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SYSTEMIC APPROACHES TO DIAGNOSE URINARY TRACT INFECTION

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Abstract

An infection of the urinary system is known as a urinary tract infection (UTI). This sort of infection can affect your urethra (a condition known as urethritis), kidneys (a condition known as pyelonephritis), or bladder (a condition called cystitis). Bacteria are often absent in normal urine . Our filtration mechanism, the kidneys, produces urine as a by-product. Urine is produced when your kidneys filter waste materials and extra water out of your blood. Urine typically passes through your urinary system uncontaminated. The urinary system, however, can become infected or swollen when bacteria from outside the body enter it. A large portion of the workload in clinical microbiology laboratories is attributed to urinary tract infections (UTIs), which are among the most prevalent bacterial infections. Although the distribution of UTI-causing pathogens is shifting, enteric bacteria, in particular Escherichia coli, still account for the majority of cases. There are only a few tests that doctors may use to differentiate UTIs from other diseases with comparable clinical presentations, and none of them have sufficient sensitivity and specificity when used alone. Urinalysis is one of the diagnostic tests that is most useful for ruling out bacteria.

Keywords: *Urinary tract infections, Bacteria, Inpatient and Outpatient Laboratories, Urinalysis, Pathogenic organisms, Antimicrobials, Urine Culture.*

1. Introduction

A bacterial infection of the bladder and related organs is known as an uncomplicated urinary tract infection (UTI). These patients are free of anatomical abnormalities and concomitant conditions including pregnancy, immunocompromised status, or diabetes. Cystitis and lower UTI are other names of uncomplicated UTI. A UTI without symptoms cannot be diagnosed based solely on bacteriuria. Urinary urgency, frequency, soreness above the pubic bone, and dysuria are typical symptoms. Since UTIs are rare in circumcised men, any male UTI is typically regarded as complex. Although many patients seek medication for symptom relief, many cases of simple UTIs heal on their own without treatment. A sizable portion of antibiotic prescriptions are written for urinary tract infections (UTI), one of the most common conditions treated in adult primary care medicine. A high degree of diagnostic accuracy is necessary because this issue is so prevalent and important in everyday therapeutic practice. Particularly in light of the rising prevalence of antibiotic resistance, unnecessary antibiotic prescriptions should be avoided. One of the most common illnesses treated with antibiotics in primary care is acute cystitis, an infection of the lower urinary tract.

Age and gender play a significant role in predominance. The likelihood that a female patient will have an infection of the urinary tract is 50% to 80% if she appears to a primary care office with the normal symptoms. The instructions in the guidelines for the use of antibiotics in the treatment of urinary tract infections are frequently not followed in actual

practice. Fluoroquinolones should only be used sparingly and cautiously when necessary, according to national and international regulations [1,2]. The sheer number of prescriptions reveals just how frequently these suggestions are disregarded in real-world situations [3]. The use of fluoroquinolones in serious infections is put at risk by these prescription practices, which have increased resistance [4]. According to estimates, symptomatic UTIs cause up to 7 million visits to outpatient clinics, 1 million trips to emergency rooms, and 100,000 admissions to hospitals each year [5]. As much as 35% of nosocomial infections now occur from UTIs, which are also the second most common cause of bacteremia in hospitalised patients. UTIs have emerged as the most prevalent hospital-acquired illness [6,7,8]. The presence of clinical symptoms along with pathogen identification is the gold standard for the diagnosis of a urinary tract infection. Urine culture is used to detect and identify the infection (using midstream urine). This enables estimation of the amount of bacteriuria. However, neither the scientific literature nor the standards set by microbiological laboratories specify the minimal degree of bacteriuria demonstrating an infection of the urinary tract. The cutoff is typically 10^5 colony forming units (cfu)/mL urine, according to several laboratories. The problem is that many important infections are missed by this threshold. Consequently, depending on the types of bacteria found, some suggestions advocate making the diagnosis of UTI at a level of 10^3 cfu/mL [9,10,11].

2. Etiology

The causes of community- and hospital-acquired UTIs are different [12,13,14]. Regarding changes in the frequency of causative agents among outpatients, only a little quantity of data has been reported. Although there is some evidence that the percentage of UTIs caused by E. coli is declining, enteric bacteria, particularly Escherichia coli, have historically been and continue to be the most common cause [15,16,17]. The causes of nosocomial UTI, however, have undergone considerable modifications since 1980, according to reports [18].

- E Coli:

1. Introduction:Gram negative bacilli, motile non capsulated,non-spore forming bacteria, facultativeanaerobic, grows in 35-37 degree Celsius, PH 7.2-7.4.Lactose-fermenting Enterobacteriaceae (all ferment glucose, are oxidase-negative, and reduce nitrates to nitrites).The most common cause of UTIsoccurring after contamination/colonization of the genital area with fecal microbiota.
2. Culture media: Eosin Methylene Blue Media, Mac Conkey, CLED etc.
3. Characteristics : Produce metallic sheen on EMB ,Yellow color in CLED ,Pink color in Mac Conkey due to lactose fermentation. Indole and Methyl RED test positive. On TSI slant it produce an acid/acid reaction with gas [19].

- Pseudomonas:

1. Introduction:*Pseudomonas aeruginosa* is the most common member of this genus, which causes human infections and is commonly associate with burn wound, respiratory tract and Urinary tract infection, Septicemia. It found in soil,water,plants,water baths,soap dishes etc.These are often referred as Opportunist organism that tend to attack those patients whose defenses has been compromised because of age,long illness.
2. Culture Media: Blood Agar,Mac Conkey,CLED.
3. Characteristics: Gram negative bacilli,aerobic, capsulated,non-sporing

motile bacteria.Oxidase positive.Colonies on blood agar are large,flat and grey white with a ground glass appearance and produce a zone of hemolysis.The colonies have grape like odour.It produces pyocyanin,a blue green pigment that diffuse into the medium and most easily seen on a clear medium as MacConkey [20].

❖ Proteus

1. Introduction: It a member of Enterobacteriaceae. *P mirabilis* is responsible for UTI.
2. Culture media:Blood Agar, Mac Conkey, CLED etc.
3. Characteristics: Gram negative bacilli,aerobic,non-capsulated,non-sporing motile bacteria.Colonies on blood agar swarm with a single colony covering the entire plateon mac conkey it produces colourless colonies. In CLED it produces blue color.It is phenylalanine deaminase,urease, and H2S positive.*P mirabilis* indole negative but *P. vulgaris* is indole positive [21].

❖ Klebsiella

1. Introduction: It a member of Enterobacteriaceae whichis responsible for UTI.
2. Culture media:Blood Agar, Mac Conkey, CLED etc.
3. Characteristics: Gram negative bacilli,aerobic, capsulated,non-sporingnon motile bacteria.Colonies on blood agar shows mucoid colonies.On mac conkey it produces pink mucoid colonies.In CLED it produces big yellow colonies [22].

❖ Staphylococcus

1. Introduction:Gram positive cocci, appear as grape like structure,non-capsulated, non-sporing, non-motile aerobic bacteria grow at 35–37-degree centigrade PH 7.2-7.4.
2. Culture media:Blood Agar, Nutrient agar,Salt Milk Agar,Ludlam media,Mannitol salt agar.
3. Characteristics: Produce golden yellow colonies and in blood agar produce beta hemolysis.It is catalase and coagulase positive [23].

❖ Streptococcus

1. Introduction: Gram positive cocci, appear as chain like structure,non-capsulated, non-sporing, non-motile aerobic bacteria grow at 35–37-degree centigrade PH 7.2-7.4.
2. Culture media:Blood Agar, Nutrient agar, Crystal violet blood agar, Pikes media.
3. Characteristics: Produce beta hemolysisin blood agar. It is catalase and coagulase negationist is bacitracin sensitive.Dick test positive [24].

❖ Enterococcus

1. Introduction: Gram positive dip cocci, appear as chain like structure,non-capsulated, non-sporing, non-motile aerobic bacteria grow at 35–37-degree centigrade PH 7.2-7.4.
2. Culture media: Bile esculin agar.
3. Characteristics: Produce black colonies in this media [25].

3. Point of contention

- lingering sensations of the lower urinary tract.
- Renal calculi in the staghorn.
- Pyelonephritis.

- Endometrial hyperplasia with granulomatous pyelonephritis.
- Incontinence.
- Targeted glomerular nephropathy.
- kidney infection.
- enduring prostatitis.
- testicular disease.
- Hypertension.
- kidney failure.

4. Prevalence and incidence

The most common bacterial infections in women are urinary tract infections. More than 40% to 60% of women experience an illness at least once in their lifetime, and they often strike between the ages of 16 and 35, affecting 10% of females annually. Nearly half of patients had a recurrence within a year, which is rather normal. Compared to men, women experience urinary tract infections at least four times more frequently [26,27].

5. Pathophysiologic mechanisms

The bladder is typically the sole organ affected by an avirulent UTI. Cystitis is an inflammatory response that develops as a result of bacterial invasion of the bladder mucosal wall. Enteric coliforms, which often live in the periurethral vaginal introitus, are the most common germs responsible for UTIs. UTIs are brought on by these microorganisms, which enter the bladder through the urethra. Due to the fact that it encourages bacterial migration into the bladder, sexual activity frequently results in UTIs. UTI risk is typically lower in people who routinely void and empty their bladder [28].

6. Collection and Analysis of Sample

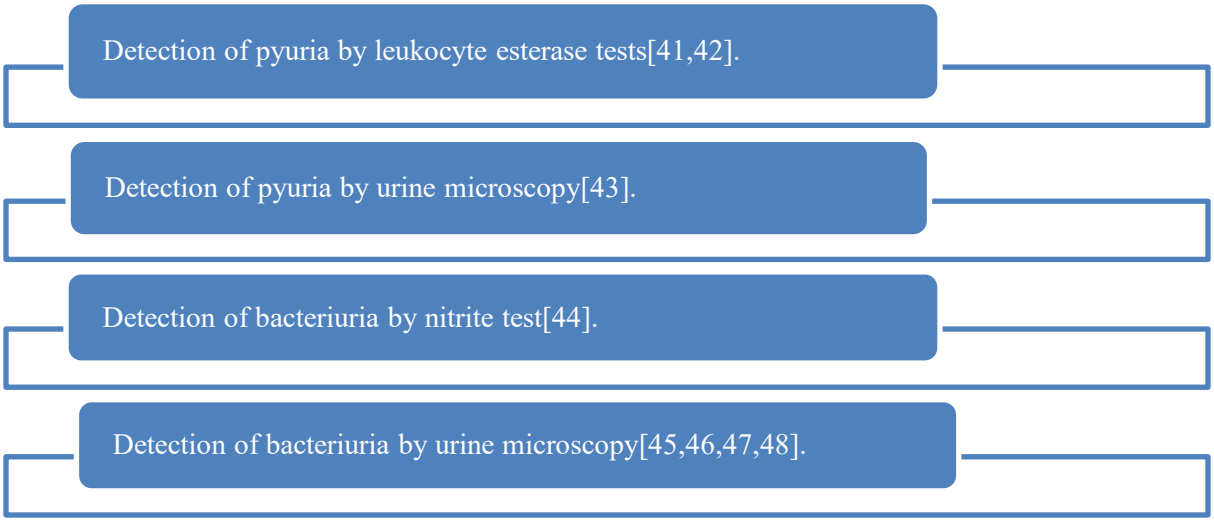
The clean-catch midstream approach is used to capture the majority of urine samples from adult patients. This method has the following benefits: it is neither invasive nor uncomfortable, it is straightforward and affordable, it can be used in practically any therapeutic setting, there is no chance of problems, and there is no risk of introducing bacteria into the bladder through catheterization. Colony counts from urine samples obtained using this approach and those obtained using straight catheterization or suprapubic aspiration had a fair amount of agreement [29,30]. Because the urine sample travels through the distal urethra and has the potential to pick up commensal bacteria, this method obviously has some drawbacks. Cleaning the skin and mucous membranes at the urethral orifice before micturition, letting the first portion of the urine stream go into the toilet, and collecting urine for culture from the midstream are just a few of the straightforward techniques that have been established to reduce the contamination rate [31]. The clean-catch midstream method is generally acknowledged and employed, although the evidence suggests that the cleansing operations may not considerably reduce urine contamination rates and may thus not be essential on a regular basis [32,33]. Delays in the transportation or processing of urine samples have been shown to have a negative impact on their quality in a number of studies [34,35,36].

7. Sample Testing

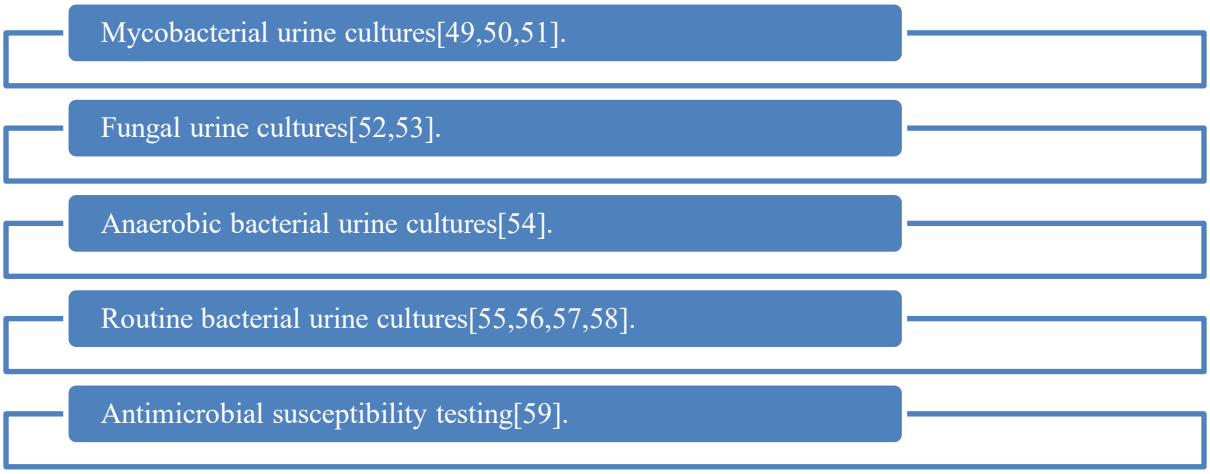
Utilizing calibrated loops, routine urine cultures should be plated when using the semiquantitative approach. With this approach, isolated colonies can be used for susceptibility testing and identification, as well as information on the quantity of cfu/mL. Blood agar and MacConkey's agar should be the only media types utilized for routine cultures. Since nearly all UTIs in outpatients are caused by facultative and aerobic gram-negative bacteria, it is not required to routinely inoculate a medium that is selective for gram-positive bacteria with urine specimens acquired from outpatients [37,38]. Use of

selective media is not required, not even in patient populations where Staphylococcus saprophyticus is a frequent cause of UTIs. On the other hand, urine samples taken from hospitalised patients are more likely to include enterococci, the second most prevalent source of nosocomial infections. Using a medium that is selective for gram-positive cocci, laboratories may wish to think about inoculating urine samples from hospitalised patients or from individuals in whom gram-positive bacterial infection is suspected but not confirmed. A medium like phenylethyl alcohol inhibits the growth of swarming Proteus species and other gram-negative bacteria that could cause the specimen's gram-positive cocci to overgrow. Before reading, urine cultures should be cultured for an entire night at 35°C–37°C in room air. Routine urine cultures shouldn't be incubated for longer than 24 hours, and 48 hours should only be spent incubating urine samples with more than 10^4 uropathogens or samples from people who may have funguria [39,40].

❖ Non-Culture Method



❖ Culture Method



8. Interpretation of urine culture results

To decide if additional identification and testing for antimicrobial susceptibility are required, microbiologists must assess the microbiologic relevance of growth on culture plates. The majority of culture results can be easily understood, no growth, severe contamination, and pure cultures of common pathogens growing in an amount of >105 cfu per milliliter of urine are all unambiguous outcomes. For samples collected by suprapubic aspiration or direct catheterization, the interpretation of cultures that produce pure growth in lesser numbers is similarly evident [60]. On the other hand, it can be challenging to interpret urine cultures that produce mixed bacteria in different concentrations.

Probablity of Contamination(Low)	Quantitation(cfu/ml)	Interpretation
•1	•<10^2	•Probable Contaminant
•1	•>=10^2	•Significant isolate
•2	•<10^2 for each	•Probable Contaminant
•2	•>=10^2 for each	•Significant isolate
•2	•>=10^2 for 1	•Significant isolate and contaminant
•3	•>=10^5 for 1	•Significant isolate and contaminant
•3	•>=10^5 for each	•Probable Contaminant

Table 1 In case of Low Probability of Contamination, Urine sample is collected from bladder, ureter, renal pelvis, kidney, catheterization, operation room, patient with antimicrobial therapy.

Probablity of Contamination(High)	Quantitation(cfu/ml)	Interpretation
•1	•<10^2	•Probable Contaminant
•1	•>=10^2	•Significant isolate
•2	•>=10^5 for each	•Significant isolate
•2	•>=10^5 for 1	•Significant isolate and contaminant
•2	•<10^5 for each	•Probable Contaminant
•3	•>=10^5 for 1	•Significant isolate and contaminant
•3	•>=10^5 for each	•Probable Contaminant

Table 2 In case of High Probability of Contamination, Urine sample is collected from Clean catch technique, nephrostomy tube, ureterosmy tube, ileal loops.

Name of Antibiotic	Dose	Duration	Side effects	Note
Trimethoprim sulfamethoxazole	160/800 mg	Twice daily, for 3 days	nausea, vomiting, anorexia, rash, urticarial, photosensitivity, hematologic complications Rare	Avoid if resistance prevalence is greater than 20%, in some regions, trimethoprim 100 mg alone for three days may be equal.
Nitrofurantoin monohydrate/macrocrystals	100 mg	Twice daily, for 5 days	nausea, headache, flatulence, diarrhea Rare: pulmonary fibrosis, hepatitis, pancreatitis	When there is a possibility of pyelonephritis, avoid, modest renal impairment (creatinine clearance of 30 mL/min) suggests that you are probably safe.
Pivmecillinam	400 mg	Twice daily, for 3-7 days	nausea, vomiting, diarrhea	Not available everywhere so avoid if suspicion for pyelonephritis
Fosfomycin trometamol	3 g	Once, may be repeated 48 hr later	diarrhea, nausea, headache, vaginitis Rare: dizziness, rash, abdominal pain, weakness, elevated liver enzymes	Whenever there is a possibility of pyelonephritis, avoid,
Ciprofloxacin Levofloxacin	250 mg 250 or 500 mg	Twice daily, for 3 days. Once daily, for 3 days	Nausea, vomiting, abdominal discomfort, headache, dizziness, insomnia Rare: Peripheral neuropathy, tendinopathy, tendon rupture, QT interval prolongation, hepatotoxicity	Its efficacy is limited by increased resistance, pyelonephritis should be its sole indication. elderly people or immunosuppressed patients have an increased risk of tendon rupture

Table 3 Guidelines for treating urinary tract infections [64,65,66,67,68,69,70]

Antibiotic	Dose	Duration	Note
Amoxicillin	500 or 875 mg	Every 8 h (500 mg) or 12 h (875 mg), for 3-7 days	The populace is becoming more resistant.
Fosfomycin trometamol	3 g	Once, may be repeated 48 hr later	Avoid if suspicion for pyelonephritis
Nitrofurantoin monohydrate/macrocrystals	100 mg	Twice daily, for 5 days	Avoid if pyelonephritis is suspected, avoid during the first trimester (because to a rare link with birth abnormalities in case-control studies, despite prospective studies showing no association), causes hemolytic anaemia in term G6PD deficient patients
Cephalexin	500 mg	Every 6 hr, for 3-7 days	The populace is becoming more resistant.
Amoxicillin-clavulanate	500 or 875mg	Every 8 hr (500 mg) or 12 hr (875 mg), for 3-7 days	The populace is becoming more resistant.
Trimethoprim-sulfamethoxazole	160/800 mg	Twice daily, for 3 days	Due to its effect as a folic acid antagonist, its link to birth abnormalities, despite not having been confirmed in humans, and its potential to cause kernicterus at term, it should be avoided throughout the first trimester.

Table 4 Therapeutic guidelines for pregnant women with urinary tract infections [71,72,73,74,75]

9. Surveillance and Therapeutic interventions

Historically, the course of treatment has ranged from three to six weeks. 'Mini-dose therapy,' which is a three-day course of therapy, has good cure rates. Varied regions of the nation have different levels of E. coli resistance to conventional antibiotics, if the resistance rate is higher than 50%, pick a different medication. The three-day mini-dose therapy with trimethoprim and sulfamethoxazole is effective, but resistance is widespread. If local resistance is higher than 20%, it shouldn't be used. The best options for mini-dose therapy are first-generation cephalosporins. Although it is bacteriostatic rather than bactericidal and needs to be taken for 5–7 days, nitrofurantoin is a suitable option for simple UTI. Although fluoroquinolones have significant resistance, they are a preferred medication among urologists due to their high levels of tissue penetration, particularly in the prostate. This makes fluoroquinolones less desirable than other antibiotics, with the exception of infections involving the prostate and those that are difficult. Attention should be paid to recent FDA warnings about the potential negative effects of fluoroquinolones [61,62,63].

10. Conclusion

UTIs are quite typical, although it can be difficult to understand test results and symptoms. Careful identification of UTI is necessary to prevent increased uropathogen resistance from overusing antibiotics. The most readily identifiable UTI symptoms include a change in frequency, dysuria, urgency, and the presence or absence of vaginal discharge, however older women may experience UTIs in a different way. Young women with obvious UTI symptoms who don't have vaginal discharge can begin treatment right once, and additional testing may not be required unless the woman keeps getting UTIs. Dipstick urinalysis is a common laboratory test because it is accessible and simple to use, but results must be understood in the context of the patient's pretest probability based on symptoms and other features. Positive testing does not exclude the possibility of UTI in patients with a high pretest likelihood. In comparison to other dipstick tests for UTI, nitrites are probably more sensitive and specific, especially in the elderly. Dipstick urinalysis is not the preferred test, however positive dipstick testing is likely specific for asymptomatic bacteriuria in pregnancy. Positive testing might make UTI more likely, but the decision to start treatment should be made based on the post-test probability. Further testing should be carried out in circumstances when the likelihood of a UTI is uncertain. Only when the gold standard—urine culture—was routinely applied would absolute diagnostic reliability and maximally tailored therapy be possible. The number of antibiotic prescriptions could be drastically decreased with this strategy, but it would require a lot more work. The delay in specialised antibiotic medication, however, would result from this. The preparation of a urine culture concurrently with empirical therapy is currently in demand. At least in some circumstances, such as in nursing homes, this is another option. For the treatment of urinary tract infections, new approaches are required due to the rising development of resistance. The use of diagnostic algorithms can assist in improving the specificity of antibiotic use.

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