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Protein/Creatinine Ratio in Random Urine Sample for Quantitation of Proteinuria Compared with 24 Hour Urine Collection in Patients with Pre-Eclampsia

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Abstract

Objective: To evaluate the diagnostic value of protein/creatinine (p/c) ratio in a single voided urine sample for quantitation compared to those of 24h urine sample in patient with pre-eclampsia.

Patients and Methods: A prospective study was conducted in Basrah maternity and child hospital during the period from October 2013 to October 2014. The study involved 60 pregnant women with hypertension attending the antenatal clinic and admitted to obstetrics ward regardless the severity of the disease. The main measurement was estimation the urinary protein to urinary creatinine ratio by random direct measurement and a 24-hour urinary protein excretion. The data obtained was statically analyzed.

Results: Out of 60 patients with gestational hypertension, 49 patients had significant proteinuria (>300 mg/day) and 11 patients had proteinuria less than (300 mg/day). Also, 17 out of 60 patients had p/c ratio <3 mg/dl and 43 patients had p/c ratio >3.5 mg/dl. The p/c ratio was able to correctly identify 42 out of 49 patients with significant proteinuria. It has been estimated that protein/creatinine ratio with sensitivity of 81.6%, specifity of 27.7% positive predictive value 93%, negative predictive value 70%, false positive rate 27.2%, false negative rate 18.3%.

Conclusion: The study suggest that the p/c ratio in single voiding urine is highly accurate test (P<0.01) for discriminating between in significant proteinuria. This could be a reasonable alteration to the 24-hour collection for detection of significant proteinuria in hospitalized pregnant women with suspected pre-eclampsia.

Keywords: Pre-eclampsia; Protein/creatinine ratio; Proteinuria; Urinary system

Introduction

Precamplsia is idiopathic disorder of pregnancy characterized by hypertension and proteinuria [1]. About 10% of women will develop Pre-eclampsia in the rst pregnancy. It usually occurs a er 20 weeks of gestation most o en near term [1]. In severe disease there may be thrombocytopenia, hemolysis, impair liver and renal function, swelling, dyspnea or visual disturbance [2].

Maternal death worldwide is 12% and is due to hypertension disorder of pregnancy and it has been shown that patients with signi cant proteinuria have signi cant reduction in mean birth weight for gestational age due to intra-uterine growth retarded compared to the patients with hypertension alone. While, the mean birth weight for gestational age among women with hypertension alone same as normotensive [3].

So, early detection and proper management of patients with proteinuria is therefore, bene cial for mother and fetus [3]. Pre-eclampsia can be perceived as an Pre-eclampsia impairment of maternal immune system which prevent it from recognizing the fetoplacental unit. Excessive production of immune cells causes secretion of tumor necrosis factors alpha and induce apoptosis of extra villous cytotrophlpast. e Human Leukocyte Antigen (HLA) system also appears to play a role in defective invasion of the spiral arteries [1].

e use of the term albuminuria to describe proteinuria is incorrect because there is an increase permeability to large molecular weight protein with any glomerulopathy. us, albumin excretion is accompanied by other protein such as globulines, haemoglobuline and transferring [4]. Normally, those of a large protein molecules are not ltered by the glomeruli and thus their appearance in urine signi es glomerulopathic process [5].

Proteinuria of Pre-eclampsia involves predominantly high molecular weight proteins such as albumin and large amount of IgM, IgG, bronectin and B2 microglobulin are found in urine. It is caused by reversible structural alteration of glomerular lter resulting from injury of endothelial cells in glomerular capillaries [6]. Both proteinuria and alteration of glomerular histology develop late in the course of pre-eclampsia [7].

erefore, the aim of the study is to evaluate the diagnostic value

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of protein/creatinine (p/c) ratio in a single voided urine sample for quantitation compared to those of 24h urine sample in patient with pre-eclampsia.

Patients and Methods

is prospective study was conduct in AL-Basrah Maternity and Child Hospital during the period from October 2013 to October 2014. Sixty inpatient pregnant women more than 20 weeks with gestational hypertension (de ned as blood pressure more than 140/90 mmHg in 2 di erent measurements obtained at interval more than 6 hours). eir ages ranged between 16-39 years and parity (0-6) .

Patients with chronic renal disease, chronic hypertension, diabetes mellitus, bacteruria, urinary tract infection or catheter not insert a er rupture of membrane were excluded from the study.

On admission all patient were interviewed and examined carefully, gestational age was determined by the Last Menstrual Period (LMP) and any previous Ultra Sound (U/S). en each patient was asked for:-

24h urine collection on clean bottle was started before midday. First morning sample was discarded and the time was noted .

A single voided urine specimen for spot protein/creatinine ratio was obtained as soon as possible a er the 24h collection.

Morning sample was excluded for estimation of urine P/C ratio.

e data obtained was statistically analyzed.

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

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

$$\text{Positivity predictive value} = \frac{\text{True positive}}{(\text{True positive+False positive})}$$

$$\text{Negative predictive value} = \frac{\text{True negative}}{\text{True negative} + \text{False positive}}$$

Results

Study population

A total of 60 pregnant women were admitted for the evaluation and the age group 30-39 contributed the highest percentage (45%) followed by age ≥ 20-29 (34%) Table 1.

Table 2 shows the distribution of the patients according to the parity. Majority of the studied group were multiparty patient ≥ 3 (39%) followed by para 2 (25%) and prim gravida (20%).

Table 3 shows the distribution of the studied subjects according to 24 urine protein. Out of 60 patients 26 (34%) had signi cant protein urea of the range more than 300 gm/day.

Table 4 shows the distribution of patients according to p/c ratio in spot urine sample. Among 60 patients, 17 (28%) had p/c ratio less than 3.5 mg/dL and 26 (44%) greater than 4.5 mg/dL.

Table 1: Distribution of the studied subjects (n=60) according to age.

Age (in years)	Number (n)	Percentage (%)
<20	13	21
20-29	20	34
30-39	27	45
Total	60	100

Table 2: Distribution of the studied subjects (n=60) according to parity.

Parity (p)	Number (n)	Percentage (%)
0	12	20
1	10	16
2	15	25
≥ 3	23	39
Total	60	100

Table 3: Distribution of the studied subjects (n=60) according to 24 hour urine protein.

24 hour urine protein (mg/day)	Number (n)	Percentage (%)
<300	11	18
300-400	23	39
>400	26	43
Total	60	100

Table 4: Distribution of the studied subjects (n=60) according to protein/ creatinine ratio.

Protein creatinine ratio mg/dL	Number (n)	Percentage (%)
<3.5	17	28
3.5-4.5	17	28
>4.5	26	44
Total	60	100

Table 5: Comparison of protein/creatinine ratio in single voided urine sample to 24 hour urine protein in the studied subjects (n=60).

Protein/ creatinine ratio in single voided urine sample	24 hour urine protein		Total (n)
	Positive 300 mg	Negative <300 mg	
Positive 3.5 mg/dL	40 TP	3 FP	43
Negative <3.5 mg/dL	9 FN	8 TN	17
Total	49	11	60

Table 5 shows the comparison of p/c ratio in single voided urine sample to 24h urine protein in the studied group. Out of the total 60 patients with gestational hypertension 49 patients had 24h urine protein excretion more than 300 mg and out of 49 positive protein urea there was 40 positive p/c ratio and 9 patient were false negative (protein/creatinine ratio <0.3 mg/dL) on the other hand 11 patients with gestational hypertension had negative 24h protein urine (<300 mg) out of them 3 patients were false positive for p/c ratio >3.5 mg/dL and 8 patients with true negative (<3.5 mg/dL).

Table 6 shows test of validity for p/c ratio in patients with pre-eclampsia. P/c ratio had 81.6% sensitivity, 72.7% speci city and positive predictive value of 93%, negative predictive value of 70%, false negative rate 27.2%, false negative rate 18.3%, Odds ratio 11.85%, P <0.01.

Table 6: Diagnostic value of protein/creatinine ratio patients with suspected preeclampsia (n=60) compared to 24 hour urine protein.

Test of validity	Protein/ Creatinine ratio
Sensitivity	81.60%
Specificity	72.70%
Positive Predictive value	93%
Negative Predictive value	70%
False Positive rate	27.20%
False Negative rate	18.30%

Discussion

Pre-eclampsia with various severity (mild, moderate, severe), proteinuria is estimated ≥+1 on dipstick test or urine protein ≥300mg/24h is mandatory for diagnosis and evaluation of the severity of pre-eclampsia beside maternal and perinatal morbidity and mortality increased with amount of proteinuria [8]. Several methods are available for measuring proteinuria but 24h urine protein excretion has long been regarded as the gold standard. is test has some disadvantages such as inconvenience for patients, inaccuracy due to incomplete collection, cost and delay of diagnosis and management, which make it di cult for wide use for clinician [9].

One of most commonly used is the urinary dipstick test because it is simple and cheap but this method has high false positive and false negative rate beside associated with uctuation throughout the day due to water intake, exercises, diet, posture, and properly trained laboratory sta [9,10]. us, the determination of the protein/ creatinine ratio in single urine sample in pregnancy seems a su cient valid method to assess the amount of protein excretion.

e socio demographic variable shows that the peak age more than 30 years (45%) and multiparty (≥3) 39% which in contrast to what is usually reported and shows that prim gravida and age peak of 20-29 years to be at high risk of developing pre-eclampsia [11]. Various studies have shown that women aged more than 40 years twice risk of pre-eclampsia regardless of parity [12].

In this study, sensitivity of 81.6% allows the clinician to correctly identify greater than 8 out of 10 cases a signi cant protein urea. Speci city of a diagnostic test is the probability that patient without proteinuria will have a negative result. In the present study, the speci city was (72.7%) which higher than urine dipstick test had a (47%) speci city. e false positive rate of (27%) in contrast with studies have demonstrated that false positive reaction was (14%) false positive lead to error in diagnosis and early interference increase maternal and fetal complications. Positive predictive value (93%) and negative predictive value (70%) which is higher than that for the dipstick test (48%) which demonstrated the unreliability of the dipstick test.

e e ectiveness or validity of a test is important to aid clinical decision making the above method is faster in comprising to 24h protein collections as well as the di cult in ensuring complete collection make it un t for routine use in clinical practice.

Conclusion

P/c ratio had a sensitivity of 81.6%, which will allow the clinician to correctly identify greater than 8 0ut of 10 cases of signi cant proteinuria. erefore, routine use of either p/c ratio quantitation of proteinuria in patient with pre-eclampsia could be adapted which is reliable, relatively faster and correlating well with 24h urinary protein excretion in clinical practice.

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