sFlt/PlGF Ratio in the Management of Suspected Pre-eclampsia

TARGET AUDIENCE	All in Maternity
PATIENT GROUP	Maternity patients

Clinical Guidelines Summary

Pre-eclampsia is a leading cause of admissions, maternal and fetal morbidity

Many of the symptoms of pregnancy and the signs of medical conditions, such as essential hypertension and renal disease, mimic Pre-eclampsia and often the diagnosis is unclear

The sFlt/PLGF ratio is one test that has been recommended by NICE and by the recent Scottish Health Technologies Group (SHTG) report which have recommended this as one of the tests that can be use in the exclusion and prediction of suspected pre-eclampsia

The test is used between 20+0 weeks and 36+6 weeks in cases where the clinical diagnosis of pre-eclampsia is uncertain

Due to its high negative predictive value when the ratio is $\leq$38 (The likelihood of these women developing PET in the next 7 days is 0.4% (1.2% in 14 days and <3% in the next 28 days). Women can safely be discharged and manages as outpatients.

This guideline outlines the test, the inclusion and exclusion criteria and how it should be used in the clinical setting

It had now been prospectively audited continuously for a full four months and had been presented to the Department.

The data has informed changes in this updated version

Contents

Key Recommendations

- The sFlt/PlGF ratio is an aid for the exclusion of pre-eclampsia (PET). **It should not be used in patients admitted for PET, nor used to decide the timing of delivery.**
- The sFlt/PlGF ratio should be collected in addition to other investigations already taken for suspected PET. (Gold and purple blood tubes to be sent to lab)
- Amongst women with suspected PET where the clinical picture is unclear. The sFlt/PlGF ratio can be used to identify those women with a very low risk or to identify those with an increased risk. It should be used only in conjunction with existing local guidance for Hypertension/PET in pregnancy.

Background

PET is a multisystem disorder that carries a significant risk of maternal and/or fetal morbidity and mortality.

The current management of suspected PET usually involves admission to hospital for treatment and/or maternal and fetal monitoring. However, the manifestation and development of PET is varied, meaning that it is difficult to identify which women and babies are the most at risk of developing complications.

A blood test can be used to identify those women at very low or very high risk of imminently developing PET.[1] The sFlt/PlGF ratio measures the ratio of two biomarkers, soluble fms-like tyrosine kinase 1 (sFlt) and placental growth factor (PlGF).[2] This is raised in women with PET, as well as those who are developing PET.

This test can be used to assess the risk of developing PET, enabling appropriate admission or follow- up plans to be made.

Aims

By using the sFlt/PlGF ratio in women with suspected PET, we aim to guide admissions and follow-up by:

- Identifying women who are very unlikely to develop PET in the next 7-14 days.
- Identifying women who are at increased risk of developing PET in the next 7-14 days.
- Preventing unnecessary admissions for women with a low risk of developing PET.
- Increasing surveillance of women with a high risk of developing PET.

Scope

This guideline is intended to outline the minimum standard of care for all women with suspected PET within NHS Lanarkshire.

- This guideline is not intended for women with confirmed PET.
- This guideline should be regarded as additional to local hypertension/PET guidelines and should not replace it.

Definitions

Term	Definition
sFlt	Soluble fms-like tyrosine kinase 1
PlGF	Placental growth factor
PET	Pre-eclampsia
PCR	Protein:creatinine ratio (urine)
HELLP	Haemolysis Elevated Liver Low Platelets
DIC	Disseminated intravascular coagulation
HTN	Hypertension
FBC	Full blood count
U&Es	Urea and electrolytes (renal function)
LFTs	Liver function tests
G&S	Group and save/screen

Executive Summary

The sFlt/PlGF ratio can be used to identify women with a very low risk of developing PET within 7 days, or to identify those with an increased risk.

Where sFlt/PlGF may be used

- The sFlt/PlGF ratio should be taken in women of **20-36^{+6} weeks gestation with a singleton pregnancy** with suspected PET. It should not be used in patients who are already admitted.
- PET should be suspected in women with hypertension (≥140/90 mmHg) with significant proteinuria (PCR ≥30 mg/mmol or ≥2+ protein on urine dipstick) and/or evidence of end- organ dysfunction. For the listed criteria of suspected PET see the full guideline (Identifying Risk).
- Initial management of suspected PET should be commenced in accordance with existing local/national guidance, which may include referral to an assessment unit, review by a senior doctor, treatment of hypertension, quantification of proteinuria, PET blood tests and fetal monitoring.
- The sFlt/PlGF ratio should not be repeated within 14 days
- The sFlt/PlGF ratio should be clearly documented in the patient's notes along with the results of other investigations.

Interpretation (see Appendix 1, Page 8)

Amongst women of 20-36^{+6} weeks gestation with a singleton pregnancy and suspected PET:

- sFlt/PlGF ratio ≤38 represents a very low risk of developing PET within 7 days. Discharge may be considered, following review by a senior doctor (of at least registrar grade) if there is no other cause for clinical concern and if there is a suitable plan for outpatient monitoring.
- sFlt/PlGF ratio >38 but ≤85 represents an increased risk of developing PET within 7 days.
- Amongst women with an sFlt/PlGF ratio >38 but ≤85 and no evidence of significant proteinuria or end-organ dysfunction discharge may be considered, after review by a senior doctor (of at least registrar grade), if there is no other cause for clinical concern and if there is a suitable plan for outpatient monitoring.
- Women with an sFlt/PlGF ratio >38 but ≤85 **and** significant proteinuria or end-organ dysfunction should be reviewed by a senior doctor (of a least registrar grade). Admission and monitoring as per local PET guidance should be strongly considered.
- sFlt/PlGF ratio >85 represents a very high risk of developing PET within 7 days. The woman should be reviewed by a senior doctor (of a least registrar grade). Admission and monitoring as per local PET guidance should be strongly considered.

Women of at least 35^{+0} weeks gestation with suspected PET have a high risk of developing PET within 7 days. The woman should be reviewed by a senior doctor, admitted and monitored as per local PET guidance.

Guideline

Identifying Risk

Women with suspected PET should be referred to the maternity day assessment unit, as per local guidance. Several criteria contribute towards clinical suspicion of PET, which may include as isolated symptoms:[3] Those listed below represent likely PET and are **exclusion criteria** for the test

Hypertension >140/90 mmHg or significant rise from booking blood pressure

And/or including

- New onset proteinuria or worsening of pre-existing proteinuria
- Elevated serum creatinine
- Elevated transaminases
- Unexplained Right/upper abdominal pain
- Unexplained Seizures/ Altered mental state
- New-onset significant visual disturbance
- Signs/symptoms of stroke
- Hyperreflexia and/or clonus
- Severe headache
- Shortness of breath or other signs/symptoms of pulmonary oedema
- Low or decreasing haemoglobin or other signs/symptoms of haemolysis
- Severe Thrombocytopaenia (platelets <100,000/dL)
- Antepartum haemorrhage (Placental Abruption) or other signs/symptoms of DIC

Initial Management

Initial management of suspected PET should be commenced in accordance with existing local/national guidance, which may include referral to an assessment unit, review by a senior doctor, treatment of hypertension, quantification of proteinuria, PET blood tests and fetal monitoring.

For women of **20-36^{+6} weeks gestation with a singleton pregnancy** and **suspected** PET the following steps should be undertaken **in addition** to the usual management of suspected PET:

When doing a MAT-PET Screen please phone the lab at **6446** to let them know the MAT-PET Screen test is being sent

a. They will then do the quality control in anticipation of receiving the sample
   i. Takes 20-30 minutes

- On TRAK request: "**MAT-PET Screen**"(FBC, U&Es, LFTs, urate, +/-PCR and the sFlt/PlGF test will be in this order set)(gold and purple tops).
- SFlt-1/PlGF can also be requested on its own on TRAK
- The result should be awaited before a decision is made by a doctor (of at least registrar level) for discharge or admission (unless there is evidence of maternal/fetal compromise e.g. uncontrolled hypertension, suspected fetal distress).
- The sFlt/PlGF ratio should be clearly documented on Badger along with the results of other investigations.
- The sFlt/PlGF ratio should not be repeated within 14 days.
- The order set on TRAK for PET bloods is "**MAT-PET**" (FBC, U&Es, LFTs, urate, PCR)

Management at 20-36^{+6} weeks gestation

The algorithm for the interpretation of sFlt/PlGF ratio in women with suspected PET at 20-36^{+6} weeks gestation is displayed in **Appendix 1.**

For the purposes of this guideline the sFlt/PlGF ratio will be used.

sFlt/PlGF ratio ≤38

- These women are at very low risk of developing PET.
- The likelihood of these women developing PET in the next 7 days is 0.4% (1.2% in 14 days and <3% in the next 28 days).
- Women with sFlt/PlGF ≤38 should not be admitted for suspected PET, if this is deemed appropriate after review by a senior doctor (of at least registrar grade), **but** should be admitted if there is any other clinical reason, including uncontrolled hypertension.
- Outpatient treatment and follow-up should be considered for other conditions (e.g. hypertension, obstetric cholestasis) as per local guidance, following a medical review.
- Routine antenatal care should resume. The patient's consultant should be made aware of any new medical issues and seen at their high risk clinic as appropriate
- If there is new suspicion of PET following discharge, the woman should be re-referred for investigation as per local guidance, but sFlt/PlGF ratio should not be repeated within 14 days.

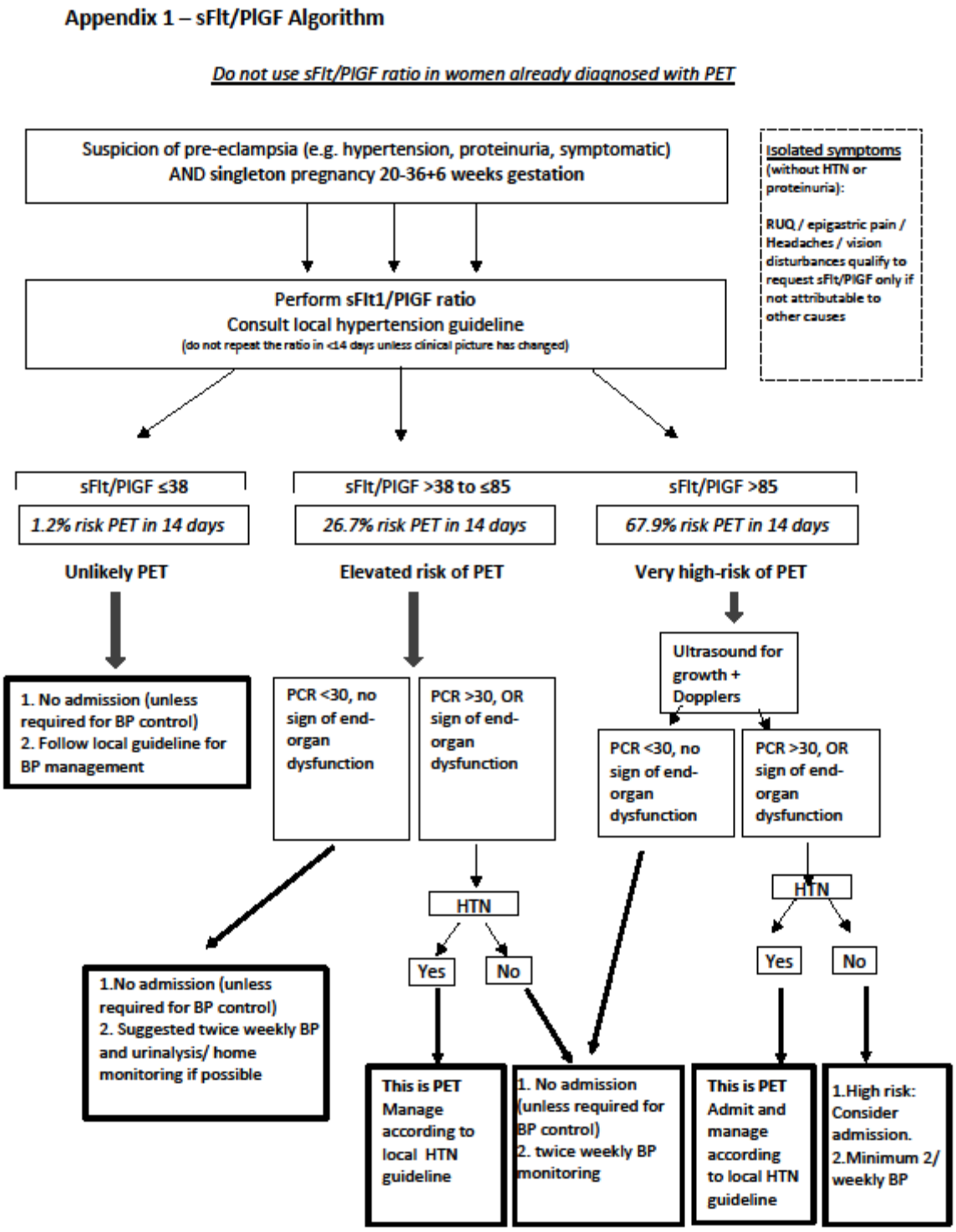
sFlt/PlGF ratio >38 but ≤85

- These women are at somewhat increased risk of developing PET.
- The likelihood of these women developing PET in the next 7 days is 20%(26.7% at 14 days)
- If there is no evidence of significant proteinuria or end-organ dysfunction (see "Identifying Risk" and ISSHP criteria[1]) the woman should not be admitted for suspected PET **but** should be admitted for any other clinical reason, including uncontrolled hypertension. A plan should be made for twice-weekly blood pressure checks and urinalysis with the community midwife.
- If discharged, a referral should be made from the maternity day assessment unit for a consultant antenatal clinic within 1 week.
- If there is evidence of significant proteinuria or end-organ dysfunction the woman should be reviewed by a senior doctor (of a least registrar grade). Admission and monitoring as per local PET guidance should be strongly considered.

sFlt/PlGF ratio >85

- These women are at very high risk of developing PET.
- The likelihood of these women developing PET in the next 7 days is 56% (67.9% in 14 days)
- The woman should be reviewed by a senior doctor (of a least registrar grade). Admission and monitoring as per local PET guidance should be strongly considered.

Appendix 1: sFlt/PlGF Algorithm



Appendix 2: Criteria for pre-eclampsia diagnosis or high suspicion of PET

(exclusion criteria for sFlt/PlGF test)

- **Hypertension ≥140/90 mmHg**

and *at least one of the following features:*

- Significant proteinuria (PCR ≥30 mg/mmol or ≥2+ protein on urine dipstick)
- Serum creatinine ≥90 micromol/L
- Elevated tranaminases (≥2 times the normal range)
- Unexplained Right/upper abdominal pain
- Unexplained Seizures
- Unexplained altered mental state
- New-onset visual disturbance
- Features of HELLP syndrome
- And may include
  - Low or decreasing haemoglobin or other signs/symptoms of haemolysis
  - Thrombocytopaenia (platelets <150,000/dL)
  - Antepartum Haemorrhage (Abruption) or other signs/symptoms of DIC
  - Signs/symptoms of stroke
  - Hyperreflexia and/or clonus
  - Severe headache

References

1. H Zeisler, et al. Predictive value of the sFlt:PlGF ratio in women with suspected preeclampsia. *New England Journal of Medicine* 2016; 374(1).

2. AS Cerdeira, et al. Angiogenic factors: potential to change clinical practice in pre-eclampsia? *British Journal of Obstetrics and Gynaecology* 2017. https://doi.org/10.1111/1471-0528.15042.

3. ISSHP. The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. *Pregnancy Hypertension* 2014; 4:97-104.

4. NICE: PLGF-based testing to help diagnose suspected preterm pre-eclampsia Diagnostics guidance [DG49]Published: 27 July 2022

5. Health Improvement Scotland, SHTG Recommendation March 2023. Placental growth factor (PlGF)-based testing to help diagnose suspected preterm pre-eclampsia

6. Scottish Government letter to Chief Executives, Medical Directors and Nurse Directors on pre-eclampsia and placental growth factor (plgf) testing in Scotland March 2024

7. Oxford and Thames Heath Innovation guideline: sFlt/PlGF ratio in the management of suspected preeclamsia 2018. Updated algorithm 2023. Last updated June 2024

Clinical Governance Appendices

1. Governance information for Guidance document

Lead Author(s):	Dr Surindra Maharaj
Endorsing Body:	Maternity Clinical Effectiveness Group
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Responsible Person (if different from lead author)	

CONSULTATION AND DISTRIBUTION RECORD	
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CHANGE RECORD

Date	Lead Author	Change	Version No.
18/10/24	S Maharaj	Original	1
17/6/2025	S Maharaj	Update following local audit Changes to lab procedures Changes to Gestational ages for test Amendment to Clinical Summary	2
			3
			4
			5

2.You can include additional appendices with complimentary information that doesn't fit into the main text of your guideline, but is crucial and supports its understanding.

e.g. supporting documents for implementation of guideline, patient information, specific monitoring requirements for secondary and primary care clinicians, dosing regimen/considerations according to weight and/or creatinine clearance