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Can the Urine Dipstick Test Be Used As A Proteinuria Screening Test?

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ABSTRACT

The present study aimed to evaluate the diagnostic performance of the chemical dipstick protein measurement method, which can be used for screening purposes, in the detection of proteinuria.

The results from 795 individuals were retrospectively scanned. In order to evaluate the urine dipstick's accuracy in detecting proteinuria, the current study accepted protein/creatinine ratio (PCR) as the reference value, and three different criteria were used according to different age groups [PCR: ≥ 0.2 g/g (>2 years), ≥ 0.5 g/g (6 months-2 years), and ≥ 0.8 g/g (0-6 months)]. While evaluating diagnostic sensitivity, specificity, positive predictive value, and negative predictive value, two cut-off values [trace and 1(+)] were evaluated. Area under the curve (AUC) by Receiver operating characteristic analysis were analyzed.

The calculated sensitivity levels were lower than 70% for all age groups, with an AUC of 0.680, 0.780, and 0.768 for the age groups of 0–6 months, 6 months–2 years, and > 2 years, respectively.

When the PCR was taken as a reference for proteinuria, the chemical dipstick test only proved suitable for screening proteinuria in the >6 months age group. Nonetheless, its performance could benefit from further improvement. Although the use of dipsticks is fast, simple, and inexpensive, this research indicates that they cannot replace PCR and 24-hour urine protein amount tests in the diagnosis and follow-up of renal diseases, which are generally known to be asymptomatic until their progression and complications are detected.

Keywords: Urine dipstick, tetrabromophenol blue dye method, protein/creatinine ratio, proteinuria

Introduction

Urinary protein analysis, which plays an important role in the evaluation of renal function, is a frequently used biochemical test (1, 2). This analysis is critical to the early diagnosis of patients with proteinuria and the initiation of preventive treatment (2). The amount of proteinuria can provide information about the prognosis of the disease and the success of the treatment (3). Three main analysis methods are used to detect proteinuria: chemical dipstick-based urinalysis, spot urine protein creatinine ratio, or, protein/creatinine ratio (PCR), and 24-hour urinary protein excretion analysis (4).

The accurate collection of samples for 24-hour urinary protein excretion analysis, which is accepted as the gold standard test in proteinuria analysis, is a time-consuming and difficult process. PCR has been the preferred method by clinicians as it prevents errors related to 24-hour urine collection. (5,6). For PCR (g/g), proteinuria is accepted to be ≥ 0.8 g/g in the 0–6 month age group, ≥ 0.5 g/g in the 6 months–2 years age group, and ≥ 0.2 g/g in the > 2 years age group (7–11).

Various methodologies are used to determine the amount of protein in urine. The cost of immunometric-based tests limits their use for screening purposes (12). Although the dipstick urine test is used as a screening test due to its ease of use and relatively low cost, questions about the test's reliability have been raised by inconsistent study results that have shown a range of sensitivity and specificity values (4).

The present study aimed to evaluate the diagnostic performance of the chemical dipstick protein measurement method, which can be used for screening purposes, in the detection of proteinuria.

Materials and Methods

The results from 795 individuals whose spot urine protein, spot urine creatinine, and complete urinalysis analyses were made from simultaneously provided samples were retrospectively scanned from the hospital information system.

Dipstick protein was measured semiquantitatively in AX 4280 (Arkray, Kyoto, Japan) systems using the

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tetrabromophenol blue dye method and an Aution Sticks brand dipstick. Spot urine protein was measured using an Architect urine/CSF protein kit and the turbidimetric benzethonium chloride method on an Abbott Architect C8000 (CA, USA) analyzer. According to the manufacturer's specification the limit of blank (LOB), the limit of detection (LOD) and the limit of quantitation (LOQ) were 1.8 mg/dL, 2.6 mg/dL and 6.75 mg/dL, respectively. Spot urine creatinine was measured using an Architect brand creatinine kit and the kinetic alkaline picrate method on an Abbott Architect C8000 (CA, USA) analyzer. According to the manufacturer's specification the LOB, LOD and LOQ were 1.38 mg/dL, 4.0 mg/dL and 5 mg/dL, respectively.

Statistical analysis: In order to evaluate the urine dipstick's accuracy in detecting proteinuria, the current study accepted PCR as the reference value, and three different criteria were used according to different age groups [PCR: ≥ 0.2 g/g (Group I: > 2 years), PCR≥ 0.5 g/g (Group II: 6 months–2 years), and PCR≥ 0.8 g/g (Group III: 0-6 months), (7-11)]. While evaluating diagnostic sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), two cut-off values [trace and 1(+)] were evaluated. Diagnostic sensitivity, specificity, PPV, NPV, and area under the curve (AUC) by receiver operating characteristic (ROC) analysis were evaluated. Youden index (J=maximum (sensitivity + specificity −1) and acceptable sensitivity value were used to determine the optimal cut-off values. Statistical analysis of the data was performed using the SPSS Statistics 22 program.

Results

Of the 795 individuals who were between 2 days old and 87 years old, 52.1% were female. At least 88% of the individuals were > 2 years old, 5.6% were 6 months old–2 years old, and 6.4% were 0–6 months old. For the dipstick protein measurements of all age groups, 46.6% were negative, 15.9% were trace, 16.4% were 1(+), 12% were 2(+), 7.5% were 3(+), and 1.6% were 4(+).

The PCR was ≥ 0.2 g/g in 72.2% of the measurements for Group I (> 2 years). Of the samples with a PCR of ≥ 0.2 g/g, 33.3% were negative on the dipstick, 14.2% were trace, 20.8% were 1(+), 17.6% were 2(+), 11.5% were 3(+), and 2.6% were 4(+).

The PCR was ≥ 0.5 g/g in 70.4% of the measurements for Group II (6 months–2 years). Of the samples with a PCR of ≥ 0.5 g/g, 35.5% were negative, 19.4% were trace, 35.5% were 1(+), 6.4% were 2(+), and 3.2% were 3(+) on the dipstick.

In Group III (0–6 months), 70.6% of the PCR measurements were ≥ 0.8 g/g. Of the samples with a PCR of ≥ 0.8 g/g, 58.3% were negative, 13.9% were trace, 13.9% were 1(+), 11.1% were 2(+), and 2.8% were 3(+) on the dipstick.

By using a PCR of ≥ 0.2 g/g as a reference for Group I, the ROC analysis determined that the AUC was 0.768 and that the optimal cut-off value was at the trace level (Figure 1). When the cut-off was determined to be at the trace, the sensitivity was 66.7%, the specificity was 75.8%, the PPV was 87.8%, and the NPV was 46.7%. When values of 1(+) or above were considered positive, the sensitivity was 52.5%, the specificity was 95.4%, the PPV was 96.7%, and the NPV was 43.5%. (Table 1).

When a PCR of ≥ 0.5 g/g was taken as the reference for Group II, the ROC analysis determined that was 0.780 and that the optimal cut-off value was at the trace level (Figure 2). When the dipstick cut-off value was at trace value, the sensitivity was 64.5%, the specificity was 84.6%, the PPV was 90.9%, and the NPV was 50%. When values of 1(+) or higher were determined to be positive, the sensitivity was 45.2%, the specificity was 100%, the PPV was 100%, and the NPV was 43.3% (Table 1).

When a PCR of ≥ 0.8 g/g was taken as the reference for Group III, the ROC analysis determined that the AUC was 0.680 (Figure 3). However, when the dipstick value was accepted to be at the trace and upper limit value, the sensitivity was 41.7%, the specificity was 80%, the PPV was 83.3%, and the NPV was 36.4%. When values of 1(+) and above were found to be positive, the sensitivity was 27.8%, the specificity was 80%, the PPV was 83.3%, and the NPV was 36.4% (Table 1).

Discussion

This study aimed to evaluate the diagnostic performance of the chemical dipstick tetrabromophenol blue dye method in detecting proteinuria using the spot urine PCR as a reference. Although previous studies on this subject have focused on the general population or specific pediatric or adult age groups, the present study included a broad age group and evaluated them according to the PCR reference standards accepted for each group. Age-adjusted PCR is recommended as the reference value for proteinuria (11). Therefore, PCR values of ≥ 0.2 g/g, ≥ 0.5 g/g, and ≥ 0.8 g/g were accepted as the cut-off values for each age group in the current study (7–10). The ROC analysis for all

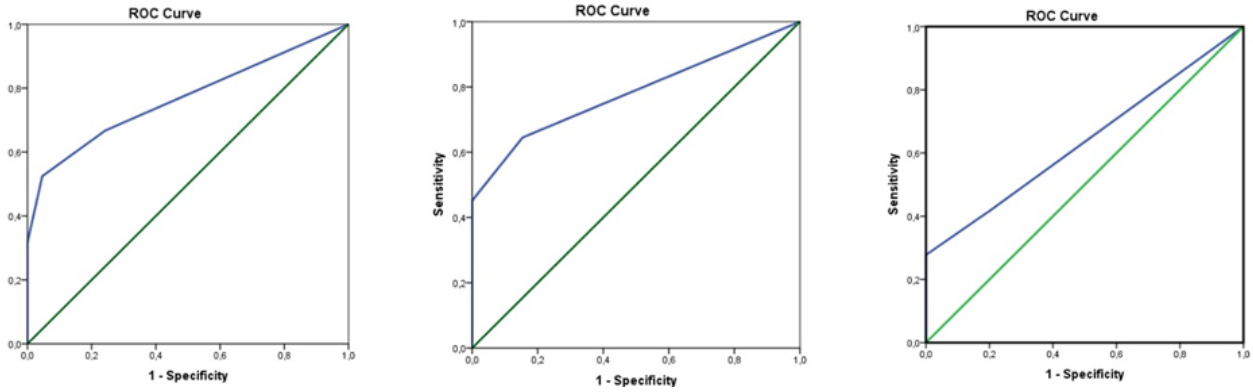

Fig. 1. Evaluation of the urine dipstick test in the diagnosis of proteinuria (based on PCR) using an ROC curve. (A) > 2 years, PCR ≥ 0.2 g/g; (B) 6 months–2 years, PCR ≥ 0.5 g/g; (C) 0–6 months, PCR ≥ 0.8 g/g. For each group, the AUC was calculated as 0.768, 0.780, and 0.680, respectively. PCR; protein/creatinine ratio, ROC:receiver operating characteristic, AUC; area under the curve

Table 1. Data on The Diagnostic Performance of Strip Protein In Proteinuria (Based on PCR)

PCR (g/g)	Dipstick Protein	Sensitivity (%) (%95 Cl)	Spesifity (%) (%95 Cl)	PPV (%) (%95 Cl)	NPV (%) (%95 Cl)	AUC (%95 Cl)
Group I ≥0,2 (%95 Cl)	Trace	66,7 (62,6-70,8)	75,8 (70,0-81,6)	87,8 (85,3-90,3)	46,7 (43,0-50,4)	0,768 (0,750-0,786)
	1(+)	52,5 (48,0-57,0)	95,4 (92,9-97,9)	96,7 (95,2-98,2)	43,5 (41,2-45,8)	
Group II ≥0,5 (%95 Cl)	Trace	64,5 (48,7-80,8)	84,6 (71,1-98,1)	90,9 (84,4-97,4)	50,0 (37,1-62,9)	0,780 (0,710-0,850)
	1(+)	45,2 (27,3-63,1)	100 (-)	100 (-)	43,3 (35,7-50,9)	
Group III ≥0,8 (%95 Cl)	Trace	41,7 (25,5-57,9)	80 (64,3-95,7)	83,3 (72,6-93,7)	36,4 (28,2-44,6)	0,680 (0,443-0,917)
	1(+)	27,8 (14,2-41,4)	100 (-)	100 (-)	36,6 (32,0-41,2)	

PCR: Protein/creatinin ratio, PPV: Positive predictive value, NPV: Negative predictive value, AUC:Area Under the Curve, CI: Confidence Interval

the age groups resulted in an AUC of less than 0.8. The calculated sensitivity levels were lower than 70% for all the age groups, with an AUC of .680, 0.780, and 0.768 for the age groups of 0–6 months, 6 months–2 years, and > 2 years, respectively.

Although the dipstick protein method could be used to screen individuals in the 6 months–2 years and > 2 years age groups, its performance requires improvement. Conversely, the urine dipstick tests were less successful in evaluating proteinuria in the 0-6 months age group. The results obtained for the 0–6 month age group were less diagnostically accurate because of the PCR reference intervals, which were not created to assess narrower age groups (i.e., age groups arranged by hour, day, and month). The low number of results included in this group may also have contributed to this situation.

In Lim et al.'s study of an elderly patient group, the sensitivity was > 80%, and the area under the curve from the ROC analysis was > 0.9 for the trace and 1(+) values at PCRs of ≥ 0.2 g/g and ≥ 0.5 g/g. In lieu of these findings, the researchers reported that the dipstick method could be used as a screening method (7). According to the present study, although

moderate diagnostic performance adequacy was observed during the ROC analysis of the 6 month–2 years and > 2 years age groups, the sensitivity levels were calculated at lower levels. In another study conducted on hypertensive pregnant women, using the 1(+) level as the limit value in dipstick measurements provided a higher overall accuracy than the trace level. The study also determined that additional clinical findings and tests would be needed for measurements of < 1(+) in proteinuric patients who had yet to be diagnosed (4).

In a study of a patient group with chronic renal failure, the sensitivity was calculated as > 90% for the 1(+) and 4(+) levels of the dipstick results, respectively, when PCR levels of 1 g/g and 3 g/g were used as the references (13). In the current study, because a PCR level of ≥ 0.2 g/g was taken as the reference, which was a much lower value than the PCR levels used in the abovementioned study, the sensitivity ratios were low for the trace and 1(+) values. According to a study of patients with rheumatological diseases, while the dipstick test was found to be 100% sensitive in detecting 300 mg/24h protein loss at values ranging from 1(+) to 3(+), the test was reported to be insufficient, with a false positive rate of 48% (14) Another study, which evaluated six different studies of obstetric patients, reported that dipsticks did not perform well in detecting or excluding proteinuria (8). To summarize, there are both differences and similarities between the current study and the aforementioned researchs. There is evidence that test strips from different manufacturers perform differently at breakpoint concentrations. It is also known that values expressing positivity among producers do not always correspond to the same protein concentrations (8). In addition, protein concentrations in urine are closely related to hydration. High specific gravity can cause a positive color change within the strip, even when protein excretion is within normal ranges (15). Cases that cause pH changes in the urine, such as urinary tract infections or the presence of quaternary ammonium compounds, can also lead to incorrect results. High levels of hemoglobin, contrast agents, disinfectants containing quaternary ammonium compounds, excessively acidic urine (pH ≤ 3), and alkaline urine (pH ≥ 8) may cause interference in protein measurements with a dipstick (16).

Although urine dipsticks are known to be sensitive to albumin, it is worth noting that PCR values are calculated according to protein measurements. When evaluating a patient's results, the dipstick test can provide advantages by ruling out overt proteinuria with a spot urine sample, eliminating the need for specially collected samples, and reducing the requirement for lengthy and costly quantitative laboratory tests. According to the present study, while the performance of the urine dipstick test could only be used as a proteinuria screening test in the > 6 months age group, its performance could benefit from further improvement.

The current study aimed to evaluate the diagnostic performance of the chemical dipstick protein measurement method for detecting proteinuria. The spot urine PCR was used as a reference for proteinuria. When the PCR was taken as a reference for proteinuria, the chemical dipstick test only proved suitable for screening proteinuria in the >6 months age group. Nonetheless, its performance could benefit from further improvement. Although the use of dipsticks is fast, simple, and inexpensive, this research indicates that they cannot replace PCR and 24-hour urine protein amount tests in the diagnosis and follow-up of renal diseases, which are generally known to be asymptomatic until their progression and complications are detected.

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