



Gynecology

A SPOT URINE PROTEIN CREATINE RATIO IS AN ALTERNATIVE TO 24 HOURS URINARY PROTEIN FOR DETECTION OF PIH AND ITS SEVERITY.

Atin Halder

Associate Professor , Department of Gynaecology and Obstetrics, Burdwan Medical College , Burdwan

Himadri Sekhar Das *

Junior Resident , Department of Gynaecology and Obstetrics ,Burdwan Medical College , Burdwan *Corresponding Author

Ankit Halder

Junior Resident , Department of Gynaecology and Obstetrics, KPC Medical College , Jadavpur, Kolkata.

ABSTRACT Protein/creatinine ratio of a single voided urine specimen may have a role in the management of ambulatory women with suspected PIH, which necessitates further research in the field.

We did a systematic review of the literature and multivariate meta-analysis with the objective of determining the diagnostic accuracy of the protein to creatinine ratio compared with 24 hour urine collection for the detection of significant proteinuria in patients with suspected pre-eclampsia and to look at their ability to predict adverse outcome for mother and baby & to find out its co-relation with disease severity. The spot urinary protein /creatinine ratio can be used as an alternative to 24-hours urinary protein excretion in patients with PIH.

KEYWORDS : Spot, Urinary , Protein /creatinine, Ratio , PIH

INTRODUCTION :

The gold standard for measuring proteinuria is 24-hour urine protein. Microalbuminuria is a predictor of pre-eclampsia, marker of disease severity, more accurately reflect glomerular dysfunction associated with glomerular endotheliosis of pre-eclampsia and better screening test for clinically significant proteinuria and a marker of vascular disease than a pathogenic factor.

Protein/creatinine ratio of a single voided urine specimen may have a role in the management of suspected PIH, which necessitates further research in the field.

We did a systematic review of the literature and multivariate meta-analysis with the objective of determining the diagnostic accuracy of the protein to creatinine ratio compared with 24 hour urine collection for the detection of proteinuria in patients with PIH and to predict adverse fetomaternal outcome with disease severity.

The aim of study is to determine the accuracy and diagnostic value of spot urinary microalbumin: creatinine ratio in single voided urine samples in patients with pre-eclampsia for quantification of proteinuria & its correlation with severity compared to 24 hour urine protein.

MATERIALS & METHODS

This prospective comparative case control study was conducted in the Department of Obstetrics & Gynecology of Burdwan Medical College & Hospital. Total 200 women participated in the study and among them 100 women were included in the control(normal) group, while other 100 women consisted mild preeclampsia and severe pre-eclampsia patients from July,2016 to June, as cases were selected by systematic random sampling. All pregnant patients who are >20 weeks of gestation with BP>140/90 mm of Hg & positive urine dipstick 1+,2+ are included in the study group. Chronic hypertensive, renal disease, pathological vaginal discharge, urinary tract infection, are excluded.

After proper counselling & informed consent from each antenatal mother detailed history & clinical examination has been done for selection of study population. Urine dipstick test, Microalbuminuria test & Urinary creatinine was done on a random urine sample. 24 hours urine protein was done after 24 hours urine collection.

RESULTS:**TABLE 1 : BLE Distribution according to blood pressure (BP)**

	BP			Total	p value	S
	<140/90	>140/90 <160/110	>160/110			
Case Control	0	60	40	100	<0.00001	S
	100	0	0	100		
Total	100	100	100	200		

TABLE 2 : Distribution According To The Result Of Urine Dipstick Test & 24 Hours Urine Protein

			GROUP			p -Value	S
			Case	Control	Total		
Protein uria test	Urine dipstick test	Positive	65	40	105	<0.00001	S
		Negative	35	60	95		
Total			100	100	200		
24 hrs Urine Protein	Urine Protein	Case	Control	Total			
		Positive	100	0	100		
		Negative	0	100	100		
Total			100	100	200		

TABLE 3 : Distribution According To The Result Of Spot Urine P:c Ratio & 24 Hours Urine Protein

			GROUP			p Value	S
			Case	Control	Total		
Protein uria test	Spot urine P:C ratio	+	92	15	107	<0.00001	S
		-	8	85	93		
Total			100	100	200		
24 hours urine protein	24 hours urine protein	Case	Control	Total			
		+	100	0	100		
		-	0	100	100		
Total			100	100	200		

TABLE 4 : Comparison Of Spot Urine P:c Ratio To 24-hours Urine Protein.

SPOT URINE P:C RATIO >0.3	24 HOURS URINE PROTEIN >300mg		
	POSITIVE	NEGATIVE	TOTAL
POSITIVE	92(True positive)	15(False positive)	107
NEGATIVE	8(False negative)	85(True negative)	93
TOTAL	100	100	200

TABLE 5 : Comparison Of Urine Dipstick Test To 24-hours Urine Protein.

URINE DIPSTICK TEST	24 HOURS URINE PROTEIN		
	Positive	Negative	Total
Positive	65(True positive)	40(False positive)	105
Negative	35(False negative)	60(True negative)	95
Total	100	100	200

Out of 200 patients normal blood was pressure observed in control group & raised blood pressure , >160/110 mm Hg in 40% cases & <160/110,>140/90 mm Hg in 60% cases. Here p value is <0.00001, so

it is significant (**S**) **Table 1**. Urine dipstick test is positive in 65% patient & 40% patient in case & control group respectively, (**Table 2**) whereas it is negative in 35% & 60% patients in case & control group respectively. The p value is <0.00001, so it is significant. 24 hours urine protein is the gold standard test for diagnosing proteinuria in pre-eclampsia. It is positive in 100% patients in case group.

Table-3 shows spot urine P:C ratio test is positive in 92% patient & 15% patient in case & control group respectively, whereas it is negative in 8% & 85% patients in case & control group respectively. The p value is <0.00001, so it is significant. 24 hours urine protein is positive in 100% patients in case group. Spot urine P:C ratio has a sensitivity of 92%, specificity of 85%, positive predictive value & negative predictive value of 88.9% & 91.3% respectively. (**Table 4**). One interesting finding observed in our study that urine dipstick test has a sensitivity of 65%, specificity of 60%, positive predictive value & negative predictive value of 61.9% & 63.15% respectively (**Table 5**).

So there is a very good co-relation between 24 hours urine protein & spot urine P:C ratio. Therefore spot urine protein:creatinine is a good alternative for 24 hours urine protein.

DISCUSSION

Preeclampsia is considered an idiopathic multisystem disorder that is specific to human pregnancy¹. Several potential candidate biochemical markers have been proposed to predict the severity of preeclampsia. The multi organ dysfunction in preeclampsia caused by vascular endothelial damage, including maternal liver, kidney, lungs, nervous system, coagulation system leads to excessive LDH leakage and elevated levels in serum due to cellular dysfunction, which may cause the occurrence of preeclampsia.¹

Young age and primigravida are well-known risk factors for developing pre-eclampsia and 15% of pregnancies constituted mild and 1-2% develop severe preeclampsia.² The patients with severe preeclampsia in our study were significantly younger and with significant low gravidity and parity compared with the normotensive and mildly pre-eclamptic women with higher gravidity and parity. These findings are in corroborated with study done by different authors^{3,4,5}

Testing for proteinuria is very important in the detection and treatment of preeclampsia⁶. It is postulated that protein excretion varies throughout the day, which is thought to be secondary to vasoconstriction and vascular spasm producing a fluctuation in protein from moment to moment⁶. Protein excretion tends to increase with ambulation and upright body position, which produces renal vasoconstriction and altered permeability of the glomerular barrier⁶. These physiologic factors are thought to produce a diurnal variation in protein excretion. It is known that albumin excretion has a circadian rhythm that makes a 24-hour collection necessary. The proteins excreted in urine of preeclampsia women are, however, heterogeneous and variable. The gold standard testing for detection of proteinuria as 24-hour protein collection, is not always performed correctly and can cause delayed diagnosis and the application of treatment. Due to high accuracy, reproducibility, and convenience compared with 24-hour protein collection, the P/C ratio in spot urine was developed as an alternative test in the non-pregnant population.^{5,7} Gao YF et al⁸ reported the potential error in determining protein in a spot urine sample due to daily variation that does not exceed the error in collecting a 24-hour urine sample. Also, until now, the majority of cases evaluating spot urine P/C ratio in pregnant women with suspected preeclampsia have been found to be closely correlated with the 24-hour urine protein measurement. However, in pregnant women, there is no reliable evidence about the optimal cut-off value for spot urine P/C ratio for defining preeclampsia. The most recent meta-analysis implied that the optimum threshold for P/C ratio to define significant proteinuria is between 0.30 and 0.35, regarding to sensitivity and specificity values above 75%⁹. The present study indicated that P/C ratio has a good correlation with 24-hour urine protein excretion (Spearman co-relation coefficient "r" = 0.69). According to analysis of the ROC curve (AUC=0.56), the optimal P/C ratio for detection of urine protein excretion of 300 mg/day was identified as 0.3 mg/mg with a sensitivity and specificity of 92% and 85%, respectively. However, we found that P/C ratio is more sensitive and more specific for the detection of proteinuria >300mg/day.

Missed diagnosis of preeclampsia is higher with the urine dipstick test emphasising the drawback of relying on it in a clinical setting. The

detecting chromophore is tetrabromophenol blue, which, changes from yellow-green (-) to blue-green (+++) when viewed against a white background in natural light¹⁰.

However, dipsticks testing has been demonstrated to be highly observer dependent and in studies have been found to have a high false positive rate and false negative rate despite the use of experienced observers. This means with the urine dipstick test up to one quarter of patients in whom protein is not detected by dipstick have significant proteinuria⁵. Thus many patients that may need urgent intervention will be undetected. And the disease which is a multi-systemic one may worsen and patients present later with marked maternofetal complications. The sensitivity & specificity of dipstick test in our study are 65% & 60% respectively. So in our study suggested that the urinary spot protein /creatinine ratio of <0.3 excludes preeclampsia. Where as a ratio of >=0.3 detects patients of preeclampsia with 92% sensitivity.

CONCLUSION : Spot urinary P/C ratio in hospitalized women with suspected preeclampsia can be used as a screening test as a good predictor for significant proteinuria. It could be used as a rapid alternative test in patients with pre-eclampsia status in order to prevent any delay in treatment. The spot urinary protein/ creatinine ratio has a significant correlation with 24-hours urinary protein excretion in patients with pre-eclampsia and can be used as an alternative to 24-hours urinary protein excretion.

REFERENCES

1. Carty DM, Delles C, Dominiczak AF. Preeclampsia and future maternal health. *J Hypertension*. 2010;28:1349-55
2. Aziz R, Mehmood T. Relation between preeclampsia and cardiac enzyme. *ARYA Atherosclerosis J*. 2008;4(1):29-32.
3. Al RA, Baykal C, Karacay O et al. Random Urine protein creatinine ratio to predict proteinuria in new onset mild hypertension in late pregnancy. *Obstet Gynecol*. 2004;104(2):367-71
4. Rinehart BK et al. A 12 hour urine collection accurately assess proteinuria in the hospitalised hypertensive gravida. *J Perinatol*. 1999;19:556-8
5. Somnathan N, Farrell T, Galimbert A. A comparison between 24 hours and 2 - hour urine collection for the determination of proteinuria. *J Obstet Gynaecol*. 2003;23:378.
6. Institute for Health and clinical excellence clinical guideline. Antenatal care : routine care for healthy pregnant woman .2008 <http://www.nice.org.uk/guidance/CG62> Accessed 26th November 2016.
7. Moity FS, Mohamed ESEB, Alter RE, Kaffash DE. Albumin to creatinine ratio in a random sample collection with severe preeclampsia. *Alexandria J Med*. 2014;50(2):139-42.
8. Gao YF, Huang QT, Tu Y et al. Diagnostic value of random spot albumin to creatinine ratio in woman with preeclampsia. *Zhonghua Fu Chan Ke Za Zhi*. 1012;47(3):166-70.
9. Nisell H, Trygg M, Back R. Urine albumin creatinine ratio for the assessment of albuminuria in pregnancy hypertension. *Acta Obstetrica Gynecologica Scandinavica*. 2006;85(11):1327-30
10. Taki A, Nakatani Y, Misugi K, Yao M, Nagashima Y. Chromophore renal cell carcinoma: an immunohistochemical study of 21 Japanese cases. *Mod Pathol*. 1999;12(3):310-17