ORIGINAL ARTICLE

Assessment of Glycosylated Fibronectin Level in Maternal Serum at 10-15 Weeks as a Predictor of Preeclampsia

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ABSTRACT

Background: Preeclampsia is a major contributor to maternal and perinatal morbidity and mortality, particularly in low- and middle-income countries (LMICs). The early identification of at-risk women remains a clinical priority. Glycosylated fibronectin, a marker of endothelial dysfunction, has emerged as a potential early biomarker. **Objective:** This study aimed to assess maternal serum glycosylated fibronectin levels at 10–15 weeks of gestation as a predictor of preeclampsia. **Methods & Materials:** This prospective cohort study was conducted at the Dhaka Medical College Hospital from July 2021 to June 2022. A total of 115 pregnant women with viable singleton pregnancies were enrolled between 10 and 15 weeks of gestation. Maternal serum glycosylated fibronectin levels were measured using ELISA. The participants were followed up until delivery to monitor the development of preeclampsia. Statistical analysis was performed using SPSS version 25.0. **Results:** Twelve women (10.4%) developed preeclampsia and the mean serum glycosylated fibronectin levels were significantly higher in women who developed preeclampsia than in those who did not (260.58 ± 79.01 vs. 115.84 ± 61.62 µg/ml; p < 0.001). A cut-off value of 261.5 µg/ml yielded a sensitivity of 83.3%, specificity of 91.3% and AUC of 0.912. **Conclusion:** Elevated maternal serum glycosylated fibronectin levels in early pregnancy are strong predictors of preeclampsia. Its use as an early screening biomarker may improve risk stratification and enable the timely implementation of preventive strategies.

Keywords: Preeclampsia, Glycosylated fibronectin, early pregnancy, Biomarker.

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INTRODUCTION

Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality worldwide, especially in low- and middle-income countries [1]. It presents as a multisystem hypertensive disorder after 20 weeks of gestation, characterized by new-onset hypertension with or without proteinuria and maternal organ dysfunction [2]. Its pathogenesis is heterogeneous and incompletely understood, with abnormal placentation early in pregnancy marked by shallow trophoblastic invasion and inadequate spiral artery remodelling, leading to placental ischemia and the systemic release of anti-angiogenic and inflammatory factors, resulting in widespread endothelial dysfunction [2,3]. These vascular changes precede the clinical symptoms, emphasizing the need for early biomarkers that reflect these processes [4].

Fibronectin, a high-molecular-weight extracellular matrix glycoprotein, plays a key role in cell adhesion, angiogenesis and vascular integrity. Its circulating forms include plasma fibronectin, produced by hepatocytes and cellular fibronectin, which is synthesized by endothelial and other cells. Elevated fibronectin levels are associated with endothelial injury and vascular remodeling conditions, including preeclampsia [5]. Fibronectin undergoes complex glycosylation, a post-translational modification that affects its stability and function and altered glycosylation patterns have been linked to endothelial dysfunction. Glycosylated fibronectin (GlyFn) has gained attention as a promising biomarker for early vascular injury and placental dysfunction in preeclampsia [5].

Several studies have demonstrated that fibronectin levels are elevated before the onset of clinical preeclampsia, supporting its role as an early predictive marker. Maternal serum glycosylated fibronectin levels measured in early pregnancy can reliably identify women at an increased risk of developing preeclampsia [4]. Nonetheless, most screening approaches are applied during mid-pregnancy, reducing the lead time for preventive interventions such as low-dose aspirin [6]. In resource-limited settings, such as Bangladesh, there is an acute need for simple, cost-effective biomarkers applicable

early in pregnancy to stratify risk and optimize antenatal care; however, evidence on the predictive value of GlyFn in the first trimester remains limited in South Asian populations [6].

Overall, advances in proteomics and biomarker discovery continue to unravel novel mediators of preeclampsia pathophysiology and improve early detection strategies, with fibronectin and its glycosylated forms representing significant components of this evolving landscape [7,8]. An enhanced understanding of these biomarkers, alongside other emerging molecular candidates such as pregnancy-specific β-1 glycoproteins and extracellular vesicles, holds promise for improving prediction and prevention efforts globally [4,8].

Thus, integrating fibronectin glycosylation profiling with expanding biomarker panels could refine early risk stratification and guide targeted interventions to mitigate the substantial morbidity and mortality associated with preeclampsia [2,4].

Therefore, this study was designed to assess maternal serum glycosylated fibronectin levels at 10–15 weeks of gestation as a predictor of preeclampsia to contribute to early risk stratification and improved maternal outcomes.

OBJECTIVES

The objective of this study was to assess the maternal serum of glycosylated fibronectin at 10-15 weeks of gestation as a predictor of Preeclampsia.

METHODS & MATERIALS

This prospective cohort study was conducted in the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh, from July 2021 to June 2022. A total of 115 pregnant women with a viable singleton pregnancy attending the antenatal clinic between 10 and 15 weeks of gestation were included in this study.

Inclusion criteria
1) Pregnant women of 10-15 weeks of gestation
2) Age between 18 and 40 years of age
3) Women having a single pregnancy.
4) Informed consent for inclusion in the study

Exclusion criteria
1) Prior or current history of PE, chronic hypertension, chronic kidney disease, autoimmune disease such as SLE & APLA, collagen vascular disease (as they are major risk factor of preeclampsia)
2) Subjects with multiple pregnancy as it is a risk factor of PE (Gestosis score 2)
3) Generalized disorders affecting maternal haemodynamics like anaemia, obesity, thyrotoxicosis, diabetes mellitus (all are risk factors of PE), any cancer.
4) Congenital and acquired heart diseases, chronic obstructive pulmonary disease was excluded. (as fibronectin may also increase in these condition).
5) Fetal abnormalities, as the possibility that those patients might opt for a pregnancy termination existed and data collection would thus be incomplete.

Data Collection Procedure

A total of 124 eligible pregnant women were initially enrolled using a combination of purposive and convenience sampling. After exclusion due to loss to follow-up, 115 participants were included in the final analysis. Detailed socio-demographic, medical, obstetric and family histories were recorded using a structured questionnaire. Gestational age was confirmed by the last menstrual period and early ultrasonography. A thorough physical examination was performed at enrollment.

At 10–15 weeks of gestation, venous blood samples were collected under aseptic conditions. Serum glycosylated fibronectin levels were measured using an enzyme-linked immunosorbent assay (ELISA) in the Department of Clinical Pathology, DMCH. Participants were followed prospectively until delivery. Blood pressure was measured at each antenatal visit and preeclampsia was diagnosed based on the development of hypertension after 20 weeks of gestation with associated proteinuria or protein–creatinine ratio, according to standard diagnostic criteria. Ethical approval was obtained from the institutional ethical review committee and confidentiality of participant data was strictly maintained.

Statistical Analysis

Data were analyzed using SPSS version 25.0. Descriptive statistics were expressed as mean ± standard deviation and frequencies. Group comparisons were performed using the chi-square test and the independent t-test. ROC curve analysis was used to determine the optimal cut-off value of serum glycosylated fibronectin. A p-value < 0.05 was considered statistically significant.

RESULTS

Table I presents the socio-demographic and obstetric characteristics of the study population. The majority of participants were aged 21–30 years (65.2%), were housewives (89.6%) and belonged to the middle socio-economic group (60.9%). Multiparous women constituted 67.8% of the study population.

Table – I: Socio-demographic and obstetric characteristics of the study population (*n*=115)

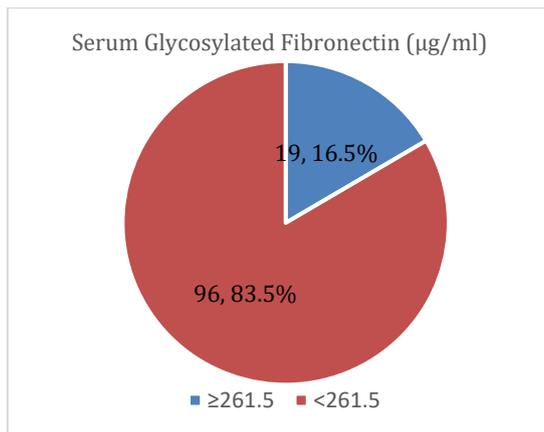| Variables		Frequency	Percentage
Age group (years)	≤20	29	25.2
	21-30	75	65.2
	31-40	11	9.6
Educational status	Illiterate	1	0.9
	Only can sign her name	8	7.0
	Primary	52	45.2
	Secondary and above	54	47.0
Occupational status	Housewife	103	89.6
	Working	12	10.4
Socio-economic status	Lower	25	21.7
	Middle	70	60.9
	Upper	20	17.4
Parity	Primiparous	37	32.2
	Multiparous	78	67.8

Figure – 1: Distribution of the study patients by serum glycosylated fibronectin (*n*=115)

Figure 1 illustrates the distribution of maternal serum glycosylated fibronectin levels among the study participants. Most women (83.5%) had serum glycosylated fibronectin levels below the cut-off value of 261.5 µg/ml, while 16.5% had elevated levels.
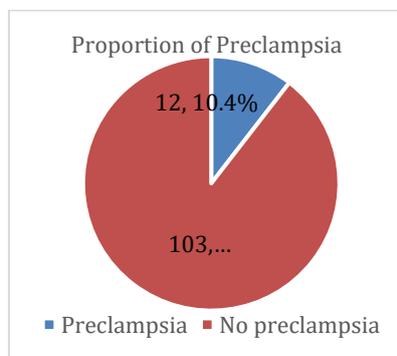

Figure – 2: Distribution of study patients by proportion of preeclampsia in the study population (*n*=115)

Figure 2 shows the proportion of women who developed preeclampsia. Out of 115 participants, 12 (10.4%) were diagnosed with preeclampsia, whereas 103 (89.6%) remained normotensive throughout pregnancy.

Table II compares serum glycosylated fibronectin concentrations between women who developed preeclampsia and those who did not. The mean serum glycosylated fibronectin level was significantly higher in the preeclampsia group compared to the non-preeclampsia group (260.58 ± 79.01 µg/ml vs. 115.84 ± 61.62 µg/ml; p < 0.001).

Table – II: Comparison of serum glycosylated fibronectin among preeclampsia and no preeclampsia women (*n*=115)

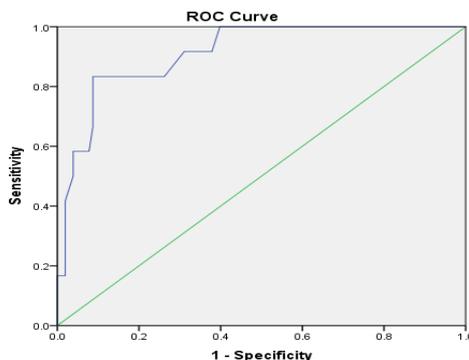| Variables	Frequency (n)	Serum glycosylated fibronectin (µg/ml) Mean±SD	p-value
Preeclampsia	12	260.58± 79.01	<0.001
No preeclampsia	103	115.84± 61.62	

Figure – 3: ROC analysis of serum glycosylated fibronectin to predict preeclampsia

Figure 3 depicts the receiver operating characteristic (ROC) curve of serum glycosylated fibronectin for predicting preeclampsia. The area under the curve (AUC) was 0.912 (95% CI: 0.838–0.986), indicating excellent discriminative ability.

ROC analysis
ROC analysis of glycosylated fibronectin to predict preeclampsia found an AUC value of 0.912 (95% CI, 0.838-0.986), which was statistically significant (p<0.001) (Table III).

Table – III: Area Under Curve

Area under curve	Cut of value	Sensitivity	Specificity	95% CI (Lower-Upper)	p-value
0.912	261.5	83.3	91.3	0.838-0.986	<0.001

Table IV presents the diagnostic accuracy indices of the derived cut-off value. The sensitivity was 83.3%, specificity 91.3%, positive predictive value 52.6%, negative predictive value 97.9% and overall accuracy 90.4%.

Table – IV: Sensitivity, specificity, PPV, NPV and accuracy gained by the derived cutoff of serum glycosylated fibronectin with 95% confidence interval

Statistic	Value	95% CI
Sensitivity	0.833	62.25% to 99.42%
Specificity	0.913	82.15% to 94.55%
Positive Predictive Value	0.526	24.65% to 66.26%
Negative Predictive Value	0.979	94.90% to 99.80%
Accuracy	0.904	81.85% to 93.80%

Table V demonstrates the association between serum glycosylated fibronectin levels and the occurrence of preeclampsia. Among women with Serum glycosylated fibronectin ≥ 261.5 µg/ml, 83.3% developed preeclampsia compared to 16.7% among those with lower levels, with a relative risk of 25.26 (p = 0.001).

Table – V: Association between serum glycosylated fibronectin with preeclampsia (*n=115*)

Serum glycosylated fibronectin	Preeclampsia (n=12)		No preeclampsia (n=103)		RR	P value
	n	%	n	%		
≥261.5 µg/ml	10	83.3	9	8.7	25.26	0.001
<261.5 µg/ml	2	16.7	94	91.3		

DISCUSSION
The present prospective cohort study demonstrates that elevated maternal serum glycosylated fibronectin (GlyFn) levels at 10–15 weeks of gestation are strongly associated with the subsequent development of preeclampsia. Women who later developed preeclampsia exhibited significantly higher mean GlyFn concentrations compared to normotensive pregnant women and the derived cut-off value showed excellent predictive performance. These findings support the hypothesis that biochemical evidence of endothelial dysfunction and abnormal placentation precedes the clinical onset of preeclampsia by several weeks.

Preeclampsia is increasingly recognized as a disorder originating in early pregnancy, with defective trophoblastic invasion and inadequate spiral artery remodeling leading to placental hypoperfusion [9,10]. This placental pathology triggers the release of circulating factors that induce systemic endothelial dysfunction, which manifests clinically later in gestation [11]. Fibronectin, particularly its glycosylated form, reflects endothelial activation and vascular injury, making it biologically plausible as an early predictive biomarker [12].

The significantly higher mean GlyFn level observed among women who developed preeclampsia in this study is consistent with earlier reports. Räsänen et al. demonstrated that maternal serum glycosylated fibronectin measured in early pregnancy was significantly elevated in women who later developed preeclampsia and showed strong diagnostic accuracy [13]. Similarly, Agarwal et al. reported elevated fibronectin levels in women who developed hypertensive disorders of pregnancy, supporting its role as an early indicator of placental dysfunction [14].

The ROC analysis in the current study yielded an area under the curve of 0.912, indicating excellent discriminative ability of GlyFn in predicting preeclampsia. This level of accuracy is comparable to and in some cases exceeds, that reported for other biochemical markers such as placental growth factor and activin A [15]. The high sensitivity (83.3%) and specificity (91.3%) observed suggest that GlyFn measurement in early pregnancy could reliably identify women at both high and low risk for developing preeclampsia.

Notably, the negative predictive value of 97.9% observed in this study highlights the potential clinical utility of GlyFn as a screening tool to rule out future preeclampsia in low-risk women. This is particularly relevant in resource-limited settings, where unnecessary referrals and interventions can strain healthcare systems. DG and Iqbal also emphasized the usefulness of fibronectin as an early predictor of gestational hypertension and preeclampsia, especially in low- and middle-income countries where access to advanced screening tools is limited [16].

The strong association between elevated glycated fibronectin (GlyFn) levels and preeclampsia, reflected by a relative risk of 25.26 in the present study, highlights the substantial risk conferred by early endothelial dysfunction. Circulating fibronectin levels are increased in preeclampsia and reflect endothelial damage characteristic of the disorder, as demonstrated by research linking fibronectin glycosylation patterns with pathological vascular remodeling rather than physiological pregnancy-related adaptations. These glycosylation modifications enhance the specificity of fibronectin as a biomarker for vascular injury and endothelial dysfunction in preeclampsia, providing a mechanistic basis

that supports the present findings on GlyFn as a predictive marker of disease severity and progression [8,17].

Early identification of women at risk for preeclampsia has important clinical implications. Preventive strategies, such as the initiation of low-dose aspirin before 16 weeks of gestation, have been shown to reduce the incidence and severity of preeclampsia when targeted to high-risk populations [18]. Incorporating GlyFn measurement into early antenatal screening protocols could therefore facilitate timely intervention and improved maternal and perinatal outcomes.

Overall, the findings of this study align with existing evidence supporting fibronectin, particularly its glycosylated form, as a robust early biomarker for preeclampsia. Further large-scale, multicenter studies are warranted to validate these findings and explore the feasibility of integrating GlyFn testing into routine antenatal care, especially in low-resource settings.

CONCLUSION

This study demonstrates that elevated maternal serum glycosylated fibronectin levels at 10–15 weeks of gestation are strongly associated with the subsequent development of preeclampsia. Glycosylated fibronectin showed high sensitivity, specificity and overall diagnostic accuracy, indicating its potential utility as an early predictive biomarker. Measurement of glycosylated fibronectin is a simple and feasible approach and its incorporation into early antenatal screening may facilitate timely risk stratification and preventive interventions, particularly in resource-limited settings.

Conflicts of interest: There are no conflicts of interest.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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