

Introduction

The uteroplacental dysfunction in pre-eclampsia is mediated by circulating angiogenic factors released by the placenta. Placental growth factor (PLGF) is a glycoprotein that exerts its activity by binding to the receptor of the angiogenic factor, vascular endothelial growth factor (VEGF). In normal pregnancies, PLGF levels increases during the first two trimesters and decrease during the third trimester. However, significantly lower levels of PLGF is associated with pre-eclampsia, leading to its use as part of pre-eclampsia assessment. PLGF based tests are recommended by NICE to help rule in/rule out pre-eclampsia leading to earlier diagnosis and help decide on care given in pregnancy. We introduced the Perkin Elmer based PLGF assay, which was cost saving at the Nottingham University Hospital NHS, and also determined the cut-off as a rule in/rule out test.

Benefits of PLGF testing

PLGF-based testing can reassure pregnant women with hypertension who are anxious about complications and risks to the baby and themselves and increase their confidence in treatment plans. Improves risk assessment and enable early planning for a safe birth including transfer to a suitably equipped centre. Help avoid stressful last-minute medical interventions. Better identification of women who is unlikely to develop preterm pre-eclampsia, reducing unnecessary hospitalisation.

Research questions

- 1) Can PLGF be used to rule out pre-eclampsia?
- 2)What is the suitable cut-off value for the DELFIA Xpress PIGF-123 assay for the rule-out of pre-eclampsia between 20 weeks and 34 weeks plus 6 days gestation.
- 3) If PLGF can rule-out pre-eclampsia what are the potential cost-savings to Nottingham University Hospital if it was introduced?

Methods

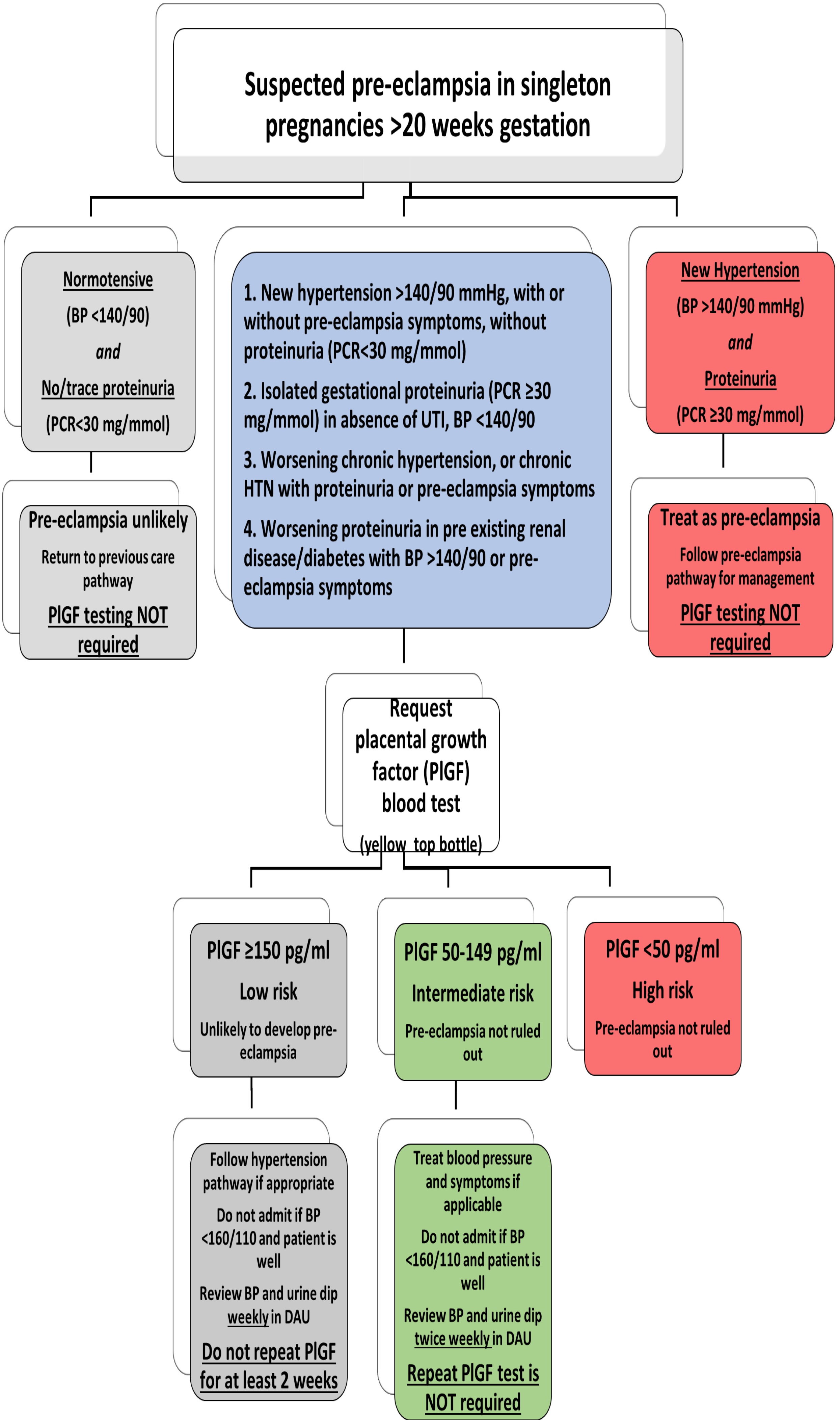
Pregnant women between 20 weeks and 34 weeks plus 6 days of gestation, presenting with hypertension and/or proteinuria, with or without symptoms consistent with pre-eclampsia had PIGF levels measured using the same serum samples utilised for current pre-eclampsia investigations. Following completion of the pregnancy the hospital system was investigated to determine if the PIGF levels correlate with patient out-comes and if PIGF can be used as a rule-out test for pre-eclampsia. If PIGF is identified as a suitable rule-out marker, the suitability of the manufacturer defined cut-off will be determined.

Result

Pre-eclampsia rule-in threshold of 50pg/ml had a sensitivity of 65% and specificity of 74.4% whereas a Pre-eclampsia rule-out threshold of 150pg/ml had a sensitivity of 96.2% and specificity of 34.9% .The negative predictive value as a rule out test is comparable to previous study at 93.8% (Bremner et al 2022, McCarthy et al 2019). The cost of this pre-eclampsia biomarker tests from NICE economic models showed that the DELFIA® Xpress PLGF 1-2-3 assay compared to its counterpart was significantly cheaper hence saving cost for the NHS.

PLGF level pg/ml	Interpretation
≥150	Rule out - Strong negative predictor for pre-eclampsia in the next four weeks
50-149	Indeterminate - Cannot be used to help plan management
<50	Rule in - Strong positive predictor of pre-eclampsia

Pre-eclampsia biomarker tests from NICE economic models	Cost per test (NICE)
Elecsys immunoassay sFlt-1/PLGF ratio (Roche)	£79.23
Triage PLGF Test (Quidel)	£49.58
DELFIA® Xpress sFlt-1/PLGF ratio	£71.41
DELFIA® Xpress PLGF 1-2-3	£37.41



Guideline implementation

Following the completion of this project, a guideline pathway was formulated for use at the department of obstetrics at Nottingham University Hospitals- (see attached pathway). This is to be used in conjunction with departmental guideline for ‘gestational hypertension and pre-eclampsia in the community and following referral to hospital’ to help to decide management for women where pre-eclampsia is suspected, not where it has been diagnosed.

PLGF levels <50 pg/ml and ≥150 pg/ml is being used to influence management decisions with respect to the need for admission to hospital, the need for BP and urine follow up checks within the community or hospital, and the frequency of this.

Conclusion

Rule in and rule out cut offs for PLGF are valid. DELFIA® Xpress PLGF 1-2-3 testing is now fully established for clinical usage at Nottingham University Hospital NHS.

References

NICE Diagnostics consultation document – PLGF-based testing to help diagnose suspected preterm pre-eclampsia (March 2022).

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Thadhani R, Mutter WP, Wolf M, Levine RJ, Taylor RN, Sukhatme VP, Ecker J and Karumanchi SA (2004). First trimester placental growth factor and soluble fms-like tyrosine kinase 1 and risk for preeclampsia. J. Clin Endocrinol Metab. 89, 770-775.

Rule-in and rule-out of pre-eclampsia using DELFIA Xpress PIGF 1-2-3 and sFlt-1: PIGF ratio. Bremner L, Gill C, Seed PT, Conti-Ramsden F, Webster L, Fleminger J, Chappell LC, Shennan A, Bramham K. 27, 2022, Pregnancy Hypertens, pp. 96-102.