Original Research Article

Diagnostic efficacy of urine dipstick in detecting chronic kidney disease

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Abstract

Background: Proponents of routine urine dipstick screening to identify patients at risk for ESRD in the primary care setting have argued that urine dipsticks are inexpensive, low risk, acceptable to patients, and now, more accurate. Proponents believe that urine dipstick screening has the potential to improve outcomes for people with early disease and increase awareness of CKD. Most primary care physicians agree that populations who are at high risk for CKD should be tested and appropriately treated to decrease complications of ESRD. However, proponents of mass screening may not appreciate the challenges, limitations, and potential harms of screening. Urine dipstick testing does not meet all of the criteria for a good screening test.

The aim of the study: To elucidate the diagnostic efficacy of the urine dipstick in detecting chronic kidney disease by assessing its validity as a screening test for detecting CKD.

Materials and methods: A community-based cross-sectional study was conducted among 287 subjects aged 20 years and above residing in the P.K. Garden area of Chennai during November 2018 to January 2019. Subjects were interviewed with a questionnaire and blood samples were collected to estimate serum creatinine and a urine sample was collected to estimate the proteinuria using urine

dipstick. eGFR was calculated using CKD – EPI equation and CKD was diagnosed using KDOQI CKD guidelines.

Results: The prevalence of Chronic Kidney Disease (<60 ml/min eGFR) in the study group was 10.45%. The Area under Curve (AUC) of the ROC curve for urine dipstick in detecting CKD was 0.948 (0.900 – 0.996) and the 2+ proteinuria was closest to the ideal test point. When proteinuria criteria set at dipstick 2+ or more, the sensitivity was 83.33% and specificity was 98.36%, positive predictive value was 83.33% and κ coefficient of agreement of proteinuria with CKD was 0.81.

Conclusion: The urine dipstick test can be used as an effective screening tool in detecting CKD in primary care level. Non Communicable Diseases screening at primary health care level should include the screening of proteinuria using urine dipstick especially for people with risk factors like Diabetes and Hypertension.

Key words

Chronic Kidney Disease, Urine Dipstick, Proteinuria, Diagnostic efficacy, eGFR.

Introduction

Chronic Kidney Disease (CKD) is a global public health problem with a rising trend in prevalence. By the time the symptoms of CKD manifest, the disease would have progressed to advanced stage leading to End Stage Renal Disease (ESRD). In India, the projected number of deaths due to chronic kidney disease was around 5.21 million in 2008 and is expected to rise to 7.63 million by 2020 (66.7% of all deaths) [1]. Indeed, it has been recently estimated that the age-adjusted incidence rate of ESRD in India to be 229 per million population [2]. More than 100,000 new patients enter renal replacement programs annually in India [3]. Hence, early screening offers the advantage of delaying the progression and modification of risk factors identified. Early screening programs in high-risk groups including those with diabetes mellitus, hypertension, neglected urinary tract infection and first-degree relatives of CKD patients will have a major impact on the overall health status of the population [4]. Growing evidence indicates that the presence of relatively high levels of urine protein can be an early marker of increased risk of progressive kidney disease, poor cardiovascular outcomes, and death [5]. Prescription of angiotensin-converting enzyme (ACE) inhibitor or Angiotensin II-receptor blocker (ARB) therapy in persons with proteinuria and chronic kidney disease has been demonstrated to decrease both the progression of kidney disease toward ESRD as well the incidence of cardiovascular events and death [6]. The urine dipstick test can be used as an initial screening tool for detecting proteinuria (a predictor of CKD) in primary health care level because of its low cost and ability to provide rapid information to clinicians and patients [7, 8]. The urine dipstick as a screening tool for detecting CKD has not been sufficiently validated in our population. So this study tends to elucidate the diagnostic efficacy of the urine dipstick in detecting chronic kidney disease by assessing its validity as a screening test for detecting CKD [9].

Materials and methods

A community-based cross-sectional study was conducted from November 2018 to January 2019 among the people residing in the P.K. Garden area, an urban slum in Chennai. People aged 20 years and above irrespective of sex were included in the study. People already diagnosed of chronic kidney disease (confirmed by health records), pregnant women and women during active menstruation and those who had a history of acute illness like diarrhea and fever in the week prior to the study were excluded from the study. The sensitivity of the urinary dipstick ranges from 83% to 98% [10, 11]. Taking average sensitivity of urine dipstick, Sn = 91%, absolute precision, Δ = 8%, with a confidence level of 95%, Z = 1.96, with a prevalence of

CKD, p = 17.2%, the sample size was calculated by the following Buderer's formula [12], $\mathbf{N = Z^2 * Sn * (1 - Sn) / \Delta^2 * p}$ and was estimated to be 287 subjects.

Interview with the structured questionnaire was conducted to collect the information from the participants. After information was given about the study and obtained the informed consent of the participants, relevant information was obtained from the respondent using the questionnaire. The questionnaire contained questions about the socio-demographic profile of the subject and the history regarding exposure of the subject to the risk factors. Two ml of a venous blood sample (random) was collected from all the study participants with the subject in the sitting position using disposable syringes and collected in a fresh, clean pilot tube. Adrenaline injections were kept in hand for emergency situations like pain shock. The blood samples collected were transported to the laboratory in a vaccine carrier to maintain cold chain. Blood was centrifuged and analyzed in Institute of Biochemistry Laboratory. Blood samples were analyzed on the same day of collection. Using Jaffe Colorimetric method, serum creatinine was measured in the semi-auto analyzer. Quality control was ensured by analyzing standard sample before checking for the test samples. Proteinuria was detected by urine dipstick method (DIRUI H- series urinalysis strips H10). The study participants were provided with a clean container in which fresh urine was collected. A urine sample was mixed well before taking the test. The urine tests were done within 2 hours of sample collection. In-room temperature, the reagent area of the strip was immersed in the urine and then the strip was removed quickly. The strip was held horizontally and the color changes on the strip were compared with the color chart on the bottle label. A semi-quantitative result was read according to the time specified (60 seconds) on the color chart.

Operational Definitions

CKD (Chronic Kidney Disease) is defined as eGFR <60 ml /min/1.73 m^2 with or without kidney damage [13]. eGFR is calculated using the CKD-EPI equation [14]. CKD – EPI gives the best estimation of GFR compared to MDRD and Cock Graft Equations [15].

Proteinuria is defined as excretion of albumin in urine in an increased amount and is graded by the urine dipstick as follows. < 0.15 mg/dl protein level in urine is considered as negative; 15 to 30 mg/dl as trace; 30 to 100 mg/dl as 1; 100 to 300 mg/dl as 2+; 300 to 2000 mg/dl as 3+; >2000 mg/dl as 4+.

Statistical analysis: The data collected were entered in Microsoft Excel 2013 version and double-checked for errors. The data was analyzed using Statistical Package for Software Solutions (SPSS) version 21. The validity of the screening test was evaluated using sensitivity and specificity. The diagnostic efficacy of the test was calculated using positive predictive value and the κ coefficient of agreement.

Results

There were totally 287 subjects, out of which 88 were males and 199 were females. Almost the distribution of gender in all age groups was equal. The age wise distribution of the proteinuria and CKD status of the subjects was illustrated in **Table - 1**. Totally 182 (63.41%) of the subjects had negative or trace proteinuria, 75 (26.13%) had 1+ proteinuria, 16 (5.57%) had 2+ proteinuria, 10 (3.48%) had 3+ proteinuria and 4 (1.39%) had 4+ proteinuria. About 43% had CKD in 60 years and above followed by almost 12% in both 40-49 years and 50-59 years age group with 3% in 30-39 years age group. There was no CKD in less than 30 years age group. The distribution of proteinuria characteristic and CKD status of the subjects is illustrated in **Table - 2**. 87.5% (14 subjects) of 2+ proteinuria and 80% (8 subjects) of 3+ proteinuria subjects and 75% (3 subjects) had CKD. **Figure - 1** demonstrated the ROC curve of urine dipstick proteinuria in detecting CKD in the study population. The Area Under Curve (AUC) was 0.948 (0.900 – 0.996). When proteinuria criteria

set at dipstick 1+ or above for detecting CKD among all subjects, the sensitivity was 96.7% and specificity was 70.4%; when 2+ or more, the sensitivity was 83.33% and specificity was 98.36%; when 3+ or more, the sensitivity was 36.67% and specificity was 98.83%; when 4+ or more, the sensitivity was 10% and specificity was 99.61% (**Table – 3**).

Table - 1: The age-wise distribution by the proteinuria and CKD status of the subjects.

Age categories	Proteinuria					Chronic Kidney Disease		Total
	Neg/trace	1+	2+	3+	4+	Present	Absent	
20 - 29 years	59	15	1	0	0	0	75	75
30 - 39 years	40	20	1	1	1	2	61	63
40 - 49 years	41	19	3	5	1	8	61	69
50 - 59 years	25	17	1	1	1	5	40	45
60 & above	17	4	10	3	1	15	20	35
TOTAL	182	75	16	10	4	30	257	287

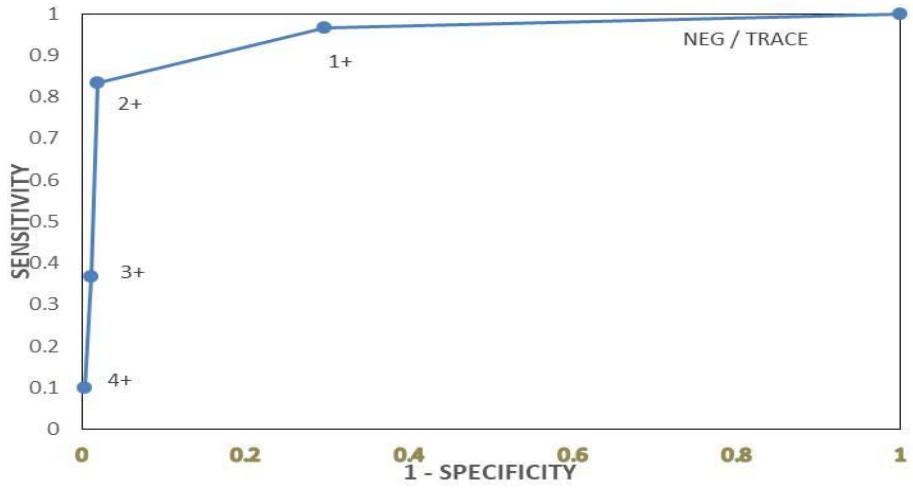
Table - 2: Distribution of proteinuria characteristic and CKD status of all the subjects.

Proteinuria	Chronic Kidney Disease		Total
	Present	Absent	
Neg / trace	1	181	182
1+	4	71	75
2+	14	2	16
3+	8	2	10
4+	3	1	4
TOTAL	30	257	287

Table - 3: Comparison of validity of urine dipstick in detecting CKD among the subjects with proteinuria cut-off as ≥ 1+ and ≥ 2+.

Proteinuria	CKD		Sensitivity	Specificity	positive predictive value	negative predictive value	κ agreement
	Yes	No					
1+ or above	29	76	96.67%	70.42%	27.61%	99.45%	0.3188
2+ or above	25	5	83.33%	98.05%	83.33%	98.05%	0.8138

Figure - 1: ROC curve of urine dipstick proteinuria in detecting CKD in the subjects.



Discussion

The prevalence of Chronic Kidney Disease (<60 ml/min eGFR) in the study group was 10.45% which was lower than the prevalence of 17.2% stated in SEEK study The SEEK study used the MDRD equation to calculate eGFR which has a slight difference with the eGFR calculated using the CKD-EPI equation which was also shown in the same study. Also, the SEEK study had participants all over India whereas the present study included only from Chennai. Of the subjects with CKD, 96.66% had proteinuria 1+ or above and 83.33% had proteinuria 2+ or above. In the SEEK study, 79.5% of the CKD subjects had proteinuria. It almost correlates with the present study [10]. The area under Curve (AUC) of the ROC curve was 0.948 (0.900 – 0.996) and the 2+ proteinuria was closest to the ideal test point with a sensitivity of 83.33% and specificity of 98%. The positive predictive value for detecting CKD was 83.33% when the proteinuria was taken as dipstick 2+ or more compared to 27.61% at 1+ or above. The κ coefficient of agreement of proteinuria with CKD increased from 0.32 at dipstick 1+ or above to 0.81 at dipstick 2+ or more which denotes an excellent agreement. So 2+ or more proteinuria in urine dipstick can be taken as a best cut off for detecting CKD in this study population [11]. In Bruderer, et al. [12], the sensitivity, and specificity of urine dipstick evaluated against protein creatinine ratio and albumin-creatinine ratio were more than 80% when 1+ or more proteinuria was used as cut off for proteinuria. White, et al. [9] state that a dipstick test result of <1+ or less than trace has a high negative predictive value in the general community setting. These studies had evaluated the validity of the dipstick in detecting proteinuria but not in detecting CKD. Moreover, the study population differs much from the present study population [12]. In Micheals, et al. study [15], subjects with baseline proteinuria of 2+ or more had the maximum incidence of End Stage Renal Disease (ESRD) of 18.7% in the follow up of 25 years and the hazard ratio was 15.7 (10.33-23.87). In that study, the incidence of ESRD in those subjects who had baseline proteinuria of 2+ or more and eGFR < 60 ml/min was 40.91% with a hazard ratio of 32.87 (15.20 to 71.10). This study adds evidence to the present study results that 2+ proteinuria in urine dipstick can be used as a cut-off for detecting CKD which also ultimately reduces ESRD if those identified as CKD were treated adequately [13, 14, 15]. The study was done in a selected area in Chennai so that generalization of the results has some constraints. Mostly female subjects were available in the household at the time of data collection which reflected more percentage of females among the study subjects. To establish the validity of urine dipstick as a screening tool to detect CKD among the general population, a large scale study may be conducted.

Conclusion

The urine dipstick test can be used as an effective screening tool in detecting CKD in primary care level. Non Communicable Diseases screening at primary health care level should include the screening of proteinuria using urine dipstick especially for people with risk factors like Diabetes and Hypertension.

References

1. Chronic Kidney Disease: Current Status, Challenges, and Management. chap130.pdf [Internet]. [cited 2015 Dec 31]. Available from: ttp://www.apiindia.org/medicine_update_2013/chap130.pdf
2. Modi GK, Jha V. The incidence of end-stage renal disease in India: a population-based study. Kidney Int., 2006 Dec; 70(12): 2131–3.
3. Kher V. End-stage renal disease in developing countries. Kidney Int., 2002 Jul; 62(1): 350–62.
4. Jaar BG, Khatib R, Plantinga L, Boulware LE, Powe NR. Principles of Screening for Chronic Kidney Disease. Clin J Am Soc Nephrol., 2008 Mar 1; 3(2): 601–9.

5. Mann JF, Gerstein HC, Pogue J, Bosch J, Yusuf S. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. Ann Intern Med., 2001 Apr 17; 134(8): 629–36.
6. Lindholm LH, Ibsen H, Dahlöf B, Devereux RB, Beevers G, de Faire U, et al. Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomized trial against atenolol. Lancet Lond Engl., 2002 Mar 23; 359(9311): 1004–10.
7. Gerstein HC, Mann JF, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA, 2001 Jul 25; 286(4): 421–6.
8. Ishani A, Grandits GA, Grimm RH, Svendsen KH, Collins AJ, Prineas RJ, et al. Association of Single Measurements of Dipstick Proteinuria, Estimated Glomerular Filtration Rate, and Hematocrit with 25-Year Incidence of End-Stage Renal Disease in the Multiple Risk Factor Intervention Trial. J Am Soc Nephrol., 2006 May 1; 17(5): 1444–52.
9. White SL, Yu R, Craig JC, Polkinghorne KR, Atkins RC, Chadban SJ. Diagnostic accuracy of urine dipsticks for detection of albuminuria in the general community. Am J Kidney Dis Off J Natl Kidney Found., 2011 Jul; 58(1): 19–28.
10. Waheed S. Acknowledgements. Assessment of proteinuria [Internet]. [cited 2016 Feb 8]. Available from: http://bestpractice.bmj.com/best-practice/monograph/875.html
11. Singh AK, Farag YMK, Mittal BV, Subramanian KK, Reddy SRK, Acharya VN, et al. Epidemiology and risk factors of chronic kidney disease in India - results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. BMC Nephrol., 2013; 14: 114.
12. Buderer NMF. Statistical Methodology: I. Incorporating the Prevalence of Disease into the Sample Size Calculation for Sensitivity and Specificity. Acad Emerg Med., 1996 Sep 1; 3(9): 895–900.
13. KDOQI CKD Guidelines [Internet]. [cited 2015 Oct 18]. Available from: http://www2.kidney.org/professionals/KDOQI/guidelines_ckd/p4_class_g1.htm
14. GFR Calculator [Internet]. CKD-EPI. [cited 2016 Jan 2]. Available from: http://ckdepi.org/equations/gfr-calculator/
15. Michels WM, Grootendorst DC, Verduijn M, Elliott EG, Dekker FW, Krediet RT. Performance of the Cockcroft-Gault, MDRD, and New CKD-EPI Formulas in Relation to GFR, Age, and Body Size. Clin J Am Soc Nephrol CJASN, 2010 Jun; 5(6): 1003–9.