Research Article

Inflammatory and insulin resistance markers in gestational diabetes mellitus

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is defined as "carbohydrate intolerance with recognition or onset during pregnancy," irrespective of the treatment with diet or insulin. Metabolic features of GDM are hyperglycemia, insulin resistance (IR), and hyperlipidemia. IR during pregnancy is multifactorial. Most important causes of IR are placental hormones, and inflammatory markers include interleukin-6, high sensitivity C reactive protein (HsCRP), tumor necrosis factor α, increased free fatty acids, and increased oxidative stress. **Objectives:** The objective of this study is to evaluate the role of biomarkers of IR like fasting insulin and inflammatory markers like HsCRP in the development of hyperglycemia in GDM. **Materials and Methods:** The study population was derived by screening pregnant females attending for their routine antenatal checkup from 24 to 28 weeks of gestation. 159 females were enrolled after giving consent. A sample of venous blood was collected to assess the fasting insulin and HsCRP. **Results:** On comparing the HsCRP, fasting insulin levels and body mass index of GDM and non-GDM cases diagnosed by any of the criteria values were found to be higher among GDM as compared to non-GDM and differences were found to be statistically significant for HsCRP and fasting insulin. **Conclusion:** Fasting insulin levels are significantly increased in GDM patients as compared to non-GDM, which concluded that gestational diabetes is an insulin-resistant state. Inflammatory markers such as HsCRP are also significantly increased in GDM patients, which also favors that pregnancy is a state of mild inflammation.

KEY WORDS: Gestational Diabetes Mellitus; High Sensitivity C Reactive Protein; Fasting Insulin

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as "carbohydrate intolerance with recognition or onset during pregnancy," irrespective of the treatment with diet or insulin.[1] The importance of GDM is that the future generations are at risk of developing diabetes in the future. Women with a history of GDM are at increased risk of future diabetes, predominately Type 2 diabetes, and so are their children over a period of time.[1]

Metabolic features of GDM (hyperglycemia, insulin resistance (IR), and hyperlipidemia) are components of Type 2 DM (T2DM) and the metabolic syndrome.[2,3] Women with GDM have both increased peripheral IR (mainly in skeletal muscle) and impaired insulin secretion.[4,5] Insulin sensitivity is reduced 30–40% in women with GDM compared to controls, and insulin secretion is significantly impaired in response to hyperglycemia.[5] This suggests a major β-cell defect that makes compensation for increased IR difficult to achieve and implies multiple defects in insulin action along with impaired compensatory insulin secretion in the etiology of GDM,[4-6] suggesting a higher fasting insulin levels in pregnancy.

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IR during pregnancy is multifactorial. Most important causes of IR are as follows:

- Placental hormone experimental studies outside of human pregnancy suggested that hPL also increases peripheral IR[7] and may be a potent insulin antagonist.
- Inflammatory markers such as interleukin (IL)-6, high sensitivity C reactive protein (HsCRP), and tumor necrosis factor α: Pregnancies complicated by obesity and GDM stimulate the dysregulation of metabolic vascular and inflammatory pathways by increasing circulating concentrations of inflammatory molecules.[8,9] It has also been observed that the increased cytokine levels parallel increasing IR.[10]

This suggests that the pregnancy complicated by GDM has IR as its primary pathology. Previous studies which are done in this context suggest the same.

The aim of this study is to evaluate the role of (1) fasting insulin levels in patients with GDM and (2) high sensitivity C reactive levels in patients with GDM.

MATERIALS AND METHODS

This was a cross-sectional observational study, conducted at King George's Medical University, Lucknow, Uttar Pradesh, between August 2016 and September 2017. The participants were recruited from the outpatient departments of Department of Endocrinology, Medicine and Obstetrics and Gynaecology. Pregnant women between 24 and 28 weeks of gestation fulfilling the inclusion and exclusion criteria were included in the study after obtaining a written informed consent.

Inclusion Criteria

- Pregnant females at 24–28 weeks of gestation period were included in the study.

Exclusion Criteria

The following criteria were excluded from the study**:**

- Prior known T2DM, Type 1 DM, secondary or another form of diabetes.
- Chronic/acute kidney disease.
- Patients on steroid therapy.

The study population was derived by screening pregnant females attending for their routine antenatal checkup from 24 to 28 weeks of gestation. A total of 180 consecutive pregnant females fulfilled the inclusion criteria, of which 159 gave consent for participation in the study. Plasma glucose levels were measured following 8 h of overnight fasting. The pregnant females were given 82.5 glucose (equivalent to 75 g anhydrous glucose). The venous blood sample was collected for estimating plasma glucose at 0, 1, and 2 h, respectively.

RESULTS

GDM according to the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria was 22.64% while that as per modified Carpenter and Coustan criteria was 17.61% and as per Diabetes In Pregnancy Study group India (DIPSI) criteria was 13.21% [Table 1].

On comparing the HsCRP, fasting insulin levels and body mass index (BMI) of GDM and non-GDM cases diagnosed by any of the criteria mentioned above IADPSG, DIPSI, or modified C and C values were found to be higher among GDM as compared to non-GDM, and differences were found to be statistically significant for HsCRP (19.40 [5.95–24.60] vs. 7.40 [4.48–10.23] $P < 0.001$), fasting insulin (5.20 [4.25–5.80] vs. 4.15 [3.20–4.60] $P < 0.001$), and BMI (25.10 ± 2.32 vs. 23.50 ± 2.09 kg/m^2; $P < 0.001$) [Table 2].

HsCRP levels of GDM females with BMI ≥23 kg/m^2 (19.23 ± 8.68 mIU/ml) was found to be significantly higher ($P < 0.001$) as compared to females with BMI <23 kg/m^2 (7.08 ± 6.20 mIU/ml). HsCRP levels of non-GDM females with BMI ≥23 kg/m^2 (10.64 ± 6.63 mIU/ml) was found to be significantly higher ($P < 0.001$) as compared to females with BMI <23 kg/m^2 (5.15 ± 3.89 mIU/ml) [Table 3].

DISCUSSION

The findings of the study show that the HsCRP, fasting insulin levels, and BMI of GDM versus non-GDM cases diagnosed by any of the criteria mentioned above IADPSG, DIPSI, or modified C and C values were found to be higher among GDM as compared to non-GDM, and differences were found to be statistically significant for HsCRP, fasting

Table 1: Diagnosis of GDM using different criteria (*n*=159)

Criteria used	Number of patients diagnosed (%)
IADPSG	36 (22.64)
Modified C and C	28 (17.61)
DIPSI	21 (13.21)

GDM: Gestational diabetes mellitus, IADPSG: International Association of the Diabetes and Pregnancy Study Groups, DIPSI: Diabetes In Pregnancy Study group India

Table 2: Association of HsCRP, fasting insulin, and BMI with GDM

Variables	GDM (*n*=45)		Non-GDM (*n*=114)		*P*
HsCRP	19.40 (5.95–24.60)		7.40 (4.48–10.23)		<0.001
Fasting insulin	5.20 (4.25–5.80)		4.15 (3.20–4.60)		<0.001
BMI	25.10	2.32	23.50	2.09	<0.001

HsCRP: High sensitivity C reactive protein, BMI: Body mass index, GDM: Gestational diabetes mellitus

Table 3: Comparison of HsCRP levels among GDM and non-GDM (any criteria) with different BMI

Groups	BMI≥23 kg/m²		BMI<23 kg/m²		*P*
	n	Mean±SD	*n*	Mean±SD	
GDM (n=45)	35	19.23±8.68	10	7.08±6.20	<0.001
Non-GDM (n=114)	71	10.64±6.63	43	5.15±3.89	<0.001

HsCRP: High sensitivity C reactive protein, BMI: Body mass index, GDM: Gestational diabetes mellitus, SD: Standard deviation

insulin, and BMI, suggesting that gestational diabetes is a condition of IR.

Previous studies done suggesting that the same results are, Smirnakis *et al*.[11] which showed that fasting glucose, fasting insulin, and homeostatic model assessment (HOMA) were significantly higher in women who subsequently developed GDM compared with control subjects. A study by Wei *et al*.[12] suggested that advanced age, family history of diabetes, high BMIs, and blood pressure were risk factors for GIGT and GDM, which were both caused by reduced insulin secretion and enhanced IR, a study by Kumru *et al*.[13] suggested that the HOMA, sex hormone-binding globulin, triglycerides, and low-density lipoprotein -C levels are independent predictors for subsequent development of GDM in low-risk pregnancies, but they exhibit low sensitivity, and a study by Li *et al*.[14] showed that serum levels of IL-6 and HsCRP are elevated in women with GDM, which are the most significant factors affecting HOMA-IR.

Limitations of the study were that it has small sample size.

CONCLUSION

Increased fasting insulin levels show that gestational diabetes is an insulin resistant state. Inflammatory markers such as HsCRP are also significantly increased in GDM patients, favoring that pregnancy is a state of mild inflammation. It is also seen that HsCRP levels are higher in patient with high BMI as comparison to low BMI patients in both GDM and non-GDM. Hence, HsCRP levels could be used for predicting GDM, but more studies need to be done in this regard.

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