concentration in GDM group was significantly higher as compared to normal controls as shown in table 2 ($p<0.01$).

Mean serum cholesterol [216.60±5.87 vs. 166.38±3.19 mg/dl], mean serum triglycerides [189.36±6.76 vs. 106.28±2.85 mg/dl], mean LDL-cholesterol [131.08±4.73 vs. 102.48±2.18 mg/dl] and mean total lipid [825.24±16.92 vs. 653.96±15.40 mg/dl] concentrations were also higher in GDM groups as compared to normal pregnant controls. While mean HDL-cholesterol showed significantly lower concentration in GDM patients as compared to normal [41.24±0.65 vs. 48.34±0.66 mg/dl] as shown in table 2.

Table 1: Clinical characteristics of the control and gestational diabetic groups (GDM).

S #	Parameters	Control (n=50)	GDM (n=50)
1	Age (years)	23.62±0.41	23.66±0.35
2	Gravida	2.22±0.18	2.00±0.15
3	Gestational age (weeks)	31.98±0.21	31.42±0.14
4	BMI	27.62±0.25	27.92±0.47

Table 2: Plasma glucose, serum insulin and lipid profile of normal and gestational tional diabetic groups.

S #	Investigations	Normal controls (n=50)	GDM (n=50)
1	FBS (mg/dl)	90.06±1.20	124.76±4.22*
2	RBS (mg/dl)	120.32±1.97	221.38±6.68*
3	Serum insulin (µIU/ml)	17.88±0.54	32.10±0.83*
4	Serum cholesterol (mg/dl)	166.38±3.19	216.60±5.87*
5	Serum triglycerides (mg/dl)	106.28±2.85	189.36±6.76*
6	HDL- cholesterol (mg/dl)	48.34±0.66	41.24±0.65*
7	LDL- cholesterol (mg/dl)	102.48±2.18	131.08±4.73*
8	Total lipids (mg/dl)	653.96±15.40	825.24±16.92*

* $P<0.01$ as compared to control denoting significance.

DISCUSSION

This study showed that fasting and postprandial glucose, serum insulin, serum cholesterol, serum triglycerides, LDL-cholesterol and serum total lipid concentrations were higher in women who developed gestational Diabetes as compared to the normal pregnant women.

Normal pregnancy has been characterized as a "diabetogenic state" because of the progressive increase in postprandial glucose and insulin response in late gestation.[3,4] There is higher glucose production and lower glucose clearance after an overnight fast as compared to normal pregnant women as shown in this study and also supported by Xiang et al.[9] These two factors (high glucose production and low clearance) contribute to elevation of fasting glucose levels in Gestational Diabetes Mellitus. Gestational diabetes does not occurr due to defective secretion of insulin as supported by Seely and Solomon.[15]

In the present study higher insulin levels (table 2) were found compatible with other studies by Catalano et al, Setji et al, Butte, and Toescu et al.[15-17] The pathophysiology of gestational diabetes is a functional decrease of maternal insulin sensitivity or increased insulin resistance. Insulin resistance is defined as the inability of a defined concentration of insulin to affect a predictable biological response of nutrient metabolism at the level of the target tissue.[6] Various hormones like cortisol, prolactin , progesterone and human placental lactogen rise with the advancement of pregnancy, so the insulin resistance occurs and becomes worse and maximum in IIIrd trimester of pregnancy. Since insulin resistance is related to defect in pancreatic beta cells functions mothers at this time with beta cell functional deficiency become glucose intolerant.

We also found that levels of serum total cholesterol and LDL-cholesterol were also higher, as noted in some other studies[3,6,7,18] While in some studies cholesterol concentrations did not differ significantly between gestational diabetic and control mothers.[19,20] Lipid metabolism changes during pregnancy and lipolysis is increased as a result of insulin resistance. VLDL remains in the plasma for longer period because of a decrease in the activity of lipoprotein lipase, and leads to accumulation of LDL. The LDL particles in plasma vary in size due to variable amount of cholesteral, Contained in them. \Pregnancy and Diabetes hav additive effect on the development of atherogenic lipid profile. Importantly,

this is exaggerated earlier in pregnancy in gestational diabetes.Therefore higher concentrations of total and LDL-cholesterol is found in gestational diabetic patients.

In this study, it was also found that with increasing insulin resistance serum triglycerides also increased while HDL-cholesterol decreased as shown in table 2. This is also supported by some others studies.[14-17] Insulin-regulated carbohydrate, lipid and protein metabolisms are affected to a variable degree. Lipid metabolism changes during pregnancy, the anabolic phase of early pregnancy encourages lipogenesis and fat storage in preparation for the rapid fetal growth in late pregnancy.[21-24] Lipolysis is increased as a result of insulin resistance, leading to increased triglycerol concentration. The ability of insulin to suppress free fatty acids with advancing gestation were found in Gestational Diabetes Mellitus, hence insulin resistance is responsible for the hypertriglyceridemia in Gestational Diabetes Mellitus.

CONCLUSION

In the view of the above findings, it is concluded that there is a positive relationship between insulin resistance and hyperlipidemia in pregnancies complicated by Gestational Diabetes. Mainly the insulin resistance is responsible for the accumulation of cholesterol and triglycerides in serum, which in turn elevates LDL-cholesterol and decreases HDL cholesterol.

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Errata

Due to inadvestent composing error, there was a discrepency in title of an article in issue 2 of volume 2 as stated in the index and the main contents. The title should be read as " Relationship of central corneal thickness with measured intraocular pressure" by Mashhooduzzafar and Ziauddin A. Shaikh.