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Utility of dipstick urinalysis in the diagnosis of urinary tract infections among outpatients in Mwanza and Dar es Salaam regions in Tanzania

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Abstract

Background Globally, urinary tract infections (UTIs) are the leading cause of hospital visits, especially among women. In many developing countries, especially in lower health facilities, the dipstick urinalysis is the most commonly requested test, as urine culture is not routinely performed. The dipstick test can potentially reduce the number of patients who could be treated with empirical antibiotics and reduce the burden of antibiotic resistance. The current study determined the utility of dipstick urinalysis in diagnosing UTIs using urine culture as a gold standard method.

Methods A cross-sectional study was conducted between July and November 2021. The study involved 1327 outpatients attending lower health centres in Mwanza ($n=678$) and Dar es Salaam ($n=649$) regions. The samples were subjected to dipstick urinalysis (nitrite and leucocytes) and quantitative bacterial culture.

Results Of all 1326 patient samples, 808(60.9%) and 48(3.6%) were positive for urinary leucocyte and nitrite, respectively, while significant urine culture was found in 364(27.4%). leucocyte test correctly diagnosed UTI in 283 (77.75%) and nitrite test in 36 (9.89%). The leucocytes and nitrites, in combination, exhibited a sensitivity of 79.40% and NPV of 85.24% but a lower specificity of 44.96% and a lower PPV of 35.29%. Urinary leucocyte test had a higher discrimination ability to detect urinary tract infection than urinary nitrite test (AUC = 0.073, 95% CI 0.043–0.103, $p<0.001$); likewise, combined results of urinary nitrite and leucocytes tests had higher discrimination ability to detect UTI than nitrite only (AUC = − 0.079, 95% CI − 0.107–0.050, $p<0.001$).

Conclusions In settings where culture is available, dipstick urinalysis can be a helpful screening method for reducing unnecessary urine cultures and related expenses because of its higher negative predictive value. In most low-resource settings where patients' diagnosis solely depends on clinical diagnosis and culture is not easily available, urine dipstick can decrease the risk of overuse of antibiotics. However, the combined (leucocytes and nitrites) dipstick urinalysis has a rather low positive predictive value, with approximately one-third of cases giving positive test results being truly UTI, subjecting over 65% of cases to unnecessary antibiotic treatment.

Keywords Leucocyte esterase, Negative predictive value, Nitrite, Positive predictive value, Sensitivity, Specificity, Urinalysis dipstick, Urine culture

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Background

Urinary tract infection (UTI) is among the most common infectious diseases, contributing to a large part of the workload in clinical laboratories (Wilson and Gaido 2004). In Tanzania, culture-based laboratory-confirmed UTIs range from 11 to 23% among different populations (Msaki et al. 2012; Chaula et al. 2017; Gidabayda et al. 2017; Mwambete and Malaba 2017). Adoption of urine culture, a gold standard technique, is limited to higher healthcare facilities such as regional and zonal referral hospitals. On the other hand, in lower healthcare facilities (dispensaries, health centres, and district hospitals), dipstick urinalysis is commonly ordered to diagnose UTI.

Usually, to initiate UTI treatment based on dipstick urinalysis, one should consider a positive leucocyte esterase and/or nitrite in conjunction with the patient's clinical history (Bates 2013). However, diagnosing UTI using dipstick urinalysis and clinical history is challenging as it can give false-positive results in patients with other underlying illnesses (Wilson and Gaido 2004). Dipstick can reduce the number of patients prescribed antibiotics in settings where diagnosis depends only on the patient's signs and symptoms. Clinical diagnosis without laboratory investigation can lead to unnecessary UTI treatment and healthcare costs from increased over-prescription of antibiotics, which is associated with the emergence and spreading of antimicrobial resistance (Bates 2013).

The biochemical reactions in dipstick urinalysis detect bacteriuria and pyuria by detecting the presence of nitrite and leucocyte esterase in a urine sample, respectively (Wilson and Gaido 2004). Nitrite results from the conversion of nitrate to nitrite by members of the family *Enterobacterales*. On the other hand, leucocyte esterase is associated with the hydrolysis of ester substrate on dipstick strips by esterolytic proteins (esterases) present in both intact and lysed leucocytes in a urine sample (Wilson and Gaido 2004; Gordon et al. 2013; Marques et al. 2017a).

Dipstick urinalysis is a common clinical practice most frequently requested test, especially at point-of-care, emergency medicine departments, and health centres in the majority of healthcare facilities across the world, including Tanzania, where urine (Lei et al. 2020). However, its utility against urine culture as a gold standard test is not well documented. (Sangeda et al. 2021). The lack of evidence-based findings limits our recommendation for the appropriate use of dipstick urinalysis in routine diagnosis of UTI in settings where urine culture is unavailable. Therefore, this study aimed to investigate the utility of dipstick urinalysis (leucocyte and nitrite) in diagnosing UTIs in lower-resource clinical settings of health facilities.

Methods

Study design and population

This cross-sectional study was conducted in lower health centres in Mwanza and Dar es Salaam for a period of five months continuously between July and November 2021. This was a nested study under a big study that determined the prevalence of multidrug-resistant bacteria in urine (Silago et al. 2022). Sampling involved participants from the age of two (men and both non-pregnant and pregnant women) who were residents of a given surveillance area and passively presented for health care. All participants were outpatients with signs and symptoms of UTI occurring <48 h before enrolment (Silago et al. 2022).

Study setting and site selection

The study was conducted in four health facilities, two from Dar es Salaam and two from Mwanza regions. Selected surveillance sites were primary health facilities, i.e. dispensaries and health centres located within 50 km of a laboratory where urine cultures were performed.

Data and urine sample collection

Quantitative data on patients' socio-demographic and clinical characteristics were collected electronically by AfyaData® version 1.4, an open-source software for collecting data from health facilities and submitting it to the main server. On the other hand, laboratory data were captured using the WHONET software 2022, a modernized and expanded version of WHONET 5.6. From each patient, 5 to 10 millilitres of mid-stream urine (MSU) were collected in a sterile urine container and immediately stored in the refrigerator to control the rate of bacterial multiplication that could affect the colony-forming unit (CFU) determination. In all facilities, samples were collected between 0900 and 1200 h and transported in a cool box to the testing laboratory for processing within two hours of collection.

Laboratory procedures

Urinalysis

A urine sample was examined macroscopically for colour and turbidity (e.g. yellow and cloudy, pale yellow and clear) and then by dipstick urinalysis to detect leucocyte esterase and nitrite. The latter was performed and interpreted according to the manufacturer's instructions (Mission® urinalysis; ACON Laboratories, San Diego, California, USA). A positive dipstick was defined as the presence of nitrites or leucocytes greater than or equal to a trace. A negative dipstick was defined as the absence of any reaction for leucocytes and nitrites. Urine dipstick bottles were stored at room temperature, and expiration dates were checked before use. Urine dipstick test results were interpreted according to the manufacturer's instructions.

Urine culture

One microlitre (1 µl) loop was used for quantitative inoculation of urine on MacConkey agar (MCA) with salt (Oxoid, UK), 5% sheep blood supplemented Columbia Blood Agar (BA) (Oxoid, UK), and cysteine–lactose–electrolyte-deficient (CLED) (Oxoid, UK). MCA and CLED plates were incubated aerobically, whereas BA plates were incubated in a candle jar to obtain 5–10% CO_2. All plates were incubated at 35 ± 2 °C for 24 h. Plates were examined for growth, colony morphology, and characteristics on a culture medium. Bacterial counts of ≥ 10^5 CFU/mL of one or two species of microorganisms indicated UTI. Contamination was defined as > 10^5 growth of more than two species or < 105 CFU/ml growth.

Data analysis

Collected data were entered in a Microsoft Excel spreadsheet and transferred to a statistical package for the social sciences (SPSS) version 27 (Armonk, NY: IBM Corp) for analysis. Frequencies and percentages were used for categorical variables, mean (standard deviation (SD)) was used for continuous variables, and descriptive statistics were computed for different attributes. The performance of dipstick urinalysis in detecting UTI cases was evaluated by receiver operating characteristic (ROC) to evaluate the discriminatory power of the urine dipstick test to diagnose UTI. An ROC curve plots the true-positive rate (sensitivity) against the false-positive rate for a diagnostic test's different possible cutoff points. The closer the curve follows the left-hand border and then the top border of the ROC space, the more accurate the test.

Results

A total of 1327 urine samples were tested for UTI using urine culture and dipstick tests for nitrite and leucocyte detection. Of all, 808(60.9%) and 48(3.6%) were positive for urinary leucocyte and nitrite, respectively (Fig. 1). Significant urine culture was found in 364(27.4%).

Performance of urinary leucocyte test

The comparison of dipstick results with urine culture showed that urinary leucocytes had correctly diagnosed the presence of UTI in 283 (77.75%) of the 364 samples with significant bacterial growth in urine culture. In addition, urinary leucocytes had correctly identified the absence of UTI in 438 (45.48%) samples among the 963 samples with no significant bacterial growth in the culture (Fig. 1). The test had a sensitivity (true positives) of 77.75% (95% CI 73.47–82.02), a specificity (true negatives) of 45.48% (95% CI 42.34–48.63%), and positive and negative predictive values of 35.02% (95% CI 31.74–38.31) and 84.39% (81.27–87.52), respectively. Furthermore, urinary leucocytes were found to have positive and negative diagnostic likelihood ratios of 1.43 (95% 1.32–1.54) and 0.49 (95% CI 0.40–0.60), as well as a discriminatory power of detecting the presence of urinary tract infection of 0.616 (95% CI 0.584–0.649), as denoted by the area under the receiver operating curve. (Fig. 2A).

Performance of urinary nitrite test

Urinary nitrite correctly diagnosed the presence of UTI in 36 (9.89%) of the 364 samples with significant bacterial growth in the culture and correctly identified the absence of UTI in 951 (98.75%) among 963 samples with no significant bacterial growth in the culture. However, urinary nitrites' false positive and negative results were 12 and 328, respectively (Fig. 1). The corresponding sensitivity, specificity, positive, and negative predictive values were 9.89% (95% CI 6.82–12.96), 98.75% (95% CI 98.05–99.45), 75.00% (95% CI 62.75–87.25), and 74.35% (95% CI 71.96–76.75), respectively. Furthermore, urinary nitrite was found to have positive and negative diagnostic likelihood ratios of 7.94 (95% CI 4.18–15.08) and 0.91 (95% CI 0.88–0.94), as well as a discriminatory ability to detect the presence of urinary tract infection of 0.543 (95% CI

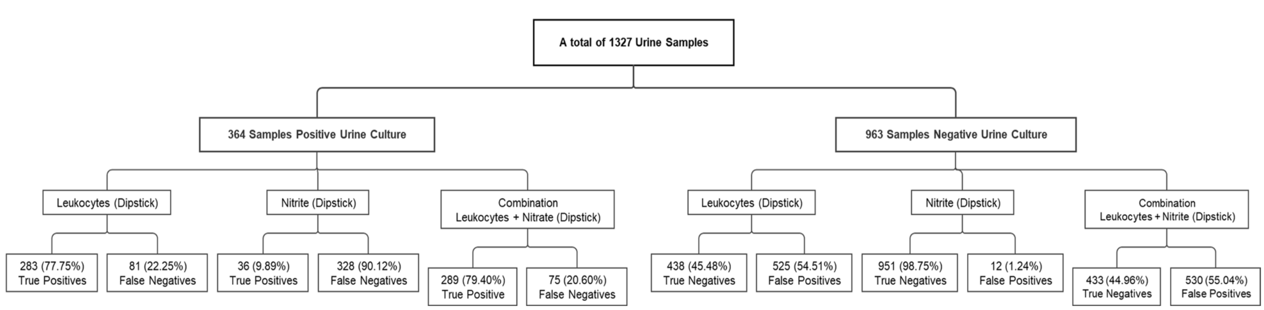

Fig. 1 Comparison of urinary leucocyte and nitrite results of the dipstick methods versus growth of significant bacteria in the urine culture

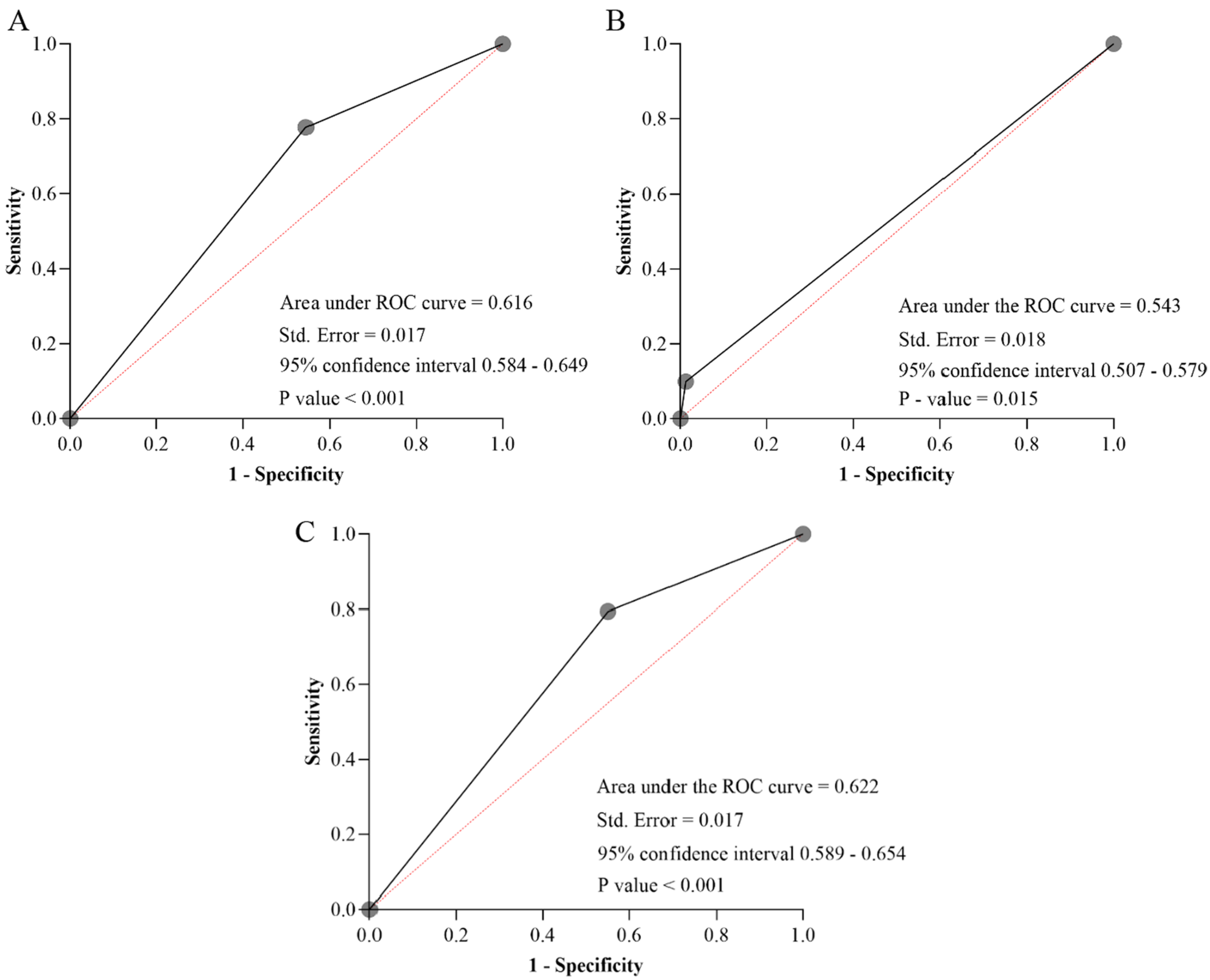

Fig. 2 **A**. Receiver operating characteristics curve of urinary leucocytes in detecting UTI. **B**. Receiving operating characteristics curve of urinary nitrite in detecting UTI. **C** Receiver operating characteristics curve of combined results or urinary leucocytes and nitrites in detecting UTI

0.51–0.58, $P=0.015$), as denoted by the area under the receiver operating curve (Fig. 2B).

Performance of leucocyte and nitrite tests

Combination of urinary leucocyte and nitrite with the presence of either one of them or both regarded as positive for UTI, the urine dipstick correctly diagnosed 289 (79.40%) among 364 samples with significant bacterial growth in the urine culture and correctly identified the absence of UTI in 433 (44.96%) among 963 samples with no significant bacterial growth in the culture (Fig. 1). The combined results of urinary leucocytes and nitrite had sensitivity, specificity, and positive and negative predictive values of 79.40% (95% CI 75.24–83.55), 44.96% (95% CI 41.82–48.11), 35.29 (95% CI 32.01–38.56), and 85.24% (95% CI 82.15–88.32), respectively (Table 1). In addition to that, the combined results were found to have positive

Table 1 Sensitivity, specificity, diagnostic accuracy, positive and negative predictive values, and positive and negative diagnostic likelihood ratios of combination urinary leucocyte and nitrite in diagnosing UTI

Characteristics	95% confidence interval		
	Estimate	Lower CL	Upper CL
Sensitivity (%)	79.40	75.24	83.55
Specificity (%)	44.96	41.82	48.11
Diagnostic accuracy (%)	54.41	51.68	57.11
Positive predictive value (%)	35.29	32.01	38.56
Negative predictive value (%)	85.24	82.15	88.32
Positive diagnostic likelihood ratio	1.44	1.34	1.56
Negative diagnostic likelihood ratio	0.46	0.37	0.57
Diagnostic odds ratio	3.15	2.37	4.18

and negative diagnostic likelihood ratios of 1.44 (95% CI 1.34–1.56) and 0.46 (95% CI 0.37–0.57), respectively, as well as a discriminatory ability to detect the presence of UTI of 0.622 (95%CI 0.59–0.65, $p<0.001$), denoted by the area under the receiver operating curve (Fig. 2C).

The urinary leucocyte test has a higher sensitivity (77.75% vs 9.89%) and a higher negative predictive value (84.39% vs 74.35%) than the urinary nitrite test. On the other hand, urinary nitrite has a higher specificity (98.75% vs 45.48%) and a higher positive predictive value (75.00% vs 35.29%) compared to urinary leucocytes. The combined results of urinary leucocytes and nitrite have even higher sensitivity (79.40%) and negative predictive value (85.24%) than either test alone (Table 2).

Urinary leucocytes had a higher discrimination ability to detect urinary tract infection than urinary nitrite (difference of AUC = 0.073, 95% CI 0.043–0.103, $p<0.001$); likewise, combined results of urinary nitrite and leucocytes had higher discrimination ability to detect UTI than nitrite only (difference of AUC = − 0.079, 95% CI − 0.107–0.050, $p<0.001$). There was no statistically significant difference in the ability to detect UTI between urinary leucocytes and combined results of urinary leucocytes and nitrites (difference of AUC = − 0.006, 95% CI − 0.013–0.001, $p=0.110$) (Fig. 2).

Discussion

This study was part of a surveillance project that aimed to (i) develop a common protocol for surveillance of antimicrobial-resistant bacteria causing community-acquired urinary tract infections in low-income countries and (ii) assess multidrug-resistant bacteria causing community-acquired urinary tract infections. This arm of the study aimed to find the utility of the nitrite/leucocyte dipstick test in screening asymptomatic community-acquired UTIs among suspected adult cases in Tanzania. The dipstick test is usually 'first-line' in the diagnosis of UTI because is easy to test, low cost, and can be used as a point-of-care test. Two components of the dipstick, leucocyte esterase, and nitrites are utilized to diagnose UTIs. leucocyte esterase is released by white blood cells (WBCs) when there is an infection in the urinary tract, which correlates with pyuria. Some gram-negative bacteria, such as Escherichia coli, routinely convert urinary nitrates in the urine into nitrite. Therefore, a positive nitrite test on the urine dipstick suggests the presence of these organisms.

When using leucocytes alone, we found moderate sensitivity (77.75%) and low specificity (45.8%) of leucocytes, while nitrites had a low sensitivity (9.89%) and a high specificity (98.75%). When the two tests were combined, the sensitivity and specificity were found to be 79.40% and 44.96%, respectively. The leucocyte test had higher sensitivity, while the nitrite test had higher specificity.

The high sensitivity and low specificity reported in this study's findings can be attributed to the high number of gram-positive bacteria isolated, evidenced by previously published articles from this research project (Silago et al. 2022). A positive nitrite test result reduces nitrate, a byproduct of some bacteria, mainly those in the *Enterobacterales* family. It is important to remember that some uropathogens, except those in the family *Enterobacterales*, cannot convert nitrate to nitrite, which might occasionally result in false-negative test findings (Demilie et al. 2014; Marques et al. 2017b). The high sensitivity reported in this study may also be attributed to leukocyturia, which is not specific to UTIs and may occur with other inflammatory disorders of the genitourinary tract. Also, false positives can occur in contaminated samples, some dietary factors, certain medications like non-steroid anti-inflammatory drugs, and some medical conditions like dehydration. Leukocyturia may persist after bacteriuria has cleared spontaneously or after treatment (Franz and Hörl 1999; Schumm and Lam 2008). False-negative leucocyte results can occur in different conditions like the presence of atypical bacteria, diluted urine,

Table 2 Comparisons of predictive values and diagnostic likelihood ratios between urinary leucocytes and nitrite in diagnosing UTI

Characteristics	Leucocytes	Nitrites	Difference	Test statistics		*P*—value
Sensitivity	77.74%	9.89%	− 67.86	235.556		< 0.001
Specificity	45.48%	98.75%	53.27	503.191		< 0.001
Characteristics	**Leucocytes**	**Nitrite**	**Ratio**	**95% Confidence Level**		***P*-Value**
				Lower CL	**Upper CL**	
Positive predictive value	35.02%	75.00%	0.47	0.39	0.56	< 0.001
Negative predictive value	84.39%	74.35%	1.14	1.10	1.18	< 0.001
Positive diagnostic likelihood ratio	1.43	7.94	0.18	0.09	0.34	< 0.001
Negative diagnostic likelihood ratio	0.49	0.91	0.54	0.44	0.66	< 0.001

and timing of sample collection. (Early morning sample collection is concentrated compared to later in the day.) (Dadzie et al. 2019)

The leucocyte urine dipstick exhibited positive and negative predictive values of 35.02% and 84.39%, respectively. This implies that when leucocytes are present, there is a 35.02% chance of a true positive, and on the other hand, the absence of leucocytes indicates an 84.39% likelihood of a true negative outcome. On the other hand, the nitrite tests displayed positive and negative predictive values of 75.00% and 74.35%, respectively. These values signify that a positive nitrite test has a 75.00% probability of being a true positive result, and a negative nitrite test has a 74.35% chance of being a true negative result.

Combining the nitrite and leucocyte results showed an increased negative predictive value (NPV) from (urine leucocytes 35.02 and nitrite 74.35 to a combined 85.24%), but a decreased positive predictive value (PPV) (urine leucocytes 84.39% and nitrite 74.35% to combined 35.29%). The combined (leucocytes and nitrites) dipstick urinalysis has a rather low positive predictive value, with 35.29% of cases giving positive test results being truly UTI, subjecting over 64.7% of cases to unnecessary antibiotic treatment. This suggests that the NPV attributed to the combined nitrite, and leucocyte test is a value indicator for ruling out UTI. The increase in NPV is similarly reported in multiple studies showing the importance of urine dipstick screening for community-acquired UTIs (Demilie et al. 2014; Marques et al. 2017b).

A screening urine dipstick test with a high NPV rules out the presence of UTI, eliminating the additional urine culture testing and reducing unnecessary tests and associated costs for the patient and the healthcare system. The estimated cost per urine dipstick is $1, and approximately $7 for urine culture, including additional costs of consumables and personnel. The urine dipstick has a low diagnostic accuracy compared to urine culture; however, with a high NPV and a low cost provides a strong rationale for nominating the urine dipstick as a frontline screening test for community-acquired UTIs (Schumm and Lam 2008; Mignini et al. 2009).

Moreover, combining nitrite and leucocyte esterase tests allows for quicker diagnosis and therapy. When screening tests yield a reliable negative result, healthcare professionals may rule-out UTIs as the underlying cause of the patient's symptoms. The exclusion of UTIs enables healthcare professionals to focus on investigating and addressing other potential conditions, leading to improved patient care and a reduction in unnecessary antibiotic usage (Flokas et al. 2017; Childers et al. 2022). A similar study suggested that urine dipstick should follow a *rule-out* strategy as a negative dipstick test is indicative of a low probability of a positive urine culture, making the diagnosis of UTI unlikely, thus reducing the number of samples for culture and the use of empirical antimicrobial therapy (Ginting et al. 2018). This study finding reports a high NPV of the urine dipstick, supporting this strategy for setting where culture can be performed. The challenge for the rule-out strategy is false-negative urinalysis results. Still, these patients may be asked to return for further testing if symptoms persist, as in some patients, uncomplicated UTIs are a self-limiting condition. The alternative of the *rule-in* strategy is the commonly used method in a setting where culture is unavailable. The urine dipstick is the sole diagnosis method and an indication to start antibiotic treatment (Rousham et al. 2019). The *rule-in* strategy could lead to reduced antimicrobial use compared to clinical diagnosis, where only signs and symptoms are used as criteria to start treating UTI (Ginting et al. 2018). This practice, however, has the potential to overuse antibiotics, fostering the emergence of bacterial strains, reducing the effectiveness of crucial antibiotics as culture is not performed, and treating patients according to antibiotic susceptibility results (Rousham et al. 2019; Ginting et al. 2018).

In countries where culture is not available in most healthcare settings, and most patients are treated empirically by clinical diagnosis, the dipstick test can be applied to reduce the use of antibiotics, given its high NPV. The disadvantage of this test, when used alone without confirmation of culture, is that it has high false-positive results, which can increase the overuse of antibiotics, which may lead to an increase in antibiotic resistance.

Conclusions

Combining leucocytes and nitrite in a dipstick test has a low specificity and PPV. However, the sensitivity and NPV increase. An actual urinary tract infection (UTI) is confirmed only in around one-third of cases with positive results. This situation leads to over 65% of cases receiving unnecessary antibiotic treatment. An inexpensive urine dipstick is useful for excluding UTIs and minimizing the need for needless urine culture tests and related expenses. This test can be used in lower healthcare settings where clinical diagnosis reduces over-prescription of antibiotics. In higher health care settings where culture can be performed, dipstick can be used as a screening tool to reduce the number of samples for culture.

Abbreviations

UTI	Urinary tract infection
CFU	Colony-forming unit
WBCs	White blood cells
PPV	Positive predictive value
NPV	Negative predictive value
ROC	Receiver operating characteristics

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Author contributions
M.I.M., S.E.M., S.S.M., M.M., N.M., E.K., M.M.M., and E.M designed the study and supervised the study; S.S.M, V.S., M.M, F.X.M., S.E.M., H.N., and M.M.M. participated in oversee the laboratory work; S.S.M, V.S., and P.K performed data interpretation, cleaning, and analysis; all authors participated in drafting the manuscript, led by S.S.M, P.K, V.S, M.M, M.I.M., and S.E.M. All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials
All data for this article are presented in this manuscript; more data can be requested from the corresponding author.

Declarations

Ethics approval and consent to participate
Ethical clearance to conduct this study was received from the National Institute for Medical Research (NIMR); certificate numbered NIMR/HQ/R.8a/Vol. IX/3580. Permission to conduct the study was requested from the Regional Medical Officers (RMOs) of Mwanza and Dar es Salaam. Medical Officer In-charges (MOIs) of each health facility where sampling was done. Patients were requested to sign written informed consent forms before enrolling after the study's main objective was explained. For patients below 18 years, parents or guardians provided signed consent forms and assent for children aged between 5 and 18 years. Unique identification numbers were used to identify patients throughout this study to maintain confidentiality.

Consent for publication
Not applicable.

Competing interests
There were no reported potential conflicts of interest relevant to this article.

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