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"Serum adiponectin in Gestational diabetes mellitus."

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Abstract:
Introduction:
Gestational diabetes mellitus (GDM) is associated with a state of decreased insulin sensitivity along with increased body mass index. It has been studied that serum adiponectin produced by human placenta and adipose tissue has profound insulin sensitizing properties along with anti-inflammatory and anti-atherogenic effects. A decreased level of serum adiponectin is an independent risk factor for future development of diabetes. Conversely, increased level of serum adiponectin reduces the chances of Type 2 DM.
Aims & Objectives:
To study the association of serum adiponectin levels with GDM.
Materials & method:
Thirty pregnant women between 24th to 28th weeks of pregnancy with GDM and no other co-morbidities and thirty age-matched healthy control pregnant women without GDM were included in the study, presenting in the out-patient department of the hospital over a period of one year and fulfilling the inclusion criteria.
Result:
The data shows that the GDM group have a higher pre-pregnancy BMI, lipid profile and HbA1c levels as compared to those with normal pregnant women and a lower serum adiponectin level. A significant inverse correlation was seen between serum adiponectin and blood glucose levels at GCT and OGTT, HbA1c, BMI and lipid profile. Also, HbA1c level shows a positive correlation with GCT, BMI and serum cholesterol.
Conclusion:
Gestational Diabetes mellitus is significantly associated with associated with low levels of serum adiponectin.
Key words:*Adiponectin, HbA1c, GDM, GCT, OGTT, cholesterol,*

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I. Introduction

Gestational Diabetes (GDM) is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy"[1]. This definition acknowledges the possibility that patients may have previously undiagnosed diabetes mellitus or may have developed diabetes coincidentally with pregnancy.

Pregnancy is associated with alterations in the regulation of glucose metabolism caused by actions of various hormones such as placental lactogen, placental growth hormone production[2] and other substances that antagonize the action of insulin, leading to a state of relative insulin resistance as pregnancy progress. These changes occur to meet the increasing metabolic needs of the mother as well as the growing fetus.

Recent studies have shown that human placenta and adipose tissue produce various cytokines such as Adiponectin [3]. It is an adipose tissue derived protein with profound insulin sensitizing, anti-inflammatory and anti-atherogenic effects. Low serum adiponectin levels are an independent risk factor for future development of Diabetes Mellitus. Conversely, higher adiponectin levels are consistently associated with a lower risk of type–2 diabetes in prospective studies of diverse populations.

Since, Gestational Diabetes is associated with increased body mass index (BMI) and decreased insulin sensitivity, the evaluation of plasma Adiponectin levels in these patients can have a potential role in the future management and further followup of women who have a higher risk of developing Type-2 Diabetes Mellitus later in life.

II. Aims & Objective:

The aim of this study is to evaluate the serum level of adiponectin in women with gestational diabetes and correlate its level with blood glucose levels,HbA1c and lipid profile in these women.

III. Materials And Methods

Thirty pregnant women between 24^{th} to 28^{th} weeks of pregnancy with Gestational Diabetes and no other co-morbidities and thirty age-matched healthy control pregnant women without Gestational diabetes presenting in the out-patient department of the hospital over a period of one year and fulfilling the inclusion criteria were included in the study.

An informed consent was taken from all the patients participating in the study and a detailed clinical history along with meticulous general physical examination was conducted.

Anthropometric measurement:Pre–pregnancy body mass index (BMI) was calculated for all the patients using the formula BMI =weight (kg)/height $(meter)^2$.

Screening and diagnosis of case of Gestational Diabetes:A screening test was performed on pregnant females attending the antenatal clinic in the hospital at 24^{th} to 28^{th} weeks of pregnancy. A 50 gms, glucose challenge test (GCT) was done and 1 hour blood glucose level measured. All patients with 1 hour blood glucose level >/=140mg/dl were further taken up for confirmation of diagnosis. Gestational Diabetes was diagnosed after a 100-gram Oral glucose tolerance test (OGTT) as per the American Diabetes Association criteria.

Biochemical Assay: The Quantitative determination of serum adiponectin (DRG) and IL-1beta (Gen-Probe Diaclone) was done by ELISA and determination of HbA1c was done using an RX Daytona automated analyser.

Statistical analysis:The statistical analysis was done by using the Statistical Package for Social Sciences (SPSS) version 20.0. The data were expressed as mean+/-standard deviation. Besides descriptive statistics, the comparison of the parameters (serum adiponectin, IL-1beta and HbA1c) between the cases and controls was done using "Mann Whitney U test" for non-parametric data and "independent sample t test" for parametric data. Correlation of the parameters was done using Pearsons correlation test among the parameters themselves and also with GCT, OGTT, BMI, lipid profile and parity in both the study groups. The "p value" of <0.05 was considered to be significant. Also, a receiver–operator characteristic curve was plotted for determination of their sensitivity and specificity in the detection of cases of gestational diabetes.

IV. Results:

Anthropometric and metabolic characteristics of the study participants in the normal and Gestational Diabetes group are shown in table 1.

Table 1. Mean and standard deviation of baseline level of anthropometric and metabolic characteristics of studied subjects.

Variables	Cases(GDM group)	Control group
Age (years)	27.06+/-4.8	26.64 +/- 3.1
Pre-pregnancy BMI (kg/m^2)	23.49 +/- 2.1	20.95 +/- 1.1
GCT (mg/dl)	152.6 +/- 13.5	98.9 +/- 33.9
S. cholesterol (mg/dl)	196.36 +/- 41.7	161.83 +/- 24.9
HbA1c (%)	5.89 +/- 0.79	4.63 +/- 0.38
S. adiponectin (microgm/dl)	5.76 +/-2	14.12 +/- 4.9

The data shows that the GDM group have a higher pre-pregnancy BMI, lipid profile and HbA1c levels as compared to those with normal pregnant women and a lower serum adiponectin level.

Using Pearson'smethod, a significant inverse correlation was seen between serum adiponectin and blood glucose levels at GCT and OGTT, HbA1c, BMI and lipid profile. Also, HbA1c level shows a positive correlation with GCT, BMI and serum cholesterol.

By plotting an ROC curve, at a critical value of 8.75microgm/ml, serum adiponectin has a sensitivity and specificity of 100% for detection of GDM cases. While HbA1c> 5.15% has a sensitivity of 80% and a specificity of 96.7%.

V. Discussion:

Serum adiponectin is known for its insulin sensitizing and anti- atherosclerotic actions[2-3]. In the present study, its level was significantly lower in cases of GDM as compared with normal pregnant women. Similar findings were observed by Altinova AE et al (2007)[4], Vitoratos N et al (2008)[5] and Culha C et al (2011)[6]. Williams MA et al (2004)[7] also reported lower adiponectin levels in women with GDM compared with normal pregnancy controls and that women with adiponectin concentrations below 6.4 ug/ml has an increased risk for

developing GDM by 4.6-fold compared with the risk at higher concentrations. On the contrary, McLachlan KA et al (2006)[8] found no difference in the adiponectin level between pregnant women with and without GDM.

An inverse correlation was found between adiponectin level pre – pregnancy BMI, glucose level at GCT, lipid profile including serum cholesterol and triglyceride levels as well as with HbA1c(Figure 1). Pre-pregnancy body mass index is known to be the primary factor in determining BMI during pregnancy, with high pre-pregnancy BMI being a risk factor for GDM as well as postpartum glucose intolerance. Torloni M R, et al (2009)[9] in their systematic review with meta-analysis found that for every 1 kg/m2 increase in BMI, the prevalence of GDM increased by 0.92% (95% CI 0.73 to 1.10).

Similar to our findings, Sedigheh S et al (2009)[10], Culha C et al (2011)[6] andSahriian V et al (2012)[11] also found that the amount of serum adiponectin has an inverse relationship with the body mass index in normal pregnant women and that reduction in adiponectin in- turn increased the synthesis of lipids and fatty acids and accumulation of the surplus in the tissue. In contrast Worda C et al (2006)[12] found no correlation between BMI and serum adiponectin level. The negative correlation seen between pre-pregnancy BMI and the adiponectin levels during pregnancy may suggest that a decrease in adiponectin occurs even before the development of GDM and that change in the adiponectin level in GDM precedes the onset of insulin resistance and abnormal glucose levels.

Also changes in adiponectin level is known to be related to decreased insulin sensitivity and glucose disposal and are reported to be negatively correlated with triglyceride levels and positively correlated with HDL levels and that these relationships are independent of systemic insulin resistance and are affected by central obesity.

In the present study, serum cholesterol and triglyceride levels were significantly higher in the GDM group as compared to the normal controls. Also, their levels were inversely correlated with the level of adiponectin. Similarly, Kinalski M et al (2005) [13] and Altinova AE et al (2007) [4] also found a significant correlation between serum adiponectin and triglyceride levels in normal glucose tolerant pregnant females.

Also, an inverse correlation between serum adiponectin level and blood glucose level at GCT and OGTT was found.This study was consistent with Weerakiet s, et al (2006)[14] who also found that adiponectin concentration was negatively correlated with gestational age and plasma glucose levels of the GCT and each OGTT and using logistic regression analysis, they demonstrated adiponectin as an independent predictive factor for GDM.Sedigheh S, et al (2009) [10] also found significant correlation between serum levels of adiponectin and plasma glucose at GCT ($r = -0.344$, $p = 0.002$).Similarly, Nicholson W, et al (2013) [15] found that at baseline, higher adiponectin concentrations were inversely and statistically significantly associated with maternal response to GCT and adjustment for lifestyle factors like BMI did not alter the association of adiponectin with GCT. Altinova AE, et al (2007)[4] also found that adiponectin levels correlated negatively with insulin resistance and 0 hour and 1 hour glucose both at glucose challenge test and oral glucose tolerance test in GDM cases.

Glycated Haemoglobin (HbA1c) is formed by a non–enzymatic glycation pathway by hemoglobin's exposure to plasma glucose [12]. And as the average amount of plasma glucose increases, the fraction of glycated hemoglobin increases in a predictable way. This serves as a marker for average blood glucose levels over the previous 4 weeks to 3 months prior to the measurement [16] and can help in identification of women who were already diabetic before pregnancy but undiagnosed and thereby distinguishing them from women who have true gestational diabetes[17-18]. However, as a screening test for gestational diabetes, HbA1c is not recommended because of its low sensitivity.

Our study findings showed that HbA1c level was below the cut off level of 6% but significantly higher in women with gestational diabetes (GDM) as compared to that of controls and was inversely correlated with serum adiponectin level.

VI. Conclusion:

Gestational Diabetes which is characterized by marked insulin resistance is associated with hypoadiponectinemia.

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Nil

CONFLICT OF INTEREST:
There are no conflicts of interest.

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