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A STUDY OF CHEMERIN FOR THE EARLY PREDICTION OF GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Gestational diabetes mellitus (GDM), a common metabolic disorder in pregnancy, poses risks to both maternal and fetal health and is associated with future development of type 2 diabetes mellitus. Recent studies suggest that biomarkers such as Chemerin—regulators of intestinal permeability and metabolic processes—may play a role in the pathogenesis of GDM. This prospective case-control study aimed to evaluate the predictive role of Chemerin in GDM and to analyze associated biochemical parameters including glucose, insulin, HbA1c, HOMA-IR, serum creatinine, ALT, and AST. Conducted at Janana Hospital, JLN Medical College, Ajmer, the study included 160 pregnant women categorized into GDM cases and healthy controls based on OGTT results. Results indicated significantly elevated levels of Chemerin in GDM subjects, correlating positively with insulin resistance and hyperglycemia. These findings support the potential of Chemerin as early predictive biomarkers for GDM, highlighting their utility in risk assessment and early intervention strategies.

Keywords: Gestational Diabetes Mellitus (GDM) , Chemerin , OGTT , Insulin Resistance , Biomarkers.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable degree with onset or recognition during pregnancy, has been recently identified as a potential risk factor for Type II Diabetes Mellitus[1]. According to the American Diabetes Association criteria, GDM is defined as diabetes diagnosed in the second or third trimester of pregnancy that was not overt prior to gestation[2].

GDM is the most common metabolic complication to occur during pregnancy and is classed as a mild form of diabetes. It is normally diagnosed at 24–28 weeks gestation and is characterized by hyperglycemia[3]. GDM develops as a consequence of either unusually high IR(Insulin Resistance), perhaps because of contribution of pre-existing IR in overweight women, or because of inadequate β-cell expansion and concomitant insulin insufficiency[4].

As per International Diabetes Federation (2017) one in seven births is affected by GDM. 16.2% (21.3 million) of live births is to women with hyperglycemia in pregnancy (HIP)[5]. India, being home to 69.2 million diabetic subjects, has also become the "diabetes capital of the world" harbouring around four million women with GDM alone[6]. Approximately 7% of all pregnancies are complicated by GDM, resulting in more than 200,000 cases annually. The prevalence may range from 1 to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed[7].

Chemerin is a novel chemoattractant 14 kDa protein, described as retinoic acid receptor responder protein 2 (RARRES2), secreted as a prochemerin[8]. This inactive precursor is changed into the active molecule by coagulation and inflammatory serine proteases. Chemerin plays an important role in adipocyte differentiation, and insulin signaling results in an impact on the regulation of inflammation and major metabolic processes. Its elevated levels are observed in obesity and metabolic syndrome.[9] Chemerin and the receptor of chemerin, chemokine-like receptor 1 (CMKLR1, also known as ChemR23) are almost exclusively expressed and synthesized in white adipose tissue[10].

Chemerin plays a vital role in adipocyte differentiation and development, and it may act as a modulator of different metabolic pathways in mature adipocyte namely, in the expression of adipocyte genes involved in glucose and lipid homeostasis[11].

Chemerin is an adipokine that regulates adipocyte development and metabolic function as well as glucose metabolism in the liver and skeletal muscle tissue. Chemerin has the biological effects of regulating adipocyte differentiation and lipolysis as well as promoting the insulin signal transduction pathway in adipose cells[12]. Chemerin is expressed in the body's adipose tissue, adrenal gland, liver, lung, pancreas, placenta, ovary and skin particularly in white adipose tissue[13].

MATERIALS AND METHODS

The present study comprised a case-control study design involving 160 individuals diagnosed with GDM. Diagnosis was established through clinical history, physical examination, and OGTT and HbA1c%. Cases were selected from the Obstetrics and Gynaecology dept of Janana Hospital, Ajmer. Concurrently, age and gender-matched controls (n=100) were selected from the Outpatient Department of the same institution. A comparative analysis of patient data was conducted against the 100 healthy controls. Patients with GDM who are taking Insulin, smokers, alcoholics, heart disease patients, Hypertensive, endocrine disorders, liver disease and Kidney disease were excluded. Overt Diabetes Type 1 and Type 2 DM cases are also excluded. Also those who didn't provide consent all were excluded from the study.

Procedure Blood samples were collected after administrating 50 gm anhydrous Glucose in plain vial or clot activator vial and one on EDTA Vail under aseptic conditions from all the study participants. All samples were centrifuged and analysed after 1 hour. Serum Glucose was estimated using GOD POD method using Beckman Coulter Biochemistry Analyzer (DXC700). HbA1C is estimated using HPLC method on D10 biochemical analyzer. Chemerin was estimated by using ELISA Method. Overnight fasting sample was also taken for the estimation of Fasting Serum Insulin and Fasting Glucose on the same day before 1 hour PP Sample. HOMA-IR is calculated using fasting glucose and fasting insulin levels, and it provides a simple, cost-effective way to assess the degree of insulin resistance in a patient. The formula to calculate HOMA-IR is: -

$$\text{HOMA-IR} = \frac{\text{Fasting Insulin } (\mu U/mL) \times \text{Fasting Glucose } (mg/dL)}{405}$$

A value greater than 2.5 is commonly considered indicative of insulin resistance, though this threshold can vary based on population and study.

Data analysis

Collected data were entered into Microsoft Excel spreadsheet and then analysed by IBM SPSS (version 26). Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. A p value <0.05 was considered significant.

RESULTS

TABLE 1
AGE DISTRIBUTION

Age (in years)	Group I Without GDM (n = 100)		Group II With GDM (n = 160)		P value
	Number	Percent (%)	Number	Percent (%)	
≤ 30 years	66	66	80	50	p-value <0.0001(HS)
> 30 years	34	34	80	50	
Total	**100**	**100**	**160**	**100**	

The above table shows age distribution in our study. Out of 100 patients in Group I (without GDM) 66 patients (66%) were in the age group of ≤ 30 years and 34 patients were in the age group of >30 years. But in Group II (with GDM) out of 160 patients 80 patients were in the age group of ≤ 30 years and 80 patients were in the age group of > 30 years.

The Chi-square reveals a highly significant association between age and GDM status (p-value <0.0001). Women with GDM (Group II) were more likely to be above 30 years of age (50%) compared to women without GDM (Group I), who were more likely to be below 30 years of age (66%).

GRAPH 1
AGE DISTRIBUTION

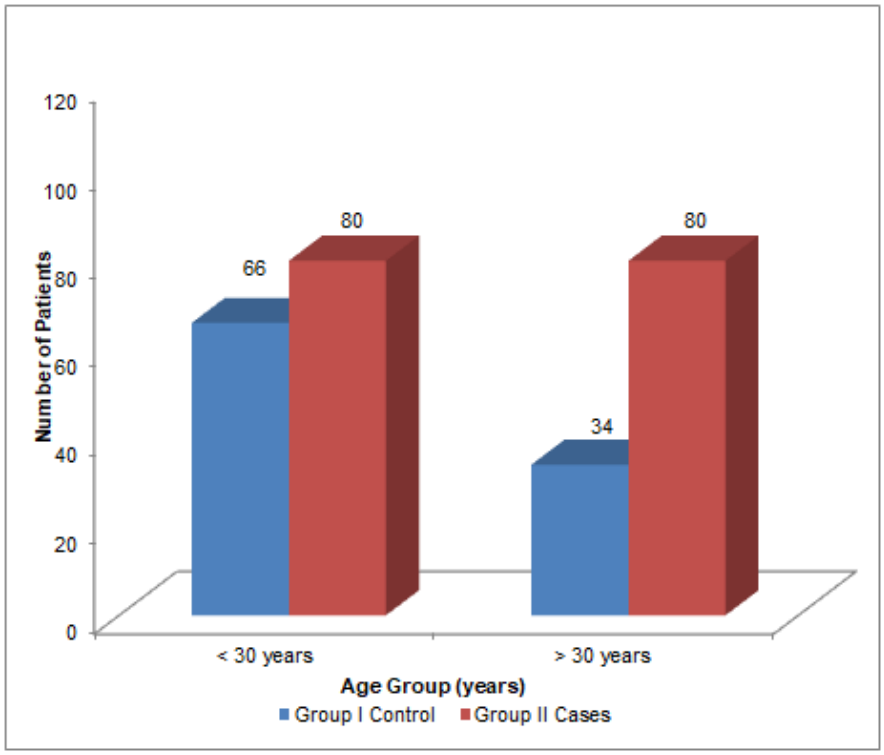


TABLE 2
COMPARISON OF GLYCEMIC MARKERS

Test	Group 1 Without GDM (n = 100)		Group 2 With GDM (n = 160)		P Value
	Mean	±SD	Mean	±SD	
Homeostatic model assessment for insulin resistance (HOMA-IR)	1.123	0.16	3.95	0.8	p<0.0001
Glycated Haemoglobin (HbA1c)	4.9	0.8	6.64	1.17	p<0.0001

The mean HOMA-IR values were significantly higher in Group II (With GDM) (3.95±0.8) compared to Group I (Without GDM) (1.123±0.16), indicating higher insulin resistance in women with GDM.
The mean HbA1c values were also significantly higher in Group II (With GDM) (6.64±1.17 %) compared to Group I (Without GDM) (4.9±0.8 %), indicating poorer glycemic control in women with GDM.

GRAPH 2
COMPARISON OF GLYCEMIC MARKERS

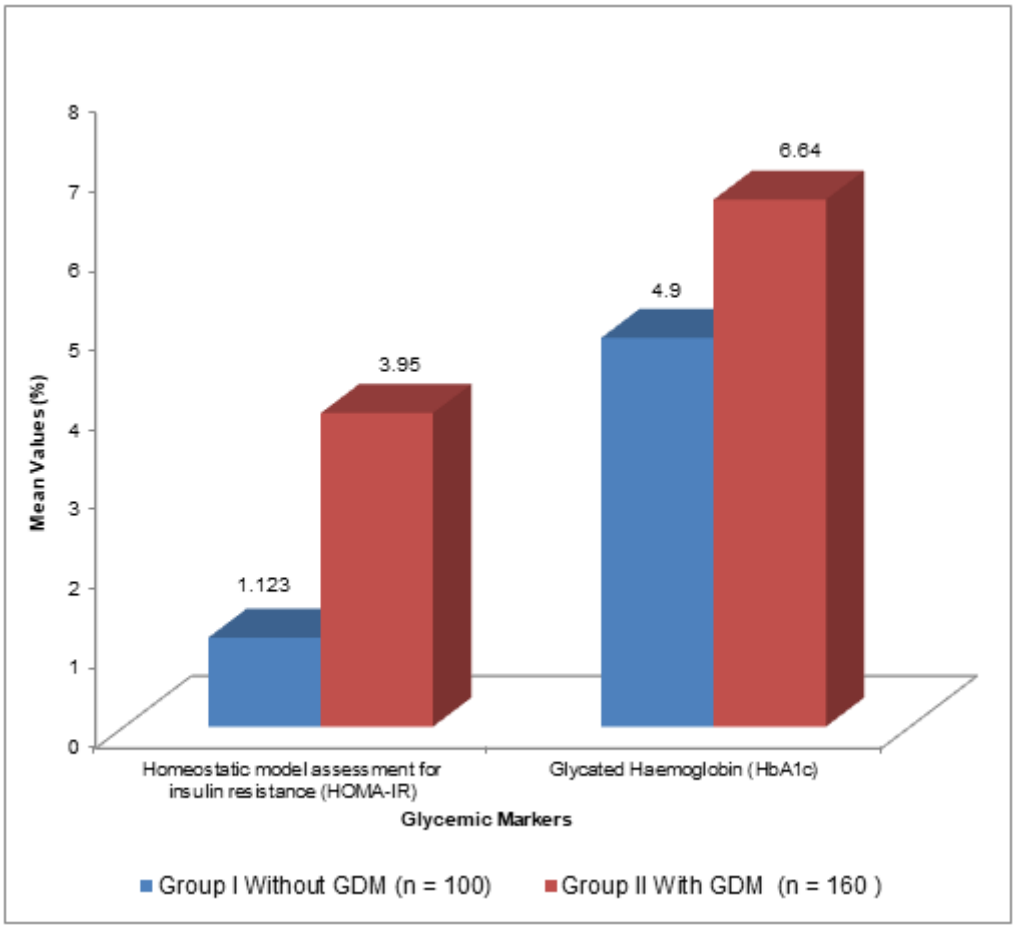


TABLE 3
CORRELATION OF SERUM CHEMERIN LEVELS
WITH GLYCEMIC MARKERS IN CONTROL AND CASE GROUP

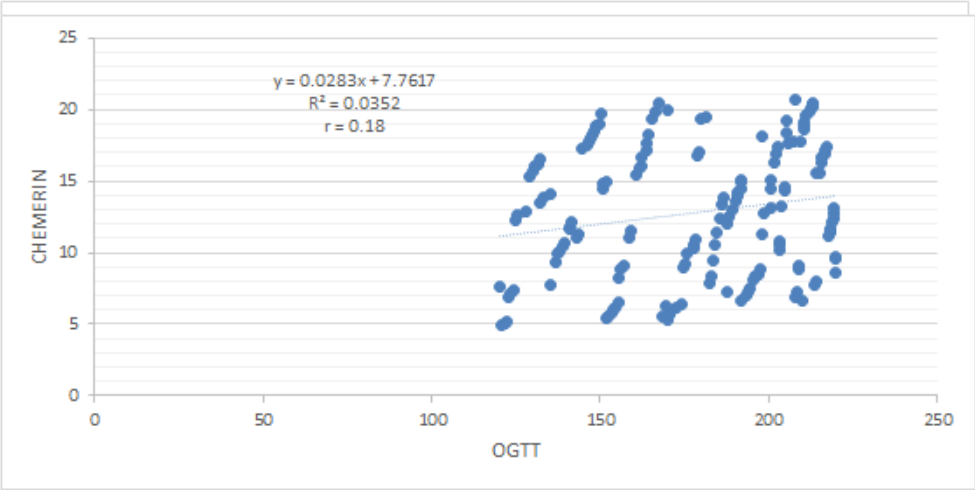
Correlation of Serum Chemerin with HOMA-IR and OGTT		**Group I Without GDM (n = 100)**	**Group II With GDM (n = 160)**
HOMA- IR	Pearson Correlation	0.1764	0.37
	P Value	0.0792	<0.0001
OGTT	Pearson Correlation	0.2414	0.18
	P Value	0.0329	0.0227

p value <0.0001 (HS) Highly significant p value <0.05 (S) Significant

In Group I - HOMA-IR values show a positive correlation (Pearson Correlation = 0.1764) with Serum Chemerin levels, which is statistically non- significant (P-Value = 0.0792). In Group I - OGTT values show a positive correlation (Pearson Correlation = 0.2414) with serum Chemerin levels which is statistically significant (P-Value = 0.0329).

In Group II - HOMA-IR values show a positive correlation (Pearson Correlation = 0.37) with Serum Chemerin levels which is statistically highly significant (P-Value = <0.0001). In Group II - OGTT values show a positive correlation (Pearson Correlation = 0.18) but it's statistically significant (P-Value = 0.0227).

GRAPH 3
CORRELATION OF SERUM CHEMERIN LEVELS WITH GLYCEMIC MARKERS IN CONTROL AND CASE GROUP



DISCUSSION

Chemerin, an adipokine encoded by the RARRES2 gene, plays a significant role in the pathophysiology of gestational diabetes mellitus (GDM) through its involvement in metabolic regulation, adipocyte differentiation, and inflammation. Elevated levels of chemerin have been consistently reported in women with GDM, suggesting its potential role as a biomarker and contributor to the disease's metabolic dysfunctions.

The mean HOMA-IR value was significantly higher in women with GDM (3.95±0.8) compared to those without GDM (1.123±0.16), with a p-value of <0.0001.

Furthermore, in our study it was found that women with GDM had significantly higher levels of glycated hemoglobin (HbA1c) compared to women without GDM. The mean HbA1c value was 6.64±1.17% in women with GDM, compared to 4.9±0.8% in women without GDM, with a p-value of <0.0001.

The mean HOMA-IR values in the present study were 1.123±0.16 for women without GDM and 3.95±0.8 for women with GDM, with a significant p-value. These findings are consistent with Ademoghu E et al. (2015)[14] and Abd El Alla NK et al. (2022)[15], who also reported significant differences in HOMA-IR values between women with and without GDM.

Regarding HbA1c levels, in the present study it was found significant differences between women with and without GDM, with mean values of 4.9±0.8% and 6.64±1.17%, respectively. These findings are consistent with Ademoghu E et al. (2015)[14] and Hare KJ et al. (2014)[16], who also reported significant differences in HbA1c levels between women with and without GDM.

A higher HOMA-IR value indicates greater insulin resistance. Gestational diabetes mellitus (GDM) is a condition characterized by glucose intolerance first recognized during pregnancy. Pregnancy naturally induces a state of insulin resistance due to hormonal changes (e.g., increased levels of human placental lactogen, progesterone, and cortisol). However, in women with GDM, insulin resistance is excessive, leading to hyperglycemia[17].

Our study is consistent with study by Bender w et al (2022)[18] on HbA1c in which it is explained that increase in insulin resistance causes persistent hyperglycemia which in turn causes increase in HbA1c. Impaired beta-cell function causes increase in fasting glucose which increases HbA1c. If the person has consistent postprandial hyperglycemia before pregnancy it can cause increase in HbA1c.

Our study reported that Women with GDM had significantly higher levels of Serum Chemerin (12.77±4.53 ng/ml) compared to women without GDM (6.08±1.08 ng/ml).

Liang Z et al. (2018)[19] reported a significant difference in chemerin levels between GDM cases (20.11±3.28 ng/mL) and non-GDM controls (17.63±3.63 ng/mL). Zhang et al. (2017)[20] also reported higher chemerin levels in GDM cases (11.2±1.17 ng/mL) compared to non-GDM controls (5.76±0.03 ng/mL).

Our present study draw a positive analysis with the study of Wang x et al(2020)[21] that Chemerin is an adipokine (a signaling protein secreted by fat cells) that plays a role in inflammation, metabolism, and insulin resistance. It is involved

in glucose homeostasis and has been linked to metabolic disorders, including gestational diabetes mellitus (GDM). Increased chemerin contribute to impaired insulin sensitivity and glucose dysregulation. Chemerin is involved in adipose tissue inflammation and insulin resistance, both of which are key factors in GDM development. Elevated chemerin correlates with higher HOMA-IR (insulin resistance index) and higher fasting glucose levels. Chemerin acts as a pro-inflammatory molecule, increasing levels of cytokines like TNF-α and IL-6, which are linked to insulin resistance. Chronic low-grade inflammation is a known contributor to GDM pathogenesis

Chemerin is primarily secreted as an inactive precursor, which is then activated by various proteases involved in coagulation and inflammation. The active form of chemerin impacts insulin signaling, adipogenesis, and inflammatory pathways, all of which are crucial in the development of insulin resistance—a hallmark of GDM. The adipokine influences glucose metabolism by modulating insulin signaling pathways and promoting insulin resistance in adipose tissue, liver, and skeletal muscle, contributing to the hyperglycemic state characteristic of GDM.

CONCLUSION

Chemerin plays a significant role in the development and progression of gestational diabetes mellitus (GDM) through its regulatory effects on adipogenesis, glucose metabolism, insulin signaling, and inflammation. Elevated chemerin levels in maternal plasma, adipose tissue, and placenta have been consistently associated with increased insulin resistance, higher BMI, dyslipidemia, and poor glycemic control in GDM patients. Several studies have demonstrated significantly higher circulating chemerin concentrations in GDM compared to healthy pregnancies, with positive correlations to insulin resistance indices such as HOMA-IR.

Despite some variations in chemerin levels across different pregnancy stages and populations, the overall evidence supports its involvement in the metabolic and inflammatory disturbances characteristic of GDM. Thus, chemerin holds promise as a potential biomarker for early prediction of GDM and may serve as a therapeutic target to mitigate insulin resistance and adverse metabolic outcomes during pregnancy. Further research is warranted to clarify its mechanistic pathways and to establish standardized thresholds for its clinical application in GDM risk assessment and management.

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