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Rule-in and rule-out of pre-eclampsia using a novel point-of-care placental growth factor test

James Rogers [1], Alice Hurrell [*,1], Gaayen Ravii Sahgal, Louisa Samuels, Chileshe Mabula-Bwalya, Katy Kuhrt, Carolyn Gill, Anna Brockbank, Katie Dalrymple, Antonio De Marvao, Paul T. Seed, Lucy C. Chappell, Andrew H. Shennan [1], Kate Bramham [1]

Department of Women and Children's Health, School of Life Course Sciences, King's College London, London, UK

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ABSTRACT

Objective: To evaluate test performance of the point-of-care Lepzi® Quanti placental growth factor (PlGF) test to rule-in and rule-out pre-eclampsia at various time points, in women presenting with suspected preeclampsia.
Study design: 242 frozen plasma samples from women with suspected pre-eclampsia were analysed from a prospective cohort study. Participants were recruited from two obstetric tertiary referral centres in London.
Main outcome measures: PlGF concentration was quantified using the Lepzi® Quanti PlGF test, which is a point-of-care PlGF test. Test performance for diagnosis of pre-eclampsia was evaluated at various thresholds, and at different gestations. The area under the receiver operator curve (AUROC) was determined for the Lepzi® Quanti PlGF test and compared to that of the nationally recommended Delfia® Xpress PlGF1-2–3 test, in the same cohort of participants.
Results: The LEPZI® Quanti PlGF test showed high test performance for rule-out of pre-eclampsia within seven and 28 days. A threshold of $\geq$ 129 pg/ml (in plasma) had high negative predictive value (NPV) for rule out of preeclampsia within seven days of sampling: NPV 96.9 % at $<$ 34 weeks' gestation (95 % confidence interval (CI) 91.2–99.4), NPV 97.0 %; at 34 – 37 weeks' gestation (95 % CI 84.2–99.9), NPV 80.0 % at $\geq$ 37 weeks gestation (95 % CI 44.4–97.5).
Conclusion: The LEPZI® Quanti PlGF test demonstrates high test performance for diagnosis of pre-eclampsia, comparable to test performance for validated, nationally recommended PlGF tests. The LEPZI® Quanti PlGF test is a whole blood, point-of-care option to optimise risk stratification, enhanced surveillance, and appropriate management strategies; this would be suitable for low- and middle-income settings, as well as high-income settings.

1. Introduction

Preeclampsia and associated hypertensive disorders of pregnancy (HDP) are a leading cause of maternal and perinatal morbidity and mortality, affecting up to 10 % of pregnancies worldwide [1,2]. Delivery of the placenta is the only definitive preeclampsia treatment, and delayed or missed diagnosis is associated with adverse maternal and perinatal outcomes [3].

Diagnostic criteria for preeclampsia have evolved, and diagnosis can be made on the basis of new onset or worsening chronic hypertension, with at least one of: proteinuria, evidence of organ dysfunction, and more recently uteroplacental dysfunction, including angiogenic imbalance and fetal growth restriction [6,7]. The conventional use of blood pressure and proteinuria to diagnose preeclampsia are associated with limited predictive capacity and lack of accuracy [5]; identifying more sensitive and accurate screening modalities is an active area of research. The clinical application of angiogenic biomarkers is recognised as one of the key advancements in the prediction, diagnosis, and management of preeclampsia [13].

Evidence has shown preeclampsia is driven by placental dysfunction and angiogenic imbalance, with abnormally high concentrations of placental-secreted antiangiogenic soluble fms-like tyrosine kinase 1

* Corresponding author at: Department of Women and Children's Health, School of Life Course Sciences, King's College London, Westminster Bridge Road, London SE1 7EH, UK.
E-mail address: alice.hurrell@kcl.ac.uk (A. Hurrell).
[1] Contributed equally.

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(sFlt-1) and abnormally low concentrations of proangiogenic placental growth factor (PlGF) [8,9]. PlGF is a member of the vascular endothelial growth factor (VEGF) family that plays a critical role in placenta angiogenesis throughout gestation.[10] In women with preeclampsia, the marked elevation in sFlt-1 binds vascular endothelial growth factor-A (VEGF-A) and PlGF, associated with distinctive low concentrations of PlGF detectable prior to the onset of clinical symptoms [11].

The PARROT Trial, a stepped-wedge cluster-randomised controlled trial of revealed PlGF testing, compared to usual care, demonstrated reduced time to diagnosis of pre-eclampsia (time ratio 0.36, 95 % CI 0.15–0.87; p = 0.027) and reduced severe maternal adverse outcomes (adjusted odds ratio 0.32, 95 % CI 0.11–0.96; p = 0.043) [14] associated with revealed PlGF testing. The National Institute for Health and Care Excellence (NICE) now recommends the use of PlGF-based testing to help rule-in and rule-out preeclampsia in suspected cases up to 37 weeks' gestation. [17] Currently, the QuidelOrtho PlGF test, the Roche sFlt-1/PlGF ratio, and the Delfia Xpress PlGF and sFlt-1/PlGF tests are recommended [17].

PlGF assays provide scope for enhanced risk stratification, appropriate surveillance and re-allocation of resources, and a health economic analysis within the PARROT trial demonstrated that PlGF testing also provides cost savings of up to £149 per patient in the NHS [14–20]. The potential impact extends to high-burden settings constrained by human resource capacity and limited laboratory infrastructure [21]. However, most of the current NICE-recommended PlGF testing platforms are lab-based tests on plasma or serum, requiring skills and resources that potentially limit their scalability to lower-resourced settings. The availability of point-of-care testing platforms, such as the LEPZI® Quanti PlGF POC test, which can be used on whole blood, has the potential to improve the reach and utility of PlGF testing.

This study aimed to:

a) assess the test performance for diagnosis of preeclampsia within two, seven, 14 and 28 days, at different gestational ages
b) explore optimised thresholds for rule-in and rule-out of preeclampsia
c) compare test performance to a validated, recommended assay.

2. Methods

This study utilized all available archived plasma samples collected from women with suspected pre-eclampsia during a prospective cohort study in two obstetric tertiary referral centres in London [22]. Details of data collection and outcomes in Table 1 have been previously described [22]. The inclusion criteria were women between 18 and 50 years with suspected preeclampsia and singleton pregnancy between 20- and 40 + 6-weeks' gestation. Women with multi-fetal pregnancy, existing HIV, Hepatitis B or C infection and a diagnosis of pre-eclampsia, eclampsia or HELLP at the time of sampling were excluded from the study. Hypertensive disorders of pregnancy were defined according to ISSHP classification [6]. Laboratory staff were masked to the maternal and perinatal outcomes.

The LEPZI® Quanti PlGF test is an immunofluorescence assay for rapid quantification of PlGF concentration in EDTA-anticoagulated blood or plasma specimens. The LEPZI® Quanti PlGF test is comprised of a single use cartridge and the LEPZI® reader. The cartridge contains polyclonal PlGF antibody conjugated with fluorescent microparticles which binds PlGF in the sample and is captured on the reaction zone of a cartridge by murine monoclonal antibodies against PlGF. The remaining fluorescent particles are captured by the polyclonal antibody on the control line. Once the sample is added to the cartridge it is inserted into the LEPZI® Quanti reader and quantitative measurements of PlGF is displayed in the range of 12–3000 pg/mL. The limit of detection is 9 pg/mL and the linear correlation coefficient of the assay is 0.97 within the range of 23 pg/mL-2900 pg/mL.

The LEPZI® kit contains 25 test cartridges, an electronic quality control (EQC) cartridge used to verify the functionality of the LEPZI® Quanti reader before sample testing and a lot specific radio frequency identification (RFID) card used to register new test lot information (which contains the LOT ID, test name, number of lines and expiry date) on the LEPZI® Quanti reader. The EQC verification and RFID card lot registration was performed before using each kit.

Plasma was thawed to room temperature and mixed by inversion. 200 μl of plasma was pipetted into the sample well of a test cartridge and immediately inserted into the LEPZI® Quanti reader which verifies the test run and displays the results in pg/mL. The multi cartridge mode was used, and quality control checks were performed according to Westguard rules [26].

Statistical analysis was performed using Stata version 17 (College Station, TX: Stata Corp. LLC) [29]. Area under the receiver operating characteristics curves (AUROC) were calculated to show test performance for diagnosis of pre-eclampsia within two, seven, 14, and 28 days, at different gestation bands (commonly utilised in clinical practice), including < 34 weeks', < 37 weeks', 34–37 weeks' and ≥ 37 weeks' gestation. Optimal thresholds for the LEPZI® Quanti PlGF test were derived by matching specificity to specificities of established thresholds for the Delfia Xpress PlGF test for pre-eclampsia within seven days, taken from a previous study in the same cohort of women [19]. Sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated for optimal thresholds, and other previously used thresholds (included in the supplementary appendix).

AUROC was used to compare test performance between the LEPZI® Quanti PlGF and the Delfia Xpress PlGF1-2–3 assays, as has been done previously and recommended for comparing test performance [16]. We have previously published test performance of the Delfia Xpress PlGF1-2–3 test to rule-in and rule-out pre-eclampsia within seven and 28 days, at < 34 weeks' gestation in the same cohort of participants; therefore, this was used for comparison [19]. A value of $p < 0.05$ was considered statistically significant.

3. Results

242 plasma samples were included in the study. Participant characteristics are presented in Table 1 [19].

3.1. Rule-in and rule-out of pre-eclampsia within seven and 28 days

AUROC for pre-eclampsia within seven days was 0.88, and similarly high for all other end points (Tables 2-4). The optimal threshold identified was < 12 pg/ml for rule-in and ≥ 129 pg/ml for rule-out of pre-eclampsia within seven days. Details of test performance for other exploratory thresholds and time points are included in the supplementary appendix. The prevalence of pre-eclampsia was 22 %.

There was high test performance to rule-out pre-eclampsia for all end points. Sensitivity for pre-eclampsia within two to 28 days ranged between 75.0 – 87.5 % (Tables 2, 3 and S4). NPV for pre-eclampsia within 7 days was 96.9 % for women presenting before 37 weeks' gestation, and 95.4 % for pre-eclampsia within 14 days. (Tables 2, 3, S5 and Fig. 1). The corresponding positive predictive value (PPV) for PlGF < 12 pg/ml ruling in pre-eclampsia within 28 days was 88.2 % (95 % CI 63.6–98.5), and the specificity was 98.0 % (95 % CI 92.9–99.8) (Table 2). Test performance was highest before 37 weeks' gestation: NPV was 80.0 % beyond 37 weeks' gestation for rule-out of pre-eclampsia within seven and 28 days ≥ 37 weeks' (95 % CI 44.4–97.5) (Table 4). (See Fig. 2).

Test performance for the Lepzi® Quanti PlGF test was compared to data evaluating the Delfia Xpress PlGF1-2–3 test in the same women, previously published [19]. For prediction of pre-eclampsia within seven days at < 34 weeks' gestation, the AUROC for the Lepzi test was 0.88 (95 % CI 0.79–0.96), whereas the AUROC for the Delfia Xpress test was 0.85 (95 % CI 0.76–0.94) [19]. For this endpoint and gestation, the sensitivity of the Lepzi test was 75.0 % (95 % CI 42.8–94.5) and NPV 96.9 % (95 % CI 91.2–99.4), corresponding values for the Delfia Xpress test were 72.2 % (95 % CI 46.5–90.3) and 94.8 % (88.4–98.3). For

Table 1
Maternal characteristics and pregnancy outcomes (242 participants).

Age at booking (years) Median (IQR)	35.0 (32.0,38.0)
BMI (kg/m^2) Median (IQR)	27.2 (23.5,32.9)
Ethnicity *(available for 236 participants)*	
White	104 (44.1 %)
Black	68 (28.8 %)
Asian	24 (10.2 %)
Mixed	10 (4.2 %)
Other	30 (12.7 %)
Nulliparous n (%)	124 (51.2 %)
Family History − Pre-eclampsia n (%)	22 (9.1 %)
SBP Median (IQR)	132.0 (122.0,141.0)
DBP Median (IQR)	85.5 (78.0,93.0)
Smoking: At any time, n (%)	31 (12.8 %)
Smoking: Never n (%)	211 (87.2 %)
Chronic Hypertension n (%)	159 (65.7 %)
Chronic Kidney Disease n (%)	25 (10.3 %)
Aspirin n (%)	152 (62.8 %)
Gestation at time of sampling Median (IQR) (weeks)	33.7 (30.0,36.0)
Gestation of sample n (%)	
20–33 + 6 weeks' gestation	126 (52.1 %)
34–36 + 6 weeks' gestation	79 (32.6 %)
≥37 weeks' gestation	37 (15.3 %)
Time from sampling to pre-eclampsia diagnosis Median (IQR) (days)	7.0 (0.0,22.0)
Time to PE diagnosis n (%)	
Never	188 (77.7 %)
0–2 days	24 (9.9 %)
3–7 days	3 (1.2 %)
8–14 days	7 (2.9 %)
15–28 days	18 (7.4 %)
After 28 days	2 (0.8 %)
Pregnancy outcomes N (%)	
Live birth n (%)	241 (99.6 %)
Intrauterine fetal death n (%)	1 (0.4 %)
Haemolysis Elevated Liver Enzymes Low Platelets (HELLP) n (%)	1 (0.4 %)
Gestation at Delivery Median (IQR) (Weeks)	38.4 (37.4,39.1)
Low birth weight (<2.5 kg) n (%)	45 (18.6 %)

Table 2
Clinical performance of Lepzi® Quanti PlGF Test to rule-in or rule-out pre-eclampsia within seven days and 28 days of sampling at < 34 weeks' gestation.

Test <34 Weeks N = 126	LEPZI PLGF Rule In within 7 days	Rule Out within 7 days	Rule In within 28 days	Rule Out within 28 days
Threshold	<12 pg/ml% (95 % CI)	≥129 pg/ml% (95 % CI)	<12 pg/ml% (95 % CI)	≥129 pg/ml% (95 % CI)
Sensitivity	50.0 % (21.1–78.9) 6/12	75.0 % (42.8–94.5) 9/12	55.6 % (35.3–74.5) 15/27	77.8 % (57.7–91.4) 21/27
Specificity	90.4 % (83.4–95.1) 103/114	82.5 % (74.2–88.9) 94/114	98.0 % (92.9–99.8) 97/99	91.9 % (84.7–96.4) 91/99
PPV	35.3 % (14.2–61.7) 6/17	31.0 % (96.9 %) 9/29	88.2 % (63.6–98.5) 15/17	72.4 % (52.8–87.3) 21/29
NPV	94.5 % (88.4–98.0) 103/109	96.9 % (91.2–99.4) 94/97	89.0 % (81.6–94.2) 97/109	93.8 % (87.0–97.7) 91/97
AUROC (95 % CI)	0.88 (0.79–0.96)		0.91 (0.83–0.98)	

PlGF: Placental Growth Factor; PPV: Positive Predictive Value; NPV: Negative predictive value; AUROC: Area under the receiver operating characteristics curve.

Table 3
Clinical performance of Lepzi® Quanti PlGF Test to rule-in or rule-out pre-eclampsia within seven days and 28 days of sampling between 34–37 weeks' Gestation.

Test 34–37 Weeks N = 79	LEPZI PLGF Rule In within 7 days	Rule Out within 7 days	Rule In within 28 days	Rule Out within 28 days
Threshold	<12 pg/ml% (95 % CI)	≥129 pg/ml % (95 % CI)	<12 pg/ml% (95 % CI)	≥129 pg/ml % (95 % CI)
Sensitivity	85.7 % (42.1–99.6) 6/7	85.7 % (42.1–99.6) 6/7	56.3 % (29.9–80.2) 9/16	87.5 % (61.7–98.4) 14/16
Specificity	75.0 % (63.4–84.5) 54/72	44.4 % (32.7–56.6) 32/72	76.2 % (63.8–86.0) 48/63	49.2 % (36.4–62.1) 31/63
PPV	25.0 % (9.8–46.7) 6/24	13.0 % (4.9–26.3) 6/46	37.5 % (18.8–59.4) 9/24	30.4 % (17.7–45.8) 14/46
NPV	98.2 % (90.3–100.0) 54/55	97.0 % (84.2–99.9) 32/33	87.3 % (75.5–94.7) 48/55	93.9 % (79.8–99.3 %) 31/33
AUROC (95 % CI)	0.77 (0.56–0.98)		0.72 (0.58–0.87)	

PlGF: Placental Growth Factor; PPV: Positive Predictive Value; NPV: Negative predictive value; AUROC: Area under the receiver operating characteristics curve.

Table 4
Clinical performance of Lepzi® Quanti PLGF Test to rule-in or rule-out pre-eclampsia within seven days and twenty-eight days of sampling at ≥ 37 weeks' Gestation.

Test ≥37 Weeks N = 37	LEPZI PLGF Rule In within 7 days	Rule Out within 7 days	Rule In within 28 days	Rule Out within 28 days
Threshold	<12 pg/ml% (95 % CI)	≥129 pg/ml% (95 % CI)	<12 pg/ml% (95 % CI)	≥129 pg/ml% (95 % CI)
Sensitivity	75.0 % (34.9–96.8) 6/8	75.0 % (34.9–96.8) 6/8	77.8 % (40.0–97.2) 7/9	77.8 % (40.0–97.2) 7/9
Specificity	62.1 % (42.3–79.3) 18/29	27.6 % (12.7–47.2) 8/29	64.3 % (44.1–81.4) 18/28	28.6 % (13.2–48.7) 8/28
PPV	35.3 % (14.2–61.7) 6/17	22.2 % (8.6–42.3) 6/27	41.2 % (18.4–67.1) 7/17	25.9 % (11.1–46.3) 7/27
NPV	90.0 % (68.3–98.8) 18/20	80.0 % (44.4–97.5) 8/10	90.0 % (68.3–98.8) 18/20	80.0 % (44.4–97.5) 8/10
AUROC (95 % CI)	0.66 (0.46–0.87)		0.69 (0.50–0.88)	

PlGF: Placental Growth Factor; PPV: Positive Predictive Value; NPV: Negative predictive value; AUROC: Area under the receiver operating characteristics curve.

prediction of pre-eclampsia within 28 days at < 34 weeks' gestation, the AUROC for the Lepzi test was 0.91 (95 % CI 0.83–0.98); for the Delfia Xpress test the AUROC was 0.90 (95 % CI 0.83–0.97). For this endpoint and gestation, the sensitivity of the Lepzi test was 77.8 % (57.7–91.4) and NPV 93.8 % (87.0–97.7), corresponding values for the Delfia Xpress test were 80.6 % (95 % CI 64.0–91.8) and 92.8 % (95 % CI 85.7–97.0). There were no significant differences observed between the two tests ($p > 0.05$).

4. Discussion

In this study assessing the test performance of a novel point-of-care PlGF test in 242 stored plasma samples from women with suspected

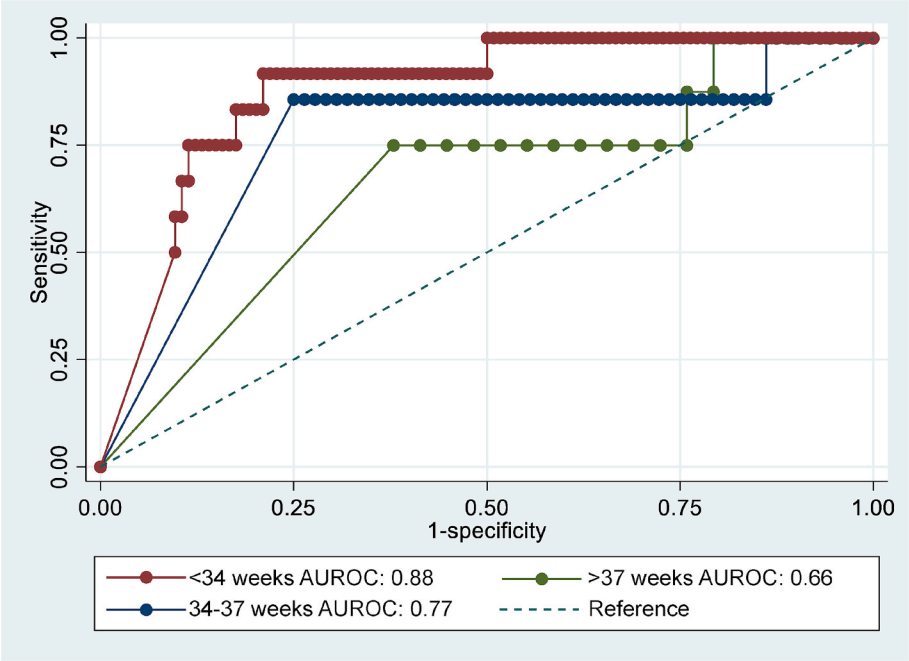

Fig. 1. AUROC for test performance for diagnosis of pre-eclampsia within seven days, for Lepzi® Quanti PLGF Test.

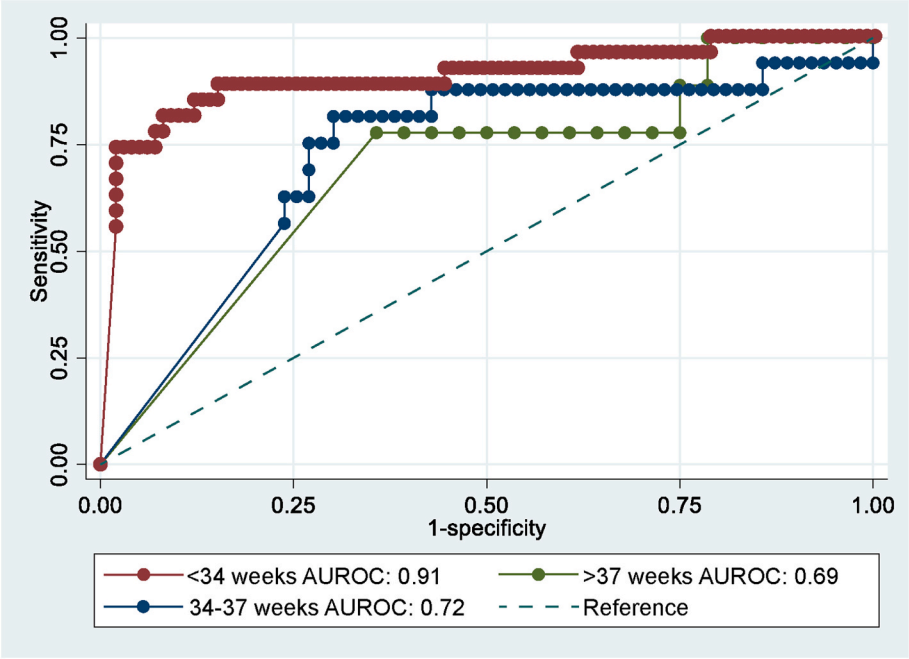

Fig. 2. AUROC curves for predictive performance of Lepzi® Quanti PLGF Test within 28 days of sampling.

pre-eclampsia, we demonstrated that the Lepzi® Quanti PlGF test could be used as an effective point-of-care test for diagnosis of pre-eclampsia.

Our study determined an optimal rule-out threshold of 129 pg/mL for this cohort using plasma; this may be different for whole blood and will need to be determined in prospective validation studies of the Lepzi Quanti point-of-care test. PlGF is mainly synthesised by the syncytiotrophoblasts and is expressed as four isomers (PlGF 1–4) [10–12]. Differences in analytical methodology and the PlGF isoform targeted by various commercially available assays [14] make direct comparisons between tests challenging. The COMPARE study assessed three commercially available PlGF assays, observing that equivalent clinical thresholds varied by up to 50 % for different tests (e.g., 150 pg/ml for Delfia Xpress PlGF 1–2-3 and 100 pg/ml for QuidelOrtho PlGF) [16]. A side-by-side comparison of areas under the ROC curve demonstrated that the point-of-care Lepzi® Quanti test and the NICE recommended Delfia Xpress 1–2-3 PlGF assay [19] had comparable performance for diagnosing preeclampsia within 7 and 28 days. This finding presents a substantial opportunity for the use of point-of-care angiogenic biomarker tests as diagnostic adjuncts for pre-eclampsia.

We demonstrated excellent test performance to rule-out pre-eclampsia below 37 weeks' gestation, that is likely to have clinical utility. High sensitivity and NPV reflect the clinical utility as a rule-out

test to determine which women are likely to need delivery for pre-eclampsia within seven, 14 and 28 days. Rule-out performance is important for risk stratification, enabling safe discharge home and thus reducing burden on healthcare costs associated with unnecessary admission for inpatient monitoring. Although the AUROC declined above 34 weeks' gestation, this is similar to other biomarker tests for pre-eclampsia. The diagnostic accuracy supports testing in women up to 37 weeks' gestation (AUROC 0.82), and is comparable to other nationally recommended tests [16].

The observed positive predictive value (PPV) of 88.2 % for pre-eclampsia developing within 28 days with a PlGF concentration < 12 pg/ml at < 34 weeks' gestation also had high capability to determine diagnosis of pre-eclampsia. This is important for risk stratification, enabling healthcare providers to tailor prenatal care and monitoring based on individualised risk profiles. Pregnant individuals with low concentrations of PlGF may benefit from closer surveillance and timely delivery, although low PlGF alone is not an indication for delivery, and caution must be exercised to avoid an unnecessary increase in iatrogenic preterm birth. This PPV compares favourably to a previously published study which demonstrated a PPV of 71.7 % for pre-eclampsia within 28 days, for a Roche Elecsys sFlt-1/PlGF ratio at a cut-off of 85 [25].

The results of this study suggest the point-of-care Lepzi® Quanti PlGF test could be integrated into clinical practice guidelines and algorithms for preeclampsia diagnosis and management. As a near-patient, whole-blood, rapid, low-cost test, this is a substantial change to current technology. The test is applicable to varied settings offering immediate results without the need for expensive and resource-intensive laboratory facilities, additional training, or venepuncture skills. This would enhance accessibility, ensuring the benefits of PlGF testing can reach low- and middle-income settings, where the great disease burden of pre-eclampsia lies.

Strengths of the study include the prospective collection of samples from a demographically diverse population in London. This cohort has previously had test performance evaluated for a range of angiogenic biomarker tests, including Delfia Xpress PlGF1-2–3 and Delfia Xpress sFlt-1/PlGF; therefore, it is possible to make direct comparisons on the same samples and same study population. All samples only underwent a single freeze thaw cycle, and clinical outcomes have been verified.

There were some limitations to our study. This study used plasma samples, and not prospectively collected whole blood samples; thresholds for whole blood may need to be adjusted. This study demonstrates high test performance when testing plasma, which may be advantageous in some settings alongside other blood tests for pre-eclampsia on spun EDTA blood, platelet count for example. Freeze-thaw cycles can impact the integrity and stability of biological samples. However, the potential effects are minimal as samples analysed were single freeze thaw aliquots stored at −80 °C. Finally, the optimal thresholds identified in this study should be clinically validated in independent prospective cohort studies of pregnant women, including from low- and middle-income settings.

The Lepzi® Quanti PlGF test is part of an ongoing multicentre prospective cohort study in Sierra Leone and the Zambia designed to test point-of-care biomarker testing to assess hypertensive women between 24 – 37 weeks of pregnancy. In this context, where severe outcomes such as stillbirth and maternal death are common, the value of this test could be considerable. Furthermore, there is some data to suggest that there is an effect of ethnicity on median PlGF concentration, and future work should interrogate this in large cohorts. However, in other fields such as creatinine testing, we have seen a move away from thresholds adjusted for ethnicity. Finally, there is promising emerging evidence for metabolic biomarker testing for pre-eclampsia [27,28]; as there are vascular and metabolic aspects of the pathophysiology of pre-eclampsia, angiogenic and metabolic biomarker testing may be synergistic, and future work could evaluate prediction of pre-eclampsia by combining these biomarkers.

5. Conclusion

This study demonstrates excellent test performance for the Lepzi® Quanti PlGF test as a point-of-care adjunct for diagnosis of preeclampsia; test performance is comparable to validated, nationally recommended laboratory PlGF tests. This represents a step forward in leveraging point-of-care biomarker-based technologies to improve the precision and efficiency of antenatal care for pregnant women at risk of complications related to preeclampsia. The advent of point-of-care PlGF testing means that we are on the tipping point of a diagnostic adjunct becoming more widely available, including beyond high-income settings.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.preghy.2025.101215.

References

[1] R. Fu, Y. Li, X. Li, W. Jiang, Hypertensive Disorders in Pregnancy: Global Burden From 1990 to 2019, Current Research Hotspots and Emerging Trends, Curr. Probl. Cardiol. 48 (12) (2023) 101982, https://doi.org/10.1016/j.cpcardiol.2023.101982.

[2] M.K. Jena, N.R. Sharma, M. Petitt, D. Maulik, N.R. Nayak, Pathogenesis of Preeclampsia and Therapeutic Approaches Targeting the Placenta, Biomolecules 10 (6) (2020) 953, https://doi.org/10.3390/biom10060953.

[3] L. Creswell, N. O'Gorman, K.R. Palmer, F. da Silva Costa, D.L. Rolnik, Perspectives on the Use of Placental Growth Factor (PlGF) in the Prediction and Diagnosis of Pre-Eclampsia: Recent Insights and Future Steps, Int. J. Womens Health 15 (2023) 255–271, https://doi.org/10.2147/IJWH.S368454.

[5] L.C. Chappell, C.A. Cluver, J. Kingdom, S. Tong, Pre-eclampsia, Lancet (London, England) 398 (10297) (2021) 341–354, https://doi.org/10.1016/S0140-6736(20)32335-7.

[6] L.A. Magee, M.A. Brown, D.R. Hall, S. Gupte, A. Hennessy, S.A. Karumanchi, L. C. Kenny, F. McCarthy, J. Myers, L.C. Poon, S. Rana, S. Saito, A.C. Staff, E. Tsigas, P. von Dadelszen, The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice, Pregnancy Hypertension 27 (2022) 148–169, https://doi.org/10.1016/j.preghy.2021.09.008.

[7] Brown, M. A., Magee, L. A., Kenny, L. C., Karumanchi, S. A., McCarthy, F. P., Saito, S., Hall, D. R., Warren, C. E., Adoyi, G., Ishaku, S., & International Society for the Study of Hypertension in Pregnancy (ISSHP) (2018). Hypertensive Disorders of Pregnancy: ISSHP Classification, Diagnosis, and Management Recommendations for International Practice. Hypertension (Dallas, Tex. : 1979), 72(1), 24–43. doi: 10.1161/HYPERTENSIONAHA.117.10803.

[8] S. Rana, E. Lemoine, J.P. Granger, S.A. Karumanchi, Preeclampsia: Pathophysiology, Challenges, and Perspectives, Circ. Res. 124 (7) (2019) 1094–1112, https://doi.org/10.1161/CIRCRESAHA.118.313276.

[9] E.V. Kuklina, C. Ayala, W.M. Callaghan, Hypertensive disorders and severe obstetric morbidity in the United States, Obstet. Gynecol. 113 (6) (2009) 1299–1306, https://doi.org/10.1097/AOG.0b013e3181a45b25.

[10] B. Huppertz, Biology of preeclampsia: Combined actions of angiogenic factors, their receptors and placental proteins. Biochimica et biophysica acta, Molecular Basis of Disease 1866 (2) (2020) 165349, https://doi.org/10.1016/j.bbadis.2018.11.024.

[11] S.E. Maynard, S.A. Karumanchi, Angiogenic factors and preeclampsia, Semin. Nephrol. 31 (1) (2011) 33–46, https://doi.org/10.1016/j.semnephrol.2010.10.004.

[12] Stepan, H., Hund, M., & Andraczek, T. (2020). Combining Biomarkers to Predict Pregnancy Complications and Redefine Preeclampsia: The Angiogenic-Placental Syndrome. Hypertension (Dallas, Tex. : 1979), 75(4), 918–926. doi: 10.1161/HYPERTENSIONAHA.119.13763.

[13] A. Hurrell, K. Duhig, B. Vandermolen, A.H. Shennan, Recent advances in the diagnosis and management of pre-eclampsia, Faculty Reviews 9 (2020) 10, https://doi.org/10.12703/b/9-10.

[14] K.E. Duhig, J. Myers, P.T. Seed, J. Sparkes, J. Lowe, R.M. Hunter, A.H. Shennan, L. C. Chappell, PARROT trial group, Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial, Lancet (london, England) 393 (10183) (2019) 1807–1818, https://doi.org/10.1016/S0140-6736(18)33212-4.

[15] D. Hayes-Ryan, K. Hemming, F. Breathnach, A. Cotter, D. Devane, A. Hunter, F. M. McAuliffe, J.J. Morrison, D.J. Murphy, A. Khashan, B. McElroy, A. Murphy,

E. Dempsey, K. O'Donoghue, L.C. Kenny, PARROT Ireland: Placental growth factor in Assessment of women with suspected pre-eclampsia to reduce maternal morbidity: a Stepped Wedge Cluster Randomised Control Trial Research Study Protocol, BMJ Open 9 (2) (2019) e023562, https://doi.org/10.1136/bmjopen-2018-023562.

[16] F.P. McCarthy, C. Gill, P.T. Seed, K. Bramham, L.C. Chappell, A.H. Shennan, Comparison of three commercially available placental growth factor-based tests in women with suspected preterm pre-eclampsia: the COMPARE study, Ultrasound in Obstetrics & Gynecology : the Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology 53 (1) (2019) 62–67, https://doi.org/10.1002/uog.19051.

[17] M.Y. Tan, D. Wright, A. Syngelaki, R. Akolekar, S. Cicero, D. Janga, M. Singh, E. Greco, A. Wright, K. Maclagan, L.C. Poon, K.H. Nicolaides, Comparison of diagnostic accuracy of early screening for pre-eclampsia by NICE guidelines and a method combining maternal factors and biomarkers: results of SPREE, Ultrasound in Obstetrics & Gynecology : the Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology 51 (6) (2018) 743–750, https://doi.org/10.1002/uog.19039.

[18] J. Binder, E. Kalafat, P. Palmrich, P. Pateisky, A. Khalil, Should angiogenic markers be included in diagnostic criteria of superimposed pre-eclampsia in women with chronic hypertension? Ultrasound in Obstetrics & Gynecology : the Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology 59 (2) (2022) 192–201, https://doi.org/10.1002/uog.23711.

[19] L. Bremner, C. Gill, P.T. Seed, F. Conti-Ramsden, L. Webster, J. Fleminger, L. C. Chappell, A. Shennan, K. Bramham, Rule-in and rule-out of pre-eclampsia using DELFIA Xpress PlGF 1-2-3 and sFlt-1: PlGF ratio, Pregnancy Hypertension 27 (2022) 96–102, https://doi.org/10.1016/j.preghy.2021.12.008.

[20] Y. Carlsson, A. Sandström, L. Bergman, P. Conner, S. Hansson, M. Kublickas, U. Görmüş, P. Lindgren, G. Oleröd, A.K. Wikström, A. Larsson, Comparing the results from a Swedish pregnancy cohort using data from three automated placental growth factor immunoassay platforms intended for first-trimester preeclampsia prediction, Acta Obstet. Gynecol. Scand. 102 (8) (2023) 1084–1091, https://doi.org/10.1111/aogs.14615.

[21] E.R. Lawrence, T.J. Klein, T.K. Beyuo, Maternal Mortality in Low and Middle-Income Countries, Obstet. Gynecol. Clin. N. Am. 49 (4) (2022) 713–733, https://doi.org/10.1016/j.ogc.2022.07.001.

[22] K. Bramham, P.T. Seed, L. Lightstone, C. Nelson-Piercy, C. Gill, P. Webster, L. Poston, L.C. Chappell, Diagnostic and predictive biomarkers for pre-eclampsia in patients with established hypertension and chronic kidney disease, Kidney Int. 89 (4) (2016) 874–885, https://doi.org/10.1016/j.kint.2015.10.012.

[25] S. Verlohren, S.P. Brennecke, A. Galindo, S.A. Karumanchi, L.B. Mirkovic, D. Schlembach, H. Stepan, M. Vatish, H. Zeisler, S. Rana, Clinical interpretation and implementation of the sFlt-1/PlGF ratio in the prediction, diagnosis and management of preeclampsia, Pregnancy Hypertension 27 (2022) 42–50, https://doi.org/10.1016/j.preghy.2021.12.003.

[26] J.O. Westgard, S.A. Westgard, Establishing evidence-based statistical quality control practices, Am. J. Clin. Pathol. 151 (4) (2019) 364–370, https://doi.org/10.1093/ajcp/aqy158.

[27] S.R. Nagalla, V. Janaki, A.R. Vijayalakshmi, K. Chayadevi, D. Pratibha, P.V. Rao, K. M. Sage, D. Nair-Schaef, E. Bean, C.T. Roberts Jr, M.G. Gravett, Glycosylated fibronectin point-of-care test for diagnosis of pre-eclampsia in a low-resource setting: a prospective Southeast Asian population study, BJOG 127 (13) (2020) 1687–1694, https://doi.org/10.1111/1471-0528.16323.

[28] N. Sokratous, M. Bednorz, A. Wright, K.H. Nicolaides, N.A. Kametas, Prediction of imminent pre-eclampsia by serum glycosylated fibronectin in women with new onset hypertension, Ultrasound in Obstetrics & Gynecology: the Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology (2023), https://doi.org/10.1002/uog.27458.

[29] StataCorp., Stata Statistical Software: Release 18, StataCorp LLC, College Station, TX, 2023.