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To Study the Diagnostic Accuracy of Spot Urinary Protein-Creatinine Ratio for Proteinuria in Pregnancy Induced Hypertension

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Abstract: ***Aim: To evaluate the diagnostic accuracy of spot urinary protein-creatinine ratio in single voided urine sample for quantification of proteinuria by comparing it with 24-hour urinary protein in patients with pregnancy induced hypertension. Material & Methods: 150 cases of Pregnancy Induced Hypertension admitted in ward/Labour room of Deptt of Obstt & Gynae, SRMSIMS were studied and grouped into mild and severe pre-eclampsia depending upon blood pressure, clinical and biochemical parameters. Midstream urine sample estimation for protein-creatinine ratio and 24-hr urine collection was done. Urine protein estimation was done by Pyrogollol red method and creatinine estimation was done by Jafee's method. The derangements in fundoscopy, liver function and renal function tests with increasing grades of proteinuria and effects of Pre-eclampsia on maternal and fetal outcomes were also studied. Results: There is a strong correlation between the spot urinary protein-creatinine ratio with severity of pre-eclampsia. Severity of organ dysfunction is significantly related to Protein-creatinine ratio > 0.3. Conclusion: 24-hr urine protein is considered as gold standard; however collection is cumbersome, time consuming. Spot urine protein-creatinine is an accurate, reliable, and time saving which can be used as an alternative method for evaluation of proteinuria in Pre-eclampsia and it can substitute 24-hr urine protein estimation in clinical practice. The optimal spot protein-creatinine ratio cut off point was 0.3. This protein-creatinine ratio can be used in predicting disease severity in form of organ involvement, maternal and perinatal outcome. Clinical Significance: Determination of protein-creatinine ratio is a valuable tool to determine the severity of disease and adverse maternal and perinatal outcome.***

Keywords: Pre-eclampsia, proteinuria, protein-creatinine ratio

1. Introduction

Hypertensive disorders are the most common medical complications of pregnancy rampant globally.[1] Of the hypertensive disorders of pregnancy, pre-eclampsia remains the leading cause of maternal and perinatal morbidity and mortality that complicates 2-8% of all pregnancies.[2]

The basic underlying pathology remains endothelial dysfunction and vasospasm resulting from increased circulating pressor substances, increased sensitivity of the vascular system to normally circulating pressor substances.[3] It is a multisystem disorder leading to widespread endothelial disease affecting almost all the vessels, particularly those of uterus, kidney, liver, placental bed and brain.

Kidneys are the most commonly affected organ and 'glomerular endothelosis' is the characteristic lesion seen in patients of preeclampsia.[4] The chain of events follows: Spasm of the afferent glomerular arterioles → anoxic change to the endothelium of the glomerular tuft → glomerular endotheliosis → increased capillary permeability → increased leakage of proteins. In a nonpregnant women without kidney disease, urinary protein excretion is less than 150 mg daily but in pregnancy urinary protein excretion increases substantially due to increased glomerular permeability and when exceeds 300 mg/24 hours is considered abnormal.[5]

Screening programme directed at the detection of pre-eclampsia with regular measurements of blood pressure and urinalysis for proteinuria is considered one of the "cornerstones" of antenatal care. Heat coagulation test is an easy, convenient, bedside test, good in detecting proteinuria of > 500 mg/day but is less sensitive than > 1+ on the dipstick test in detecting lesser degrees of proteinuria and also associated with large number of false negative results.[6] Most dipstick tests measure protein in excess of 10 mg/dl, they are roughly quantitative, and their use should be limited to screening and to rough estimates required before

concentrating the specimen for electrophoresis or diluting it for quantitative assays.[7]

Therefore, quantitative assay for total proteins or for individual proteins is necessary in patients where dipstick results are abnormal.[8] 24-hour urinary protein remains 'Gold Standard' test for proteinuria and patients with hypertension have only < 300 mg, those with mild preeclampsia have 300 mg to 5000 mg, and those with severe preeclampsia have >5000 mg of protein[7] but cumbersome, time consuming, delay in diagnosis and treatment, subject to errors (inaccuracies in 13-68% of collections).[1] The Protein Creatinine Ratio in a single urine specimen rapid and accurate and avoids collection errors.

Early diagnosis of preeclampsia with a protein/creatinine ratio would be a valuable diagnostic tool if the accuracy is acceptable. It could prevent unnecessary hospitalizations, cumbersome testing, and lead to earlier diagnosis. Currently, different providers use different cut points of protein/ creatinine ratio for the diagnosis of preeclampsia.

Aim: To evaluate the diagnostic accuracy of spot urinary protein- creatinine ratio in single voided urine sample for quantification of proteinuria by comparing it with 24-hour urinary protein in patients with pregnancy induced hypertension.

2. Material & Methods

This was a prospective case study conducted in the Department of Obstetrics and Gynaecology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly on 150 women diagnosed with hypertension attending the antenatal clinic (out-patient department) and those admitted in the ward and labor room from November 2018-May 2020. A protein- creatinine ratio of 0.3 and 24 hour urinary protein of 300 mg/24 hr was taken as cut-off for prediction of pre-eclampsia among patients with mild and severe preeclampsia.

Inclusion Criteria

Previously normotensive and normo-proteinuric women with gestational age > 20 weeks calculated from the first day of last menstrual period with singleton pregnancy and Systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg on two occasions at least 4 hours apart.

Exclusion Criteria

- History of chronic hypertension and proteinuria before conception or development of hypertension before 20 weeks of gestation.
- Patients with chronic renal disease.
- Patients with history of recurrent urinary tract infection.
- Molar pregnancy.
- Multiple pregnancies.
- Patients with associated liver dysfunction.
- Patients who require delivery before completion of collection of 24-hour urine sample.

Cases were recruited according to inclusion criteria and grouped into mild (72) and severe pre-eclampsia (78) depending upon blood pressure, clinical and biochemical parameters. Midstream urine sample estimation for protein-creatinine ratio and 24-hr urine collection was done. Urine protein estimation was done using Pyrogollol red method and Creatinine estimation by Jafee's method and the results were analysed on software IBM SPSS version 20.0.

3. Observations

Table 1: Demographic Parameters of Study Population

Demography	
Age Group (years)	24.9± 4.5 years (53.3%)
Body Mass Index (kg/m^2)	25.9± 3.7 kg/m^2 (41.3%)
Parity	Primigravidae (57.3%)
Socioeconomic Status	Lower Class (50.7%)

53.3% cases were between 20-25 years of age with maximum cases being primigravidae with normal BMI but belonging to lower socio-economic status.

The mean systolic BP among mild preeclampsia was 143.94 ± 14.1 mm Hg, whereas severe preeclampsia was 167.26 ± 17.6 mm Hg and the mean diastolic BP among mild pre-eclampsia and severe preeclampsia was 93.67 ± 10.2 mm Hg and 105.74 ± 99.9 mm Hg respectively.

Table 2: Comparison of Spot Urinary Protein - Creatinine and 24 hours Urine Protein With Severity of Pre-Eclampsia.

Spot Urinary Proteins (mg/dl)	**Value**	**1-50**	**51-100**	**>100**	**Mean± SD**
	Mild PE	44 (61.1%)	17 (23.6%)	11 (15.3%)	47.33 ± 33.6
	Sever PE	20 (25.6%)	32 (41.0%)	26 (33.3%)	128.6 ± 105.5
Spot Urinary creatinine (mg/dl)	**Value**	**1-60**	**61-120**	**>120**	**Mean± SD**
	Mild PE	17 (23.6%)	36 (50.0%)	19 (24.3%)	111.2 ± 73.1
	Sever PE	49 (62.8%)	24 (30.8%)	5 (6.41%)	60.2 ± 35.6
24 hours Urinary Proteins (mg/24 hrs)	**Value**	**0-300**	**301-5000**	**>5000**	**Mean± SD**
	Mild PE	34 (47.2%)	37 (51.4%)	0	360.0 ± 213.3
	Sever PE	10 (12.8%)	60 (76.9%)	8 (10.3%)	2184.7 ± 1928.3

The mean value of spot urinary proteins in cases of mild and severe preeclampsia is 47.3 ± 33.6 mg/dl and 128.6 ± 105.5 mg/dl respectively while for spot urinary creatinine is 111.2 ± 73.1 mg/dl and 60.2 ± 35.6 mg/dl respectively. 24 hr urinary protein among mild and severe preeclampsia is 360.0 ± 213.3 mg/24 hr and 2184.7 ± 1928.3 mg/24 hr respectively.

Table 3: Comparison of Spot Urinary Protein – Creatinine with Severity of Pre-Eclampsia.

PCR		Mild PE (n=72)	Severe PE (n=78)
<0.3	No. of pt (n=43)	37 (51.38%)	6 (7.69%)
	Mean ± SD	0.19 ± 0.06	025 ± 0.07
	Total Mean ± SD	0.22 ± 0.007	
>0.3	No. of pt (n=107)	35 (48.61%)	72 (92.30%)
	Mean ± SD	1.00 ± 0.79	1.5 ± 2.2
	Total Mean ± SD	1.95 ± 1.87	

The mean value of cases with protein creatinine ratio ≤ 0.3 was 0.22 ± 0.007 and > 0.3 was 1.95 ± 1.87 respectively.

The mean values of Spot urinary protein – creatinine ratio (1.95 ± 1.87) had statistically significant positive correlation with mean values of 24 hours urinary protein (1770.24 ± 1732.87 mg/24hours) {p value < 0.01}.

24 hr urinary proteins value in preeclampsia was found to be 47.88% sensitive, 87.18% specific, with positive and negative predictive value of 77.27% and 64.76% respectively while protein creatinine ratio > 0.3 was 51.39% sensitive, 92.31% specific, with positive and negative predictive value of 86.05% and 67.29% respectively.

Abnormal fundoscopy was seen in 29.45% cases of severe pre-eclampsia compared to 5.56% in mild pre-eclampsia. Liver function tests and renal function tests were deranged in 92.30% and 97.43% cases of severe preeclampsia when compared to mild pre-eclampsia where liver and renal function tests were deranged in 33.33% and 70.83%.

Table 4: Comparison of Organ Function with Protein-Creatinine Ratio

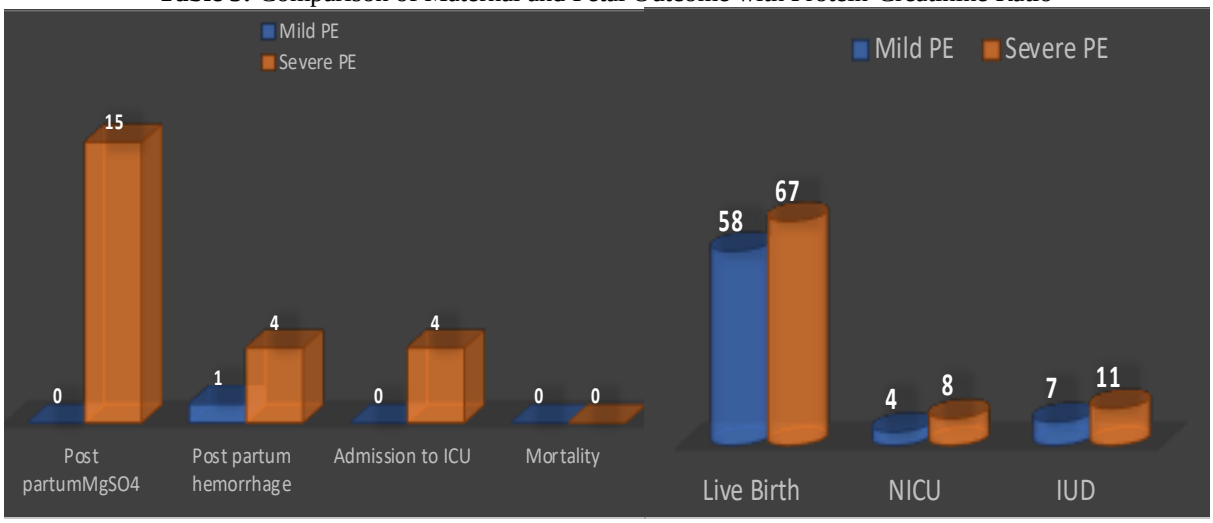
PCR	Fundus Examination		RFT		LFT	
	Normal % (n=123)	Abnormal % (n=27)	Normal % (n=23)	Deranged % (n=127)	Normal % (n=54)	Deranged % (n=96)
≤0.3 (n=43)	39 (31.07%)	4 (14.81%)	12 (52.18%)	31 (24.40%)	25 (46.2%)	18 (18.75%)
>0.3 (n=107)	84 (68.29%)	23 (85.18%)	11 (47.82%)	96 (75.60%)	29 (53.0%)	78 (81.25%)
P Value	0.0078		0.0067		0.0003	

85.18%, 75.6% and 81.25% cases of abnormal fundoscopy, deranged renal function and deranged liver function test had protein creatinine ratio > 0.3.

Out of total 150 cases, 143 women delivered, only 7 patients among mild pre-eclampsia were discharged antenatally. All cases of severe preeclampsia were delivered. Among 143 cases, 52.30% cases underwent cesarean section out of which 12.59% cases were taken up for elective caesarean section and rest cases were emergency caesarean section. 48.95% delivered vaginally. However, the p value was not statistically significant.

15 cases in severe pre-eclampsia required MgSO4. 4 cases had postpartum complication and 4 needed ICU admission. Live birth were 87% cases out of which 10 % required NICU admission. 13% perinatal mortality was observed.

Table 5: Comparison of Maternal and Fetal Outcome with Protein-Creatinine Ratio



4. Discussion

It was observed that with increasing severity of pre-eclampsia, frequency of organ involvement increases. The derangement of organ dysfunction is more closely related with protein-creatinine ratio > 0.3. 24-hr urinary protein helps in better grading the severity of disease but we observed its sensitivity, specificity, positive and negative predictive value comparable to protein-creatinine ratio > 0.3 with significant p value of both tests.

Sami Jan et al (2017)[1], concluded that a spot protein-creatinine ratio cut off point of 0.33 for 300 mg per 24 hours of protein excretion had sensitivity and specificity of 82.8% and 76.1% and positive and negative predictive value observed was 58.8% or 91.5% respectively.

Nedaa Obeid et al (2018)[9], in their study on 98 pregnant women with suspected preeclampsia concluded that protein-creatinine ratio at a cutoff of 0.02 g/mmol had sensitivity and specificity of 97.6% and 44% respectively in predicting proteinuria of 300 mg/24 hour. The positive and negative predictive value observed for this correlation was 58% and 96% respectively.

Hanumant et al (2018)[10], concluded that if cut-off value for the protein-to-creatinine ratio as an indicator of protein excretion of 300 mg/day was 0.285, then sensitivity, specificity positive and negative predictive value were 100%, 99%, 100% and 99% respectively.

Kaminskaei al (2020)[11], stated that spot urine protein-creatinine ratio of > 20 mg/mmol (0.2 mg/mg) is the most commonly reported cutoff value for detecting proteinuria, while a protein-creatinine ratio value of >350 mg/mmol (3.5 mg/mg) confirms nephrotic range proteinuria. However, the International Society for the Study of Hypertension in Pregnancy recommends a protein-creatinine ratio of 30 mg/mmol (0.3 mg/mg) for the classification of proteinuria in pregnant women at risk of preeclampsia. Significant degree of correlation was observed between protein-creatinine ratio and the 24-hr urine protein concentration.

In our study, 15 cases of severe pre-eclampsia required postpartum MgSO4 continuation, out of which 4 had antepartum eclampsia and rest were given prophylactic treatment. Postpartum complication occurred in four cases and all had post-partum haemorrhage. ICU admission was required in 4 cases of severe pre-eclampsia,2 needed intubation due to antepartum eclampsia, one had pulmonary oedema and one required dialysis for Acute Kidney Injury. Out of all patients who delivered, 87% had live birth due to early detection and intervention and only 10 % of them required NICU admission because of low APGAR and prematurity.

5. Conclusion

Since the level of urinary protein excretion has been seen to have considerable clinical implications in the coarse of pregnancy and on the maternal and perinatal outcome, the early detection of even minor degrees of proteinuria is important to improve both maternal and fetal morbidity and mortality. Renal affection causes increase in protein excretion and decrease clearance of urea, creatinine and uric acid. 24 hour urine collection has been considered as the standard method for quantitation of proteinuria in the management of women with pre-eclampsia. However, this method is inconvenient to patient and leads to incomplete collection causing delay in diagnosis. Our contention was, that the value of the protein/creatinine ratio in a single urine sample which may avoid collection error and give physiologically relevant information. Protein/creatinine ratio has been found to be superior diagnostic tool compared to routine urine analysis useful in out-patient setting and to monitor organ function. Protein/creatinine ratio in spot urinary sample provides valuable information for clinical purpose and can be a satisfactory substitute against protein excretion in 24 – hour urine collect, however our being a very small study, a large randomized control trial are needed before establishing its diagnostic accuracy as a predictor of pre-eclampsia.

References

[1] Jan S et al. Diagnostic accuracy of spot urinary protein/creatinine ratio for proteinurea in pregnancy induced hypertension. Int J Reprod Contracept Obstet Gynecol. 2017 May;6(5):2083-2089
[2] Miranda AL, Acosta JM, Arauz FR. Protein/ creatinine ratio in random urine samples is a reliable marker of increased 24hr protein excretion in hospitalized Women with hypertensive disorders of pregnancy. J Clin Chem. 2007;53:1623.
[3] Dutta DC. Hypertensive disorders of pregnancy. Textbook of obstetrics. Page no. 219-240.
[4] L.W. Gaber et al. Renal pathology in pre-eclampsia. Clinical medicine insights: Women's health 2011:4. Page 444-468.
[5] Osman O, Maynard S: Review on proteinuria in pregnancy. Fronts women healt vol.4: 125 ISSN:2398-2799.
[6] Vajjra H. W dissanyake, lindamorgan , Fiona broughton et al: the urine protein heat coagulation test-a useful screening test for proteinuria in pregnancy in developing countries: a method validation study: BJOG May 2004 vol. 111 pp.491-494.
[7] J Eigbefoh, J Abebe, M Odike, P Isabu. Protein/Creatinine Ratio In Random Urine Specimens For Quantitation Of Proteinuria In Pre-Eclampsia. The Internet Journal of Gynecology and Obstetrics. 2006 Volume 8 Number 1.
[8] Burtis CA, Ashwood ER. Teitz fundamentals of clinical chemistry. Seventh edition.
[9] Obeid N, Kelly R, Saadeh F, Crowley V, Daly S. A comparison of spot urine protein-creatinine ratio with 24 hr urine protein excretion for prediction of proteinuria in preeclampsia. Res Rep Gynaecol obstet. 2018;2(1):11-15.
[10] Hanumant V, Maurrya D, Susmitha S, Ravindra PN. Analysis of proteinuria estimation methods in hypertensive disorders of pregnancy. The Journal of obs& Gynaecology society of India. Nov-Dec.2018.68(6):452-455.
[11] KaminskaJ ,Piekarskaa VD, Tomaszewskab J. Diagnostic utility of protein to creatinine ratio (P/C ratio) in spot urine sample within routine clinical practice. Critical reviews in clinical laboratory sciences 2020, vol. 57, no. 5, 345–364.