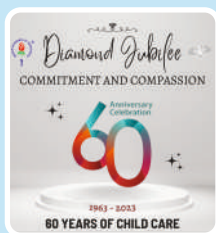


Indian Academy of Pediatrics (IAP)



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Newer **R**esearch and recommendations **I**n **C**hild **H**ealth

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UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023

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Dear fellow IAPans,

nRICH

Newer Research and recommendations In Child Health-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialties of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology, vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

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Diagnostic test accuracy of dipstick urinalysis for diagnosing urinary tract infection in febrile infants attending the emergency department

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BASED ON ARTICLE

Thomas Waterfield, Steven Foster, Rebecca Platt, Michael J Barrett, Sheena Durnin, Julie-Ann Maney, Damian Roland, Lisa McFetridge, Hannah Mitchell, Etimbuk Umana, Mark D Lyttle: On behalf of Paediatric Emergency Research in the UK and Ireland (PERUKI). Arch Dis Child. 2022;107:1095–1099.

SUMMARY

This study was conducted in emergency departments (EDs) of 8 hospitals based in the UK and Ireland. Hospitals in the UK follow NICE CG54 guidelines for UTI which recommends that infants under 3 months of age undergo urine laboratory microscopy analysis rather than point-of-care (POC) urine dipstick analysis.[1]

This retrospective cohort study's objective was to determine the accuracy of the urine dipstick test in correctly diagnosing urinary tract infection (UTI) in infants aged less than 90 days presenting to the ED. The researchers used data from the Febrile Infants Diagnostic Assessment and Outcome (FIDO) study, a multicentre cohort study. Infants up to 90 days of age attending between 31 August 2018 and 1 September 2019 were screened for inclusion by searching clinical software databases. Patients with a recorded fever ($\geq 38^{\circ}\text{C}$) at triage were eligible for inclusion. Exclusion criteria for this secondary analysis included not having either the index test (Siemens Multistix) or the reference test (urine culture) reported or urine collection via either a urine pad or bag.

The Siemens Multistix is a semiquantitative urine test that reports the absence (negative) or presence of leucocytes and nitrites ('trace' to '3+'). On dipstick test leukocyte positive correlate to pus cells and nitrite positive to bacteria in urine routine microscopy respectively. The reference standard was confirmation of UTI defined as the growth of ≥ 100000 cfu/mL of a single organism excluding likely contaminants (lactobacilli, corynebacteria, and coagulase-negative staphylococci) and the presence of pyuria (>5 white blood cells per high-power field) on laboratory microscopy.

A total of 1942 eligible infants were screened, of which 275 were included in the final analysis. Out of the 275 urine samples, 252 (92%) were clean catch samples and 23 (8%) were transurethral bladder catheters (TUBC). In total, 38 (13.8%) participants had a confirmed (non-contaminant) UTI. Of these, 35 (92%) were Escherichia coli; 2 (5%) were Klebsiella; and 1 (3%) was Enterococcus. The median length of stay of infants with confirmed UTI was 72 hours (IQR 45-102). The most sensitive individual dipstick result for UTI was the presence of leucocytes. Including trace as positive resulted in a sensitivity of 0.84 (95% CI 0.69 to 0.94) and a specificity of 0.73 (95% CI 0.67 to 0.79). The most specific individual dipstick result for UTI was the presence of nitrites. Including trace as positive resulted in a specificity of 0.91 (95% CI 0.86 to 0.94) and a sensitivity of 0.42 (95% CI 0.26 to 0.59).

The study concluded that Siemens Multistix as a point of Care urine analysis (POC) is a moderately sensitive and highly specific test to diagnose UTI in febrile infants under 90 days of age. The optimum cut-point for excluding UTI was leucocytes (1+) and the optimum cut-point for confirming UTI was nitrites (trace). Thus, POC urinalysis in infants under 90 days of age has a moderate sensitivity of 0.82 and a specificity of 0.82 for identifying UTIs in this group.

COMMENTARY

It is a very well-known fact that UTI accounts for 80-90% of all serious bacterial infections (SBI) seen in infants.[2] The diagnosis of UTI in young infants is based on urinalysis as the symptoms are non-specific being fever, lethargy, vomiting, and poor feeding. Most Paediatric ER protocols advocate a tailored approach to the assessment and management of febrile infants, including the community management of well-appearing infants with suspected UTIs. [3,4] The advantages of POC urine dipstick analysis over routine urine microscopy are that of quick results, requiring fewer resources, and can be done at sites where the laboratory is unavailable for 24 hours. It is important to diagnose UTI promptly in these febrile infants as it may reduce the length of hospital stay, the need for lumbar puncture, and reduce the use of IV antibiotics. [5,6] In the FIDO study cohort group, the optimum cut point was 1+ leucocytes and trace for nitrite for Siemens Multistix POC dipstick testing. A sensitivity of 82% and specificity of 82% were observed at this cut point. It was observed that the presence of nitrites was highly specific for UTI. The study thus concluded that the presence of nitrites on Siemens Multistix POC urine dipstick is more accurate in confirming UTI than the presence of leucocytes (using cut-point 1+). This is of potential benefit as early identification of UTI in this cohort could minimize the need for further invasive investigations such as a lumbar puncture.

There was a similar study done by Glissmeyer et al for a period of 7 years from 2004 to 2011 and it included a larger sample size of 770. The results showed that the negative predictive value of dipstick was very high being >98% in their study. Also, it was found that urine culture showed some growth within 24 hours in 83% indicating good accuracy of urine dipstick. The sensitivity and specificity of urine dipstick testing of febrile infants as between (95% CI 0.83 to 0.94) and (95% CI 0.91 to 0.94). Higher sensitivity and specificity were seen as in this study urine collection was done by suprapubic aspiration (SPA) or TUBC. However, a study on the subject by Gurang R et al had contrasting results and they found the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of urine dipstick test were 43.75%, 77.51%, 35.59%, and 82.91% respectively. They thus concluded that the dipstick test strip for screening UTI was associated with many false positive and false negative results as compared to the gold standard culture method and that the dipstick nitrite test alone should not be used as the sole method for screening UTI. [7]

The study by Waterfield had a few limitations, like it was a retrospective study, and thus did not include all febrile infants who might have attended the ED at all sites. Also, retrospective data collection adds bias to the study. This study was conducted in pediatric hospitals EDs and thus results cannot be generalized to hospitals without dedicated pediatric EDs. Also, the study population was small, and thus subgroup analysis was not done such as age or symptoms. Additionally, as per the NICE CG54 recommendation, a non-invasive method for urine collection is used at the POC, increasing the chances of contamination and lowering the accuracy of the dipstick test. However, the strengths of the study are that it is a relatively large multicentric study and the first to report the

diagnostic test accuracy of POC dipstick urine analysis in the UK and Ireland. The applicability of this study in an Indian setting needs to be validated by more studies. It looks promising as this is a rapid and cost-effective method, easily available, and feasible for bedside diagnosis of UTI. And logically, it should have been by now the standard of care, however, surprisingly not many studies are reported. Detailing further on the subject, the diagnostic accuracy of dipstick testing has been found to widely vary between studies. When applying quality assessment of diagnostic accuracy studies there could be four major reasons behind the variability. First, some studies were laboratory-based, while others were done in outpatient clinics or ED as was the study analyzed. Second, the clinical syndrome of UTI contains an extensive variety of clinical severity which may exert a spectrum impact at the diagnostic accuracy of dipstick testing. Third, most of the research articles did not consider the clinical pre-test probability while interpreting the dipstick results. Finally, in nearly all research articles urine culture showing bacteriuria above a certain threshold was used as the gold standard to diagnose UTI. However, it is well known that not all patients with significant bacteriuria have UTI, and not all cases of UTI yield growth on urine culture. A considerable proportion of patients with suspected UTI presenting in tertiary Care ER settings have received empirical antibiotics which might result in negative cultures. Hence when a new test is compared against an imperfect gold standard with sub-optimal sensitivity, the true prevalence of the disease could be underestimated. Also, the specificity of the new test could be estimated falsely low. One such interesting study in the Indian context in the adult population was done by Bafna P et al [8] in a teaching institute in south India using dipstick tests to diagnose UTI using Bayesian latent class analysis (LCM) to improve diagnostic accuracy. Here the researchers used the statistical analysis method and concluded that in the true diagnostic accuracy of urine dipstick testing for Leucocyte Esterase and nitrite as compared to the classical gold standard approach, a negative dipstick LE helped in ruling out UTI, while a positive dipstick nitrite helped in ruling in UTI. [7] In summary urine dipstick at the point of care would be the future method for diagnosing infants and children with UTI as its rapid, feasible, and cost-effective. However, its applicability in office practice and ERs should be re-evaluated for its true diagnostic accuracy in children using Bayesian LCMs.

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