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ORIGINAL PAPER

Interleukin 6 as a key inflammatory predictor of gestational diabetes – clinical and biochemical evidence

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ABSTRACT

Introduction and aim. Gestational diabetes mellitus (GDM) is a prevalent metabolic disorder in pregnancy associated with significant maternal and fetal complications. Chronic low-grade inflammation is increasingly recognized as a key contributor to GDM pathophysiology, with interleukin 6 (IL-6) emerging as an important mediator of insulin resistance. The aim was to investigate the relationship between IL-6 levels and metabolic parameters in pregnant women with and without GDM, and to evaluate the diagnostic performance of IL-6 for distinguishing GDM.

Material and methods. A total of 45 pregnant women with GDM and 45 normoglycemic controls between 24 and 28 weeks of gestation were enrolled. Clinical data age, body mass index (BMI), gestational age, fasting insulin, oral glucose tolerance test (OGTT), and lipid profile were assessed. IL-6 was quantified by high-sensitivity enzyme-linked immunosorbent assay. Correlation analysis, multiple linear regression, and receiver operating characteristic (ROC) curve analysis were performed using SPSS.

Results. Women with GDM exhibited significantly higher IL-6 levels (25.35±11.76 ng/L) than controls (11.02±3.59 ng/L, $p<0.001$). IL-6 showed strong positive correlations with fasting insulin ($r=0.900$, $p<0.001$) and OGTT ($r=0.684$, $p<0.001$). Multiple regression indicated that gestational age, BMI, and total cholesterol were significant predictors of IL-6 in GDM ($p<0.05$). ROC analysis revealed an area under the curve of 0.923 ($p<0.001$) for IL-6, with a sensitivity of 88.9% and specificity of 78.3% at the cutoff of 13.243 ng/L.

Conclusion. Elevated IL-6 is strongly associated with insulin resistance and dyslipidemia in GDM, suggesting a potential role as an inflammatory biomarker for early risk stratification. Incorporating IL-6 measurement into GDM screening protocols may enhance diagnostic accuracy and facilitate timely interventions to improve pregnancy outcomes.

Keywords. gestational diabetes mellitus, insulin resistance, interleukin-6, maternal inflammation, metabolic dysregulation, pregnancy complications

Introduction

Gestational diabetes mellitus (GDM) is a common metabolic disorder characterized by glucose intolerance that first arises during pregnancy, with a global prevalence ranging from 5% to 20% depending on diagnostic criteria and population characteristics.[1] It has significant short- and long-term implications for both maternal and fetal health, including increased risk of hypertensive disorders, cesarean delivery, macrosomia, and future development of type 2 diabetes.[2]

A growing body of evidence indicates that inflammation plays a pivotal role in GDM, linking excess adiposity, insulin resistance, and placental hormonal changes to a pro-inflammatory state.[3] Among the

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various inflammatory mediators implicated in metabolic dysfunction, interleukin 6 (IL-6) has gained considerable attention for its multifaceted role in glucose homeostasis and insulin signaling.[4] IL-6 is primarily secreted by adipose tissue and the placenta in pregnancy, though it can also be produced by immune cells and skeletal muscle in response to stressors such as infection or hypoxia.[5] Elevated IL-6 concentrations have been observed consistently in pregnant women with GDM compared to those with normal glucose tolerance, supporting the hypothesis that chronic low-grade inflammation contributes to the development and progression of gestational dysglycemia.[5]

Mechanistically, IL-6 modulates insulin signaling through several pathways. Experimental models suggest that IL-6 can induce serine phosphorylation of insulin receptor substrate-1 (IRS-1), thereby impairing downstream insulin signaling and promoting insulin resistance.[6] In addition, IL-6 appears to regulate hepatic gluconeogenesis by influencing key enzymes, including phosphoenolpyruvate carboxykinase and glucose-6-phosphatase, leading to increased endogenous glucose production.[7] During pregnancy, the placenta itself can be an abundant source of IL-6, and circulating levels tend to rise as gestation advances, further challenging maternal glucose homeostasis.[8]

Several clinical investigations have demonstrated a strong correlation between IL-6 and impaired glucose tolerance in pregnant populations. Nonetheless, most of these studies have focused solely on establishing this association, with limited exploration into the diagnostic utility of IL-6. In our study, we not only confirm the link between elevated IL-6 and GDM but also propose a specific cutoff value of ≥13.243 ng/L based on receiver operating characteristic (ROC) curve analysis. This threshold, which exhibits a sensitivity of 88.9% and a specificity of 78.3%, offers a valuable clinical tool for distinguishing GDM from normoglycemic pregnancies. By defining this diagnostic parameter, our work advances current understanding and holds promise for enhancing early screening strategies and guiding timely interventions in gestational diabetes management. Despite mounting evidence of IL-6 pathogenic significance, there is still a need to elucidate its precise relationship with classical metabolic and lipid parameters in pregnancy. Clarifying the interplay between IL-6, insulin resistance, and dyslipidemia may illuminate novel diagnostic or therapeutic avenues. Early identification of elevated IL-6 could help pinpoint those at the highest risk for GDM and enable timely interventions such as lifestyle modifications or pharmacotherapy.[8] Additionally, further exploration of IL-6 potential as a predictive biomarker may guide individualized management, ultimately improving maternal and neonatal outcomes.

Aim

Against this backdrop, the present study was designed to examine IL-6 levels in pregnant women with and without GDM, with particular emphasis on its correlation with insulin resistance indices and lipid abnormalities. Our investigation integrates both cross-sectional measurements and regression analyses to delineate factors influencing IL-6 in GDM, alongside a ROC curve assessment to determine the diagnostic accuracy of IL-6. By focusing on the multifaceted role of IL-6, we aim to contribute novel insights into the inflammatory underpinnings of GDM and to explore the potential clinical utility of this cytokine in enhancing early screening and risk stratification.

Material and methods

Study design and ethical approval

This study was conducted between September 10, 2024, and February 10, 2025, at Al-Najaf Al-Ashraf Teaching Hospital and Al-Hakim General Hospital in Najaf City, Iraq. The study protocol was reviewed and approved by the Institutional Review Board of the Najaf Health Directorate, Training and Human Development Center (Approval No. 33652), ensuring compliance with the ethical principles outlined in the Declaration of Helsinki.[9] Informed consent was obtained from all participants prior to enrollment in the study.

Study population and diagnostic criteria

Pregnant women between 13 and 27 weeks of gestation were screened. Those meeting the standard diagnostic criteria for GDM, based on the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) 75 g oral glucose tolerance test (OGTT) thresholds (fasting plasma glucose ≥92 mg/dL, 1 h ≥180 mg/dL, or 2 h ≥153 mg/dL)[10], were enrolled as cases (GDM group). Pregnant women within the same gestational age range but without GDM served as controls. Exclusion criteria included known diabetes prior to pregnancy, hypertension, preeclampsia, multiple gestation, chronic inflammatory conditions, and use of corticosteroids or immunosuppressive therapy. A total of 45 pregnant women with GDM and 45 normoglycemic pregnant women were included in the final analysis. The sample size was determined using the formula for comparing two means. Based on an anticipated difference in IL-6 levels of 14.33 ng/L, a standard deviation of 8.7 ng/L, an alpha level of 0.05, and a power of 80%, the calculated minimum sample size per group was 6. To account for potential dropouts and to ensure adequate power, a total of 90 participants were recruited.[11]

Anthropometric and clinical assessment

Comprehensive anthropometric and clinical assessments were performed for all participants at the time of enrollment, which was between 13 and 27 weeks of

gestation. Maternal age, gestational age, and body mass index (BMI) were recorded and participants were categorized based on the World Health Organization (WHO) classification.[12] BMI was calculated using the formula: BMI=weight (kg)/height (m^2), with body weight and height measured using a calibrated stadiometer and digital weighing scale. It is important to note that these BMI values reflect maternal adiposity during the second trimester of pregnancy, rather than pregestational BMI.

Blood sample collection

Venous blood samples (5 mL) were collected from each participant at a single time point between 09:00 and 10:00 a.m. following a standardized 12-hour fasting period. Participants were enrolled at various stages of pregnancy, and the gestational age at the time of blood collection was recorded. For the purpose of analysis, participants were grouped according to their gestational age into the following categories: 13–16 weeks, 17–20 weeks, and ≥21 weeks. This approach enabled a cross-sectional analysis of IL-6 levels at different stages of gestation. Serum was separated by centrifugation at 3,000 rpm for 5 minutes at 4°C, aliquoted, and stored at -20°C until further processing.

Biochemical and biomarker analysis

OGTT

The 75 g OGTT was administered following IADPSG guidelines. Fasting, 1-hour, and 2-hour plasma glucose concentrations were measured using the Mindray Chemistry Analyzer (Shenzhen Mindray Bio-medical Electronics, China), providing precise and reproducible glucose measurements. Fasting plasma glucose (FPG) was measured as part of the 75 g OGTT protocol. To assess insulin resistance, the homeostatic model assessment of insulin resistance (HOMA-IR) was calculated for each participant using the formula:

HOMA-IR fasting insulin (mIU/L)/FPG (mmol/L)/22.5

For calculations, FPG values measured in mg/dL were converted to mmol/L by dividing by 18.

Glycated hemoglobin (HbA1c) measurement

HbA1c levels were quantified using a high-performance liquid chromatography (HPLC) method (Tosoh G8 Automated HPLC Analyzer, Tosoh Bioscience, USA), with results expressed as percentages (%), reflecting the average blood glucose levels over the preceding 2–3 months.

Lipid profile assessment

Serum lipid profile, including total cholesterol, triglycerides, HDL-C, and LDL-C, was evaluated using enzymatic colorimetric methods (Clinichem, Hungary) with the Biolis30i analyzer. Assays were calibrated daily, ensuring adherence to quality control protocols.

Fasting serum insulin

Insulin concentrations were measured through a highly sensitive sandwich enzyme-linked immunosorbent assay (ELISA) (BT Lab, China; Cat. No. E0010Hu). This method employed specific monoclonal antibodies for precise detection of serum insulin levels, with optical density measured at 450 nm using a Paramedical microplate reader (Italy).

IL-6

Serum IL-6 levels were determined using a Human IL-6 ELISA Kit (BT Lab, China; Cat. No. E0090Hu). The assay utilized a sandwich ELISA technique, incorporating wells pre-coated with anti-IL-6 antibodies. The colorimetric detection involved biotinylated antibodies and Streptavidin-HRP, with optical density measured at 450 nm. The assay featured a sensitivity of 1.03 ng/L and a detection range of 2–600 ng/L, providing robust data on the inflammatory status of participants.

Statistical analysis

All statistical analyses were conducted using SPSS software version 28 (IBM, Armonk, NY, USA). Prior to performing regression analyses, we assessed the assumptions of linear regression, including linearity, normality of residuals, homoscedasticity, and independence of observations. Scatter plots and normal probability plots were utilized to evaluate these assumptions, while the Durbin-Watson statistic was employed to assess the independence of residuals. When necessary, data transformations were applied to meet these assumptions.

Furthermore, potential confounders such as maternal age, BMI, and gestational age were included in the regression models as covariates to isolate the independent effect of IL-6 on metabolic parameters. Multicollinearity among predictors was examined by calculating the variance inflation factor (VIF), ensuring that all VIF values remained below 5, which supports the reliability of our estimates. These steps helped ensure that our statistical models were robust and that our findings are both valid and reliable.[13]

Results

In Table 1, no statistically significant differences were observed in maternal age (p=0.485) or gestational age (p=0.510) between the GDM and control groups. However, participants with GDM exhibited significantly higher BMI (p=0.0001), triglyceride (p=0.0001), and total cholesterol levels (p=0.030). Differences in HDL (p=0.064) and LDL (p=0.297) did not reach statistical significance. Although the HbA1c values did not differ significantly (p=0.153), the GDM group displayed markedly elevated fasting insulin (p=0.0001) and OGTT (p=0.0001) values, indicating pronounced glucose intolerance. Furthermore, GDM was associated

with a heightened inflammatory profile, as evidenced by significantly elevated IL-6 (p=0.0001).

Table 1. Comparison of clinical and biochemical parameters between GDM and non-GDM pregnant women

Variables	Pregnancy women Mean±SD		p
	GDM (HG) n=45	Controls (NG) n=45	
Age (years)	26.18±4.99	25.52±3.88	0.485
BMI (kg/m^2)	29.36±3.3	26.2±3.11	0.0001
Gestational age (weeks)	19.02±4.14	18.46±4.03	0.510
TG (mg/dL)	176.8±46.57	130.55±18.44	0.0001
Chol (mg/dL)	224.69±42.78	204.99±42.29	0.030
HDL (mg/dL)	51.2±11.68	55.84±11.91	0.064
LDL (mg/dL)	124.77±31.23	117.8±32.11	0.297
HbA1c (%)	5.41±0.36	5.27±0.5	0.153
Fasting insulin (mIU/L)	7.89±1.85	5.46±1.35	0.0001
OGTT (mg/dL)	159.43±15.89	81.45±5.69	0.0001
IL-6 (ng/L)	25.35±11.76	11.02±3.59	0.0001
HOMA1-IR	3.17±1.03	1.09±0.25	0.0001

In Figure 1, the mean IL-6 concentration was substantially higher among women with GDM (25.35 ng/L) than in those without GDM (11.27 ng/L), a difference that reached statistical significance (p<0.001). This notable increase in IL-6 suggests an intensified inflammatory state in GDM, potentially reflecting a pivotal pathophysiological mechanism.

In Table 2, fasting insulin, OGTT, and IL-6 levels in the GDM group increased significantly with advancing gestational age (p=0.0001 for each), indicating progressive insulin resistance and an augmented inflammatory response. By contrast, these parameters remained stable over the same interval in the control group (p>0.05), suggesting a consistent metabolic and inflammatory profile.

In Figure 2, IL-6 levels exhibited a strong positive correlation with both OGTT (r=0.684, p<0.001) and fasting insulin (r=0.900, p<0.001). These findings imply that elevated IL-6 is linked to deteriorating glucose tolerance and increased insulin levels, underscoring the crucial role of inflammation in exacerbating insulin resistance during pregnancy.

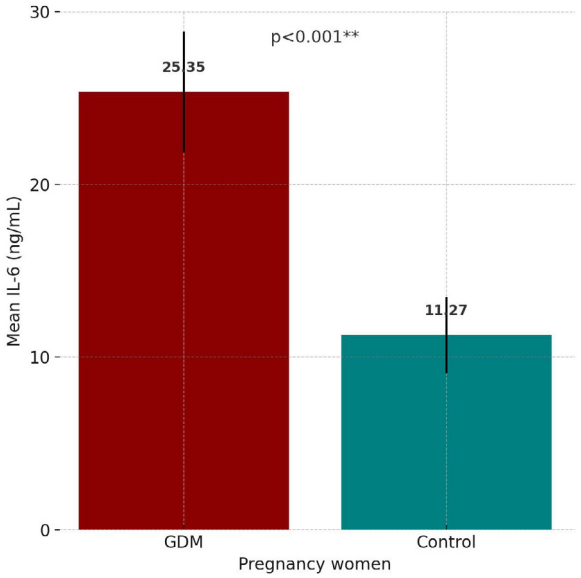

Fig. 1. Mean serum IL-6 levels in GDM versus control pregnant women

Table 2. Changes in fasting insulin, OGTT, and IL-6 levels by gestational age in GDM versus control pregnant women*

Pregnancy women		Mean±SD			
		13–16 weeks	17–20 weeks	≥21 weeks	p
GDM	Fasting insulin (mIU/L)	6.56±0.86	7.66±1.58	9.16±1.77	0.0001
	OGTT (mg/dL)	146.66±9.86	165.82±16.17	168.69±12.47	0.0001
	IL-6 (ng/L)	16.6±4.27	22.03±6.37	34.39±11.34	0.0001
Control	Fasting insulin (mIU/L)	5.58±1.42	5.89±1.38	4.91±1.11	0.159
	OGTT (mg/dL)	80.85±5.73	79.53±5.62	83.97±5.16	0.113
	IL-6 (ng/L)	11.35±4.15	10.41±2.82	11.08±3.48	0.780

* values represent mean±SD for each parameter across gestational age groups based on the single time point at which each participant's blood sample was collected (i.e., 13–16, 17–20, and ≥21 weeks) These groupings allow for a cross-sectional comparison of metabolic and inflammatory markers at different stages of pregnancy

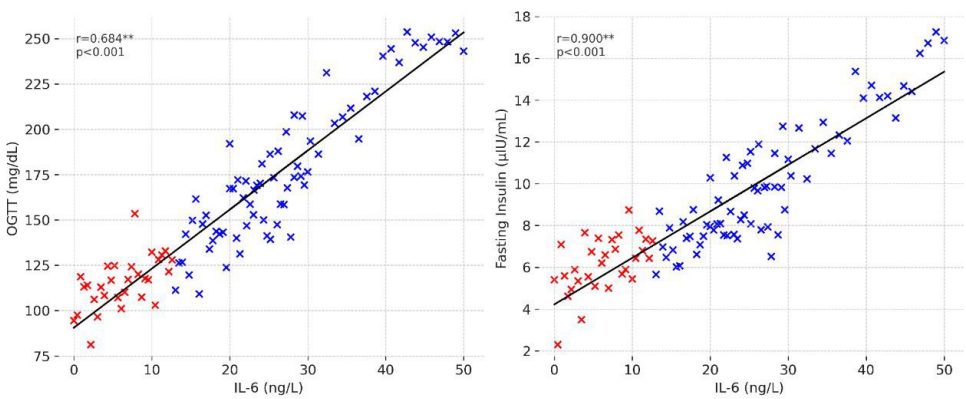

Fig. 2. Correlations between serum IL-6 levels and A: OGTT and B: fasting insulin in pregnant women, in these scatter plots, red dots represent women diagnosed with GDM and blue dots represent normoglycemic control women

Correlation analysis in Figure 3 demonstrated a significant positive association between IL-6 and HOMA-IR ($r=0.879$, $p<0.001$), further confirming the link between elevated IL-6 levels and insulin resistance in GDM. These findings are consistent with the observed relationships between IL-6, fasting insulin, and OGTT values.

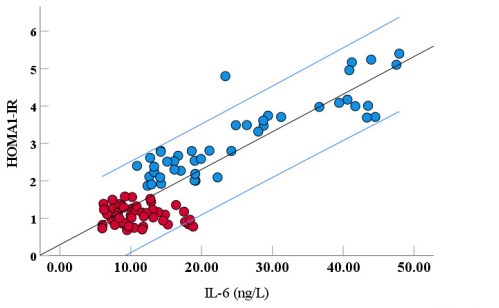

Fig. 3. Correlations between serum IL-6 Levels and HOMA-IR, in these scatter plots, red dots represent women diagnosed with gestational diabetes mellitus (GDM) and blue dots represent normoglycemic control women

Table 3 shows that among pregnant women with GDM, BMI ($\beta=0.451$, $p=0.010$) and gestational age ($\beta=0.399$, $p=0.017$) emerged as significant predictors of IL-6, whereas age did not exhibit a significant association ($\beta=-0.110$, $p=0.307$). These results suggest that both increased adiposity and advanced gestational age independently contribute to an elevated inflammatory status, as indicated by higher IL-6 levels.

Table 3. Linear regression analysis of demographic predictors of IL-6 in GDM

Pregnancy women	Predictors	Dependent variable: IL-6 (ng/L)		
		Standardized coefficients Beta	t	Sig.
GDM	Age	-0.110	-1.034	0.307
	BMI (kg/m²)	0.451	2.71	0.010
	Gestational age (weeks)	0.399	2.481	0.017

* This table presents the standardized beta coefficients, t-values, and significance levels (p) for demographic variables (age, BMI, gestational age) predicting serum IL-6 levels among women with GDM

In Table 4, of the lipid parameters analyzed, only total cholesterol significantly predicted IL-6 ($\beta=0.528$, $p=0.001$). Triglycerides ($p=0.362$), HDL ($p=0.535$), and LDL ($p=0.558$) were not significant predictors. These findings indicate that heightened cholesterol levels may critically influence the inflammatory processes in GDM, further highlighting the multifactorial pathophysiology of this condition.

Table 4. Linear regression analysis of lipid profile predictors of IL-6 in GDM

Pregnancy women	Predicators	Dependent variable: IL-6 (ng/L)		
		Standardized coefficients Beta	t	Sig.
GDM	TG (mg/dL)	0.139	0.923	0.362
	Chol (mg/dL)	0.528	3.450	0.001
	HDL (mg/dL)	-0.076	-0.625	0.535
	LDL (mg/dL)	0.089	0.591	0.558

Table 5, IL-6 demonstrated a strong diagnostic performance for distinguishing GDM, with an area under the curve (AUC) of 0.923 ($p=0.0001$; 95% CI: 0.873–0.973). A cutoff value of ≥13.2425 ng/L yielded a sensitivity of 88.9% and a specificity of 78.3%. These findings highlight IL-6 as a promising biomarker for identifying GDM risk, supported by the high accuracy depicted in the ROC curve.

Table 5. ROC analysis of IL-6 in differentiating GDM from control pregnant women

Predictors	Area under the curve					
	Area	Sig.	95% CI	Cutoff	Sensitivity	Specificity
IL-6 (ng/L)	?	0.0001	0.873-0.973	≥13.2425	0.889	0.783

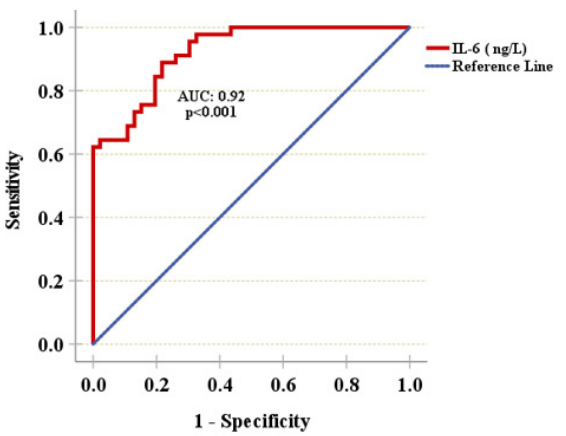

Fig. 4. ROC curve for IL-6 in GDM vs. non-GDM pregnant women

Discussion

The present study aimed to investigate the role of IL-6 in the pathophysiology of GDM by comparing clinical, biochemical, and inflammatory markers between pregnant women with and without GDM. Our data demonstrate significantly elevated IL-6 levels in the GDM group, alongside higher BMI, total cholesterol, fasting insulin, and impaired oral glucose tolerance. The strong positive correlations of IL-6 with fasting insulin and OGTT, coupled with our regression analyses, underscore IL-6 as a key inflammatory predictor of GDM.

Our findings revealed elevated IL-6 levels in GDM patients, aligning closely with previous studies that have demonstrated a comparable increase in this pro-inflam-

matory cytokine among diabetic pregnancies. (14)reported a similar pattern, showing nearly triple the IL-6 concentration in GDM women compared to healthy controls. Likewise,[6] observed a pronounced elevation in IL-6 among GDM participants, significantly surpassing levels seen in normoglycemic pregnancies. Although methodological differences, such as assay techniques and sample processing, can influence IL-6 measurements, the consistency across these studies underscores the robust association between heightened IL-6 and GDM.

Mechanistically, IL-6 is known to be secreted by adipose tissue and the placenta in response to heightened metabolic demands and insulin resistance in pregnancy.[16] Elevated IL-6 can exacerbate insulin resistance by interfering with insulin signaling pathways in both hepatic and skeletal muscle tissues, leading to increased hepatic gluconeogenesis and reduced peripheral glucose uptake.[7] In the context of GDM, expanding adipose tissue and placental size across gestation may further stimulate IL-6 production, This pro-inflammatory milieu can, in turn, amplify insulin resistance, creating a vicious cycle that contributes to hyperglycemia.[16]

Our findings also highlight the significant association between IL-6 and lipid abnormalities—particularly total cholesterol – a phenomenon that has been implicated in vascular inflammation and endothelial dysfunction.[17] Elevated cholesterol may promote oxidative stress and inflammation, thus driving IL-6 production and contributing to the progression of GDM.[18] In addition, the high BMI observed in GDM participants likely reflects excess adipose tissue, which is a key source of pro-inflammatory cytokines like IL-6.[16] These interrelated metabolic and inflammatory derangements point to the multifactorial etiology of GDM.

Building on our findings, the clinical implications of IL-6 measurement in GDM screening merit further consideration. Incorporating IL-6 as an adjunct to conventional glucose-based screening methods could enhance early risk stratification, particularly by identifying patients who might be missed by standard tests alone. The diagnostic cutoff of ≥13.243 ng/L, as derived from our ROC analysis, offers a promising threshold for flagging pregnant women at heightened risk of GDM. In practice, IL-6 assays could be performed concurrently with routine OGTT or fasting glucose measurements, thereby providing an additional layer of diagnostic accuracy and enabling earlier lifestyle or pharmacological interventions.

Looking ahead, future research should aim to validate the diagnostic utility of IL-6 in larger, multi-center, and longitudinal studies. Such studies could assess the predictive power of IL-6 over the course of pregnancy, examine its relationship with long-term maternal and neonatal outcomes, and potentially refine the optimal cutoff value for clinical use. Additionally, research exploring the cost-effectiveness and feasibility of integrating IL-6 screening into existing prenatal care protocols will be essential to inform its translation into clinical practice.

A key strength of this study is the focused investigation of IL-6 as both an inflammatory and diagnostic biomarker in GDM, encompassing correlations with metabolic parameters and lipid profiles. By establishing a specific cutoff for IL-6, we propose a potentially valuable clinical screening tool. The integration of comprehensive biochemical assessments, including insulin and lipid measurements, further strengthens our conclusions regarding the interplay between inflammation and metabolic dysfunction in pregnancy.

Despite the robust associations observed between IL-6 levels and GDM, several limitations of our study warrant consideration. First, the single-center design may limit the generalizability of our findings to broader populations, as patient demographics and clinical practices might differ in other settings. Second, the relatively small sample size (n=90) may reduce the statistical power and limit the detection of more subtle associations. These factors, combined with potential variability in IL-6 assay measurements, suggest that caution should be exercised when extrapolating our results. Future studies involving larger, multi-center cohorts are needed to confirm these findings and to further delineate the role of IL-6 in the pathophysiology and early diagnosis of GDM.

Nonetheless, we recognize that expanding the scope of inflammatory profiling could further enhance our understanding of GDM. Future research should consider analyzing the interactions between IL-6 and other emerging biomarkers, such as C-reactive protein (CRP) and tumor necrosis factor-alpha (TNF-α), within the same patient cohort. Such studies could help determine whether IL-6 adds significant diagnostic and prognostic value over existing markers. Additionally, tracking pregnancy outcomes – both short-term (e.g., preeclampsia, preterm birth) and long-term (e.g., development of type 2 diabetes post-pregnancy) – would further underscore the clinical relevance of these inflammatory markers.

It would also be valuable to assess how IL-6 levels fluctuate across different stages of pregnancy. Our current study was limited to measurements between 24 and 28 weeks of gestation; however, evaluating IL-6 across all trimesters could identify critical windows when inflammatory changes are most predictive of GDM. Finally, while we controlled for key confounders such as BMI, age, and gestational age, other factors – including smoking, dietary habits, physical activity, and comorbid conditions – may influence IL-6 levels and should be addressed in future, larger-scale studies to improve generalizability.

While our study demonstrates that IL-6 levels are significantly elevated in women with GDM and suggests

a potential diagnostic cutoff of ≥13.243 ng/L, it is important to note that IL-6 is an acute-phase cytokine that lacks specificity. Elevated IL-6 is observed in a variety of inflammatory and metabolic disorders – including type 2 diabetes and obesity – and may be affected by factors such as dietary habits, physical activity, and stress. To mitigate these confounding effects, we excluded patients with known inflammatory conditions and controlled for variables such as BMI, age, and gestational age. Nonetheless, unmeasured factors (e.g., red meat consumption, exercise levels, and stress) could have contributed to the observed IL-6 levels.

Given these limitations, the diagnostic utility of IL-6 as a stand-alone marker for GDM must be interpreted with caution. Our study was not designed as a diagnostic trial with blinded protocols and focused sensitivity and specificity evaluations. Therefore, while our data support the potential of IL-6 as an adjunct biomarker, future studies employing specially designed, blinded protocols are warranted. In addition, exploring the interactions of IL-6 with other inflammatory markers – such as CRP and TNF-α – could enhance the specificity and clinical relevance of the inflammatory profile in GDM.

Conclusion

In conclusion, our findings indicate that elevated IL-6 levels are associated with gestational diabetes mellitus and may serve as a useful adjunct to conventional screening methods. However, because IL-6 is a non-specific marker affected by various confounding factors, further research using rigorously designed, blinded protocols is necessary to confirm its diagnostic value. Future investigations should also explore the combined use of IL-6 with other inflammatory biomarkers to improve the specificity of GDM screening and better predict both short- and long-term clinical outcomes.

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Declarations

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Author contributions

Conceptualization, S.H. and R.D. ; Methodology, S.H.; Software, S.H.; Validation, S.H., R.D., and A.U.; Formal Analysis, S.H.; Investigation, S.H.; Resources, R.D.; Data Curation, S.H.; Writing – Original Draft Preparation, S.H.; Writing – Review & Editing, R.D.; Visualization, A.U.; Supervision, A.U.; Project Administration, R.D.; Funding Acquisition, A.U.

Conflicts of interest

We declare that there are no conflicts of interest associated with this manuscript.

Data availability

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The study protocol was reviewed and approved by the Institutional Review Board of the Najaf Health Directorate, Training and Human Development Center (Approval No. 33652).

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