Original Research Article

Role of resistin in gestational diabetes in Eastern India

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Received: 11-01-2021 / Revised: 18-03-2021 / Accepted: 21-04-2021

Abstract

Background: Gestational diabetes leads to complications due to glucose intolerance whereas resistin induces insulin resistance concerned in the pathogenesis of obesity and type 2 diabetes commonly associated with GDM. Thus the aim of the study is to investigate the relationship between resistin levels and GDM and the possible benefits of the metabolic profile. **Methods:** The cross-sectional study consists of 36 pregnant females routinely examined for GDM with a 75 g 2 hour oral glucose tolerance test (OGTT) at the gynecological out-patient clinic were taken as cases whereas 32 women with normal glucose tolerance (NGT) were taken as control subjects. The cases as well as controls were assayed for serum resistin as well as serum insulin after matched for age, gestational age as well as BMI for this study. **Results:** Serum resistin levels were increased in GDM cases as compared to controls and were statistically significant (36.24 ± 14.62 vs 15.29 ± 8.51 ng/ml; $p < 0.0001$). Moreover, serum Insulin levels were higher in GDM cases as compared to controls which were statistically significant (16.92 ± 8.23 versus 8.84 ± 4.11 µ IU/ml; **P** < 0.0001). **Conclusion:** Our study reveals higher serum resistin and higher serum insulin values in GDM cases may be used for screening tests in the diagnosis of the disease.

Keywords: Gestational diabetes, resistin, insulin, diabetes mellitus, glucose, oral glucose tolerance test (OGTT)

Introduction

Gestational diabetes mellitus (GDM) is a metabolic disorder commonly recognised during gestation in pregnancy leads to acute and chronic complications due to glucose intolerance. It contributes to approximately 16% of pregnancies globally with an estimate of 25% in Southeast Asia and the percentage continues to increase, contributing significantly to the increased prevalence of diabetes and obesity [1, 2].Moreover, it is a heterogeneous disorder due to exchanges between environmental and genetic factors. The placenta plays an important role in fetal growth and development by supplying nutrients and oxygen. GDM alters placental structure and function with aberrant vascularization, increased inflammation, and impaired energy metabolism [3]. Maternal hyperglycaemia known to be associated with C-peptide levels above the 90th percentile, primary caesarean section, clinical neonatal hypoglycaemia, gestational hypertension, birth injury, premature delivery, neonatal hyperbilirubinaemia, preeclampsia and neonatal intensive care admission [4]. The associated factors such as obesity, diabetes mellitus advanced maternal age are said to be linked with GDM. Moreover, it enhances the potential risk of type 2 diabetes onset in the mother and her offspring [5]. The pathogenesis of GDM has not been clearly unstated but since the disease has been linked with associated risk factors with obesity, type 2 diabetes mellitus (T2DM), a connection between these two diseases may be established [1].

On the other hand, resistin is a secreted protein discovered in rodents as an adipocyte-derived factor which induces insulin resistance concerned in the pathogenesis of obesity and type 2 diabetes which are associated risk factors for GDM [6]. Human and murine resistin shares 59% homology only at the amino acid level [7]. The human resistin is primarily produced by peripheral blood mononuclear cells (PBMCs), macrophages, and bone marrow cells [8]. Human resistin has been associated with inflammation as well as endothelial dysfunctions by showing the expression of proinflam-matory cytokines.Moreover, human resistin involves in the pathological process of metabolic disease which includes obesity,

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diabetes, and cardiovascular diseases [9, 10]. The resistin level has been inconsistent in several studies and does not establish the link between resistin and the development of GDM. Moreover, no studies have been done in Eastern India which establishes the link between resistin and development of GDM. Therefore our aim was to investigate the relationship between resistin levels and GDM and the possible benefits of the metabolic profile.

Materials & Methods

The cross-sectional study consists of 36 pregnant females routinely examined for GDM with a 75 g 2 hour oral glucose tolerance test (OGTT) at the gynecological out-patient clinic were taken as cases whereas 32 women with normal glucose tolerance (NGT) were taken as control subjects in a tertiary care teaching hospital, Haldia, West Bengal. The cases as well as controls were matched for age, gestational age as well as BMI for this study. The diagnosis of GDM was made if one or more plasma glucose levels were elevated during a 75 g, 2 h oral glucose tolerance test (OGTT) according to the criteria of the American Diabetes Association [10]. The following threshold plasma glucose levels were used: fasting ≥100 mg/dl (5.5 mmol/l), 1 h ≥ 180 mg/dl (10.0 mmol/l) and 2 h ≥ 140 mg/dl (7.8 mmol/l). Patients with multiple pregnancy, pre-existing glucose intolerance, pregnancy-induced hypertension, bronchial asthma, preeclampsia, acute or chronic inflammation, as well as active smokers were not included. Routine biochemical parameters were done for both cases as well as controls. Informed consent was taken by cases and control groups. The study was approved by the Institution Ethics committee.

Overnight fasting venous blood samples were obtained from all participants by arm venous puncture to assess serum resistin levels and other biochemical parameters in the second trimester (24–28th weeks of gestation) during GDM screening. The samples were primarily stored at room temperature for 30 min to allow the blood to clot, followed by centrifugation at 2500 rpm for 15 – 20 min to separate serum. Serum specimens were aliquoted and stored at −80 °C until resistin levels were analyzed. Glucose levels were measured with the hexokinase method using a commercially available kit whereas Insulin levels were determined using a chemiluminescent assay (Beckman Coulter, CA). Serum resistin levels were assayed using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Raybiotech, USA). Statistical analysis of different biochemical parameters was performed by Students' *t*-test. All variables were expressed as mean ± SD (standard deviation). Means obtained from two normally distributed sample groups were compared by Student's unpaired two-tailed "*t*"-test and for nonparametric Mann-Whitney *U* "*t*" test. To find out the correlation between two variables, Pearson's product moment correlation coefficient was used. A value of $P < 0.05$ was considered as statistically significant. All statistical analyses were performed by using Graph Pad prism software (version 5, 2007, San Diego, California, USA).

Results

The demographic and biochemical profile of the GDM subjects and healthy controls is presented in Table 1. There was no significant difference in age and BMI in either of the two groups between GDM cases and control subjects (Table 1). OGTT levels were elevated in GDM cases as compared to controls which were found statistically significant (Table 1). Serum resistin levels were increased in GDM cases as compared to controls and were statistically significant (36.24 ± 14.62 vs 15.29 ± 8.51 ng/ml; p < 0.0001) (Figure 1). It was also observed that serum Insulin levels were higher in GDM cases as compared to controls which was statistically significant (16.92 ± 8.23 versus 8.84 ± 4.11 µ IU/ml; **P** < 0.0001) (Figure 2). However, no correlation was observed between serum insulin with serum resistin level (**r** = 0.341; **P** = 0.298) among GDM subjects.

Table 1: Demographic and biochemical profile of the subjects

	Control (n = 32)	Cases (n = 36)
Age	26.42 ± 6.91	27.82 ± 5.72
BMI	26.64 ± 2.64	27.12 ± 1.62
Gestational age at blood sampling (in weeks)	25.68 ± 1.16	25.82 ± 1.84
FBG (mg/dl)	86.23 ± 9.52	102.54 ± 14.36 *
OGTT 2 h (mg/dl)	119.2 ± 11.24	142.64 ± 21.44*
Total Cholesterol (mg/dl)	188.24 ± 29.18	208.26 ± 58.42

FBG, fasting blood glucose; OGTT, Oral Glucose Tolerance Test; Age, BMI, and serum levels of biochemical parameters were expressed as the means ± SD. Statistically significant, * p < 0.001 vs Control.

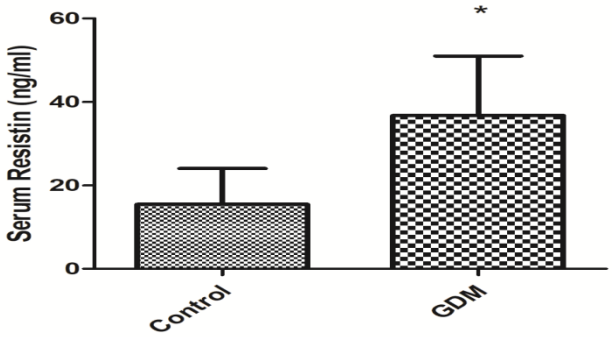

Fig 1: Serum levels of Resistin in control and GDM subjects.

Serum levels of Resistin were determined as described in methods for control and GDM subjects. Values expressed as the means ± SD. Statistically significant, * p < 0.0001, vs GDM.

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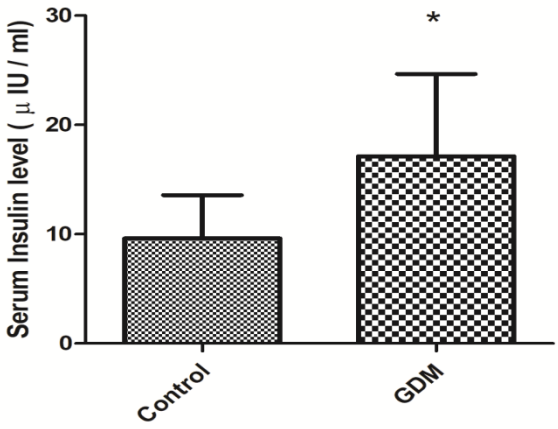

Fig 2: Serum levels of Insulin in control and GDM subjects.

Serum levels of Insulin were determined as described in methods for control and GDM subjects. Values expressed as the means ± SD. Statistically significant, * $p < 0.0001$, vs GDM

Discussion

GDM is recognised in pregnant women when the compensatory increase in insulin is not sufficient to maintain glycemic homeostasis. The results of studies on the association between resistin and GDM risk severely vary. Few studies have recommended that higher circulating resistin is a risk factor for GDM [11-15], while some studies have suggested elevated circulating resistin is a protective factor[16-19]. Moreover, few studies reported that serum resistin circulating level is not associated with GDM risk [20 -24]. A study assayed by Steppan et al [6] found that resistin expression was adipocyte-specific whereas recent reports reported that resistin is also expressed in multiple other tissues, such as pancreatic islets, skeletal muscles, mononuclear cells, placenta, and liver cells [25-26]. Another study found that resistin protein expression in placental tissue was much higher than that in subcutaneous adipose tissue in pregnant women's abdomens, indicating that the placenta is a major contributor of resistin in pregnancy [27]. Several studies have shown maternal circulating level of resistin gradually increases with gestational age and decreases significantly after delivery [28-30] . Moreover, few studies noticed no association between circulating resistin levels and GDM [31].

The association between elevated serum resistin level and GDM was only found in the third-trimester subgroup according to the gestational age because of the serum level of resistin is higher with gestational age [28-30]. A study done by Choi et al [11] found higher circulating resistin levels in women with pre GDM than in women with normal glucose tolerance during pregnancy and one year after delivery. Our study reveals higher serum resistin values in GDM cases than controls which accounts for several studies done. However, our study does not reveal a correlation between serum resistin and insulin which fewer studies have found out. The link between serum resistin with insulin may be due to increase in the gestational age. However, there were few limitations in our study which needs to be mentioned. The sample size of the study was less. Secondly, few of the patients were taking some other drugs such as antihistamines, topical corticosteroids which might interfere with serum resistin or insulin levels. Despite these limitations it has been observed that serum resistin levels and serum Insulin levels were higher in GDM patients. Though correlation has not been seen between resistin and insulin in GDM cases there is a significant rise in their levels indicating early screening of these markers could be of diagnostic importance in the prevention of the pathogenesis of gestational diabetes. Moreover it would be recommended that a longitudinal study needs to be done for better understanding the pathogenesis of GDM.

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Conflict of Interest: Nil
Source of support:Nil