



Original Article

Association of Serum Interleukin-6 with Gestational Diabetes Mellitus: A Prospective Observational Study

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Received: 01-01-2026

Accepted: 03-01-2026

Available online: 23-02-2026

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Medical and Pharmaceutical Research

ABSTRACT

Background: Gestational Diabetes Mellitus (GDM) is increasingly recognized as an inflammatory metabolic disorder. Interleukin-6 (IL-6), a key pro-inflammatory cytokine, has been implicated in insulin resistance, but its clinical relevance in GDM remains under evaluation.

Objective: To assess serum IL-6 levels in women with GDM and normal glucose tolerance (NGT) and to examine its association with glycaemic parameters and body mass index (BMI).

Methods: A prospective observational study included 160 pregnant women (80 GDM, 80 NGT) between 24–28 weeks of gestation at a tertiary care hospital. GDM was diagnosed using DIPSI criteria. Glycaemic parameters and Serum IL-6 were measured, and anthropometric indices were recorded. The p-value <0.05 considered as significant.

Results: Mean serum IL-6 levels were significantly higher in the GDM group compared to NGT (8.33 ± 1.41 vs 3.45 ± 0.98 pg/mL; $p < 0.001$). HbA1c levels were also significantly elevated in GDM ($6.01 \pm 0.54\%$ vs $5.23 \pm 0.38\%$; $p < 0.001$). IL-6 showed no significant correlation with BMI or weight but demonstrated positive associations with glycaemic parameters in the combined population.

Conclusion: Elevated IL-6 levels are strongly associated with GDM and appear independent of adiposity, supporting its role as an immune-metabolic biomarker. Incorporation of IL-6 into antenatal screening may enhance early identification of high-risk pregnancies.

Keywords: Gestational diabetes mellitus, Interleukin-6, Inflammation, Insulin resistance, Pregnancy.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as glucose intolerance first recognized during pregnancy and is associated with adverse maternal and fetal outcomes [1]. Globally, approximately 14% of pregnancies are affected by hyperglycaemia, with higher prevalence reported in South-East Asia and the Middle East [2]. India is considered a high-risk region due to genetic susceptibility, increasing maternal age, urbanization, and lifestyle transitions [3]. Emerging evidence suggests that GDM is not merely a disorder of carbohydrate metabolism but is strongly influenced by chronic low-grade inflammation [4].

Interleukin-6 (IL-6) is a pro-inflammatory cytokine secreted by immune cells, adipocytes, and placental tissue. It interferes with insulin signaling, promotes hepatic gluconeogenesis, and contributes to systemic insulin resistance [5]. Elevated IL-6 levels have been reported in women with GDM compared to normoglycemic pregnant women, suggesting

its role in metabolic dysregulation during pregnancy [6–8], however, findings regarding its association with BMI and glycaemic control remain inconsistent.

The present study was undertaken to measure serum IL-6 levels in women with GDM and normal glucose tolerance (NGT).

MATERIALS AND METHODS

Study Design and Setting

A hospital-based prospective observational study was conducted at SMS Medical College and Attached Hospitals, Jaipur, from November 2023 to October 2024.

Study Population

A total of 160 pregnant women (24–28 weeks gestation) were enrolled:

- Gestational Diabetes Mellitus (GDM) group: 80 women
- Normal Glucose Tolerance (NGT) group: 80 age- and gestation-matched controls

The diagnosis of Gestational Diabetes Mellitus (GDM) was based on the Diabetes in Pregnancy Study Group in India (DIPSI) criteria [9].

Inclusion Criteria

- Age 20–35 years
- Singleton pregnancy
- Willing to provide informed consent

Exclusion Criteria

- Pre-existing diabetes
- Chronic inflammatory or endocrine disorders
- Steroid or NSAID use

Laboratory Investigations

- Fasting Blood Glucose (FBG) and post-prandial blood glucose (PPBG) (GOD-POD method)
- Glycated Haemoglobin (HbA1c) (latex turbidometric immunoassay)
- Serum IL-6 (chemiluminescent immunoassay, ADVIA Centaur)

Statistical Analysis

Data were analyzed using SPSS version 22. Student's *t*-test and Pearson's correlation were applied. $p < 0.05$ was considered significant.

RESULTS

The age distribution of participants, family history of diabetes mellitus, blood pressure and body mass index were comparable between the two groups, with no statistically significant difference. The majority of women in both groups were multigravida (≥ 3 pregnancies), with 57.5% in the GDM group and 47.5% in the NGT group. Statistical analysis revealed that the differences in obstetric history were non-significant for either gravida ($p = 0.576$) or parity ($p = 0.586$).

Table 1: Biochemical parameters comparison between GDM and NGT Groups

Parameters	GDM Group (Mean \pm SD)	NGT Group (Mean \pm SD)	p-value
FBG (mg/dL)	108.61 \pm 12.13	85.08 \pm 09.91	<0.001
PPBG (mg/dL)	165.54 \pm 16.90	117.27 \pm 11.19	<0.001
HbA1c (%)	06.01 \pm 00.54	05.23 \pm 00.38	<0.001
IL-6 (pg/mL)	08.33 \pm 01.41	03.45 \pm 00.98	<0.001

Table 1 shows the statistically significant difference in glycaemic parameters (FBG and PPBG) between the two groups. HbA1c levels were significantly higher in the GDM group compared to the NGT group ($p < 0.001$), indicating sustained hyperglycaemia during mid-pregnancy. Serum IL-6 levels were also markedly elevated in women with GDM compared to NGT group and the difference was highly significant ($p < 0.001$).

Correlation analysis (Figure 1) revealed no significant association between IL-6 levels and BMI. IL-6 levels showed a statistically significant ($p < 0.05$) strong positive correlation with PPBG ($r = 0.734$, $R^2 = 0.5386$), a moderate correlation with FBG ($r = 0.627$, $R^2 = 0.393$), and a moderate correlation with HbA1c ($r = 0.517$, $R^2 = 0.2677$).

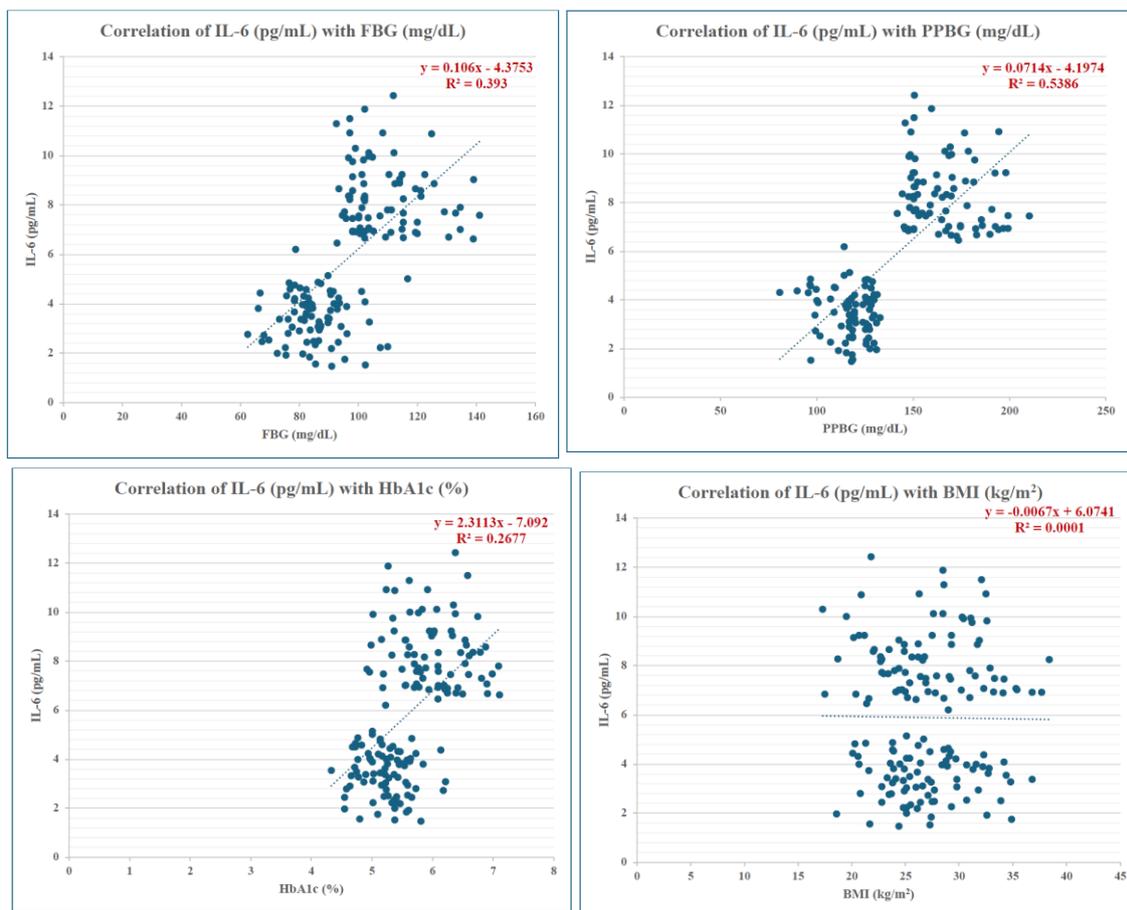


Figure 1: Correlation of Interleukin-6 with glycaemic parameters and body mass Index

DISCUSSION

The present study showed fasting blood glucose, postprandial blood glucose and HbA1C were significantly elevated ($p < 0.001$) in GDM compared to NGT. IL-6 levels were also significantly elevated in GDM versus NGT ($p < 0.001$). Moreover, IL-6 showed strong positive correlations with FBG ($r = 0.627$), PPBG ($r = 0.734$), and moderate correlation with HbA1c ($r = 0.517$) in the total population.

These results confirm the classical glycaemic derangement in gestational diabetes and align closely with previous findings reported by Siddiqui S et al, Srivastava N et al, Zhao X et al [10-12]. The consistent elevation in both FBG and PPBG in present study reflects impaired insulin sensitivity and β -cell dysfunction characteristic of GDM.

Elevated serum IL-6 in GDM group in present study were also reported by Srivastava N et al , Kuzmicki et al. and Nergiz S et al identified IL-6 as a potential biomarker for GDM risk prediction. IL-6 (Interleukin-6) plays a central mechanistic role in the development and progression of Gestational Diabetes Mellitus (GDM) by linking inflammation, insulin resistance, and placental dysfunction [11,13,14].

Notably, our observed IL-6 levels are numerically higher than those in most earlier studies, which could be attributed to differences in assay sensitivity (chemiluminescent immunoassay vs. ELISA), timing of sample collection, and ethnic or genetic predispositions. Nonetheless, the highly significant elevation in our GDM group strongly corroborates the role of IL-6 as a potential biomarker for GDM-associated inflammation and highlights its relevance in metabolic dysregulation during pregnancy.

In the present study, significant strong positive correlation with PPBG, a moderate correlation with FBG and HbA1c suggest that IL-6 increases in parallel with worsening glycaemic control, supporting its role in the metabolic-inflammatory axis of GDM. Our results are in agreement with Siddiqui S et al., who observed significant positive correlations between IL-6 and FBG ($r = 0.54$), PPBG ($r = 0.62$), and BMI ($r = 0.49$), highlighting the proinflammatory influence on glycaemic regulation [10]. Srivastava N et al. reported similar findings, with IL-6 showing strong positive correlations with FBG ($r = 0.68$) and PPBG ($r = 0.70$), as well as a moderate correlation with HbA1c ($r = 0.58$), suggesting that IL-6 tracks both acute and chronic hyperglycaemia, also supported by Zhao X et al [10,12]. These correlations in present study reinforce the concept of “meta-inflammation” in pregnancy, where cytokine mediated

pathways contribute to insulin resistance and beta-cell dysfunction. The particularly strong association between IL-6 and postprandial glucose may reflect IL-6's rapid response to metabolic stress, especially in the dynamic post-meal phase of glucose metabolism.

Moreover, IL-6 levels in present study showed minimal correlation with BMI, suggesting that inflammatory activation in GDM may occur independently of adiposity. This finding aligns with reports by Abell et al. and Liu & Wang, who demonstrated IL-6 as an independent predictor of GDM even after adjustment for BMI and adiponectin levels [15,16].

CONCLUSION

Serum IL-6 is significantly elevated in gestational diabetes mellitus and correlates with glycaemic dysregulation independent of BMI. IL-6 may serve as a valuable inflammatory biomarker for early identification and risk stratification of GDM.

Conflict of Interest

None declared

Financial Support

None

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