

Do We Have Enough Evidence to Lower the Urinary Bacterial Colony Counts for the Diagnosis of Urinary Tract Infection in Children?

JITENDRA MEENA, PANKAJ HARI*

Division of Nephrology, Department of Pediatrics, ICMR Centre for Advanced Research in Nephrology,

All India Institute of Medical Sciences, New Delhi.

*pankajhari@hotmail.com

Urinary tract infection (UTI) is one of the commonest bacterial infections in childhood, affecting almost 2% boys and 7-8% girls in the first seven years of life [1]. Almost a third of these children would experience recurrence of UTI during childhood; hence, these patients require further imaging to identify underlying abnormality of urinary tract. UTIs may lead to post-infectious kidney scarring, subsequently causing proteinuria and hypertension. It is crucial to diagnose UTI quickly and appropriately to initiate prompt antibiotic therapy within 72 hours of onset of fever to reduce risk of kidney scarring [2]. However, it is also important to avoid over diagnosing UTI as it may increase antibiotic misuse. Overdiagnosis of UTI also exposes children to unnecessary investigations, increasing the cost and burden of healthcare.

Diagnosis of UTI in children, especially infants, can be problematic due to non-specific clinical features and difficulty in collecting urine. Many International guidelines recommend diagnosing UTI based on significant growth of bacteria in urine culture in the appropriate clinical context [4,5]. The threshold for positive urine culture is based on the assumption that it discriminates between true urine infection from false positive infection, and is chiefly extrapolated from studies performed in the adult population [6]. Since many uropathogens are also present in periurethral area and gut, collection of urine by clean catch and catheter is always fraught with risk of contamination.

While most recommendations agree on the cutoff for urine sample collected by suprapubic aspiration as 10^3 CFU/mL, the specific cutoff for defining positive culture by clean catch and catheter specimen remains controversial. Presently, the most commonly used threshold for positive bacterial colony count ($>10^5$ CFU/mL) was derived from studies by Kass and colleagues based on urine collected by non-invasive methods [6]. Even at that time, authors had stated that this specific cutoff would result in missing some patients with true UTI. Over the

years, some studies have challenged this specific cutoff in identifying children with true UTI. Overall, review of these studies suggests that almost 10-25% of children with positive bacterial growth (CFU $>10^3$ /mL) in urine sample collected by suprapubic aspiration had lower bacterial count ($<10^5$ CFU/mL) on simultaneously collected urine by mid-stream clean catch [7-9]. Most of these studies included children less than 2 years of age. Growth of bacteria in urine is affected by incubation period in bladder, transportation of sample, and type of culture media used in laboratory. Short incubation period in infants due to frequent voiding is one of the factors reported to contribute to lower bacterial CFUs.

In this issue of the Journal, Nyayadhish and colleagues [10] compared the characteristic of patients between two group of children with low counts (10^{4-5} CFU/mL) and those with counts $>10^5$ CFU/mL. Authors observed that 9 (4.2%) children had low bacterial CFUs and there was no significant difference in parameters between two groups except the antibiotic treatment rates and *E.coli* growth in urine [10]. The follow-up findings of the children in lower bacterial CFUs groups who did not receive antibiotics would be of interest. As these observations will provide us the clue whether culture in these children becomes sterile without antibiotic therapy. The authors [10] have done a commendable job in carrying out this prospective study and reporting that using conventional cutoff for clean catch and catheter urine sample may result in missing few children with true UTI. Based on conclusion from present study, we may be missing one in nine children with underlying abnormality of urinary tract.

While the authors conclude that nine (4.2%) children were diagnosed to have UTI if lower bacterial CFUs is considered but we do not have gold standard test to say with conviction that all of these children have true UTI. Previous studies have used $>10^3$ CFU/mL in urine sample collected by suprapubic aspiration as a surrogate for gold standard test. While lower CFUs did identify one patient

with abnormal tract but it would also increase the use of antibiotics in children who may not have true UTI. However, in the present study [10], authors left the decision of antibiotic therapy to the primary physician; hence, four out of nine patients with lower bacterial CFUs received antibiotics. Going forward, the ideal study design to answer this question would be to randomize children with lower CFUs in urine culture into treatment with antibiotics or placebo groups and compare the resolution of symptoms, repeat urine culture and kidney scarring on late-phase DMSA.

To conclude, a lower cutoff of bacterial CFUs to diagnose UTI can be considered in children, especially the infants, where shorter incubation period may not allow enough CFU in urine culture. However, one should not rely on a specific precise cutoff of bacterial growth alone in urine; rather, clinicians should use their wisdom keeping the clinical context in mind to make a diagnosis of UTI even with lower bacterial CFUs than that used conventionally.

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