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Systematic Review

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The Accuracy of Diagnosing Proteinuria in Pregnancy Using Urine Protein to Creatinine Ratio Compared to 24-Hour Urine Collection: A Systematic Review and Meta-Analysis

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Abstract

Objective: Proteinuria in pregnancy is commonly assessed following a positive urine dipstick using either a 24-hour urine collection or the urine protein-to-creatinine ratio. While the 24-hour urine collection is considered the gold standard, it is time-consuming and often limited by patient compliance, prompting interest in faster and more practical alternatives. To evaluate whether the urine protein-to-creatinine ratio can serve as an alternative to the gold standard 24-hour urine collection to diagnose proteinuria in pregnancy.

Methods: A systematic review and diagnostic meta-analysis were conducted to directly compare the two diagnostic methods. Studies were identified through structured database searches and screened based on predefined inclusion criteria. Five studies (n = 1,811) were included. The inclusion criteria included studies of pregnant patients who used both the urine protein-to-creatinine ratio and 24-hour urine protein to test for proteinuria, and that were available to the public and written in English. A bivariate random-effects model was used to estimate pooled sensitivity and specificity, and analyses of heterogeneity and threshold effect were performed.

Results: The pooled sensitivity was 91% (95% CI: 0.80-0.96), and the pooled specificity was 89% (95% CI: 0.69-0.97). The area under the curve was 0.95, indicating excellent diagnostic performance. A strong negative correlation between sensitivity and specificity was observed (correlation = -0.93), suggesting a potential threshold effect. Forest plot-based estimates indicated substantial heterogeneity ($I^2 \approx 88$-95%), whereas the Zhou and Dendukuri method, which accounts for sensitivity-specificity correlation, suggested moderate heterogeneity ($I^2 = 47.3\%$).

Conclusion: The urine protein-to-creatinine ratio demonstrates high diagnostic accuracy and may serve as a practical alternative to 24-hour urine collection, particularly in settings requiring rapid decision-making or when patient compliance is limited. However, variability across studies suggests that results should be interpreted with caution.

The review was registered in PROSPERO (registration number: 1369716) on April 15, 2026. No major deviations from the protocol were made.

Keywords

Pregnancy, Proteinuria, Proteinuria in pregnancy, Urine protein-to-creatinine ratio, 24-hour urine collection

Introduction

Proteinuria in pregnancy is the presence of excess protein in urine, including albumin, globulin, Bence-Jones protein, and mucoprotein [1]. It occurs due to elevated plasma protein levels, increased glomerular permeability, decreased tubular reabsorption, and renal hemodynamic changes. In a healthy pregnancy, the urine protein level should double because of renal adaptation. By 16 weeks, renal plasma flow increases by 75%; by 5-7 weeks, glomerular filtration rate (GFR) increases by 50%. Increased proteinuria is due to the rise in GFR, likely

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driven by hypervolemia and increased renal blood flow. Proteinuria can suggest other pregnancy issues, such as pre-eclampsia, chronic kidney disease, gestational hypertension, infections, or diabetes. Prompt diagnosis and management are crucial [2].

During routine prenatal visits, a urine dipstick test is performed first to screen for proteinuria. Dipsticks are both semi-quantitative and qualitative. The degree of proteinuria cannot be quantified by dipstick; a 24-hour urine collection is warranted if 1+ or higher is observed [3]. A 24-hour collection is positive if 300 mg or more is collected over 24 hours. Urine protein-creatinine ratio (UPCR) is another alternative for detecting proteinuria. A UPCR of 0.3 mg/mg or higher is abnormal in pregnancy [2]. There are few studies on the accuracy of UPCR compared with 24-hour collection in pregnancy. In non-pregnant patients, UPCR, with a cutoff of 0.3 mg/mg, has sensitivities and specificities of 82-90% and 80-90%, respectively, for predicting progression of chronic kidney disease [4].

The gold standard, 24-hour urine collection, is considered more accurate for quantifying proteinuria. It shows a sensitivity of 83.3% and specificity of 92.8% in pregnant patients, with validation studies reporting over 95% for both, but accuracy relies on complete collection [5,6]. The 24-hour collection displays daily protein variations, whereas UPCR provides a single snapshot. UPCR could improve follow-up and is useful for diagnosing proteinuria. One study reported that over 30% of 24-hour collections were incomplete, and 50% were under collected [7]. The 24-hour urine test is time-consuming and may not be suitable for emergency settings or quick decisions [8].

This meta-analysis aimed to determine the accuracy and reliability of UPCR compared to 24-hour urine protein in diagnosing proteinuria in pregnant patients. A literature review was conducted to identify studies comparing UPCR and 24-hour urine protein in pregnant patients. Five studies published between 2003 and 2013 were reviewed. Further discussion and future research areas are included later in this paper.

Methods

Literature review

The literature search was conducted using PubMed, Nature, and Cochrane Library. This approach may have limited the retrieval of potentially relevant studies. The search used the keywords:

Keywords = “24-hour urine protein test” OR “urine protein to creatinine ratio” AND “in pregnancy”

The references of identified articles were also reviewed to locate additional relevant studies. This allowed inclusion of studies that assessed both UPCR and 24-hour urine protein testing in pregnant patients, even if the primary search keywords were not present.

Source inclusion and exclusion criteria

Studies included in this meta-analysis were selected based on the following criteria:

1. Written in English

2. Available to the public via online databases

3. Studies included pregnant patients and used both UPCR and 24-hour urine protein to assess proteinuria.

4. The studies included quantitative clinical data on the accuracy of both UPCR and 24-hour urine protein in diagnosing proteinuria.

Studies were excluded if they lacked published quantitative data, used a UPCR cut-off other than 0.30 mg/mg, or involved non-pregnant populations.

Search strategy

PubMed

1. "Proteinuria"[Mesh] OR proteinuria OR "urinary protein"

2. "Pregnancy"[Mesh] OR pregnancy OR pregnant OR preeclampsia

3. "Protein Creatinine Ratio" OR "protein-to-creatinine ratio" OR UPCR OR "spot urine protein"

4. "24-hour urine" OR "24-hour urine protein" OR "timed urine collection"

5. 1 AND 2 AND 3 AND 4

6. Filters applied: Humans, English

Cochrane Library

(proteinuria OR "urinary protein") AND

(pregnancy OR pregnant OR preeclampsia) AND

("protein creatinine ratio" OR "protein-to-creatinine ratio" OR UPCR) AND

("24 hour urine" OR "24-hour urine protein")

Nature

("proteinuria in pregnancy" OR "preeclampsia proteinuria") AND

("protein creatinine ratio" OR UPCR) AND

("24-hour urine protein")

Study selection

One reviewer independently screened titles, abstracts, and full-text articles, and the results were checked by two other reviewers. Disagreements were resolved through discussion. Studies that did not meet the inclusion criteria were removed.

Full-text articles were then retrieved and assessed for eligibility. Studies were included if they involved pregnant patients, directly compared the urine protein-to-creatinine ratio (UPCR) with 24-hour urine protein collection for the diagnosis of proteinuria using a cutoff of 0.3 mg/mg, and reported sufficient quantitative data to assess diagnostic accuracy.

A total of 187 records were identified; 14 duplicates were removed, leaving 173 for screening. After reviewing titles

and abstracts, 160 records were excluded. Thirteen full-text articles were assessed for eligibility, of which 8 were removed due to inconsistent or unreported UPCR cutoff values. Five studies met the inclusion criteria and were included in the final meta-analysis.

The study selection process is summarized in Figure 1 (PRISMA flow diagram).

Assembly of data

Data extraction was performed independently by one reviewer using a standardized form and checked by two other reviewers. Discrepancies were resolved by consensus.

For each included study, sample size, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for UPCR were extracted and recorded in a spreadsheet. Using reported sensitivity, specificity, and sample size, true-positives, true-negatives, false-positives, and false-negatives were calculated using standard formulas. Table 1 presents the raw data extracted for meta-analysis.

Assessment of risk of bias

The risk of bias assessment using QUADAS-2 demonstrated moderate methodological quality across the included studies. The reference standard domain was consistently low risk, as all studies used 24-hour urine protein collection as the gold standard. Patient selection bias was generally low in studies with prospective or consecutive enrollment, though some studies lacked sufficient reporting. The index test domain showed unclear risk in several studies due to the lack of blinding reporting. Flow and timing bias were most notable in Saikul, et al. where exclusions due to incomplete urine collection introduced potential bias.

Software and reproducibility

A bivariate random-effects meta-analysis for diagnostic accuracy was performed using the mada package. The analysis used true positive, true negative, false positive, and false negative data from the five included studies. Calculated metrics included pooled sensitivity, pooled specificity, area

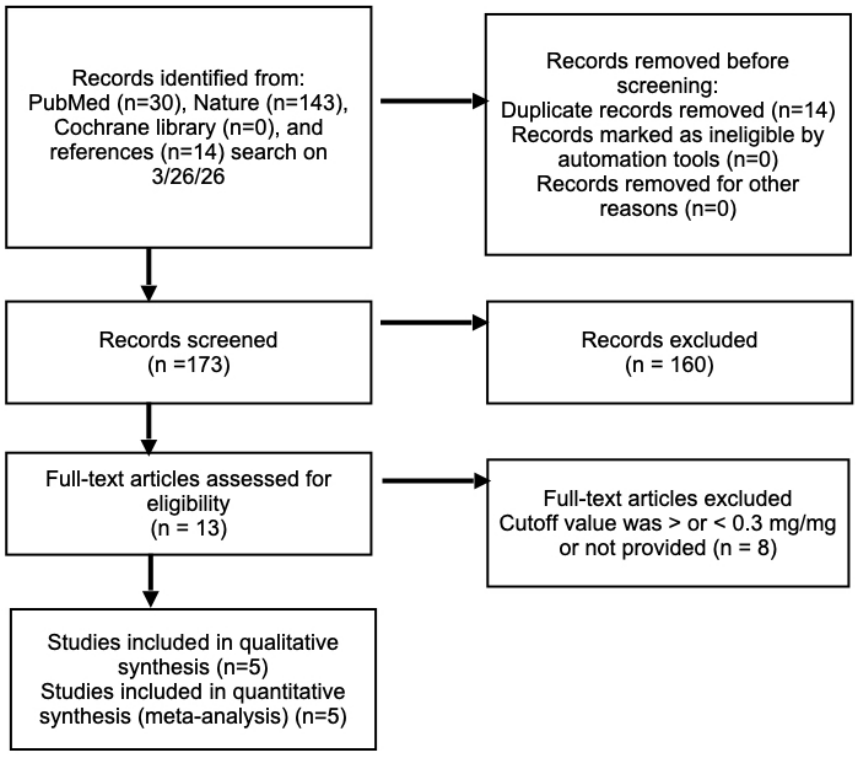

Figure 1: PRISMA flow diagram of study selection.

Table 1: The data for each included study.

Study	nexp	nctrl	TP	FN	FP	TN	sens	spec	ppv	npv
Durnwald_2003	220	220	136	32	23	29	81	55.8	85.5	47.5
Leanos-Miranda_2007	282	927	277	5	8	637	98.2	98.8	97.2	99.2
Saikul_2006	164	164	88	21	6	49	81	88	93	71
Kumari_2013	400	400	270	30	16	84	90	84	95	72
Saudan_2005	100	100	55	4	3	38	93	92	95	90

Abbreviations: Nexp: Experimental Group; Nctrl: Control Group; TP: True Positive; FN: False Negative; FP: False Positive; TN: True Negative; Sens: Sensitivity; Spec: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value

under the curve (AUC), heterogeneity, and the summary receiver operating characteristic (SROC) curve. Statistical significance was set at $p < 0.05$. A bivariate random-effects model and the restricted maximum likelihood (REML) model were used for this data and meta-analysis. The bivariate random-effects model is a statistical method that analyzes two related outcomes, such as sensitivity/specificity, by accounting for study variability and heterogeneity, and constructs an SROC [9]. The REML model produces a nearly unbiased estimate with consistent variance components by dividing the data into two parts: one used to estimate fixed effects and the other to estimate variance components. This allows the effects to be independent of fixed effects [10]. This model is often used with small sample sizes.

Receiver operating characteristic (ROC) curvers are used to evaluate diagnostic performance by plotting sensitivity against the false positive rate. False positive rate (FPR) is located on the x-axis (1-specificity), and the y-axis (sensitivity) contains the true positive rate (TPR) [11].

Forest plots were obtained for sensitivity and specificity for each study.

ChatGPT (OpenAI) was used as an assistive tool to generate research questions, outline the manuscript structure, and refine language for clarity. All outputs were critically reviewed, edited, and verified by the authors, who assume full responsibility for the content.

Meta-analysis was performed using RStudio (version 2025.09.1+401) and R (version 4.5.3) with the mada package.

Certainty of evidence was not formally assessed using GRADE due to the diagnostic nature of the studies and their small number.

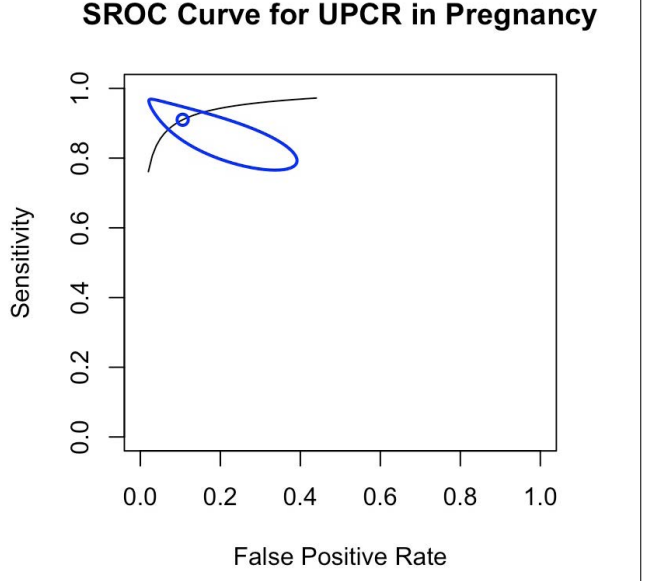

Figure 2: Demonstrates the ROC-space plot with the FPR on the x-axis (1- specificity) and the TPR on the y-axis (sensitivity).

Results

The studies included in this analysis were selected using the flow diagram. The studies were required to include quantitative clinical data on the accuracy of both UPCR and 24-hour urine protein in diagnosing proteinuria. All included studies used a UPCR threshold of 0.30 mg/mg.

A bivariate diagnostic random-effects meta-analysis was performed using the Reitsma model, based on five studies [12-16]. Figure 1 demonstrates the study selection in a flow diagram.

Study characteristics

The included studies were conducted in hospital-based obstetric populations and primarily included patients evaluated for suspected preeclampsia. Study designs were predominantly prospective or cross-sectional.

Diagnostic accuracy

The pooled sensitivity for UPCR for detecting proteinuria was 0.91 (95% CI: 0.80-0.96). The pooled specificity was 0.89 (95% CI: 0.69-0.97), demonstrating that approximately 89% of individuals without proteinuria were correctly classified.

The summary receiver operating characteristic (SROC) curve demonstrated excellent diagnostic performance, with an area under the curve (AUC) of 0.951 and a partial AUC of 0.921. The ROC-space plot is demonstrated in Figure 2.

The pooled sensitivity and specificity are illustrated in a forest plot in Figure 3 and Figure 4.

A strong negative correlation between sensitivity and specificity was observed ($\rho = -0.93$), suggesting a threshold effect across studies. This suggests that variation in diagnostic thresholds or clinical interpretation contributed to differences in reported sensitivity and specificity.

Moderate between-study heterogeneity was identified, with an I^2 of 47.3% (Zhou and Dendukuri method). This indicates that diagnostic accuracy varies across studies, likely due to differences in study populations, clinical settings, and measurement techniques.

Overall, the included studies demonstrated a moderate risk of bias. Patient selection was often unclear due to limited reporting of enrollment methods. The index test (urine protein-to-creatinine ratio) showed unclear risk because blinding between the index and reference test interpretations was not consistently reported. The reference standard (24-hour urine collection) was considered low risk across studies. Flow and timing were also rated as unclear due to insufficient reporting of the interval between tests and potential missing data.

Reporting bias, such as publication bias, was not formally assessed due to the small number of included studies ($n < 10$), which limits the reliability of these analyses.

Risk of bias of included studies

Study-level risk of bias assessment using the QUADAS-2 tool, including domain-specific judgment and supporting

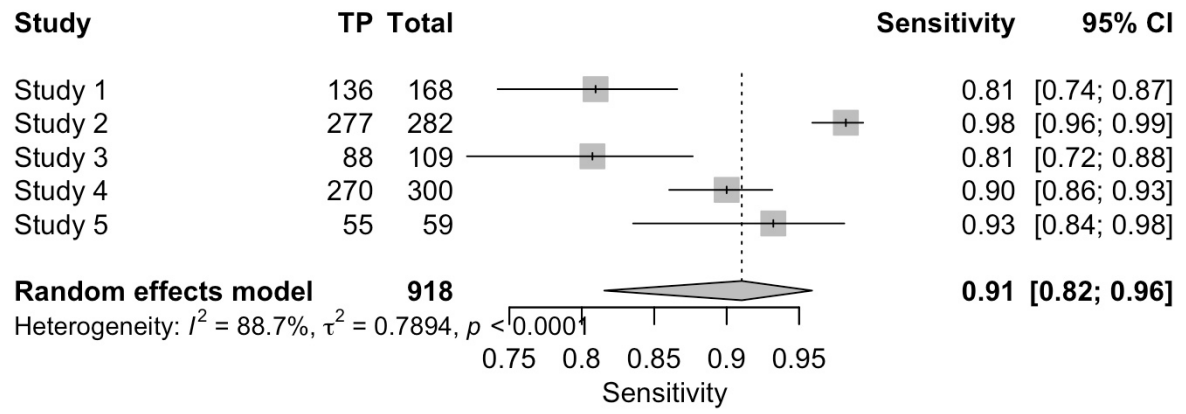

Figure 3: Demonstrates a forest plot for sensitivity.

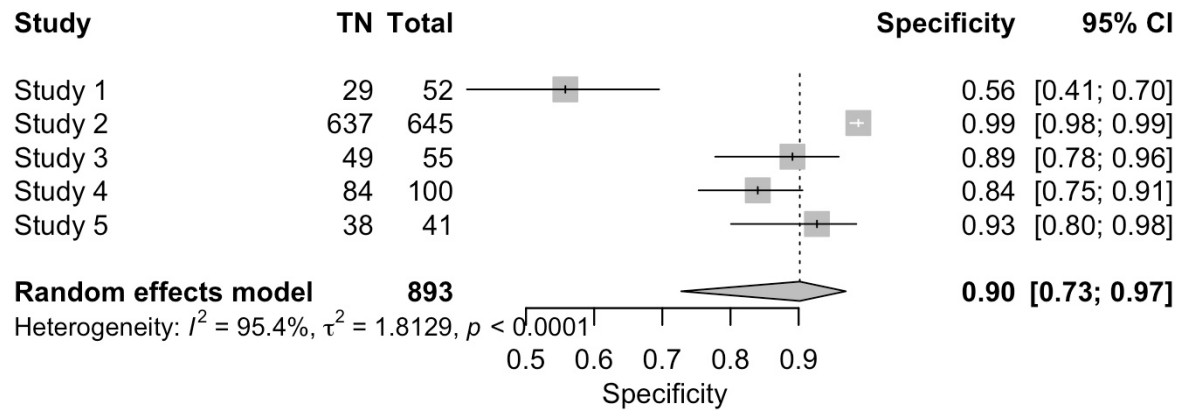

Figure 4: Demonstrates a forest plot for specificity.

Table 2: Risk of bias assessment of included studies using the QUADAS-2 tool.

Study	Patient Selection	Index Test (UPCR)	Reference Standard (24-hr urine)	Flow and Timing	Overall Risk	Substantiation from original study/ rationale
Durnwald & Mercer, 2003 [12]	Low	Unclear	Low	Low	Moderate	Prospective design with defined inclusion/ exclusion criteria (excluded chronic HTN, renal disease). UPCR obtained before 24-hour urine. Blinding not reported (unclear index text bias).
Leanos-Miranda, et al. 2007 [13]	Low	Low	Low	Low	Low	Large cross-sectional study (>1,000) with clearly defined population and standardized testing. Random urine collected before/after 24-hr collection and physicians blinded to results.
Saikul, et al. 2006 [14]	Unclear	Low	Low	High	High	Clear diagnostic test design with gold standard (>300 mg/24 hr). However, patients excluded for incomplete 24-hr urine collection, introducing flow bias.
Kumari, et al. 2006 [15]	Low	Unclear	Low	Low	Moderate	400 consecutive patients which creates a low selection bias. Prospective design with standardized UPCR cutoff (0.3). Blinding not reported (unclear index text bias).
Saudan, et al. 2005 [16]	Unclear	Unclear	Low	Unclear	Moderate	Uses accepted gold standard (24-hr urine), but limited reporting of enrollment, timing, and blinding.

justifications from the original studies. This is demonstrated in (Table 2).

Diagnostic accuracy meta-analysis

The meta-analysis evaluated the diagnostic accuracy of the urine protein-to-creatinine ratio (UPCR) compared with 24-hour urine collection for detecting proteinuria in pregnancy. The findings demonstrate that UPCR has high diagnostic performance, with a pooled sensitivity of 0.91 and a pooled specificity of 0.89, and an area under the curve (AUC) of 0.951, indicating excellent overall accuracy.

These results suggest that UPCR is a reliable method for identifying proteinuria in pregnant patients. The high sensitivity supports its utility as a screening tool, minimizing the risk of missing clinically significant proteinuria. At the same time, the relatively high specificity indicated that UPCR also has a reasonable ability to confirm disease, making it useful not only for ruling out but also for supporting diagnosis in appropriate clinical contexts. Sensitivity analyses were not performed due to the small number of included studies.

Threshold effect and correlation

The correlation between sensitivity and FPR (1-specificity) was -0.925, indicating a strong negative correlation between sensitivity and specificity. The threshold effect suggests that variation in diagnostic thresholds, patient populations, or clinical interpretation contributed to differences in reported accuracy.

Heterogeneity

Heterogeneity estimates differed by method. Forest plot-based estimates suggested high variability ($I^2 \approx 88$-95%), whereas the Zhou and Dendukuri method, which accounts for sensitivity-specificity correlation, indicated moderate heterogeneity ($I^2 = 47.3\%$). This discrepancy reflects methodological differences in heterogeneity estimation and underscores the importance of using approaches that account for the correlation between sensitivity and specificity in diagnostic meta-analysis. The observed heterogeneity likely arises from differences in patient populations, timing of urine collection, disease severity, and laboratory measurement techniques.

These findings suggest that the UPCR has high sensitivity and is an effective screening test for ruling out proteinuria in pregnancy. The specificity also suggests a strong rule-in capability of proteinuria in pregnancy. The overall accuracy of the UPCR is excellent with an AUC of 0.95. This supports the use of the urine protein-to-creatinine ratio as an alternative to the gold-standard 24-hour urine collection for classifying the degree of proteinuria in pregnancy after screening with a urine dipstick. The small number of included studies (n = 5) limits the stability of pooled estimates and reduces the generalizability of the study.

Discussion

The outcomes of the meta-analysis in this paper supported the urine protein-creatinine ratio as a highly sensitive screening test and an accurate test for proteinuria, with excellent diagnostic accuracy. UPCR, based on this meta-analysis, is considered clinically useful in pregnancy to reduce the 24-hour urine collection required to assess the degree and severity of proteinuria. These findings apply to the UPCR value of 0.3 mg/mg. The sensitivity, specificity, and diagnostic accuracy are comparable to those of the 24-hour urine collection. In situations where the 24-hour test is not strictly required, patient compliance or follow-up is uncertain, or in emergency settings, UPCR can be used to quickly “rule out” significant proteinuria.

This is among the few meta-analyses that use a strict cut-off value of 0.3 mg/mg for UPCR; however, others have used varying cut-off values or assessed the risk of maternal complications based on UPCR. A meta-analysis was performed comparing UPCR and 12-hour urine collection, which showed a sensitivity of 87% (95% CI: 83-91%) and specificity of 86% (95% CI: 79-91%); however, the cut-off value ranged from 0.15 to greater than 0.3 mg/mg [17]. Another meta-analysis using twenty-four trials (n = 3,186) to investigate the diagnostic accuracy of the protein-to-creatinine ratio in diagnosing proteinuria in women being evaluated for preeclampsia was found to have a sensitivity of 91.0% (95% CI: 87.0 - 93.9) and specificity of 86.3% (95% CI: 78.4 - 91.7) [18]. However, the cut-off value varied; >0.3 mg/mg was found to have the best accuracy in this study.

The data used in this paper were limited by the scarcity of studies directly comparing UPCR to 24-hour urine collection, as well as the wide range of cut-offs for classifying proteinuria using UPCR. There needs to be further research and more data collection on the diagnostic accuracy of proteinuria in pregnancy using UPCR compared to 24-hour collection, with a focus on different disease populations in pregnancy, such as how accurate UPCR is in cases of chronic hypertension, preeclampsia, and eclampsia.

Conclusion

According to the data used in this analysis, the urine protein-creatinine ratio is a highly sensitive and accurate test that can be used as an alternative to 24-hour urine collection to quantify proteinuria and may be a practical option for diagnosing proteinuria in pregnancy.

Acknowledgement

This research was funded by Lincoln Memorial University-Debusk College of Osteopathic Medicine Research Department.

PRISMA checklist

PRISMA checklist with the page numbers identifying the location of information, demonstrated in Figure 5.

The datasets and R code used for this meta-analysis are available from the corresponding author upon reasonable request.

Author Contributions

Dr. Kamran Hasni contributed to the study conception and design, supervised the project, and provided critical revision

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	p. 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	p. 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	p. 3-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	p. 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	p. 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	p. 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	p. 6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each reco and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	p. 7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	p. 7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	p. 7-8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	p. 7-8
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed eac study and whether they worked independently, and if applicable, details of automation tools used in the process.	p. 8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	p. 8-9
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	p. 8-9
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	p. 8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	p. 9

Figure 5: PRISMA checklist with page number identification.

for the manuscript for important intellectual content. Taylor Campbell contributed to the conception and design of the study, conducted the literature search, performed data extraction and statistical analysis, and drafted the manuscript. Kacie Coy contributed to data interpretation and critically reviewed and edited the manuscript.

All authors contributed to the interpretation of the data, reviewed and revised the manuscript critically for important intellectual content, approved the final version for publication, and agreed to be accountable for all aspects of the work, ensuring the accuracy and integrity of the study.

Conflicts of Interest

No conflicts of interest for any of the authors.

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