

Author's declarative title

Urine Concentration should be taken into account when interpreting pyuria in infants, but machine-read leucocyte esterase has greater diagnostic value

Citation

Urine Concentration and Pyuria for Identifying UTI in Infants
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PEDIATRICS Volume 138, number 5, November 2016:e20162370

Context

The relationship between pyuria and true urinary tract infection (UTI) remains controversial. Most studies have assessed pyuria using manual microscopy in centrifuged urine. However, standard practice at most centres now involves automated urinalysis of un-centrifuged urine, thus pyuria in dilute samples may have more significance than pyuria in concentrated urine samples. It may therefore be important to consider the possible impact of urine concentration on the significance of white cell counts [WCC] or leukocyte esterase [LE] assessment.

Methods

This was a retrospective study of routinely collected data from infants aged less than three months with suspected UTI who presented to a busy US emergency department over five years. Automated urinalysis and culture was available for each eligible child. UTI was defined as $\geq 50\,000$ colony-forming units/mL of a pathogenic organism, and all analysed samples were collected by catheter. Dipstick urinalysis was performed by an automated laboratory machine, and included specific gravity measurements. Dipstick positivity for LE, nitrite, or blood automatically triggered a microscopic urinalysis that measured cell counts on un-centrifuged urine. Positive urinalysis led to culture. Negative dipstick for LE was considered equivalent to a negative microscopic urinalysis. Cultures yielding non-pathogenic organisms or mixed organisms were considered contaminated and were excluded from analysis, rather than being classified as negative. Cultures yielding pathogenic organisms at $< 50\,000$ CFU/mL were also considered negative. Test characteristics were calculated across a range of WCC and LE cut-points between two specific gravity groups (dilute < 1.015 ; concentrated ≥ 1.015).

Findings

The analysis included data from 2700 ethnically diverse infants with a mean age of 1.7 months, half of whom were febrile ($\geq 38^{\circ}\text{C}$) at presentation. 211 (7.8%) had a positive urine culture. Receiver operating curves showed that optimal WBC cut-points associated with UTI culture positivity were 3 WBC/high-power field [HPF] in dilute urine (likelihood ratio positive [LR+] 9.9, negative [LR-] 0.15) and 6 WBC/HPF in concentrated urine (LR+ 10.1, LR- 0.17). For dipstick analysis, positive LE was strongly associated with the culture

positivity regardless of urine concentration (LR+ 22.1, LR– 0.12 in dilute urine; LR+ 31.6, LR– 0.22 in concentrated urine). Subgroup analysis found similar test characteristics in both febrile and afebrile infants.

Commentary

The authors have collected an impressive number of urinalyses and corresponding culture results (but not quite as impressive as the typo in the abstract suggests!). All infants aged less than three months in whom UTI was considered were identified during the study period, but it is unclear what the clinical criteria were for sampling urine, especially as non-febrile babies were included: this hampers judgments about applicability to other settings.

It is also unclear which electronic medical records were accessed from the hospital's data warehouse for the primary data collection, and which records were manually reviewed in the audit of a randomly selected 5% of cases. The former analysis appears to have identified 49% of eligible infants with fever, whilst the latter identified 83% with fever before or during the ED course. More thoroughly unwrapping the relationship between fever and urine WCC would be a welcome further analysis.

The prevalence of UTI in the study population was similar to that quoted in other studies. Could the 5% gender imbalance have resulted from the inherent difficulty in catheterising female neonates? However, catheterisation is an uncommon sampling method in most paediatric settings in many countries.

The authors considered a negative urine dipstick test to be equivalent to negative microscopic urinalysis, and so such samples were not cultured. However, there must have been exceptions, as 5.7% of the positive culture results had a negative urinalysis. Positive culture results were found in about a third of urine samples that had minimal WCC in large, multi-centre, prospective study of older children, (DUTY, ****)(Shaikh et al, 2016). Thus, there were probably false negatives among the discarded samples, which could have affected the reported correlation between WCC and culture, and so a negative predictive value for LE/WCC cannot be determined as reliably as in other studies (Glismeyer et al, 2014). Contrary to the authors' suggestion, many of the samples with low WCCs and growth on culture would have been unlikely to represent simple bacteriuria as they were taken from infants with a pre-test clinical suspicion of UTI.

They also excluded (the somewhat surprisingly few) contaminated samples (1.4%): such samples may include both false negative and false positive results. It would have been interesting to know the WCCs in these samples; consistently low WCC or LE results may have provided reassurance that 'contaminated' cultures indeed were true negatives.

The authors conclude that urine concentration should be incorporated into the

interpretation of automated microscopic urinalysis in young infants. However, they also point out that automated dipstick LE has superior diagnostic value, that was not affected by urine concentration, so white cell estimation may be superfluous when automated LE is available.

Implications for practice

The degree of urine concentration should be considered when interpreting the significance of WCC microscopy in infants' un-centrifuged urine. However, automated LE assessment at urinalysis of infants' urine predicts culture positivity better, and this is not affected by urine concentration.

References

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Competing interests

Chris Butler has done studies of urinary tract infection diagnosis and management, and on antibiotic use in the community and holds several grants in the field.