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Prediction using serum glycosylated fibronectin of imminent pre-eclampsia in women with new-onset hypertension

N. SOKRATOUS[1], M. BEDNORZ[1], A. WRIGHT[2], K. H. NICOLAIDES[1] and N. A. KAMETAS[1]

[1]*Fetal Medicine Research Institute, King's College Hospital, London, UK;* [2]*Institute of Health Research, University of Exeter, Exeter, UK*

KEYWORDS: angiogenic factor; antiangiogenic factor; glycosylated fibronectin; imminent pre-eclampsia; placental growth factor; soluble fms-like tyrosine kinase-1

CONTRIBUTION

What are the novel findings of this work?
In women with a singleton pregnancy presenting with new-onset hypertension at 24–41 weeks' gestation, the predictive performance for delivery with pre-eclampsia (PE) within the subsequent 2 weeks of maternal serum glycosylated fibronectin (GlyFn) was similar to that of serum placental growth factor (PlGF) and the soluble fms-like tyrosine kinase-1 (sFlt-1) to PlGF ratio, with detection rates of about 60%, at a screen-positive rate of about 45%.

What are the clinical implications of this work?
GlyFn is a simple test that can be carried out using a point-of-care device without need for a laboratory and provide results within 10 min of testing. In this respect, it could potentially replace other tests that are used currently in the prediction of PE in women presenting with new-onset hypertension. However, the predictive performance for all tests is relatively poor.

ABSTRACT

Objective *To compare the predictive performance for delivery with pre-eclampsia (PE) within 2 weeks after assessment in women with new-onset hypertension at 24–41 weeks' gestation between serum glycosylated fibronectin (GlyFn) concentration, serum placental growth factor (PlGF) concentration and soluble fms-like tyrosine kinase-1 (sFlt-1) to PlGF concentration ratio.*

Methods *This was a prospective observational study of 409 women with a singleton pregnancy presenting at 24–41 weeks' gestation with new-onset hypertension. The recommended cut-off for sFlt-1/PlGF ratio for the prediction of PE in the platform used in this study is 85; the appropriate cut-offs for GlyFn and PlGF were determined to achieve the same screen-positive rate as that of sFlt-1/PlGF ratio > 85. We then compared the predictive performance for delivery with PE within 2 weeks after presentation between GlyFn, PlGF and sFlt-1/PlGF, both overall and in subgroups according to gestational age at presentation.*

Results *Delivery with PE within 2 weeks occurred in 93 (22.7%) cases. The screen-positive rate for sFlt-1/PlGF ratio > 85 was 46.2%. The cut-off corresponding to a screen-positive rate of 46.2% was 75 pg/mL for PlGF and 510 μg/mL for GlyFn. The overall detection rate for delivery with PE within 2 weeks after presentation was 62.4% (95% CI, 51.7–72.2%) for GlyFn and sFlt-1/PlGF and 60.2% (95% CI, 49.5–70.2%) for PlGF. In all women who delivered with PE within 2 weeks after presentation at < 34 weeks' gestation and in about 60–70% of those presenting at < 38 weeks, GlyFn and sFlt-1/PlGF were increased and PlGF was reduced. However, the screen-positive rate for these tests was very high at about 45%. The predictive performance for delivery with PE within 2 weeks after presentation at ≥ 38 weeks' gestation was poorer for all three methods of screening, with detection rates of 47–63% at screen-positive rates of 40–50%.*

Conclusions *In women with new-onset hypertension, the predictive performance for delivery with PE within 2 weeks after presentation for serum GlyFn is similar to that of PlGF and the sFlt-1/PlGF ratio, but GlyFn may be the preferred option because it is a rapid point-of-care test. However, the predictive performance for all tests is relatively poor.* © *2023 International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Pre-eclampsia (PE) complicates about 5% of pregnancies and is a leading cause of maternal and perinatal mortality

Correspondence to: Prof. K. H. Nicolaides, Fetal Medicine Research Institute, King's College Hospital, 16–20 Windsor Walk, Denmark Hill, London SE5 8BB, UK (e-mail: kypros@fetalmedicine.com)

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and morbidity[1]. Development of PE is preceded by a decrease in the maternal serum concentration of angiogenic placental growth factor (PlGF) and an increase in the level of antiangiogenic soluble fms-like tyrosine kinase-1 (sFlt-1)[2–9]. In women presenting to specialist clinics with signs and/or symptoms of hypertensive disorder, cut-offs in PlGF concentration and the ratio of concentrations of sFlt-1 to PlGF have been used to predict the development of PE within the subsequent 1–4 weeks[5,7,8].

Another potentially useful biomarker of PE in women presenting with signs and/or symptoms of the disease is glycosylated fibronectin (GlyFn)[9–11]. However, a panel of experts for the National Institute of Health and Care Excellence reported that there is currently insufficient evidence to determine the test accuracy compared with standard care in the UK and that larger studies are needed[12].

The objective of this prospective study in women with a singleton pregnancy presenting to a specialist clinic with new-onset hypertension at 24–41 weeks' gestation was to compare the predictive performance for delivery with PE within 2 weeks after assessment between maternal serum GlyFn concentration, PlGF concentration and sFlt-1/PlGF concentration ratio.

METHODS

Study design and participants

This was a prospective observational study of women with a singleton pregnancy presenting to a specialist hypertension clinic at King's College Hospital, London, UK, at ≥ 24 weeks' gestation with new-onset hypertension. The women were examined between November 2016 and October 2022. Patients are referred to this clinic by obstetricians and midwives if hypertension is diagnosed during a routine antenatal clinic appointment or after an emergency clinical examination in those presenting with symptoms of hypertensive disease. The diagnosis of gestational hypertension (GH) was based on the finding of systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on at least two occasions 4 h apart in previously normotensive women. Blood pressure was measured using validated automated devices[13]. During the first visit to the specialist clinic, all women had blood taken for the measurement of serum creatinine concentration, serum aspartate transaminase and platelet count and quantification of serum concentration of PlGF and sFlt-1 in pg/mL by an automated biochemical analyzer (BRAHMS KRYPTOR compact PLUS; Thermo Fisher Scientific, Hennigsdorf, Germany), in addition to either a 24-h urine collection for protein quantification or a urine sample for measurement of the protein-to-creatinine ratio. Gestational age was determined by the measurement of fetal crown–rump length at 11–13 weeks or fetal head circumference at 19–24 weeks[14,15]. Serum was stored at −80°C for subsequent research. PlGF and sFlt-1 measurements were not made available to the obstetricians managing the pregnancies, but were collected as part of a research project, which was approved by the NHS Research Ethics Committee (REC reference: 02-03-033). All participants gave written informed consent to participate in the study.

All women had regular visits at the specialist clinic, which varied from once per week to daily, depending on the severity of hypertension, evolution to PE, gestational age and condition of the fetus, including estimated fetal weight and oxygenation, as determined by Doppler assessment of flow in the umbilical arteries, ductus venosus and middle cerebral artery. Gestational age and the maternal and fetal condition dictated the timing and method of delivery.

Included in the study were singleton pregnancies delivering a non-malformed liveborn or stillborn fetus at ≥ 24 weeks' gestation. Excluded were pregnancies with aneuploidy or major fetal abnormality.

Measurement of glycosylated fibronectin

The frozen serum samples were thawed and then analyzed for GlyFn using a point-of-care test (Lumella™ PE test; DiabetOmics, Inc., Hillsboro, OR, USA). Briefly, 5 µL of serum was diluted 1:350 in running buffer and 120 µL of diluted serum was added to a test strip and inserted into a hand-held reader system. Test strips were configured with monoclonal antibodies against GlyFn labeled with gold particles. The GlyFn concentration was displayed on the reader after 10 min. According to the manufacturer, the measurable range of the Lumella™ assay is 50–800 µg/mL and the intra- and interassay coefficients of variation at mean concentrations of 50–800 µg/mL are 5–10% and 6–10%, respectively.

Outcome measure

The outcome measure was delivery with PE within 2 weeks after presentation to the hypertension clinic. Data on pregnancy outcome were collected from the women's hospital maternity records. PE was defined according to the 2019 American College of Obstetricians and Gynecologists criteria as hypertension with development of one or more of the following: new-onset proteinuria (≥ 300 mg/24 h or protein-to-creatinine ratio ≥ 30 mg/mmol or ≥ 2+ on dipstick testing), renal insufficiency with serum creatinine > 97 µmol/L in the absence of underlying renal disease, hepatic dysfunction with blood concentration of transaminases more than twice the upper limit of normal (≥ 65 IU/L for our laboratory), thrombocytopenia (platelet count < 100 000/µL), headache or visual symptoms, or pulmonary edema[16].

Statistical analysis

Data were summarized as median (interquartile range) for continuous variables and *n* (%) for categorical variables. Outcome groups were compared using Student's *t*-test for continuous data and the chi-square test or Fisher's exact test for categorical data. The following three steps were used to compare the predictive performance for delivery

with PE within 2 weeks after presentation by GlyFn, PlGF and sFlt-1/PlGF ratio. First, we examined the distribution of GlyFn concentration, PlGF concentration and sFlt-1/PlGF concentration ratio in women who delivered with PE within 2 weeks after presentation and those that did not. Second, we defined a screen-positive group using the recommended cut-off of 85 for the sFlt-1/PlGF ratio[17] and, to allow for fair comparison, we calculated cut-offs for PlGF and GlyFn that corresponded to the same screen-positive rate. We then determined the detection rate and false-positive rate for development of PE within 2 weeks after presentation, overall and grouped by gestational age at presentation (< 34 weeks, 34 + 0 to 35 + 6 weeks, 36 + 0 to 37 + 6 weeks and ≥ 38 weeks). We compared the detection rate and false-positive rate within these gestational-age groups using Fisher's exact test. Third, we compared the area under the receiver-operator-characteristics (ROC) curve (AUC) in the prediction of delivery with PE within 2 weeks after presentation by GlyFn, PlGF and sFlt-1/PlGF in all women and in those presenting at < 36 weeks' gestation.

The statistical software package R, with packages PropCIs and pROC, was used for data analysis[18].

RESULTS

Study participants

The study population of 409 singleton pregnancies presenting with new-onset hypertension included 93 (22.7%) that delivered with PE within 2 weeks after presentation. Maternal and pregnancy characteristics of the study population are summarized in Table 1. There were no significant differences between those that delivered with PE within 2 weeks after presentation and unaffected pregnancies in most maternal and pregnancy characteristics, including diastolic blood pressure at presentation. However, in the PE group, compared with unaffected pregnancies, systolic blood pressure, GlyFn and sFlt-1/PlGF were higher and PlGF was lower.

The screen-positive rate for sFlt-1/PlGF ratio of 85 was 46.2%. The cut-off corresponding to a screen-positive rate of 46.2% was 75 pg/mL for PlGF and 510 µg/mL for GlyFn. Correlations between $\log_{10}$ GlyFn and $\log_{10}$ sFlt-1 was 0.531 (95% CI, 0.457–0.597), between $\log_{10}$ GlyFn and $\log_{10}$ PlGF was −0.405 (95% CI, −0.483 to −0.321) and between $\log_{10}$ PlGF and $\log_{10}$ sFlt-1 was −0.644 (95% CI, −0.698 to −0.584).

Table 1 Maternal and pregnancy characteristics of study population, according to whether they delivered with pre-eclampsia (PE) within 2 weeks after presentation

Characteristic	*No PE ≤ 2 weeks* (n = *316*)	*PE ≤ 2 weeks* (n = *93*)	P*
Maternal age (years)	34.5 (30.5–37.2)	34.0 (30.0–37.5)	0.869
Maternal weight (kg)	75.0 (64.0–87.3)	74.0 (63.0–84.0)	0.231
Maternal height (cm)	165 (161–170)	165 (161–171)	0.606
BMI (kg/m^2)	27.0 (23.4–32.7)	26.7 (23.6–30.5)	0.173
GA at presentation (weeks)	35.6 (32.7–37.4)	36.7 (36.0–38.4)	< 0.0001
Ethnicity			0.736
White	195 (61.7)	53 (57.0)	
Black	100 (31.6)	32 (34.4)	
South Asian	20 (6.3)	8 (8.6)	
Mixed	1 (0.3)	0 (0)	
Type-1 DM	5 (1.6)	1 (1.1)	0.443
Type-2 DM	5 (1.6)	0 (0)	0.443
Smoker	4 (1.3)	1 (1.1)	1
Family history of PE	41 (13.0)	14 (15.1)	0.731
Method of conception			0.558
Natural	285 (90.2)	83 (89.2)	
In-vitro fertilization	28 (8.9)	10 (10.8)	
Ovulation drugs	3 (0.9)	0 (0)	
Parity			0.715
Nulliparous	197 (62.3)	62 (66.7)	
Parous, no previous PE	77 (24.4)	21 (22.6)	
Parous, previous PE	42 (13.3)	10 (10.8)	
Biomarker			
SBP (mmHg)	142 (138–146)	144 (140–150)	0.003
DBP (mmHg)	91.5 (89.0–95.0)	92.0 (89.8–94.8)	0.125
GlyFn (µg/mL)	453 (333–616)	585 (424–804)	< 0.0001
PlGF (pg/mL)	86.7 (50.8–170.6)	58.9 (31.4–103.3)	< 0.0001
sFlt-1/PlGF	64.1 (18.2–146.9)	143.3 (64.2–329.7)	< 0.0001

Data are given as median (interquartile range) or *n* (%). *Chi-square test or Fisher's exact test for categorical variables and Student's *t*-test for continuous variables. BMI, body mass index; DPB, diastolic blood pressure; DM, diabetes mellitus; GA, gestational age; GlyFn, glycosylated fibronectin; PlGF, placental growth factor; SBP, systolic blood pressure; sFlt-1, soluble fms-like tyrosine kinase-1.

Predictive performance

The distribution of GlyFn, PlGF and sFlt-1/PlGF ratio in pregnancies delivering with PE within 2 weeks after presentation and unaffected pregnancies is shown in Figure 1. The proportions of screen-positive cases that delivered with PE within 2 weeks overall and in each gestational-age range at presentation (< 34 weeks, 34 + 0 to 35 + 6 weeks, 36 + 0 to 37 + 6 weeks and ≥ 38 weeks) are presented in Table 2 and compared in Figure 2.

For each one of the three approaches, GlyFn, PlGF and sFlt-1/PlGF ratio, there was a good separation between those that delivered with PE within 2 weeks and those that did not deliver with PE when the gestational age at sampling was < 34 weeks and, with increasing gestational age at sampling, there was increasing overlap in the proportions between the two groups (Figure 2).

ROC curves for the prediction of delivery with PE within 2 weeks after presentation by GlyFn, PlGF and sFlt-1/PlGF are shown in Figure 3. For all women,

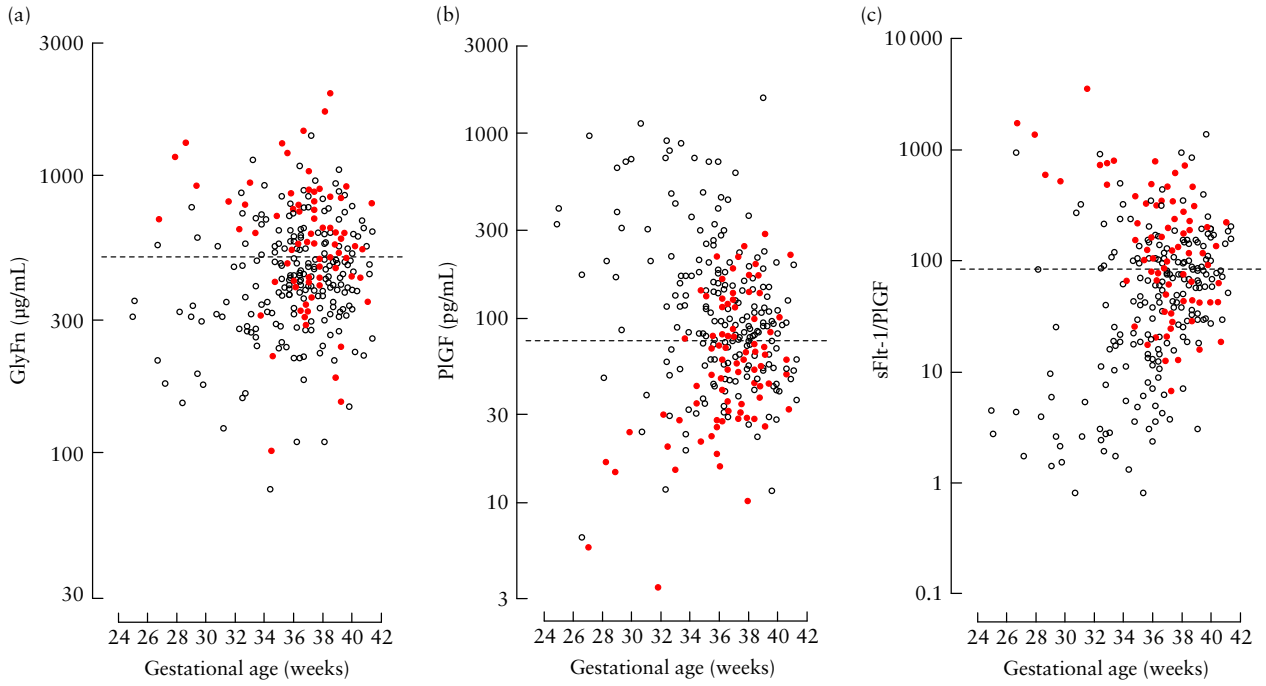

Figure 1 Distribution of glycosylated fibronectin (GlyFn) (a), placental growth factor (PlGF) (b) and soluble fms-like tyrosine kinase-1 (sFlt-1) to PlGF ratio (c) in women delivering with pre-eclampsia within 2 weeks after presentation with new-onset hypertension (●) and unaffected pregnancies (○). Dashed line indicates cut-off at screen-positive rate of 46.2%.

Table 2 Predictive performance for delivery with pre-eclampsia within 2 weeks after presentation with new-onset hypertension, according to gestational age at blood sampling

Method of screening	*SPR (n/N (%))*	*FPR (n/N (%))*	*DR (n/N (%, 95% CI))*
GlyFn ≥ 510 μg/mL			
Total	189/409 (46.2)	131/316 (41.5)	58/93 (62.4, 51.7–72.2)
< 34 weeks	54/118 (45.8)	44/108 (40.7)	10/10 (100, 69.2–100)
34 + 0 to 35 + 6 weeks	41/92 (44.6)	32/79 (40.5)	9/13 (69.2, 38.6–90.9)
36 + 0 to 37 + 6 weeks	49/102 (48.0)	24/62 (38.7)	25/40 (62.5, 45.8–77.3)
≥ 38 weeks	45/97 (46.4)	31/67 (46.3)	14/30 (46.7, 28.3–65.7)
PlGF ≤ 75 pg/mL			
Total	189/409 (46.2)	133/316 (42.1)	56/93 (60.2, 49.5–70.2)
< 34 weeks	58/118 (49.2)	48/108 (44.4)	10/10 (100, 69.2–100)
34 + 0 to 35 + 6 weeks	37/92 (40.2)	30/79 (38.0)	7/13 (53.8, 25.1–80.8)
36 + 0 to 37 + 6 weeks	45/102 (44.1)	25/62 (40.3)	20/40 (50.0, 33.8–66.2)
≥ 38 weeks	49/97 (50.5)	30/67 (44.8)	19/30 (63.3, 43.9–80.1)
sFlt-1/PlGF ≥ 85			
Total	188/409 (46.0)	130/316 (41.1)	58/93 (62.4, 51.7–72.2)
< 34 weeks	56/118 (47.5)	46/108 (42.6)	10/10 (100, 69.2–100)
34 + 0 to 35 + 6 weeks	43/92 (46.7)	35/79 (44.3)	8/13 (61.5, 31.6–86.1)
36 + 0 to 37 + 6 weeks	49/102 (48.0)	25/62 (40.3)	24/40 (60.0, 43.3–75.1)
≥ 38 weeks	40/97 (41.2)	24/67 (35.8)	16/30 (53.3, 34.3–71.7)

DR, detection rate; FPR, false-positive rate; GlyFn, glycosylated fibronectin; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1; SPR, screen-positive rate.

irrespective of gestational age at presentation, the area under the ROC curve (AUC) was 0.653 (95% CI, 0.587–0.718) for GlyFn, 0.643 (95% CI, 0.581–0.705) for PlGF and 0.685 (95% CI, 0.626–0.744) for sFlt-1/PlGF ratio. For women presenting at < 36 weeks' gestation, the AUC was 0.739 (95% CI, 0.618–0.861) for GlyFn, 0.785 (95% CI, 0.686–0.885) for PlGF and 0.818 (95% CI, 0.727–0.909) for sFlt-1/PlGF. There were no significant differences in performance between the three methods of screening, either for all patients or for those presenting at < 36 weeks.

DISCUSSION

Main findings

This study in women with a singleton pregnancy presenting with new-onset hypertension at 24–41 weeks' gestation found that the predictive performance for delivery with PE within 2 weeks after presentation of serum GlyFn is similar to that of PlGF and the sFlt-1/PlGF ratio, but GlyFn may be the preferred option because it is measured using a rapid point-of-care test. However, the

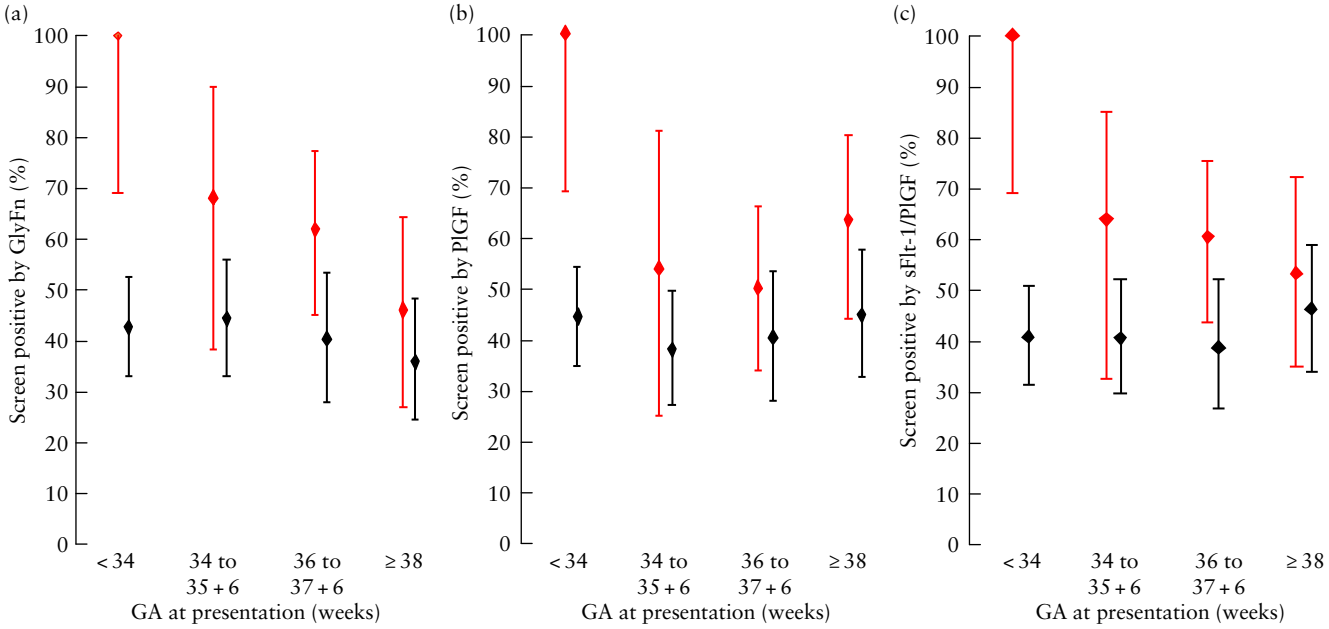

Figure 2 Proportion of women that delivered with pre-eclampsia (PE) within 2 weeks of sampling (◆) and those that did not deliver with PE within 2 weeks (◆) screening positive by glycosylated fibronectin (GlyFn) (a), placental growth factor (PlGF) (b) and soluble fms-like tyrosine kinase-1 (sFlt-1) to PlGF ratio (c). GA, gestational age.

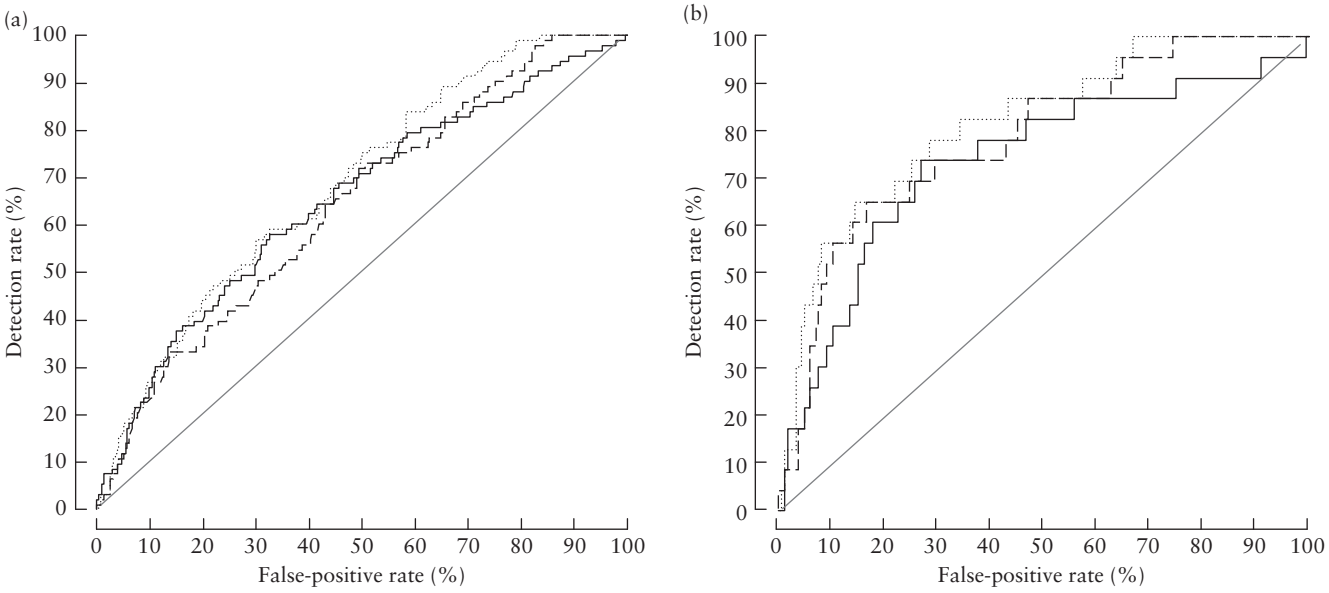

Figure 3 Receiver-operating-characteristics curves for prediction of delivery with pre-eclampsia within 2 weeks after presentation in women with new-onset hypertension by glycosylated fibronectin (——), placental growth factor (PlGF) (- – -) and soluble fms-like tyrosine kinase-1 to PlGF ratio (·····), in all women (a) and in those presenting at < 36 weeks' gestation (b).

predictive performance for all tests was relatively poor, with detection rates of about 60%, at a screen-positive rate of about 45%.

Comparison with findings of previous studies

Previous studies have demonstrated that PlGF, mean arterial pressure (MAP) and uterine artery pulsatility index are useful biomarkers in screening for preterm PE at 11–13 weeks' gestation, with detection rates for preterm PE of 75% at a screen-positive rate of 10%[19,20]. In a recent study, we suggested that GlyFn is a potentially useful first-trimester biomarker for preterm PE[21]. We have also reported that prediction of term PE is achieved by screening at 35–37 weeks' gestation by a combination of maternal risk factors with MAP, PlGF and sFlt-1, with a detection rate for term PE of about 70% at a screen-positive rate of 10%[22–24].

In relation to women presenting to specialist clinics, a landmark study of Zeisler *et al.*[7] examined the predictive performance of sFlt-1/PlGF ratio > 38 in a heterogeneous group of women presenting with signs and/or symptoms of hypertensive disorders at 24–37 weeks' gestation. The detection rate and false-positive rate for PE within 1 week after assessment were 80% and 22%, respectively. Another study in women presenting with signs and/or symptoms of hypertensive disorders highlighted the importance of using low serum PlGF (< 5th percentile)[5]. The detection rate and false-positive rate for PE within 2 weeks after assessment in pregnancies presenting at < 35 weeks' gestation were 96% and 45%, respectively; the respective values in those presenting at 35 + 0 to 36 + 6 weeks were 70% and 36%[5]. The authors of these studies[5,7] suggested that their biomarker cut-offs are highly predictive of imminent PE and that high sFlt-1/PlGF ratio or low PlGF could be used to stratify women into a high-risk group in need of intensive surveillance or hospitalization and delivery and a low-risk group that could be reassured that imminent PE was unlikely. The findings from these two studies[5,7] are consistent with those of the present study regarding PlGF and sFlt-1/PlGF ratio, i.e. moderate detection rate of imminent PE, but at high screen-positive rate.

In the case of GlyFn, Huhn *et al.*[10] examined 151 women with risk factors for PE or clinical signs and symptoms of PE at 20–37 weeks' gestation; 32 (21%) women developed PE within 4 weeks. The predictive performance of GlyFn for imminent PE was very high (AUC, 0.94; detection rate, 91%; false-positive rate, 14%) and similar to that of other serum biomarkers, including PlGF (AUC, 0.90; detection rate, 81%; false-positive rate, 17%) and sFlt-1 (AUC, 0.92; detection rate, 84%; false-positive rate, 9%)[25]. Another study by Nagalla *et al.*[11] reported on 798 pregnant women at ≥ 20 weeks' gestation who were enrolled in a prospective case–control study; 135 had PE, 194 had GH and 469 were normotensive. The predictive performance for PE was very high for GlyFn (AUC, 0.99; detection rate, 98.5%; false-positive rate, 7.2%) and PlGF (AUC, 0.96; detection rate, 91.9%; false-positive rate 7.9%), but not so for sFlt-1 (AUC, 0.86; detection rate, 97%; false-positive rate, 56.3%). The findings of these two studies[10,11] indicate a much higher detection rate for PE and much lower false-positive rates compared with the present study. One possible explanation for this discrepancy is that Huhn *et al.*[10] and Nagalla *et al.*[11] did not include cases of GH when calculating false-positive rates, whereas in our study, all false-positive cases had GH.

Interpretation of results and implications for clinical practice

We have demonstrated previously the value of screening for preterm PE at 11–13 weeks' gestation and screening for term PE at 35–37 weeks with use of the competing-risks approach; essentially, information from maternal demographic characteristics and medical history are combined with multiples of the median values of biomarkers, adjusted for maternal factors, to provide accurate and reproducible personalized assessment of risks[19–26]. We have also advocated that the same approach be used in the prediction of imminent PE in women presenting to specialist clinics with some signs and/or symptoms of hypertensive disorder[24–26]. We suggested that use of cut-offs in measured biomarkers or their ratio to define clinical management has the advantage of simplicity. However, such simplicity would be truly advantageous only if there was no overlap in the distributions of biomarkers between women that would develop imminent PE and those that would not; in this case, the test would be diagnostic. However, the findings of this study indicate that this is not so for the proposed biomarkers.

The use of risk cut-offs for stratification of pregnancy care is limited because: first, it does not take into account the prior risk of the individual patient based on maternal characteristics and medical history; second, it does not adjust the measured biomarkers for those maternal and pregnancy characteristics that are known to affect these measurements; third, it ignores the level of deviation from normal of blood pressure, which is an integral part of the condition under investigation; and fourth, it does not quantify the patient-specific risk and lacks the necessary flexibility of allowing healthcare professionals to select the desired proportion of cases with imminent PE that can be allocated to the high-risk group[25,26]. We proposed that use of the competing-risks approach overcomes these limitations and can form the basis of future research that would quantify and incorporate into the model symptoms, such as headache and visual symptoms, as well as proteinuria, creatinine, liver enzymes and platelets. However, in this study, we used the traditional approach of risk cut-offs in order to make our results comparable to those of previous studies advocating such an approach, because the objective was to evaluate a new biomarker by comparison with the traditional ones. Moreover, in our population of women presenting with new-onset hypertension, there was no significant difference in maternal characteristics and diastolic blood pressure between those who delivered with PE within 2 weeks after presentation and those who persisted with GH (Table 1).

Strengths and limitations

The main strength of this study is the examination of a large population of pregnant women with new-onset hypertension, rather than a heterogeneous group with signs and/or symptoms of hypertensive disorder, as was the case for previous studies, in which measurement of blood pressure and demonstration of hypertension was not an inclusion criterion. For example, in the two studies advocating for the use of PlGF[5] or sFlt-1/PlGF ratio[7] for stratification of care, new-onset hypertension or worsening pre-existing hypertension was present in only 79% and 41% of patients, respectively. As all women in our study had hypertension, we were able to examine the performance of GlyFn, by comparison with other biomarkers, in the prediction of subsequent development of PE.

We found no significant difference between GlyFn and other screening methods in predictive performance for PE. Despite, to our knowledge, our study being the largest to date to investigate this topic, the number of cases is still small for definitive conclusions to be drawn. Another limitation of the study is that sFlt-1 and PlGF were measured at the time of presentation in fresh maternal blood samples, introducing potential bias because of interassay variation over the duration of the study; in contrast, GlyFn was measured in one batch over a period of a few days in stored serum samples.

Conclusions

Measurement of GlyFn is a simple test that can be carried out using a point-of-care device without need for a laboratory and provide results within 10 min of testing. In this respect, it could potentially replace other tests that are used currently in the prediction of PE in women presenting with new-onset hypertension. However, the predictive performance for all tests is relatively poor, with detection rates of about 60%, at a screen-positive rate of about 45%.

ACKNOWLEDGMENT/DISCLOSURES

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