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Correlation of Spot Urine Protein:Creatinine Ratio with 24-hour Urinary Protein in Preeclampsia: A Cross Sectional Study

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Authors' contributions

This work was carried out in collaboration between all authors. Authors SVK and GSK carried out the design and coordinated the study, participated in most of the experiments and prepared the manuscript. Authors MR and SVK provided assistance in the design of the study, coordinated and carried out all the experiments and participated in manuscript preparation. Authors MR and KH provided assistance for all experiments. All authors have read and approved the content of the manuscript.

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ABSTRACT

Aims: The present study was undertaken to evaluate the diagnostic value of protein:creatinine ratio in spot voided urine sample for detection of proteinuria as compared to those of 24 hour urine sample in patients with preeclampsia, and also to determine the optimal cut-off value of protein:creatinine ratio with best sensitivity and specificity for the prediction of significant proteinuria.
Study Design: Cross sectional study.

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Place and Duration of the Study: The study was conducted at teaching hospital in North Karnatak, India. The study was conducted from Jan 2012 to February 2013.
Methods: This study was conducted on 52 preeclampsia patients. The 24 hour urine protein and random urine protein:creatinine ratio was determined. Pearson's correlation, sensitivity and specificity were determined using 24-hour urinary protein as a gold standard for spot urine protein:creatinine ratio. Receiver operators characteristic (ROC) curve and area under curve was also determined using SPSS (11.5) software. All the results were expressed in mean±SD.
Results: Fifty two preeclampsia patients participated in this study. The average 24 hour urinary protein was 1643.3±2079.5 mg/day. The spot urine protein:creatinine ratio was 1.47±1.68. There was a positive correlation between 24 hour urinary protein and spot urine protein:creatinine ratio (r = 0.86, *P*<0.0001). The area under the receiver operators characteristic curve for urine protein:creatinine ratio at various cut-off was 0.914 (95% confidence interval: 0.800-0.975, *P*<0.0001). The sensitivity and specificity was 71.5% and 100% respectively at protein:creatinine ratio cut-off of 0.66.
Conclusion: The random urine protein:creatinine ratio predicts the amount of 24-hour urinary protein excretion with high accuracy. Hence it can be used as a faster diagnostic substitute for 24-hour urinary protein estimation in preeclampsia.

Keywords: Preeclampsia; 24-hour urine protein; urine protein:creatinine ratio.

1. INTRODUCTION

Pre-eclampsia (PE) has been named the "disease of theories" and was described as early as 3000 years ago by the ancient Egyptians. PE is a pregnancy specific disorder, most common, serious multisystem disease and is only cured by delivery [1-5]. According to the International Society for the Study of Hypertension in Pregnancy, PE can be defined as de novo hypertension occurring after 20 weeks of gestation associated with proteinuria, with previously normotensive and nonproteinuric women. Hypertension is defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg measured at two occasions with at least 4 hours apart and proteinuria is defined as ≥ 300 mg per day [6]. The PE has two stages. The first stage is an altered formation of the placenta. The second stage is characterised by clinical manifestations, which include hypertension and proteinuria, seen from 20 weeks of gestation and above [7-9].

Proteinuria is because of two mechanisms 1) The abnormal transglomerular passage of proteins due to damage to glomerular capillary wall which becomes permeable to high molecular weight proteins and 2) because of increased concentration of proteins in tubular lumen which crosses the reabsorption capacity of epithelial cells of the proximal tubuli and damages them [5]. Proteinuria is defined as the protein in urine, the amounts exceeding 0.3 g in a 24 hour urine collection or in concentrations more than 1 g per litre (1+ on urine dipstick), in two random samples that are collected at least four hours apart. When protein excretion exceeds these levels in pregnant women, it is considered abnormal and a sign of PE [2,5,10,11].

Proteinuria in PE is usually done by routine simple visual dipstick urine analysis of a voided midstream sample. The dipstick is inexpensive, easy to use, and provides a rapid result but has been shown to have low sensitivity and specificity, inaccurate, high false positive and negative results over 24 hour urine protein [2,11].

Urine collection over 24 hours is the gold standard method and considered the traditional method for quantification of proteinuria in pregnancy, but has several limitations [11-14]. Mitchell et al. [15] had to discard 20% of the samples because of incomplete collection; Chitalia et al. [16] in their study had to discard 10% of the 24 hour urine samples because of similar cause. Also, it may not be possible to complete the urine collection if delivery occurs [11]. The results are not available to the clinician before 24 hours, delay in clinical diagnosis and ideal strategy for the immediate management of hypertension during pregnancy [17] that results in prolonged hospital stay, thereby increasing patient anxiety and healthcare costs [2,11]. The protein excretion during the day varied from 100% to 500%. This variation is attributed to several factors like variation in water intake and excretion, rate of diuresis, physical exercise, recumbency and diet intake. The variation may be further exacerbated by changes in blood pressure and renal pathology [18]. Thus, Newman et al. [19] found that the mean

intraindividual variation in the P:C ratio was 38.6%, whereas that of the protein excretion was 96.5%. Koopman et al. [20] also found similar results.

There is a need of an alternative method which is rapid, as well as a valid and accurate test to identify significant urinary proteinuria. Sufficient evidence from studies show a strong association between random P:C ratio and 24 hour protein excretion, and the International Society for the Study of Hypertension in Pregnancy has accepted this test as a method for identification of significant proteinuria. However, a consensus has been poorly described and standardized, to be used in clinical practice, specifically in ethnic group with suspected PE [11,12].

Estimation of total protein in spot urine sample, avoids the 24-hour urine collection, but is largely influenced by the body hydration. This variation can be eliminated by factoring the spot urine total protein concentration by urine creatinine concentration, i.e. the urine P:C ratio. Random urine sampling for P:C ratio would be more acceptable and less time consuming. The P:C ratio takes into account the fact that creatinine excretion remains fairly constant in presence of a stable glomerular filtration rate. The protein excretion would also be fairly stable. Therefore, the ratio of the two in a single voided sample would reflect the cumulative protein excretion over the day, as the two stable rates would cancel out the time factor. Measurement of total P:C ratio on random (spot) urine sample correlates well with 24 hour total protein excretion [18,21,22].

In this context, the present study was undertaken to evaluate the diagnostic value of P:C ratio in spot voided urine sample for detection of proteinuria as compared to those of 24 hour sample in patients with PE, and also to determine the optimal cut-off value of P:C ratio with best sensitivity and specificity for the prediction of significant proteinuria.

2. MATERIALS AND METHODS

The study was conducted on PE subjects admitted in Hanagal Shri Kumareshwara hospital, Bagalkot. The study was approved by S. Nijalingappa Medical College ethical committee. Informed consent was obtained. The study was conducted from Jan 2012 to February 2013. Singleton pregnant women with more than 20 weeks of gestation were included on the basis of clinical findings, new- onset proteinuria of ≥1+ on urinary dipstick, hypertension (≥140/90,≤160/110), and/or oedema (International Society for the Study of Hypertension in Pregnancy). Detailed history taking and clinical examination were carried out. Patients with urinary tract infection, hematuria, chronic renal failure, glomerular nephritis due to other systemic conditions, previously existing hypertension, diabetes mellitus were excluded from the study.

The sample size was calculated using Open epi software, version 2.3.1. According to the study done by Pacarizi H [23], the mean ± SD of blood urea nitrogen and creatinine index in controls and cases were 12±3 and 19±7.7 respectively. At 95% of confidence level and 80% power of the study, the sample size was calculated to be 52. A total number of 84 patients were selected for the study but 27 patients did not turn-up and 57 subjects participated in the present study. Five participants were excluded from the study, because of improper collection of 24- hour urine, and finally, the study was stopped when we got 52 PE patients, which was the required sample size. For each patient, a random urine collection was collected for the calculation of the P:C ratio. All random samples were collected before the 24-hour urine collections. Twenty four hour urine sample was collected by instructing subjects to begin collection immediately after completion of first voiding in morning and to collect all urine into same container having 5mL of 10% thymol in isopropanol as a preservative for 24 hours, including final void at completion of 24 hour period [24]. This was thoroughly mixed and a sample of 2 mL was taken for evaluation of proteins. Total volume was noted and calculation was done for 24 hours. Urinary protein quantification was determined by turbidometric method, and urinary creatinine was determined by the modified Jaffe reaction, kits were supplied by Biolab Diagnostics (I) and Pvt Ltd and CPC diagnostics Pvt Ltd India, respectively. P:C ratio was calculated by dividing the urinary protein concentration by urinary creatinine concentration. Proteinuria ≥ 300 mg in 24-hour urine sample was considered as significant proteinuria [22].

2.1 Statistical Analysis

Statistical package for social science (SPSS for window version; SPSS, 11.5 Inc, Chicago IL) software was used for statistical analysis. Pearson's correlation coefficient was used to show the correlation between the spot urine P:C ratio and 24 hour urine total protein. Sensitivity,

specificity, predictive values of random urine P:C ratio at various cut-off values were evaluated using 24 hour urine total protein level as the gold standard. Receiver operator characteristic (ROC) curves were evaluated to determine an optimal P:C ratio value that maximized the sensitivity and specificity in identification of significant proteinuria that was based on 24-hour urine collections. Area under the curve was calculated. All the results were expressed as mean±SD.

3. RESULTS

The general characteristics like blood pressure and biochemical parameters of the study subjects are shown in Table 1. The mean age was 28.1±4.88 years. The mean gestational age was 33.5±4.40 weeks. The systolic and diastolic blood pressures met the diagnostic criteria of preeclampsia. Serum Urea and blood urea nitrogen (BUN) were within normal limits, whereas serum creatinine and uric acid were slightly higher than the normal range.

Table 2 shows the correlation between the 24 hour urine protein and various biochemical parameters in blood and urine P:C ratio. There is a positive correlation between urine P:C ratio and 24 hour urine protein (Fig. 1). BUN, Serum Urea and Serum Uric acid had statistically significant (*P*<0.05) positive correlation with 24 hour urine protein. Serum creatinine was also positively correlated with 24 hour urine protein, but was not statistically significant.

Sensitivity, specificity, predictive values of random urine P:C ratio at various cut-off values were evaluated using 24 hour urine total protein level as the gold standard. A receiver operator characteristics (ROC) curve was determined. The area under the ROC curve for random urine P:C ratio at various cut-off was 0.914 (95% confidence interval, 0.800-0.975; *P*<0.0001) (Fig. 2). Sensitivity and specificity of P:C ratio to detect proteinuria at various cut-off values is shown in Table 3. A sensitivity of 71.05% and specificity of 100% were achieved to detect proteinuria at P:C ratio greater than 0.66. At cut-off value of greater than 0.12, sensitivity was 100% but specificity reduced to 25%.

4. DISCUSSION

In the present study BUN, Serum Urea and Serum Uric acid were positively correlated with 24 hour urine protein which was found to be statistically significant ($p < 0.05$). Nischintha S et al. [25] in their study found statistically significant correlation between P:C ratio and Serum uric acid (r=0.355, *P*<0.002). In the present study, serum creatinine was also positively correlated with 24 hour urine protein, but it was not statistically significant, this can be overcome by further study with large sample size.

Table 1. General characteristics of study subjects

	Mean±SD	Minimum	Maximum
Age (years)	28.1±4.88	20.00	38.00
Gestational (weeks)	33.5±4.40	21.00	39.00
SBP (mmHg)	163.4±20.2	140.00	240.00
DBP (mmHg)	106.4±10.8	90.00	140.00
Urea (mg/dl)	18.7±8.38	10.00	43.00
Creatinine (mg/dl)	0.82±0.28	0.50	1.70
Uric acid (mg/dl)	4.9±1.44	1.20	9.40
BUN (mg/dl)	8.7±3.9	4.67	20.09
24 hr urine protein (mg/24 hours)	1643.3±2079.5	116	8536
P:C ratio	1.47±1.68	.10	5.90

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood Urea Nitrogen; P:C ratio: Protein: Creatinine ratio

Table 2. Correlation between various biochemical parameters and 24 hour urine protein levels

Parameters	Correlation coefficient (r)	*P* value
Urine P:C ratio	0.86	0.0001
BUN	0.32	0.02
Serum urea	0.32	0.02
Serum creatinine	0.20	0.14
Serum uric acid	0.30	0.03

BUN: Blood Urea Nitrogen; P: C ratio: Protein:Creatinine ratio

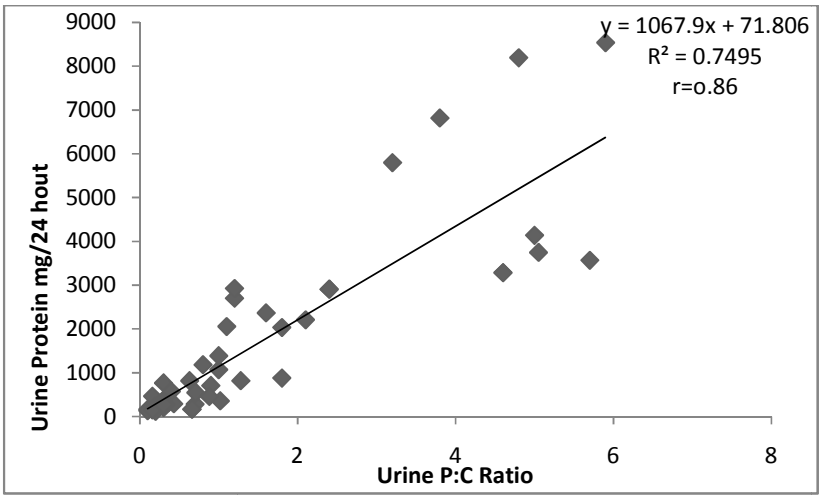

Fig. 1. Correlation between 24 hour urine protein excretion and urine P:C ratio

Table 3. Criterion values and coordinates of the ROC curve

Criterion	Sensitivity	95% CI	Specificity	95% CI
>=0.1	100	90.7 - 100.0	0	0.0 - 26.5
>0.12	100	90.7 - 100.0	25	5.5 - 57.2
>0.16	97.37	86.2 - 99.9	41.67	15.2 - 72.3
>0.2	97.37	86.2 - 99.9	58.33	27.7 - 84.8
>0.24	94.74	82.3 - 99.4	58.33	27.7 - 84.8
>0.3	86.84	71.9 - 95.6	75	42.8 - 94.5
>0.32	81.58	65.7 - 92.3	75	42.8 - 94.5
>0.33	81.58	65.7 - 92.3	83.33	51.6 - 97.9
>0.63	71.05	54.1 - 84.6	83.33	51.6 - 97.9
>0.66 *	71.05	54.1 - 84.6	100	73.5 - 100.0
>5.9	0	0.0 - 9.3	100	73.5 - 100.0

CI: Confidence interval

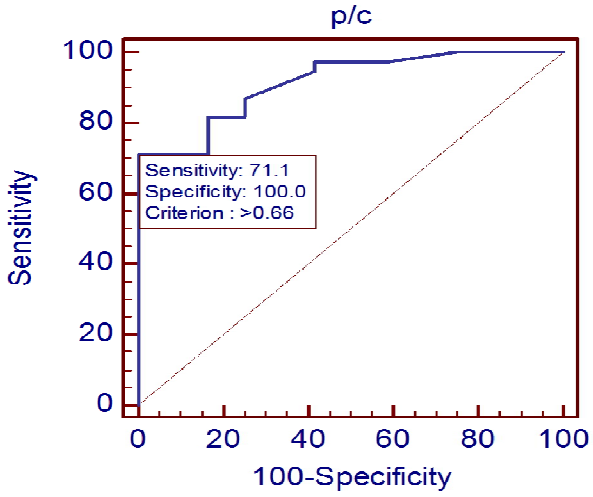

Fig. 2. ROC (Receiver operator characteristics) curve showing the diagnostic ability of P:C ratio in diagnosing preeclampsia

Area under the curve (95% Confidence limits): 0.914(0.800 - 0.975), p=0.0001

Several studies on PE have already established the usefulness of the random urine P:C ratio, including some that have presented evidence of good correlation with acceptable sensitivity in predicting significant proteinuria [26-28]. Furthermore, some reports indicate maternal age, gestational age, parity and maternal body size are not confounding factors with regard to random urine P:C ratio [29]. Studies have shown a high correlation between random urinary P:C ratio in both normotensive and hypertensive pregnant women [30-32]. The current study also showed, 24 hour urine protein has statistically significant positive correlation with P:C ratio. Park JH et al. [33] in their study in Korea showed a strong correlation between the spot P:C ratio and 24 hour urine protein with correlation coefficient of 0.82 (P<0.01). Correlation coefficients reported range from 0.80 to 0.995 [34,35]. The correlation coefficient of 0.86 yielded in the present study is similar compared to other studies. In a study conducted on PE patients, the correlation between random urinary P:C ratio and 24-hour urine total protein was poor [36].

When considering PE, one would wish a replacement test to limit the number of false negative and false positive results, to avoid under detection and over monitoring of patients respectively. The optimum threshold for P:C ratio to detect significant proteinuria is between 0.30 and 0.35, relating to sensitivity and specificity values above 75% [37]. Park JH et al. [33] also found the optimal cut-off points by analyzing ROC curves for significant (≥300 mg per 24-hours) proteinuria and severe (≥5,000 mg per 24-hours) proteinuria as 0.63 and 4.68 and were found to provide optimal sensitivity and specificity for the detection of significant and severe proteinuria, respectively. The present study revealed that the random urinary P:C ratio is an outstanding test for discriminating between significant and insignificant proteinuria as demonstrated by an area under the ROC curve of 0.914. Sensitivity of 71.05% and specificity of 100% were achieved to detect proteinuria at the P:C ratio greater than 0.66. At cut-off value of greater than 0.12, sensitivity was 100% but specificity reduced to 25%. A cut-off below 0.12 ruled out significant proteinuria, however the specificity was only 25%. As shown in Table 3, to maximize the specificity while maintaining a sensitivity of ≥90%, we set our criterion of positivity as 0.66. A cut-off point of >0.66 that was suggested by the optimization of sensitivity and specificity through ROC analysis. Some reports indicate appropriate cut-off points ranging from 0.15 to 0.5 and sensitivities and specificities from 77.5% to 89.7% and from 72.6% to 80%, respectively [38]. However, some prior studies that evaluated the accuracy of random urine P:C ratio in predicting 24-hour urine protein excretion in PE reveal some conflicting results for determining an optimal cut off point for significant proteinuria. This is because of the study-to-study variability in laboratory methods for measuring proteinuria, which precludes valid comparison among the studies.

Young et al. [39] found no single value to distinguish ideally significant proteinuria after ROC analysis but found that a value of <0.15 efficiently ruled out significant pregnancy-induced hypertension. Rodriguez-Thompson and Lieberman [40] performed ROC analysis and found a high area under the curve (0.91) but were unable to identify a clear cut-off point for delineating significant proteinuria, with a cut-off point of 0.190. Durnwald et al. [41] found 0.390 as “optimal” cut-off value for the P:C ratio in the detection of significant proteinuria by ROC analysis. They concluded that P:C ratio was not useful for the exclusion of significant proteinuria in women with suspected PE. Although these studies showed a strong linear association, the ROC curves did not reveal a reliable cut-off. Different cut-off points were published, which are quite different, because of the variability in the units used for cut-off points for urinary protein and urinary creatinine, such as mg/mmol, mg/ g, mg/mg, and g/g. This was more complicated further by the different populations of pregnant women and variations in the sensitivities and specificities in the studies of the spot P:C ratio [11].

In hospitalized patients, the 24-hour urine collection can be extrapolated in ambulatory patients compared to non- ambulatory patients [42]. As this study was done only in hospitalized patients, further studies are required with large sample size, including outpatients. Patients should be followed up till termination of pregnancy so as to predict the disease progression. Uniformity of units is one of the most important point that has to be followed by all researchers in the future studies.

5. CONCLUSION

Based on the results of present study, we conclude that the random urinary P:C ratio have shown significant correlation with 24-hour urine protein excretions in PE, with high accuracy. This

test could be used as a reasonable alternative to quantification of 24-hour urine protein excretion in PE.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the Institutional Ethics Committee of S. N. Medical College Bagalkot, Karnataka, India.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Stevens JM. Gynaecology from ancient Egypt: The Papyrus Kahun: A translation of the oldest treatise on gynaecology that has survived from the ancient world. Med J Aust. 1975;2(25-26):949-52.
2. Waugh JJ, Clark TJ, Divakaran TG, Khan Ks, Kilby MD. Accuracy of urinalysis by dipstick techiniques in predicting significant proteinuria in pregnancy. Obstet Gynecol. 2004;103:769-77.
3. Adelberg AM, Miller J, Doerzbacher M, Lambers DS. Correlation of quantitative protein measurements in 8-, 12-, and 24h urine samples for the diagnosis of preeclampsia. Am J Obstet Gynecol. 2001;185:804-7.
4. Anderson UD, Olsson MG, Kristensen KH, Akerstrom B, Hansson SR. Review: Biochemical markers to predict preeclampsia. Placenta 33, Supplement A, Trophoblast Research. 2012;26:s42-7.
5. Sheikh F, Venyo A. Proteinuria in Pregnancy: A review of the literature. Web Med Central Obstetrics and Gynaecology. 2012;3(11):WMC003814.
6. Brown MA, Lindheimer MN, De Swiet M, Van Assche A, Moutquin JM. The classification and diagnosis of the hypertensive disorders of pregnancy: statement from the international Society for the Study of Hypertension in Pregnancy (ISSHP). Hypertens Pregnancy. 2001;20:9-14.
7. Roberts JM, Hubel CA. The two stage model of preeclampsia: Variations on the theme. Placenta. 2009;30:S32-7.
8. Brosens JJ, Pijnenborg R, Brosens IA. The myometrial junctional zone spiral arteries in normal and abnormal pregnancies: A review of the literature. Am J Obstet Gynecol. 2002;187(5):1416-23.
9. Lipstein H, Lee CC, Crupi RS. A current concept of eclampsia. Am J Emerg Med. 2003;25(3):223-6.
10. Hladunewich M, Karumanchi SA, Lafayette R. Pathophysiology of the Clinical Manifestations of Preeclampsia. Clin J Am Soc Nephrol. 2007;2:543-9.
11. Cote AM, Brown MA, Lam EM, Von DP, Firoz T, Liston RM, et al. Diagnostic accuracy of urinary spot protein:creatinine ratio for proteinuria in hypertensive pregnant women: Systematic review. BMJ. 2008;336:1003-6.
12. Keana WF, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): A position paper of the National Kidney Foundation. Am J Kidney Dis. 1999;33:1004-10.
13. Cote AM, Firoz T, Mattman A, Lam EM, Von Dadelszen P, Magee LA. The 24 hour urine collection: Gold standard or historical practice? Am J Obst Gynecol. 2008;199:e1-6.
14. Waugh J, Bell SC, Kilby MD, Lambert P, Shennan AH, Halligan AWF. Urine protein estimation in hypertensive pregnancy: which thresholds and labortatory assay best predict clinical outcome? Hypertens Pregnancy. 2005;24:291-302.
15. Mitchell SCM, Sheldon TA, Shaw AB. Quantification of proteinuria: A re-evaluation of the protein/creatinine ratio for elderly subjects. Age Ageing. 1993;22:443-9.
16. Chitalia VC, Kothari J, Wells EJ, Livesey JH, Robson RA, Searle M, et al. Cost-benefit analysis and prediction of 24-hour

proteinuria from the spot urine protein-creatinine ratio. Clin Nephrol. 2001;55:436-47.
17. Rizk DEE, Agarwal MM, Pathan JY, Obineche EN. Predicting proteinuria in hypertensive pregnancies with urinary protein-creatinine or calcium-creatinine ratio. Journal of Perinatology. 2007;27:272–7.
18. Price CP, Newall RG, Boyd JC. Use of protein:creatinine ratio measurements on random urine samples for prediction of significant proteinuria: A systematic review. Clinical Chemistry. 2005;51(9):1577–86.
19. Newman DJ, Pugia MJ, Lott JA, Wallace JF, Hiar AM. Urinary protein and albumin excretion corrected by creatinine and specific gravity. Clin Chim Acta. 2000;294:139–55.
20. Koopman MG, Krediet RT, Koomen GCM, Strackee J, Arisz L. Circadian rhythem of proteinuria: consequences of the use of protein:creatinine ratios. Nephrol Dial Transplant. 1989;4:9-14.
21. Biradar SB. Kallaganad GS, Manjula R, Kashinakunt SV, Revathy R. Correlation of spot urine protein- creatinine ratio with 24-hour urinary protein in type 2 diabetes mellitus patients- a cross sectional study. JRMS. 2011;16(5):634-639.
22. Stevens LA, Levey AS. Current status and future perspectives for CKD testing. American Journal of Kidney Diseases. 2009;53(3):17-26.
23. Paçarizi H, Begolli L, Lulaj S, Gafurri Z. Blood urea nitrogen/creatinine index is a predictor of prerenal damage in preeclampsia. Journal of Health Sciences. 2012;2(1):61-5.
24. Varley H, Gowenlock AH. Collection of specimens and some general techniques. In: Varley H, editor. Practical clinical biochemistry: general topics and commoner tests. 5th ed. London: Butterworth-Heinemann Ltd. 1980;379-80.
25. Nischintha S, Pallavee P, Ghose S. Correlation between 24-h urine protein, spot urine protein/creatinine ratio, and serum uric acid and their association with fetomaternal outcomes in preeclamptic women. J Nat ScBiol Med. 2014;5:255-60.
26. Silpraset S, Praloprakarn C, Manussirivithyaya S, Wiriyasirivaj B. A six-hour urinary protein-creatinine ratio for predicting significant proteinuria in preeclampsia. Thai J Obstet Gynecol. 2009;17:30-6.
27. Saikul S, Wiriyasirivaj B, Charoenchinont P. First 4-hour urinary protein-creatinine ratio for diagnosis of significant proteinuria in preeclampsia. J Med Assoc Thai. 2006;89(4):42-6.
28. Wiwanitkit V. Periodic urinary protein creatinine ratio for predicting significant proteinuria in preeclampsia in different alternatives: Time effectiveness analysis. Arch Gynecol Obstet. 2010;281:571-3.
29. Leanos-Miranda A, Marquez-Acosta J, Romero-Arauz F, Cardenas-Mondragon GM, Rivera-Leanos R, Isordia-Salas I, et al. Protein:creatinine ratio in random urine samples is a reliable marker of increased 24-hour protein excretion in hospitalized women with hypertensive disorders of pregnancy. Clin Chem. 2007;53:1623-8.
30. Boler L, Zbella EA, Gleicher N. Quantitation of proteinuria in pregnancy by the use of single voided urine samples. Obstet Gynecol. 1987;70(1):99-100.
31. Jaschevatzky OE, Rosenberg RP, Shalit A, Zonder HB, Grunstein S. Protein/creatinine ratio in random urine specimens for quantitation of proteinuria in preeclampsia. Obstet Gynecol. 1990;75(4):604-6.
32. Robert M, Sepandj F, Liston RM, Dooley KC. Random protein-creatinine ratio for the quantitation of proteinuria in pregnancy. Obstet Gynecol. 1997;90(6):893-5.
33. Park JH, Chung D, Cho HY, Kim YH, Son GH, Park YW, et al. Random urine protein/creatinine ratio readily predicts proteinuria in preeclampsia. Obstet Gynecol Sci. 2013;56(1):8-14
34. Quadri KH, Bernardini J, Greenbery A, Laifer S, Syed A, Holly JL. Assessment of renal function during pregnancy using a random urine protein to creatinine ratio and Cockcroft-Gault formula. Am J Kidney Dis. 1994;24(3):416-20.
35. Combs CA, Wheeler BC, Kitzmiller JL. Urinary protein/creatinine ratio before and during pregnancy in women with diabetes mellitus. Am J Obstet Gynecol. 1991;165(4 Pt 1):920-3.
36. Durnwald C, Mercer B. A prospective comparison of total protein/creatinine ratio versus 24-hour urine protein in women with suspected preeclampsia. Am J Obstet Gynecol. 2003;189(3):848-52.
37. Morris RK, Riley RD, Deeks JJ, Kilby MD. Diagnostic accuracy of spot urinary protein and albumin to creatinine ratios for detection of significant proteinuria or adverse pregnancy outcome in patients

with suspected pre-eclampsia: systematic review and meta-analysis. BMJ. 2012;345:e4342.
38. Eslamain L, Behnam F, Tehrani ZF, Jamal A, Marsoori V. Random urine protein creatinine ratio as a preadmission test in hypertensive pregnancies with urine protein creatinine ratio. Acta Med Iran. 2011;49:81-4.
39. Young RA, Buchanan RJ, Kinch RA. Use of the protein/creatinine ratio of a single voided urine specimen in the evaluation of suspected pregnancy-induced hypertension. J Fam Pract. 1996;42(4):385-9.
40. Rodriguez- Thompson DR, Lieberman ES. Use of a random urinary protein-to-creatinine ratio for the diagnosis of significant proteinuria during pregnancy. Am J Obstet Gynecol. 2001;185(4):808-11.
41. Durnwald C, Mercer B. A prospective comparison of total protein/creatinine ratio versus 24-hour urine protein in women with suspected preeclampsia. Am J Obstet Gynecol. 2003;189(3):848-52.
42. Taherian AA, Dehbashi S, Baghban M. The relationship between random urinary protein-to-creatinine ratio and 24-hours urine protein in diagnosis of proteinuria in mild preeclampsia. JRMS. 2006;11(1):6-12.

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