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Predictive performance of the sFlt-1/PlGF ratio for subsequent preeclampsia in a prospective Algerian high-risk cohort

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Abstract

Preeclampsia is characterised by an imbalance between anti-angiogenic and pro-angiogenic pathways. We evaluated the predictive performance of soluble fms-like tyrosine kinase-1 (sFlt-1), placental growth factor (PlGF), and their ratio in a prospective two-centre Algerian high-risk cohort of 405 singleton pregnancies, including 75 women who subsequently developed preeclampsia. The median sFlt-1/PlGF ratio was higher in women who developed preeclampsia than in those who did not (111.59 [42.57-357.63] vs 20.53 [6.07–38.18]; P < 0.001). The ratio showed the highest discrimination (AUC 0.841, 95% CI 0.774–0.901). In the expanded multivariable model, each doubling of the ratio remained independently associated with preeclampsia (adjusted OR 2.08, 95% CI 1.57–2.74), and its addition to prespecified clinical predictors increased the AUC from 0.897 to 0.943. These findings suggest that the sFlt-1/PlGF ratio may improve risk stratification in high-risk pregnancies, although external validation is required before adoption of a population-specific threshold.

Introduction

Preeclampsia is a pregnancy-specific multisystem disorder that remains an important cause of maternal and perinatal morbidity worldwide [1–3]. Although the diagnosis is clinically established after the onset of hypertension with proteinuria and/or maternal or uteroplacental dysfunction, the pathological process begins earlier than the clinical diagnosis. Identifying women who are likely to develop preeclampsia before the full clinical syndrome becomes apparent therefore remains a major objective of antenatal care.

Placental dysfunction is accompanied by a shift towards an anti-angiogenic maternal environment. Increased release of soluble fms-like tyrosine kinase-1 (sFlt-1) reduces the bioavailability of vascular endothelial growth factor and placental growth factor (PlGF), contributing to endothelial dysfunction and maternal manifestations of preeclampsia [4, 5]. Because circulating sFlt-1 increases whereas PlGF decreases with placental dysfunction, their ratio integrates these reciprocal angiogenic changes into a single biomarker.

The sFlt-1/PlGF ratio is one of the most extensively evaluated angiogenic markers of preeclampsia. A ratio of 38 has been validated mainly for short-term rule-out in women with suspected disease, whereas higher gestational age-specific values have been proposed for rule-in assessment [6–8]. However, predictive performance varies according to gestational age, baseline risk, clinical setting, ethnicity, disease prevalence, and the interval between biomarker measurement and diagnosis [8–10]. Recent studies have therefore moved from a single universal threshold towards context-specific validation and integration of angiogenic biomarkers with maternal and clinical characteristics [10–13].

Prospective validation data from North African populations remain scarce. We therefore evaluated the predictive performance of sFlt-1, PlGF, and the sFlt-1/PlGF ratio for subsequent preeclampsia in a prospective Algerian high-risk cohort. We also examined whether the ratio added discriminatory information beyond readily available clinical characteristics.

Results

Study population and baseline characteristics

Among 755 women screened, 421 were enrolled and prospectively followed. Following 3 spontaneous miscarriages and 13 losses to follow-up, 405 women were included in the final analysis (Fig. 1). Seventy-five women developed preeclampsia during follow-up, whereas 330 did not. Women who developed preeclampsia were older and had a higher prepregnancy BMI. A history of preeclampsia, gestational hypertension or gestational diabetes, as well as chronic hypertension, pregestational diabetes and isolated proteinuria at enrolment, was also more frequent among women who subsequently developed preeclampsia (Table 1).

Table 1
Baseline characteristics according to subsequent preeclampsia status

Characteristic	No preeclampsia (n = 330)	Preeclampsia (n = 75)	P value
Maternal age, years	31.0 [27.0–35.0]	34.0 [30.0–37.0]	P < 0.001
Prepregnancy BMI, kg/m²	29.4 [26.6–33.0]	32.9 [27.6–36.3]	P < 0.001
Age > 35 years	78/330 (23.6%)	29/75 (38.7%)	P = 0.013
BMI ≥ 30 kg/m²	127/330 (38.5%)	49/75 (65.3%)	P < 0.001
Nulliparity	77/330 (23.3%)	25/75 (33.3%)	P = 0.078
History of preeclampsia	12/330 (3.6%)	12/75 (16.0%)	P < 0.001
History of gestational hypertension	31/330 (9.4%)	33/75 (44.0%)	P < 0.001
History of gestational diabetes	9/330 (2.7%)	11/75 (14.7%)	P < 0.001
Chronic hypertension	16/330 (4.8%)	9/75 (12.0%)	P = 0.031
Pregestational diabetes	21/330 (6.4%)	15/75 (20.0%)	P = 0.001
Nephropathy	4/330 (1.2%)	2/75 (2.7%)	P = 0.308
Isolated proteinuria at enrolment	113/330 (34.2%)	65/75 (86.7%)	P < 0.001

Continuous variables are median [IQR] and were compared using two-sided Mann-Whitney U tests; categorical variables are n/N (%) and were compared using two-sided Fisher exact tests.

Angiogenic biomarker concentrations

All three angiogenic measures differed between outcome groups. PlGF concentrations were lower, whereas sFlt-1 concentrations and the sFlt-1/PlGF ratio were higher in women who developed

preeclampsia. The sFlt-1/PlGF ratio showed the numerically highest AUC (Table 2).

Table 2
Angiogenic biomarkers and ROC performance for subsequent preeclampsia

Biomarker	No PE, median [IQR]	PE, median [IQR]	n	AUC (95% CI)	P value
PlGF, pg/mL	107.80 [30.51–331.00]	37.79 [17.41–80.60]	405	0.693 (0.625–0.757)	P < 0.001
sFlt-1, pg/mL	1491.00 [928.50–2347.00]	7721.60 [2628.75-10119.50]	405	0.782 (0.690–0.867)	P < 0.001
sFlt-1/PlGF ratio	20.53 [6.07–38.18]	111.59 [42.57-357.63]	405	0.841 (0.774–0.901)	P < 0.001

P values refer to two-sided Mann-Whitney U tests comparing biomarker distributions between outcome groups. AUCs were calculated in the full analytical cohort (n = 405).

Predictive performance

In the full analytical cohort (n = 405; 75 preeclampsia events), the sFlt-1/PlGF ratio showed an AUC of 0.841 (95% CI 0.774–0.901), compared with 0.693 for PlGF and 0.782 for sFlt-1 (Fig. 2). At the widely used threshold of 38, sensitivity was 75.9% (95% CI 62.4–86.5) and specificity was 75.0% (95% CI 69.0-80.3), with a positive predictive value of 40.6% and a negative predictive value of 93.3%. ROC analysis identified an exploratory, data-derived Youden cut-off of 73.12, with sensitivity 63.0% (95% CI 48.7–75.7) and specificity 93.3% (95% CI 89.4–96.1); the corresponding positive and negative predictive values were 68.0% and 91.8%, respectively.

Incremental predictive value of the sFlt-1/PlGF ratio

The expanded multivariable analysis included 405 women, including 75 preeclampsia events. Clinical predictors were selected a priori on clinical grounds and comprised maternal age, prepregnancy BMI, nulliparity, chronic hypertension, pregestational diabetes, isolated proteinuria at enrolment, a history of preeclampsia, a history of gestational hypertension, and gestational age at biomarker sampling (< 34 vs ≥ 34 weeks). Each doubling of the sFlt-1/PlGF ratio remained independently associated with subsequent preeclampsia (adjusted OR 2.08, 95% CI 1.57–2.74; P < 0.001) (Table 3). The clinical model had an apparent AUC of 0.897 (95% CI 0.857–0.933), which increased to 0.943 (95% CI 0.910–0.970) after the addition of the ratio, an absolute increase of 0.046 (95% bootstrap CI 0.013–0.078) (Fig. 3).

Table 3
Expanded multivariable model for subsequent preeclampsia

Variable	Adjusted OR	95% CI	P value
sFlt-1/PlGF ratio, per doubling	2.08	1.57–2.74	P < 0.001
Maternal age, per year	1.04	0.95–1.15	P = 0.354
Prepregnancy BMI, per kg/m²	1.07	0.99–1.17	P = 0.104
Nulliparity	1.52	0.48–4.78	P = 0.478
Chronic hypertension	4.07	0.90-18.38	P = 0.068
Pregestational diabetes	2.34	0.59–9.30	P = 0.228
Isolated proteinuria at enrolment	10.14	3.09–33.27	P < 0.001
History of preeclampsia	25.55	3.84-169.81	P < 0.001
History of gestational hypertension	3.58	1.22–10.51	P = 0.021
Gestational age at sampling < 34 weeks	0.85	0.19–3.77	P = 0.825

Model n = 405, including 75 preeclampsia events. The sFlt-1/PlGF ratio was log2-transformed; its odds ratio represents the change in odds associated with a doubling of the ratio. Gestational age was modelled as < 34 vs ≥ 34 weeks.

Internal validation using 1,000 successful bootstrap resamples yielded optimism-corrected AUCs of 0.873 for the clinical model and 0.924 for the model including the ratio. The corresponding optimism-corrected Brier scores were 0.119 and 0.087, and the calibration slopes were 0.816 and 0.809, respectively. No relevant multicollinearity was detected (maximum variance inflation factor 1.26).

Discussion

In this prospective Algerian high-risk cohort, the sFlt-1/PlGF ratio was the angiogenic measure most strongly associated with preeclampsia. Women who developed the disease had a markedly higher median ratio than those who remained free of preeclampsia, and the ratio showed good discrimination. After expansion of the clinical model to include established maternal and obstetric risk factors, each doubling of the ratio remained associated with approximately a twofold increase in the odds of preeclampsia. The increase in apparent AUC from 0.897 to 0.943, together with the corresponding optimism-corrected AUCs of 0.873 and 0.924, indicates that angiogenic information provided additional discrimination beyond the prespecified clinical predictors, although the magnitude of improvement was more modest than in the initial parsimonious model.

These findings are consistent with the central role of angiogenic imbalance in preeclampsia pathophysiology. Excess placental sFlt-1 binds circulating VEGF and PlGF, thereby reducing pro-angiogenic signalling and contributing to endothelial dysfunction [4, 5]. The ratio integrates both sides of

this biological imbalance and may therefore be more informative than either marker alone. A similar pattern was reported in a prospective Vietnamese high-risk cohort, in which PlGF was lower, the ratio was higher, and the ratio achieved an AUC of approximately 0.80 while sFlt-1 alone was less discriminative [9]. A 2025 systematic review and meta-analysis similarly reported pooled AUCs of 0.92 for the ratio, 0.89 for sFlt-1, and 0.87 for PlGF, although substantial heterogeneity was attributed to study design, disease subtype, sample size, and cut-off selection [10]. Our results therefore fall within the range of contemporary evidence while emphasising the importance of population- and setting-specific validation.

The predictive performance of the ratio in this high-risk cohort deserves particular attention. The exploratory cut-off identified in our cohort was 73.12. This value is numerically close to the cut-off of 74 recently derived and externally validated by Pan et al. for prediction of early-onset preeclampsia within one week among Chinese women with high blood pressure [12]. In that study, the validated threshold of 74 achieved a sensitivity of 87.7% and a specificity of 97.0% before 34 weeks. The numerical agreement is noteworthy but should not be interpreted as direct validation because the populations and prediction horizons differ substantially. Our threshold was selected and assessed in the same dataset and was not evaluated against a prespecified short-term prediction horizon. It should therefore remain an exploratory, data-derived finding rather than a proposed clinical decision limit.

The widely used threshold of 38 showed a different operating profile in our cohort, with sensitivity of 75.9% and specificity of 75.0%. This is lower than the short-term rule-out performance reported in cohorts of women with suspected preeclampsia. In a 2025 multicentre Japanese study, Yamazaki et al. reported a negative predictive value of 98.4% for excluding preeclampsia within one week at a threshold of 38, whereas the positive predictive value increased when higher thresholds were used [11]. This difference is expected because predictive values depend on disease prevalence, the clinical spectrum of the population and, critically, the interval over which disease occurrence is assessed. A threshold of 38 is therefore best interpreted as a short-term triage tool in women with suspected disease rather than as a universal screening threshold for all high-risk pregnancies.

Our multivariable findings also support moving beyond interpretation of angiogenic biomarkers in isolation. Chen et al. showed that combining the sFlt-1/PlGF ratio with maternal characteristics, uterine artery Doppler indices and laboratory variables improved prediction across several gestational windows [13]. In the present study, the clinical model deliberately incorporated established risk information available at enrolment, including isolated proteinuria, previous preeclampsia, previous gestational hypertension and gestational age at sampling. Even against this stronger clinical benchmark, addition of the ratio improved discrimination by 0.046. Internal bootstrap validation attenuated the apparent performance but preserved a higher corrected AUC and a lower Brier score for the model containing the ratio, supporting incremental predictive information while also demonstrating some degree of model optimism.

However, strong discrimination does not necessarily imply improved clinical outcomes when a test is introduced into routine care. The 2025 PRECOG randomised study, conducted in women hospitalised for suspected preeclampsia before 35 weeks of gestation, found that use of the sFlt-1/PlGF ratio did not reduce hospitalisation duration or improve maternal and neonatal outcomes [14]. A biomarker may therefore refine risk classification without automatically changing management unless it is embedded in a clearly defined clinical pathway. Recent work has also shown that markedly elevated ratios, especially before 34 weeks, are associated with adverse maternal and fetal outcomes and shorter intervals to delivery [15], further supporting the ratio as a marker of placental disease burden while underscoring the need for gestational age-specific interpretation.

The present study has several strengths. It was based on prospective recruitment in two Algerian centres, focused on a clinically relevant high-risk cohort, used standardised Elecsys assays on the cobas platform, and evaluated both the standalone and incremental predictive value of the ratio. The study also adds data from a North African population that remains poorly represented in contemporary biomarker validation studies. Several limitations should nevertheless be considered. Recruitment was non-probabilistic, both centres were located in the same geographical region, biomarker measurements were obtained at a single time point, and the exploratory threshold was derived internally without external validation. Gestational age at biomarker sampling was available as prespecified categories rather than as a continuous measurement, and the interval between biomarker sampling and clinical onset was not standardised. The multivariable model was developed with a limited number of events relative to the number of predictors; bootstrap internal validation therefore remains important but cannot replace independent external validation.

In conclusion, the sFlt-1/PlGF ratio provided better discrimination for subsequent preeclampsia than PlGF or sFlt-1 alone and added predictive information to a clinically enriched model incorporating maternal, obstetric and gestational-age characteristics. The exploratory cut-off of approximately 73 should be regarded as hypothesis-generating. Prospective multicentre validation with prespecified gestational windows and clinically defined prediction horizons is required before a population-specific decision threshold can be recommended.

Methods

Study design and setting

This prospective two-centre high-risk cohort study was conducted in the obstetrics departments of EHS Mère et Enfant El Bouni, Annaba, and EPH El Okbi, Guelma, Algeria. Women were recruited between December 2017 and October 2018 and were followed throughout pregnancy. The final analytical cohort comprised 405 women at risk of preeclampsia with singleton pregnancies at ≥ 20 weeks of gestation.

Participants

Women aged ≥ 18 years with singleton pregnancies at ≥ 20 weeks of gestation were screened for eligibility. Among 755 pregnant women assessed, 421 presenting at least one predefined risk factor for preeclampsia were enrolled and prospectively followed. The predefined risk factors included maternal age > 35 years, nulliparity, a history of preeclampsia, chronic hypertension, pregestational diabetes mellitus, prepregnancy body mass index (BMI) ≥ 30 kg/m², nephropathy, isolated proteinuria ≥ 300 mg/24 h in the absence of hypertension, or autoimmune disease, including antiphospholipid syndrome. Women without any of these predefined risk factors were not eligible for inclusion. Multiple pregnancies and pregnancies complicated by major fetal, placental or chromosomal abnormalities were also not eligible. During follow-up, 3 pregnancies were excluded because of spontaneous miscarriage and 13 women were lost to follow-up because delivery outcome data were unavailable, leaving 405 women for the final analysis.

Outcome definition

The primary outcome was preeclampsia. Preeclampsia was defined according to the prespecified diagnostic criteria in use during the study period, based on the expert consensus of the French Society of Hypertension [16]. The study protocol defined preeclampsia as new-onset systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg from 20 weeks of gestation together with significant proteinuria (≥ 300 mg/24 h or urine protein/creatinine ratio > 30 mg/mmol).

Sample collection and biomarker assays

Maternal venous blood was collected at enrolment. Serum was separated by centrifugation at 2500 g for 10 min, aliquoted, and stored at -80°C until analysis. Serum PlGF and sFlt-1 concentrations were measured using automated electrochemiluminescence sandwich immunoassays (Elecsys PlGF and Elecsys sFlt-1) on a cobas e 411 analyser (Roche Diagnostics). The analytical sample volumes were 50 µL for PlGF and 20 µL for sFlt-1, with an 18-min analytical cycle. The analytical measurement ranges were 3–10,000 pg/mL for PlGF and 10–85,000 pg/mL for sFlt-1. Manufacturer-reported repeatability was ≤ 2% and reproducibility was ≤ 5% for both assays. Analytical quality control used two levels of PreciControl MultiMarker (Roche Diagnostics). The sFlt-1/PlGF ratio was calculated from paired concentrations. Angiogenic biomarker measurements were not included in the prespecified clinical definition used to adjudicate preeclampsia.

Statistical analysis

Distributional assumptions were assessed using histograms, Q-Q plots and the Shapiro-Wilk test. Non-normally distributed continuous variables are presented as median [interquartile range] and were compared using two-sided Mann-Whitney U tests. Categorical variables are presented as n/N (%) and were compared using two-sided Fisher exact tests. Baseline comparisons were exploratory; no

adjustment for multiple testing was applied, and P values should therefore be interpreted descriptively. The alpha level was 0.05 for all inferential tests.

Receiver operating characteristic (ROC) curves were used to quantify discrimination of PlGF, sFlt-1 and the sFlt-1/PlGF ratio in the full analytical cohort (n = 405). AUC confidence intervals were estimated using 3,000 stratified bootstrap resamples. Exploratory cut-offs were selected using the Youden index. Sensitivity and specificity confidence intervals were calculated using exact binomial methods.

To evaluate incremental predictive value, clinical covariates were prespecified on clinical grounds rather than selected from univariable P values. The clinical model included maternal age, prepregnancy BMI, nulliparity, chronic hypertension, pregestational diabetes, isolated proteinuria at enrolment, a history of preeclampsia, a history of gestational hypertension, and gestational age at biomarker sampling (< 34 vs ≥ 34 weeks). Maternal age and BMI were retained as continuous variables. The sFlt-1/PlGF ratio was log2-transformed, so its odds ratio represents the change in odds associated with a doubling of the ratio. The multivariable models included 405 women (75 preeclampsia events). Collinearity was assessed using variance inflation factors, with all values < 1.27. Internal validation used 1,000 successful bootstrap resamples to estimate optimism-corrected AUCs, Brier scores and calibration slopes. Statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA) with Python integration for bootstrap resampling, model validation and calibration analyses.

Declarations

Ethics approval and informed consent

The study and use of clinical and laboratory data were approved by the Ethics Committee of the Faculty of Medicine, Badji Mokhtar University of Annaba (No. 23 FACMED/CSF/2017). Written informed consent was obtained from all participants. Study data were anonymised, and all procedures were conducted in accordance with applicable institutional and national regulations and the principles of the Declaration of Helsinki.

AI-assisted manuscript preparation

OpenAI ChatGPT was used to assist English-language editing, manuscript organisation and statistical code development. All analyses, numerical results, interpretations and references were independently verified by the authors, who retain full responsibility for the data, statistical methods, interpretation and manuscript.

Code availability

The Python code used for bootstrap resampling, model validation and calibration analyses is available from the corresponding author on reasonable request.

Data availability

The de-identified data supporting the findings of this study are not publicly available because of participant privacy and institutional ethics requirements. They are available from the corresponding author (adel.gouri@univ-annaba.dz) on reasonable request, subject to approval by the relevant institutional ethics and data-protection authorities.

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Author contributions

A.G. conceived and designed the study, supervised laboratory analyses, performed and interpreted the statistical reanalysis, and drafted the manuscript. H.A. contributed to obstetric recruitment, clinical assessment and data collection. A.D. contributed to clinical assessment and data collection. S.B. supervised the study, contributed to interpretation and critically revised the manuscript. All authors reviewed and approved the final manuscript.

Additional information

Competing interests

The authors declare no competing interests.

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References

1. Dimitriadis, E. et al. Pre-eclampsia. *Nat. Rev. Dis. Primers*. **9**, 8 (2023).
2. Magee, L. A. et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. *Pregnancy Hypertens.* **27**, 148–169 (2022).

3. Chappell, L. C., Cluver, C. A., Kingdom, J. & Tong, S. Pre-eclampsia. *Lancet* **398**, 341–354 (2021).
4. Phipps, E. A., Thadhani, R., Benzing, T. & Karumanchi, S. A. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. *Nat. Rev. Nephrol.* **15**, 275–289 (2019).
5. Levine, R. J. et al. Circulating angiogenic factors and the risk of preeclampsia. *N Engl. J. Med.* **350**, 672–683 (2004).
6. Zeisler, H. et al. Predictive value of the sFlt-1:PlGF ratio in women with suspected preeclampsia. *N Engl. J. Med.* **374**, 13–22 (2016).
7. Verlohren, S. et al. Clinical interpretation and implementation of the sFlt-1/PlGF ratio in the prediction, diagnosis and management of preeclampsia. *Pregnancy Hypertens.* **27**, 42–50 (2022).
8. Stepan, H. 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.* **61**, 168–180 (2023).
9. Nguyen, T. H. et al. Predictive value of the sFlt-1 and PlGF in women at risk for preeclampsia in the south of Vietnam. *Pregnancy Hypertens.* **14**, 37–42 (2018).
10. Zhang, L. et al. Predictive performance of sFlt-1, PlGF and the sFlt-1/PlGF ratio for preeclampsia: a systematic review and meta-analysis. *J. Gynecol. Obstet. Hum. Reprod.* **54**, 102925 (2025).
11. Yamazaki, T. et al. Predictive accuracy of sFlt-1/PlGF ratio for preeclampsia and adverse outcomes: prospective, multicenter including primary, secondary, and tertiary care institutions, observational study in Japan. *Hypertens. Res.* **48**, 2548–2557 (2025).
12. Pan, X. et al. sFlt-1/PlGF ratio thresholds for diagnosing pre-eclampsia in pregnant women with high blood pressure. *Ultrasound Obstet. Gynecol.* **66**, 631–640 (2025).
13. Chen, G. et al. A dynamic prediction model for preeclampsia using the sFlt-1/PLGF ratio combined with multiple factors. *BMC Pregnancy Childbirth*. **24**, 443 (2024).
14. Sibiude, J. et al. sFlt-1/PlGF ratio use does not reduce hospitalisation duration in suspected preeclampsia: the PRECOG study, a multicentre randomised trial. *Sci. Rep.* **15**, 39299 (2025).
15. Ohkuchi, A. et al. Elevated sFlt-1/PlGF ratio in women with suspected or confirmed early-onset preeclampsia and super-imposed preeclampsia complicated by HELLP syndrome as well as abnormal umbilical artery Doppler findings and non-reassuring fetal status requiring immediate delivery: a prospective cohort study. *Hypertens. Res.* **48**, 3101–3112 (2025).
16. Mounier-Vehier, C. et al. Hypertension artérielle et grossesse. Consensus d'experts de la Société française d'hypertension artérielle, filiale de la Société française de cardiologie. *Presse Med.* **45**, 682–699 (2016).

Figures

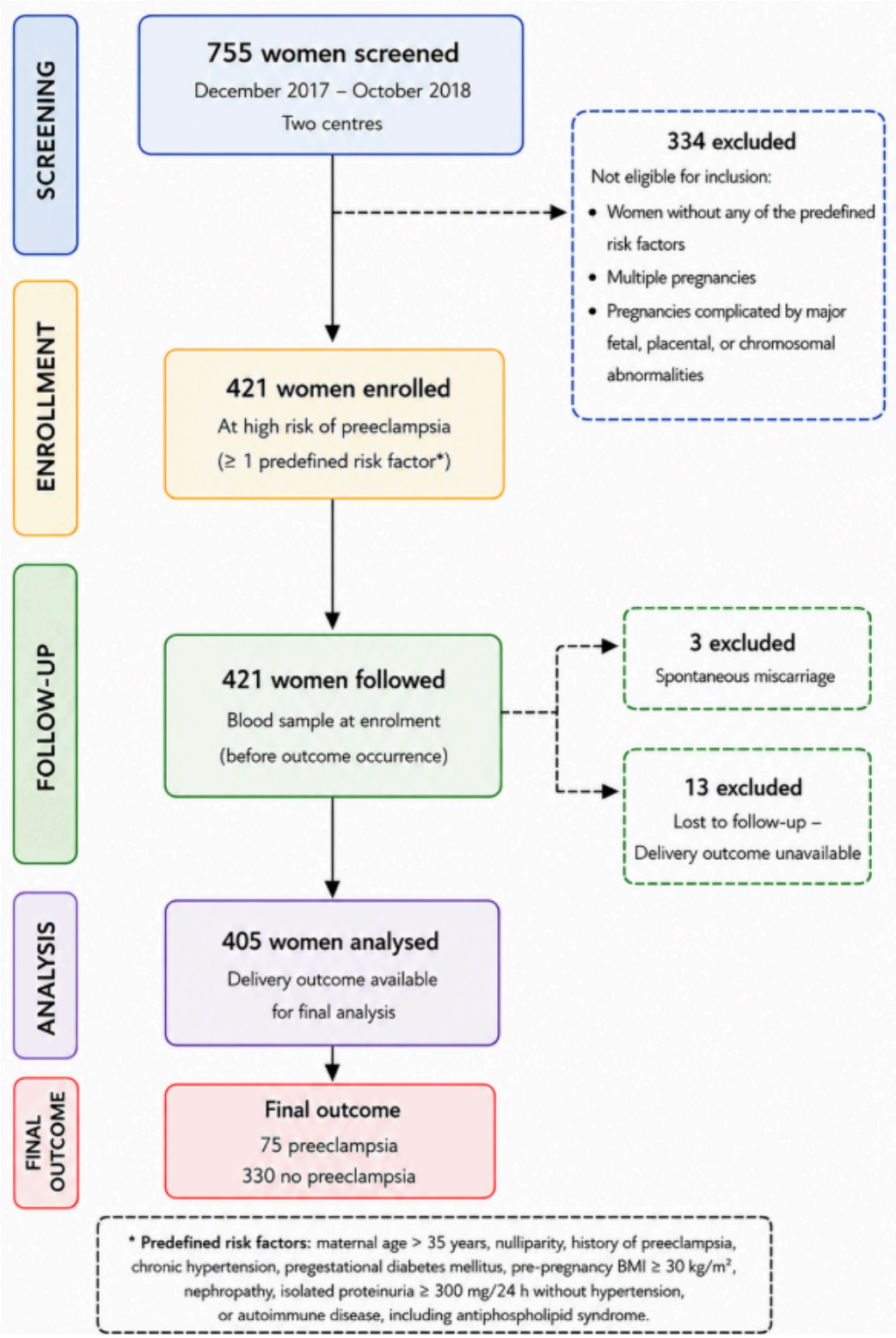


Figure 1

Participant flow from screening through enrolment and follow-up to final analysis.

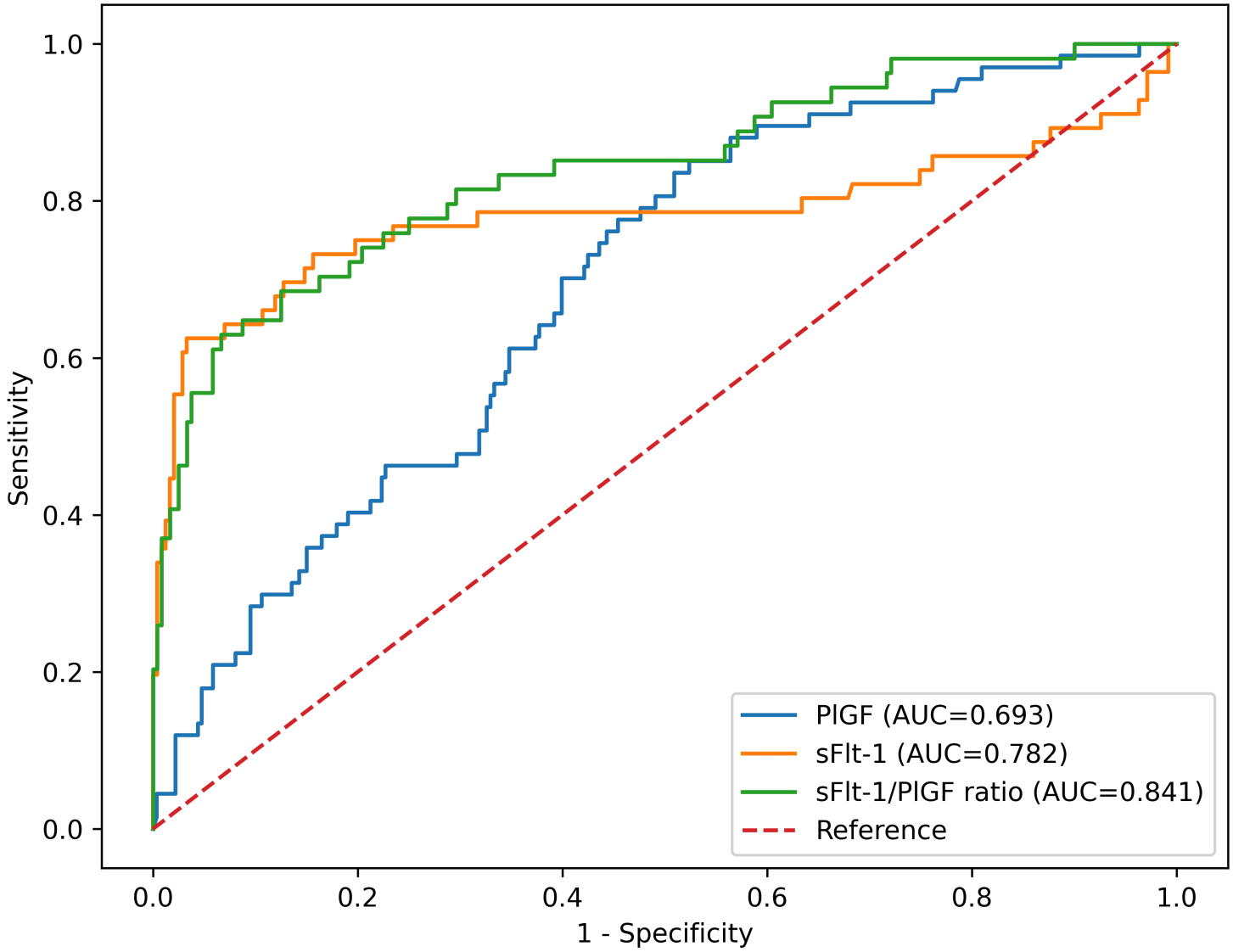


Figure 2

Receiver operating characteristic curves of PlGF, sFlt-1 and the sFlt-1/PlGF ratio for subsequent preeclampsia in the full analytical cohort (n=405).

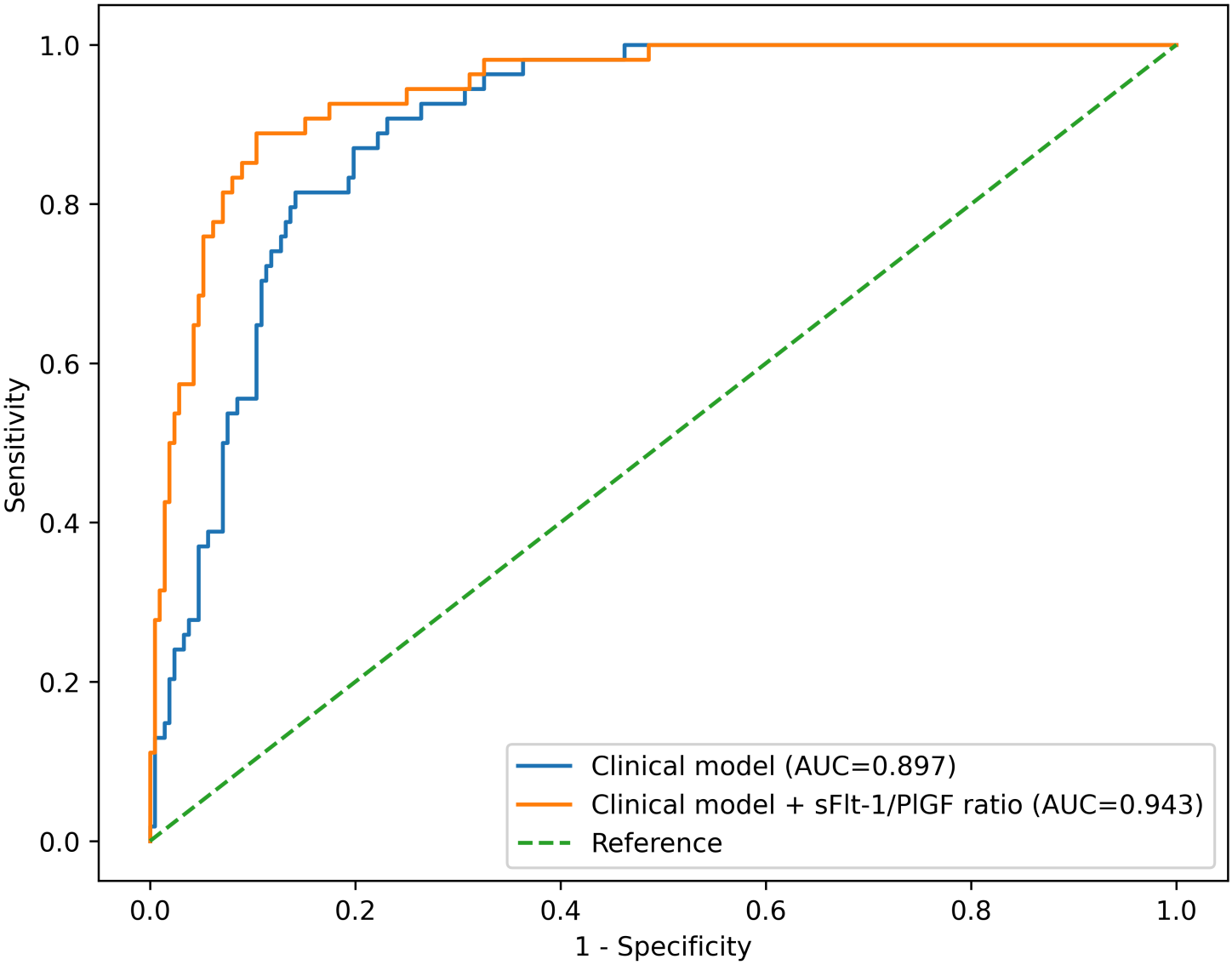


Figure 3

Incremental discrimination after addition of the sFlt-1/PlGF ratio to the clinical prediction model. The clinical model included maternal age, prepregnancy BMI, nulliparity, chronic hypertension, pregestational diabetes, isolated proteinuria at enrolment, history of preeclampsia, history of gestational hypertension and gestational age at biomarker sampling. Analyses included n=405 women (75 preeclampsia events). Apparent AUC increased from 0.897 to 0.943.