Diagnostic accuracy of a urine dipstick for detecting albuminuria in hypertensive patients [version 2; peer review: 2 approved with reservations]

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Abstract

Background: Screening for albuminuria is generally recommended among patients with hypertension. While the urine dipstick is commonly used for screening urine albumin, there is little evidence about its diagnostic accuracy among these patients in Thailand. This study aimed to assess the diagnostic accuracy of a dipstick in Thai hypertensive patients for detecting albuminuria.

Methods: This study collected the data of 3,067 hypertensive patients, with the results of urine dipstick and urine albumin-to-creatinine ratio (ACR) from random single spot urine being examined in the same day at least once, at Lampang Hospital, Thailand, during 2018. For ACR, a reference standard of ≥ 30 mg/g was applied to indicate the presence of albuminuria.

Results: The sensitivity, specificity, positive predictive value (PPV), and negative predictive value of the trace result from dipsticks were 53.6%, 94.5%, 86.5%, and 75.5%, respectively. The area under the receiver operating characteristic curve of the dipstick was 0.748.

Conclusion: Using the dipstick for screening albuminuria among hypertensive patients should not be recommended for mass screening due to its low sensitivity. In response to high PPV, a trace threshold of the dipstick may be used to indicate presence of albuminuria.

Keywords
hypertension, albuminuria, urine dipstick, diagnostic test

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2

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15 Oct 2020

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2. Polathep Vichitkunakorn, Prince of Songkla University, Songkhla, Thailand

Any reports and responses or comments on the article can be found at the end of the article.
Introduction

Strong evidence has indicated that the presence of albuminuria in hypertensive patients is associated with the development of chronic kidney disease (CKD), which increases the risk of cardiovascular-related morbidity and mortality\(^1,2\). Early detection of CKD is important as either angiotensin-converting-enzyme inhibitor drugs or angiotensin II receptor blocker drugs can be added to a patient’s treatment regimen to slow down the progress of the disease and thus reduce all-cause mortality.

Detection of albumin in urine plays an important role in diagnosing CKD in the early stages. Regarding the detection of albumin in urine, urine albumin-to-creatinine ratio (ACR) has widely been recommended to be used in diagnosing albuminuria, which is defined as the amount of urine albumin divided by urine creatinine \(\geq 30 \text{ mg/g} \geq 3 \text{ mg/mmol}\)\(^3,4\).

Despite the recommendations, performing ACR in all patients with hypertension is not always applicable, particularly in a primary care unit in rural or outreach areas where the necessitated resources may be unavailable. Practically, the urine dipstick is a test that has widely been used to identify the presence of albumin in the urine due to its low cost and high accessibility.

Although using the urine dipstick is pragmatic, existing literature has not affirmed the accuracy of the test. Previous research has revealed a variety of diagnostic accuracy of the urine dipstick, compared with ACR. While some studies suggest that the dipstick is inappropriate for screening albuminuria\(^5,6\), others conclude that trace albuminuria from a dipstick can be used to indicate the presence of urine albumin\(^7\).

Owing to result inconsistencies, it is still arbitrary as to whether or not positive findings of albumin from a urine dipstick could be used to confirm presence of albuminuria. Additionally, there is as yet no evidence to demonstrate if diagnostic results would be consistent across populations. Therefore, this study aimed to assess the diagnostic accuracy of a dipstick in Thai hypertensive patients for detecting albuminuria.

Methods

Participants

This analysis is based on retrospective data from patients who visited Lampang Hospital from January to December 2018. The study included patients aged 18 years and over who were diagnosed with hypertension, ICD10 code “I10-14”, with the results of urine dipstick and ACR from random single spot urine being examined in the same day at least once. Laboratory results from the last visit were used if multiple results of a urine dipstick and ACR on the same day were presented within the same patient. Patients with urinary tract infections were excluded from the study.

This study protocol was approved by the Ethics Committee at Lampang Hospital (No.79/62). Consent of the patients to use their data in the study was waived by the ethical committee due to the retrospective nature of the study.

Reference standard and index test

ACR was a reference standard to indicate the level of urine albumin. Evaluation of ACR was performed at Lampang Hospital using the immunoturbidimetric essay by AU5800/DxC700AU. The result of ACR \(\geq 30 \text{ mg/g}\) indicates the presence of albuminuria\(^8\).

This study employed the urine dipstick, “URiSCAN 9 SG” and the analyzer “URiSCAN SUPER+”, as an index test. Interpretation of the results were based on the color changes on the indicator tetrabromophenol blue in the presence of urine albumin. A positive reaction is indicated by a color change to yellow or green, reflecting the albumin results of negative, trace, 1+, 2+,3+, and 4+.

Covariates

Demographic characteristics including age and sex were collected for use in the analysis. Body mass index was calculated by weight in kilograms divided by squared height in centimeters\(^9\). Glomerular filtration rate (GFR) was estimated using the formula eGFR = 141 × min(S\(_\text{cr}/\text{k}, 1)\(^{10}\) × max(S\(_\text{cr}/\text{k}, 1)\(^{11}\) 1.209 × 0.993\(_{\text{se}} \times 1.018 \text{ [if female]}\) × 1.159 \text{ [if Black]}\(^11\). Information about patients’ underlying disease of diabetes was obtained from the diagnosis in the hospital’s electronic medical record with ICD10 code “E10-14”\(^16\).

Statistical analysis

Chi-squared test and t-test were applied to explore the association between the presence of albuminuria from ACR and covariates, with a significance level of 0.05. Sensitivity, specificity, positive predictive value, and negative predictive value of the dipstick were calculated, with 95% confidence intervals. The area under the receiver operating characteristic curve was approximated to demonstrate the test performance\(^17\). Subgroup analyses using the trace threshold of dipstick were performed to elucidate the diagnostic accuracy of the test among subgroups. Statistical analyses were performed using STATA version 13\(^18\).

Results

A total of 3,067 hypertensive patients matched the study criteria and were included in the analysis (Table 1). Approximately 39.8% of the samples presented with albuminuria. The mean age of the patients was 63.7 year, with ~40% being men. Diabetes appeared among 73.7% of the patients; 17.7% of them had eGFR <60 ml/min/1.73m\(^2\). Albuminuria was present in 24.5% of those with negative result from the dipssticks. Distribution of albumin-creatinine ratios with respect to results of urine dipssticks were exhibited in Figure 1.
Table 1. Demographic characteristics of the patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Albumin-to-creatinine ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;30 mg/g</td>
<td>≥30 mg/g</td>
</tr>
<tr>
<td>Total, n</td>
<td>1,847</td>
<td>1,220</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>736 (39.9)</td>
<td>484 (39.7)</td>
</tr>
<tr>
<td>Female</td>
<td>1,111 (60.2)</td>
<td>736 (60.3)</td>
</tr>
<tr>
<td>Age years, mean±SD</td>
<td>63.52±10.3</td>
<td>64.0±10.7</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>1,326 (71.8)</td>
<td>934 (76.6)</td>
</tr>
<tr>
<td>eGFR &lt;60 mL/min/1.73 m², n (%)</td>
<td>350 (19.0)</td>
<td>194 (15.9)</td>
</tr>
</tbody>
</table>

Table 2 demonstrated the sensitivity, specificity, positive and negative predictive values of urine dipstick in detecting albuminuria. It is seen that sensitivity of 53.6% was observed when the trace threshold was applied, whereas cutoff of ≥2+ and higher yields 100% test specificity. The area under the receiver operating characteristic curve was 0.7482 (Figure 2).

Comparing diagnostic accuracy of the dipstick, it appears that sensitivity, specificity, along with positive and negative
Table 2. Sensitivity, specificity, positive and negative predictive values of urine dipstick to detect albuminuria.

<table>
<thead>
<tr>
<th>Cutoffs</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥Negative</td>
<td>100.0</td>
<td>0.0</td>
<td>39.8</td>
<td></td>
</tr>
<tr>
<td>≥Trace</td>
<td>53.6</td>
<td>94.5</td>
<td>86.5</td>
<td>75.5</td>
</tr>
<tr>
<td>≥1</td>
<td>31.1</td>
<td>99.6</td>
<td>98.2</td>
<td>68.6</td>
</tr>
<tr>
<td></td>
<td>95% CI 28.5-33.1</td>
<td>95% CI 99.2-99.8</td>
<td>95% CI 96.3-99.3</td>
<td>95% CI 66.8-70.4</td>
</tr>
<tr>
<td></td>
<td>95% CI 50.8-56.4</td>
<td>95% CI 93.3-95.5</td>
<td>95% CI 83.9-88.9</td>
<td>95% CI 73.7-77.3</td>
</tr>
<tr>
<td>≥2</td>
<td>12.5</td>
<td>100.0</td>
<td>100.0</td>
<td>63.4</td>
</tr>
<tr>
<td></td>
<td>95% CI 10.7-14.5</td>
<td>95% CI 99.8-100.0</td>
<td>95% CI 97.6-100.0</td>
<td>95% CI 61.6-65.1</td>
</tr>
<tr>
<td>≥3</td>
<td>2.7</td>
<td>100.0</td>
<td>100.0</td>
<td>60.9</td>
</tr>
<tr>
<td></td>
<td>95% CI 1.9-3.8</td>
<td>95% CI 99.8-100.0</td>
<td>95% CI 89.4-100.0</td>
<td>95% CI 59.1-62.6</td>
</tr>
<tr>
<td>≥4</td>
<td>0.7</td>
<td>100.0</td>
<td>100.0</td>
<td>60.4</td>
</tr>
<tr>
<td></td>
<td>95% CI 0.3-1.3</td>
<td>95% CI 99.8-100.0</td>
<td>95% CI 63.1-100.0</td>
<td>95% CI 58.6-62.1</td>
</tr>
</tbody>
</table>

CI, confidence interval.

Figure 2. Receiver operating characteristic curve for the performance of dipsticks in detecting albuminuria.

predictive values were approximately the same in all subgroups (Table 3).

Discussion
Existing studies have manifested a wide range of positive predictive values (PPVs) of urine dipsticks among patients with hypertension, ranging from 27 to 82%. However, none have been conducted in a Thai population. Results of this study, exploring the diagnostic accuracy of the dipstick in a Thai population, not only illustrates the outcomes in this specific population, but can also be used in comparison with results from other populations for a better understanding of test accuracy.

Previous research has documented the differences in sensitivity and specificity of the dipstick across populations. A Japanese study showed sensitivity, specificity, and PPV of 37.1%, 97.3%, and 71.4%, respectively. Another study conducted in Australian adults showed sensitivity, specificity, and PPV of 69.4%, 86.8%, and 27.1%, respectively. One possible explanation for the difference in diagnostic accuracy of the dipstick was owing to differences in the characteristics...
Table 3. Diagnostic performance of the urine dipstick result of trace and higher for detection of albumin-to-creatinine ratio ≥ 30 mg/g.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All samples</td>
<td>53.6</td>
<td>94.5</td>
<td>86.5</td>
<td>75.5</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>54.6</td>
<td>94.2</td>
<td>86.0</td>
<td>75.9</td>
</tr>
<tr>
<td>Female</td>
<td>53.0</td>
<td>94.7</td>
<td>86.9</td>
<td>75.6</td>
</tr>
<tr>
<td>Age group, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>52.6</td>
<td>93.8</td>
<td>84.7</td>
<td>75.3</td>
</tr>
<tr>
<td>≥60</td>
<td>54.1</td>
<td>94.8</td>
<td>87.5</td>
<td>75.6</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>54.2</td>
<td>94.3</td>
<td>87.1</td>
<td>74.5</td>
</tr>
<tr>
<td>No</td>
<td>51.8</td>
<td>94.8</td>
<td>84.6</td>
<td>78.1</td>
</tr>
<tr>
<td>eGFR category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥60 mL/min/1.73 m²</td>
<td>54.4</td>
<td>94.3</td>
<td>86.8</td>
<td>75.1</td>
</tr>
<tr>
<td>&lt;60 mL/min/1.73 m²</td>
<td>49.5</td>
<td>95.1</td>
<td>85.0</td>
<td>77.3</td>
</tr>
<tr>
<td>Body mass index category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;23</td>
<td>56.1</td>
<td>93.3</td>
<td>83.6</td>
<td>77.8</td>
</tr>
<tr>
<td>≥23</td>
<td>52.6</td>
<td>95.0</td>
<td>87.9</td>
<td>74.5</td>
</tr>
</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value

of the populations\(^7\). The other study points out variation in the calibration of the dipstick as another explanation for differences between populations\(^8\). Compared with previous reports, diagnostic parameters shown in this study affirms variation in diagnostic performance of the dipstick across populations. This implies that the assessment of dipstick performance should be recommended for different populations.

It should be noted that false positive results of the dipstick could come from highly alkaline urine and contamination of antiseptics. Moreover, urine specimens used in this study came from random spot urine collection, which may be subjected to false positive results. Likewise, false negative results may have occurred due to excessive hydration before collecting the urine specimen, which leads to a decrease in concentration of urine albumin and subsequently a smaller chance of detecting albuminuria.

Such low sensitivity of 53% from the urine dipstick indicates that almost half of the patients with albuminuria cannot be identified using just the urine dipstick. It is also seen that among patients with a negative albumin result from the dipstick, albuminuria was found in nearly a quarter of them. This outcome well aligns with previous studies asserting low sensitivity of the dipstick in detecting albuminuria\(^6,11\). Given strong evidence indicating the high probability of cases being undetected, using the dipstick alone should not be recommended for use in screening of albuminuria among hypertensive patients.

Results from the study revealed a rather high predictability of the dipstick in detecting urine albumin. Concerning the dipstick cutoffs, applying the trace threshold yields a PPV of 86.5%, compared with 98.2% and 100% using the 1+ and 2+ thresholds, respectively. Though a rather high chance of predicting albuminuria once hypertensive patients have these results of trace or higher from the dipstick, it should be borne in mind that albuminuria may be overly diagnosed with the application of the trace threshold, compared with using the higher cutoffs.

Although excellent PPV can be achieved when employing higher thresholds of the dipstick, drawbacks remain when the recommendation for using the high threshold is applied due to fewer patients being applicable. Considering the trade-off between PPV and applicability of the dipstick results, the trace threshold may be recommended for indicating the presence of albuminuria in hypertensive patients.

Even though the KDIGO guidelines\(^3\) have recommended the use of ACR to indicate the presence of albuminuria, this is proven
to be rather costly and not readily available in some regions. Limitations, regarding the availability and costs of ACR, may arise when considering the application of ACR for routine screening of hypertensive patients. Nonetheless, evidence has demonstrated a low sensitivity of urine dipsticks, which should not be recommended for screening albuminuria. Hence, ACR is deemed the option for screening albuminuria in the setting where resources are available.

Conclusion

While existing evidence is controversial to whether the urine dipstick should be recommended for screening albuminuria in hypertensive patients, results from this study demonstrated that the dipstick has such low sensitivity in detecting albumin in urine in the Thai population. These results suggest that the urine dipstick not be recommended for screening urine albumin in patients with hypertension. In contrast, results of trace or higher yields high PPV, indicates a very high possibility of the presence of microalbuminuria.

Data availability

Underlying data


Reporting guidelines


Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Acknowledgements

The authors would like to thank Dr. Thanawat Vongchaudomchoke, nephrologist, and Dr. Napat Phetkub for their valuable comments.

References

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Current Peer Review Status:  

Reviewer Report 16 July 2021

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Surendran Deepanjali
Department of Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, Puducherry, India

The authors have modified the manuscript based on some of the suggestions given in the last review. However, a few points still require further clarification.

1. Abstract: If the authors’ point is that the high PPV is helpful in interpreting the result of an already performed test in that particular study population, then it should be made sufficiently clear in the manuscript. I would like to maintain that discussing the utility of the high PPV of the test after recommending against the use of the test is confusing.

2. Introduction: Reference no.4 is a study comparing 24-hour urinary albumin estimation versus urine spot ACR in patients with diabetic patients. How are the results from this study relevant?

3. Methods: “Laboratory results from the last visit were used if multiple results of a urine dipstick and ACR on the same day were presented within the same patient.” Do the authors mean that the last one of the multiple tests done on the same day was considered for inclusion in the study?

4. The method used to exclude patients with UTI should be mentioned in the manuscript.

5. Results: In my opinion, giving the PPV for \( \geq \) negative test result is not intuitive (in Table 2). This could be modified as > Negative.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: urinary tract infections, medical philosophy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have
significant reservations, as outlined above.

Author Response 23 Sep 2021

Win Techakehakij, Lampang Hospital, Thailand, Amphur Muang, Thailand

Abstract: If the authors' point is that the high PPV is helpful in interpreting the result of an already performed test in that particular study population, then it should be made sufficiently clear in the manuscript. I would like to maintain that discussing the utility of the high PPV of the test after recommending against the use of the test is confusing.

- We rechecked throughout the manuscript to ensure emphasis of the Thai population was appropriately addressed.
- As stated in the previous response, implication of the use of sensitivity and PPV information are different. Thus, we briefly provided the key messages of both issues for the audiences.

Introduction: Reference no.4 is a study comparing 24-hour urinary albumin estimation versus urine spot ACR in patients with diabetic patients. How are the results from this study relevant?

- We removed the reference no.4.

Methods: “Laboratory results from the last visit were used if multiple results of a urine dipstick and ACR on the same day were presented within the same patient.” Do the authors mean that the last one of the multiple tests done on the same day was considered for inclusion in the study?

- It is correct that the last UA results were used in the study if multiple tests were done on the same day. This is as, in reality, there is sometimes errors in performing laboratory test or in reporting results, which require a re-test. Thus, we decidedly chose the last result to minimize these errors.

The method used to exclude patients with UTI should be mentioned in the manuscript.

- We added “Patients with the urine results containing white blood cell more than 5-10 cells per high power field were suspected of having urinary tract infections, and thus were excluded from the study” in the method section.

Results: In my opinion, giving the PPV for ≥ negative test result is not intuitive (in Table 2). This could be modified as > Negative.

- We suggest to keep the ≥ negative results as providing the results of “≥ negative” is beneficial to audiences to know the prevalence of albuminuria among the study population.
Polathep Vichitkunakorn
Department of Family and Preventive Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

The authors examined the diagnostic accuracy of urine dipstick on albuminuria among hypertensive patients in Thailand. This study tried to reveal the sensitivity, specificity, positive predictive value, and negative predictive value of the tool. This is very useful for urine dipstick in many health care settings.

The manuscript is clear and well documented. The rationale is well established. The authors applied appropriate methods for data analysis and the results were convincing.

However, to improve paper readability, minor changes are required. I suggest the following:
- The introduction did not discuss the heterogeneity of various accuracy of urine dipstick.
- The authors selected the laboratory results from the last visit. It would be great if you can provide the rationale for this selection method.
- The logic for calculating the sample size is missed in this manuscript. The authors may add the calculation of sample size or power analysis.
- Table 1: Regarding rounding decimals, the “63.52” should be “63.5”.
- Figure 1: Please explain or discuss the outlier (i.e., ACR ~ 5000+ in the Negative group).
- Table 2: the “95%CI” can be moved to the first row of the table.
- For discussion, the limitations and implications for this research should be mentioned for the readers.

Thank you for the opportunity of reading and evaluating this paper.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 05 Jul 2021

**Win Techakehakij**, Lampang Hospital, Thailand, Amphur Muang, Thailand

The heterogeneity of dipstick results was discussed in details in the discussion.

In case that there are more than one laboratory results within the same person, we decided to include only one result from each sample to reduce the bias from individuals who had undertaken the tests many times. Results from the last visit were decidedly selected in order to obtain the most recent outcomes in this regard.

From the Bujang and Adnan (2016), with the prevalence of approximately 40%, the minimum sample size of 408 would yield the conventionally acceptable power of 0.804. However, this study contained a lot more samples of 3,067, which far exceeds the minimum to reassure the accuracy and reliability of the analysis.

Decimal points were rounded to one digit for percentage and 3 digits for p-value.

False negative results from dipsticks, including some outliers, ordinarily exist to indicate imperfect predictability of the index test. Possible explanation was described in the discussion part “Likewise, false negative results may have occurred with excessive hydration before collecting the urine specimen, which leads to a decrease in concentration of urine albumin and subsequently a smaller chance of detecting albuminuria.”.

Owing to the limited space available in the table, we moved the 95%CI to the second line to improve readability for the audiences.
The main limitation of this research is the externality of the results. This is because the samples were chosen from only one hospital in the northern Thailand, which may not well represent the diagnostic accuracy of the test in other populations, particularly with differential prevalence of albuminuria. This limitation is genuinely the gaps and rationale of this research, which was mentioned in the introduction.

Concerning the implication, this research mentioned the interpretation and applicability of the results in the discussion part: “results from this study demonstrated that the dipstick has such low sensitivity in detecting albumin in urine. These results suggest that the urine dipstick not be recommended for screening urine albumin in patients with hypertension. In contrast, results of trace or higher yields high PPV, which indicates a very high possibility of the presence of microalbuminuria.”

Reference


Competing Interests: None declared

Review Report 14 June 2021

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Surendran Deepanjali
Department of Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, Puducherry, India

Panta P et al conducted a retrospective study to evaluate the performance of urine dipstick testing for albumin compared to urine albumin-creatinine ratio (ACR) in patients with hypertension. The study population included 3067 subjects of Thailand. The authors found that urine dipstick at the trace positive cut-off has modest sensitivity for detecting ACR of 30mg/g or more. The authors conclude that urine dipstick test cannot be used to screen albuminuria in hypertensive patients. Overall the manuscript is well-written. However, there are a set of issues to be addressed in the study.

Major comments:

Abstract
1. Authors state that “there is little evidence” about the diagnostic accuracy of dipstick testing
for albuminuria. This information is not accurate since the authors themselves cite studies addressing this issue in the Introduction and Discussion.

2. The conclusion reads “Using the dipstick for screening albuminuria among hypertensive patients should not be recommended due to its low sensitivity. In response to high PPV, a trace threshold of the dipstick may be used to indicate presence of albuminuria.” After having stated that dipstick testing should NOT be recommended, it is redundant to suggest a ‘trace’ threshold for albuminuria.

Introduction

1. Although ACR is the ideal test for albuminuria, urine dipstick analysis finds mention as part of initial work up of hypertension in existent guidelines on hypertension (ISH CPG 2020, ESH 2018). Hence in the Introduction authors should elaborate more on the advantages and disadvantages of using the dipstick in comparison to ACR. The references 3-5 do not seem to be appropriate as evidence of recommending ACR for measuring albuminuria.

2. In the last paragraph of Introduction, it is given whether urine dipssticks “confirm” the presence of albuminuria which is not conforming to the ideas in the previous paragraph where it is mentioned as a tool for “screening”.

Methods

1. It is mentioned under Participants that “Laboratory results from the last visit were used if multiple results of a urine dipstick and ACR on the same day were presented within the same patient.” It is not clear whether some patients had both the tests repeated on multiple days or multiple results on the same day were available.

2. How did authors exclude patients with UTI?

3. It is not clear whether the urine dipstick reading was done by visual inspection or automated analyzer. An internet search for EH 2080 reveals it is a urine sediment analyzer. Why was this instrument used for interpreting dipsticks?

4. For calculating BMI and eGFR data on height and weight and serum creatinine were collected. Was it done on the same visit as the urine tests or within any given time frame?

Results

1. The authors have not stated what proportion of the study population was detected to have albuminuria in the text. The information has to be deducted from Table 1. Also, it will be more informative if the albuminuria estimated by ACR is quantified into meaningful groups like moderately or severely increased albuminuria. How the dipstick performed in these two groups can also be compared; for example, as given in Reference no.19.

2. It is not clear why statistical tests of significance were used for comparison of 2 ACR groups in Table1. It seems like proportion of diabetic patients with albuminuria is less compared to those without diabetes. The same for CKD also. If the authors want to point out any specific finding through these comparisons it has to be stated in the text. Likewise, comparison of dipstick results between the two groups conveys no extra information.

3. The information provided in Table 2 is not clear. Terms like “≥Negative” and “≥trace” are confusing. A sensitivity of 100% and PPV of 40% for a negative test?

Discussion

1. Although the authors have compared their results, especially the low sensitivity of dipstick, with other studies in literature, they have not interpreted their study results thoroughly. The trade-off between the low sensitivity and the good PPV have to be interpreted in terms of population in which the dipstick testing will be employed. According to this study, a trace positive result has 98% PPV in this particular hypertensive population where 70% were
diabetic too. The authors could discuss whether the test is still worthy of use from the cost-benefit point of view.
2. If the authors however are maintaining that the test should not be recommended because of low sensitivity, then suggesting a trace threshold for interpretation of test result is superfluous.
3. The ‘variation in calibration’ as a cause for differing diagnostic performance characteristics across populations is not clear enough. Does this apply only to automated analyzer results?
4. The authors state that proteinuria will be over-diagnosed with trace threshold. This point is also not substantiated since a test with a PPV of 98-100% will not have a high false-positivity rate.

Conclusion
1. As mentioned previously in the comments on Abstract, the conclusion has to be re-written without ambiguities.

Minor comments:
1. References 3, 5, 14, 15 & 16 are not correctly cited.
2. The figshare dataset shows age and BMI represented with almost 10 decimal points precision. I would suggest approximating it 2 or 3 decimal points for better representation.
3. The figshare dataset does not give the results of dipstick testing.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: urinary tract infections, medical philosophy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
Win Techakehakij, Lampang Hospital, Thailand, Amphur Muang, Thailand

Abstract
1. We added “in Thailand” in the text to clarify the scarce of evidence in this area of research.

1. The sentence, “Using the dipstick for screening albuminuria among hypertensive patients should not be recommended due to its low sensitivity”, interprets the implication of the sensitivity of the test, in which it may not be appropriate to apply for mass screening. In this regard, we added “for mass screening” in the text to improve clarity of the content.

On the other hand, the sentence, “In response to high PPV, a trace threshold of the dipstick may be used to indicate presence of albuminuria”, reflects another practical point of using of PPV result when the patients already presenting with results from dipsticks. Unlike the suggestion for mass screening, the PPV suggests that a trace result yields a rather high possibility of the presence of albuminuria and thus may be recommended for use in clinical practice.

Introduction
1. The use of ACR as the gold standard for detecting albuminuria is recommended by the Renal Association, with supportive evidence. All the evidence was available in reference 3-5. The pros and cons of using dipsticks in comparison with ACR were discussed in the latter 2 paragraphs with supportive references 6-11.

2. To figure whether urine dipsticks “confirm” the presence of albuminuria does conform the ideas of this paper, which is to explore diagnostic accuracy of the test. Results from diagnostic accuracy can be applied to recommendations for both public screening and clinical diagnosis, as demonstrated in this paper.

Methods
1. This means in case of that the patients had multiple results on the same day, as mentioned in the previous sentence, “The study included patients aged 20 and over who were diagnosed with hypertension, ICD10 code “I10-14”, with the results of urine dipstick and ACR from random single spot urine being examined in the same day at least once."

2. Results of urine dipsticks presenting with red blood cell or white blood cell to the diagnostic criteria of urinary tract infection were construed as urinary tract infection.

3. The urine dipstick reading was done by the automated analyzer. The EH2080 was removed.

4. BMI and eGFR were calculated on the same visit.

Results
1. We added “Approximately 39.8% of the samples presented with albuminuria” to describe the proportion of samples with albuminuria.

Concerning the demonstration of albuminuria level, we decidedly omitted this information...
as this is considered out of the scope of this paper.

1. Statistical analyses shown in Table1 are deemed a compliment to the demonstration of the samples’ characteristics.

2. The terms, e.g., “≥Negative” and “≥trace”, are used when applied the cutoffs for diagnostic test is considered. “≥Trace”, for instance, means that any results with albuminuria higher than the trace level, trace, 1+, 2+, 3+, 4+, were counted.

A 100% sensitivity when applying the negative threshold is explained by the fact that the negative result is the lowest possible outcome of dipsticks. Using the negative threshold, all the samples, with or without albuminuria, would be identified as having albuminuria, resulting in a 100% sensitivity.

**Discussion**

1. For the purpose of mass screening in the population level, it may be appropriate to consider only sensitivity, which exhibits the test ability to uncover all diseased patients from the population. Narrative about this was described in the discussion. In addition, issues about high PPV were also provided in the discussion.

2. The issues about difference in interpretation of sensitivity and PPV were above-mentioned.

3. The ‘variation in calibration’ as a cause of the difference in diagnostic performance could apply to not only automated analyzer, but also the visual analyzer.

4. Albuminuria will be over-diagnosed with trace threshold because of PPV of 86.5%. This means that only 865 of 1,000 patients with trace-or-above results will really have albuminuria. Approximately 13.5% will thus be wrongly/overly diagnosed with albuminuria.

**Conclusion**

Explanation was described above.

**Minor comments:**

1. References were re-checked respecting to the Vancouver style.

2. Information in the dataset was provided with details for the users.

3. Results of the dipsticks were provided with labels.

**Competing Interests:** None declared
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