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Spot protein/creatinine ratio as an accurate quantification of proteinuria to replace the use of the 24 hours urine protein in pre-eclamptic women

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Abstract

The objective of the study was to know if a spot protein/ creatinine ratio would provide an accurate quantification of proteinuria and whether it can replace the use of the 24 hours urine protein in preeclamptic women. 60 women with preeclampsia were recruited for the study. A stable renal function was ascertained by doing serum creatinine and blood urea nitrogen. The patients were instructed to collect the 24 hours urine starting from the second urine sample in the morning till the first urine sample the next day morning. A single voided urine specimen was obtained thereafter for determination of the protein/ creatinine ratio. The urine protein and creatinine were measured using a standard methods. In the present study it was observed that with proteinuria <300 mg a negative correlation exists between 24 hour urine protein and spot p/c ratio. This observation can be explained by the fact, that, the number of patients in this range of proteinuria was less and also in the exclusion criteria those patients with dipstick <1+ (like traces and negative) is excluded from the study

Keywords: 24 hour urine protein, preeclampsia, spot protein creatinine ratio

INTRODUCTION

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with hemorrhage and infection that results in much of the maternal morbidity and mortality related to pregnancy Proteinuria is essential for the diagnosis of preeclampsia. Proteinuria develops late in the course of the hypertensive disease and its presence is a sign of worsening hypertensive disease, specifically preeclampsia. As the Proteinuria increases, the likelihood of complications also increases and hence a rapid and accurate detection and quantization of Proteinuria are essential for the management of hypertensive pregnant women. In pregnancy Proteinuria is detected and measured either by visual dipstick urine analysis or by the 24 hrs urinary protein measurement. The visual dip stick urinalysis in recent studies has been found inaccurate, giving a high number of false positives and false negatives. The 24 hrs urinary collection has been the standard in most places for quantifying Proteinuria. Though reliable indicator, it has the disadvantages of being a cumbersome and time consuming process, for both the patient and laboratory; it is subjected to collection error; requires good patient compliance and there is a delay of 24 hrs from the time of collection till the diagnosis is made. 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. The protein creatinine ratio in a single urine specimen has been used for the rapid and accurate detection of proteinuria in hypertensive pregnant women it avoids collection errors and gives physiologically more relevant information.

How to Cite this Article:

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Proteinuria

It is defined as urinary protein excretion of >150mg/day in a 24 hour urine collection. It reflects an increase in the glomerular permeability for the normally non filtered plasma macromolecules like albumin. In a

normal person the urine protein excretion is <150mg/day and consists mostly of plasma proteins-60% (mainly albumin) and tubular Tamm Horsfall protein-40%. In pregnancy proteinuria is defined as a urinary protein excretion of >300mg/day in a 24 hr urine collection. 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. Prevalence: Proteinuria and pregnancy- 5%

Pathophysiology

There are 4 types of proteinuria:

Glomerular Proteinuria:

It is the commonest type of proteinuria and the most serious one. Because most of the protein excreted is albumin it is called albuminuria. It is seen in glomerular disease where there is an injury to the basement membrane. The glomerular filtration barrier is composed of the endothelial cell, basement membrane and the epithelial foot processes. The glomerulus behaves as an ultra filter for the plasma proteins. The degree to which the proteins are filtered depends on-

a) Molecular size: as the size of the molecule increases their transport through the glomerular membrane decreases. HMW proteins like IgM (MW 900, 00) do not normally appear in the glomerular filtrate except in trace amounts whereas relatively LMW proteins like albumin (66,000) pass into the filtrate.
b) Ionic charge: Normally the basement membrane and endothelial cells possess a negative charge. Plasma albumin which also possesses a negative charge is repelled by the normal negative charge on the basement membrane and endothelial cells.
c) Plasma concentration: Albumin has a high concentration in the plasma and hence appears in the urine. Very LMW proteins (15,000- 40,000) do not appear in the urine because of their low plasma concentration.
d) Extent of reabsorption by the renal tubules: LMW proteins are better absorbed by the renal tubules and hence their concentration is less in the urine. 60% of albumin appears in the urine.

Hence increased glomerular permeability is first signaled by the appearance of increased amounts of albumin in the urine. If there is a defect in the tubular reabsorption, LMW proteins are seen. As long as the molecular weight (MW) determines which proteins are filtered it is called Selective proteinuria. With progressively severe glomerular lesions, there is less selective proteinuria and proteins of all MW are filtered i.e.; Nonselective proteinuria. Glomerular diseases like lipoid nephrosis, membranous glomerulo nephritis etc. are the commonest causes of proteinuria and can manifest as hypertension, nephritic syndrome or progressive renal failure

Functional or benign Proteinuria:

It is a form of glomerular proteinuria which is probably related to changes in the blood flow throughout the glomeruli. It is seen with exercise, pyrexia, hypertension etc. Protein excretion rates are <1gm/day and urinary protein excretion returns to normal after recovery from the precipitating event.

Postural or orthostatic proteinuria:

It is associated with the upright position. Protein excretion may exceed 1gm/day. But if it is transient it is benign and if it is persistent it is associated with an underlying pathology.

Tubular Proteinuria:

It is characterized by the appearance of LMW proteins in the urine which are normally completely reabsorbed by the renal tubules.

It is usually associated with tubular or interstitial injury which results in impaired reabsorption of these molecules. Glomerular proteinuria usually accompanies tubular proteinuria. LMW proteins that are excreted are BMG (MW-11,800), lysosyme (14,500), alfa-1 microglobulin, polypeptide hormones, and enzymes.

Acute tubular proteinuria:

It is seen with severe metabolic disturbances like burns, heavy metal poisoning etc. & is reversible.

Chronic tubular proteinuria:

It is irreversible & is seen in hereditary conditions like Fanconi's syndrome.

Overload Proteinuria:

Increased excretion of LMW proteins might be seen in states where there is significant increased production of these proteins like in multiple myeloma. Proteinuria results from the fact that the amount of proteins filtered exceeds its reabsorptive capacity.

Post renal proteinuria:

Arises from the urinary tract below the kidneys & is usually due to inflammation or malignancy.

Microalbuminuria:

It is defined as the presence of >30mg & <300mg/day of albuminuria. Its detection in TypeI DM is the earliest clinical evidence of diabetic nephropathy.

Clinical Features: Most patients with proteinuria have no signs & symptoms. In states of heavy proteinuria (nephrotic range, >3gm/day), the patient may present with foamy urine –due to increased lipid content in the urine & edema- due to decrease in the plasma oncotic pressure. Other manifestations of renal disease like haematuria, hypertension should be sought for.

Diagnosis: All pregnant patients are routinely screened for proteinuria at their first antenatal visit and at regular

intervals thereafter by either the dipstick test or the heat coagulation test. If the test is negative, clinically significant proteinuria is precluded but if it is positive further evaluation is necessary.

Qualitative detection of Proteinuria :
- Dipstick test
- Sulfosalicylic acid “cold” test
- Heat coagulation test

Dipstick test:

A dipstick contains reagents for just one test or for multiple tests.

Eg: protein, glucose, ketone bodies etc. The reactive portion of the stick is coated with a buffered indicator that changes color in the presence of protein. The dipstick for protein consists of a cellulose test pad impregnated with tetrabromophenol blue& citrate ph3 buffer. Tetra bromophenol blue which is green turns yellow in the presence of protein (test is read after 60 s). Lower detection limit is 200-300mg/ml. The test is carried out on the first morning specimen of urine preferably because it tends to be more concentrated and is not affected by postural factors. The dipsticks are more sensitive to albumin than to other plasma proteins. They are therefore excellent screening tests for albuminuria. They are not suitable to detect tubular proteinuria which is done by electrophoresis.

Dipstick testing is associated with a large number of false positives which can be due to a very concentrated & alkaline urine (sp.gr>1.030), if contaminated with quaternary ammonia compounds, chlorhexidine or vaginal discharge. The incidence of false positives can be up to 25% in trace reactions and up to 6% in those with 1+ reaction. False negative results also occur and are due to very dilute urine (sp.gr <1.010).

Sulfosalicylic acid test and Heat coagulation test: Used for protein detection by acid precipitation & detects any type of protein in the urine. It is done by mixing 1 part urine with 3 parts of 3% SSA.

Heat coagulation test is done by adding 3-4 drops of acetic acid to the urine after heating. Results are graded depending on the turbidity and hence are subjective they are also associated with a number of false positives & false negatives.The result is graded depending on the turbidity.

Quantitative assay of proteinuria:

Persistent dipstick proteinuria requires further evaluation. Quantification of proteinuria helps in differentiating the various renal diseases causing proteinuria. Proteinuria of <1-2gm/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

Proteinuria of pregnancy:

There are two entities:
- Gestational proteinuria &
- Gestational proteinuric hypertension

Gestational Proteinuria: includes all proteinuric conditions of known or unknown origin that develop during pregnancy in the absence of hypertension and disappear either on treatment or after delivery.

Causes: urinary tract infections, chronic nephritis and nephrotic syndrome, essential hyperension, orthostadischarge; rare causes: anemia, congestive heart failure, SLE with renal involvement etc

Gestational Proteinuric hypertension:

It is synonymous with pre-eclampsia and is associated with specific changes in the renal glomeruli. It also includes acute nephritis & an exacerbation of chronic nephritis, but these conditions are so rare that the occurrence of gestational proteinuria hypertension is assumed to be pre-eclampsia unless otherwise proved.
Protein excretion in pregnancy is increased because of increase in the GFR. Proteinuria >300mg/24hrs is considered abnormal.

Proteinuria and preeclampsia:

Presence of proteinuria is essential for the diagnosis of PE. It develops late in the course of the disease & its presence is a sign of worsening hypertensive disease.

Renal Pathology in Pre-eclampsia

Pre-eclampsia affects kidneys both functionally and morphologically. Renal hemodynamic decrease and urine protein excretion increases, in part due to lesions affecting the glomerulus, where a combination of changes produce a characteristic appearance and permits differentiation of preeclamptic nephropathy from other glomerular alterations associated with hypertension in pregnancy.

In pre-eclampsia, glomerulus is diffusely enlarged and bloodless, due not to proliferation, but hypertrophy of intercapillary cells. These alterations best described ultra-structurally, include hypertrophy of cytoplasm organelles in endothelium and occasionally mesangial cells, particularly lysosomes which undergo marked enlargement and vacuolization(due to accumulation of free lipids).This reactive lesion is classically described as glomeruli endotheliosis. Other lesions- sub endothelial and mesanglial electron dense deposits as well as interposition of mesanglial cell cytoplasm or meningeal matrix along an otherwise normal basement membrane.
Some have even described immune-histological findings (IgM, IgG, and fibrin) which they believe is specific for pre-ecalmpsia.

It has been shown that in pre-eclampsia renal lesions are fully reversible and the disease has no renal effects in future. Acute renal failure which is a rare complication of pre-eclampsia occurs due to tubular necrosis. Rarely renal cortical necrosis develops when a major portion of the cortex is damaged and is irreversible.

Pathophysiology of Proteinuria in Pre-eclampsia

Spasm of glomerular arteries—anoxia of glomeruli—endothelial damage—escape of proteins into the urine. Proteinuria in pre eclampsia is a nonselective type of proteinuria. When it is overt and persistent, maternal and fetal risks are increased. But the degree of proteinuria does not always indicate the severity of the disease.There is no evidence that the level of proteinuria correlates with the degree of risk. In the more severe disease, the proteinuria is less specific, being associated with tubular proteins and indicative of tubular damage.

Objectives of the Study

- To study the clinical profile of preeclampsia patients.
- To assess the degree of Proteinuria by 24hour urine protein and spot urine protein creatinine ratio in the study population
- To study if the spot urine protein and creatinine ratio will provide accurate quantification of proteinuria in hypertensive pregnant women.

MATERIALS AND METHODS

Type of study: Observational study

Period of study: 1 year
Sample size: 60 cases

Source of Data

Pregnant women with preeclampsia admitted to KING GEORGE HOSPITAL, VISAKHAPATNAM, between October 2012 and October 2013.

Criteria for Selection of Patients

Inclusion Criteria

Pregnant women with pre eclampsia – for pre-eclampsia to be diagnosed, there should be a minimum criteria of hypertension i.e.; a blood pressure of 140/90 mmHg or more on two occasions at least 4 hours apart or a single diastolic reading of >= 110 mmHg and the presence of proteinuria of > = 1+as detected by a qualitative test done on a random sample of urine.

Patients were categorized as severe preeclampsia if any of the following criteria were met:

- Diastolic BP> / = 110mmHg or higher
- Proteinuria persistent > / = 2+
- Headache, vomiting, epigastric pain, visual Disturbances, brisk deep tendon reflexes, oliguria, Presence of IUGR
- Raised liver enzymes, thrombocytopenia, raised serum creatinine

Mild pre-eclampsia was a BP>=140/90 and <150/100 mmHg with 1+ protein by dipstick.

Exclusion Criteria

Preexisting renal disease – A stable renal function was ascertained by doing blood urea nitrogen and serum creatinine. Urine analysis was done for all the patients to exclude the presence of microscopic haematuria, casts and bacteruria.

Procedure

All the patients satisfying the above criteria were selected for the study. The tests were carried out in hospitalized, non-ambulatory patients.

1) A detailed history was taken, general physical and systemic examination including the obstetric examination. Per speculum examinations were done to look for any evidence of vaginal infection clinically.
2) If urine microscopy suggested the presence of infection a urine culture was done.
3) A qualitative test for urinary protein was carried out on a random sample of urine using the dipstick method. Protein by the dipstick method was graded as follows:
   Traces = 300 mg/ dl
   1+ = 500 mg/dl
   2+ = 1gm/dl
   3+ = 2gms/dl
   4+ = 3gms/dl
4) The test was repeated on an additional sample of urine immediately and if the subsequent tests showed 1+ or more, quantitative tests for proteinuria were carried out.
5) The tests were carried out as follows: The patients were instructed to collect the 24 hours urine starting from the second urine sample in the morning (i.e.; after discarding the first morning specimen) till the first urine sample the next day morning. A single voided urine specimen was obtained soon after the 24 hour urine collection, before mid day.
6) The samples were sent to the Biochemistry laboratory where:
   - Urine protein was measured by the UCFP method (Urinary-Cerebrospinal fluid protein), which is an adaptation of the pyragallol red molybdate method. The test was performed on an automated analyzer.
   - Urine creatinine was measured by the CREA method which is a modification of the Jaffe's reaction. The test was performed on an automated analyzer.
7) The urine protein and creatinine ratio was obtained by dividing the urine protein concentration (mg /dl) by the urine creatinine (mg/dl).
8) Normal values for protein excretion

9) The data thus collected were analyzed using appropriate statistical methods. The mean and standard deviations were computed. The statistical test used for analysis were:
   - Pearson's Correlation Coefficient which is expressed as — r
   - A value of p < 0.05 has been considered to be statistically significant.

	24 hours urine protein(mg/24 hours)	Protein / creatinine Ratio
Negative	<300	<0.3 (<30)
Clinically significant proteinuria	>300	>0.3 (>30)
Severe proteinuria	>3000	Ratio >3

RESULTS AND ANALYSIS

In the present study it was observed that with proteinuria <300 mg a negative correlation exists between 24 hour urine protein and spot p/c ratio. This observation can be explained by the fact, that, the numbers of patients in this range of proteinuria are less and also in the exclusion criteria those patients with dipstick <1+ (like traces and negative) is excluded from the study.

Table – 1. Correlation coefficient between 24 hour urine protein and spot urine protein creatinine ratio.

VARIABLE	Mean	Standard Deviation
24 hour urine protein	1645.72mg/24hrs	2098.43
Spot urine protein creatinine ratio	1.991	2.463

Correlation coefficient r = 0.906 (p value <0.001)

For n number of subjects n = 60
Degree of freedom =n-2 =58
At 58 degrees of freedom table value =0.408 at pvalue <0.001, and observed value =0.906

It implies that there is a good correlation between 24hr urine protein and spot urine protein creatinine ratio which is significant at p value <0.001 in 60 patients with preeclampsia.

The graph (Figure-1) shows the distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with preeclampsia. The central line is the best fit due to regression. The overall correlation coefficient (r) between 24 hr urine protein and spot protein creatinine ratio r = 0.906 at pvalue <0.001,

1. When 24 hour urine protein values were <3gms, spot p/c ratio values were <3- in the above graph all the observations are clustered around this range which has a good correlation coefficient of r =0.641 with p value <0.001.
2. when 24 hour urine protein values were >3gms , spot p/c ratio values were along the line but not clustered ,the correlation coefficient r =0.88 at value <0.01 ,it implies that even at higher ranges of proteinuria though significance decreases, a fair correlation exists between 24 hour urine protein and spot p/c ratio.

Table 2. Correlation coefficient between 24 hour urine protein and spot urine protein creatinine ratio based on severity.

24hr urine protein	n	Correlation coefficient r	*P* value
>3gms	7	0.88	<0.01
<3gms	53	0.641	<0.001
>2gms	12	0.885	<0.001
<2gms	48	0.536	<0.001
300-2000mgs	45	0.494	<0.001
<300mgs	3	-0.87	>0.1

Table-3 shows that there is a good correlation between 24hr urine protein and spot urine protein creatinine ratio which is significant at p value <0.001 in 38 patients with severe preeclampsia.

Table-3. Correlation coefficient between 24 hour urine protein and spot urine protein creatinine ratio in Mild preeclampsia and severe preeclampsia

Mild Preeclampsia (n=22)	Mean	Standard Deviation
24 hour urine protein	**745.18**	425.118
Spot urine protein creatinine ratio	**0.845**	0.48
Severe Preeclampsia (n =38)		
24 hour urine protein	**2167.1**	2481.2
Spot urine protein creatinine ratio	**2.65**	2.84

For n number of subjects with mild preeclampsia n = 22.
Degree of freedom =n-2 =20
At 20 degrees of freedom table value =0.652 at p value <0.001, and observed value =0.801.

Correlation Coefficient – 'r'

Severity	R	P value
Mild Preeclampsia (n=22)	0.801	<0.001
Severe Preeclampsia (n =38)	0.895	<0.001

For n number of subjects with severe preeclampsia n = 38.

Degree of freedom =n-2 =36
At 36 degrees of freedom table value =0.519 at pvalue <0.001, and observed value =0.895.

It implies that there is a good correlation between 24hr urine protein and spot urine protein creatinine ratio which is significant at p value <0.001 in 22 patients with mild preeclampsia.

. Figure-2 shows the distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with mild preeclampsia.

Figure-3 shows the distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with severe preeclampsia.

Figure-1. The distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with preeclampsia

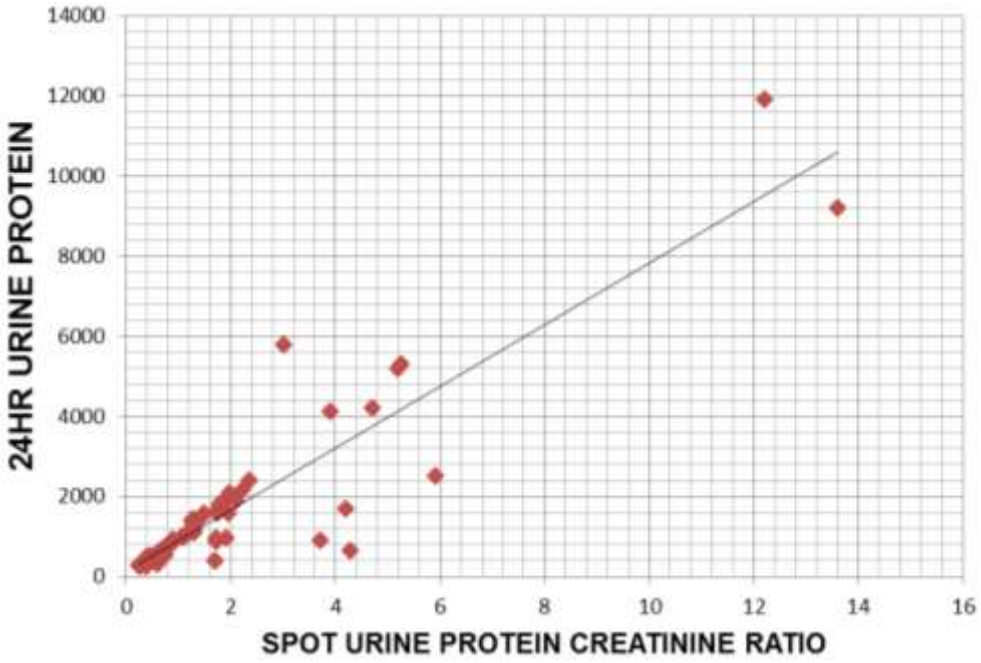
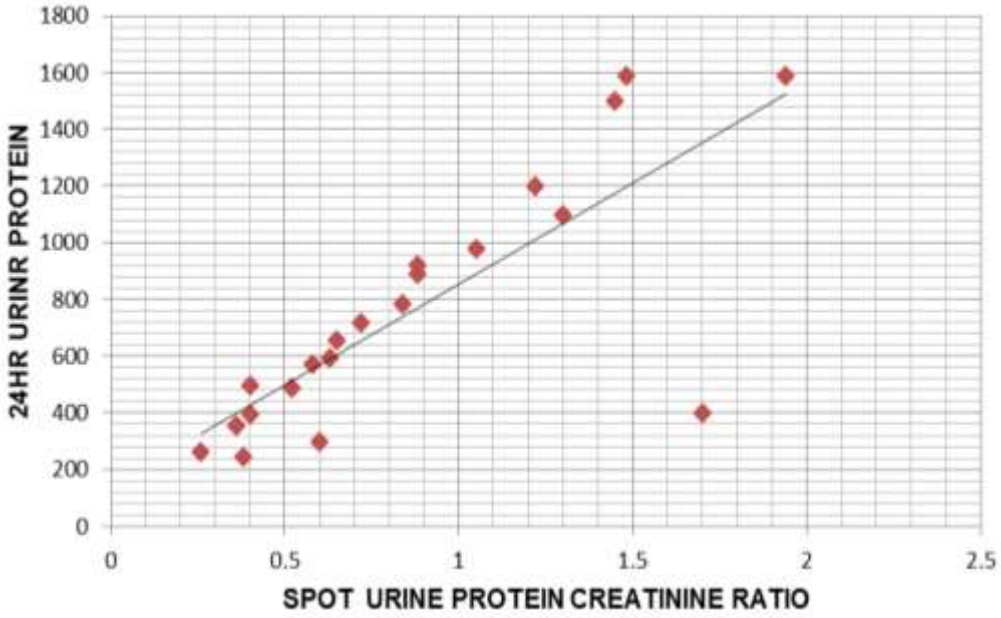


Figure-2. The distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with mild preeclampsia.



Considering 24hour urine protein as gold standard test
24 hour urine protein

Spot p/c ratio	+ve >300 mg	-ve <300mg
+ve >0.3	57 TP	1 FP
-ve <0.3	0 FN	2 TN

Sensitivity Of Spot Urine P/C Ratio-100% (a/a+c)*100
SPECIICITY OF SPOT URINE P/C RATIO-66.67% (d/b+d)*100
Positive Predictive **Value** Of Spot P/C Ratio-**98.27% (a/a+b)*100**

Figure-3 showing distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with preeclampsia

DISCUSSION

An accurate and rapid detection and quantification 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 60 pre-eclamptic women, the mean age of the patients was 23.1 years and the mean gestational age was 37.7 weeks. 22 (37%) had mild preeclampsia and 38 (63%) had severe preeclampsia ,3 patients(5%) had proteinuria <300mg , 45(75%) had proteinuria between 300-2000mg and 12(20%) had proteinuria >2000mg based on gold standard test 24hour urine protein compared to spot p/c ratio ,2 pts (3%) had p/c ratio <0.3, 51pts (85%) had p/c ratio 0.3-3 ,and 7 pts (12%) with p/c ratio >3.

The incidence of preeclampsia was higher in primigravidas 42(70%) than in multigravidas 18(30%), majority 42 (70%) of them were in the age group of 21-30 years. In patients with age <20 years 82% had severe preeclampsia. It was observed that, 40 patients (67%) were in the gestational age of 36-40 weeks. And severe preeclampsia was a found to be the most common in this period of gestation 27 cases(68%).It was also observed that the earlier the onset of disease in pregnancy the more severe it is.

The overall correlation coefficient (r) between 24 hr urine protein and spot protein creatinine ratio r = 0.906 at p value <0.001.

Of the 60 subjects 22(37%) of them undergone cesearean section commonest indication being severe preeclampsia and associated fetal distress.5 (8%) of subjects had a preterm delivery.

Of the 60 subjects delivered at our hospital ,33% have birth weight between 2-2.5 kgs, one baby was still born and 3 babies died in IPCU in view of low apgar and preterm .The perinatal outcome in women with severe preeclampsia was poor with increased incidence of IUGR, LBW ,preterm births ,meconium stained liquor and requiring higher need for NICU admission.

Figure-3. The distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with severe preeclampsia.

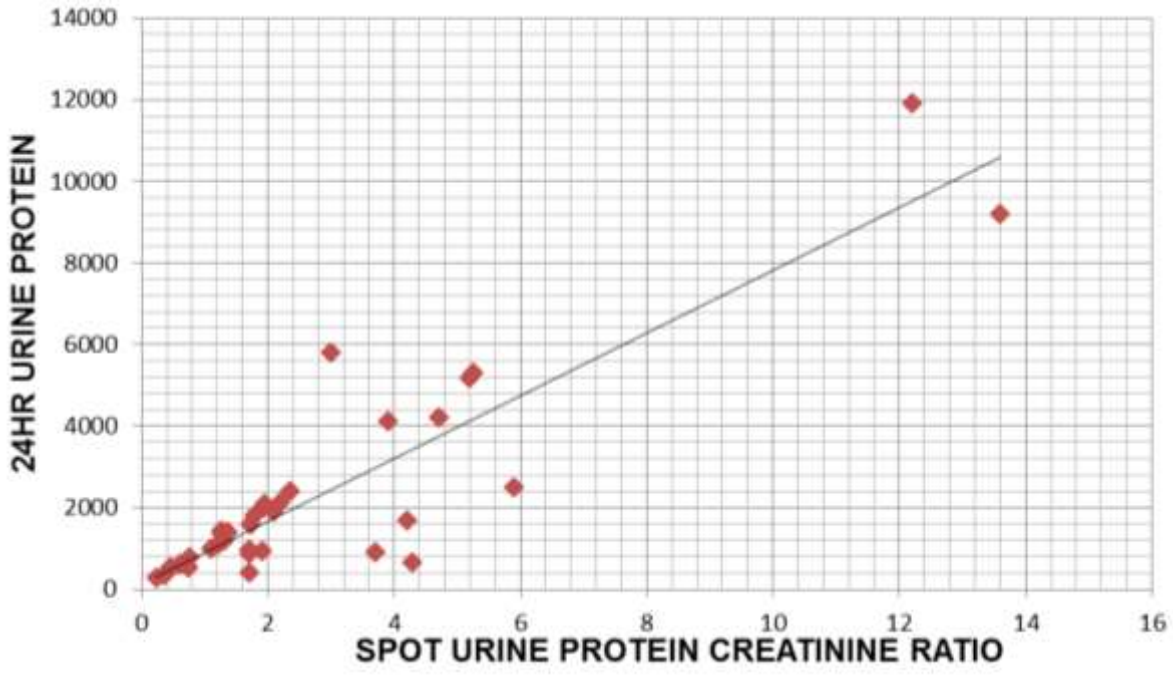
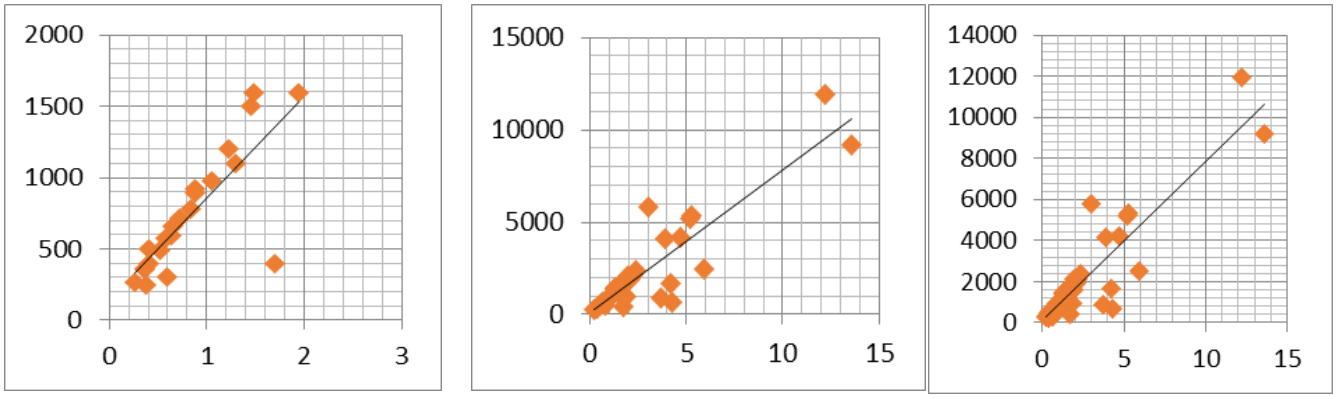


Table-4. The distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with severe and mild preeclampsia

	Mild Preeclampsia	Severe Preeclampsia	Total
No.Of Cases	22	38	60
Mean Age (Years)	24	23	23.1
Mean Pog (Weeks)	38	37.4	37.7
No. Of Primi	13	29	42
No. Of Multi	9	9	18
Mean Hb Gm/Dl	9.06	95	9.34
Platelet Count Lac/Mm3	2.02	1.91	1.95
Blood Urea Mg/Dl	21.5	23.46	22.93
Serum Creatinine Mg/Dl	0.754	.93	0.87
Serum Uric Acid Mg/Dl	4.55	5.9	5.41
Elevated Lft		8	8
Grade 1 Fundus-Htn		3	3
Mean Systolic Blood Pressure Mmhg	140	161.84	155.7
Mean Diastolic Blood Pressure Mmhg	90	113.42	104.67
Mean Spot Urine Protein Creatinine Ratio	0.845	2.65	1.99
Mean 24 Hr Urine Protein Mg/24hrs	745.18	2167.1	1645.72
Correlation Ratio	0.801	0.895	0.96
	Mild Preeclampsia	Severe Preeclampsia	Total
P Value	<0.001	<0.001	<0.001
Ft Nvd	17	16	33
Pt Nvd	1	4	5
Cesarean Section	4	18	22
No. Of Iugr Cases	5	15	20
Mean Birth Weight Kgs	2.55	2.272	2.37
Meconium Liquor	3	15	18
Nicu Admission	4	24	28
Live	22	34	56
Still Birth		1	1
Dead		3	3

Figure-4. Distribution of 24hr random urine protein and spot urine protein creatinine ratio in patients with Mild and Severe Preeclampsia.



MILD PREECLAMPSIA **SEVERE PREECLAMPSIA** **PREECLAMPSIA**

Of the 60 patients with preeclampsia, 7 patients developed eclampsia, 2 patients had abruption and 2 cases developed partial HELLP syndrome.

In the present study Spot Urine P/C Ratio Sensitivity 100% ,Speciicity 66.67% , Positive Predictive Value Of 98.27%. The study was limited to hospitalized non ambulatory 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.

We found a good degree of correlation in our study, when the 24 hours urine protein and the random urine protein-creatinine ratios were correlated with r = 0.906 and the p value being highly significant at <0.001, when all the observations were considered.

The correlation was also found to be good at r = 0.641 and p<0.001, for lesser degrees of proteinuria < 3 gms/24 hours and protein/ creatinine ratio also < 3. But when the correlation was computed for higher degrees of proteinuria i.e.; > 3gms/24 hrs, there was a fair correlation with r = 0.88 and p value being <0.01 which is statistically significant but to a lesser degree than proteinuria < 3 gms/24 hours.

In a similar study (Table-5) 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.

Table 5. Comparison Of Present Study With Similar Studies.

Study	Correlation Coefficient R	P value
Ginsberg et al	0.93	<0.001
Neithardt et al 2000	0.93	<0.001
Robert et al	0.94	<0.001
Boler et al	0.99	<0.001
Sauden et al	0.93	<0.001
Young et al	0.80	<0.001
Jaschevatzky et al 1990	0.92	<0.001
Nahid shahbazian 2008	0.84	<0.001
Bansal Bhavana 2009	0.83	<0.001
Present study	**0.906**	**<0.001**

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.

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.

We have also found the 24 hours urine collection to be cumbersome and inconvenient for a pregnant woman. 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 to mildly impaired renal function (<1.6 mg%). The mean serum creatinine value in our study group was 0.87mg/dl.

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.

CONCLUSION

Since the level of urinary protein excretion has considerable clinical implications in the course of pregnancy and on the perinatal and maternal outcome, the early detection of even minor degrees of proteinuria is important. Dipstick analysis as a screening for proteinuria lacks reliability with a high rate of false positives. For years, 24 hour urine collection has been the standard for quantification 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.

Quantitating proteinuria in a random sample has found to be far more cost effective and acceptable to the patient than a 24 hour urine collection. Since pre-eclampsia is a progressive disease, repeated laboratory examinations to quantitate proteinuria are required. Protein/ creatinine ratio has been found to be a superior diagnostic tool compared to the routine urinalysis which would otherwise be used for daily quantification of Proteinuria. It is especially found to be useful in an outpatient setting to predict clinically significant Proteinuria and to monitor renal functions in such women with lesser degrees of proteinuria thus avoiding unnecessary hospital admissions. The present study indicates that this method for quantization of proteinuria, when properly interpreted, can provide valuable information, that for clinical purposes is a satisfactory substitute for the determination of protein excretion in a 24 hour collection.

Ethics statement

Ethics approval was not sought for this article.

Competing interests

The authors have declared that no competing interests exist.

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