

Urinary placental growth factor stability as a critical factor in the reliability of preeclampsia diagnosis

Eva Martínez-Marzo^{*1,2}, María Peran^{1,2}, Juan Lerma-Irureta¹, Ana Medel-Martínez¹, Cristina Paules^{1,3,4,5}, Daniel Oros^{1,3,4,5}, Marta Fabre^{1,2,4}

¹Instituto de Investigación Sanitaria de Aragón (IIS Aragón), Zaragoza, Spain

²Biochemistry Department, University Clinical Hospital Lozano Blesa, Zaragoza, Spain

³Obstetrics Department, University Clinical Hospital Lozano Blesa, Zaragoza, Spain

⁴Red RICORS "Primary Care Interventions to Prevent Maternal and Child Chronic Diseases of Perinatal and Developmental Origin", RD21/0012/0001, Instituto de Salud Carlos III, Madrid, Spain

⁵University of Zaragoza, Zaragoza, Spain

*Corresponding author: emartinezmarz@salud.aragon.es

Highlights

- Urinary placental growth factor (PIGF) may support diagnosis and prediction of preeclampsia
- First structured study assessing PIGF stability in urine samples
- The stability protocol used improves consistency across laboratories
- Urinary PIGF is stable for up to 48 hours when stored at 2-8 °C
- Urinary PIGF remains stable after two freeze-thaw cycles

Abstract

Introduction: Placental growth factor (PIGF) is a key biomarker for diagnosing and predicting preeclampsia (PE). While serum-based PIGF assays are well established, urine has emerged as a promising non-invasive alternative matrix. However, the absence of urinary PIGF stability data remains a major preanalytical limitation. This study aimed to assess urinary PIGF stability under common preanalytical conditions, including refrigerated storage and a double freeze-thaw cycle.

Materials and methods: A prospective study was conducted using urine samples from ten pregnant women. Each sample was processed under standard laboratory conditions and aliquoted into five tubes. One aliquot was immediately frozen at - 80 °C (T0), three were stored at 2-8 °C for 48, 96, and 168 hours before freezing, and one underwent a double freeze-thaw cycle. Urinary PIGF concentrations were measured using the Elecsys PIGF immunoassay on Roche Cobas e801 analyzer. Percent degradation (PD%) was calculated relative to baseline. A linear regression model was applied to estimate the time to exceed a maximum permissible instability (MPI) of $\pm 10\%$.

Results: Urinary PIGF remained stable at 2-8 °C for up to 48 hours, with a mean PD% of - 6 % (95% confidence interval (CI): - 9.1 to - 2.8). The regression model ($PD\% = - 0.0834 \times \text{Time (h)}$) estimated the - 10 % threshold at approximately 120 hours. After a double freeze-thaw cycle, the mean PD% was - 1.5 % (95% CI: - 3.4 to 0.4%).

Conclusions: Urinary PIGF shows acceptable stability for up to 48 hours under refrigeration and is stable over two freeze-thaw cycles. These findings provide essential preanalytical data supporting its potential use in clinical and research settings.

Keywords: placental growth factor; preanalytical phase; preeclampsia; stability; urine

Submitted: August 8, 2025

Accepted: January 15, 2026

Introduction

Preeclampsia (PE) is a leading cause of maternal and perinatal morbidity and mortality worldwide (1). It is characterized by placental dysfunction and

typically manifests after 20 weeks of gestation with new-onset hypertension and proteinuria (2). Early and accurate diagnosis is essential to reduce

<https://doi.org/10.11613/BM.2026.020701>

Biochem Med (Zagreb) 2026;36(2):020701

associated complications. The pathophysiology of PE has been strongly linked to an imbalance between angiogenic and antiangiogenic factors. Serum concentrations of soluble fms-like tyrosine kinase-1 (sFlt-1), an antiangiogenic molecule, are elevated in women with PE, while free circulating concentrations of placental growth factor (PIGF), a proangiogenic protein, are decreased (3). The serum sFlt-1/PIGF ratio has been incorporated into clinical algorithms and is recommended by international guidelines due to its high negative predictive value for PE diagnosis (4,5). Additionally, serum PIGF alone has demonstrated notable diagnostic performance (6,7).

While serum remains the standard matrix for angiogenic markers (sFlt-1 and PIGF), urine has gained increasing attention as a promising alternative sample. Its non-invasive and spontaneous collection, greater patient acceptability, and feasibility for repeated testing make it especially suitable for use in non-specialized or low-resource settings (8,9). Several studies have investigated urinary biomarkers for PE diagnostic. Proteomic analyses have identified candidates such as SERPINA1, uromodulin, albumin fragments and fibrinogen-derived peptides, which reflect endothelial and renal dysfunction in PE (10). Other analytes like activin A, inhibin A and sFlt-1 have also shown potential, particularly in multimarker models. However, PIGF has emerged as one of the most promising urinary biomarkers, showing consistent diagnostic performance even without creatinine adjustment (11).

A thorough understanding of an analyte's properties is essential prior to its clinical application. Assessing its stability under real-world preanalytical conditions is critical to ensure reliable measurement. Clinical laboratories often depend on published literature and manufacturer specifications to define acceptable storage times (12). Multiple studies have evaluated the stability of PIGF in serum over periods ranging from 48 hours to 30 days; however, their findings vary depending on storage conditions, analytical methods, and stability criteria (13-15). To our knowledge, no study has systematically assessed the stability of PIGF in urine, highlighting a key preanalytical gap that must be addressed before this matrix can be reliably implemented in clinical or research settings.

The aims of this study were to assess the stability of PIGF in urine samples stored refrigerated at 2-8 °C for up to seven days as well as after a double freeze-thaw cycle, reflecting typical preanalytical conditions encountered in hospital settings.

Materials and methods

Subjects

This prospective study was carried out at the University Clinical Hospital Lozano Blesa (Zaragoza, Spain) within the framework of project PI22/143, supported by the Instituto de Salud Carlos III (ISCI-III), Government of Spain. Following the protocol published by the Spanish Society of Laboratory Medicine (SEQC-ML) for the stability testing of biochemical analytes, ten urine samples were collected from pregnant women with suspected PE at various gestational ages (16). Sample collection was conducted between January and February 2025 and laboratory analysis was performed in April 2025.

The study was approved by the Research Ethics Committee of the Community of Aragón (C.I. PI19/346 and PI23/102) and all patients provided written informed consent.

Methods

From each participant, 10 mL of midstream urine was collected in sterile, additive-free VACUETTE Z urine no additive 10 mL tubes (Greiner Bio-One GmbH, Kremsmünster, Austria). All urine samples were centrifuged at 3500 rpm for five minutes at room temperature and the supernatant was aliquoted into five sterile round-bottom polystyrene tubes (500 µL each) (Deltalab, Barcelona, Spain). One aliquot was immediately frozen at - 80 °C (T_0), while the remaining three were stored refrigerated at 2-8 °C for 48, 96 and 168 hours, respectively, before being frozen at - 80 °C. An additional aliquot from each participant underwent a double freeze-thaw cycle to simulate a common preanalytical condition in research. All double freeze-thaw aliquots were frozen at - 80 °C immediately after collection (T_0). Four days later, each aliquot was completely thawed at room temperature for

approximately 30 minutes, ensuring full homogenization, and subsequently refrozen at -80°C , completing the first freeze–thaw cycle. The second thaw occurred on the day of laboratory analysis, when all aliquots were thawed simultaneously and analyzed in a single batch within two hours to minimize analytical variability. Because samples were collected on different dates, the interval between the second freezing and final thaw varied from 38 to 80 days. A flowchart illustrating the sample processing workflow is presented in Figure 1.

Urinary PIGF concentrations were measured using the Elecsys PIGF immunoassay (lot 796564), run on Roche Cobas e801 analyzer (Roche Diagnostics, Basel, Switzerland). As no immunoassay is currently validated for urinary PIGF measurement, analytical performance of the system was monitored using routine serum internal quality controls at low ($\approx 50\text{ pg/mL}$) and high ($\approx 100\text{ pg/mL}$) concentration levels, showing inter-assay coefficients of variations (CVs) of 3.1 % and 3.3 %, respectively. All

samples were analyzed in duplicate, and the average of both replicates was used in all calculations.

Statistical analysis

For each time point, the percent degradation (PD%) was calculated relative to baseline using the following formula: $\text{PD}\% = ((T_x - T_0) / T_0) \times 100$, where T_0 is the baseline PIGF concentration and T_x the concentration at the specified time point. The mean PD%, standard deviation (SD) and 95% confidence interval (CI) were calculated for each storage condition. According to the SEQC-ML protocol, an analyte was considered stable if the mean $\text{PD}\% \pm 95\%$ CI remained within the maximum permissible instability (MPI) (16). An MPI threshold of $\pm 10\%$ was adopted for defining analyte stability.

To model the degradation trend over time, a linear regression analysis was performed using the PD% values. The regression line was constrained to pass through the origin, in accordance with the SEQC-

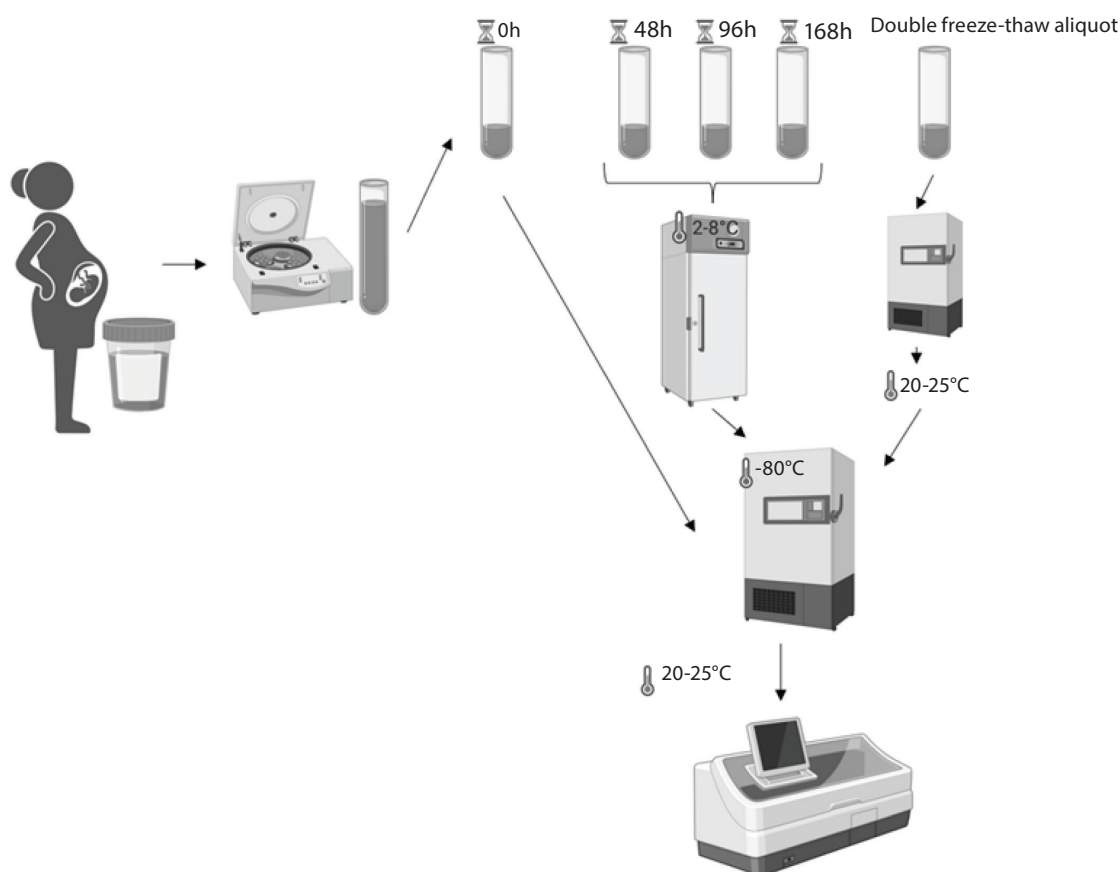


FIGURE 1. Flowchart of the stability study process from sampling to analysis. The figure was created using BioRender.com.

ML comprehensive stability protocol, reflecting the biological assumption of no degradation at time zero (16). The resulting regression equation was: $PD\% = -0.0834 \times \text{Time (h)}$, with a coefficient of determination $R^2 = 0.97$.

All statistical analyses were performed using Jamovi v2.6 (The jamovi project, Sydney, Australia) and Microsoft Excel 365 MSO version 2505 (Microsoft Corporation, Redmond, USA).

Results

Urinary stability of PIGF was evaluated in samples obtained from ten pregnant women. Baseline concentrations ranged from 97 to 371 pg/mL. The mean PIGF concentration for each individual sample at every storage time point is shown in Figure 2, allowing a visual comparison of analyte behavior over time.

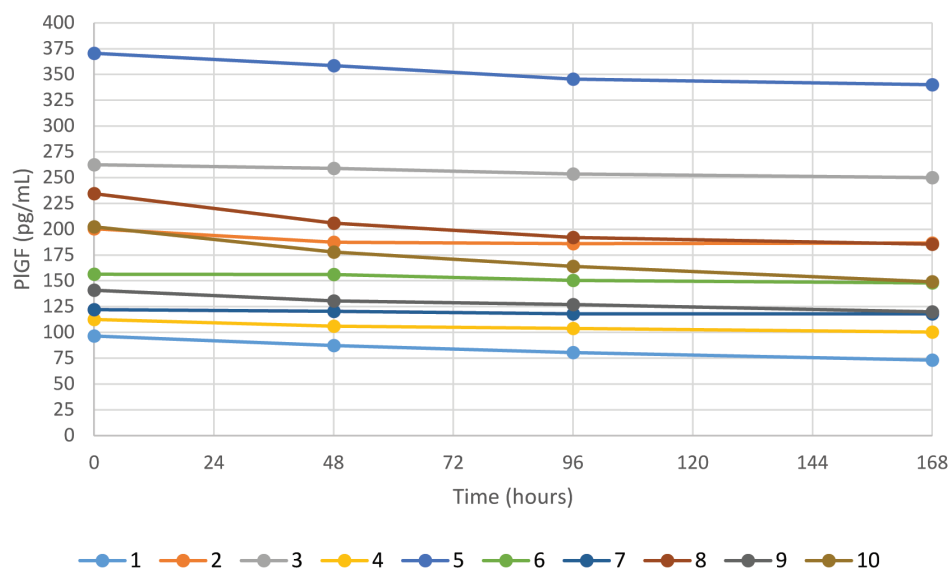


FIGURE 2. Urinary PLGF concentrations for all samples at each time point. PIGF - placental growth factor.

TABLE 1. Individual percent degradation (PD%) values and group means with 95% confidence intervals for urinary PIGF concentrations

Individual PD%	48 hours	96 hours	168 hours
Sample 1	- 9.5 %	- 16.7 %	- 24.3 %
Sample 2	- 6.5 %	- 7.2 %	- 7 %
Sample 3	- 1.3 %	- 3.4 %	- 4.8 %
Sample 4	- 5.8 %	- 7.6 %	- 10.8 %
Sample 5	- 3.2 %	- 6.8 %	- 8.2 %
Sample 6	- 0.3 %	- 3.5 %	- 5.1 %
Sample 7	- 1.2 %	- 3.3 %	- 3.3 %
Sample 8	- 12.2 %	- 18.1 %	- 20.9 %
Sample 9	- 7.5 %	- 9.9 %	- 14.9 %
Sample 10	- 12.1 %	- 19 %	- 26.4 %
Average PD% (95% CI)	- 6% (- 9.1 to - 2.8)	- 9.6% (- 14 to - 5.1)	- 12.6% (- 18.7 to - 6.4)

PIGF - placental growth factor.

To assess analyte stability, the PD% relative to the baseline value was calculated for each sample after 48, 96 and 168 hours of refrigerated storage at 2-8 °C with the corresponding average PD% and 95% CI (Table 1).

At 48 hours, mean degradation remained within the acceptable MPI threshold of - 10 %, indicating adequate analyte stability. At 96 hours, however, the lower bound of the 95% CI crossed this threshold, suggesting that analyte stability may no longer be guaranteed. By 168 hours, a marked increase in degradation was observed and most samples exceeded the instability limit (Figure 3A).

Based on the linear regression equation, the estimated time at which PD% reaches the - 10 % MPI threshold is approximately 120 hours (5 days) (Figure 3B).

Finally, the effect of a double freeze-thaw cycle on PIGF stability was evaluated. The mean PD% following the second thaw was - 1.5 %, with a 95% CI of - 3.4 % to 0.4 %, indicating minimal impact on stability (Figure 4).

Discussion

This study provides the first structured assessment of urinary PIGF stability under conditions that sim-

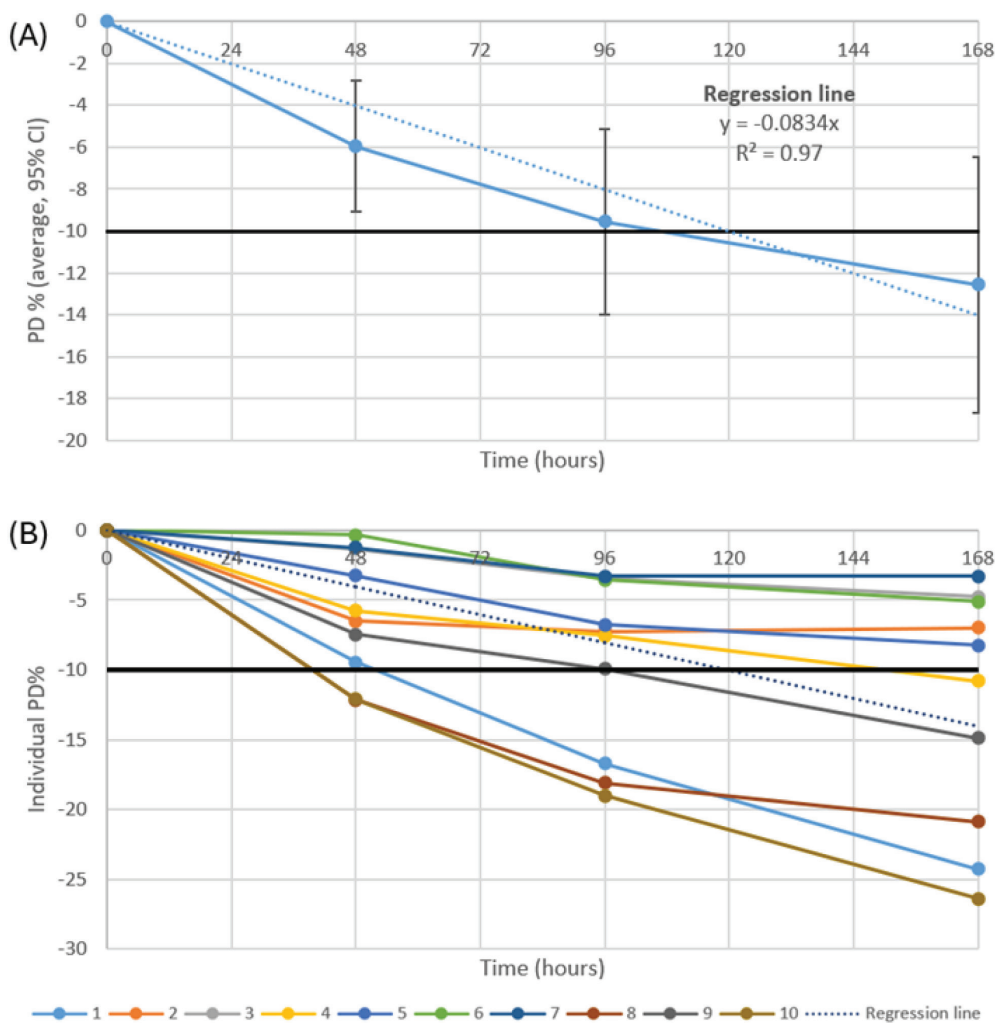


FIGURE 3. (A) Average PD% with 95% confidence intervals at each storage time point for PIGF stability measurement; (B) Individual PD% trajectories for each sample. The dashed line indicates the regression model and the solid black line marks the MPI threshold of - 10 %. PIGF - placental growth factor. PD% - percent degradation. MPI - maximum permissible instability.

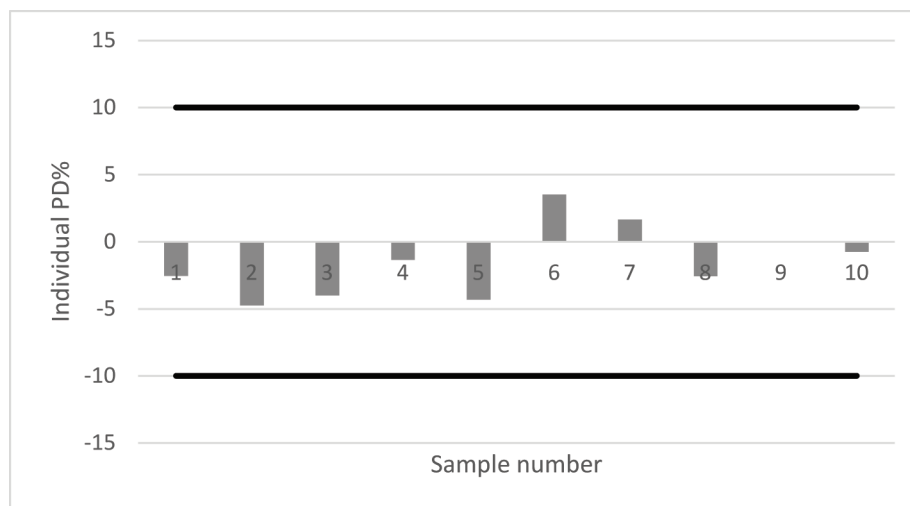


FIGURE 4. Individual PD% values after a double freeze-thaw cycle. PIGF - placental growth factor. PD% - percent degradation.

ulate typical hospital workflows. Our results show that PIGF remains adequately stable at 2-8 °C for up to 48 hours, with the mean PD% and its 95% CI remaining within the predefined MPI of $\pm 10\%$. Beyond this time point, progressive degradation was observed, with the 95% CI at 96 hours exceeding the MPI threshold and most samples surpassing it at 168 hours. Additionally, PIGF remained stable after two freeze-thaw cycles, with a mean PD% of -1.5% (95% CI: -3.4% to 0.4%).

Stability studies on biomarkers have often used heterogeneous acceptance criteria, which limit comparability and reproducibility of results across laboratories (15,17,18). To improve consistency, the SEQC-ML proposed a structured protocol using MPI, PD% and regression modeling, which was followed in our study (16).

According to the consensus of the Milan Strategic Conference, clinical outcome-based specifications (model 1) could not be applied because no established clinical decision limits are available for urinary PIGF (19). Likewise, the biological variation-based approach (model 2) was not applicable due to the absence of urine-specific biological variation data. Although biological variation data exist for serum PIGF (intra-individual CV = 7.9 %, inter-individual CV = 12.9 %), suggesting an allowable bias of approximately 5.7 %, these data were derived from non-pregnant women and PIGF con-

centrations are known to fluctuate with gestational age during pregnancy (20,21). Moreover, they refer to a different biological matrix, further limiting their relevance for the present study. Finally, the state-of-the-art approach (model 3) was also not applicable because no validated method is currently available for urinary PIGF measurement, as all existing immunoassays are designed for serum. Therefore, a pragmatic MPI threshold of $\pm 10\%$ was adopted in the absence of previously reported urinary PIGF stability data and in line with previous thresholds used in serum PIGF stability studies (13,14,22,23).

The evidence available on PIGF stability is limited exclusively to studies performed in serum, which cannot be extrapolated to urine due to the fundamentally different biochemical composition of both matrices. Based on our results, urinary PIGF appears stable for at least 48 hours when stored at 2-8 °C. Beyond this period, degradation becomes more pronounced, with several samples exceeding the predefined instability limit, likely reflecting the intrinsic variability of urine, including differences in pH, ionic strength and the presence of proteases or bacterial enzymes. The degradation pattern observed is comparable to that of other urinary biomarkers, such as inflammatory proteins, which have also shown similar stability limitations at 4 °C (9,24). Overall, these findings highlight the

need for further research on urinary PIGF stability, as no prior data exists and current knowledge from serum-based studies cannot inform urine-specific preanalytical behavior.

Recent studies have investigated urinary PIGF as a potential biomarker for PE, including its correlation with serum concentrations. Hebert-Schuster *et al.* reported a very strong correlation between urinary and serum PIGF concentrations ($\rho = 0.983$, $P < 0.05$), particularly when serum PIGF exceeded 100 pg/mL, suggesting that urinary PIGF may reliably reflect circulating concentrations (25). Similarly, Martín-Palumbo *et al.* found that urinary PIGF showed the strongest correlation with its serum counterpart ($R^2 = 0.73$) among all markers studied and demonstrated high predictive value for PE (area under curve (AUC) = 0.866), comparable to that of serum PIGF (AUC = 0.853) (26). Although these studies support the clinical potential of urinary PIGF, none have addressed analyte stability, a key preanalytical requirement for reliable measurement. Demonstrating stability during refrigerated storage and over two freeze-thaw cycles is essential for its future implementation in both research and clinical workflows. The analyte's acceptable performance under typical storage conditions supports its suitability for use in outpatient and non-specialized healthcare settings, where sample transport and delayed processing are common.

One of the main strengths of this study is its real-world applicability, as sample collection and handling were conducted under standard clinical laboratory conditions, reflecting typical preanalytical variability. Furthermore, applying a validated and structured stability protocol (SEQC-ML model) reinforces the methodological consistency and reliability of the results (16). All samples were processed in a single analytical batch, using the same reagent lot, minimizing analytical variability as much as possible. However, several limitations must be acknowledged. First, while the time-to-instability estimation (≈ 120 hours) derived from regression modeling provides useful insight, only the 48-hour time point showed consistent stability across all samples. Two of the ten aliquots exceeded the 10 % MPI at 48 hours; however, according to the SEQC protocol, stability is determined by

the mean PD% and its 95% CI rather than individual sample variability, reinforcing that the maximum acceptable stability is up to 48 hours. Second, there is currently no commercially available immunoassay and material controls for measuring urinary PIGF concentrations; available tests are validated only for serum. Lastly, although the sample size was sufficient for preliminary conclusions, a larger cohort would be necessary to confirm these findings.

In conclusion, urinary PIGF exhibits good stability under refrigerated conditions and shows minimal impact from freeze-thaw events, supporting its utility in clinical and translational research. Nevertheless, the sharp decline in stability beyond 48 hours and the high inter-sample variability emphasize the need for prompt processing and consistent preanalytical procedures. Our findings provide new preanalytical evidence on urinary PIGF stability, which is essential for its reliable implementation in clinical practice.

Acknowledgments

We are grateful to all pregnant women who provided urine samples at the Biochemistry Department of the University Clinical Hospital Lozano Blesa (Zaragoza, Spain). This study was supported by grants from the Government of Aragon, Spain, co-financed by FEDER ("Una manera de hacer Europa, Construyendo Europa desde Aragón" / European Social Funds: B46_20R and B46_23R), and by project PI22/143 funded by the Instituto de Salud Carlos III, Government of Spain. A.M.-M. and M.F. were supported by research grants from the Instituto de Salud Carlos III (FI21/00224 and CM22/00045, respectively).

Author contributions

E Martinez-Marzo: Conceptualization, Methodology, Investigation, Writing – original draft; M Peran: Writing – original draft; J Lerma-Irureta: Formal analysis, Data curation, Investigation; A Medel-Martinez: Resources, Data curation; C Paules: Supervision, Writing – review & editing; D Oros: Supervision, Writing – review & editing; M Fabre: Conceptualization, Methodology, Supervision, Writing – review & editing.

Potential conflict of interest

None declared.

Data availability statement

The data generated and analyzed in the presented study are available from the corresponding author on request.

References

- Duley L. The Global Impact of Pre-eclampsia and Eclampsia. Vol. 33, *Seminars in Perinatology*. 2009. p. 130–7. Duley L. The Global Impact of Pre-eclampsia and Eclampsia. *Semin Perinatol*. 2009;33:130-7. <https://doi.org/10.1053/j.semperi.2009.02.010>
- Young BC, Levine RJ, Karumanchi SA. Pathogenesis of preeclampsia. *Annu Rev Pathol*. 2010;5:173-92. <https://doi.org/10.1146/annurev-pathol-121808-102149>
- Maesa JM, Romero-Tabares A, Benot-López S. Diagnostic validity of the sFlt-1/PIGF ratio in the identification of preeclampsia: A systematic review. *Clin Investig Ginecol Obstet*. 2020;47:30-7. <https://doi.org/10.1016/j.gine.2019.04.001>
- Zeisler H, Llorba E, Chantraine F, Vatish M, Staff AC, Sennström M, et al. Predictive Value of the sFlt-1:PIGF Ratio in Women with Suspected Preeclampsia. *N Engl J Med*. 2016;374:13-22. <https://doi.org/10.1056/NEJMoa1414838>
- National Institute for Health and Care Excellence (NICE). PLGF-based testing to help diagnose suspected preterm pre-eclampsia *Diagnostics guidance* [Internet]. London; 2022 Jul. Available from: www.nice.org.uk/guidance/dg49. Accessed May 15th 2025.
- Chappell LC, Duckworth S, Seed PT, Griffin M, Myers J, MacKillop L, et al. Diagnostic accuracy of placental growth factor in women with suspected preeclampsia: A prospective multicenter study. *Circulation*. 2013;128:2121-31. <https://doi.org/10.1161/CIRCULATIONAHA.113.003215>
- Zhang L, Li W, Chi X, Sun Q, Li Y, Xing W, et al. Predictive performance of sFlt-1, PIGF and the sFlt-1/PIGF ratio for preeclampsia: A systematic review and meta-analysis. *J Gynecol Obstet Hum Reprod*. 2025;54:102925. <https://doi.org/10.1016/j.jogoh.2025.102925>
- Saude EJ, Sykes BD. Urine stability for metabolomic studies: Effects of preparation and storage. *Metabolomics*. 2007;3:19-27. <https://doi.org/10.1007/s11306-006-0042-2>
- Chang C, Obeid W, Thiessen-Philbrook H, Parikh CR. Sample Processing and Stability for Urine Biomarker Studies. *J Appl Lab Med*. 2021;6:1628-34. <https://doi.org/10.1093/jalm/jfab082>
- Kolialexi A, Mavreli D, Tounta G, Mavrou A, Papantoniou N. Urine proteomic studies in preeclampsia. *Proteomics Clin Appl*. 2015;9:501-6. <https://doi.org/10.1002/prca.201400092>
- Wu J, Yao Y, Wang T, Xu T, Jiang R. Pregnancy urine biomarkers for effectively preeclampsia prediction: a systematic review and meta-analysis. *Hypertens Pregnancy*. 2025;44. <https://doi.org/10.1080/10641955.2025.2487794>
- Gomez-Rioja R, Von Meyer A, Cornes M, Costelloe S, Vermeersch P, Simundic AM, et al. Recommendation for the design of stability studies on clinical specimens. *Clin Chem Lab Med*. 2023;61:1708-18. <https://doi.org/10.1515/cclm-2023-0221>
- Armstrong-Buisseret LK, Haslam S, James T, Bradshaw L, Heazell AEP. Verification of placental growth factor and soluble-fms-like tyrosine kinase 1 assay performance in late pregnancy and their diagnostic test accuracy in women with reduced fetal movement. *Ann Clin Biochem*. 2020;57:223-33. <https://doi.org/10.1177/0004563220911993>
- Cowans NJ, Alfthan H, Stenman UH, Spencer K. Stability of first trimester placental growth factor in serum and whole blood. *Prenat Diagn*. 2011;31:1193-7. <https://doi.org/10.1002/pd.2894>
- Lian IA, Dypdalsbakk T, Åsberg A. Stability of serum placental growth factor (PIGF) and soluble fms-like tyrosine kinase 1 (sFlt-1). *Scand J Clin Lab Invest*. 2024;84:160-7. <https://doi.org/10.1080/00365513.2024.2340037>
- Gómez-Rioja R, Amaro MS, Diaz-Garzón J, Bauçà JM, Espartosa DM, Fernández-Calle P, et al. A protocol for testing the stability of biochemical analytes. Technical document. *Clin Chem Lab Med*. 2019;57:1829-36. <https://doi.org/10.1515/cclm-2019-0586>
- Rowson S, Reddy M, Rolnik DL, Da Silva Costa F, Palmer KR. Stability of placental growth factor, soluble fms-like tyrosine kinase 1, and soluble fms-like tyrosine kinase 1 e15a in human serum and plasma. *Placenta*. 2019;86:1-3. <https://doi.org/10.1016/j.placenta.2019.08.001>
- Čičak H, Bulat S, Jeličić J, Ivković A, Radončić KM, Radišić Biljak V, et al. Short- and long-term stability of synovial fluid calprotectin. *Biochem Med (Zagreb)*. 2024;34:030704. <https://doi.org/10.11613/BM.2024.030704>
- Sandberg S, Fraser CG, Horvath AR, Jansen R, Jones G, Oosterhuis W, et al. Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine. *Clin Chem Lab Med*. 2015;53:833-5. <https://doi.org/10.1515/cclm-2015-0067>
- Braga F, Ferraro S, Borille S, Panteghini M. Biological variation of two serum markers for preeclampsia prediction. *Clin Chem Lab Med*. 2020;58:e27–8. <https://doi.org/10.1515/cclm-2019-0649>
- Schiettecatte J, Russcher H, Anckaert E, Mees M, Leeser B, Tirrelli AS, et al. Multicenter evaluation of the first automated Elecsys sFlt-1 and PIGF assays in normal pregnancies and

- preeclampsia. *Clin Biochem.* 2010;43:768-70. <https://doi.org/10.1016/j.clinbiochem.2010.02.010>
22. Higgins V, Ma L, Ragosnig BL, Melamed N, Hladunewich M, James T, et al. Analytical Performance and Quality Indicators of Fully Automated Immunoassays for sFlt-1 and PlGF. *J Appl Lab Med.* 2022;7:555-67. <https://doi.org/10.1093/jalm/jfab135>
23. Law LW, Sahota DS, Wai Chan L, Chen M, Kin Lau T, Leung TY. Effect of long-term storage on placental growth factor and fms-like tyrosine kinase 1 measurements in samples from pregnant women. *J Matern Fetal Neonatal Med.* 2010;23:1475-80. <https://doi.org/10.3109/14767051003678242>
24. Parikh CR, Butrymowicz I, Yu A, Chinchilli VM, Park M, Hsu CY, et al. Urine stability studies for novel biomarkers of acute kidney injury. *Am J Kidney Dis.* 2014;63:567-72. <https://doi.org/10.1053/j.ajkd.2013.09.013>
25. Hebert-Schuster M, Ranaweera T, Fraichard C, Gaudet-Chardonnet A, Tsatsaris V, Guibourdenche J, et al. Urinary sFlt-1 and PlGF levels are strongly correlated to serum sFlt-1/PlGF ratio and serum PlGF in women with preeclampsia. *Pregnancy Hypertens.* 2018;12:82-83. <https://doi.org/10.1016/j.preghy.2018.03.011>
26. Martín-Palumbo G, Alcorta MD, de Aguado MP, Antolín E, Bartha JL. Urinary sFlt-1 and PlGF as preeclampsia predictors: sFlt-1/creatinine ratio improves the prediction value. *European Journal of Obstetrics and Gynecology and Reproductive Biology.* 2024;298:53-60. <https://doi.org/10.1016/j.ejogrb.2024.05.002>