Acta Biomed 2025; Vol. 96, N. 2: 16902 DOI: 10.23750/abm.v96i2.16902

Review

Diagnostic accuracy of urinary PlGF levels for preeclampsia in pregnancy: Systematic review and meta-analysis of case-control studies

Rashida Bliyeva[1], Andrey Gaiday[1], Saule Bermagambetova[2], Svetlana Sachanova[3], Bibigul Karimsakova[4], Akylbek Tussupkaliyev[1]

[1]Department of Obstetrics and Gynecology, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan; [2]Department of Hygienic Disciplines with Professional Diseases, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan; [3]Scientific and Practical Center, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan; [4]Department of General Medical Practice #1, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan.

Abstract. *Background and aim:* Despite growing interest in placental growth factor (PlGF) as a promising biomarker for preeclampsia, a comprehensive synthesis of urinary PlGF levels in this condition remains lacking. This systematic review and meta-analysis aim to quantify mean urinary PlGF levels (pg/mL) in women with preeclampsia compared to healthy controls, with and without creatinine adjustment. *Methods:* A systematic search of five databases was conducted by two independent researchers using the following keywords: "urine" AND "PlGF" OR "placental growth factor" AND "preeclampsia" OR "hypertensive disorders of pregnancy" OR "gestational hypertension," according to the standard guidelines. Studies were included if they provided the mean and standard deviation of urinary PlGF levels among pregnant women with preeclampsia and healthy controls, with or without creatinine adjustment. *Results:* Seven articles were included. Five studies, encompassing seven groups, reported the mean urinary PlGF levels without creatinine adjustment. Using a random-effects model, the pooled mean PlGF level across these groups was 101.41 pg/mL (95% CI, 53.66–149.15) among healthy controls, compared with 32.24 pg/mL (95% CI, 21.48–43.02) in patients with preeclampsia. In three studies comprising five groups, the mean urinary PlGF levels were adjusted for creatinine. The pooled mean PlGF level for these groups, was 303.53 pg/mL (95% CI, 186.49–420.56) among healthy controls, versus 40.31 pg/mL (95% CI, 20.32–60.29) in patients with preeclampsia. *Conclusions:* Our findings demonstrate significantly reduced urinary PlGF levels in preeclampsia regardless of creatinine adjustment, supporting its potential as a non-invasive diagnostic biomarker. Further research should establish standardized measurement protocols and clinical thresholds for implementation. (www.actabiomedica.it)

Key words: preeclampsia, placental growth factor, urinary biomarkers, pregnancy complications, diagnostic biomarkers, systematic review, meta-analysis, case-control studies, biomarker validation, pregnancy, placental proteins

Introduction

According to the World Health Organization (WHO) 2024 report on maternal mortality, nearly 800 women died each day in 2020 from largely preventable complications related to pregnancy and childbirth (1). This number shows the urgency of strengthening preventative strategies, which have shown potential for significant impact: between 2000 and 2020, Eastern Europe saw an exemplary 70% reduction in maternal

mortality due to interventions addressing the fundamental causes of pregnancy-related complications (1). However, stark inequalities in maternal mortality persist between high- and low-income countries, further highlighting the effectiveness of preventive measures. Low-income countries report maternal mortality rates as high as 430 per 100,000 live births, compared to just 13 per 100,000 in high-income regions (1). Top five causes, including severe haemorrhage, infections, hypertensive disorders of pregnancy, complications from delivery, and unsafe abortions, collectively account for approximately 75% of maternal deaths worldwide (2). As the global health community shifts toward a post-pandemic, endemic response to COVID-19, the focus on hypertensive disorders in pregnancy remains essential (3–6). These disorders, including preeclampsia, are critical contributors to maternal morbidity and mortality, third only to complications exacerbated by bleeding and infectious diseases in 2020. Preeclampsia, a hypertensive disorder of pregnancy, is not only a major cause of maternal mortality but also has profound implications for neonatal health, with prevalence rates ranging from 2–3% to as high as 6% depending on the region (5–7). Preeclampsia typically presents after 20 weeks of pregnancy and resolves within 48 hours postpartum, indicating that placenta plays a pivotal role in its pathophysiology. Emerging evidence highlights the role of placental growth factor (PlGF), a proangiogenic factor, as a promising biomarker for preeclampsia (8). During normal pregnancy, PlGF expression rises to support adequate placental perfusion. In preeclampsia, however, impaired trophoblastic invasion and defective spiral artery remodelling lead to placental ischemia and a substantial reduction in PlGF production (9-10). This dysregulation contributes to endothelial dysfunction and the clinical manifestations of the disease, including hypertension and proteinuria (8-10). Numerous studies report significantly lower levels of PlGF in both serum and urine samples of patients with preeclampsia compared to healthy pregnant individuals, with the decline in PlGF often preceding the onset of clinical symptoms (8–10). No correlation exists between PlGF levels and renal function antepartum (11). Monitoring PlGF levels could therefore offer predictive and diagnostic value for preeclampsia, enabling earlier and potentially life-saving interventions. Urinary measurement of PlGF may be especially advantageous for pregnant patients, offering a non-invasive and more acceptable alternative to serum assessment, which involves venipuncture and is particularly burdensome for frequent and continuous monitoring (12).

Despite the potential of urinary PlGF as a biomarker, there is no comprehensive synthesis of existing research on urinary PlGF levels in preeclampsia. The aim of this systematic review and meta-analysis is to address this gap by determining mean urinary PlGF levels (in pg/ml) in women diagnosed with preeclampsia compared to healthy controls, both with and without creatinine adjustment. This analysis assesses whether urinary PlGF levels consistently differ between preeclamptic and normotensive pregnancies according to the published literature results, ultimately contributing to the evidence base for its use as a diagnostic biomarker in clinical settings.

Materials and Methods

The study protocol is registered with PROSPERO, the International Prospective Register of Systematic Reviews, ID: CRD42024608833. (13).

Search strategy, eligibility criteria, and data extraction

A search in the PROSPERO database aimed to identify registrations of comparable studies found one study protocol that assessed urinary PlGF as a predictor of complications in hypertensive disorders of pregnancy (14). Since the aim of the present study was different from that of the identified study, the authors proceeded with registering the current study protocol in the PROSPERO database. Following this, a systematic search of the literature was conducted across PubMed, Web of Science, Scopus, ScienceDirect, and Google Scholar databases to identify studies published up to October 2, 2024. The search strategy incorporated the following keywords: “urine” AND “PlGF” OR “placental growth factor” AND “preeclampsia” OR “hypertensive disorders of pregnancy” OR “gestational hypertension.” No restrictions on publication date were applied. However, the search results were

limited to English-language publications and studies conducted on humans. Where relevant, filters were also applied to include only research articles and exclude other publication types. The types of studies to be included were determined using the following eligibility criteria: Inclusion Criteria: 1. Studies that report the mean and standard deviation (SD) of urinary PlGF levels (in pg/ml) among pregnant women, with or without creatinine adjustment. 2. Studies that include both preeclampsia patients and healthy control groups. 3. Studies published in English. 4. Peer-reviewed articles, including observational studies, cohort studies, case-control studies, and cross-sectional data from randomized clinical trials on PlGF levels. Exclusion Criteria: 1. Studies that report serum PlGF levels. 2. Animal studies, in vitro studies, and studies unrelated to human pregnancy. 3. Studies on pregnant patients with chronic conditions. 4. Reviews, editorials, letters, commentaries, and abstracts. 5. Studies without extractable data on mean and SD PlGF values in pg/ml. The literature review and synthesis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (15). Two authors (R.B. & A.T.) independently screened the titles and abstracts of the search results, after duplicate removal, to assess relevance. Full texts of studies meeting the initial criteria were then retrieved and evaluated against the inclusion and exclusion criteria. Data extracted from eligible studies included the first author's last name, year of publication, country, study design, number of pregnant women with preeclampsia and healthy controls, gestational age, mean PlGF values (pg/mL), and the standard deviation of mean PlGF values. Any discrepancies in data extraction were resolved through consultation with a third author (B.K.), ensuring consensus among all three authors responsible for this process.

Risk of bias (quality) assessment

The risk of bias (quality) of studies included in this systematic review and meta-analysis was assessed using the Newcastle-Ottawa Scale (NOS), as recommended by the Cochrane Non-Randomized Studies Methods Working Group. The NOS evaluated each study based on eight items organized into three categories: selection of study groups (four items), comparability of groups (one item), and outcome ascertainment (three items). Each item was scored up to one point. The total score ranged from 0 to 8, with higher scores indicating greater methodological quality. Two authors (R.B. & A.T.) independently conducted the quality assessment following an initial consensus on the assessment protocol. The level of inter-rater agreement between the two authors was calculated by a third author (B.K.) to ensure reliability. For this review, studies scoring seven or more points were classified as satisfactory quality, and were included to the final analysis.

Meta-analysis plan

The pooled mean value of urinary PlGF for patients with preeclampsia and healthy controls was calculated using a random-effects model for meta-analysis in RStudio (version 4.3.2), with 95% confidence intervals (95% CI) provided. Data analysis and visualization were conducted using two R packages for meta-analysis: "meta" and "metafor" (16). The outcomes from the random-effects model were presented in forest plots. To assess heterogeneity across studies, the I^2 statistic was calculated, accompanied by an additional examination through influence analysis. Publication bias was evaluated using Egger's test statistics and visualized through funnel plots. Subgroup analyses were performed based on the categorization of the included study participants into those with preeclampsia and healthy controls (17).

Results

Included studies with mean PlGF values

The initial database search identified 203 articles. After applying the "Humans" and "English language" filters, 2 articles were excluded. Following the removal of 81 duplicate records, 120 unique articles remained for screening. Of these, 72 articles were sought for retrieval for full-text review, after exclusion of the 48 non-relevant titles. Upon further assessment, 7 articles met the inclusion criteria. One study was excluded due to duplicative data overlapping with an already included

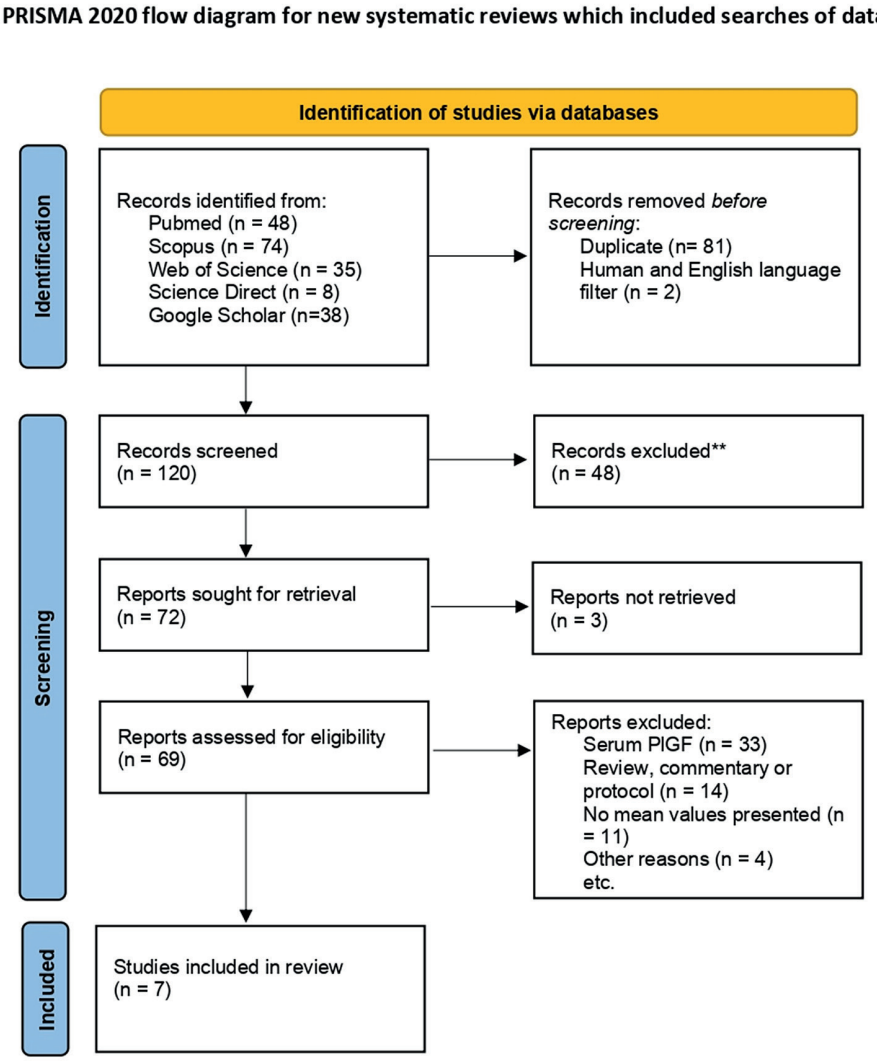

Figure 1. PRISMA flow chart of study inclusion process.

study (18), another focused on pregnant patients with diabetes (19), and two additional studies were excluded for other specified reasons not presented in the flowchart (20,21). A PRISMA flow chart detailing the study inclusion process is provided in Figure 1 (15).

Among the seven studies included, one provided mean PlGF values both without and with creatinine adjustment. Four studies reported mean PlGF values without creatinine adjustment, and two studies reported values adjusted for creatinine. Geographically, two studies were conducted in India, while China, Korea, Spain, France, and Italy each contributed one study. With respect to study design, all but one were case-control studies, and one was a supplementary study within a randomized controlled trial. Sample sizes varied widely, ranging from 6 to 168 participants, with a combined total of 221 participants with preeclampsia across all studies. Gestational age data was available for all studies except one. A detailed summary of the included articles is provided in Table 1.

Table 1. Summary of the included studies.

Study	Country	Study design	Number of patients/PE	Gestational age	Groups of patients
No adjustment to creatinine					
Aggarwal, 2006 (22)	India	Case-control	66/35	30.16±0.89 & 30.28±1.28	Control & PE
Varughese, 2012 (23)	India	Case-control	80/40	< 34W & >34W	Control & PE < 34W & PE > 34W
Tang, 2016 (24)	China	Case-control	120/80	22.5 ± 2.3 & 22.6 ± 2.2	Control & Mild PE & Severe PE
Kim, 2024 (25)	Korea	Case-control	6/3	Not provided	Control & PE
Martin-Palumbo, 2024 (26)	Spain	Case-control	49/26	36.42 ± 1.24 & 31.99 ± 3.61	Control & PE
With creatinine adjustment					
Aggarwal, 2006 (22)	India	Case-control	66/35	30.16±0.89 & 30.28±1.28	Control & PE
Lecarpentier, 2019 (27)	France	RCT (longitudinal obs)	168/16	22-25 & 26-29 & 30-33	Control & PE: 22-25W (a) & 26-29W (b) & 30-33W (c)
Valsecchi, 2022 (28)	Italy	Case-control	39/21	35.7 ± 4.3 & 33.4 ± 5.3	Control & PE

Abbreviations: obs – observations; PE – preeclampsia; RCT – randomized controlled trial.

Mean urinary PlGF values in patients with preeclampsia vs. healthy control

Five studies, encompassing seven groups, reported the mean urinary PlGF levels without creatinine adjustment. Using a random-effects model, the pooled mean PlGF level across these groups was 101.41 pg/mL (95% CI, 53.66–149.15) among healthy controls, showing high heterogeneity, compared with 32.24 pg/mL (95% CI, 21.48–43.02) in patients with preeclampsia, also with high heterogeneity (Figure 2A). In three studies comprising five groups, the mean urinary PlGF levels were adjusted for creatinine. The pooled mean PlGF level for these groups, analyzed with a random-effects model, was 303.53 pg/mL (95% CI, 186.49–420.56) among healthy controls, again exhibiting high heterogeneity, versus 40.31 pg/mL (95% CI, 20.32–60.29) in patients with preeclampsia, with similar heterogeneity noted (Figure 2B).

An influence analysis was conducted to identify studies with the greatest impact on the pooled estimate. In the group of studies without creatinine adjustment, the pooled mean PlGF value was primarily influenced by study #1, the Aggarwal 2006 study (22) (Figure 3A). In contrast, within the group of studies with creatinine adjustment, no single study exhibited a substantial effect on the pooled mean PlGF value (Figure 3B).

Upon visual inspection of the funnel plot, in the group of studies without creatinine adjustment, an asymmetry is evident (Figure 4A). This finding was further confirmed by significant results from Egger's test for publication bias ($p<0.001$). Upon visual inspection of the funnel plot, in the group of studies with creatinine adjustment, no assymetry is observed (Figure 4B). This finding was further confirmed by non-significant results from Egger's test for publication bias ($p>0.05$).

A meta-regression analysis did not identify a significant effect of year of publication on the pooled mean PlGF levels without creatinine adjustment and after creatinine adjustment ($p = 0.89$; Figure 5A and $p = 0.93$; Figure 5B, respectively).

Risk of bias (quality) assessment

All included studies had a NOS score of 7 or above, indicating high quality and a low risk of bias in all three areas of assessment, as detailed in Table 2.

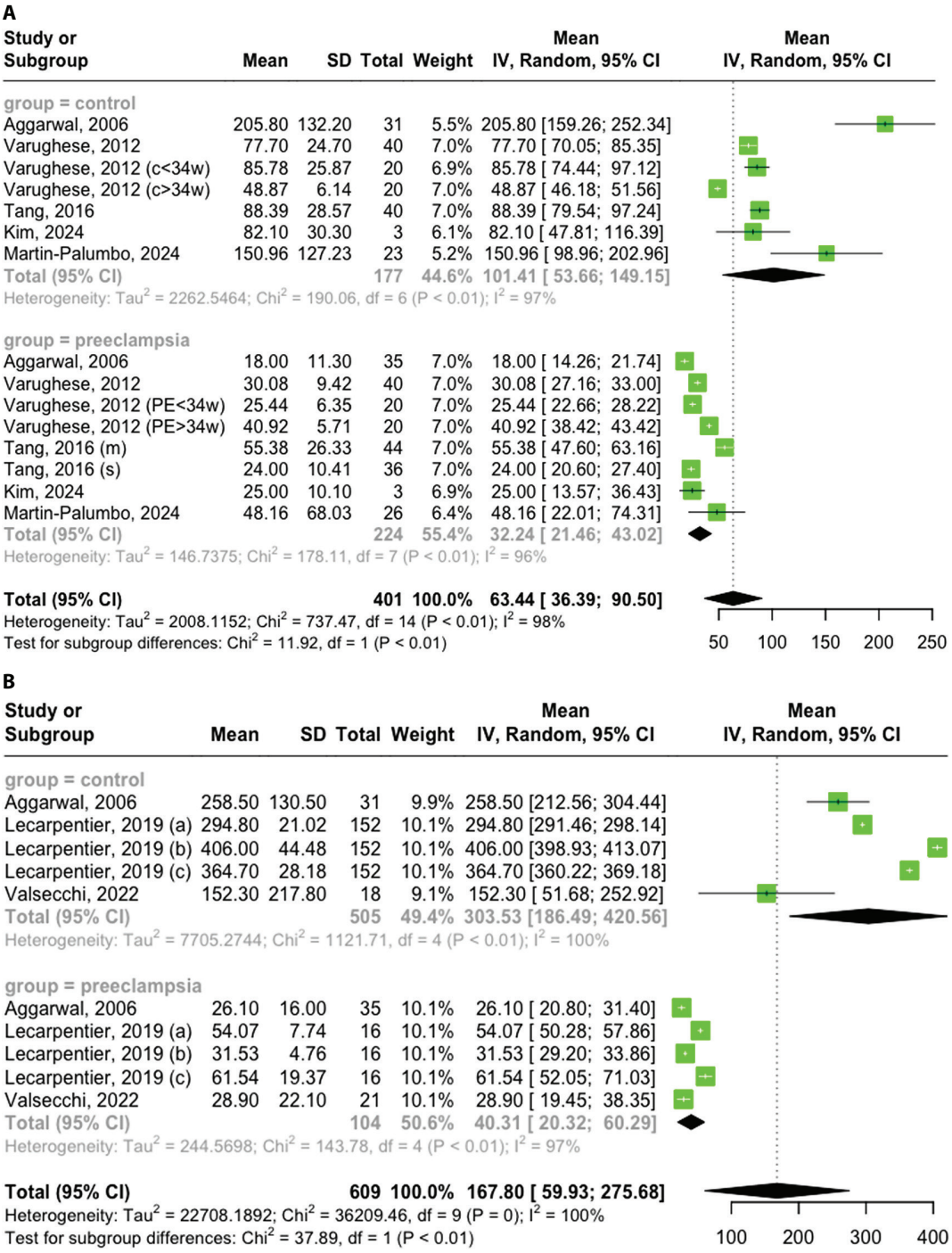

Figure 2. Forest plot of mean urinary PlGF levels: A) Unadjusted values (pg/mL): Preeclampsia vs. Healthy Controls; B) Creatinine-adjusted values (pg/mL): Preeclampsia vs. Healthy Controls. *Abbreviations:* SD – standard deviation. Group definitions: Varughese, 2012 (c<34w) – healthy controls < 34 weeks; Varughese, 2012 (c>34w) – healthy controls > 34 weeks; Tang, 2016 (m) – mild preeclampsia; Tang, 2016 (s) – severe preeclampsia.

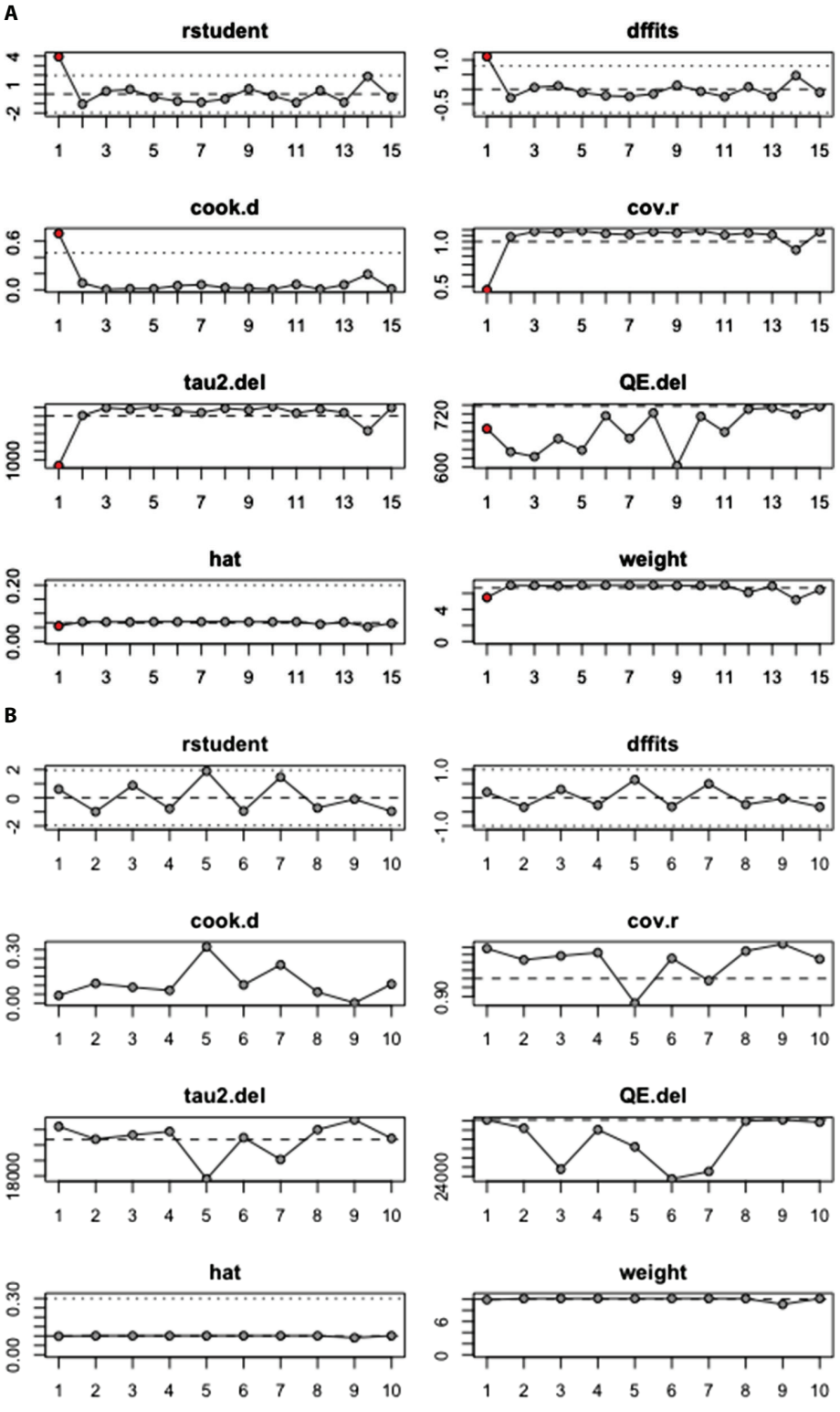

Figure 3. Influence analysis of pooled urinary PlGF estimates: A) unadjusted values; B) creatinine-adjusted values

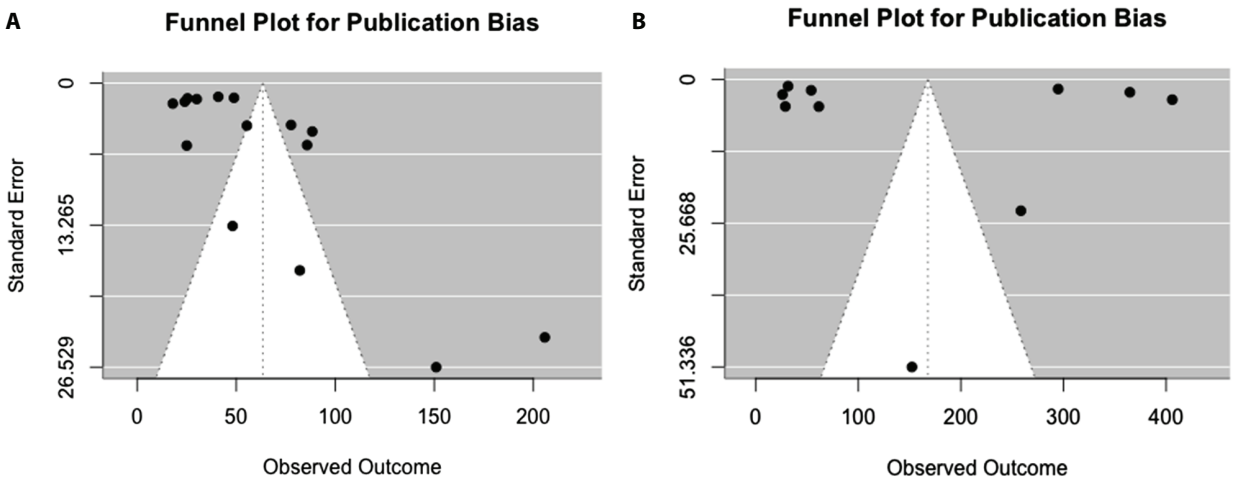

Figure 4. Assessment of publication bias for urinary PlGF studies: A) Funnel plot of unadjusted values; B) Funnel plot of creatinine-adjusted values.

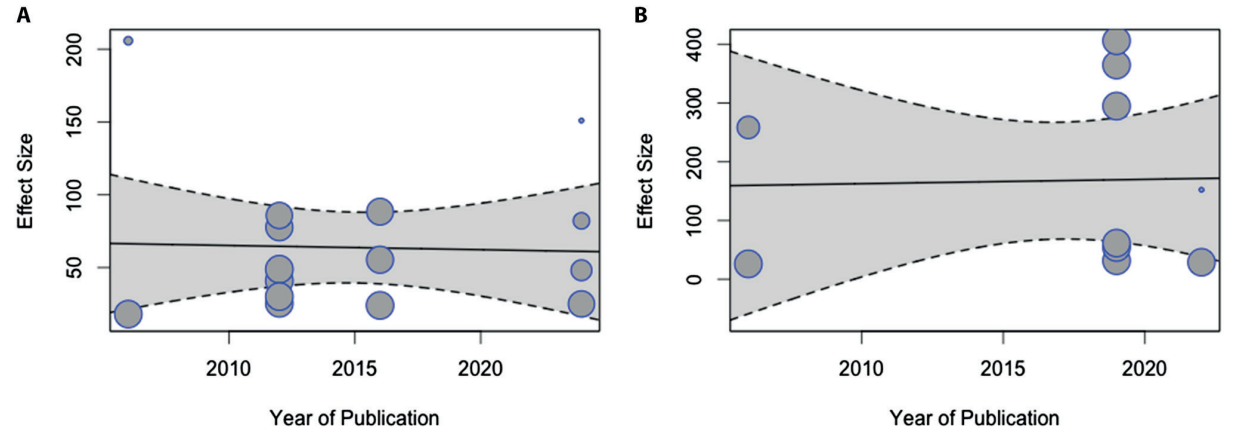

Figure 5. Meta-regression of urinary PlGF levels by year of publication: A) unadjusted values; B) creatinine-adjusted values

Discussion

We conducted a systematic review and meta-analysis of the literature to determine mean urinary PlGF levels in women diagnosed with preeclampsia compared to healthy controls, both with and without creatinine adjustment. Five studies, encompassing seven groups, reported the mean urinary PlGF levels without creatinine adjustment. Using a random-effects model, the pooled mean PlGF level across these groups was 101.41 pg/mL (95% CI, 53.66–149.15) among healthy controls, compared with 32.24 pg/mL (95% CI, 21.48–43.02) in patients with preeclampsia. In three studies comprising five groups, the mean urinary PlGF levels were adjusted for creatinine. The pooled mean PlGF level for these groups, was 303.53 pg/mL (95% CI, 186.49–420.56) among healthy controls, versus 40.31 pg/mL (95% CI, 20. 32–60.29) in patients with preeclampsia. Our results show that the mean urinary PlGF levels in patients with preeclampsia were consistently lower compared to healthy controls.

The results of the present study are in line with previous research findings on this topic. A meta-analysis examining the discriminatory performance of serum PlGF in predicting preeclampsia in asymptomatic

Table 2. New-Castle Ottawa risk of bias (quality) assessment results

Study	Selection	Comparability	Exposure	Total
Aggarwal, 2006 (22)	4	1	3	8
Varughese, 2012 (23)	3	1	3	7
Tang, 2016 (24)	4	1	2	7
Kim, 2024 (25)	4	1	3	8
Martin-Palumbo, 2024 (26)	4	1	2	7
Lecarpentier, 2019 (27)	3	1	3	7
Valsecchi, 2022 (28)	4	1	3	8

pregnant women showed high test accuracy (29). This review also showed that PlGF levels vary by gestational age (29). The authors of the present study did not have sufficient data to perform a subgroup analysis based on gestational age to assess urinary PlGF values. However, this could be a potential area for future research. A narrative review on urinary biomarkers for preeclampsia further supports the potential of urinary PlGF as one of the most promising screening tools, alongside other biomarkers such as urinary soluble fms-like tyrosine kinase-1 (sFlt-1) and the sFlt-1/PlGF ratio (30). The use of urinary screening tests in pregnant women may offer clinical advantages in the context of viral infections associated with vascular dysfunction. Emerging evidence suggests that conditions such as Zika virus and COVID-19 may exacerbate maternal endothelial dysfunction, potentially increasing the risk of hypertensive disorders of pregnancy, including preeclampsia, and their complications (31–33). Preeclampsia itself has also been associated with an elevated risk of postpartum haemorrhage (PPH), possibly mediated by impaired vascular and coagulation pathways (34). In light of the consistently reduced urinary PlGF levels observed in preeclampsia, further investigation is warranted to evaluate whether urinary biomarker-based diagnostics could support clinical decision-making in infectious or inflammatory states that elevate PPH risk. This consideration is particularly timely given the documented rise in maternal morbidity during COVID-19 surges and the associated shifts in obstetric care delivery (35–37). Several articles examine the cost-effectiveness of incorporating PlGF screening into standard care for pregnant women. These articles consistently demonstrate cost reductions associated with decreased hospitalization rates among low-risk patients, as well as improved screening and management for those at high risk of developing preeclampsia (38–41). However, all of these studies focused on the utility of serum PlGF assessment, and none evaluated the cost-effectiveness of urine PlGF assessment. This gap presents a promising area for future research, as findings could strengthen preventive strategies in effective pregnancy management and play a significant role in improving maternal and neonatal outcomes. Although our meta-analysis focused on synthesizing pooled mean urinary PlGF levels rather than estimating diagnostic accuracy metrics, this was a methodologically appropriate choice given the nature of the included data. The studies analyzed reported continuous PlGF values without standardized diagnostic thresholds, which are essential for deriving sensitivity, specificity, or other performance metrics. Therefore, diagnostic accuracy measures could not be calculated. Future research employing threshold-based classification is warranted to evaluate the clinical performance of urinary PlGF as a diagnostic or screening tool for preeclampsia. Limitations of the present study. There is a potential for selective reporting bias, where studies reporting significant findings on PlGF levels in preeclampsia might be overrepresented. This can skew the positive results of the meta-analysis and affect its conclusions. Secondly, differences in methods for measuring PlGF levels and their adjustment (e.g., for creatinine) add to the heterogeneity of the results, which could impact the clinical applicability of findings regarding urinary PlGF as a biomarker. We addressed this limitation by separately reporting the adjusted and non-adjusted values; however, substantial

heterogeneity in the estimates remains. Finally, this study did not aim to assess or synthesize data on the relationship between proteinuria or the extent of kidney damage and urinary PlGF levels in patients with preeclampsia.

Conclusions

This systematic review and meta-analysis demonstrate significantly lower urinary PlGF levels in women with preeclampsia compared to healthy controls, supporting its potential as a non-invasive biomarker. While our findings align with established evidence for serum PlGF's predictive value, important knowledge gaps remain regarding urinary PlGF's clinical utility. Notably, our analysis could not directly compare the diagnostic performance of urinary versus serum PlGF due to heterogeneity in measurement methods and reporting formats across studies. Furthermore, while existing cost-effectiveness analyses of serum PlGF screening suggest potential healthcare savings through improved risk stratification, similar evaluations for urinary testing remain unexplored - a critical consideration for clinical implementation given urine testing's potential practical advantages.

To advance the clinical applicability of urinary PlGF testing, future research should focus on: (1) defining gestational-age–specific reference ranges, (2) establishing diagnostic thresholds for clinical use, (3) comparing its diagnostic accuracy and cost-effectiveness to serum-based assays, and (4) evaluating its role in infection-related maternal morbidity. Although methodological limitations including measurement variability and potential reporting bias affect the current evidence base, urinary PlGF measurement represents a promising complementary tool that could enhance preeclampsia screening protocols, particularly in resource-limited settings where non-invasive testing may offer practical advantages.

Supplementary Materials: Table S1. Summary of variables included in the analysis.

Ethic Approval: Ethical review and approval were waived for this study as this is a systematic review of the literature.

Conflicts of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article".

Authors' Contribution: Conceptualization: RB, AT, BK. Methodology: RB, AT, AG, BK. Software: RB. Validation: RB, AT, BK. Formal Analysis: RB, AT, BK. Investigation: RB, AT, AG, BK. Data Curation: RB, AT, AG, BK. Writing – Original Draft Preparation: RB, AT, AG, SB, SS, BK. Writing – Review and Editing: RB, AT, AG, SB, SS, BK. Visualization: SB, SS. Resources: SB. Supervision: SB, SS. Project Administration: AG, SB, SS. Funding Acquisition: RB, AT, BK. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work were ap-propriately investigated and resolved.

Declaration on the Use of AI: None.

Consent for Publication: Not applicable.

Acknowledgments: None.

Funding: The project of the Ministry of Education and Science of Kazakhstan, grant number: AP14869445. Project title: Prediction of preeclampsia based on the concentration of placental growth factor (PLGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) in urine in the first trimester of pregnancy.

Data availability Statement: The original contributions presented in this study are included in the supplementary material. Further inquiries can be directed to the corresponding author.

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Correspondence:
Received: 20 February 2025
Accepted: 26 March 2025
Rashida Bliyeva, MD
Department of Obstetrics and Gynecology
West Kazakhstan Marat Ospanov Medical University
68, Mares'ev street, Aktobe, Kazakhstan. 030000
ORCID ID: 0000-0002-8109-6109
E-mail: brmed07@gmail.com

Annex

Author, year	year	country	patients	Group	group	PLGF measure	pmean	psd	age	bmi
Aggarwal, 2006 (22)	2006	India	31	healthy	control	adjusted to creatinine	258,5	130,5		
Aggarwal, 2006 (22)	2006	India	31	healthy	control	before creatinine adjustement	205,8	132,2	26.13±4.22	
Aggarwal, 2006 (22)	2006	India	35	PE	preeclampsia	before creatinine adjustement	18	11,3	26.9±5.06	
Aggarwal, 2006 (22)	2006	India	35	PE	preeclampsia	adjusted to creatinine	26,1	16		
Varughese, 2012 (23)	2012	India	40	PE	preeclampsia	before creatinine adjustement	30,08	9,42		24.91 ± 4.75
Varughese, 2012 (23)	2012	India	40	healthy	control	before creatinine adjustement	77,7	24,7		22.85 ± 3.50
Varughese, 2012 (c<34w) (23)	2012	India	20	healthy	control	before creatinine adjustement	85,78	25,87		
Varughese, 2012 (c>34w) (23)	2012	India	20	healthy	control	before creatinine adjustement	48,87	6,14		
Varughese, 2012 (PE<34w) (23)	2012	India	20	PE	preeclampsia	before creatinine adjustement	25,44	6,35		
Varughese, 2012 (PE>34w) (23)	2012	India	20	PE	preeclampsia	before creatinine adjustement	40,92	5,71		
Tang, 2016 (24)	2016	China	40	control	control		88,39	28,57	29.9 ± 4.6	22.5 ± 2.3
Tang, 2016 (m) (24)	2016	China	44	mild	preeclampsia	before creatinine adjustement pg/ml	55,38	26,33	30.6 ± 3.8	22.6 ± 2.2
Tang, 2016 (s) (24)	2016	China	36	severe	preeclampsia		24	10,41	31.1 ± 3.2	22.5 ± 1.9
Lecarpentier, 2019 (a) (27)	2019	France	152	control	control	adjusted to creatinine pg/ml	294,8	21,02	31.8 ± 0.3	25.9 ± 0.4
Lecarpentier, 2019 (a) (27)	2019	France	16	PE	preeclampsia	adjusted to creatinine	54,07	7,737	31.8 ± 0.3	25.9 ± 0.4
Lecarpentier, 2019 (b) (27)	2019	France	152	control	control	adjusted to creatinine	406	44,48		
Lecarpentier, 2019 (b) (27)	2019	France	16	PE	preeclampsia	adjusted to creatinine	31,53	4,756		

(*Continued*)

Author, year	year	country	patients	Group	group	PLGF measure	pmean	psd	age	bmi
Lecarpentier, 2019 (c) (27)	2019	France	152	control	control	adjusted to creatinine	364,7	28,18		
Lecarpentier, 2019 (c) (27)	2019	France	16	PE	preeclampsia	adjusted to creatinine	61,54	19,37		
Valsecchi, 2022 (28)	2022	Renal dysfunction and podocyturia in pre-eclampsia may be explained by increased urinary VEGF	18	healthy	control	adjusted to creatinine	152,3	217,8	36.6 ± 5.4	25.2 ± 4.2
Valsecchi, 2022 (28)	2022	Italy	21	PE	preeclampsia	adjusted to creatinine	28,9	22,1	34.2 ± 6.5	25.0 ± 3.7
Kim, 2024 (25)	2024	Korea	3	healthy	control		82,1	30,3		
Kim, 2024 (25)	2024	Korea	3	PE	preeclampsia	before creatinine adjustement pg/ml	25	10,1		
Martin-Palumbo, 2024 (26)	2024	Spain	23	control	control	before creatinine adjustement	150,96	127,23	35.26 ± 4.87	
Martin-Palumbo, 2024 (26)	2024	Spain	26	PE	preeclampsia	before creatinine adjustement pg/ml	48,16	68,03	34.31 ± 5.87	