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Original Work

Role of leptin and adiponectin in gestational diabetes mellitus: a study in a North Indian tertiary care hospital

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ABSTRACT: Gestational Diabetes Mellitus (GDM) exposes women to a higher risk for development of type 2 diabetes mellitus in later years of life. Newborns of mothers with GDM are at increased risk for acute perinatal complications including hypoglycaemia, jaundice and being large for gestational age. One of the mechanisms underlying glucose metabolism in pregnancy are a group of substances, which includes leptin and adiponectin, produced mainly in the adipose tissue; in this paper we analyze the role of these mediators in women with GDM. This case control study was performed in 90 females (30 GDM patients and 60 control subjects without GDM) referred to a tertiary care hospital. Blood samples were analyzed for fasting blood glucose, leptin and adiponectin. Leptin and Adiponectin were analyzed using ELISA technique. In our study, the levels of fasting blood glucose were statistically significantly higher (p=0.000) in gestational diabetes patients as compared to controls. There was statistically significant positive correlation between blood glucose and leptin (p = 0.000, r = 0.585). There was statistically significant negative correlation between blood glucose and adiponectin(p = 0.000, r = -0.661). An amplification of the low-grade inflammation already existing in normal pregnancy may lead to increase in leptin and decrease in adiponectin. These factors may play a role in development of gestational diabetes mellitus. Further studies are required for establishing them as a marker for gestational diabetes mellitus.

KEY WORDS: ***Gestational diabetes mellitus; Leptin; Adiponectin***

INTRODUCTION

Pregnancy is a hyperglycemic period of life, with the hyperglycemia serving a highly important role in the nutrition and development of the fetus by providing it with adequate levels of glucose[1]. Gestational diabetes mellitus is a complication of pregnancy that is characterized by impaired glucose tolerance with onset or first recognition during pregnancy[2].

Gestational Diabetes Mellitus and gestational dysregulation of blood glucose levels expose the women affected to a higher risk for subsequent development of type 2 diabetes mellitus and cardiovascular disease later in their lives. Both mother and newborn have a significantly increased risk for metabolic and vascular disease after a diabetic pregnancy[3-5]. Newborns of mothers with GDM are typically at increased risk for acute perinatal complications including hypoglycaemia, jaundice and being large for gestational age[6], the risk being proportional to the degree of the dysregulation and hormones produced by the placenta[7] and increased maternal fat mass[8].

One of the mechanisms underlying glucose metabolism in pregnancy are a group of substances, produced mainly in the adipose tissue which includes leptin and adiponectin[9]. In recent years, the adipokines adiponectin and leptin have been shown to play a role in normal pregnancy, as well as in complications of pregnancy, including GDM[10]. In this paper we analyse the role of these mediators in women with GDM.

METHODOLOGY

This case control study was performed in 90 females (30 GDM patients and 60 control subjects without GDM) referred to the Department of

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Biochemistry, Lady Hardinge Medical College and associated hospitals, New Delhi in 2011-12. It was approved by the institutional ethical committee. Informed consent was obtained from each participant after explanation of the nature and purpose of the study. Gestational age was estimated from participants' last normal menstrual period which was further confirmed or modified by ultrasound. The diagnosis of GDM was made using a two-step approach. Patients were initially screened by measuring the plasma glucose concentration 1 h after a 50g oral glucose challenge test at ~28 weeks of gestation. A diagnostic oral glucose tolerance test was performed on the subset of women whose plasma glucose concentrations exceeded the glucose threshold value (>140 mg/dl). The diagnostic criteria for GDM were the Carpenter/Coustan conversion as recommended by the American Diabetes Association[11].

Sample collection and analytic procedures

Blood samples collected from study participants were refrigerated and centrifuged at 4°C. Plasma and serum samples were stored at −70°C until assayed. Fasting blood glucose was done by fully automated autoanalyser (CX-4 analyser by Beckman Coulter USA). Leptin and adiponectin were analysed by DRG ELISA kit. Statistical analysis (SPSS version 20) was done to analyse the significance and correlation of leptin and adiponectin with blood glucose in GDM patients.

RESULT

In our study the levels of blood sugar were statistically significantly higher (p = 0.000) in gestational diabetes patients (177.33 ± 22.96 mg/dl) as compared to controls (106.30 ± 16.152mg/dl). The leptin concentrations were higher in women with gestational diabetes mellitus (42.96 ± 19.47 ng/ml) as compared with those who have normal glucose tolerance (16.53 ± 7.58 ng/ml). Adiponectin concentrations were lower in women with gestational diabetes mellitus (5.43 ± 2.28 µg/ml), compared with those having a normal pregnancy (13.03 ± 5.53 µg/ml). The change in leptin and adiponectin was highly significant statistically (p = 0.000) (**Table 1**).

Table 1: Levels of blood sugar, leptin and adiponectin in gestational diabetes mellitus patients and controls

	Controls (n=60) Mean ± SD	**Cases (n=30) Mean ± SD**	**P value**
Sugar	106.30 ±16.152	177.33 ±22.96	0.000
Leptin (ng/ml)	16.53 ±7.58	42.96 ±19.47	0.000
Adiponectin (µg/ml)	13.03 ±5.53	5.43 ±2.28	0.000

The levels of leptin and adiponectin were correlated significantly with fasting blood glucose (**Table 2**). There was statistically significant positive correlation between blood glucose and leptin(p = 0.000, r = 0.585). There was statistically significant negative correlation between blood glucose and adiponectin (p = 0.000, r = -0.661).

Table 2: Correlation of blood glucose with leptin and adiponectin

	Leptin		Adiponectin	
	p	r	P	R
Blood glucose	0.000	0.585**	0.000	-.661**

***Correlation is significant at the 0.01 level (2-tailed)*

DISCUSSION

In our study, the levels of leptin were higher in GDM and correlated positively with blood sugar. Most studies have found increased leptin concentrations in GDM[12-15]. Leptin increases insulin sensitivity by influencing insulin secretion, glucose utilization, glycogen synthesis and fatty acid metabolism, regulates gonadotrophin releasing hormone secretion from the hypothalamus and activates the sympathetic nervous system[16,12]. Besides its effect on regulating gonadotrophin releasing hormone secretion, leptin plays a functional role in implantation[17,13]. Moreover, it induces human chorionic gonadotrophin production in trophoblast cells, regulates placental growth, enhances mitogenesis and stimulates amino acid uptake[17,13]. Hyperleptinaemia in early pregnancy appears to be predictive of an increased risk to develop GDM later in pregnancy independent of maternal adiposity[18].

GDM is characterized by an amplification of the low-grade inflammation already existing in normal pregnancy[19]. The concentrations of inflammatory molecules like TNFα and IL-6 increases in GDM pregnancies and these are responsible for causing insulin resistance. Conversely, leptin itself increases production of TNFα and IL-6 by monocytes and stimulates the production of CC-chemokine ligands[20]. Thus, a vicious circle develops, aggravating the inflammatory situation. Thus, hyperinsulinaemia in GDM might further stimulate leptin production. Insulin increases leptin secretion by adipocytes and elevated leptin concentrations in turn amplify inflammation[21]. The increased leptin may adversely affect the outcome of pregnancy and women who have gestational diabetes mellitus (GDM) are at a greater risk of developing type 2 diabetes mellitus (type 2 diabetes) within 10-20 years of their index pregnancy[22].

The levels of adiponectin were lower in GDM patients and it was negatively correlated with blood sugar levels. Adiponectin is considered an insulin-sensitizing, anti-inflammatory and anti-atherogenic

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adipokine[23]. Adiponectin concentrations were lower in women with gestational diabetes mellitus, compared to those having a normal pregnancy. Lower adiponectin levels have notably been associated with subclinical inflammation, while low levels of adiponectin in pregnancy have been associated with women of South Asian origin and this may have a significant impact on the development of GDM[10]. Moreover, downregulation of adiponectin in the first trimester of pregnancy is an independent predictor of impending GDM[24-25]. Moreover, quantification of adiponectin has been included in a prediction model using a panel of maternal demographic and clinical characteristics[26-28].

In conclusion, the results of the present study can be applied to a broader understanding of the significance of adiponectin and leptin in GDM. Further studies in larger populations are required, to determine whether the adiponectin and leptin could represent a potential biomarker of insulin resistance in pregnancy, and provide information beyond the Homeostasis Model Assesment Insulin Resistance (HOMA-IR.)

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