Vol. 16, No. 3
ORIGINAL PAPER

GYNAECOLOGY & OBSTETRICS

MEDICAL CHANNEL
JULY - SEPTEMBER 2010

OPTIMAL DIAGNOSTIC VALUE OF RANDOM URINE PROTEIN-TO- CREATININE RATIO OVER 24-HOURS URINE PROTEIN EXCRETION IN WOMEN WITH PRE ECLAMPSIA AT CHANDKA MEDICAL COLLEGE HOSPITAL LARKANA

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ABSTRACT

OBJECTIVE: *To determine correlation of random urine protein-to- creatinine ratio with 24-hours urine protein excretion as simple, steadfast and effective method of diagnosis of proteinuria in patients with pre eclampsia and to determine its value as time saving test.*
STUDY DESIGN: *Cross-sectional analytical.*
PLACE AND DURATION OF STUDY: T*his study was conducted at obstetrics unit of Sheikh Zyed Hospital for women and department of pathology Chandka Medical College Larkana between the periods of January 2008 to June 2009.*
METHODOLOGY: *Random urine sample was collected in 53 consecutive patients who were admitted and diagnosed as case of pre-eclampsia in the department of obstetrics and gynaecology, for protein –to- creatinine ratio and also urine was collected in same patients for estimation of 24-hour urinary protein excretion to see the association in between them. Patients of chronic hypertension, renal diseases, autoimmune diseases and urinary tract infections were excluded from study.*
RESULT: *Strong correlation was seen (r=+0.97, P<0.001) between random urine protein-to-creatinine ratio and 24-hours urine protein excretion, which was found by Pearson correlation coefficient (r) test. The mean ±standard deviation 24-hours urinary total protein excretion rate was 3.90±2.91g/24-hours and protein: creatinine ratio 3.85 ± 3.16.*
CONCLUSION: *Protein –to-creatinine ratio in random urine sample specimens provides an accurate, convenient, and reliable method to estimate proteinuria in pre eclamptic patients. Due to strong correlation in both tests, in mild to moderate proteinuria the cumbersome test 24-hours urinary protein excretion estimation can be substituted with random urine protein-to-creatinine ratio measurement. Also this test will be steadfast and time saving in earlier decision to ensure good feto-maternal out come.*

KEY WORDS: Random urine protein: creatinine ratio, pre-eclampsia, 24-hours urinary proteinexcretion.

INTRODUCTION

Hypertensive disorders of pregnancy complicates up to 10% of pregnancies[1] and preeclampsia is a major cause of maternal and perinatal mortality and morbidity world wide causing 15% of all direct maternal deaths in the UK and 24% of all maternal deaths in india[2-4]Pre eclampsia is defined as hypertension (blood pressure>140/90mmhg) associated with proteinuria (300mg or more in 24-our urine)[5.] Presence of proteinuria differentiates pre-eclampsia from other hypertensive disorders of pregnancy like non proteinuric gestational hypertension and chronic hypertension, so the latter two conditions bear good feto-maternal prognosis, hence earlier the detection of proteinuria better is the understanding of disease. Davey and MacGillivary, defined significant proteinuria as one 24-urine collection with a total protein excretion of 300mg or more.[6] Proteinuria in pregnancy is categorized as mild 300-499mg/day), severe (5-10g/day) and massive (>10g/day)[7]
Measurement of protein excretion in a 24-hours urinary collection is a gold standard for the quantitative evaluation of proteinuria. However, this method is a cumbersome and inconvenient, since it is difficult to collect a complete 24-hour urine sample accurately, especially in those patients who are going to deliver before completion of 24-hours. Diagnosing

significant proteinuria could help clinician make more timely decision regarding delivery and seizure prophylaxis. Studies have shown that the urinary dipstick test is poor predictor of 24-hour urinary total protein level[8].An alternative method for quantitative evaluation of proteinuria is the measurement of protein:creatinine ratio in a random urine sample, which provides a more convenient method to assess protein excretion .Many studies conducted in non pregnant women have strengthened the idea of detecting proteinuria with good accuracy results .[9]In this study, our aim is to correlate the random urine protein:creatinine ratio with 24-hours urinary protein excretion rate and attempt to find a discriminant value for protein: creatinine ratio that reliably determines a significant threshold level of proteinuria. This will be helpful in those hospitals where women with hypertensive diseases report very late and quicker results may shorten their hospital stay for long time.

MATERIALS AND METHODS

This cross sectional analytical study was carried out in the obstetrics ward, labour room unit II Sheikh Zyed Hospital for Women at Larkana and department of pathology chandka medical college larkana during the period of January 2008 to June 2009. A total of 53 patients with the diagnosis of pre-eclampsia were recruited in the study. Blood pressure more than 140/ 90mmhg and positive dipstick test of a value more than 30mg for proteinuria made them the candidates of study. As 3 patients were excluded due to improper collection, and the remaining 50 fulfilled the criteria

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INCLUSION CRITERIA

Patients of pre-eclampsia at more than 20 weeks of gestational age of any parity and of 19-40 years of age, in patients with hypertension occurring for the first time in pregnancy were eligible for study.

EXCLUSION CRITERIA

Patients of chronic hypertension, renal disease, auto immune diseases and urinary tract infection were not included in study. Women who needed urgent delivery were also excluded.Haematological tests like random blood sugar, blood urea, serum creatinine and serum electrolytes were done as baseline tests in all recruited patients. Their particular demographic variables are discussed later in results. Urine was tested for routine and microscopic examination to exclude patients having urinary tract infection.

The patients were advised to pass urine at 8: am (as per standard protocol to discard early morning sample) and collect all the urine subsequently till 8: am the next morning (24-hours period). Protein and creatinine concentration was measured from random sample of urine after the 24-hours collection was over (to discriminate the particular sample for urinary protein: creatinine ratio), in all same patients after giving them instruction. Both tests were done on urine analyser microlab 300 of Merek company®.

Statistical analyses were conducted by using SPSS, version (10). A descriptive analysis was done for baseline characteristics of the patients and results are presented as mean standard deviation of all variables like age, parity, gestational age, blood pressure and urinary protein values. The protein: creatinine

TABLE – I
BASE LINE CLINICAL CHARACTERISTICS OF STUDY POPULATION

Variable	Results
Age (years)	24.14 ± 3.54
Parity (range)	0-5
Gestational age (weeks	33.14 ± 2.81
Systolic blood pressure (mm Hg)	161.00 ± 15.29
Diastolic blood pressure (mm Hg)	111.60 ± 12.99
Serum creatinine (mg/dl)	1.02 ± 0.18

All figures are mean ± 1 standard deviation

TABLE – II
DISTRIBUTION OF STUDY SUBJECTS (N=50) ACCORDING TO SEVERITY OF PROTEIN UREA
PROTEINURIA

Proteinuria (g/24-hr)	Number of patients	Percentage
Mild(0.30-.99)	36	72.0
Severe (5.00-10.00)	11	22.0
Massive	3	6.0

TABLE – III
URINARY TOTAL PROTEIN EXCRETION (G/24-HR) AND VALUE OF RANDOM URINE PROTEIN AND CREATININE (MG/MG)

Parameters	Mean ± SD
24-hour urine	
Volume (L)	1-88 ± 0.73
Total protein (g)	3.90 ± 2.91
Random urine	
Protein (mg/dl)	301.65 ± 224.34
Creatinine (mg/dl)	92.54 ± 56.46
Protein : Creatinine (mg/mg)	3.85 ± 3.16

ratio in random urine samples were calculated by protein concentration (mg/dl) divided by creatinine concentration. Correlation was tested using Pearson correlation coefficient<0.05 was selected as the level of significance.

RESULTS

53 consecutive women were enrolled, out of them 3 women were excluded due to insufficient urine collection in them. In 50 patients, the demographic variable taken as mean maternal age, which was around 24 years (range 19-40 years).Majority of women recruited in study were primigravidas (75%). Mean gestational age of presentation was 32 weeks. Other variables like mean systolic and diastolic blood pressure mean serum creatinine are given in table -1

Patients were grouped according to severity of proteinuria in to mild (0.30-4.99g/24 hour) severe (5-10g/24 hour) and massive (>10g/ 24hour) proteinuric types. 72%(n=36) patient fell in category of mild proteinuria while 22%(n=11) had severe type of proteinuria and only 6%(n=3) patients were detained in group of massive proteinuria as shown in table –II.

The mean random urinary protein : creatinine ratio was 3.85±3.16mg/mg while mean 24-hour excretion rate was 3.90±2.91g/24- hour given in table- III.

The random urine protein:creatinine ratio has positive and highly significant relationship with 24-hour urinary total protein excretion rate in 50 preeclamptic patients (r= +0.978,p<0.001) shown in fig-1.

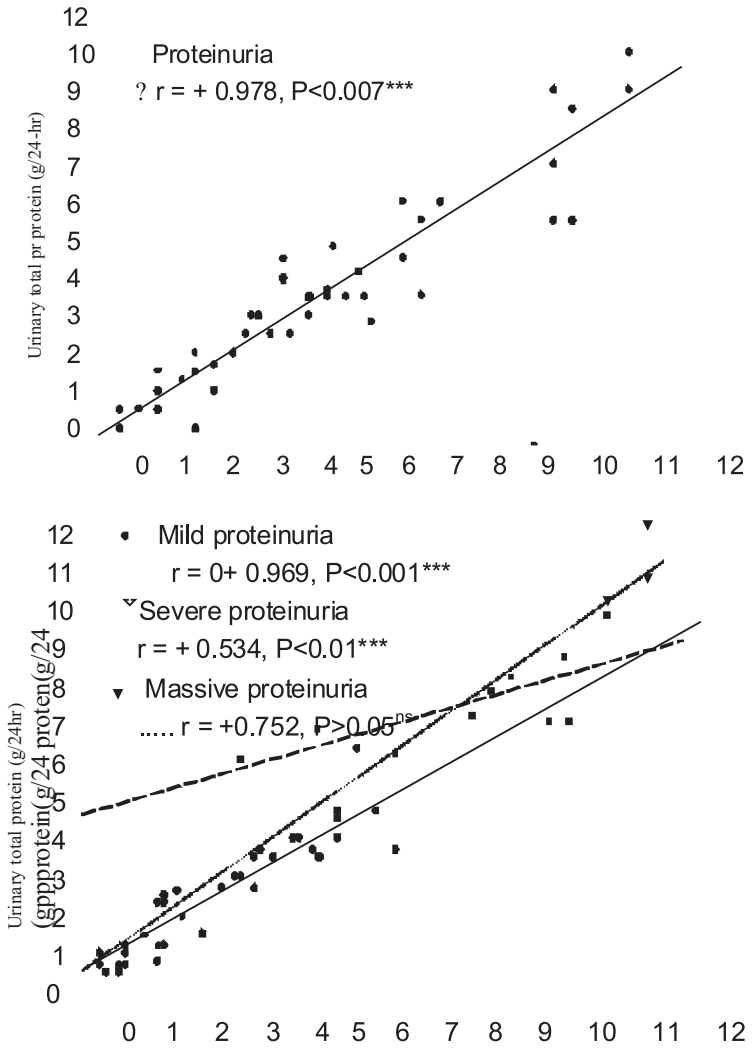
Relation ship is highly significant and positive in mild proteinuria(r=+0.969, P<0.001) significant and positive in severe proteinuria(r= +0.534, p<o.o1), but not significant in massive proteinuria (r= =0.752,p>o.o5) fig-2

Random urine protein : creatinine ratio (mg/ mg).Fig: 1 Association between random urine protein creatinine ratio and 24 hour urinary total protein excretion (n=53)

Relationship is highly significant and positive in mild proteinuria(r=+0.969, P<0.001) significant and positive in severe proteinuria(r= +0.534, p<o.o1), but not significant in massive proteinuria (r= =0.752,P>o.o5) fig-2

Random urine protein: creatinine ratio (mg/ mg)

Fig: Association between random urine protein creatinine ratio and various type of proteinuria.



DISCUSSION

The quantification of proteinuria in preeclampsia is necessary for diagnosing preeclampsia and for classifying mild versus severe disease, increasing levels of proteinuria is considered to be associated with adverse maternal and fetal outcomes.[10] The gold standard for proteinuria, a key component in the assessment of preeclampsia, is a 24-hour urine collection, which is cumbersome both for the patients and the staff handling the urine collection, and subject to error due to inaccurate timing and/or incompleteness.[11]

A shorter period to diagnosis would have clinical benefits such as shortened time to delivery and earlier use of antenatal glucocorticods. A more expedient intervention could decrease perinatal morbidity. Certainly, those women would be discharged to home earlier if a more rapid (and accurate) determination of proteinuria was available, thus resulting in lower health care costs. Patient compliance with testing may also improve if the test for proteinuria can be simplified or shortened.

The wide spread use a of 24-hours urine protein excretion measurement forced the researchers to find a simpler and quicker method to get the result. One of the simpler methods is use of random single voided urine protein: creatinine ratio as an alternative to 24 hours urine collection. Our study is also based on that method. Western journals have published number of papers on this subject but Pakistani data is lacking relatively .[12,13] This study was conducted to evaluate correlation between significant proteinuria and random urinary protein:creatinine ratio and to determine its accuracy. The present study shows that there is high degree of correlation of the random urinary protein:creatinine ratio and 24-hour urinary protein excretion rate in preeclampsia. Previously done studies have supported the results. Zadehmodarres found strong correlation between two methods and recommended it as a faster and simpler diagnostic method[14].

Studies by Boler and associates, and jaschevatzky and associates have also shown excellent correlation between 24-hour proteinuria and random urinary protein-creatinine ratio[15,16]. Boler and associates

studied the parameters in 54 patients. Excellent correlation was achieved (r=0.9935; P< .0001) between the two, and this was achieved for normal pregnancies, hypertensive pregnancies, and multiple gestation.[15] Similarly the study conducted by Jaschevatzky and associates on 35 preeclamptic patients with 70 healthy patients, found close correlation (r=0.9278; P< .001) between 24-hour proteinuria and random urinary protein-creatinine ratio.[16\ Chan P and colleagues from Australia concluded that for all ages, a high spot urine protein / creatinine ratio in pre-eclamptic women of greater than 900 mg/mmol (9g/day) or greater than 500 mg/mmol (5g/day) in women over 35 years, is associated with greatly increased likelihood of adverse maternal outcomes.[17] Our study also shows that the correlation is highly significant in mild proteinuric cases and significant in severe cases, while no significance was seen in massive type of proteinuria, which is supported by another study by Quaderi et al who found that correlation is not as strong as the proteinuria becomes higher. He also showed that correlation was maintained throughout the pregnancy and remained independent of gestational age.[18] So in massive type of proteinuria 24-hour urinary protein excretion should be measured. Many studies in non pregnant and pregnant women have shown that the random urinary protein to creatinine ratio can be used to quantify the degree of proteinuria with good accuracy with a level greater than or equal to 0.2 considered evidence of significant proteinuria.[19] Calculation of a cut off protein:creatinine ratio needs study of both normotensive and hypertensive women. But the present study consisted of only the diagnosed cases of preeclampsia. Also many studies have stressed on early detection and prompt management of patients with proteinuria that is beneficial for patient and fetus.[20,21]

As this study was conducted in a hospital of interior sindh which recruits mostly patients of low socio economic class, usually they report late, so total time from diagnosis to treatment is important. The result of urinary dipstick is available immediately but it is a poor predictor, while the urine protein /creatinine ratio result is obtained in 30 minutes. When compared with the 24-hours protein estimation whose result takes about 25 hours to get, so the method of detection ofproteinuria with random urine protein: creatinine ratio is faster and within safe limits to aid diagnosis and in early start of treatment ,hence ensuring better feto-maternal out come.

CONCLUSION

It is clear that in women with preeclampsia there is obvious association between the degree of proteinuria at the time of diagnosis and subsequent adverse maternal or fetal out come Random urinary: protein ratio may be used for closer monitoring of the severity and progression of proteinuria in pregnancy. Another benefit of this method may be in institutions where women with hypertensive disorders of pregnancy are admitted, women with insignificant proteinuria may be identified within a minute of hours and follow-up care can be handled on an out patient basis. Shortening the period for the diagnosis of preeclampsia would be valuable for management purposes, as well as for decreasing hospital cost and patient inconvenience. For the better understanding of the correlation and to find out a cut off value further studies are recommended including both normo-tensive and hypertensive pregnant women.

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