Is Urine dipstick as accurate as 24 hour urine protein? A Comparative Study.

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ABSTRACT

Introduction

Hypertensive disorder in pregnancy (HDP) is one of the most common medical complications affecting approximately 5-10% of pregnancies. It remains a major cause of maternal/perinatal mortality and morbidity. Proteinuria is a sign of preeclampsia where there is >300 mg of protein in 24 hour urine collection. This usually correlates with 30mg/dl or 1+ reading in a random urine specimen. The main objective of this study is to find out whether urine dipstick correlates with 24 hour urine protein.

Methodology

This is a hospital based comparative study, where proteinuria by dipstick method was compared with 24 hour urinary protein in 60 cases of pre eclampsia at Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu.

Results

The dipstick method of detecting proteinuria significantly correlated with the total 24 hour urine protein excretion by Esbach Albuminometer. A dipstick factor of ≥300mg/24 hour indicates proteinuria with sensitivity of 97.5%, specificity of 65%, positive predictive value of 84.78% and negative predictive value of 92.85%. 3+ value in dipstick had high significance with 24 hour urine protein by Esbach's Albuminometer (R=0.983). The cost of dipstick was Nepalies Rs (NPR) 14 in comparison to 24 hour dipstick which cost NPR 80.Time needed to get report was immediate in case of dipstick but takes 48-50 hour in case of 24 hour urine protein.

Conclusion

Timely collection of six hourly urine for detection of proteinuria by dipstick is comparable to 24 hour urinary protein determination in laboratory by Esbach Albuminometer, which is more time consuming and expensive.

Key Words: Dipstick, Pre eclampsia, Proteinuria

INTRODUCTION

Hypertensive disorder in pregnancy (HDP) a common medical complication affecting approximately 5-10% of pregnancies and remains a major cause of maternal and perinatal mortality and morbidity.[1] Pregnancy induced hypertension, pre eclampsia and eclampsia are responsible for 70% and chronic hypertension represents 30% of hypertensive disorders of pregnancy.[2] Incidence of gestational hypertension ranges between 6 and 18 % in nullipara and 6 and 8% in multipara.[3,4] Incidence of preeclampsia ranges between 3 and 7% in nullipara and between 0.8 % and 5% in multipara.[5]

Approximately, 25 % of patients with gestational hypertension develop preeclampsia.[6]

Proteinuria is the sign of preeclampsia where there is >300 mg of protein in 24 hour urine collection. The presence of proteinuria signifies a greater likelihood of both maternal and fetal complications.[7] Patients with significant proteinuria have significant reduction in mean birth weight for gestational age compared with patients with hypertension alone. Early detection and prompt management of patients with proteinuria is therefore beneficial to patients and fetus.[8]

The 24 hour urine collection for protein is the gold standard method in the diagnosis of preeclampsia,

though it is also not without errors. The result is not only affected by variable and incomplete collection but also inconvenient and is associated with delays in lab analysis and availability of results.[9] It is time consuming which limits its clinical usefulness and often results in a protracted inpatient stay if day care facilities are not available. It often entails inaccuracy with collection and lack of correction for creatinine excretion and there remains a lack of certainty about the upper limit of normal 24 hour protein excretion in pregnancy.[10]

The dipstick method of detecting proteinuria remains the mainstay of screening for proteinuria worldwide but has more false positive results, possibly due to contamination of urine by vaginal discharge, antiseptics, concentrated urine and urinary tract infections. False positive result may subject patient to inconvenience of unnecessary investigations and interventions, while false negative results may jeopardize the health of the woman and the infant.[11]

There are around 22,674 obstetrical admissions at Paropakar Maternity and Women's Hospital in a year and around 100 to 120 cases of HDP get admitted every month. The screening method used in this and most other hospital is dipstick method and the gold standard is taken as 24 hour urinary protein estimation. In this study an attempt is made to see whether the 4 to 6 hourly urine dipstick method is as effective as 24 hour urinary protein estimation. This study also verifies the accuracy of current hospital protocol to manage pre eclampsia on the basis of results of dipstick method and 24 hour urinary protein estimation for selected patients only.

MATERIALS AND METHODS

This was a cross sectional study where comparison was done in two methods of detection of protein in urine with patients of pre eclampsia. The study was conducted at Paropakar Maternity and women's hospital, Thapathali, Kathmandu from August 2010 to February 2011.The proposal as well as questionnaire was sent to Institutional Review Board, National Academy of Medical Sciences for approval. Informed consent was taken from the patients prior to enrolling them in study. During this period 60 antenatal diagnosed pre eclampsia cases were randomly enrolled. The sample size was determined by using statistical method. All cases admitted with the diagnosis of pre eclampsia were enrolled for the study where the blood pressure was ≥140/90 mm Hg with 1+ protein in random urine sample. The patients had dipstick method of detecting proteinuria 6 hourly and the same sample was sent for 24 hour urine protein test. Cases were enrolled till sample size was complete. Exclusion criteria included pregnancy associated with UTI, eclampsia, pregnancy with chronic renal disease, chronic hypertension, presence of pathological vaginal discharge and diabetes in pregnancy.

For 24 hour urine collection, a collection jar with 3 liter capacity was obtained from lab. The urine protein by dipstick was done every 6 hours. Urine passed in within 6 hour was collected in a single jar and dipstick test was done for it, then this urine was transferred to the 24 hour collection jar. In this way dipstick was done 6 hourly and total urine for 24 hour was sent to lab in collection jar. The time of voiding of urine was recorded and the urine was measured in volume every 6 hour. The urine protein by dipstick was measured at the same time or the other day by putting the sample in room temperature.

If the patient is in continuous Foleys catheter then the bag was emptied every 6 hour from the urobag into collection jar and then dipstick was done and the total collected urine in 24 hour was sent to lab.

The dipstick method was done by visual reading technique where the reagent area of the strip was immersed in urine collected in the container, then the strip was removed immediately and the excess urine was removed by running the edge of the strip against the container. The strip immersed in urine was kept horizontally and compared with the colour chart on the bottle label closely and the result was noted. The result was read within 1 min, as colour change beyond 2 min was of no diagnostic value. The test area in the strip was impregnated with the indicator tetrabromo phenol blue (Bayer) and buffered to an acid PH. In the presence of protein there was change in colour of the indicator from light yellow to green blue depending upon the amount of protein present. Dipstick value was interpreted as negative, 1+(0.3gram/Litre), 2+(1 gram/Litre), 3+(3gram/Litre) and 4+ (>20gram/Litre)

The 24 hour urinary protein was done by Esbachs albuminometer by the hospital laboratory, the collected 24 hour urine was measured for volume and 100 ml of urine was taken from the 24 hour urine collection jar and kept in measuring test tube till mark 'U' and the reagent was kept till 'R' and kept like that for 24 hour. The reagent R contains picric acid and acetic

acid. The precipitate formed in 24 hour was read and interpreted in gm/ lit protein.

The value of >0.3gm/dl was interpreted from 1+ to 4+ proteinuria. The dipstick determined protein was calculated by multiplying the dipstick value (mg/dl) and the volume of void (ml) in that 6 hour and adding all these products in 24 hour. The final value was divided by 100 since dipstick value is in mg/dl.

For example

Dipstick total protein = {dipstick value (mg/dl) x volume of urine (in 6hour)} x 4/100 mg of protein

If there is 1+ proteinuria and she voids 240 ml of urine in 6hour

30 x240 =7200

4 times 7200 = 28800

28800/100=288mg

Statistical analysis was done by paired t test and correlation coefficient, the P value of <0.05 was considered significant.

RESULTS

Total of 60 patients were screened by dipstick and 24 hours urine protein by Esbach's albuminometer for pre-eclampsia. The sensitivity, specificity, positive and negative predictive values of 24 hours and dipstick were calculated using 24 hours proteinuria as gold standard. Among the 11,886 obstetrical admissions during the study period of 6 month from August 2010 to February 2011, there were 762 cases of PIH admitted (6.4%). Among which there were 189 cases of pre eclampsia i.e. 1.5% of total admission and constitute 24.8 % of all PIH cases. Similarly there were 50 cases of severe pre eclampsiaia (0.4%) and constitute (6.5%) of all PIH cases.

Among the 60 patients who were enrolled in the study with preeclampsia, majority 65% (n=39) of them were in the age group of 20-29 years. Similarly most of the patients were primigravida (60%, n=36) and 31 patients (51.67%) were at the gestational age between 37- 42 weeks.

On measuring proteinuria by dipstick in patients with BP range of 140-159/90-109 mm of Hg, the mean was 1.05 g/24hour, which was comparable with the 24 hour. urine protein detection by Esbach's albuminometer i.e. 1.07 g/24 hour. There was strong correlation between these two [correlation coefficient (R) =0.968].

Similarly in case of BP≥ 160/110 the proteinuria detected by dipstick had the mean of 1.2 g/24 hour which was comparable with 24 hour urine protein by Esbach'salbuminometer i.e. 1.22g/24 hour. This also had very strong correlation i.e, R= 0.982.

Among 60 cases of preeclampsia 240 dipstick values were obtained and were changed to 24 hour value of dipstick using a formula mentioned in methodology. Among them 3+ protein in dipstick had high correlation with 24 hour urine protein R=0.983 and least with 1+ i.e. R=0.871.

In 60 samples of pre eclampsia, 24 hour proteinuria by Esbach's albuminometer was used as gold standard in the calculation of sensitivity, specificity, positive and negative predictive values. The cut off value of 0.75 g of protein in 24 hour protein was used as there was less biasness in this value. All these showed that almost all timed collection was accurate in detecting proteinuria.

Among the cost of various methods for detecting proteinuria cheapest was dipstick which cost(NPR) 14 i.e. for one time it cost only NPR 3.5. The Esbach'salbuminometer for detecting 24 hour urine protein was the expensive which cost NPR 80 for it.

Similarly for the time of getting the report, dipstick gives report immediately for detecting protein but 24 hour urine protein takes 24 hours to collect the sample and takes more than other 24 hours to interpret the report which means it takes 48 hours to 50 hours to get the report.

DISCUSSION

The incidence of HDP in our study was 6.4 % which was comparable with the study done by Zhang J and Helewa who reported the incidence of 6.1% and 5.9%.[12,13] This study showed that the incidence is low in relation to the study conducted by Yucesay G ie 8.49%.[14] Gangaram found very high incidence of HDP i.e. 18 % which is much higher than in this study.[11] In a study done by Lawler J and Vatten they found very low incidence of HDP 1.1% and 2.6% respectively in comparison to this study.[15,16]

The incidence of pre eclampsia and severe preeclampsia in this study was 1.5% and 0.4% respectively. The incidence was low in relation to the study conducted by Abdul Aziza (2.47%) and Rmnaug A (2.5%).[17,18] Overall the incidence of preeclampsia in this study is comparable with many studies but less incidence may be due to small sample size.

The most common age which was seen in this study was in between 20-29 yrs which accounts for 65% of total cases. Similar type of result was seen in a study

done by F Tara where the incidence was higher at age group of 19-38 yrs with the mean of 25 yrs.[19]

In contrast to this study, there were few studies which showed the increased incidence of pre eclampsia in extremes of age group. Abdul Aziz Al Mulhim et al showed the incidence was high at age <20 yrs and >40 yrs.[17]

In our study the mean age where preeclampsia has high incidence was 25 yrs which is in close proximity with the study by Abdul Aziz Al Mulhim et al.

Preeclampsia was most common in primigravida, i.e. 60 % in our study. Similar finding was noted in studies conducted by Vatten et al, F Tara et al, Shazia et al, Abdul Aziz Al Mulhim and Rmnaug A et al, where preeclampsia was found more commonly in primigravida compared to other order of birth.[15-19]

As for the gestational age, preeclampsia was more common at term i.e. 37-42 weeks (51.67%) followed by 28.33% at gestation of 35- 36 weeks and 20 % were less than 34 weeks. F Tara et al showed that 92.3% were at third trimester followed by 7.7% at second trimester which is higher than this study at term and lower in pre term.[19] Similarly Abdul Aziz Al Mulhim et al reported 30.2% of preeclampsia at pre term in comparison to only 20% in our study.[17]

The discrepancy in this result comparing to other result may be due to small sample size and distribution problem of gestational age. It may be classified as early second trimester, late second trimester and third trimester which may yield similar result to other observer.

The Sensitivity, Specificity, PPV and NPV for dipstick in this study was 97.5%, 65%, 84.78% and 92.85% respectively. Many of the studies have sensitivity and specificity of less than 80% which seems to be poor predictor of protein in urine like R Gangaram, F paruk and J Abebe.[11,20,8] Similary many of the studies have sensitivity and specificity more than 80% which may be more acceptable range for detection of proteinuria like F Tara.[19]

Accuracy may be improved at higher thresholds (greater than 1+ proteinuria), but available data is sparse and of poor methodological quality. In this study dipstick value at 3+ highly correlates with 24 hour urine protein followed by 2+ and then 1+ (R= 0.983, 0.955 and 0.871 respectively).

Similar results was obtained by Loran k Phelam where the false positive dipstick was 7% at 3+ level to 71% at 1+ level.[10] HelleKieler found 2+ protein in dipstick almost fit closely with 24 hour urine protein.[21]

There have now been several studies investigating the relationship between semi quantitative dipstick urinalysis on random voided urine samples and a subsequently collected 24-hour urine sample. Kuo et al in 1992 found a poor correlation with 1+ dipstick proteinuria and subsequent 24-hour protein estimation. They report a false positive rate of 18% and false negative rate of 40%.[22] In 1994 Meyer et al in a retrospective study found that among 300 samples of urine from hypertensive pregnant women, 66% of the women had false negative dipstick urinalysis where significant proteinuria was defined as ≥300 mg/24 hours.[23] In the same series they report a false positive rate of 26% at the 1+level. The series of Brown et al in 1995 produced false negative results of 8–18% and a very high false positive rate of 67% with 1+ scores. [7]

To explain the persistent false positive rate of 1 in 4 they suggest that the dipstick is too sensitive at the 1+ threshold and that as such it is useful for the management of pre-eclampsia as it will minimize the false negative results (missed proteinuria) but the test will be incorrect at least half of the time.

All of this data suggests that the correlation between dipstick urinalysis and 24-hour protein estimation is imprecise. False positive results may result in over investigation and intervention whereas the potentially more serious issue of a false negative result may place a woman and her pregnancy at risk.

There are several reasons why such a poor correlation may occur. These include observer error, the characteristics of the dipstick tests, the units of protein estimation, the differing nature of the urine specimens involved, as well as possible variation in the “gold standard” assay employed in the laboratory setting.

Accuracy may be improved at higher threshold (>1+ proteinuria) but available data is sparse and of poor methodological quality. It is not therefore possible to make meaningful inferences about accuracy at higher urine dipstick thresholds.

If the 24 hour urine protein is divided into different intervals like 2 hour, 6 hour or 8hour collection, then the sensitivity will also be increased which is shown by R Gangaram and F paruk where the sensitivity was more than 90%.[11,20]

Similarly some suggest if the dipstick method is done in 24 hour aliquot then the sensitivity can also be increased which as shown by R Gangaram where the PPV increased from 64.9% to 94.2%.[11]

When dipstick urinalysis is performed on a random sample of urine, it gives a measure of the protein concentration in that specimen and as such it is affected by a number of variables such as contamination (false positive), exercise (increased excretion), posture, osmolality and urinary pH. It is unusual to find data on urine specific gravity or pH on reports of dipstick accuracy. It is also widely accepted that protein excretion has its own circadian variation and that this can change dipstick values from negative to as much as 3+ (i.e. non-proteinuric to proteinuric) over a 24-hour period. This has been reported in pregnancy in a study of 17 women with hypertension and proteinuria where considerable variation in protein excretion was observed thouroughout a 24 hour period.[24]

In this study the good result of dipstick to 24 hour urine protein collection was due to timed collection of urine every 6 hour which is also shown by many of the literatures cited above.

The method which was used in this study was Esbach'sAlbuminometer which is the oldest method of all. It may not be absolutely correct and may be adapted in cases of higher protein excretion. Esbach's method is untrustworthy so it is seldom used as stated by Otto Folin.[25]

The values which were obtained by Esbach's Albuminometer cannot be taken as gold standard as almost all the literature had said about its ineffectiveness. As it is an old method but can be used easily by all the health personal and can be used in low resource setting. The time has now come to change the conventional 24 hour protein detection to change to protein/creatinine ratio which has got higher efficacy.

In this study the cost of Dipstick was Rs 14 in comparison to Rs 80 for 24 hour urine protein. In many of the studies it has indicated the cheap price of dipstick .[8,19]

Dipstick result can be obtained immediately within seconds but 24 hour urine protein needs48-50hours to get the report which was shown in this study. Similarly many other studies showed the similar result.[8,19] As the result is obtained immediately dipstick can be used as the screening tool for detecting preeclampsia rather than waiting for more than 48 hours to get the report.

CONCLUSION

Timely collection of 6 hourly urine sample for detection of proteinuria by dipstick is comparable to more time consuming and expensive 24 hour urinary protein detection in laboratory by Esbach Albuminometer. However, these screening tests need to be validated by better and newer techniques of estimating 24 hour urinary protein in lab as gold standard.

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