Effect of Gestational Diabetes on Serum Leptin during Pregnancy and Postpartum Period

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is associated with marked increase in insulin resistance. The objective of study is to determine the relation of gestational diabetes with serum leptin and serum insulin levels during pregnancy and postpartum period.

Methods: This case control study conducted on total ninety samples that include cases and controls taken after 24 weeks of gestation. The case sample included 40 pregnant women with GDM and 10 women with GDM at postpartum stage. The control sample included 30 normal pregnant women with no GDM and 10 normal women at postpartum. Fasting serum leptin and fasting serum insulin were measured by ELISA. HOMA index was calculated by fasting serum insulin and fasting blood glucose.

Results: Serum leptin (30.89 ± 1.35), serum insulin (27.67 ± 1.32) and HOMA index (8.33 ± 0.53) significantly high in gestational diabetic women than normal pregnant (p<0.05) during pregnancy. However, after delivery of fetus, serum leptin, serum insulin and HOMA index in gestational diabetics significantly decreased compared to during gestation period. Hence a positive correlation of GDM was determined against serum leptin and HOMA index.

Conclusion: Serum leptin level is raised in GDM which has a positive correlation with insulin resistance. This study finds that the serum leptin levels may use as a marker to early screen and diagnose Gestational diabetes.

Introduction

Pregnancy is associated with a series of physiological changes that include increased food intake, accumulation of body fat and progressively raised insulin resistance (1). During the first trimester of pregnancy, there is an increase in the insulin secretion and maternal fat cells while insulin sensitivity either remains unchanged or increases. However, from mid trimester onwards, insulin sensitivity decreases. So, for maintenance of euglycemic state, a 2-fold increase in insulin secretion is required. Any abnormality in the physiological pregnancy that can’t compensate the insulin necessity will contribute to the complications like gestational diabetes (2). The pathogenesis of GDM is related to either insufficient insulin production against the demand during pregnancy or the raised-up insulin resistance (3). Food intake stimulates leptin production but in the presence of resistance it fails to induce satiety. Serum leptin deficiency or leptin resistance both promote food intake leading to obesity (4).

The expression of the placental leptin and increased adipose tissue coincide with the raised maternal serum leptin levels. Hence, the maternal serum leptin levels attain peak level till the 28th week of gestation then gradually decreases and after the delivery becomes normal due to expulsion of placenta (5). Leptin increases the body’s insulin sensitivity through the regulation of insulin-mediated glucose metabolism by skeletal muscles and by hepatic regulation of gluconeogenesis (6,7).

Pregnancy is associated with leptin resistance as leptin mRNA receptor is found to decrease during pregnancy. During early pregnancy, increase in Serum leptin, is found to be associated with the increased risk of Gestational diabetes in later pregnancy. A vicious cycle develops between insulin and leptin as increase in insulin level in pregnancy stimulates adipose tissue to produce serum leptin which in turn promotes secretion of cytokines i.e. IL-6 &TNF-α leading to inflammation and further increase in serum leptin. These cytokines increase the insulin resistance, resulting in hyperinsulinemia which results in hyperleptinemia. This study was planned to find correlation b/w GDM and serum leptin levels among Pakistani women as limited research data is available.
Materials and Methods:
This case-control study was approved by Ethical Committee of University of Lahore Teaching Hospital, Lahore. The case sample included 40 pregnant women with GDM and 10 women with GDM at postpartum stage. The control sample included 30 normal pregnant women with no GDM and 10 normal women at postpartum. An informed, written consent was taken from each participant of study. The maternal blood samples were collected from all the participants after taking a detailed history regarding bio data, address, age, Gestation age, parity, gravida, previous history of the GDM, family history of Diabetes, sibling history of diabetes, drug history and past history of chronic illness. The general physical examination included measurement of weight, height, body mass index and blood pressure. The Case participants involved in the research were pregnant women aged between 18 to 40 years with the Gestational diabetes, after 24-28 week of gestation. GDM was confirmed by oral glucose tolerance test (OGTT). The Control participants include normal healthy pregnant women. Cases and control included in study during postpartum period were taken 4 weeks after delivery of fetus. All the women with the known history of metabolic disorders, diabetes mellitus and preeclampsia or any other complication of pregnancy were excluded from the study.

At the 24–28th week of the gestation, a standard 2 hour OGTT was performed. After screening of pregnant women with glucose challenge test, the subject asked for overnight fast of 8 - 14 hours (drink only water), the subject was offered 75 g oral glucose in 250 – 300 ml water over five minutes. Fasting, after 1 hour and after 2 hours, blood sample was taken. Gestational Age was estimated by last menstrual period date and confirmed by ultrasound. After confirmation of case and control by OGTT, maternal fasting plasma samples were collected in the volume of 6 ml tubes. These samples were span 3000 rpm for 15 minutes by centrifuge machine and then sera separated into appropriate tubes and frozen at -20ºC until analysis were done. At time of procedure, the samples thawed by keeping them at the room temperature and serum leptin and serum insulin were measured by ELISA. The homeostasis model assessment index-insulin resistance (HOMA-IR), the important determinant of insulin resistance, measured by an equation:

$$\text{HOMA Index} = \frac{\text{[fasting insulin (mIU/L) x fasting glucose (mmol/L)]}}{225}$$

HOMA index less than 3 is considered normal, person with no insulin resistance. The value than 3 more is associated with insulin resistance (10).

The data was analyzed by using SPSS 21. For the continuous variables we used mean and the standard error of mean. Categorical data was expressed as numbers (n) and percentages (%). For the comparison of serum leptin, serum insulin and HOMA index in cases and controls during pregnancy, ANOVA was performed. Paired t-test was performed to analyze serum leptin, serum insulin and HOMA index of cases and controls during pregnancy and postpartum period. The p-value less than 0.05 was considered statistically significant.

Results:
Mean Age± standard deviation (years) of the cases with Gestational diabetes was 25.28 ± 0.72 and among the control group it was 23.76 ± 0.83. Basal metabolic index (BMI) (Kg/m2) of gestational diabetics (26.95 ± 0.88) is greater than that of the controls(20.59 ± 0.34).

Gestational diabetics showed OGTT fasting (6.74mmol/L ± 0.12), OGTT after 1 hours (12.56mmol/L ± 0.14), OGTT after 2 hours (10.04mmol/L ± 0.12), Serum insulin (27.48mIU/L ± 0.49), HOMA index (8.26 ± 0.23) and Serum Leptin (31.08ng/ml ± 0.70) significantly higher than that of control i.e. 4.46 ± 0.09,8.48 ± 0.16, 6.74 ± 0.14,14.63 ± 0.37, 2.90 ± 0.09 and 11.48 ± 0.16 respectively.

Table I shows comparison of cases during pregnancy with Gestational diabetes and during postpartum period, done by paired t test. Results showed significant decrease (p < 0.05) in serum Insulin, serum leptin and HOMA index from pregnancy to postpartum period.

Table II showed correlation of blood glucose against HOMA index and serum leptin. Results showed a positive significant correlation of blood glucose with HOMA index. Blood glucose level also represents a significant positive correlation with serum leptin.

Discussion
Our results have depicted that the pregnant ladies with GDM have significantly higher serum leptin level,
and subsequently serum insulin levels raise but the gestational diabetes progresses. As serum leptin shows positive association with insulin resistance, hence our future recommendation is to use serum leptin as a marker to early screening and diagnosis of gestational diabetes. This will help in combating GDM associated maternal and fetal complications.

Conflict of interest: Authors do not have any conflict of interest to declare.
Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

References


### TABLE II: PEARSON CORRELATION RESULTS

<table>
<thead>
<tr>
<th></th>
<th>HOMA INDEX</th>
<th>Serum Leptin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Glucose</td>
<td>$r = 0.786$</td>
<td>$r = 0.360$</td>
</tr>
<tr>
<td>p</td>
<td>0.000</td>
<td>0.022</td>
</tr>
</tbody>
</table>

$r$ represents correlation, $p$ value represents significance.

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

* Correlation is significant at the 0.05 level (2-tailed)