Comparison of protein/creatinine ratio in Single voided urine sample with 24 hoursUrine protein for estimation of proteinuria in pregnancy induced hypertension

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Abstract

Background : Hypertensive disorder in pregnancy is a common disease. The incidence of pregnancy induced hypertension (PIH) in India range from 5-15%.Proteniuria is essential for the diagnosis of pre eclampsia. Its presence is a sign of worsening hypertensive disease, specifically pre eclampsia.When proteniuria is overt and persistent, maternal and fetal morbidity are increased even more. As the proteinuria increases, the likelihood of complications also increases and hence a rapid and accurate detection and quantitation of protenuria are essential for the management of hypertensive pregnant women. The 24 hrs urinary collection was subjected to collection error; requires good patient compliance and there is a delay of 24hrs form the time of collection till the diagnosis is made. Hence, there is a need to evaluate protein / creatinine ratio in single voided urine sample, which can be used to quantify the protenuria accurately and rapidly and at the same time overcome the limitations of the 24 hrs urinary protein estimation.

Aim: To compare protein / creatinine ratio (P:C) in single voided sample with 24 hrs urine protein for estimation of proteinuria in pregnancy induced hypertension.

Materials and methods : A total of 50 pregnant women with pre eclampsia and gestational hypertension patients attending the teaching hospital attached to J.J.M.Medical college, Davangere, were selected consequently as and when they presented with following inclusion and exclusion criteria. **Inclusion Criteria**: Pregnant women with, pre eclampsia of blood pressure 140/90 mmHg or more recorded on two occasions at least 6 hours apart or single diastolic reading of >/= 110 mmHg and the presence of proteinuria of > trace as detected by a qualitative test done on a random sample of urine.

Exclusion Criteria: Pre existing renal disease .

Results: In the present study of 50 pre eclamptic women, the mean age of the patients was 27.14 years and the mean gestational age was 33.45 weeks. We found a fair degree of correlation in our study, when the 24 hours urine protein and the random urine protein - creatinine ratios were correlated with r=0.90 and the p value being highly significant at <0.001. Our contention was, that the value of the protein /creatinine ratio in a single urine sample is potentially more accurate, because it avoids collection errors and may give more physiologically relevant information.

Conclusion : For years, 24 hour urine collection has been the standard for quantitation of proteinuria in the management of women with pre eclampsia. However, this method is cumbersome, subjective to collection errors, requires good patient compliance and results in the delay in the diagnosis of > 24 hours from the start of collection. Our contention was, that the value of the protein /creatinine ratio in a single urine sample is potentially more accurate, because it avoids collection errors and may give more physiologically relevant information.

Keywords : pre eclampsia. Protein creatinine ratio, proteinuria.

Introduction

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with hemorrhage and infections, that results in much of the maternal morbidity and mortality related to pregnancy. The incidence of pre eclampsia is 5-7% of all pregnancy. proteinuria is essential for the diagnosis of pre eclampsia. Proteinuria develops late in the course of the hypertensive disease and its presence is a sign of worsening hypertensive disease, specifically pre eclampsia..In pregnancy proteinuria is detected and measured either by visual dipstick urine analysis or by the 24hrs urinary protein estimation. Though reliable indicator, it has the disadvantages of being a cumbersome and time consuming process, for both

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the patient and laboratory. Hence, there is a need to evaluate other tests which can be used to quantify the proteinuria accurately and rapidly and at the same time overcome the limitations of the routinely performed tests. Thus protein creatinine ratio in a single urine specimen has been used for the rapid and accurate detection of proteinuria in hypertensive pregnant women as it avoids collection errors and gives physiologically more relevant information. Ginsberg et al in their study of estimating quantitative proteinuria in a single urine sample, concluded that, in the presence of a stable renal function, Protein /Creatinine ratio of >3.5 can be taken to represent nephrotic range proteinuria and a ratio of <0.2 as normal [1] Ferrazzani and associates have said that the combination of proteinuria and hypertension during pregnancy markedly increases the risk of perinatal morbidity and mortality, and found the perinatal mortality rates were four times higher in women with proteinuric pre eclampsia than in women with chronic hypertension and the non proteinuric gestational hypertension [2]. Saudan et al in their study have emphasized the need for quantitation of proteinuria, as the likelihood of complications increases with nephrotic range proteinuria [3]. Meyer et al found that urinary dipstick is a poor predictor of absent or severe proteinuria, having a negative predictive value of only 34% for absent proteinuria and a positive predictive value of 36% for severe proteinuria [4]

PROTEINURIA: In pregnancy proteinuria is defined as an urinary protein excretion of >300mg/day in a 24 hr urine collection[5]. Prevalence: Proteinuria and pregnancy- 5%.Although proteinuria in pre eclampsia is indicative of severe disease, the absence of it does not preclude a severe form of the pre eclampsia. Eclampsia and severe pre-eclampsia can occur without proteinuria [6]

Quantitative assay of proteinuria: Persistent dipstick proteinuria requires further evaluation. Quantification of proteinuria helps in differentiating the various renal diseases causing proteinuria. Proteinuria of <l-2gm/day, usually is associated with tubulo interstitial disease and those with >3.5gm/day have glomerular disease. Quantitative assay for total proteins or individual proteins is usually performed on timed collections, usually a 24 hr urine specimen or by determining the protein/creatinine ratio in a random urine sample. There is delay of 24 hrs from the time of collection till the diagnosis is made [7]

Urine protein/creatinine (P/C) ratio:

Studies have shown that the urine protein/creatinine ratio in a random sample has an excellent correlation with the 24hr urinary protein excretion and has been used for rapid detection of proteinuria.

Though there is a marked day to day variation in plasma protein concentrations and protein excretions, certain levels of proteinuria have come to be accepted on the basis of empirical observations as having particularly important clinical implications. In the presence of a stable RFT, a P/C ratio of >3.5 represents a nephrotic range proteinuria & correlates with a 24hr urine protein excretion of >3.5gm and a value <0.2 is said to be within normal limits & correlates with a protein excretion of <0.2 gm/day. Studies have shown that, because urinary creatinine excretion in the presence of a stable GFR is fairly stable , a simple ratio of the concentrations of urinary protein & creatinine in a single voided urine sample, would reflect the cumulative protein excretion over a day [8,9].

Materials and methods

A total of 50 pregnant women with pre eclampsia and gestational hypertension patients attending the teaching hospital attached to J.J.M.Medical college, Davangere, were selected consequently as and when they presented with following inclusion and exclusion criteria.

Inclusion Criteria Pregnant women with, pre eclampsia of blood pressure 140/90 mmHg or more recorded on two occasions at least 6 hours apart or single diastolic reading of >/= 110 mmHg and the presence of proteinuria of > trace as detected by a qualitative test done on a random sample of urine.

Exclusion Criteria Pre existing renal disease .

Results

In the present study of 50 pre eclamptic women, the mean age of the patients was 27.14 years and the mean gestational age was 33.45 weeks. We found a fair degree of correlation in our study, when the 24 hours urine protein and the random urine

protein - creatinine ratios were correlated with r=0.90 and the p value being highly significant at <0.001. Our contention was, that the value of the protein /creatinine ratio in a single urine sample is potentially more accurate, because it avoids collection errors and may give more physiologically relevant information.

Table 1. Normal values for protein excretion

	24 hours urine protein (mg/24 hours)	Protein / creatinine Ratio
Negative	<300	<0.3
Clinically significant proteinuria	>300	>0.3
Severe proteinuria	>3000	> 3

The data thus collected were analyzed for both groups using appropriate statistical methods. The mean and standard deviations were computed. The statistical test used for analyses was the Pearson's Correlation Coefficient which is expressed as "r" Student chi square test expressed as p. A value of $p < 0.05$ has been considered to be statistically significant (Table 1).

Table 2. Demography

Variable n=50	Mean	Std. deviation	Min	Maximum
Age	27.14	4.06	19	36
Period of gestation	33.45	3.32	26.7	40
Systolic BP	155.08	12.89	130	200
Diastolic BP	101.2	8.2	90	120
Primi	32(64%)			
Multi	18(36%)			

In the present study, it is observed that the mean ±SD of age of the subjects studied was 27.14±4.06 yrs, gestational age was 33.45±3.32, Systolic blood pressure was 155.08 ±12.89 mm of Hg, Diastolic blood pressure was 101.2±8.2 mm of Hg. 64% of them were primigravidas (Table 2).

Table 3. Distribution of subjects according to degree of proteinuria

24 hour urine protein	Number	Percentage
<300mg	12	24
300 mg to 2gm	24	48
More than 2gm	14	28
Total	50	100

In our study there were 12 patients (24%) had less than 300mg proteinuria, 24 patients (48%) had 300mg to 2gm of proteinuria and 14 patients (28%) had more than 2gm of proteinuria (Table 3).

Table 4. Distribution of subjects in to gest. HTN, mild or severe PE using both 24 hr protein and BP recordings

	Number	percentage
Gest. HTN	12	24
Mild PE	23	46
Severe PE	15	30
Total	50	100

In our study there were 12 patients (24%) gestational hypertensives,23 patients (46%) were mild preeclamptic ,and 15 patients (30%) were severe preeclamptic (Table 4).

Table 5. Mean and SD of 24 hour urine protein and P/C ratio according to gest. HTN, mild and severe PE group

	Mean	Std deviation
Gestational hypertension 24hr protein pc ratio (n=12)	 173.2545 0.12	 82.84927 0.12
Mild preeclampsia 24hr protein PC ratio (n=23)	 1010.79 1.29	 457.38614 0.78
Severe eclampsia 24 hr protein PC ratio (n=15)	 3387.00 4.65	 1867.07 3.56

Mean and std deviation of 24 hr protein and P/C ratio was 173.25±82.8,0.12±0.12 in gestational hypertensive group, 1010.79 ±457.38,1.29 ±0.78 in mild preeclampsia group, and 3387.00 ±1867.07,4.65 ±3.56 in severe preeclampsia (Table 5).

Table 6. Mean and std deviation of 24 hour urine protein and P/C ratio of all 50 subjects

Variable	Mean	Std. deviation
24 hour urine protein	1542	1640 (wide range 54-9616)
Spot protein/creatinine ratio	2.06	2.65

Mean proteinuria was 1542 ± 1640 when all 50 subjects were considered , and mean P/C ratio was 2.06 ± 2.65 (Table 6).

Creatinine ratio, and 24 hour sample of urine protein (mg), in all subjects A fair correlation coefficient of r = 0.902 was observed between the 24 hours urine protein and spot urine protein/ creatinine ratio among 50 subjects which was statistically significant at p value <0.001 (Table 7).

Table 7. Correlation coefficient between spot Protein

Variable	**Bansal Bhavana et al**	**Present Study**
Mean age	26.9 **yr**	27.14
Correlation coefficient 'r'	**0.83**	0.902

Studies	**Correlation Coefficient (r)**	**p-value**
Boleretal. (1987) n=54	0.99	< 0.001
Jaschevatzky et al.(l990) n=105	0.94	< 0.001
Robert et al. (1995to96) n=71	0.94	< 0.001
Saudenetal. (1997) n=100	0.93	< 0.001
Neithardt et al. (2000) n=30	0.93	< 0.001
Present study n=50	0.902	< 0.001

Discussion

An accurate and rapid detection and quantitation of proteinuria are essential in the management of hypertensive disorders in pregnancy. This can help us know the severity of proteinuria much earlier and hence the severity of the disease process, which can alter the course of management.In the present study of 50 pre eclamptic women, the mean age of the patients was 27.14 years and the mean gestational age was 33.45 weeks. Except for two women with gestational hypertension, all others were on anti hypertensive's. We found a fair degree of correlation in our study, when the 24 hours urine protein and the random urine protein-creatinine ratios were correlated with r = 0.90 and the p value being highly significant at <0.001, when all the observations were considered. The study was limited to hospitalized patients. Since the protein excretion is affected by postural change, being higher in the standing than in supine position, the ambulatory

status of the patients is important while interpreting the results. Even though the number of subjects were only 9 with the severe degree of proteinuria (>3 gms), the correlation was found to be good at r = 0.77 and p<0.001, and protein/ creatinine ratio also >3. The table I and III show the values of the 24 hour urine protein and protein /creatinine ratio of the 9 patients with severe degree of proteinuria In a similar study conducted by Jaschevatzky et al in 1990, the degree of correlation between the two variables at > 2gms/ 24 hrs proteinuria was lower but still significant at p <0.05.

All of the previous studies demonstrate an excellent correlation between the 24 hrs urine protein and the protein/ creatinine ratio. The p values are also statistically very significant at <0.001 which is also seen in our study. It was noticed in our study that the correlation coefficient at lesser degree of proteinuria (i.e. less than 300mg) was less (0.59), as compared to other two groups, but statistically significant at p value 0.05 Boler et al in their study, again found an excellent correlation between the 24 hrs urine protein and the protein/ creatinine ratios at lower levels of proteinuria but when the protein losses were > 1 gm/24 hrs, the variation was more pronounced (upto 65%) [10]. The variation in the results at severe degrees of proteinuria, indicates the need for careful interpretation of the results especially when clinical decisions are to based on them. We have found the use of this alternative test to 24 hours urine protein to be much more cost effective as shown with many studies previously. Since the present study included women only with a stable renal function, our study supports the use of the protein/creatinine ratio in women with normal renal function. But Robert et al in 1997 and Quadri et al in 1994 have proved in their studies, that the protein/creatinine ratios are independent of renal function and reliable, even in the presence of underlying renal disease and have advocated their use to monitor renal function in pregnancy [9]. Neithardt et al In their study showed a significant correlation between the 24 hour urine protein and the protein creatinine ratio with a r = 0.93 and p< 0.001 and the P/C ratio was also helpful in predicting the protein excretion over time [8]. It was noticed in our study that, of 50 subjects studied 12 (24%) were having Gestational HTN, 23 (46%) were having mild pre eclampsia and 15 (30%) were having severe pre eclampsia. The perinatal outcome in women with higher levels of proteinuria was poor with increased incidences of IUGR, prematurity, low birth weight and the need for NICU care was increased in such babies.

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