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A Comparative Study of Spot Urine Protein Creatinine Ratio With 24 Hours Urine Protein Excretion For Estimation Of Proteinuria In Preeclampsia.

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Abstract
Objective: *To determine the correlation between single voided sample (spot urine PCR) and 24 hours urine protein excretion in patients being evaluated for preeclampsia. This study was conducted in Niloufer hospital and sample size is 100.*
Methods: *A random urine sample was collected after discarding the first morning specimen. A single voided urine specimen was obtained soon after the 24 hour urine collection, before midday. Urine protein was performed on semiautomated analyser. Urine creatinine was measured by the Jaffes reaction. The protein creatinine ratio was calculated by dividing the urinary protein concentration by the urinary creatinine concentration and the correlation with the 24 hours urine protein was assessed.*
Results: *A fair correlation coefficient of r=0.902 was observed between the 24 hour urine protein and spot urine protein creatinine ratio among 100 subjects which was statistically significant at P value <0.001.*
Conclusion: *There is strong correlation between spot pcr and 24 hour urine protein estimation. The present study indicate that this method for quantification of proteinuria can provide valuable information.Its is a satisfactory substitute for the determination of protein excretion in 24 hours collection.*
Keywords: *Preeclampsia,p/c ratio ,Hypertensive disorders of pregnancy, Proteinuria,Renal functional tests.*
Abbreviations: *pcr=protein creatinine ratio .*

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I. Introduction:

Preeclampsia and eclampsia are common and form one of the deadly triad along with hemorrhage and infections that result in maternal mortality and is a leading cause of perinatal mortality. The incidence of preeclampsia is 5-10% of all pregnancy. It is a multisystem endothelial disease that leads to increased permeability of glomerular basement membrane to protein with resulting proteinuria. The working group of the National high blood pressure education programme 2000 defined mild preeclampsia as Bp>140/90 mm Hg after 20 weeks of gestation with proteinuria >300mg in 24 hours or 1+dipstick.severe preeclampsia as BP >160/110mm Hg, proteinuria >2 grams in 24 hours or 2+dipstick, serum creatinine >1.1mg/dl, platelets <100000/cumm, microangiopathic heamolysis, fetal growth restriction, pulmonary edema. Proteinuria develop late in the course of preeclampsia and it increases the likelyhood of complications. The measurement of protein excretion in urine over a period of 24 hours is the gold standard for quantitative evaluation of proteinuria in pregnancy. Though reliable indicator it has the disadvantage of being a cumbersome process for both patient and laboratory. It is subjected to collection error, requires good patient compliance and there is a delay of 24hous from the time of collection till the diagnosis is made. There is a need for a quick, realiable, acceptable and cost effective alternative test. The spot protein/creatinine ratio has been prepared as an alternative test for the diagnosis of preeclampsia .A good correlation between the two tests has been demonstrated in pregnant women by many studies. The International society for the study of hypertension in pregnancy has accepted this test to identify significant proteinuria. Although proteinuria is indicative of severe disease the absence of it does not preclude severe form of preeclampsia. Eclampsia and severe preeclampsia can occur without proteinuria .Prevalence of proteinuria in pregnancy is 5%.The accepted upper limit of normal proteinuria in pregnancy is 300mg in 24 hours. PCR would be a very useful test as it is quick, cheap and convenient to patient and staff. The aim of our study was to examine the correlation between spot urine, PCR and 24 hour urine excretion in preeclampsia and its value in predicting significant proteinuria in preeclamptic patients.

II. Methods:

A prospective study was performed on pregnant women on preeclampsia with a gestational age > 20weeks. The ethical committee permission was taken. The inclusion criteria are pregnant women booked and unbooked cases, new onset of blood pressure of 140/90mm of Hg or more on two occasion atleast 6 hours apart as a single diastole reading of >110mm of Hg, and new onset proteinuria on urinary dipstick. The exclusion criteria are those with <20 weeks of gestational age, patients with >20weeks of gestational age having urinary tract infections , Diabetes mellitus ,chronic hypertension, preexisting renal disorders, hypothyroidism, thyrotoxicosis, and those receiving corticosteroids, NSAIDS, and sympathomimetic drugs. The study was conducted at Niloufer hospital a tertiary care hospital with 6500 deliveries per annum. The 24 hours urine collection was performed as an inpatient or outpatient. The urine samples were collected starting from the 2^{nd} urine sample in the morning (after discarding the 1^{st} morning specimen) till the 1^{st} urine sample the next day morning. A single voided urine specimen was obtained soon after the 24 hours urine collection before midday. Urine protein was measured by turbidometry method and the test was measured on semi automated analyzer. Urine creatinine was measured by Jaffes reaction. The test was performed on a semi automated analyzer. The urine protein and creatinine ratio was obtained by dividing the urine protein concentration (mg/dl) by urine creatinine (mg/dl). The data collected were analyzed using appropriate statistical method. The mean and standard deviations were computed. The standard tests used for analyses was the chi square test expressed as P . A P value of $p< 0.05$ has been considered to be statistically significant.

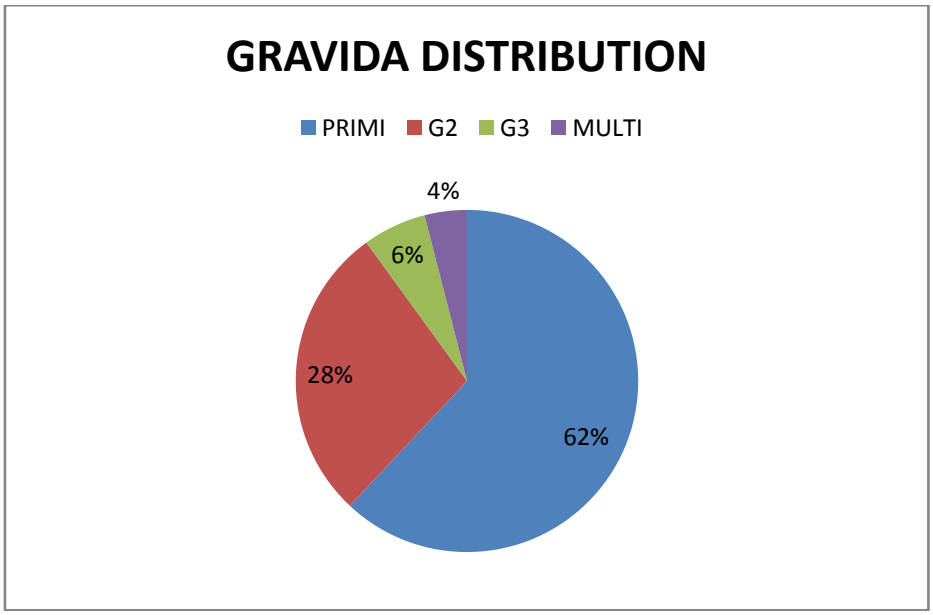
III. Results:

A total of 100 women with preeclampsia were studied. 18 had severe degree of proteinuria >3grams and the correlation was found at $r=0.77$, $p<0.01$. The mean maternal age of the patient was 27.14 years. 78% were primigravida and mean gestational age was 33.45weeks. Most of the women were having systolic blood pressure between 140-159mm Hg, diastolic blood pressure was 101.2mm of Hg . We found a fair degree of correlation in our study when the 24 hours urine protein and the random urine protein/creatinine were correlated with $r=0.90$ and the p value is being highly significant at < 0.001 when all the observations were considered. In our study the correlation coefficient at lesser degrees of proteinuria(<300mg) was less (0.59) as compared to other two groups but statistically significant p value 0.055. The study was limited to hospitalized patients. We found the use of spot test was more cost effective as shown in many studies previously. We have found the 24hours urine collection to be cumbersome and inconvenient to the pregnant women.

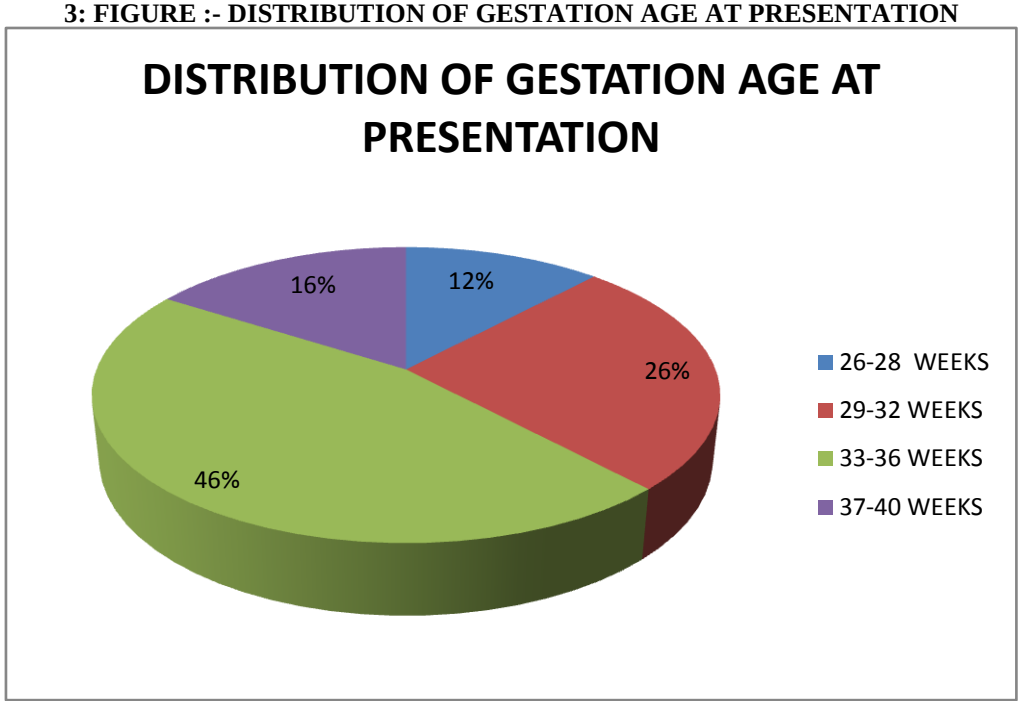
1: TABLE: AGE DISTRIBUTION IN THE STUDY GROUP

AGE GROUP	NO. OF WOMEN	PERCENTAGE
18-20 YEARS	8	8%
21-25 YEARS	22	22%
26-30 YEARS	52	52%
31-35 YEARS	16	16%
36-40 YEARS	2	2%
TOTAL	**100**	**100%**
MEAN ±std de	27.14±4.06 yrs	

2: FIGURE: GRAVIDA DISTRIBUTION IN THE STUDY GROUP



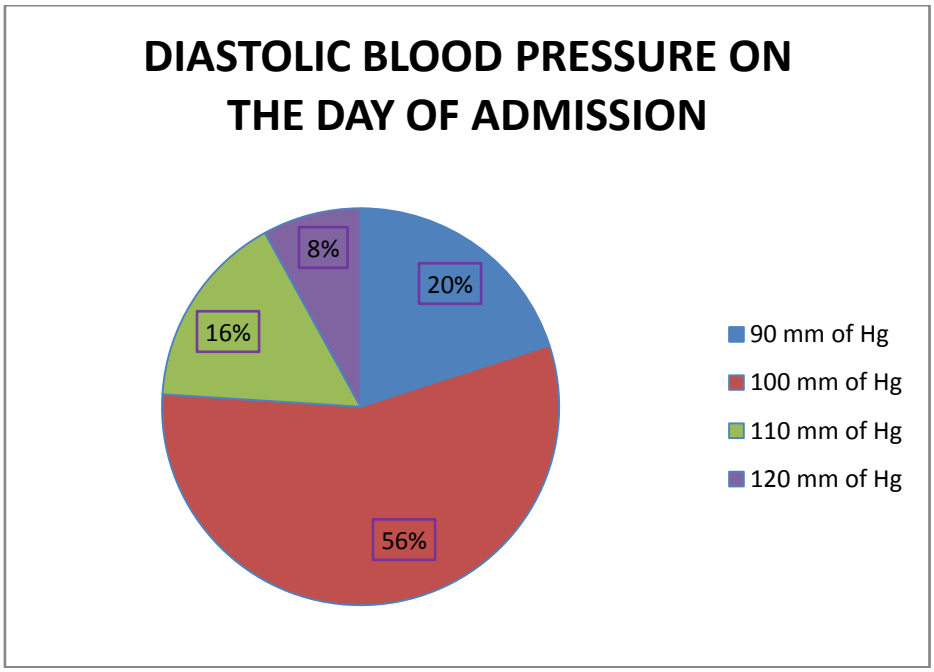
3: FIGURE :- DISTRIBUTION OF GESTATION AGE AT PRESENTATION



4: TABLE:- SYSTOLIC BLOOD PRESSURE IN THE STUDY GROUP ON THE DAY OF ADMISSION.

SBP	n(100)	PERCENTAGE
140-159 mm of Hg	58	58%
160-180 mm of Hg	40	40%
181-200 mm of Hg	2	2%
TOTAL	**100**	**100%**

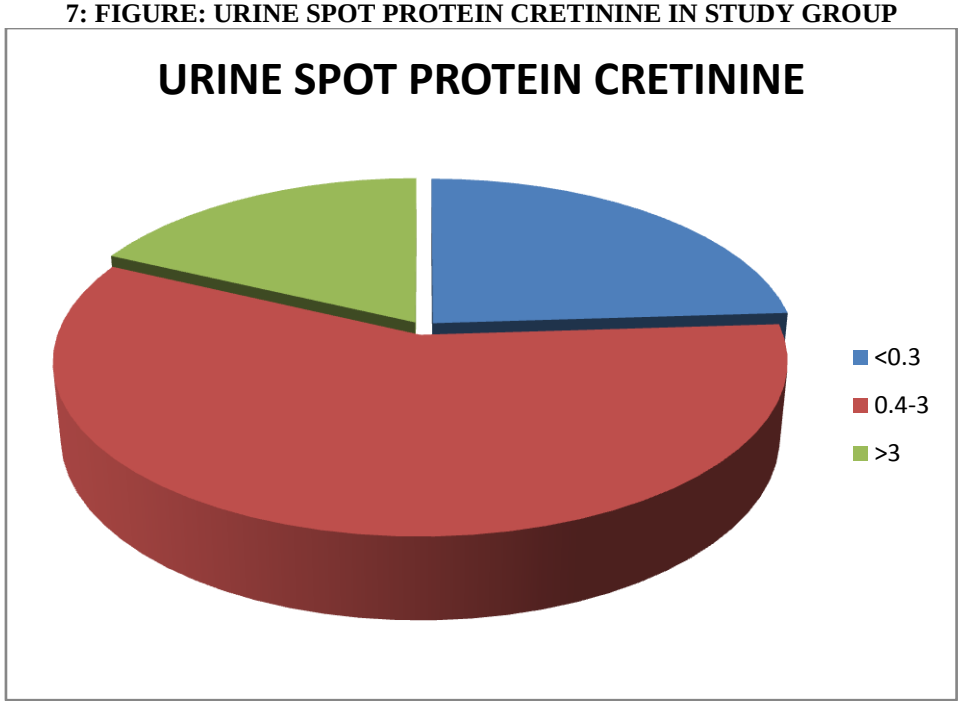
5: FIGURE :- DIASTOLIC BLOOD PRESSURE ON THE DAY OF ADMISSION



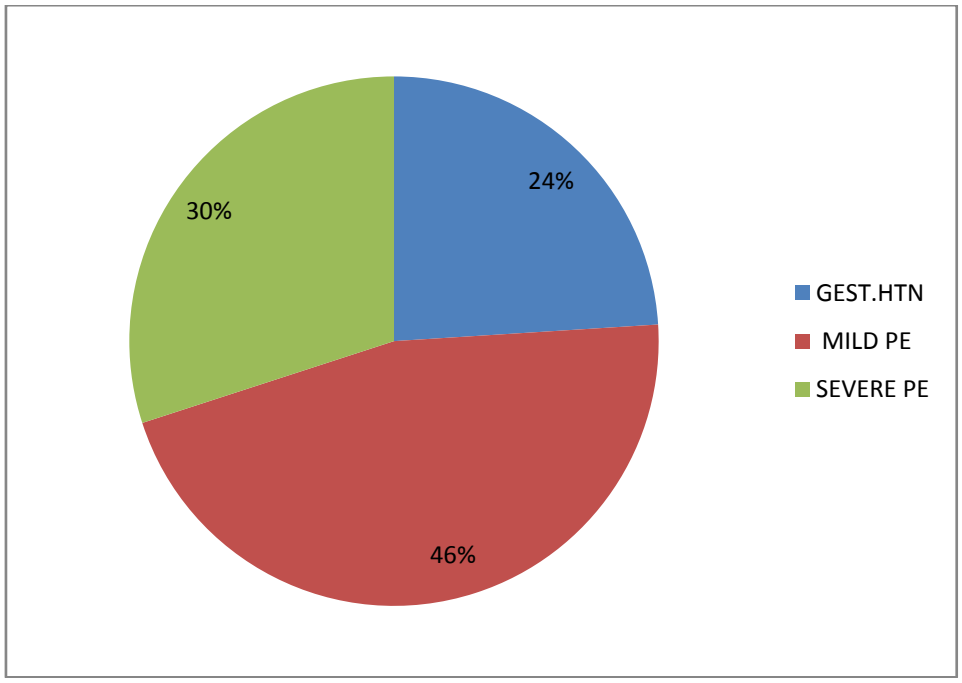
6: **TABLE :24 HOURS URINE PROTIEN.**

24 Hr urine protein	**n(100)**	**Percentage**
< 300mg	24	24%
300-1mg	28	28%
1-2mg	20	20%
2-3mg	10	10%
>3mg	18	18%

7: FIGURE: URINE SPOT PROTEIN CRETININE IN STUDY GROUP



8: FIGURE: DISTRIBUTION OF SUBJECT IN TO GEST.HTN, MILD OR SEVERE PE


24%
30%
46%
GEST.HTN
MILD PE
SEVERE PE

9:TABLE: Mean and SD of 24 hour urine protein and P/C ration.

	Mean	**Std deviation**
Gestational hypertension 24 hr protein PC ratio(n=24)	 173.2545 0.12	 82.84927 0.12
Mild preeclampsia 24 hr protein PC ratio(n=46)	 1010.79 1.29	 457.38614 0.78
Severe eclampsia 24 hr protein PC ratio(n=30)	 3387.00 4.65	 1867.07 3.56

10.Table: Mean and Standard deviation of 24 hrs urine protein and P/C ratio of all 100 subject.

Variable	**Mean**	**Std.deviation**
24 hour urine protein	1542	1.64
Spot protein/ creatinine ratio	2.06	2.65

11. Correlation between 24 hour urine protein verse PC ratio.

Studies	**Correlation Coefficient(r)**	**p-value**
Boler et al (1987)n=54	0.99	<0.0001
Jaschevatzky et al (1990)n=105	0.94	<0.001
Sauden et al (1997)n=100	0.94	<0.001
Netithardt et al(2000)n=30	0.93	<0.001
Present study (2018)n=100	0.93	<0.001

IV. Discussion:

An accurate and rapid detection and quantification of proteinuria are essential in the management of preeclampsia. Early diagnosis and treatment of preeclampsia is essential for prevention of eclampsia. Accurate diagnosis is important to prevent unnecessary interventions in hypertensive pregnant women for further testing or treatment. Although 24 hours urine collection for total protein estimation as either outpatient or in patient is the gold standard test. It has its limitations like there will be delay in time, inconvenience for both patient and staff. There may be errors in sample collection. PCR can be practical alternative tests to minimize errors and it can be done rapidly. The study supports the use of a single voided pc ratio to predict 24 hour urine protein. Though the PCR ratio shows promising diagnostic values a balance is required between sensitivity and specificity that is based on a chosen threshold. The use of PCR to replace the 24hours urinary protein measurement would ideally use a cutoff level that limits number of false negative results. If PCR were to be use as a screening test with positive result requiring a 24hours urine collection to verify then false negative rates to be minimized. In our study PCR of 0.03 was identified as the optimal threshold to detect urine protein excretion of 300mg per 24 hours.

Various studies compared 24 hours urine protein with urine spot protein creatinine ratio:

1) Jung-Hwa Park, Dawn Chung, Hee-Young cho, Young-Han Kim, Ga-Hyun son, Yong-Won Park, and Ja-Young Kwon-Random urine P/C ratio highly correlated with 24 hour protein excretion($r=0.823$, $P<0.01$). The optimal random urine P/C ratio cut off points were 0.63 and 4.68 for 300 mg/24 hr and 5000 mg/24 hr of protein excretion, respectively.

2) Amith Sharma, Pandey Kiran, Bhagoliwal Ajai-The correlation between the spot P/C ratio and 24 Hour urine protein amount was done with logistic regression analysis and ROC curve analysis. The optimal spot P/C ratio cutoff point was 0.25, for 300mg/24hr of protein excretion, with sensitivity and specificity of 69% and 75% respectively.

3)Nahid Shahbazian, Farzaneh Hosseini-Asl- The correlation between the spot p/c ratio and 24 hour urine protein excretion was assessed . Diagnostic value of p/c ratio was expressed in terms of specificity and sensitivity. There was a strong correlation between the spot p/c ratio and 24 hour protein excretion ($r=0.84$;$P<0.001$). The optimal spot p/c ratios cut off point was 0.20 for 300mg/24 hr urine protein excretion(preeclampsia).

4) Choudhary Jaya, VineetaGarg etal,-The relationship between protein-creatinine ratio and 24 hour protein excretion was assessed by Pearson correlation coefficient.

5) Gurupadappa Shantappa Kallagananda and Kavitha hiremath-The sensitivity and specificity was 71.5% and 100% respectively at protein:creatinine ratio cutoff of 0.66.
Various other studies also confirms the same findings.

V. Conclusion:

The value of protein creatinine ratio in a single urine sample is accurate because it avoids collection error. Quantitating proteinuria in a random sample has found to be more cost effective and acceptable to patient. The present study indicates that this method for quantification 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.

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