ORIGINAL ARTICLE

Correlation of Spot Urine Albumin to Creatinine Ratio and 24-Hrs. Urinary Protein Excretion in Pregnancy Induced Hypertension Cases

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ABSTRACT

Background: Preeclampsia remains a leading cause of maternal morbidity and mortality worldwide. 24-hour urinary protein estimation remains the gold standard method for the diagnosis of preeclampsia. However, there was a controversy in the existing literature regarding the positive predictive value of spot urinary protein to creatinine ratio, which caused the present study.
Aim: The aim of this study was to determine the positive predictive value of spot urinary protein to creatinine ratio for the diagnosis of preeclampsia taking 24-hour urinary protein as the gold standard.
Study Design: It was a cross-sectional survey.
Setting: Research was conducted at the Department of Obstetrics & Gynecology Civil Hospital, Hyderabad.
Duration: 6 months after the approval of synopsis 17th October 2020 to 16th April 2021
Material and Methods: This study involved 114 pregnant women aged between 18-40 years presenting for a routine antenatal checkup after 28 weeks of gestation (as per dating scan) and having raised blood pressure ≥160/110mmHg on at least two occasions at least 4 hours apart. Preeclampsia was suspected if the spot urinary protein to creatinine ratio was ≥0.2. 24-hour urinary protein excretion was estimated and diagnosis of preeclampsia was confirmed if it was ≥300mg in 24 urine specimens.
Results: The mean age of the women was 26.6±6.2 years while the mean gestational age was 34.3±1.6 weeks. 26 (22.8%) women were primiparas and 88 (77.2%) women were multiparas. The mean BMI of these women was 26.7±4.2 Kg/m^2 and 32 (28.1%) women were obese. Diagnosis of preeclampsia was confirmed in 111 (97.4%) women on 24-hour urinary protein excretion. It yielded a positive predictive value of 97.4% for spot urinary protein to creatinine ratio in the diagnosis of preeclampsia, taking 24-hour urinary protein excretion as the gold standard. A similar positive predictive value was noted across various subgroups of women based on age, gestational age, parity, and BMI.
Conclusion: In the present study, the positive predictive value of spot urinary protein to creatinine ratio was found to be 97.4% in predicting preeclampsia in hypertensive pregnant women regardless of patient's age, gestational age, parity, and BMI which along with the associated advantage of spot specimen collection and timely results (compared to the routine practice of 24-hour urinary protein estimation which wastes precious time and delays the patient's treatment), advocates the preferred use of spot urinary protein to creatinine ratio in the evaluation of hypertensive pregnant women in future obstetric practice.
Keywords: Preeclampsia, 24-Hour Urinary Protein, Spot Urinary Protein to Creatinine Ratio, Positive Predictive Value

INTRODUCTION

Pregnancy-induced hypertension is a common but serious complication that can have life-threatening consequences for both the unborn child and the mother and her unborn child. 7 percent of pregnancies are complicated by this disorder. Preeclampsia can be diagnosed after 20 weeks of pregnancy if high blood pressure and proteinuria are present.[1] Pre-eclampsia is considered to be present in women who have gestational hypertension and new proteinuria.[2]

Pre-eclampsia is a condition that affects about 5% to 8% of pregnant women worldwide. In low- and middle-income countries, it is the most common cause of maternal and perinatal morbidity and mortality, with an annual death toll of 50 000–60 000. Many questions remain unanswered about the cause and pathogenesis of this multi-systemic disorder. The mother and her child are also more likely to develop cardiovascular complications and diabetes mellitus in the future.[3] Aside from the fact that PE is an interdisciplinary condition, it has no known treatment other than cesarean section, which is the only known method of curing it.[4]

Preeclampsia is defined by proteinuria. Urinary albumin excretion varies throughout the day, causing proteinuria to fluctuate widely throughout 24 hours.[5] Several other factors, such as contamination, urine specific gravity, and pH are also influencing factors. There may be a delay in diagnosis and treatment because of the 24-hour collection period for urine.[6] This may cause a longer hospital stay. An earlier diagnosis of preeclampsia would be helpful in terms of patient care, hospital costs, and the overall experience of the patient.[7,8]

Basharat et al.[9] in 2017 conducted a study on spot protein to creatinine ratio a good alternative to 24-hour urinary protein for diagnosis of preeclampsia and found that the positive predictive value (PPV) of spot protein to creatinine ratio in predicting preeclampsia was 99.1%. Demirci et al.[10] in 2015 conducted a similar study and found that the positive predictive value was 95.2%. Shrestha et al.[11] conducted a similar study in 2018 and found that the positive predictive value was 97.2%. Mohseni et al.[12] (2013) in a similar study reported the PPV to be 92.0%. Huang et al.[13] (2012) reported the performance of Albumin creatinine ratio (ACR) as a diagnostic tool of preeclampsia among pregnant women and reported the PPV to be 56.80%.

Rational: There is a conflict in the PPV of the ACR in predicting preeclampsia among pregnant women (99.1%[9], 92.0%[12], 56.80%).[13]

To the best of the candidates' knowledge, there is no local published data on this topic and this study will help in determining the PPV of the spot protein to creatinine ratio for diagnosing preeclampsia in pregnant women and can help in reducing the complications associated with 24-hour urinary protein for the diagnosis and hence can help in reducing the mortality and morbidity in these patients.

Because of the lack of local publish data and the above conflict, there is a need to conduct this study in the local population, the results of the present study will give an insight into the magnitude of the problem and will provide local baseline statistical data for further research.

MATERIALS AND METHODS

This cross-sectional study was conducted on 114 patients at the Department of Obstetrics & Gynecology, Civil Hospital Hyderabad for six months after the approval of synopsis from 17th October 2020 to 16th April 2021.

Patients with a singleton pregnancy with age between 18-40 years with suspicion of pre-eclampsia on ACR (as per operational

definition) and who signed written informed consent to take part in the study were included

while Patients with urinary tract infection (pyuria >10WBC/mm^3), hematuria, chronic renal failure (serum creatinine ≥2mg/dl), glomerular nephritis because of other systemic conditions, previously existing hypertension, and diabetes mellitus (fasting blood glucose level ≥153 mg/dl) and those patients who took antibiotics in past 10 days as per history and clinical record were excluded.

Data collection procedure: 114 women were enrolled in the study at the Civil Hospital, Hyderabad, who met the study's eligibility criteria, were informed of the study's details, and could take part. Each patient provided written informed consent and detailed medical history. Each participant had a blood pressure reading of 140/90mmHg at the 20th week and was tested for 24-hour urine protein levels. Age, the number of pregnancies, and the gestational age were all noted in the report. The gold standard for diagnosis was the collection of 24-hour urine samples from all patients, as well as two random samples (10 am and 4 pm) to determine the protein to creatinine ratio. The first-morning urine sample did not contain any specimens. All samples were subjected to urine analysis. The 24-hour sample with creatinine 10mg/kg/day was considered an adequate sample for further analysis among the 24-hour samples available.

A biuret colorimetric assay was used to determine the urine's total protein concentration (Cobas Integra Analyzer, F Hoffman-La Roche, Basel, Switzerland). The Jaffe test was used to determine the level of urine creatinine (Hitachi 7170 autoanalyzer, Hitachi, Tokyo, Japan). The threshold for the patient was set at 0.2. The patient's demographic information was also entered into the attached proforma. To avoid bias, all of the samples were taken from the same laboratory (hospital lab) and confounding variables were eliminated.

Data Analysis: All the collected data were entered and analyzed through SPSS version 21.0. Numerical variables i-e age, gestational age, and BMI have been presented by mean±SD. Categorical variables i-e parity and pre-eclampsia confirmed on 24-hour urinary protein have been presented as frequency and percentage. Positive predictive value has been calculated by the following formula and is presented as frequency and percentage.

$$PPV = \frac{\text{True positive}}{\text{True positive} + \text{False positive}} \times 100$$

Data has been stratified for age, gestational age, parity, and BMI to address effect modifiers. Post-stratification chi-square test has been applied taking p-value ≤0.05 as significant and positive predictive value has been recalculated.

RESULTS

The age of the women ranged from 18 years to 40 years, with a mean of 26.6±6.2 years. The majority (n=74, 64.9%) of the women were aged between 18-29 years followed by 40 (35.1%) women aged between 30-40 years. The gestational age ranged from 29 weeks to 36 weeks, with a mean of 34.3±1.6 weeks. The parity ranged from 1 to 4 with a mean of 2.5±1.1. 26 (22.8%) women were primiparas and 88 (77.2%) women were multiparas. The BMI of these women ranged from 21.1 Kg/m^2 to 34.8 Kg/m^2 with a mean of 26.7±4.2 Kg/m^2 and 32 (28.1%) women were obese, as shown in Table 1.

Diagnosis of pre-eclampsia was confirmed in 111 (97.4%) women on 24-hour urinary protein excretion as shown in Table 2. Thus there were 111 true positive and 3 false-positive cases. It yielded a positive predictive value of 97.4% for spot urinary protein to creatinine ratio in the diagnosis of preeclampsia taking 24-hour urinary protein excretion as gold standard as shown in Table 2. A similar positive predictive value was noted across various subgroups of women based on age, gestational age, parity, and BMI as shown in Tables 3, respectively.

Table 1: Demographic Characteristics of included Patients (n=114)

Characteristics	Participants n=114
Age (years)	26.6±6.2
• 18-29 years	74 (64.9%)
• 30-40 years	40 (35.1%)
Gestational Age (weeks)	34.3±1.6
• 29-32 weeks	13 (11.4%)
• 33-36 weeks	101 (88.6%)
Parity	2.5±1.1
• Primiparas	26 (22.8%)
• Multiparas	88 (77.2%)
BMI (Kg/m^2)	26.7±4.2
• Non-Obese	82 (71.9%)
• Obese	32 (28.1%)

Table 2: Frequency of Pre-eclampsia on 24-Hour Urinary Protein Excretion and Positive Predicative Value of Spot Urinary Protein to Creatinine Ratio (n=114)

Diagnosis on 24-Hour Urinary Protein Excretion	Frequency (n)	Percent (%)
Pre-eclampsia (True Positive)	111	97.4
No (False Positive)	3	2.6
Total	114	100

Positive Predictive Value = $\frac{111}{111 + 3} \times 100$

Positive Predictive Value = 97.4%

Table 3: Positive Predictive Value of Spot Urinary Protein to Creatinine Ratio across Age in groups, gestational age, parity, and Body Mass Index (n=114)

Variables	Diagnosis on 24-Hour Urinary Protein Excretion		Total	PPV	P-Value
	True Positive (n=111)	False Positive (n=3)			
Age in groups					
18-29 years (n=74)	72(97.3%)	2(2.7%)	74(100%)	(97.3%)	0.949
30-40 years (n=40)	39(97.5%)	1(2.5%)	40(100%)	(97.5%)	
Gestational Age					
29-32 weeks (n=13)	13(100.0%)	0(0.0%)	13(100%	(100.0%)	0.529
33-36 weeks (n=101)	98(97.0%)	3(3.0%)	101(100%)	(97.0%)	
Parity					
Primiparas (n=26)	25(96.2%)	1(3.8%)	26(100%)	(96.2%)	0.660
Multiparas (n=88)	86(97.7%)	2(2.3%)	88(100%	(97.7%)	
Body Mass Index					
Non-Obese (n=82)	80(97.6%)	2(2.4%)	82(100%)	(97.6%)	0.837
Obese (n=32)	31(96.9%)	1(3.1%)	32(100%)	(96.9%)	

Chi-square test, observed difference was statistically insignificant, PPV: positive predictive value

DISCUSSION

If a pregnant woman is diagnosed with chronic hypertension or pre-eclampsia (a condition in which the mother's blood pressure rises above 140/90 mm Hg), she is at risk for both her health and the health of her unborn child.[14–16] One of the most dreaded outcomes of pregnancy is preeclampsia, which is dangerous.[14] Pre-eclampsia can quickly progress to serious complications,

including the death of both mother and fetus when it first appears as new-onset hypertension and proteinuria in the third trimester.[14,15]

Timely diagnosis and intervention is the key to improved outcomes in pregnancies complicated by pre-eclampsia.[16]

Urinary protein excretion increases during normal pregnancy.[15,16] Proteinuria is further increased in women with pre-eclampsia; therefore, a proteinuria of ≥300mg in 24 urine specimens is taken as diagnostic of pre-eclampsia.[1,3,16] However, collection of a 24-hour urinary specimen substantially delays the diagnosis of preeclampsia and patient management, which jeopardized the maternal and fetal outcome.[2] Recent studies claimed that urinary protein to creatinine ratio in a spot urine specimen was equally reliable in the diagnosis of preeclampsia but it was relatively quicker in sample collection and reporting and could improve the outcome by saving valuable time.[9–12] However, there was a controversy in the existing literature[9–13] regarding the positive predictive value of spot urinary protein to creatinine ratio, which caused the present study. The aim of this study was to determine the positive predictive value of spot urinary protein to creatinine ratio for the diagnosis of pre-eclampsia, taking 24-hour urinary protein as the gold standard.

In the present study, the mean age of the pre-ecliptic women was 26.6±6.2 years. A similar mean age among pre-eclamptic women has been reported in other local studies by Khan et al.[17] (26.87±5.22 years), Shoaib et al.[18] (26.06±5.01 years), and Naseeb et al.[19] (26.94±5.5 years). Triq et al.[20] and Hossain et al.[21] reported comparatively higher mean age of 27.99±5.11 years and 27±5.37 years among pre-eclamptic women presenting at Lahore General Hospital, Lahore and Civil Hospital, Karachi respectively while comparatively lower mean age of 25.24±0.54 years and 24.65±4.25 years has been reported by Nazli et al.[22] and Aziz et al.[23] among pre-eclamptic pregnant women presenting at Khyber Teaching Hospital Peshawar and Holy Family Hospital, Karachi respectively. Nabanita et al.[24] (2016) reported comparable mean age of 25.42±5.21 years among Indian women. In another similar study, Xiong et al.[25] reported a comparable mean age of 25.7±2.7 years among Canadian women with pregnancy-induced hypertension.

We observe that the mean gestational age of pre-eclamptic women was 34.3±1.6 weeks. A similar mean gestational age has been reported previously by Naseeb et al.[19] (34.42±4.02 weeks) in 2015 and Khan et al.[17] (33.10±2.60 weeks) in 2017 in the local population. Hossain et al.[21] (36±2.84 weeks) in Pakistan and Kanagal et al.[26] (36.9±0.9 weeks) in India reported comparatively higher mean gestational age among pre-eclamptic women while Shoaib et al.[18] (33.28±4.24 weeks) and Aziz et al.[23] (32.31±1.19 weeks) reported comparatively lower mean gestational age among such women at the time of diagnosis. Sajith et al.[27] (2014) also reported a relatively lower mean gestational age of 32.7±4.6 weeks on presentation in Indian women with pregnancy-induced hypertension.

In the present study, the mean BMI of the pre-eclamptic women was 26.7±4.2 Kg/m^2 and 32 (28.1%) women were obese. Saeed et al.[28] (2011) reported a similar frequency of obesity (25.1%) among pre-eclamptic women presenting at Aga Khan University Hospital, Karachi. Our observation is also in line with that of Emanuel et al.[29] (2015) who reported a slightly higher frequency of 33.8% for obesity among pre-eclamptic women presenting at Jinnah Post-Graduate Medical Centre, Karachi.

In the present study, the positive predictive value of spot urinary protein to creatinine ratio was found to be 97.4% in the diagnosis of preeclampsia, taking 24-hour urinary protein excretion as the gold standard. A similar positive predictive value was noted across various subgroups of women based on age, gestational age, parity, and BMI.

Our observation is in line with that of Shagufta et al.[30] (2019) who studied 253 pregnant women presenting at Lady Reading Hospital, Peshawar, and reported a similar positive predictive value of 97.7% for spot urinary protein to creatinine ratio in the diagnosis of pre-eclampsia taking 24-hour urinary protein excretion as the gold standard.

In a similar study involving Indian pregnant women, Shrestha et al.[11] (2018) reported a similar positive predictive value of 97.2% for spot urinary protein to creatinine ratio in the diagnosis of pre-eclampsia. Similar results have also been reported by Bhadarka et al.[31] (2018) and Shreya et al.[32] (2015) in other Indian studies who observed the PPV of spot urinary protein to creatinine ratio to be 95.0% and 94.0% respectively. A comparable positive predictive value of 95.2% has been reported by Demirci et al.[10] (2015) in Turkey.

A much higher positive predictive value of 99.1%, 100.0%, 100%, and 100.0% has been reported by Basharat et al.[9] (2017) in Pakistan, Baba et al.[33] (2016) in Japan, Park et al.[34] (2013) in Korea and Gaddy-Dubac et al.[1] (2012) in the USA respectively while a relatively lower positive predictive value of 58.0%, 56.8%, and 40.0% has been reported by Obeid et al.[148] (2018) in Ireland, Huang et al.[13] (2012) in China and Upadhyay et al.[35] (2018) in India respectively.

These differences in observation among studies can be because of the difference in the prevalence of disease in the studied population.

The present study adds to the limited already published local research evidence on the topic. The strengths of the present study were its large sample size of 114 cases and strict exclusion criteria. We also stratified the data across patients' age, gestational age, parity, and BMI to address various effect modifiers. In the present study, the positive predictive value of spot urinary protein to creatinine ratio was found to be 97.4% in predicting preeclampsia in hypertensive pregnant women regardless of the patient's age, gestational age, parity, and BMI. This spot urinary sampling and estimation of ratio allows prompt reporting and thus saves valuable time, which is otherwise wasted by routine practice of 24-hour urinary protein estimation. It will thus allow early identification of pre-eclamptic women so that timely intervention may improve the outcome of such cases. Its preferred use is therefore advocated in the evaluation of hypertensive pregnant women in future obstetric practice.

A very strong limitation to the present study was that we only considered cases where pre-eclampsia was suspected on spot urinary protein to creatinine ratio while negative cases were not included which could have enabled determination of negative predictive value and diagnostic accuracy and could have established the role of spot urinary protein to creatinine ratio in the evaluation of hypertensive pregnant women more precisely. Such a study is highly recommended in future clinical research.

CONCLUSION

In the present study, the positive predictive value of spot urinary protein to creatinine ratio was found to be 97.4% in predicting preeclampsia in hypertensive pregnant women regardless of patient's age, gestational age, parity, and BMI which along with the associated advantage of spot specimen collection and timely results (compared to the routine practice of 24-hour urinary protein estimation which wastes precious time and delays the patient's treatment), advocates the preferred use of spot urinary protein to creatinine ratio in the evaluation of hypertensive pregnant women in future obstetric practice.

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