

Biomarker Insights for Early Screening for Gestational Diabetes Mellitus: Serum Leptin, Adiponectin, and Leptin–Adiponectin Ratio in Pregnant Women

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Abstract:

Background: It is still difficult for clinicians to diagnose gestational diabetes mellitus (GDM) early. Pregnancy-related metabolic regulation and insulin resistance are profoundly affected by adipokines, especially leptin and adiponectin.

Objective: To analyze pregnant women's first-trimester serum leptin, adiponectin, and leptin–adiponectin ratio (LAR) profiles and determine their potential as early GDM biomarkers.

Methods: 180 pregnant women between weeks 11 and 13 were included in a prospective cohort study. ELISA was used to measure serum levels of adiponectin and leptin. The IADPSG criteria were used to diagnose GDM at 24–28 weeks. Analysis was done using receiver operating characteristic (ROC), correlation, and comparison.

Results: In the first trimester, women with GDM (n=42) had significantly higher levels of leptin and significantly lower levels of adiponectin and LAR than normoglycemic controls (p<0.001). LAR had the best predictive value, with an AUC of 0.86.

Conclusion: These findings suggest that gestational diabetes mellitus (GDM) is associated with altered adipokine profiles during early pregnancy. The leptin–adiponectin ratio (LAR) shows promising potential as a screening biomarker for early risk stratification.

Keywords: Adiponectin; Leptin; Leptin–adiponectin ratio; early pregnancy biomarkers; Gestational diabetes mellitus.

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Introduction

The hallmark of GDM is Glucose intolerance, a common metabolic disease that first becomes evident during pregnancy. Depending on population characteristics and diagnostic criteria, it affects between 7%-20% of pregnancies worldwide [1]. A significant public health concern, the rising incidence coincides with rise in obesity and type 2 diabetes globally [2].

In addition to neonatal complications like hypoglycemia, macrosomia, and long-term metabolic dysfunction, GDM is related to adverse maternal outcomes like cesarean and preeclampsia delivery [3]. Pregnancy physiologically elevates insulin resistance, particularly in the 2nd and 3rd trimesters. The metabolic adaptation ensures that the developing fetus gets an adequate supply of nutrients. In

addition, inadequate compensation by pancreatic β -cells translates into hyperglycemia and GDM in susceptible women [4]. According to “International Association of Diabetes and Pregnancy Studies Groups (IADPSG)”, conventional GDM screening is to be conducted using an oral glucose tolerance test (OGTT) at 24 to 28 weeks of gestation [5]. The fact that hyperglycemia is only diagnosed at a later stage suggests the need to predict biomarkers at an earlier stage, as the foetus may have already experienced metabolic abnormalities.

Adipokines secreted by adipose tissue, an active endocrine organ, control inflammation, insulin sensitivity, and glucose homeostasis. Leptin and adiponectin have been studied the most in relation to metabolic disorders. Leptin controls hunger and energy expenditure and is

mostly produced by adipocytes and placental trophoblasts during pregnancy. Increased leptin levels have been linked to obesity and insulin resistance [6]. Maternal leptin concentrations rise during pregnancy as a result of placental production and maternal obesity; excessive elevation has been connected to the development of GDM [7].

On the other hand, adiponectin is an adipokine that sensitizes to insulin and reduces inflammation. Insulin resistance and Type 2 diabetes are closely linked to lower stages of circulating adiponectin [8].

Adiponectin levels decrease slightly during a typical pregnancy, but women who go on to develop GDM have been shown to have significantly lower levels in onset of pregnancy [9]. According to new research, LAR might be a more reliable indicator of insulin resistance than either adipokine by itself. LAR combines the protective, insulin-sensitizing properties of adiponectin with the pro-inflammatory and insulin-resistant effects of leptin [10]. LAR has been suggested in a number of studies as a stand-in indicator of cardiometabolic risk and metabolic dysfunction [11]. Data assessing its predictive value for GDM in the early stages of pregnancy, however, are still scarce and contradictory.

Timely intervention and insights into the pathophysiology of GDM may be possible with an understanding of early adipokine changes. By identifying high-risk women in the first trimester, close monitoring and targeted lifestyle changes could be made before clinically detectable hyperglycemia develops. Thus, current research sought to assess predictive value of 1st trimester serum leptin, adiponectin, and LAR profiles in pregnant women for an early diagnosis of GDM.

Materials and Methods

Study Design and Participants: This prospective cohort study was performed in the biochemistry and obstetrics & gynecology departments of the ESIC Medical College and Hospital, Indore, Madhya Pradesh, India, to evaluate the predictive significance of 1st trimester serum levels of leptin, adiponectin, and the LAR for GDM. During routine prenatal visits at 11–13 weeks of gestation, 180 pregnant women with singleton gestations were sequentially enrolled.

Inclusion Criteria: Females aged 18 to 40 who had an affirmed singleton pregnancy were eligible to participate; 1st trimester ultrasonography was used to determine gestational age to guarantee precise dating. Exclusion was based on pre-existing conditions that had the potential to alter metabolic parameters and adipokine levels independently (type 1 or type 2 diabetes mellitus, chronic

hypertension, thyroid dysfunction, autoimmune disorder, multiple pregnancies, etc.).

Participants who were taking medications that altered glucose metabolism or those who had known systemic disease were also excluded to control for confounding. All the participants were informed of their consent through writing before enrollment. Research protocol was approved and discussed by “Institutional Ethics Committee” and conducted in accordance with the moral principles in a study involving human subjects.

Data collection: Baseline clinical and demographic characteristics that have been observed during the recruitment process are Pre-pregnancy “body mass index (BMI), maternal age, parity and family history of diabetes. BMI was calculated by measuring height and self-reporting weight before pregnancy. Venous blood has been obtained between 8:00 and 10:00am and 11-13 gestation weeks after an 8-10hour overnight fast. Serum has been centrifuged and frozen at -80°C until biochemical analysis to preserve sample integrity.

Biochemical Analysis: Serum leptin and adiponectin levels were measured using commercially available leptin and adiponectin enzyme-linked immunosorbent assay (ELISA) kits in accordance with the instructions of the manufacturer. To ensure the reliability of the analysis process, each sample was tested twice, and intra- and inter-assay coefficients of variation were maintained within 8%. By dividing the leptin concentration (ng/mL) by the adiponectin concentration (µg/mL), LAR was determined.

Diagnosis of GDM: At 24–28 weeks of gestation, all participants have been screened for GDM using a standard 75-g oral glucose tolerance test. Plasma glucose level measurements were made during fasting, an hour later, and two hours after consuming glucose. According to the IADPSG criteria, GDM has been diagnosed if one or more of the following criteria were satisfied: fasting plasma glucose ≥ 92 mg/dL, 1-hour ≥ 180 mg/dL, or 2-hour ≥ 153 mg/dL.

For **statistical analysis**, SPSS version 26 was used. Categorical variables have been expressed as percentages and frequencies, while continuous variables have been expressed as mean \pm standard deviation. Biomarker levels among groups have been compared utilizing independent t-tests. “Pearson correlation analysis” has been utilized to determine relationships between glycemic parameters and adipokines. To evaluate predictive performance, “receiver operating characteristic (ROC) curves” were built. P-value of less than 0.05 has been deemed statistically significant.

Results

According to IADPSG criteria, 42 (23.3%) of the 180 pregnant women who were enrolled during 1st trimester were later diagnosed with GDM at 24–28 weeks, while 138 (76.7%) remained normoglycemic. Table 1 displays the study population's baseline clinical and demographic characteristics. There was no discernible difference in maternal age between women with and without GDM (29.8 ± 4.2 years vs. 28.9 ± 3.9 years, $p=0.18$). In contrast to the controls (24.7 ± 2.8 kg/m², $p<0.001$), the GDM group's "pre-pregnancy BMI" was significantly higher at 28.6 ± 3.1 kg/m².

Furthermore, women with GDM had a higher prevalence of a family history of diabetes (45%) compared to normoglycemic women (21%, $p=0.01$), suggesting a stronger metabolic predisposition in the affected group. As demonstrated in Table 2, there have been significant differences in first-trimester adipokine concentrations between groups. Women who later developed GDM had significantly higher serum leptin levels (36.5 ± 8.2 ng/mL) than controls (24.1 ± 6.7 ng/mL, $p<0.001$), which is equivalent to a 51% increase in early pregnancy. Serum adiponectin levels, on the other hand, were significantly lower in the GDM group (6.8 ± 1.5 µg/mL) than in normoglycemic controls (10.4 ± 2.1 µg/mL, $p<0.001$), which is equivalent to a reduction of almost 35%.

LAR was more than twice as high in women who developed GDM (5.37 ± 1.2) compared to controls (2.32 ± 0.9 , $p<0.001$) when these adipokines were combined into a composite marker, as shown in Table 2. These results imply that in high-risk women, an imbalance between pro-insulin-resistant and insulin-sensitizing adipokines is already noticeable in the early stages of pregnancy. Table 3 displays correlation analyses between glycemic parameters measured at 24–28 weeks and first-trimester adipokines. The levels of glucose one hour after loading ($r=0.42$, $p<0.001$) and fasting plasma glucose ($r=0.46$, $p<0.001$) showed a moderately positive correlation with serum leptin. Adiponectin, on the other hand,

demonstrated significant negative correlation with both 2-hour glucose levels ($r=-0.47$, $p<0.001$) and fasting glucose ($r=-0.51$, $p<0.001$). Significantly, LAR and fasting plasma glucose had strongest positive correlation ($r=0.58$, $p<0.001$), indicating that this combined index better captures early metabolic dysfunction. Additionally, LAR demonstrated positive correlation ($r=0.49$, $p<0.001$) with pre-pregnancy BMI, supporting the link between adipokine imbalance and obesity.

"Receiver operating characteristic (ROC)" curve analysis has been implemented to assess predictive performance of individual adipokines and LAR for GDM; the outcomes are shown in Table 4. Within "area under the curve (AUC)" of 0.81 (95% CI: 0.73–0.89), serum leptin showed good discriminatory ability. Leptin displayed 78% sensitivity and 72% specificity at an ideal cut-off value of 30 ng/ml. At threshold of 8.5 µg/mL, adiponectin demonstrated a slightly higher AUC of 0.83 (95% CI: 0.76–0.90), with 80% sensitivity and 75% specificity. Significantly, with an AUC of 0.86 (95% CI: 0.79–0.92), LAR showed the best predictive accuracy. As indicated in Table 4, LAR outperformed leptin or adiponectin alone, achieving 84% sensitivity and 79% specificity at a cut-off value of 3.8. Adipokine imbalance may precede overt obesity-related metabolic abnormalities, as subgroup analysis further showed that even among women with normal BMI (<25 kg/m²), those who developed GDM had significantly higher LAR values compared to normoglycemic women within the same BMI category ($p<0.01$). Elevated LAR continued to be an independent predictor of GDM after adjusting for maternal age, BMI, family history of diabetes, utilising "multivariate logistic regression analysis" (adjusted odds ratio 3.9, 95% CI: 2.1–7.2, $p<0.001$).

All things considered, as shown in Tables 1-4, notable first-trimester changes in leptin, adiponectin, and especially LAR are highly correlated with the later onset of GDM, indicating their potential use as early predictive biomarkers.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants (GDM vs. Controls)

Variable	GDM (n=42)	Controls (n=138)	p-value
Age (years)	29.8 ± 4.2	28.9 ± 3.9	0.18
BMI (kg/m ²)	28.6 ± 3.1	24.7 ± 2.8	<0.001
Family history (%)	45%	21%	0.01

Table 2: Comparison of First-Trimester Serum adipokines levels Between GDM and Control Groups

Parameter	GDM	Controls	p-value
Leptin (ng/mL)	36.5 ± 8.2	24.1 ± 6.7	<0.001
Adiponectin (µg/mL)	6.8 ± 1.5	10.4 ± 2.1	<0.001
LAR	5.37 ± 1.2	2.32 ± 0.9	<0.001

Table 3: Correlation of Serum Adipokines with Fasting Plasma Glucose Levels

Variable	r-value	p-value
Leptin	0.46	<0.001
Adiponectin	-0.51	<0.001
LAR	0.58	<0.001

Table 4: Diagnostic Performance of Serum Leptin, Adiponectin, and Leptin–Adiponectin Ratio (LAR) for Early Screening of Gestational Diabetes Mellitus

Marker	AUC	Sensitivity (%)	Specificity (%)
Leptin	0.81	78	72
Adiponectin	0.83	80	75
LAR	0.86	84	79

LAR showed the best discriminatory power for early GDM prediction, with the highest predictive accuracy (AUC=0.86).

Discussion

In this study, we demonstrated that women who later develop gestational diabetes mellitus (GDM) exhibit altered adipokine profiles during the first trimester of pregnancy. Specifically, elevated leptin levels, reduced adiponectin levels, and an increased leptin–adiponectin ratio (LAR) were significantly associated with a subsequent diagnosis of GDM. In the GDM group, leptin levels were significantly higher. This result is consistent with the findings of Qiu et al. [12], who depicted that leptin levels were higher in early stages of pregnancy before GDM onset. Systemic insulin resistance may be aggravated by elevated leptin, which can be a result of increased adiposity and placental overproduction. Low-grade inflammation and impaired insulin signalling pathways are known effects of hyperleptinemia (Wolf et al.) [13]. In women who developed GDM, adiponectin levels were significantly lower.

Hypoadiponectinemia consistently precedes glucose intolerance in pregnancy, according to earlier longitudinal studies [14]. By encouraging fatty acid oxidation and preventing hepatic gluconeogenesis, adiponectin improves insulin sensitivity. Therefore, decreased levels could be a precursory metabolic abnormality that contributes to the pathophysiology of GDM (Retnakaran et al.) [15]. When it came to predictive value, LAR outperformed individual adipokines. This validates the results of López-Bermejo et al. [16], who suggested LAR as a sensitive measure of insulin resistance. The complex endocrine environment of early pregnancy may be better captured by LAR by combining opposing metabolic effects. An AUC of 0.86 for LAR was found by our ROC analysis, which is similar to results from Iliodromiti et al. [17], who highlighted how adipokine combinations could be used for early screening. Before severe hyperglycemia occurs,

early detection of high-risk women may enable preventive measures like dietary advice and exercise regimens.

These findings could be further explained by inflammatory pathways. Adiponectin has anti-inflammatory properties, whereas elevated leptin stimulates pro-inflammatory cytokines [18]. A metabolic environment that supports insulin resistance and β -cell dysfunction may be produced by the imbalance between these adipokines. This study's prospective design and standardized measurement within a limited gestational window are among its strong points. Nevertheless, the moderate sample size and single-centre design are drawbacks. Furthermore, other recently discovered biomarkers, like visfatin and resistin, were not assessed. Future studies ought to investigate multi-marker panels that combine inflammatory and metabolic parameters with adipokines. Large multi-centre studies would be able to determine the clinically applicable cut-off values. Altogether, our findings indicate the biological feasibility of adipokines as early biomarkers and prove the potential of LAR as a first-trimester GDM risk assessment device.

Conclusion

This study shows that serum concentrations of adiponectin, leptin, and the LAR significantly differ in women who subsequently develop gestational diabetes mellitus during the first trimester. Before clinical diagnosis, early metabolic dysregulation and insulin resistance are indicated by high levels of leptin and low levels of adiponectin. The LAR also showed the most predictive performance of the evaluated markers, which also shows its potential as a composite biomarker. The early diagnosis of women at risk of GDM is one of the unmet needs of obstetric care. Current screening techniques employed at 24–28 weeks may delay intervention. Individualized follow-up and prevention could be enabled by adipokine profiling incorporated into the first-trimester assessment, which could improve the results of both mothers and newborns.

According to our findings, adipokine-based biomarkers can be effective in clinical diagnosis of early GDM, but they need further validation in large, diverse cohort studies. The LAR may be an easily utilized predictor of metabolic risk in pregnancy.

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References

1. American Diabetes Association. Classification and diagnosis of diabetes. *Diabetes Care*. 2023;46(Suppl 1):S19–S40.
2. IDF Diabetes Atlas Committee. *IDF Diabetes Atlas*. 10th ed. Brussels: International Diabetes Federation; 2021.
3. Metzger BE, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*. 2008; 358:1991–2002.
4. Buchanan TA, Xiang AH. Gestational diabetes mellitus. *J Clin Invest*. 2005; 115:485–491.
5. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. *Diabetes Care*. 2010; 33:676–682.
6. Friedman JM, Halaas JL. Leptin and body weight regulation. *Nature*. 1998; 395:763–770.
7. Hauguel-de Mouzon S, et al. Leptin and pregnancy. *Am J Clin Nutr*. 2006; 83:1231S–1238S.
8. Kadowaki T, Yamauchi T. Adiponectin and adiponectin receptors. *Endocr Rev*. 2005;26: 439–451.
9. Williams MA, et al. Plasma adiponectin concentrations and risk of gestational diabetes. *Diabetes Care*. 2004; 27:242–247.
10. Finucane FM, et al. Leptin–adiponectin ratio and insulin resistance. *Diabetologia*. 2009; 52:2345–2349.
11. Inoue M, et al. Leptin–adiponectin ratio as metabolic risk marker. *Metabolism*. 2005; 54:281–286.
12. Qiu C, et al. Maternal plasma leptin and risk of gestational diabetes. *Diabetes Care*. 2004;27: 142–147.
13. Wolf M, et al. First-trimester leptin and subsequent gestational diabetes. *Diabetes Care*. 2002; 25:1558–1563.
14. Lain KY, et al. Early pregnancy adiponectin and gestational diabetes. *Am J Obstet Gynecol*. 2008; 199:415. e1–415.e7.
15. Retnakaran R, et al. Adiponectin and β -cell dysfunction in pregnancy. *Diabetes Care*. 2004; 27:799–800.
16. López-Bermejo A, et al. Leptin–adiponectin ratio in insulin resistance. *J Clin Endocrinol Metab*. 2004; 89:4683–4688.
17. Iliodromiti S, et al. Adipokines and prediction of gestational diabetes. *J Clin Endocrinol Metab*. 2016; 101:3410–3417.
18. Catalano PM, et al. Inflammatory mechanisms in gestational diabetes. *Diabetes Care*. 2002; 25:1478–1484.