

Original Research Article

Accuracy of automated urine dipstick test as a screening tool for proteinuria in hypertensive disorders of pregnancy

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ABSTRACT

Background: Progressive proteinuria implies worsening of the condition in hypertensive disorders of pregnancy and hence its quantification guides clinician in making decision and planning treatment. The gold standard is 24 hour urine protein estimation. Urine sediment cytology, also known as 'liquid renal biopsy' identifies and analyses the extent of renal damage.

Methods: Objectives of the study were to compare the efficacy of urine dipstick test to 24 hour urine protein estimation in detecting proteinuria in pre-eclampsic patients and to describe the findings in urine sediment examination in assessing proteinuria in above patients. Urine dipstick test and sediment cytology were performed on the urinary samples of 242 pregnant women with high BP recordings (BP>140/90 mm Hg) which were collected and tested in Department of Pathology, Government Medical College, Kottayam during the study period of 18 months. This was compared with 24 hour urine protein values (gold standard).

Results: About 154 patients (63.63%) had significant proteinuria of more than 300mg/24hr. Dipstick method showed 78.57% sensitivity and 81.82% specificity for prediction of significant proteinuria. Positive predictive value and negative predictive value of urine dipstick test were 88.32% and 68.57% respectively. Urine sediment examination revealed the presence of casts only in 11.98% of study population.

Conclusions: Diagnostic accuracy of automated urine dipstick test in assessing proteinuria was 79.75%. For grade 1 proteinuria, diagnostic accuracy was 79.81%, for Grade 2 it increased to 93.14% and for grade 3 & 4, accuracy was 98.68%. Urine sediment examination didn't correlate with proteinuria and hence the extent of renal damage in pre-eclampsia.

Keywords: Automated dipstick test, Diagnostic accuracy, 24 hour urine estimation, Hypertension, Pre-eclampsia, urine, Pregnant women

INTRODUCTION

Hypertensive disorders of pregnancy is one of the major cause of maternal mortality and complicate up to 10% of pregnancies. Hypertension is defined as blood pressure of more than 140/90 mm Hg on two occasion atleast 4 hours apart. Preeclampsia accounts for 5.4% of pregnancy induced hypertensive disorders in India.¹ Preeclampsia is a multisystem disorder characterized by decreased renal

perfusion and damage to glomerular basement membrane resulting in proteinuria. Normal women excrete up to 150 mg of proteins daily in the urine, but due to the renal changes occurring during pregnancy, proteinuria more than 300mg/day is considered abnormal for pregnant women.²

So, detecting proteinuria is an integral part of the management of hypertensive pregnant women. Moreover,

quantification of proteinuria is important in pre-eclampsia as the chance of complications rises with increasing protein excretion.³

The exact cause of preeclampsia is unknown, but its pathophysiology is linked to immunologic and angiogenic abnormalities in the placenta.⁴ Some of the hypotheses include:

- Abnormal trophoblast invasion of decidual spiral arteries and myometrium.
- Diminished uteroplacental circulation, leading to ischemia and oxidative stress in the placenta.
- Poor development of the fetoplacental vasculature.⁵
- Secretion of angiogenic factors into the maternal circulation resulting in hypertension and proteinuria.⁶

The methods to evaluate proteinuria vary, but till date 24-hour urine protein estimation is considered gold standard. However, 24-hour urine protein measurement is complex, time consuming and requires admission. So, alternative methods for assessing proteinuria in pregnancy like dipstick method have been considered.² Visual dipstick urinalysis which was inexpensive, easy to use, rapid and can be done by paramedical health assistants and by the patient herself was introduced initially. However, studies revealed inaccuracies in this method with high false positive and negative results. Also, it was found inadequate in quantifying proteinuria in hypertensive pregnant women. A few studies documented that use of an automated urine analysis device reduced these errors and hence improved the false negative and positive results of visual dipstick test.³

The principle of proteinuria detection in automated dipstick is 'protein error of pH indicators'. The reagent area is impregnated with bromophenol blue indicator buffered to pH 3.0 with citrate. Protein changes the colour of the indicator without actually changing the pH, since the strip is buffered.⁷ Different methods exist for quantification of protein in 24 hour urine sample including precipitation methods (sulfosalicylic acid or heat and acetic acid), dye-binding methods (Coomassie brilliant blue), chemical methods (biuret or Folin-Lowry assays), and immunological methods (radial immunodiffusion, immuno-electrophoresis, immune-turbidimetry, nephelometry, and immunoassays for specific proteins).⁸ Urine sediment cytology can assess the extent of renal damage, hence called as "liquid renal biopsy".⁹

Present study is to compare the diagnostic efficacy of dipstick test to 24-hour urine protein estimation in diagnosing pre-eclampsia and to describe urinary profile of antenatal women with preeclampsia by urine sediment cytology.

METHODS

The present study was a diagnostic test evaluation done on urinary samples of 242 pregnant women with high BP

recordings (BP>140/90 mm Hg) which were collected and tested in Department of Pathology, Government Medical College, Kottayam during December 2017 - May 2019.

According to "Improved methods of assessing proteinuria in hypertensive pregnancy" by Saudan et al, sensitivity of automated dipstick test in identifying proteinuria is 83%.³

Sample size, N is calculated as,

$$\frac{Z\alpha^2 \times \text{Sensitivity} \times (1 - \text{sensitivity})}{d^2 \times P} = \frac{(1.96)^2 \times 83 \times 17 \times 100}{400 \times 5.6} = 241.9$$

So, calculated sample size is 242.

Inclusion criteria

- All antenatal women who were admitted with high BP recordings (BP >140/90 mm Hg) on 2 occasions at least 4 hours apart.

Exclusion criteria

- Contaminated urine : if urine analysis contained >10 WBCs/hpf
- If an outpatient 24 hour urine collection was incomplete
- Gestational diabetes mellitus and other causes of proteinuria.

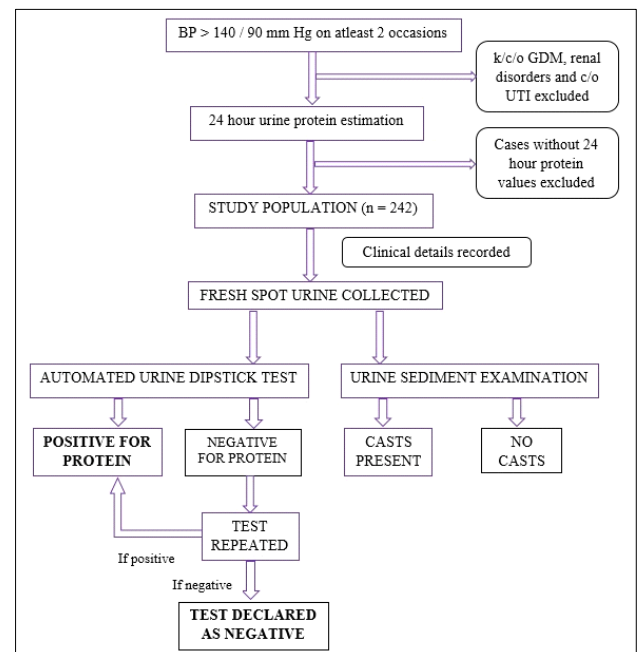


Figure 1: Study procedure.

Urine analysis was performed on all hypertensive pregnant women after obtaining informed written consent. Clinical details of each patient was recorded along with BP measurements and 24 hour urine protein values. Fresh spot urine sample was collected and

dipstick test in automated urine analyser was done. Samples with negative result were tested twice for confirmation. The result was correlated and compared with 24 hour urine protein which was analysed by Beckman Coulter AU 480 Analyser. The sample was centrifuged and sediment examined under light microscope and using polarizer for detailed cytological analysis (Figure 1).

Definition of parameters

- 24 hour urine protein estimation taken positive if > 300 mg/day and graded as:
 1+ : 300-1000 mg/day
 2+ : 1001-2000 mg/day
 3+ : 2001-3000 mg/day
 4+ : >3000 mg/day
- Automated dipstick test for protein considered positive if >30 mg/dL and graded as:
 0 <15 mg/dL and Trace 15-30 mg/dL taken as absent
 1+ : 30-100 mg/dL
 2+ : 100-300 mg/dL
 3+ : 300-2000 mg/dL
 4+ : >2000 mg/dL

Automated urine analysis

Urinalysis was made on fresh spot urine samples of hypertensive women using an automated device (Clinitek Status Analyser) with Multistix 10 SG strips. The printout result of this urinalysis was recorded.

24-hour urine protein

24-hour urine protein analysis was done in all hypertensive patients using Beckman Coulter AU 480 analyser. The procedure principle is colorimetric method.

Pyrogallol red is combined with molybdate to form a red complex with a maximum absorbance at 470 nm. Proteins, in acidic medium, combine with Pyrogallol Red and molybdate to form a blue purple coloured complex which have a maximum absorbance at 600nm.

Urine microscopy

A fresh sample of 5 to 10 mL of urine was centrifuged at 1,500 rpm for 5 minutes. The supernatant then is discarded and the sediment resuspended in the remaining liquid. A single drop is transferred to a clean glass slide, and a cover slip is applied.

Statistical analysis

The data was entered in Microsoft excel and further statistical analysis was done using SPSS software (version 24). Sensitivity, specificity, positive predictive

value, negative predictive value, likelihood ratios and diagnostic accuracy of urine dipstick tests were compared with gold standard 24 hour urine protein.

RESULTS

The mean age distribution of the present study population was 27.11 years. Minimum age was 18 years and maximum age was 36 years. Majority belong to age group >25 years (63.6%). About 77% of the study population (after excluding 64 cases which met exclusion criteria) presented with high BP of more than 140/90 mmHg at a gestational age of more than equal to 20 weeks. 57% of the study population were nulliparous women. Among the multiparous women, 62% had a past obstetric history of hypertension. Severe BP (>160/110 mmHg) at presentation was present only in 7 hypertensive women. Pedal edema was present in the majority of study population (69.4%).

Using 24 hour protein estimation, 36% of hypertensive pregnant women had absent or trace (negative) proteinuria and 63% had proteinuria hence pre-eclampsic, of which 50% had 1+ proteinuria, 12% had 2+, 1% had 3+ and only one woman had 4+ proteinuria. Prevalence of pre-eclampsia in the study population was 63.64%. With automated urine dipstick test, 43% of the hypertensive pregnant women had absent (negative or trace) proteinuria and 57% had proteinuria, hence pre-eclampsic.

When compared with 24 hour urine protein assessment, automated dipstick analysis has failed in identifying proteinuria in 6% of pre-eclampsic women. Among the 154 cases of proven proteinuria, 121 were diagnosed (78.57%) in automated urine dipstick also (Table 1).

Table 1: Proteinuria in automated dipstick test vs 24 hour urine estimation.

Dipstick test	24 hr urine protein		Total
	Present	Absent	
Positive	121	16	137
Negative	33	72	105
Total	154	88	242

Table 2: Sensitivity, Specificity, Predictive values, Likelihood ratio & Diagnostic accuracy of different dipstick grades in predicting proteinuria.

	1+	2+	3+/4+
Sensitivity (%)	77.05	82.14	75
Specificity (%)	83.72	97.3	100
PPV(%)	87.04	92	100
NPV(%)	72	93.51	98.63
LR+	4.73	30.39	-
LR-	0.27	0.18	0.25
Accuracy (%)	79.81	93.14	98.68

Sensitivity, specificity and diagnostic accuracy of automated urine dipstick test in assessing proteinuria for the diagnosis of pre-eclampsia are 78.57%, 81.82% and 79.75% respectively. Diagnostic accuracy of automated dipstick to predict Grade 1, Grade 2 and Grade 3&4 proteinuria were 79.81%, 93.14% and 98.68% respectively (Table 2).

Urine sediment examination revealed the presence of hyaline and fine granular casts only in 11.98% of study population. In majority of population, no casts or cells were visible.

DISCUSSION

The present study was conducted on the urine samples of 242 pregnant women with high BP recordings (BP>140/110 mmHg). In the present study, cases showed a range of distribution from 18-37 years, with a peak in the age group of >25 years, and mean age of 27.11 years. This finding was correlating with the study by Sapna Amin et al and Waugh et al.^{2,10} 57% of the study population were nulliparous women, which is comparable with other studies. In the present study, almost half of the study population had Grade 1+ proteinuria. But in the study done by Sapna Amin et al and Waugh et al, majority were in grade of 3+ and 0 respectively.^{2,10} This may be due to the better awareness, health seeking behavior and regular antenatal check-ups among our study population.

Sensitivity, specificity and diagnostic accuracy of automated dipstick in diagnosing proteinuria are 78.57%,

81.82% and 79.75% respectively, which is comparable with the study done by Waugh et al, (Table 3).¹⁰

Table 3: Comparison of diagnostic test characteristics of automated dipstick.

	Present study	Waugh et al ¹⁰
Year	2018	2005
Sensitivity (%)	78.57	82
Specificity (%)	81.82	81
Diagnostic Accuracy (%)	79.75	81.28

Comparing with the study done by Saudan et al, specificity of dipstick in predicting grade 1 proteinuria (83.72%) was similar, but the present study showed reduced sensitivity and considerably better PPV. Sensitivity and specificity of dipstick in predicting positive grade 2 proteinuria were 82.14% and 97.3% respectively which was similar to the former study. Specificity and positive predictive values of dipstick in predicting positive grade 3 and 4 proteinuria were similar (100%). Sensitivity is reduced (75%), which may be due to the decreased representative proportion of study population in this category (Table 3).³

Automated dipstick analysis is a more accurate screening test for the detection of proteinuria than visual testing with a better sensitivity, specificity and likelihood ratios when compared with other studies based on visual/manual urine dipstick test (Table 4).^{2,10,11}

Table 4: Comparison between present study and other visual dipstick - based studies.

	Present study (Automated)	Waugh et al ¹⁰ (visual)	Sapna Amin et al ² (Visual)	Dwyer et al ¹¹ (visual)
Year	2018	2005	2014	2008
Sensitivity	78.57	51	59	41
Specificity	81.82	78	66.7	100
LR+	4.32	2.27	1.42	-
LR-	0.26	0.635	0.34	0.59

CONCLUSION

The accurate detection of proteinuria in hypertensive pregnant women is important as it enables classification of hypertensive disorders, affects prognosis, and influences clinical management. 24-hour urine protein measurement is considered as gold standard for protein estimation, but with many disadvantages. Automated dipstick urinalysis is an alternative tool as it is quick, simple, easy to use and cost effective. It can be done on a random urine sample and does not require 24 hour collection. Most importantly, it reduces the waiting time for diagnosing pre-eclampsia and help a clinician in

making early decision and guide appropriate management.

Diagnostic Accuracy of Automated Urine Dipstick Test in assessing proteinuria is 79.75% and it increases with higher grade of proteinuria. Urine sediment examination didn't correlate with proteinuria and hence the extent of renal damage in pre-eclampsia. So performing automated dipstick test as a screening test in cases of hypertensive disorders of pregnancy to diagnose pre-eclampsia may be recommended.

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