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Research Article

Advanced Diagnostic Approaches for Urinary Tract Infections: Innovations for Rapid and Accurate Detection

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Abstract:

Urinary tract infections (UTIs) affect approximately 150 million people globally, yet diagnosing this prevalent condition remains challenging. Misdiagnosis and inappropriate antibiotic prescriptions are common, contributing to the growing problem of antibiotic resistance among pathogens. Current diagnostic methods require 2–3 days to identify the causative pathogen and determine antibiotic susceptibility, underscoring the need for innovative technologies to enhance patient care and encourage responsible antibiotic use. An ideal diagnostic tool should allow direct testing of clinical urine samples, providing pathogen identification and antibiotic susceptibility results within a few hours. This enables healthcare providers to prescribe suitable antibiotics early. Rapid screening tools like flow cytometers and advanced dipstick assays can identify negative samples efficiently, streamlining workflows and lowering costs. Significant advancements have also been made in refining mass spectrometry techniques for direct urine analysis and developing multiplex PCR panels targeting UTI pathogens and antibiotic resistance. emerging technologies, including microfluidics, biosensors, real-time microscopy, and sequence-based diagnostics, hold great promise for delivering faster and more accurate results, potentially transforming UTI diagnosis and treatment.

Keywords: urinary tract infections; antibiotics; multiplex pcr

Introduction

The urinary system, comprising the kidneys, ureters, bladder, and urethra, is responsible for filtering the blood to eliminate waste and excess water from our body. It plays a crucial role in clearing metabolic byproducts from the bloodstream, ensuring the body's proper balance and function. The system also plays a vital role in maintaining the balance of ions and solutes in the blood while helping to regulate blood volume and pressure [1]. Antibiotics should not be prescribed excessively, particularly in view of the increasing prevalence of antibiotic resistance. In healthy individuals, urine is typically sterile or contains only a minimal number of microorganisms capable of causing infection [2]. Urinary tract infections (UTIs), among the most common infectious diseases worldwide, affect approximately 150 million people annually, leading to significant health complications and high medical expenses. For instance, recurrent UTIs in the United States alone impose an economic burden exceeding $5 billion each year. These infections can occur in the urethra (urethritis), bladder (cystitis), or kidneys (pyelonephritis), with symptoms varying depending on the site of infection. UTIs negatively affect patients' social and intimate relationships, reducing their overall quality of life [3]. Antibiotics should not be prescribed excessively, particularly in view of the increasing prevalence of antibiotic resistance. (4) UTIs are categorized as either uncomplicated (uUTIs) or complicated (cUTIs) [5]. uUTIs generally occur in healthy individuals without structural or neurological issues in the urinary tract, whereas cUTIs arise in cases involving abnormalities that heighten infection risk. These abnormalities include catheterization, obstructive uropathy, urinary retention, neurogenic bladder, renal failure, pregnancy, or the presence of kidney stones. Both community-acquired and hospital-acquired UTIs are predominantly caused by bacteria from the Enterobacteriaceae family, with uropathogenic *Escherichia coli* (UPEC) being the most frequently isolated pathogen, including in complicated cases [6]. Antibiotic-resistant Gram-negative bacteria, such as carbapenemase-resistant Enterobacteriaceae, are more common in hospitals than in community settings. While UTIs are primarily bacterial in origin, infections caused by other microorganisms, like fungi and viruses, are rare. Among fungi, *Candida albicans* is the leading cause of UTIs. Viruses such as cytomegalovirus, type 1 human polyomavirus, and herpes simplex virus are also occasional contributors to UTIs [7].

UTIs according to gender: -

In females, UTI is more common than adult males. It mainly happened due to the female lower urinary tract anatomy and its proximity to the reproductive organs. UTI diagnose starting from ages 45–49 years onward. E. coli followed by *Staphylococcus saprophyticus* and *K. pneumoniae* are the commonest etiological agents of UTI. In males, UTI is much less common in the age group 18-50 years. The most common UTI in males is prostatitis an inflammation of the prostate gland.

However, above 50 years of age, due to factors like hyperplasia of Prostate and other comorbidities, UTI becomes common in males. E. coli and S. aureus are common etiological agents for UTI in males.

Classification of urinary tract infections:

Urinary tract infections (UTIs) are broadly classified into two categories: uncomplicated (uUTIs) and complicated (cUTIs). uUTIs typically occur in healthy individuals without any structural or neurological abnormalities in the urinary tract. These infections are straightforward to manage and often involve the bladder (cystitis) or urethra (urethritis). In contrast, cUTIs is associated with conditions that increase the risk of infection, such as anatomical or functional abnormalities, catheter use, kidney stones, urinary retention, neurogenic bladder, renal failure, or pregnancy. In males, hence, UTIs are almost always complicated. cUTIs often require more intensive management due to the increased complexity of the underlying conditions. Additionally, UTIs can also be classified based on the site of infection, such as lower UTIs (affecting the urethra and bladder) and upper UTIs (involving the kidneys, such as pyelonephritis). This classification aids in tailoring appropriate diagnostic and treatment strategies.

Conventional methods: -

a. Urine Suprapubic Aspirate (SPA) is standard simple and safe technique for obtaining an uncontaminated specimen of urine in children. (8)
b. Microscopy and culture of midstream urine on CLED (Cystine Lactose Electrolyte Deficient) medium is the age-old technique for diagnosis of bacteria causing UTI.CLED was first described by Sandys and later modified by Mackey and Sandys [9].
c. Other than this, dip-slide or slide culture method is also a viable option for diagnosing UTIs. People have used glass slides covered with MacConkey agar on one side and Blood agar on the other slide [10]. An image of dip-slide technique is shown below.

Figure 1: Dip-slide technique for urine culture

d. Rapid diagnostic tests like rapid urease test and rapid nitrate reductase test are also used for diagnosis of UTIs.

Gram stain is not reliable for diagnosis of UTI because the cut-off count for bacteriuria is 10^5 CFU per ml and the cut-off count for positivity of Gram stain is also 10^5 CFU per ml.

Newer methods: -

a. Recent recognition of the human urobiome, even outside the context of asymptomatic bacteriuria, has refuted the assumption that "no growth observed on CLED" means the bladder is sterile. By applying extended culture conditions to urine, like larger inoculate, microaerobic or anaerobic or CO_2-enhanced atmospheres, additional media, and longer incubation times, urine cultures frequently show more fastidious commensals that otherwise may go unrecognized [11]. One such method is the EQUC. The expanded quantitative urine culture (EQUC) leads to improved pathogen identification as compared to standard urine culture. Standard urine culture is good with common uropathogens such as *E. coli* and other Gram-negative bacilli but misses many Gram-positive bacteria and other anaerobic, fastidious, or slow-growing pathogens. The EQUC method depends on simple modifications of the standard method (like plating volumes, growth medium, and incubation conditions). As per one report, when 65 urine samples (41 from patients with overactive bladder and 24 from healthy controls) were cultured, standard culture missed 92% of the isolates that were positive by EQUC. In another study comparing the two culture methods, standard culture missed 67% of the uropathogens which could be detected by EQUC in urine samples from 150 women. Since the EQUC uses a longer incubation time than standard culture, increasing the time to result, people now recommend using the EQUC as a supplemental tool for patients with UTI symptoms that yield negative results with standard urine culture, and for patients with recurring UTIs [12].
b. Other new methods include rapid molecular-based pathogen identification and next-generation sequencing methods [13].
c. Some other novel methods are nucleic acid tests and mass spectrometry, that have been approved for clinical use and have also improved the speed and accuracy of identification of pathogens from primary cultures [14].
d. A dipstick assay has been devised for rapid diagponsis of UTI by Gurtung et al. It has reportedly sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) of 43.75%, 77.51%, 35.59% and 82.91%, respectively [15].
e. We have tried reduction of methylene blue as an accurate and rapid option for diagnosis of UTIs.

Anaerobic UTIS also occur and are grossly neglected. We have used culture of urine on Robertson's cooked meat medium for detection of anaerobes causing UTI.

Conclusion: -

Early reliable diagnosis of UTI helps to prevent misuse or overuse of antibiotics Many methods are there for conventional and new urine culture. Newer and rapid diagnostic methods save time and are equally sensitive and specific. The most apt method needs to be chosen for timely diagnosis of UTI.

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