
Urine albumin/creatinine ratio for the assessment of albuminuria in hypertensive disorders of pregnancy

Mohamed I. Taema 1, Amr Sobhy Sweed 1, Ahmed M. Radwan 2
1- Obstetrics and gynecology department, faculty of medicine, Ain shams University
2- Obstetrics & Gynecology Department, Faculty of Medicine - Zagazig University

Abstract

Background: The Protein-Creatinine ratio (P/C Ratio) measurement is an alternative diagnostic method for quantitatively evaluating proteinuria in pre-eclampsia. This study aimed to assess the precision of the protein/creatinine ratio as a diagnostic tool for proteinuria in preeclamptic pregnant patients.

Methods: A prospective study was conducted at the Obstetrics and Gynecology Department of a private hospital in KSA from July 2021 to January 2023, 100 pregnant women with preeclampsia were included in the study. All patients in the study underwent a history taking, physical examination, routine laboratory investigations, and urine protein/creatinine ratio assessment.

Results: The findings found substantial positive connections between 24-hour protein, proteinuria, and serum creatinine, as well as strong positive P/C ratio and 24-hour protein correlations. Urine creatinine and P/C ratio were shown to have strong negative correlations. The P/C ratio needs to be less than 0.29 to detect more than 300 mg of protein excretion per 24 hours, detecting 300 mg/24 hours of protein excretion with sensitivity of 95.3% and specificity of 71%.

Conclusion: Random PCR may be employed in urgent situations as a quick, simple, and accurate diagnostic for the detection of substantial proteinuria in hypertensive diseases during pregnancy.

Introduction

Many illnesses can raise blood pressure and even cause proteinuria; hence, as the diagnosis becomes more precise, so does the need for meticulous evaluation and delivery planning. (1,2).

Quantifying proteinuria in preeclampsia is essential for diagnosing the disease's severity and prognosis. (3). Although the gold standard for quantifying proteinuria, 24-hour urine collection has some drawbacks. The patient finds it difficult; it is frequently inaccurate due to under-collection, and results are delayed for at least 24 hours while the collection is finished. (4). In non-

Corresponding author:

Mohamed I. Taema
Assistant Professor Obstetrics and Gynecology Department, Faculty of Medicine, Ain Shams University.
mohamed.taema@yahoo.com

pregnant people, the threshold for urine protein excretion is typically 150 mg/day, while lower and higher amounts have been proposed. These threshold values often double during pregnancy, with 300 mg/d being the most typical value (5).

The spot P/C ratio has been tested for usage during pregnancy with inconsistent results. While some researchers have emphasized caution in its implementation because the renal function can become unstable in preeclampsia within hours, others have endorsed its use by establishing significant correlations between spot P/C and 24-hour collections. (6)

The ratios of spot albumin to creatinine and spot protein to creatinine have both been extensively studied and are used outside of pregnancy. The National Kidney Foundation currently recommends these tests (instead of 24-hour urine collection) to detect proteinuria, without addressing pregnancy specifically (7).

The Society of Obstetric Medicine of Australia and New Zealand, the International Society for the Study of Hypertension in Pregnancy, and the Society of Obstetricians and Gynecologists of Canada have all approved the spot urine ACR, but not all international consensus bodies, including the American Congress (2).

This study's objective is to evaluate the accuracy of the protein/creatinine ratio as a diagnostic tool for pregnant people with preeclampsia who have proteinuria.

Patients and methods

A prospective investigation was conducted at the Obstetrics and Gynecology Department of a private hospital in KSA in the period from July 2021 to January 2023, hundred of pregnant women with a possible preeclampsia diagnosis were included in the study after being fully told of its purpose, the necessary procedure, and the follow-up schedule. After

agreeing to participate, they signed the consent form.

Exclusion standards:

- A recognised kidney disorder.
- Vigorous workout (more than one hour of vigorous exercise on the day of urine collection).
- Bacteriuria is present.
- More than 24 hours in bed.
- Gestational diabetes.
- Ladies gave birth on the day that urine was collected.

Methods: Each pregnant participant in the study underwent:

Complete history taking and physical assessment come first:

- Vital indicators, including respiration rate, temperature, blood pressure, and heart rate.
- A thorough examination of the heart, lungs, legs, eyes, and nervous system.
- Fundal examination of the abdomen ,Leopard's manouver, FHS.

3- Investigations:

Full blood count, blood and Rh grouping, kidney function tests, urine analysis and culture, determination of urine protein/creatinine ratio, Urine from the previous 24 hours was also taken in order to measure total protein , liver function tests

The amount of protein in urine was detected using the Bradford method using BSA (also from Bio-Rad) as a calibrator (Bio-Rad Protein Assay Kit, Bio-Rad Laboratories). Spinreact kits were used to measure the creatinine levels in urine using the modified kinetic Jaffe reaction in a 96-well plate with a filter at 490 nm. The CVs for each assay were under 1.2%. By dividing the urinary protein concentration by the urine creatinine concentration, both stated in (mg/dl), one can determine the urine protein to creatinine ratio.

The shift in the complex's absorption spectra from 460 to 600 nm that happens at an acidic pH between Pyrogallol Red and Molibdate is the primary way to evaluate the presence of protein in urine (PRM) and the basic amino groups of urine. The intensity of the colored complex formed is proportional to the concentration of protein in the sample.

Statistical analysis

Data were entered checked and analyzed using Epi-Info version 6 and SPP for Windows version 8.

RESULTS

The included women's median age was 29.1 ± 6.7 years (range:19-42) At recruiting, the average gestational age was 32.2 weeks (range: 20-38). The mean blood pressure readings were 100± 12.2 mmHg for the mean diastolic reading and 154.3± 12.9 mmHg for the mean systolic reading. (table 1). Significantly favourable relationships between 24 hour protein, proteinuria, and serum creatinine were found. (table 3). Very positive relationships between the P/C ratio and the 24 hour protein were found. P/C ratio and urine creatinine were shown to have substantial negative associations. (table 4) To detect protein excretion greater than 300 mg per 24 hours, the P/C ratio must be less than 0.29..(table 5).

able (1): Demographic data

	Median (range)
Age	(19-42)
Gestational age (week)	32.2 ± 3.6 (20-38)
Systolic blood pressure	154.3 ± 12.9 (110-180)
Disatolic blood pressure	100 ± 12.2 (70-110)

Table (2): Laboratory findings, liver function tests and urine examination among studied cases

Laboratory findings	Mean ± SD
Hb	11.2 ± 1.6
Platelet x 10 ³	185.5 ± 70.7
creatinine level(mg / dl)	0.80 ± 0.12
Liver function tests	
Albumin	2.6 ± 0.7
SGOT	26± 2
SGPT	28± 6
Urine examination	
Volume (ml)	1315 ± 690.7
Protein (mg/dl)	189.6± 56
Creatinine (mg/dl)	81.5± 26
24 hour protein(mg/24h)	1965± 43
P/C ratio	2.1± 0.3

Table (3): Correlation between protein and other parameters

24 hour protein	R	P
Volume	-0.04	0.76 (NS)
Proteinuria	0.37	0.01 (S)
Creatinine	0.12	0.47 (NS)
Serum creatinine	0.47	0.00 (S)
Albumin	-0.27	0.05 (NS)
SGOT	0.04	0.76 (NS)
SGPT	0.01	0.97 (NS)
GA	-0.06	0.66 (NS)
SBP	0.17	0.25 (NS)
DBP	0.19	0.62 (NS)
Hb	0.39	0.29 (NS)
Platelets	-0.08	0.56 (NS)

Table (4): The correlation between P/C ratio and other variables

P/C ratio	R	P
Proteinuria	0.65	0.00 (S)
Volume	-0.2	0.16 (NS)
Creatinine	-0.32	0.02 (S)
24 hour proteinuria	0.122	0.039 (S)
Serum creatinine	0.12	0.41 (NS)
Albumin	0.19	0.19 (NS)
SGOT	0.03	0.86 (NS)
SGPT	0.03	0.84 (NS)
GA	-0.007	0.96 (NS)
SBP	0.12	0.41 (NS)
DBP	0.36	0.34 (NS)
Hb	0.04	0.8 (NS)

Table (5): Accuracy of P/C ratio at cut off < 0.29

cutoff value of P/C ratio	0.29
Sensitivity	95.3%
Specificity	71%
PPV	98.4%
NPV	94.8%

Discussion

Hypertensive disorders of pregnancy complicate 12-22% of pregnancies. It includes a spectrum ranging from non-proteinuric gestational hypertension to severe pre-eclampsia with heavy proteinuria (8,9).

The main goal of this study was to assess the precision of the protein/creatinine ratio as a diagnostic tool for proteinuria in a sample

of 100 preeclamptic pregnant patients. Pregnancy-related hypertension, such as gestational hypertension, mild pre-eclampsia, or severe pre-eclampsia, is present in all of the women who were included in the study. This condition is identified by a systolic arterial blood pressure of at least 140 mm Hg and a diastolic arterial blood pressure of at least 90 mm Hg, with or without proteinuria. (detected by dipsticks).

The included women's median age was 29.1± 6.7 years (range: 19-42 years). At recruiting, the average gestational age was 32.2 weeks (range: 20-38weeks).

A random urine sample from each included woman was collected to examine her levels of protein and creatinine, and the urinary protein-to-creatinine ratio was computed. Urine from the previous 24 hours was also taken in order to measure total protein.

Very positive relationships between the P/C ratio and the 24 hour protein were found. P/C ratio and urine creatinine were shown to have substantial negative associations. The cutoff value for the P/C ratio is 0.29 to identify protein excretion > 300 mg / 24 hours with sensitivity 95.3% and specificity 71%. The correlation coefficient between random urine p/c ratio and 24-hour urine protein and the cutoff point for the P/C ratio is 0.29

Numerous studies have been conducted over the past 20 years on the reliability of measuring the protein to creatinine ratio in random urine samples as an alternative to the gold standard 24-hour urinary total protein. Some of these studies found a strong correlation between the two, while others found a weak correlation.

The findings of this study concur with those of Wheeler et al(2017) 's investigation into the predictability of a random urine protein to creatinine ratio in determining the presence of severe proteinuria. The study comprised 126 women with comparable demographics who were admitted for pre-eclampsia evaluation. In this investigation, the connection between

the 24-hour urine protein and the random urine protein to creatinine ratio was highly significant ($r=0.88$, $p0.001$). Random urine protein's ideal cutoff value is used to 0.21 for 24-hour urine protein ≥ 300 mg per 24h .(10)

A P/C ratio of less than 0.21 (300 mg every 24 hours) exhibited an 83.3% NPV, or negative predictive value.

According to the International Society for the Study of Hypertension in Pregnancy's (ISSHP) guidelines for classification and diagnosis of hypertensive disorders of pregnancy, the random protein to creatinine ratio is said to be equivalent to total protein excretion in a 24-hour sample when it comes to identifying significant proteinuria (11)

The value of the random urine protein to creatinine ratio in the diagnosis of severe proteinuria was thoroughly reviewed by Price et al. (2015), who looked at 16 studies. The 24-hour urine protein concentration and the random urine protein to creatinine ratio have consistently been reported to have strong, positive associations, with correlation values ranging from 0.8 to 0.97..(12)

The first urine protein to creatinine ratio after 4 hours was investigated by Saikul et al. (2016) as a potential indicator of severe proteinuria. With similar demographics, 164 pregnant women who also experienced hypertension during pregnancy were included. The included women had a pre-eclampsia severity of 48, 74 mild cases, and 52 gestational hypertension. The optimal cutoff value according to the ROC curve was 0.3 (area under the curve = 0.845; 95% confidence interval: 0.79-0.9, $p0.001$). The sensitivity and specificity of this value were 81% and 88% respectively. (13)

(2018) Shahbazian and Hosseini-Asl investigated the relationship between spot urine P/C ratio and 24-hour urine protein excretion in patients undergoing preeclampsia evaluation. They came to the conclusion that a random urine P/C ratio can forecast the amount of protein excretion in

urine during a 24-hour period collection in pregnant women. (14)

The usefulness of this ratio to identify substantial albuminuria in patients with a suspicion of preeclampsia was also assessed by Nisell et al. in a 2016 study. They recommended that the more practical protein/creatinine ratio on spot pee can typically take the place of the more time-consuming 24-hour urine collection (15)

In order to find the optimum spot PC ratio cutoff values for moderate and severe preeclampsia, Haung et al. (2019) analysed the correlation between albuminuria as measured by PCR and the amount of albumin in a 24-hour urine collection in women with preeclampsia. It was discovered that a spot PC ratio in a midstream urine samples is less complicated, more practical, and more precise than measuring total protein in a 24-hour urine collection. (2)

The findings of a study carried out by Ragip et al. (2014) were not particularly encouraging. In the later study, records of 185 pregnant women with late-pregnancy moderate hypertension were examined. (9)s. The correlation coefficient between the 24-hour urine protein and the random urine protein to creatinine ratio was less than what was predicted in the current investigation. The random urine protein to creatinine ratio's best cutoff value was 0.19 (sensitivity: 85%, specificity: 73%).

Ragip et al(2014) .'s study came to the conclusion that the random urine protein to creatinine ratio was not a reliable indicator of severe proteinuria in this group of women. (9)

Wikstrom et al. (2016) investigated the relationship between the amount of albumin in 24-hour urine samples from women with pre-eclampsia and severe albuminuria, as defined by the protein to creatinine ratio. (11) They did not advise using a random PC ratio to detect proteinuria in manifest pre-eclampsia because this ratio varies during the

day and has a limited correlation to the 24-hour urine protein test. In order to quantify proteinuria in preeclamptic women with substantial proteinuria, they advised 24-hour urine collection with protein to creatinine ratio or total albumin measurement(11)

Conclusion

In hypertensive diseases during pregnancy, severe proteinuria might be diagnosed quickly, easily, and accurately using random PCR, making it useful in urgent cases. With sensitivity of 95.3% and specificity of 71%, PCR in random urine correlates well with 24-hour urine protein at a threshold value of 0.29.

References

1. Munir S. Role of growth factors in preeclampsia: Early detection and treatment, *Avicenna* 2013;1:1-9
2. Huang Q, Gao Y, Yu Y, Wang W, Wang S, Zhong M. Urinary Spot Albumin:Creatinine Ratio for Documenting Proteinuria in Women With Preeclampsia. *Rev Obstet Gynecol.* 2019; 5(1):9-15
3. Cunningham FG, Gant NE, Leveno KJ, Steven LB, John CH, Larry CG et al. Hypertensive disorders in pregnancy. In *Williams Obstetrics*, 22nd ed., New York, Mcgraw- Hill 2018; P.761-808.
4. Maynard SE, Thadhani R. Pregnancy and the Kidney. *J Am Soc Nephrol* 2019;20: 14–22.
5. Lindheimer MD, Kanter D. Interpreting abnormal proteinuria in pregnancy: the need for a more pathophysiological approach. *Obstet Gynecol.* 2020; 115: 365–375.
6. Waite LL, Atwood AK, Taylor RN. Preeclampsia, an implantation disorder. *Reviews in Endocrine & Metabolic Disorders* 2020; 3 (2): 151–8.
7. Côté AM, Firoz T, Mattman A, Lam EM, von Dadelszen P, Magee LA. The 24-hour urine collection: gold standard or historical practice? *Am J Obstet Gynecol.* 2008;199(6):625.e1-6.
8. James DK, Steer PJ, Weiner CP. Pregnancy antecedent of high risk pregnancy. In: *High risk pregnancy 3rd edition.* Elsevier. 2018; Chapter 1; 7-25.
9. Raqib A, Baykal C, Karacay O, Geyik PO, Altun S, Dolen I. Random urine protein-creatinine ratio to predict proteinuria in new-onset mild hypertension in late pregnancy. *Obstet Gynecol.* 2004;104(2):367-71.
10. Wheeler TL 2nd, Blackhurst DW, Dellinger EH, Ramsey PS. Usage of spot urine protein to creatinine ratios in the evaluation of preeclampsia. *Am J Obstet Gynecol.* 2007;196(5):465.e1-4.
11. Wikström AK, Wikström J, Larsson A, Olovsson M. Random albumin/creatinine ratio for quantification of proteinuria in manifest pre-eclampsia. *BJOG.* 2006;113(8):930-4.
12. Price CP, Newall RG, Boyd JC. Use of protein:creatinine ratio measurements on random urine samples for prediction of significant proteinuria: a systematic review. *Clin Chem.* 2005;51(9):1577-86.
13. Saikul FA, Mamsouri. Using 2 hour/6hour urine protein measurement as substitute. *Diagnostic Methods for evaluation of preeclampsia. The Internet Journal of Gynecology and Obstetrics.*2016 ;10:1-5
14. Shahbazian N, Hosseini-Asl F. Comparison of spot urine protein-creatinine ratio with 24-hour urine protein excretion in women with preeclampsia. *IJKD* 2018; 2:127-31.
15. Nisell H, Trygg M, Back R. Urine albumin/creatinine ratio for the assessment of albuminuria in pregnancy hypertension. *Acta Obstetrica et Gynecologica.* 2016; 85: 1327-1330.