Quantitation of Proteinuria in Women With Pregnancy Induced Hypertension: Is it Time to Abandon Use of Dipstick Strips for the Spot Urine Protein to Creatinine Ratio?

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Abstract

Context: The presence of significant proteinuria in Pregnancy Induced Hypertension is associated with worse maternal and fetal outcome. Unfortunately, Dipstick strips, currently used widely for detection and quantitation of proteinuria, have been shown to be unreliable. This creates the need for a more accurate method for early detection and quantitation of proteinuria.
Objective: To compare the accuracy of the Spot urine Protein to Creatinine ratio with that of Dipstick Tests in the quantitation of proteinuria in Nigerian women with Pregnancy Induced Hypertension.
Methods: A cross-sectional survey over a 6-month period involving 86 Nigerian women with Pregnancy Induced Hypertension.
Outcome measures: False Positive rates, False Negative rates, Sensitivity, Specificity, Positive Predictive value, Negative Predictive value, and Accuracy.
Result: The Spot urine Protein to Creatinine ratio showed better correlation with 24-hour urine protein measurement than Dipstick Tests. Comparatively, the False positive rates were 16.2% versus 53.7%, False Negative rates 6.1% versus 28.1%, Sensitivity 91.2% versus 73.5%, Specificity 88.5% versus 44.4%, Negative predictive values 93.9% versus 71.9%, and Accuracy 89.5% versus 55.8% respectively for the Spot urine Protein to Creatinine ratio and Dipstick Tests.
Conclusion: The Spot Urine Protein to Creatinine ratio is much more accurate in the quantitation of proteinuria in Nigerian women with Pregnancy Induced Hypertension than the widely used Dipstick Tests.

Key Words: Quantitation, Proteinuria, Pregnancy, Hypertension. [Trop J Obstet Gynaecol, 2004;21:136, 137, 140, 141]

Introduction

Pre-eclampsia/Eclampsia remain major causes of Maternal Morbidity and Mortality as well as Increased Perinatal Morbidity and Mortality Worldwide especially in sub-Saharan Africa[1,2,3]. It has been shown that patients with significant proteinuria coexisting with Pregnancy induced hypertension have worse maternal and fetal outcomes compared to those with hypertension alone[4,5]. This underlies the need for a quick and accurate means of quantifying proteinuria.
Unfortunately, the most widely used screening test for Proteinuria, the Dipstick test, has been shown to be fraught with error and to correlate poorly with 24-hour Urinary Protein excretion[6,7,8]. False positive results have been demonstrated to occur due to contamination of urine by vaginal discharge, use of antiseptics, alkaline urine, concentrated urine and urinary tract infection. Similarly, false negative results occur with very dilute urine and presence of Bence Jones proteins and Mucoproteins [9]. Regrettably, the gold standard for quantitation of proteinuria, the 24 hour urine protein measurement, which ideally should be done on all patients with Pregnancy induced Hypertension is cumbersome, urine collections are often incomplete and it is inconvenient especially for use in outpatients [6,8]. Therefore, there remains the need for a reliable, easy to administer, fast and accurate test for early detection and quantitation of proteinuria in hypertensive pregnant women.
The use of the Spot urine Protein to Creatinine ratio has been shown to posses the potential to fill this vacuum in nonpregnant patients[10], [11], [12]. A few studies have also reported its promise among Caucasian hypertensive pregnant women[8,13]. It measures the ratio of the urine protein to urine creatinine of the same random daytime midstream urine specimen. The assay for the protein to creatinine ratio: Urine protein in mg/l divided by the urine creatinine in mmol/l requires only a non-timed midstream aliquot of urine, which can be passed at the time of consultation. Thus a protein:creatinine ratio of 30 is consistent with 24-hour protein excretion of 300mg/l of albumin, 100 and 200 have been shown to correlate with 24 hour-protein excretion of lg/l and 2 g/l respectively[12]. Its accuracy is independent of variation in specific gravity and pH of urine in contrast to Dipstick Tests, and urine collection cannot be incomplete as in 24-hour urine protein estimation.
The objective of this study was to compare the accuracy of the Spot urine Protein to Creatinine ratio with that of Dipstick Tests in the quantitation of proteinuria in Nigerian women with Pregnancy Induced Hypertension.

Materials and Methods

The study population consisted of Antenatal Patients with Pregnancy Induced Hypertension diagnosed after the 20th week of gestation. Eighty-six consecutive cases

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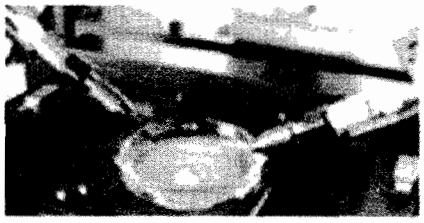

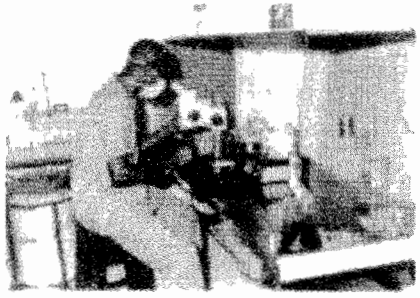

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were recruited into the study. Exclusion criteria included all cases of chronic Hypertension, chronic renal disease, pathological vaginal discharge, Urinary tract infection, and patients that had vulva or vaginal cleansing with antiseptics or skin cleansers like chlorhexidine

Diagnosis of hypertension[14,15] was based on two consecutive measurements of diastolic blood pressure of = 90mmHg 4 hours or more apart, one measurement of diastolic blood pressure of 110mmHg or more or a rise of 30mmHg or 15mmHg above the normal pre-pregnancy systolic and diastolic blood pressures respectively, after the 20th week of pregnancy using an appropriate sized cuff and korotkoff phase V (disappearance of sound) as the diastolic blood pressure .Significant proteinuria was defined by one 24 hour Urine collection with total protein excretion of 300mg and more or two random clean catch or catheter urine specimens with 2+ (1g albumin/L)or more on a reagent strip or 1+ (0.3g Albumin/L)if the specific gravity is less than 1030 and pH less than 8.[14]For each woman, information on age, parity and gestation age was collected and a dipstick test and spot urine protein and creatinine assays done. A 24-hour urine collection was then done and the protein excretion determined for comparison. Based on the results, the false positive and false negative rates, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of both dipstick tests and the spot urine protein to creatinine ratio were determined for comparison[16,17]

Measures Of Test Validity

False Positive Rate - percentage of all positive results that are truly negative

False Negative Rate - percentage of all negative results that are truly positive

Sensitivity- proportion of true positives correctly identified Spot Urine Protein to Creatinine ratio = a/a+c x 100/1 Dipstick Tests = A/A+C x 100/1

Specificity- Proportion of true Negatives correctly identified. Spot Urine Protein to Creatinine ratio = b/b+d\x100/1 Dipstick Tests = B/B+D x 100/1

Positive Predictive Value = Probability that a positive result is genuinely positive.

Spot Urine Protein to Creatinine ratio = a/a+b x 100/1

Dipstick Tests = A/A+B x 100/1

Negative Predictive Value = Probability that a negative result is genuinely negative.

Spot Urine Protein to Creatinine ratio = d/c+d x 100/1

Dipstick Test = D/C + D x 100/1

Accuracy = (True positives + True Negatives)/ Total

Spot urine Protein to Creatinine ratio= (a +d) /86

Dipstick Test=(A +D)/86

Laboratory Tests

Urinary protein estimation was done using the modified sulphur salicylic acid (SSA) method. 0.5mls of urine was added to 3.5mls of 3% SSA. This was incubated for 10minutes at room temperature and the absorbance of the test and standard were read at 660nm using a spectrophotometer. Estimation of urinary creatinine was done using the modified JAFFE method as outlined by the Manufacturers of the kit, QUIMICA CLINICAL APPLICADA S.A. SPAIN 2000.

Ethical Considerations

Approval for the study was obtained from the Ethical Committee of the University of Benin Teaching Hospital. The study was carefully explained to the patients and their informed consent obtained before being recruited into the study.

Results

The age distribution of the subjects showed that majority were aged 20-29 years (70.9%), 25.6% were 30-39 years old, 3.5% were aged 19 years or less. None of the women was aged 40 years or above. Nullipara constituted 52.3% of the study population while women who were Para 1,2,3 and 4 contributed 17.4%, 9.3%, 8.1% and 5.8% respectively while 7.0% of the women were grandmultipara. Most of the study population were at term (72.1%), 18.6% were at a gestational age greater than 32 weeks but less than 37 completed weeks and pregnancies less than or equal to 32 weeks gestation constituted 9.3%.

Tables 1 and 2 compare the results of the spot urine protein to creatinine ratio and dipstick tests respectively to that of 24-hour urinary protein estimation.

Table 1:
Comparison of Results of the Spot Urine Protein to Creatinine Ratio to that of 24Hour Urine Protein

SPOT URINE PROTEIN CREATININE	TRUE PICTURE 24 HOUR URINE PROTEIN		
RATIO	Positive	Negative	Total
Positive	(a) 31	(b) 16	a+b = 37
Negative	(c) 3	(d) 46	c+d = 49
Total	a+c = 34	b+d = 52	

Table 2: Comparison of Results of Dipstick Tests to that Of 24Hour Urine Protein

DIPSTICK TEST RESULTS	TRUE PICTURE 24 HOUR URINE PROTEIN		
	Positive	Negative	Total
Positive	(A) 25	(B) 29	A+B = 54
Negative	(C) 9	(D) 23	C+D = 32
Total	(A+C) = 34	B+D = 52	

Table 3 shows the comparison of the indices of test validity as well as the cost and time to obtain the results for both tests.

Table 3: Comparison of Indices of Test Validity, Cost, and Time to obtain Results

INDICES	DIPSTICK TESTS	SPOT URINARY PROTEIN TO CREATININE RATIO	HOUR URINE PROTEIN
False Positive rate	53.7%	16.2%	
False Negative rate	28.1%	6.1%	
Sensitivity	73.5%	91.2%	
Specificity	44.2%	88.5%	
Positive Predictive Value	44.4%	83.8%	
Negative Predictive Value	71.9%	93.9%	
Accuracy	55.8 %	89.5%	
Cost	N 20	N 300	N 400
Time to obtain test result	Immediately	30 minutes	36 hours

Dipstick tests had a false positive rate of 53.7%, false negative rate of 28.1%, sensitivity of 73.5%, specificity of 44.2%, positive predictive value of 44.4%, negative predictive value of 71.9% and overall accuracy of 55.8%. Comparatively, the spot urine protein to creatinine ratio had much less false positive and false negative rates of 16.2% and 6.1% respectively and higher sensitivity (91.2%) and specificity of 88.5%. Its positive predictive value was 83.8%, negative predictive value, 93.9% and overall accuracy, 89.5%. dipstick tests were cheaper (N20), easier to perform and results were immediately available while the spot urine protein to creatinine ratio was more expensive (N300) and it took 30 minutes for results to be available.

Discussion

The results of this study show that the spot urine protein to creatinine ratio has a much higher accuracy than dipstick tests in the quantitation of proteinuria in women with pregnancy induced hypertension. It had less than a third of the false positive rates and less than a fourth of the false negative rates associated with use of dipstick tests. These show that with use of dipstick tests, there is a much higher chance of over diagnosis of pre-eclampsia as well as under detection of patients with severe disease. This would lead to higher rates of erroneous intervention such as Induction of labour or caesarean sections in False positive cases and gives room for worsening of maternal and fetal condition causing increased maternal and perinatal morbidity and mortality in false negative cases. A high false positive rate of 40%, similar to the findings of this study, has been reported previously [8,13] for dipstick tests. The false negative rate of 28% found in this study is higher than 18% reported in Caucasian women[13].

While the false positive and false negative rates give an idea of the reliability of a test, four main indices of test validity have been widely used for over half a century: Sensitivity, specificity, positive and negative predictive values[16]. The spot urine protein to creatinine ratio was shown to have higher values of sensitivity and specificity than the dipstick tests. Thus, it demonstrates the ability to identify a higher proportion of true positives and true negatives than dipstick tests. Saudan et al [8] reported a sensitivity of 93% and specificity of 92% for the spot urine protein to creatinine ratio, similar to the findings of this study. Furthermore, the positive and negative predictive values for the spot urine protein to creatinine ratio were higher than those of dipstick tests. This signifies that both positive and negative test results are more reliable with the spot urine protein to creatinine ratio. An important finding was that dipstick tests had a much higher negative predictive value than its positive predictive value. This indicates that a negative dipstick reaction is much more reliable than a positive one.

In terms of methodology, dipstick tests are easier to perform and do not need a laboratory or trained laboratory personnel. However, the spot urine protein to creatinine ratio requires the use of a spectrophotometer (though a colorimeter may be used in poorer settings). The machine is available in most secondary and tertiary health centres and can be operated by laboratory technicians where trained laboratory scientists are in short supply. The results of the dipstick tests are instant while the spot urine protein to creatinine ratio requires about 30 minutes to be available, which is still quick enough time to allow for definitive diagnosis and prompt management. However, while dipsticks are very cheap and affordable by most patients, in comparison, the spot urine protein to creatinine ratio is about 15 times the cost of dipstick tests. Nonetheless, when the cost of the spot urine protein to creatinine ratio is weighed against the cost of unnecessary intervention and maternal and perinatal morbidity and mortality its use would prevent, the extra cost to the patient is justified.

Conclusion

Based on the results above, it is appropriate that in areas where it can be afforded by most patients and the necessary laboratory back up is available; use of dipsticks tests should be completely abandoned in favor of use of the spot urine protein to creatinine ratio. However, in settings where the test is not readily affordable, Dipstick can be used for routine screening for proteinuria, a negative result should be accepted for clinical decision making because of its greater reliability, while all positive results should be confirmed using the spot urine protein to creatinine Ratio.

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