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Impact of Reflex Algorithms on Urine Culture Utilization

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Abstract

Urine culture is the gold standard for the diagnosis of urinary tract infection (UTI), one of the most common causes of bacterial infection. As such, urine specimens are responsible for a major share of the workload in clinical microbiology laboratories. The inclusion of metrics, such as the catheter-associated UTI (CAUTI) rate, that factor into hospital reimbursements and concerns surrounding the attrition of clinical laboratory personnel have prompted scrutiny of urine culture utilization in many organizations. One strategy to improve urine culture management is the institution of urine reflex algorithms that restrict urine culture to specimens with evidence of inflammation on urinalysis. The high negative predictive value of indicators of pyuria and bacteriuria on urinalysis are useful to rule out UTI and thus the need for culture. Data from several studies support the notion that use of reflex criteria reduces urine culture utilization. However, few studies have examined the impact of reflex algorithms on CAUTI rates and antibiotic use. This article provides an overview of the laboratory diagnosis of urinary tract infections with a focus on the utility of urinalysis and reflex testing algorithms.

Introduction

Urinary tract infections (UTIs) are one of the most common causes of bacterial infection and hospital-acquired infections worldwide. With an estimate of over 10 million ambulatory and 2 million emergency department (ED) visits attributed to suspected UTIs annually, these infections have a major societal and economic impact [1]. A UTI is defined as an infection that involves any part of the urinary system and is characterized by symptoms including dysuria, frequent urination, hematuria, and suprapubic or flank pain. Clinically, UTIs are broadly categorized as uncomplicated or complicated. Uncomplicated UTI is defined as a symptomatic bladder infection that occurs in a woman with a functionally normal urinary tract. Complicated UTIs are defined as a symptomatic infection of either the bladder or kidneys in individuals with functional or structural urinary tract abnormalities, such as urinary obstruction, an indwelling catheter, or immunosuppression [2]. A key feature of both of these definitions is the requirement for symptoms, as the isolation of bacteria from urine in a patient without symptoms is defined as asymptomatic bacteriuria (ASB). ASB prevalence is increased in women who are pregnant, diabetic women, the elderly, and people with indwelling urinary catheters. With the exception of pregnant women and patients undergoing a genitourinary procedure, who are at increased risk of adverse outcomes, treatment for ASB is generally not indicated [2].

Diagnosis of UTI

The diagnosis and management of uncomplicated UTI is usually based upon presentation of symptoms consistent with UTI. Isolation of a uropathogen from urine is usually unnecessary except on the occurrence of treatment failure, where antimicrobial susceptibility results can facilitate an effective antimicrobial regimen [3]. In most cases of acute, uncomplicated UTI, urine culture results do not change management due

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to the predictable epidemiology of these infections and the 2- to 3-day turnaround time before urine culture results and susceptibility testing are available. Thus, prompt initiation of treatment is usually based on symptoms alone [4,5].

The diagnosis of recurrent or complicated UTI is commonly achieved through a combination of clinical information that includes signs or symptoms in conjunction with laboratory findings [6]. The isolation of uropathogens from urine culture is recommended for complicated UTI because of differences in the etiology of causative organisms, increased incidence of antimicrobial resistance, and higher risk of complications. Urinalysis may support the diagnosis of UTI by providing evidence of pyuria and bacteriuria, which are defined microscopically by the presence of white blood cells (WBCs) and bacteria in urine, respectively. Positive leukocyte esterase on a urine dipstick signals the presence of intact or lysed leukocytes, and positive nitrites are indicative of the presence of bacteria from the family *Enterobacteriaceae* [7]. While findings of a positive nitrite test on a urine dipstick are highly specific (92 to 100%) for diagnosis of UTI, the sensitivity of this parameter is only 19 to 48% [8]. The presence of WBCs on microscopy or leukocyte esterase on dipstick analysis is more sensitive than nitrites but less specific due to other conditions associated with inflammation. A combination of these parameters may increase the sensitivity of urinalysis for UTI [8].

Role of the Clinical Microbiology Laboratory in Diagnosis of Catheter-Associated UTI

The Centers for Medicare and Medicaid (CMS) recently established a program to promote reduction in hospital-acquired infections (HAIs). Acute care hospitals must report HAIs to the National Healthcare Safety Network (NHSN) at the Centers for Disease Control and Prevention. CMS then uses metrics such as the HAI rate to determine hospital payments. Low-performing hospitals may be penalized in the form of lost reimbursements or even financial penalties, while high performers may receive incentive payments. This has motivated many acute care hospitals to reduce HAI rates. In addition, HAI rates are freely available to the public, which empowers consumers to choose a hospital based upon quality metrics, such as the rate of HAIs.

A catheter-associated UTI (CAUTI) is a UTI that is associated with an indwelling urinary catheter. CAUTIs are among the most common causes of HAI. Between 15 and 25% of hospitalized patients are managed with short-term indwelling catheters, and the daily risk of bacteriuria with an indwelling catheter has been estimated at 3 to 8% [9]. Thus, there is enormous potential for CAUTIs to have a major impact on CMS reimbursement, as well as patient outcomes. CAUTIs are associated with increased morbidity, mortality, and hospital length of stay. In addition, catheters are a source of multi-drug-resistant organisms that may be transmitted to other patients.

Strategies to decrease CAUTI rates focus mainly upon patient-centered initiatives, such as proper catheter utilization and education about insertion and maintenance. Supplementary approaches to reduce CAUTI often involve laboratory-directed initiatives. Before a CAUTI is reported to NHSN, standardized criteria that include both a positive urine culture with growth of 1 and 2 uropathogens at a threshold above 10^5 CFU/ml and the presence of signs or symptoms of a UTI must be met. Because a positive urine culture is a requirement to meet the criteria for CAUTI, clinical microbiology laboratories are poised to assist with CAUTI reduction initiatives through a decrease in unnecessary urine cultures on patients with a low likelihood of UTI. The push to standardize definitions in order to classify an epidemiologic diagnosis of CAUTI may sometimes be at odds with a true clinical diagnosis. The requirement for the presence of symptoms in the CAUTI criteria helps ensure that only clinically significant UTIs are reported, as the likelihood of ASB is increased in patients with indwelling urinary catheters [2]. However, symptoms of a UTI are frequently non-specific yet widespread among inpatients. Thus, a clinical diagnosis of CAUTI often represents a diagnostic dilemma for a physician that is not solved by urine culture alone.

Efforts To Reduce Unnecessary Urine Cultures

Urine cultures are not indicated for uncomplicated UTI in symptomatic patients with positive urinalysis [3,6]. In spite of this, urine cultures are frequently ordered in ambulatory patients for this indication [10]. In hospitalized patients who are at increased risk for ASB, a positive urine culture result is difficult to ignore and often leads to inappropriate treatment [11]. Thus, the diagnosis of UTI relies on urine culture results and clinical signs and symptoms, which may be supported by positive results on urinalysis and/or urine microscopy [2,9]. However, a review of urine culture ordering practices at a 1,250-bed academic medical center found that over 20% of the 11,820 inpatient urine cultures were ordered in isolation, meaning without concurrent urinalysis [12]. Notably, the positivity rate of urine cultures ordered in conjunction with urinalysis was significantly higher than that of isolated urine cultures (46% versus 35%), which supports the notion that urinalysis may be effective at ruling out patients who do not have UTI.

Overutilization of urine culture in isolation is problematic and may drive treatment of ASB, which is only indicated in pregnant women or in patients undergoing urologic procedures. Indeed, an analysis of urine culture results at a Veterans' Affairs medical center found that 32% of catheterized patients with no UTI symptoms (as defined by guidelines from the Society for Healthcare Epidemiology of America) but positive urine culture results were inappropriately treated with antibiotics [13]. Overuse of antibiotics is associated with excess costs, increased risk of toxicity, development of antimicrobial resistance, and *Clostridium difficile* infection. In addition, a diagnosis of ASB as UTI may potentiate a failure to evaluate other causes of a patient's symptoms.

Extraneous urine culturing wastes the time and resources of clinical microbiology laboratories, which are increasingly faced with a shortage of skilled laboratory personnel [14]. Laboratory-directed efforts to reduce unnecessary urine culture orders for patients for whom there is a low suspicion of UTI include the implementation of an algorithm in which reflex testing for urine culture is initiated following the occurrence of defined parameters tested