

CLINICAL CASE REPORTS

Preeclampsia without proteinuria: the role of the soluble fms-like tyrosine kinase-1 to placental growth factor ratio – a case report

Miguel Martins¹ , Catarina Veiga² , Inês Brás¹ , Rosário Almeida Lopes¹ , Ana Isabel Correia¹ , Osvaldo Moutinho¹ 

ABSTRACT

Background: Preeclampsia is a hypertensive disorder of pregnancy and an important cause of maternal and perinatal morbidity. The soluble fms-like tyrosine kinase-1 to placental growth factor ratio reflects placental angiogenic imbalance and may support diagnosis and short-term risk stratification.

Case Presentation: A 29-year-old primigravida developed new-onset hypertension at 34 weeks and 1 day without significant proteinuria, with preserved renal function and hyperuricaemia. The ratio was markedly elevated at 318.4, prompting admission, antenatal corticosteroids, and close maternal-fetal surveillance. At 34 weeks and 3 days, labour was induced because of persistent hypertension and rising transaminases, culminating in caesarean section for arrest of dilatation and non-reassuring fetal status. Maternal and neonatal outcomes were favourable.

Discussion: The biomarker supported risk stratification and escalation of care in an equivocal presentation.

Conclusion: Placental growth factor-based testing may complement clinical assessment in suspected preeclampsia without proteinuria.

Keywords: angiogenic biomarkers; hypertensive disorders of pregnancy; placental growth factor; preeclampsia; risk stratification; soluble fms-like tyrosine kinase-1.

1. Department of Obstetrics and Gynecology, Unidade Local de Saúde de Trás-os-Montes e Alto Douro. 5000-508 Vila Real, Portugal. intgomiguel.martins@gmail.com; mimbras@gmail.com; rosarioalmeidalopes@gmail.com; anacorreia87@gmail.com; osvaldomoutinho@gmail.com
2. Department of Nephrology, Unidade Local de Saúde Viseu Dão-Lafões. 3504-509 Viseu, Portugal. veiga_catarina@hotmail.com

INTRODUCTION

Preeclampsia is a pregnancy-specific hypertensive disorder and a leading cause of maternal and perinatal morbidity and mortality worldwide.⁽¹⁾ It is traditionally defined by new-onset hypertension after 20 weeks of gestation associated with proteinuria and/or evidence of maternal end-organ dysfunction.⁽²⁻⁴⁾ However, a subset of women develop preeclampsia without significant proteinuria, which may complicate diagnosis and clinical decision-making.⁽²⁻⁴⁾

Placental angiogenic imbalance plays a central role in the pathophysiology of preeclampsia.^(1,5) Increased circulating soluble fms-like tyrosine kinase-1 (sFlt-1) and reduced placental growth factor (PlGF) reflect this imbalance.^(1,5) The sFlt-1/PlGF ratio has emerged as a useful adjunctive tool for short-term risk stratification in women with suspected preeclampsia, particularly in equivocal clinical scenarios.⁽⁶⁻¹⁰⁾ Current guidelines emphasise that angiogenic biomarkers should be interpreted within the overall clinical context and should not replace established diagnostic criteria.^(2-4,10,11)

We report a case of suspected preeclampsia without proteinuria at 34 weeks' gestation, in which a markedly elevated sFlt-1/PlGF ratio supported escalation of care within an institutional protocol.

CASE DESCRIPTION

A 29-year-old Caucasian primigravida, with no relevant past medical history, was followed in a high-risk pregnancy clinic because of an increased risk of preeclampsia identified at first-trimester screening. Prophylaxis with acetylsalicylic acid 150 mg/day was initiated early in pregnancy, with good reported adherence. Antenatal follow-up was regular, and serial ultrasound examinations showed appropriate fetal growth, with estimated fetal weight between the 13th and 17th percentiles for gestational age.

At 34 weeks and one day of gestation, new-onset hypertension was detected during routine assessment, with a blood pressure reading of 140/100 mmHg in a previously normotensive woman. Subsequent measurements confirmed persistent elevation in the non-severe range. The patient was asymptomatic, denying headache, visual disturbances, epigastric or right upper quadrant pain, dyspnoea, nausea, vomiting, or reduced fetal movements.

Physical examination revealed a woman in good general condition, without peripheral oedema, abdominal tenderness, or neurological abnormalities. Deep tendon reflexes were normal and clonus was absent.

Laboratory evaluation demonstrated preserved renal function and normal haematological parameters, with a platelet count of $210 \times 10^9/L$ and serum creatinine of 64 $\mu\text{mol/L}$. Liver enzymes were initially within the upper limit of normal but showed a mild upward trend during admission (aspartate aminotransferase [AST] from 32 to 48 U/L;

alanine aminotransferase [ALT] from 35 to 55 U/L). Lactate dehydrogenase and bilirubin levels were normal. Uric acid was mildly elevated (369 $\mu\text{mol/L}$).

Proteinuria assessment was performed on a spot urine sample, showing a protein/creatinine ratio of 20 mg/mmol, below the institutional diagnostic threshold for proteinuric preeclampsia (≥ 34 mg/mmol).

Given the diagnostic uncertainty between gestational hypertension and preeclampsia without proteinuria, angiogenic biomarkers were measured. The sFlt-1/PlGF ratio was markedly elevated at 318.4, exceeding the institutional high-risk cut-off for gestations beyond 34 weeks.

The patient was admitted for close maternal and fetal surveillance. Fetal assessment, including cardiotocography and ultrasound evaluation, was reassuring. Antenatal corticosteroid therapy was administered for fetal lung maturation.⁽¹²⁾

At 34 weeks and three days of gestation, in the context of persistent hypertension, rising liver transaminases, and a high sFlt-1/PlGF ratio, a multidisciplinary decision was made to proceed with delivery in accordance with the institutional protocol. The angiogenic biomarker result was interpreted as an adjunctive tool supporting increased short-term maternal risk rather than as a standalone indication for delivery.

Labour induction was initiated but was complicated by arrest of dilatation and the development of non-reassuring fetal status, leading to caesarean section. A male newborn weighing 1884 g was delivered, with Apgar scores of 6, 8, and 10 at 1, 5, and 10 minutes, respectively. The newborn was admitted to the neonatal intensive care unit, with favourable subsequent evolution.

Postpartum, the patient received magnesium sulfate for seizure prophylaxis in the context of preeclampsia with severe features (hepatic involvement) and was started on antihypertensive therapy.^(4,13) Clinical evolution was favourable, and she was discharged home on postpartum day 7, asymptomatic, with outpatient follow-up scheduled.

DISCUSSION

This case highlights the diagnostic challenges associated with preeclampsia without proteinuria. At presentation, the absence of significant proteinuria, preserved renal function, and normal platelet count could suggest gestational hypertension. However, the persistence of hypertension and the subsequent biochemical evolution raised concern for evolving preeclampsia.⁽²⁻⁴⁾

The markedly elevated sFlt-1/PlGF ratio indicated significant angiogenic imbalance and increased short-term maternal risk.⁽⁶⁻⁹⁾ Consistent with current evidence and guideline recommendations, this biomarker was used as an adjunctive tool to support inpatient surveillance and preparedness for delivery, rather than as a standalone diagnostic criterion or sole determinant of delivery timing.^(2,5-11) Ultimately, the

decision to proceed with delivery was guided by clinical and laboratory progression in the context of gestational age and fetal maturity.^(4,11,14)

The potential budget impact of sFlt-1/PlGF ratio implementation has also been evaluated from the perspective of the Portuguese public healthcare system.⁽¹⁵⁾

This case supports the use of angiogenic biomarkers as complementary tools in equivocal presentations, while reinforcing that clinical judgement and established diagnostic criteria remain central to management decisions.^(2,5-11)

Preeclampsia without proteinuria remains a diagnostic challenge. The sFlt-1/PlGF ratio may provide valuable complementary information for short-term risk stratification and support escalation of care in selected cases. However, angiogenic biomarkers should not replace clinical assessment, and decisions regarding timing of delivery should continue to be guided by maternal and fetal status in accordance with established guidelines.^(2,4,11,14)

AUTHORSHIP

Miguel Martins - Conceptualization; Data curation; Investigation; Project administration; Writing – original draft; Writing – review & editing

Catarina Veiga – Investigation; Validation; Writing – original draft; Writing – review & editing

Inês Brás – Investigation; Writing – review & editing

Rosário Almeida Lopes – Conceptualization; Supervision; Validation; Writing – review & editing

Ana Isabel Correia - Investigation; Validation; Writing – review & editing

Osvaldo Moutinho - Supervision; Validation; Writing – review & editing

REFERENCES

1. Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: pathophysiology, challenges, and perspectives. *Circ Res*. 2019;124(7):1094-1112. <https://doi.org/10.1161/CIRCRESAHA.118.313276>
2. Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Karumanchi SA, *et al*. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis and management recommendations for international practice. *Pregnancy Hypertens*. 2022;27:148-169. <https://doi.org/10.1016/j.preghy.2021.09.008>
3. Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, *et al*. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. *Hypertension*. 2018;72(1):24-43. <https://doi.org/10.1161/HYPERTENSIONAHA.117.10803>
4. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 222: Gestational hypertension and preeclampsia. *Obstet Gynecol*. 2020;135(6):e237-e260. <https://doi.org/10.1097/AOG.0000000000003891>
5. Flint EJ, Cerdeira AS, Redman CW, Vatish M. The role of angiogenic factors in the management of preeclampsia. *Acta Obstet Gynecol Scand*. 2019;98(6):700-707. <https://doi.org/10.1111/aogs.13540>
6. Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennström M, *et al*. Predictive value of the sFlt-1:PlGF ratio in women with suspected preeclampsia. *N Engl J Med*. 2016;374(1):13-22. <https://doi.org/10.1056/NEJMoa1414838>
7. Verloren S, Herraiz I, Lapaire O, Schlembach D, Moertl M, Zeisler H, *et al*. The sFlt-1/PlGF ratio in different types of hypertensive pregnancy disorders and its prognostic potential in preeclamptic patients. *Am J Obstet Gynecol*. 2012;206(1):58.e1-8. <https://doi.org/10.1016/j.ajog.2011.07.037>
8. Velegrakis A, Kouvidi E, Fragkiadaki P, Sifakis S. Predictive value of the sFlt-1/PlGF ratio in women with suspected preeclampsia: an update. *Int J Mol Med*. 2023;52(4):89. <https://doi.org/10.3892/ijmm.2023.5292>
9. Ohkuchi A, Saito S, Yamamoto T, Minakami H, Masuyama H, Kumasawa K, *et al*. Short-term prediction of preeclampsia using the sFlt-1/PlGF ratio: a subanalysis of pregnant Japanese women from the PROGNOSIS Asia study. *Hypertens Res*. 2021;44(7):813-821. <https://doi.org/10.1038/s41440-021-00629-x>
10. National Institute for Health and Care Excellence (NICE). PlGF-based testing to help diagnose suspected preterm pre-eclampsia. HealthTech guidance HTG630. London: NICE; 2022. Accessed July 2026. Available from: <https://www.nice.org.uk/guidance/htg630>
11. National Institute for Health and Care Excellence (NICE). Hypertension in pregnancy: diagnosis and management. NICE guideline NG133. London: NICE; 2023. Accessed July 2026. Available from: <https://www.nice.org.uk/guidance/ng133>
12. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev*. 2017;3(3):CD004454. <https://doi.org/10.1002/14651858.CD004454.pub3>
13. Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *Lancet*. 2002;359(9321):1877-1890. [https://doi.org/10.1016/S0140-6736\(02\)08778-0](https://doi.org/10.1016/S0140-6736(02)08778-0)
14. Broekhuijsen K, van Baaren GJ, van Pampus MG, Ganzevoort W, Sikkema JM, Woiski MD, *et al*. Immediate delivery versus expectant monitoring for hypertensive disorders of pregnancy between 34 and 37 weeks of gestation (HYPITAT-II): an open-label, randomised controlled trial. *Lancet*. 2015;385(9986):2492-2501. [https://doi.org/10.1016/S0140-6736\(14\)61998-X](https://doi.org/10.1016/S0140-6736(14)61998-X)

15. Campos A, Machado A, Martins H, São José Pais M, Ersek K, Lopes N. sFlt-1/PIGF ratio for the predictive diagnosis of preeclampsia: budget impact analysis from the public healthcare perspective in Portugal. *Acta Obstet Ginecol Port.* 2019;13(2):82-90.

CORRESPONDENCE TO

Miguel Martins
Department of Obstetrics and Gynecology
Unidade Local de Saúde de Trás-os-Montes e Alto Douro
Av. da Noruega, Lordelo,
5000-508 Vila Real
Email: intgomiguel.martins@gmail.com

Received for publication: 08.06.2026
Accepted in revised form: 13.08.2026