International Journal of Clinical and Biomedical Research

Vol. 11, No. 3 (2026)
pISSN: 2521-0394 · eISSN: 2395-0471

ORIGINAL RESEARCH

ROLE OF PLACENTAL GROWTH FACTOR (PLGF) AND THE SFLT-1/PLGF RATIO IN THE EARLY PREDICTION OF PREECLAMPSIA: A MULTI-CENTRE STUDY

Fatima Ansari[1*], **Sunaija B**[2], **Kumari Vara Prasanna G**[3]

[1] *Assistant Professor, Department of Obstetrics and Gynaecology, Indian Institute of Medical Science and Research (IIMSR), Warudi, Jalna, Maharashtra*

[2] *Assistant Professor, Department of Obstetrics and Gynaecology, Kannur Medical College, Anjarakandy, Kannur*

[3] *Assistant Professor, Department of Obstetrics and Gynaecology, Government Medical College and General Hospital, Adoni, Kurnool District, Andhra Pradesh, India.*

*Correspondence: Fatima Ansari <drfatimaubaid@gmail.com>

ABSTRACT

Background: Preeclampsia remains a leading contributor to maternal and perinatal morbidity and mortality, with a disproportionate burden in low- and middle-income countries. Conventional antenatal surveillance identifies the disorder only once hypertension and proteinuria are established. Placental growth factor (PlGF), a pro-angiogenic mediator, and soluble fms-like tyrosine kinase-1 (sFlt-1), its anti-angiogenic antagonist, diverge several weeks before clinical presentation. This study evaluated maternal serum PlGF, sFlt-1 and the sFlt-1/PlGF ratio, measured in the Antenatal period, as predictors of subsequent preeclampsia. **Methods:** A Multicenter prospective observational study was conducted over 18 months with a common study format. In total, 135 women with singleton pregnancies were recruited consecutively, 87 at 11-13 weeks and 48 at 20-24 weeks of gestation, and followed to delivery. PlGF and sFlt-1 were measured by automated electrochemiluminescence immunoassay and the ratio derived for each participant. Clinical risk stratification was performed using maternal age, body mass index, previous history of preeclampsia, mean arterial pressure (MAP), PlGF MoM, serum sFlt-1 concentration and the sFlt-1/PlGF ratio. The primary outcome was preeclampsia diagnosed according to the American College of Obstetricians and Gynecologists (ACOG) criteria. Diagnostic indices were calculated from contingency tables with Wilson binomial confidence intervals, and the area under the receiver operating characteristic (ROC) curve (AUC) was calculated using the trapezoidal method for PlGF, sFlt-1, and the sFlt-1/PlGF ratio. **Results:** Preeclampsia developed in 18 of 135 women (13.3%); 5 (3.7%) early-onset and 13 (9.6%) late-onset. Affected women had lower mean PlGF (102.6 ± 34.5 vs 268.8 ± 62.4 pg/mL), higher sFlt-1 (3248 ± 642 vs 1462 ± 385 pg/mL) and a higher ratio (39.8 ± 11.6 vs 8.9 ± 3.5); all $p < 0.001$. At a cut-off of ≥ 38 the ratio gave a sensitivity of 94.4% (95% CI 74.2-99.0), specificity 91.5% (95% CI 85.0-95.3), positive predictive value 63.0%, negative predictive value 99.1% and accuracy 91.9%, exceeding either analyte alone (both 88.9% sensitivity). The clinical risk stratification yielded an AUC of 0.903 (95% CI 0.807-0.999); classifying only the high-risk stratum as test-positive gave a sensitivity of 77.8% and specificity of 92.3%, with preeclampsia in 14 of 23 high-risk (60.9%) and 1 of 83 low-risk women (1.2%). **Conclusion:** Maternal serum PlGF, sFlt-1, and particularly the sFlt-1/PlGF ratio were effective in identifying women at risk of developing preeclampsia during early pregnancy. The sFlt-1/PlGF ratio demonstrated the highest diagnostic performance, with a negative predictive value of 99.1%, making it especially useful for confidently identifying women who are unlikely to develop preeclampsia. This may help clinicians focus closer surveillance and preventive interventions, including aspirin prophylaxis, on women at higher risk.

Keywords: Preeclampsia; Placental growth factor; Soluble fms-like tyrosine kinase-1; sFlt-1/PlGF ratio; Angiogenic biomarkers; Antenatal screening; Risk stratification

INTRODUCTION

Preeclampsia is a pregnancy-specific multisystem disorder characterised by new-onset hypertension after 20 weeks of gestation together with proteinuria, maternal end-organ dysfunction or uteroplacental insufficiency [1]. It remains among

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

the foremost causes of maternal and perinatal death worldwide and drives a substantial share of iatrogenic preterm birth, fetal growth restriction, placental abruption and eclampsia. The burden falls unevenly: in low- and middle-income settings, where access to early screening and timely obstetric intervention is constrained, case fatality is considerably higher, and hypertensive disorders of pregnancy account for a large proportion of preventable maternal deaths in India [2].

The disorder originates in early placentation. Deficient trophoblastic invasion of the maternal spiral arteries leaves a high-resistance, low-flow uteroplacental circulation; the resulting hypoperfusion and oxidative stress provoke release of soluble mediators that injure the maternal endothelium [3]. Central to this cascade is an imbalance between pro- and anti-angiogenic signalling. PlGF, a vascular endothelial growth factor (VEGF) family member required for normal placental vasculogenesis, falls in pregnancies destined to become preeclamptic, whereas sFlt-1, a truncated VEGF receptor shed by the syncytiotrophoblast, rises and sequesters both free VEGF and PlGF. Because this divergence precedes clinical signs by several weeks, it offers a window in which risk can be quantified before hypertension or proteinuria appear [3,4].

Conventional antenatal screening rests on maternal history, serial blood pressure measurement and urinalysis. These are indispensable for diagnosis but perform poorly as predictors: many women who ultimately develop severe disease are indistinguishable at booking from those who do not. The consequence is that interventions of demonstrated benefit, most notably low-dose aspirin commenced before 16 weeks, are not reliably directed to those who would gain from them [5]. This has motivated the search for biochemical markers able to detect placental dysfunction while it remains subclinical.

PlGF and sFlt-1 are the most extensively studied of these. Each is individually informative, but because they lie at opposite poles of a single pathway their ratio amplifies the signal and has generally outperformed either analyte alone. In a Chinese cohort of 118 pregnancies with suspected or confirmed disease, Lou and colleagues found the ratio discriminated preeclampsia from gestational and chronic hypertension, reporting rule-out and rule-in thresholds of 21.5 and 97.2 respectively [6]. Nikuei et al., studying 38 preeclamptic women and 20 term controls, obtained an area under the curve of 0.90 with sensitivity 84.2% and specificity 85.0% at a cut-off of 24.96 [7].

Evidence synthesis has been more measured than individual reports. Maesa and colleagues judged the diagnostic accuracy of the ratio to be moderate and positioned it as a supporting rather than stand-alone test [8]. Lim et al., pooling 33 studies comprising 9,426 women, found PlGF and the ratio predicted adverse outcomes with promising but heterogeneous performance, cautioning that few studies were poolable [9]. Zhang et al. reported summary sensitivity 0.78 and specificity 0.89 for the ratio, again favouring it over either marker alone while noting that benefit to pregnancy outcomes has not yet been demonstrated [10].

Implementation has nonetheless advanced. PROGNOSIS established that a ratio of 38 or below carried a one-week negative predictive value of 99.3% in women with clinical suspicion [11], and the PARROT trial showed that embedding PlGF-based testing in care shortened time to diagnosis and reduced severe maternal adverse outcomes [12]. Automated electrochemiluminescence platforms have brought both analytes within routine laboratory turnaround times.

Two gaps remain pertinent to Indian practice. First, most evidence derives from European, East Asian and North American cohorts; maternal age structure, body habitus, nutritional status, parity distribution and gestational age at presentation differ appreciably in Indian antenatal populations, and gestational-age-specific reference distributions are correspondingly uncertain. Second, most published data concern women already under suspicion in the late second or third trimester, whereas interventions with the greatest potential to alter outcome must begin earlier. Prospective Antenatal data from Indian tertiary centres are sparse.

Combining biochemical with clinical and biophysical information is likely to outperform either alone. Chen et al., in a cohort of 913 women, showed that adding the ratio to maternal characteristics and routine laboratory results materially improved trimester-specific prediction relative to the ratio alone [13]; multivariable architecture of this kind underpins contemporary first-trimester screening algorithms [2].

This study evaluated maternal serum PlGF, sFlt-1, and the sFlt-1/PlGF ratio, measured during the first and second trimesters of pregnancy, as predictors of subsequent preeclampsia in women attending multiple tertiary care teaching

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

hospitals in India. It also assessed the diagnostic performance of these angiogenic biomarkers for the early identification of women at increased risk of developing preeclampsia.

MATERIALS AND METHODS

Study design and setting

This prospective observational cohort study was conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of Biochemistry at three participating centers in India, over 18 months from January 2023 to June 2024. Reporting follows the STROBE statement [14].

Participants

Women with singleton pregnancies attending the antenatal outpatient clinic were recruited consecutively and followed to delivery. Eligible women were aged 18-40 years with a viable singleton pregnancy and ultra-sonograph confirmed gestational age of either 11 to 13+6 weeks or 20-24 weeks, who consented and intended to deliver at the study institution. Exclusions were chronic hypertension diagnosed before pregnancy or before 20 weeks, chronic kidney disease, pre-gestational diabetes mellitus, autoimmune disease, multiple pregnancy, known fetal structural anomaly, active systemic infection and history of malignancy. In total 135 women were enrolled, 87 in the first-trimester and 48 in the second-trimester group.

Sample size

The sample size was calculated for this diagnostic accuracy study using the formula: $n = Z^2 \times Sn\ (1 - Sn) / (d^2 \times \text{prevalence})$, where *Sn* represents the anticipated sensitivity of the diagnostic test. Based on an expected sensitivity of 90%, an estimated preeclampsia prevalence of 13% in the study population, a 95% confidence level ($Z = 1.96$), and an absolute precision of ±14%, the minimum required sample size was calculated to be 135 participants. To ensure adequate statistical power and account for potential incomplete data, a total of 135 eligible women were enrolled. Sample size estimation was performed using OpenEpi software (Version 3.01).

Clinical assessment

A structured case record form captured maternal age, residence, education, occupation, socioeconomic status, gravidity, parity, previous preeclampsia, previous adverse obstetric outcomes, family history of hypertension and mode of conception. Height, weight, body mass index and pulse rate were recorded. Blood pressure was measured with a validated automated sphygmomanometer after at least five minutes of seated rest; two readings five minutes apart were averaged. Mean arterial pressure (MAP) was calculated as (systolic + 2 × diastolic) / 3. Routine investigations comprised complete blood count, blood group and Rh typing, blood glucose, urinalysis, renal and liver function tests, viral screening and obstetric ultrasonography.

Biomarker measurement

Approximately 5 mL of venous blood was drawn under aseptic precautions, allowed to clot at room temperature and centrifuged at 3000 rpm for 10 minutes. Serum was analysed immediately or stored at −80 °C. PlGF and sFlt-1 were measured on an automated electrochemiluminescence immunoassay platform per the manufacturer's instructions, with internal and external quality control throughout. The sFlt-1/PlGF ratio was computed individually for each participant as serum sFlt-1 (pg/mL) divided by serum PlGF (pg/mL), and group values were obtained by averaging these participant-level ratios; PlGF was additionally expressed as multiples of the gestational-age-specific median (MoM).

Clinical risk Stratification score

Maternal age, body mass index, previous history of preeclampsia, mean arterial pressure (MAP), PlGF multiple of the median (MoM), serum sFlt-1 concentration, and the sFlt-1/PlGF ratio were recorded and analyzed as independent clinical

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

and biochemical variables. Their associations with the subsequent development of preeclampsia were evaluated individually to determine their diagnostic performance.

Follow-up and outcomes

Participants were reviewed at each scheduled visit with assessment of blood pressure, urinary protein, symptoms, fetal growth and obstetric complications; women developing hypertension underwent further evaluation per institutional protocol. The primary outcome was preeclampsia, defined per ACOG criteria as blood pressure ≥ 140/90 mmHg on two occasions at least four hours apart after 20 weeks in a previously normotensive woman, with proteinuria (≥ 300 mg/24 h or protein/creatinine ratio ≥ 0.3) or, in its absence, thrombocytopenia, elevated transaminases, renal insufficiency, pulmonary oedema, new cerebral or visual symptoms, or uteroplacental dysfunction [1]. Early-onset disease required delivery before 34 weeks, late-onset at or after 34 weeks. Secondary outcomes were preterm delivery, fetal growth restriction, low birth weight, neonatal intensive care admission and maternal complications.

Ethical considerations

The protocol was approved by the Institutional Ethics Committee before commencement. The study was conducted in accordance with the Declaration of Helsinki [15]. Written informed consent was obtained from every participant and confidentiality maintained throughout.

Statistical analysis

Data were compiled in Microsoft Excel and analysed in IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Normality was assessed with the Shapiro-Wilk test. Normally distributed continuous variables are presented as mean ± standard deviation and non-normally distributed variables as median with interquartile range; categorical variables as frequencies and percentages. Groups were compared with the independent-samples t-test or Mann-Whitney U test, and the chi-square or Fisher's exact test for categorical variables. Diagnostic indices were derived from 2 × 2 contingency tables, with 95% binomial confidence intervals by the Wilson score method [17]. Optimal thresholds for continuous markers were identified by the Youden index. For the risk stratification score the ROC analysis was performed using the available ordinal risk categories from its two non-trivial operating points and the area under the curve obtained by trapezoidal integration, with its standard error by the method of Hanley and McNeil [16]. A two-sided p value below 0.05 was considered statistically significant.

RESULTS

Of the 135 women enrolled, 87 (64.4%) were recruited in the first trimester and 48 (35.6%) in the second; all completed follow-up to delivery. Preeclampsia developed in 18 women (13.3%), comprising 5 (3.7%) with early-onset and 13 (9.6%) with late-onset disease, while 117 (86.7%) remained normotensive.

Baseline characteristics appear in Table 1. Women who subsequently developed preeclampsia were on average three years older, had a body mass index nearly four units higher and a mean arterial pressure some nine mmHg higher. Primigravidity and previous preeclampsia were both more frequent in the affected group; since previous preeclampsia presupposes a prior pregnancy, which is consistent with the parity distribution shown.

Table 1. Baseline maternal characteristics by outcome

Variable	Normotensive (n = 117)	Preeclampsia (n = 18)	p value
Maternal age (years)	26.8 ± 4.2	29.9 ± 4.8	0.012
Body mass index (kg/m²)	23.6 ± 2.9	27.4 ± 3.3	< 0.001
Primigravida, n (%)	54 (46.2)	13 (72.2)	0.041
Previous preeclampsia, n (%)	8 (6.8)	5 (27.8)	0.004
Mean arterial pressure (mmHg)	84.5 ± 6.1	93.8 ± 7.3	< 0.001

Values are mean ± standard deviation

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

Angiogenic marker concentrations differed markedly between groups (Table 2, Figure 1). Mean PlGF was approximately 62% lower and mean sFlt-1 approximately 122% higher in women who developed preeclampsia, with a correspondingly wide separation in the ratio.

Diagnostic performance at the thresholds identified by the Youden index is presented in Table 3, with the corresponding operating points displayed in ROC space in Figure 2. The sFlt-1/PlGF ratio at a cut-off of ≥ 38 performed best on every index, correctly classifying 124 of 135 women. Its negative predictive value of 99.1% reflects a single false-negative result among 108 women testing below the threshold, whereas its positive predictive value of 63.0% reflects the low pre-test probability of disease: 10 of the 27 women exceeding the threshold did not develop preeclampsia. PlGF and sFlt-1 used singly achieved identical sensitivity (88.9%, corresponding to 16 of 18 cases detected) and differed only marginally in specificity.

TP, true positive; FP, false positive; TN, true negative; FN, false negative; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; Acc, accuracy. Confidence intervals by the Wilson score method.

Maternal and neonatal outcomes are shown in Table 4 and Figure 3. Women with preeclampsia delivered on average 2.6 weeks earlier and experienced substantially higher rates of preterm birth, low birth weight, neonatal intensive care admission and caesarean delivery.

The clinical risk stratification was assigned 83 women to the low-risk, 29 to the intermediate-risk and 23 to the high-risk stratum (Table 5). The gradient across strata was steep, with observed incidence of 1.2%, 10.3% and 60.9% respectively — a more than fiftyfold difference between the extreme categories.

The diagnostic performance of the evaluated biomarkers was assessed using receiver operating characteristic (ROC) curve analysis. Sensitivity, specificity, and the area under the ROC curve (AUC) were calculated to determine their ability to discriminate between women who subsequently developed preeclampsia and those who remained normotensive. The AUC was estimated by the trapezoidal method and is presented in Table 6 and Figure 4.

Area under the ROC curve 0.903 (95% CI 0.807-0.999), computed by trapezoidal integration over the two operating points above, with standard error by the method of Hanley and McNeil [16].

Table 2. Maternal serum angiogenic biomarkers by outcome

Biomarker	Normotensive (n = 117)	Preeclampsia (n = 18)	p value
PlGF (pg/mL)	268.8 ± 62.4	102.6 ± 34.5	< 0.001
sFlt-1 (pg/mL)	1462 ± 385	3248 ± 642	< 0.001
sFlt-1/PlGF ratio	8.9 ± 3.5	39.8 ± 11.6	< 0.001

Values are mean ± standard deviation. Ratios were computed per participant and then averaged; the group mean ratio therefore exceeds the quotient of the group mean concentrations (5.4 and 31.7 respectively), as expected when the two analytes are inversely correlated.

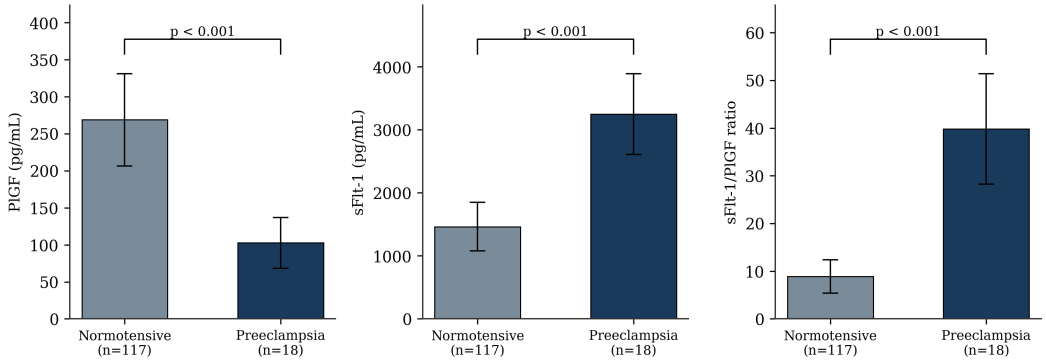

Figure 1. *Maternal serum PlGF, sFlt-1 and the sFlt-1/PlGF ratio in women who did and did not develop preeclampsia. Bars show group means; error bars indicate one standard deviation.*

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

Table 3. Diagnostic performance of individual biomarkers and the ratio

Parameter	Cut-off	TP / FP / TN / FN	Sn % (95% CI)	Sp % (95% CI)	PPV %	NPV %	Acc %
PlGF	≤ 120 pg/mL	16 / 16 / 101 / 2	88.9 (67.2-96.9)	86.3 (78.9-91.4)	50.0	98.1	86.7
sFlt-1	≥ 2500 pg/mL	16 / 15 / 102 / 2	88.9 (67.2-96.9)	87.2 (79.9-92.1)	51.6	98.1	87.4
sFlt-1/PlGF ratio	≥ 38	17 / 10 / 107 / 1	94.4 (74.2-99.0)	91.5 (85.0-95.3)	63.0	99.1	91.9

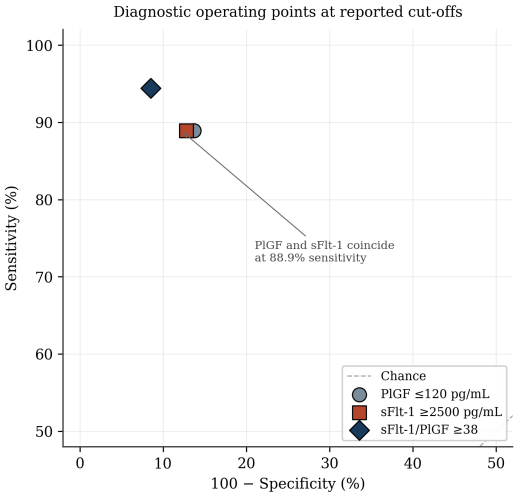

Figure 2. *Sensitivity plotted against 100 specificity for each biomarker at its cut-off.*

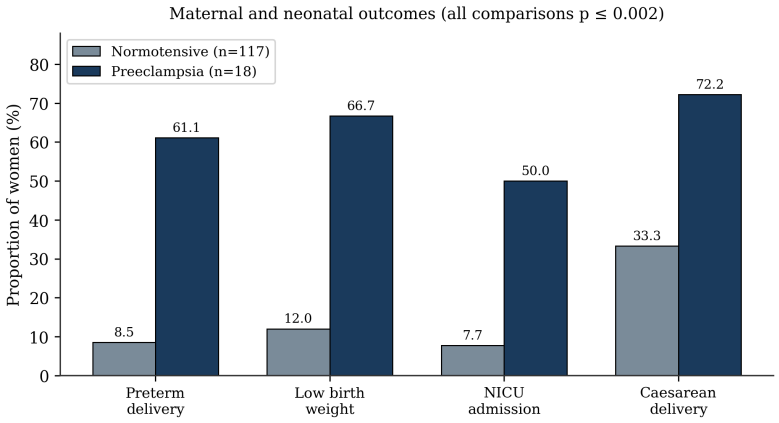

Figure 3. *Adverse maternal and neonatal outcomes by group, expressed as the percentage of women in each group.*

Table 4. Maternal and neonatal outcomes by group

Outcome	Normotensive (n = 117)	Preeclampsia (n = 18)	p value
Gestational age at delivery (weeks)	38.4 ± 1.2	35.8 ± 2.8	< 0.001
Preterm delivery, n (%)	10 (8.5)	11 (61.1)	< 0.001
Low birth weight (< 2500 g), n (%)	14 (12.0)	12 (66.7)	< 0.001
NICU admission, n (%)	9 (7.7)	9 (50.0)	< 0.001
Caesarean delivery, n (%)	39 (33.3)	13 (72.2)	0.002

Table 5. Distribution of outcomes across clinical risk stratification

Risk category	Women (n)	Developed preeclampsia, n (%)	Remained normotensive, n (%)
Low risk	83	1 (1.2)	82 (98.8)
Intermediate risk	29	3 (10.3)	26 (89.7)
High risk	23	14 (60.9)	9 (39.1)

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

Risk category	Women (n)	Developed preeclampsia, n (%)	Remained normotensive, n (%)
Total	135	18 (13.3)	117 (86.7)

Table 6. Operating characteristics of the Risk stratification scores at both available thresholds

Threshold	TP / FP / TN / FN	Sn % (95% CI)	Sp % (95% CI)	PPV %	NPV %	Acc %
High risk only	14 / 9 / 108 / 4	77.8 (54.8-91.0)	92.3 (86.0-95.9)	60.9	96.4	90.4
Intermediate + high risk	17 / 35 / 82 / 1	94.4 (74.2-99.0)	70.1 (61.3-77.6)	32.7	98.8	73.3

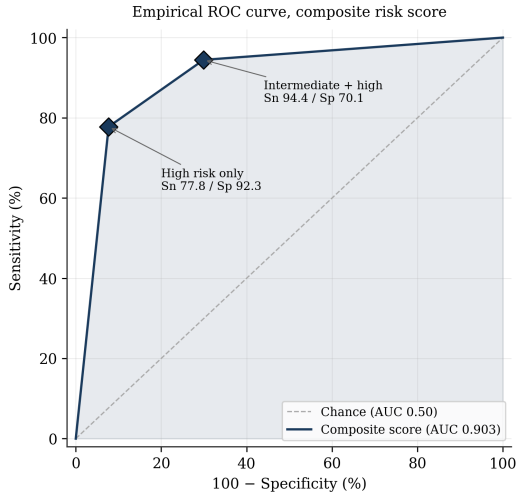

Figure 4. *Empirical ROC curve for the three-level clinical risk stratification score, constructed from the stratum counts*

DISCUSSION

In this prospective cohort of 135 Indian women screened in the first or second trimester, maternal serum angiogenic markers separated pregnancies that progressed to preeclampsia from those that did not, and the sFlt-1/PlGF ratio outperformed either analyte alone. At a threshold of 38 the ratio classified the cohort with 91.9% accuracy, detecting 17 of 18 cases.

The observed incidence of 13.3% is high relative to unselected antenatal populations, in which preeclampsia affects roughly 2-8% of pregnancies, but is consistent with the case mix of a tertiary referral centre. This bears directly on interpretation. Predictive values are functions of prevalence, and the positive predictive value of 63.0% reported here would fall considerably were the same test applied in a community antenatal clinic where disease is less common; the negative predictive value, already 99.1%, would rise further. The clinical proposition supported by these data is therefore one of exclusion rather than confirmation, which is the role the ratio has assumed internationally following prognosis [11].

The reduction in PlGF among affected women accords with its biological role. PlGF drives placental vasculogenesis, and low circulating concentrations index the defective trophoblastic invasion and consequent hypoperfusion underlying the disorder [3]. The reciprocal elevation in sFlt-1 reflects increased syncytiotrophoblast shedding of the soluble receptor, which sequesters free VEGF and PlGF and produces the generalised endothelial dysfunction manifesting as hypertension, proteinuria and multiorgan involvement. Tanner et al. have shown this relationship is modified by maternal comorbidity, so ratios require interpretation in clinical context rather than as a context-free number [18].

Performance recorded here sits at the favourable end of the published range. Nikuei et al. obtained sensitivity 84.2% and specificity 85.0% in a case-control design [7], and the pooled estimates of Zhang et al. across many cohorts were 0.78 and 0.89 respectively [10]; Maesa and colleagues characterised the accuracy of the ratio as moderate [8]. Two features of the present study probably contribute. The first is spectrum: recruitment at a tertiary centre enriches the cohort for both severe disease and clear-cut controls, widening the separation between groups. The second is that the cut-off of 38 was selected by the Youden index within this same dataset rather than applied prospectively from an external source, so the reported

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

indices are optimistic and would be expected to regress on independent validation. The 95% confidence interval around a sensitivity of 94.4% based on 18 events extends from 74.2% to 99.0%, and this imprecision should temper any claim of superiority over previously published estimates.

The clinical risk stratification, stratified risk steeply, with observed incidence rising from 1.2% in the low-risk stratum to 60.9% in the high-risk stratum. Its area under the curve of 0.903 is comparable to that reported for the ratio alone by Nikuei et al. [7] and consistent with the improvement Chen et al. obtained by adding the ratio to maternal and laboratory variables [13]. Three caveats apply. The clinical risk stratification approach was developed and evaluated in the same 135 participants, so the AUC is an in-sample estimate that will overstate performance in new data; its confidence interval, spanning 0.807 to 0.999, is wide because only 18 events inform it; and with three ordinal categories the curve rests on two operating points, so the trapezoidal area is a coarse approximation that would change were the underlying continuous score used directly. Crucially, the choice between the two available thresholds is a clinical rather than statistical decision: the high-risk-only threshold offers 92.3% specificity but misses four of eighteen cases, whereas including the intermediate stratum detects seventeen of eighteen but classifies 35 normotensive women as at risk. For a screening application intended to direct aspirin prophylaxis an intervention of low cost and low harm the more sensitive threshold is arguably preferable despite its poorer specificity.

Adverse outcomes clustered in the preeclampsia group as expected, with earlier delivery and higher rates of preterm birth, low birth weight, neonatal intensive care admission and caesarean section. Because most preterm births in this setting are iatrogenic, these figures partly reflect clinical decisions to deliver rather than the natural history of untreated disease; this is intrinsic to any observational study of a condition for which delivery is the definitive treatment. Similar associations between angiogenic imbalance and adverse outcome have been described across diverse settings, including pregnancies complicated by intercurrent illness [20].

The practical question is whether earlier identification changes outcome. Evidence that it can is strongest for two interventions: low-dose aspirin begun before 16 weeks in screen-positive women, which reduced preterm preeclampsia by 62% in the ASPRE trial [5], and PlGF-based testing embedded in clinical pathways, which shortened time to diagnosis and reduced severe maternal adverse outcomes in PARROT [12]. The Antenatal timing used here is compatible with the aspirin window, which is the principal argument for screening this early rather than awaiting clinical suspicion in the third trimester. It should be stated plainly, however, that this study measured prediction, not benefit; no outcome improvement attributable to biomarker testing can be inferred from these data.

Within these constraints, the data support the view that Antenatal angiogenic profiling identifies a subgroup of Indian women at substantially elevated risk of preeclampsia, and that a very low ratio provides strong reassurance. Confirmation in a larger multicentre cohort with gestational-age-specific reference ranges, prospective application of a pre-specified threshold, and outcome rather than prediction endpoints would be the logical next step.

CONCLUSION

Among 135 women screened during the first or second trimester across participating tertiary care hospitals, 18 (13.3%) developed preeclampsia. Women who developed preeclampsia had lower PlGF levels, higher sFlt-1 concentrations, and a significantly higher sFlt-1/PlGF ratio than those with normotensive pregnancies. At a threshold of ≥38, the sFlt-1/PlGF ratio demonstrated a sensitivity of 94.4%, specificity of 91.5%, and diagnostic accuracy of 91.9%, outperforming either biomarker alone. Receiver operating characteristic (ROC) analysis showed excellent discriminative performance with a high area under the curve (AUC). The high negative predictive value of 99.1% suggests that the sFlt-1/PlGF ratio is particularly useful for confidently identifying women at low risk of developing preeclampsia, thereby facilitating appropriate surveillance and targeted preventive interventions. Although these findings are encouraging, further large multicentre studies are warranted to validate their routine clinical application.

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

Limitations

The present study has certain limitations, including a relatively modest sample size, single-time biomarker assessment, and the absence of external validation. Therefore, larger Multicenter studies are warranted to confirm the present findings and establish their broader clinical applicability.

Declarations

Ethics approval and consent to participate: Approved by the Institutional Ethics Committee; written informed consent obtained from all participants.

Data availability: The corresponding author will provide the data upon reasonable request, subject to institutional approval.

Conflicts of interest: Nil

Funding: Nil

References

1. Gestational hypertension and preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol. 2020;135(6):e237-e260. https://doi.org/10.1097/AOG.0000000000003891
2. Poon LC, Shennan A, Hyett JA, Kapur A, Hadar E, Divakar H, et al. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: a pragmatic guide for first-trimester screening and prevention. Int J Gynaecol Obstet. 2019;145(Suppl 1):1-33. https://doi.org/10.1002/ijgo.12802
3. Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: pathophysiology, challenges, and perspectives. Circ Res. 2019;124(7):1094-1112. https://doi.org/10.1161/CIRCRESAHA.118.313276
4. Stepan H, Galindo A, Hund M, Schlembach D, Sillman J, Surbek D, et al. Clinical utility of sFlt-1 and PlGF in screening, prediction, diagnosis and monitoring of pre-eclampsia and fetal growth restriction. Ultrasound Obstet Gynecol. 2023;61(2):168-180. https://doi.org/10.1002/uog.26032
5. Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, de Paco Matallana C, et al. Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. N Engl J Med. 2017;377(7):613-622. https://doi.org/10.1056/NEJMoa1704559
6. Lou WZ, Jiang F, Hu J, Chen XX, Song YN, Zhou XY, et al. Maternal serum angiogenic factor sFlt-1 to PlGF ratio in preeclampsia: a useful marker for differential diagnosis and prognosis evaluation in Chinese women. Dis Markers. 2019;2019:6270187. https://doi.org/10.1155/2019/6270187
7. Nikuei P, Rajaei M, Roozbeh N, Mohseni F, Poordarvishi F, Azad M, et al. Diagnostic accuracy of sFlt1/PlGF ratio as a marker for preeclampsia. BMC Pregnancy Childbirth. 2020;20(1):80. https://doi.org/10.1186/s12884-020-2744-2
8. Maesa JM, Romero-Tabares A, Benot-Lopez S. Validez diagnostica del ratio sFlt-1/PlGF en la identificacion de la preeclampsia: una revision sistematica. Clin Investig Ginecol Obstet. 2020;47(1):30-37. https://doi.org/10.1016/j.gine.2019.05.004
9. Lim S, Li W, Kemper J, Nguyen A, Mol BW, Reddy M. Biomarkers and the prediction of adverse outcomes in preeclampsia: a systematic review and meta-analysis. Obstet Gynecol. 2021;137(1):72-81. https://doi.org/10.1097/AOG.0000000000004149
10. Zhang L, Li W, Chi X, Sun Q, Li Y, Xing W, et al. Predictive performance of sFlt-1, PlGF and the sFlt-1/PlGF ratio for preeclampsia: a systematic review and meta-analysis. Arch Clin Obstet Gynecol Res. 2024;4(1):1-6.
11. Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennstrom M, et al. Predictive value of the sFlt-1:PlGF ratio in women with suspected preeclampsia. N Engl J Med. 2016;374(1):13-22. https://doi.org/10.1056/NEJMoa1414838
12. Duhig KE, Myers J, Seed PT, Sparkes J, Lowe J, Hunter RM, et al. Placental growth factor testing to assess women with suspected preeclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial. Lancet. 2019;393(10183):1807-1818. https://doi.org/10.1016/S0140-6736(18)33212-4
13. Chen G, Chen Y, Shi Y, Mao Z, Lou J, Ma J. A dynamic prediction model for preeclampsia using the sFlt-1/PLGF ratio combined with multiple factors. BMC Pregnancy Childbirth. 2024;24(1):443. https://doi.org/10.1186/s12884-024-06627-4
14. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453-1457. https://doi.org/10.1016/S0140-6736(07)61602-X

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0

15. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-2194. https://doi.org/10.1001/jama.2013.281053

16. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology. 1982;143(1):29-36. https://doi.org/10.1148/radiology.143.1.7063747

17. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. Stat Med. 1998;17(8):857-872.

18. Tanner MS, de Guingand D, Reddy M, Rowson S, Rolnik DL, Davey MA, et al. The effect of comorbidities on the sFLT-1:PlGF ratio in preeclampsia. Pregnancy Hypertens. 2022;29:98-100. https://doi.org/10.1016/j.preghy.2022.06.008

19. Espinoza J, Lee W, Martin SR, Belfort MA, Nassef S, Sibai B, et al. Plasma soluble fms-like tyrosine kinase 1 to placental growth factor ratio of 11.5 multiples of median predicts preeclampsia with severe features within 2 weeks of testing. Am J Obstet Gynecol. 2024;231(3):363.e1-363.e11. https://doi.org/10.1016/j.ajog.2024.05.050

20. Pluta K, Januszewski M, Ziuzia-Januszewska L, Kudan M, Suchocka M, Kusmierczuk K, et al. sFlt-1/PlGF ratio as a predictor of preeclampsia in COVID-19 pregnant patients. BMC Pregnancy Childbirth. 2024;24(1):76. https://doi.org/10.1186/s12884-024-06263-y

© Authors 2026. IJCBR | This is an Open Access article CC-BY-NC-SA 4.0