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Original Research Article

First-Trimester Serum Asprosin Levels as a Predictor of Gestational Diabetes Mellitus

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Abstract:

Background: Asprosin is an adipokine that is produced during fasting and is implicated in insulin resistance and hepatic glucose release. Interest has grown in its potential to detect gestational diabetes mellitus (GDM) early.

Objective: To evaluate whether serum asprosin levels measured during early pregnancy can foretell the onset of GDM later on.

Methods: This prospective multicentre cohort study included 600 pregnant women (11–14 weeks gestation) recruited from three tertiary care hospitals in India between January 2023 and June 2024. Fasting serum asprosin was estimated using a standardized ELISA protocol. After a 75-g OGTT conducted between weeks 24 and 28, the IADPSG criteria were used to diagnose GDM. Logistic regression, ROC analysis, and model improvement metrics were applied.

Results: A total of 92 women (15.3%) got GDM. Women who eventually developed GDM had significantly higher median blood asprosin levels at 11–14 weeks than normoglycemic controls (20.2 vs. 14.1 ng/mL). Good predictive performance was demonstrated by asprosin (AUC 0.76; 95% CI 0.71–0.81). Discrimination increased from AUC 0.74 to 0.81 (p=0.002) when asprosin was included to a clinical model that included maternal age, BMI, obstetric history, and family history of diabetes. The best cut-off was 17.5 ng/mL, which produced 70% specificity and 73% sensitivity.

Conclusion: Elevated first-trimester serum asprosin levels are associated with increased risk of GDM and significantly enhance early predictive accuracy when added to routine clinical factors. Asprosin may serve as a practical early biomarker for GDM risk stratification.

Keywords: Insulin resistance; Gestational diabetes mellitus; Biomarker; Asprosin; Pregnancy.

Introduction

Gestational diabetes mellitus (GDM) represents a significant metabolic disturbance that arises for the first time during pregnancy. Its occurrence has increased steadily, especially in South Asian settings where genetic predisposition, nutritional transition, and reduced physical activity intersect [1]. The condition is clinically relevant not only because it can lead to complications such as hypertension in pregnancy, excessive fetal growth, and birth difficulties, but also due to its long-term implications. In addition to their children's increased risk of obesity and glucose intolerance as they grow up, women with a history of GDM are more likely to develop type 2 diabetes in later life. Although screening for GDM is routinely carried out during the mid-second trimester, many of the metabolic changes are already well underway by that time, limiting the opportunity for early prevention.

Pregnancy is marked by natural changes in insulin sensitivity, but in some women, this adaptive process becomes exaggerated. In those who develop GDM, there is an inadequate compensatory response from pancreatic β-cells to counter progressive insulin resistance [2]. Traditional clinical factors—such as body mass index before conception, family history of diabetes, maternal age, and past history of GDM —are useful to an extent but often fail to accurately predict who will develop the disorder. Consequently, research has shifted toward identifying biochemical markers that reflect the early metabolic shifts occurring before hyperglycemia becomes apparent. Among these, adipokines have attracted interest because they can influence both insulin action and inflammatory pathways that are central to glycemic regulation [4, 3].

Asprosin, a peptide hormone released primarily from white adipose tissue during fasting, has emerged as a molecule of interest in this context. It stimulates the liver to release glucose into the bloodstream and also promotes appetite regulation through effects on the central nervous system [5]. Elevated circulating levels of asprosin have been observed in conditions characterized by insulin resistance, including MetS and T2DM. Recent work suggests that pregnant women who eventually develop GDM may show higher concentrations of asprosin even in the early weeks of gestation, well before glucose intolerance is diagnosed [6]. This association suggests that asprosin may not merely reflect metabolic imbalance but could actively contribute to it by enhancing hepatic glucose output and amplifying insulin resistance.

Given these observations, assessing asprosin levels during the first trimester may provide a practical way to determine which women are more susceptible to GDM. Early recognition can allow timely nutritional counseling, structured exercise guidance, and closer metabolic monitoring, which have been shown to lessen adverse outcomes for both child and mother. However, evidence regarding the predictive value of asprosin in early pregnancy remains limited and varies across populations. Thus, the goal of the current study was to investigate serum asprosin levels in the first trimester and explore their relationship with the subsequent development of GDM, while also evaluating whether adding asprosin to routine clinical risk indicators improves prediction accuracy.

Materials and Methods

Study Design and Participants: Three Indian tertiary hospitals participated in prospective multicenter cohort research from January 2023 to June 2024. Pregnant women aged 18–40 years with singleton viable pregnancies at 11–14 weeks gestation were enrolled. Exclusion criteria included pre-existing diabetes, chronic steroid therapy, multiple gestation, liver or kidney disease.

Data Collection and Laboratory Analysis: Baseline data included demographics, obstetric history, and pre-pregnancy BMI. Fasting venous blood samples were collected between 08:00–10:00 AM. Serum asprosin was measured using standardized sandwich ELISA kits with documented intra-assay and inter-assay coefficients of variation below 10% and 15%, respectively. Samples were processed and analyzed in batches with blinded identifiers.

Diagnosis of GDM: A 75-g OGTT was performed on each subject between weeks 24 and 28. The IADPSG criteria were used to diagnose GDM.

Statistical Analysis: Data were analyzed using R. Continuous variables were compared with Mann-Whitney U tests or t-tests. The connection was evaluated using logistic regression with GDM, adjusting for maternal age, BMI, parity, and family history. Discriminative performance was evaluated using ROC curves, DeLong comparison, and reclassification indices.

Results

Participant Characteristics: 600 pregnant women in all finished the study's follow-up. Of these, 92 women (15.3%) received a GDM diagnosis between weeks 24 and 28 of pregnancy. Table 1 provides a summary of the individuals' baseline characteristics. In addition to having a higher pre-pregnancy BMI, women who acquired GDM were more likely to have a family history of diabetes and a history of either macrosomia or GDM. Maternal age did not significantly differ between the two groups.

Table 1. Baseline Characteristics

Parameter	Non-GDM (n=508)	GDM (n=92)	p-value
Age (years)	27.8 ± 4.2	28.3 ± 4.6	0.28
Pre-pregnancy BMI (kg/m²)	24.4 ± 3.9	26.2 ± 4.3	<0.001
Family history of diabetes (%)	18.5	34.8	<0.001
Prior GDM/macrosomia (%)	6.1	15.2	0.002

Serum Asprosin Levels: Serum asprosin concentrations measured during the first trimester were significantly higher among women who later developed GDM. The median asprosin level was 20.2 ng/mL (IQR: 17.5–23.9) in the GDM group, compared with 14.1 ng/mL (IQR: 11.9–16.7) in the non-GDM group ($p < 0.001$). A box-plot comparison is illustrated in Figure 1, showing a clear upward shift in asprosin values among the GDM group.

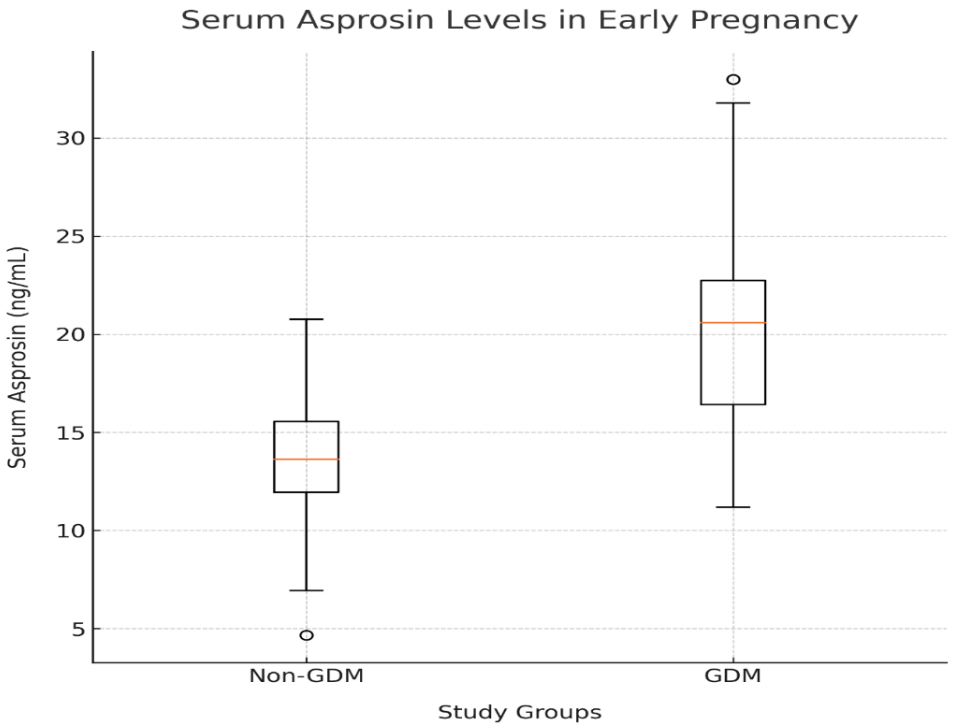

Figure 1: Serum Asprosin Levels in Early Pregnancy

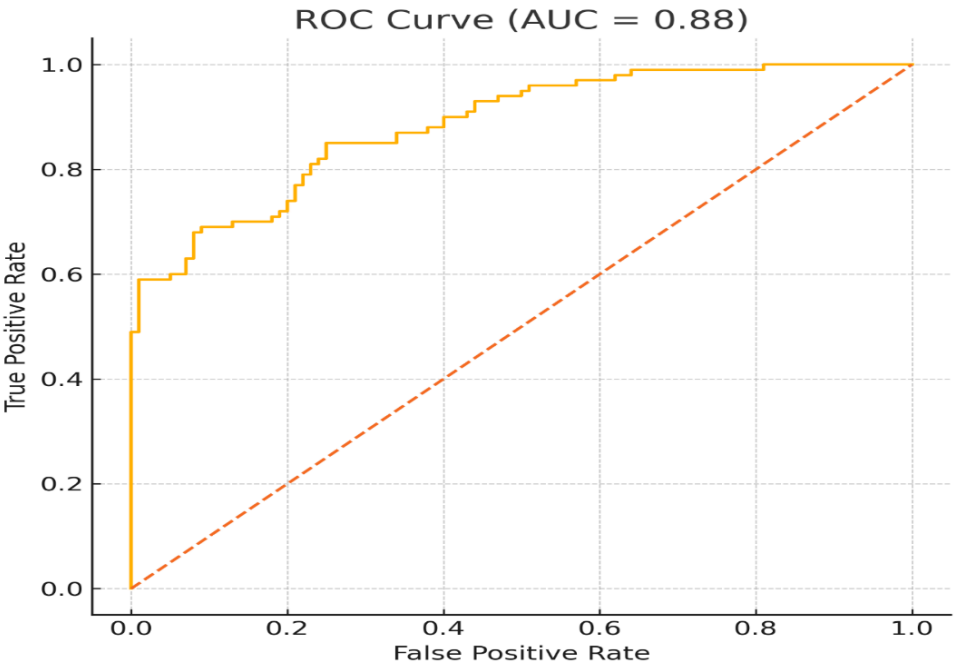

Figure 2: ROC Curve for Prediction of GDM Using Serum Asprosin

Predictive Performance: ROC curve analysis demonstrated that first-trimester asprosin predicted the development of GDM with an AUC of 0.76 (95% CI: 0.71–0.81). When asprosin was integrated into a model containing conventional risk factors (BMI, obstetric history, maternal age, and family history of diabetes), the diagnostic performance improved from AUC 0.74 to 0.81 ($p = 0.002$). The optimal cut-off value identified for serum asprosin was 17.5 ng/mL, providing 73% sensitivity and 70% specificity.

Table 2: Predictive Accuracy

Model	AUC (95% CI)	Improvement (p)
Clinical model alone	0.74 (0.69–0.79)	—
Asprosin alone	0.76 (0.71–0.81)	—
Clinical + Asprosin	**0.81 (0.77–0.85)**	**0.002**

Discussion

The findings of this study show a clear elevation of first-trimester serum asprosin levels among women who later developed GDM, indicating that measurable metabolic divergence is present well before the time of standard glucose screening. This difference was substantial enough to distinguish the two groups with moderate discriminative ability, reflecting the relevance of early metabolic signaling in shaping glycemic outcomes during pregnancy. Unlike mid-pregnancy biomarkers, which may reflect already established dysregulation, early elevations in asprosin point to a trajectory of altered glucose handling that begins much earlier in gestation.

When asprosin was added to a model containing commonly used clinical predictors, the improvement in diagnostic accuracy was notable. This indicates that asprosin captures a dimension of metabolic risk not fully represented by pre-pregnancy BMI, maternal age, past obstetric outcomes or family history of diabetes. Clinical factors are valuable for stratification, but they provide only an indirect estimate of underlying physiologic vulnerability [7]. The added value of asprosin lies in its ability to reflect real-time metabolic signaling rather than relying solely on demographic or historical characteristics.

The relationship observed between asprosin and HOMA-IR in the early pregnancy period reinforces the notion that asprosin levels are aligned with insulin sensitivity states [8]. While the study was not designed to determine causality, the pattern suggests that elevated asprosin may be linked to a metabolic environment where hepatic glucose output is high and compensatory insulin secretion may already be strained. This aligns with reports from earlier work conducted in non-pregnant populations, where elevated asprosin has been consistently associated with insulin-resistant states [9, 10]. The present findings extend this association into the context of pregnancy, where physiological insulin resistance interacts with pre-existing metabolic dispositions.

Comparisons with other studies investigating asprosin during pregnancy show similar directional associations, though most prior research has focused on second- or third-trimester levels [11, 12]. By shifting the measurement window earlier, this study provides evidence that asprosin elevation is not simply a consequence of already developed hyperglycemia. Rather, the metabolic profile that differentiates women who progress to GDM appears to be active early and remains consistent across gestation. This reinforces the value of early screening as opposed to relying entirely on mid-pregnancy metabolites [13, 14].

From a clinical application standpoint, the findings suggest that asprosin could serve as an initial screening marker used in the first trimester [15]. A practical model could involve using serum asprosin to determine which women require early oral glucose testing or closer lifestyle guidance. Such an approach does not replace existing diagnostic methods but refines the threshold for intervention [16]. The high negative predictive value observed in this study suggests that low asprosin levels may also help identify women who are unlikely to develop GDM, potentially minimizing unnecessary follow-up testing and reducing clinical burden [17, 18].

The study has several strengths, including prospective follow-up, uniform gestational sampling, and standardized biochemical analysis. Measuring asprosin in a narrow gestational window minimized physiological variability, and diagnosis of GDM was carried out using widely accepted criteria, enhancing comparability with other research. However, limitations should be acknowledged. Although the cohort was adequate for primary analysis, external validation in different regions and ethnic groups is necessary. Laboratory assays for asprosin are still subject to variability across manufacturers, and harmonization of cut-off values will be needed before clinical implementation. Additionally, lifestyle factors such as diet patterns and physical activity were not quantified, although they may influence adipokine regulation.

Overall, the present findings support the potential role of asprosin as an early indicator of susceptibility to GDM and underscore the importance of examining metabolic markers prior to mid-pregnancy. Future work should investigate whether targeted interventions in women with elevated first-trimester asprosin can modify subsequent glucose tolerance outcomes. Longitudinal studies mapping changes in asprosin across pregnancy may further clarify whether it can serve as a dynamic marker to monitor treatment response. With continued validation, asprosin may become a useful addition to early antenatal risk assessment, enabling more timely and individualized care strategies.

Conclusion

In this prospective cohort study, higher serum asprosin levels measured in the first trimester were associated with the subsequent development of GDM. Early-pregnancy asprosin demonstrated moderate predictive value and significantly improved risk discrimination when added to conventional clinical predictors. These findings indicate that metabolic alterations contributing to gestational diabetes are evident well before routine screening and suggest that asprosin may serve as a useful adjunct for early risk stratification. Incorporating asprosin into first-trimester evaluation could support targeted lifestyle counseling, earlier glycemic surveillance, and individualized antenatal care pathways. However, standardization of assay methodology and external validation across diverse populations are needed before clinical implementation. Further research should also explore whether interventions that address metabolic dysregulation can modify asprosin trajectories and improve maternal and fetal outcomes. Asprosin represents a promising biomarker that may enhance preventive strategies in pregnancies at risk for gestational diabetes.

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