INTRODUCTION

Urinary tract infection (UTI) can be defined as infection of the urinary tract structures: kidneys, ureters, bladder or urethra, occurring usually with the presence of bacteria in urine ***(Martinez et al., 2013)***.

Urinary tract infection is regarded as one of the most common serious health problems that affect millions of people each year. It is estimated that there are more than 150 million UTI in the world reported per year and it bears an economic and medical burden worldwide ***(Alshami et al., 2014)***.

Most UTI are uncomplicated, self-limited infections which are confined to the bladder and effectively treated with short-course, empiric antimicrobials. Conversely, complicated infections occur in the setting of structural or functional abnormalities, a compromised host (i.e.: pregnant, diabetic) or causative bacteria with increased virulence or antimicrobial resistance. There is a significant increase in the morbidity and mortality associated with complicated infections, ranging from loss of renal function to sepsis and death, so timely recognition is vitally important ***(Dielubanza et al., 2014)***.

Unfortunately, up to 33% of cases are being misdiagnosed because of the non-specific clinical presentation of UTI. Dipstick urinalysis for the presence of nitrite and leucocyte esterase is commonly used as a screening test.

However, these tests have a limited diagnostic accuracy. Typically, a high sensitivity is achieved at the expense of specificity or vice versa. Moreover, the subjective visual assessment of the strip can introduce an error rate up to 12%, and instrument-based reading still results in an error rate of approximately 3%. Urine culture provides a gold standard method for laboratory diagnosis of UTI; it provides quantitative information about the etiological agents and predicts antibiotic sensitivity ***(Lam et al., 2014)***.

Clearly the interpretation depends on both the clinical presentation and the causative organisms. Other pitfalls that limit the utility of urine culture include the long turnaround time (not within the same day), cost and labor intensiveness. Contamination is another problem which has been found in 15% of cases, as reported by the College of American Pathologists ***(Bekeris et al., 2008)***.

An effective screening test before culture requests can prevent unnecessary spending of time and expenditure and avoid unnecessary drug treatment ***(Kayalp et al., 2013)***.

Different screening methods have been used to screen for significant bacteriuria include; photometric system, microcalorimetry, changes in electrical impedance, detection of bacterial metabolites in urine, fluorescence staining using acridine orange, and turbidimetry***(Nnaemeka et al., 2014)***.

Recently, automated instruments capable of examining urine for cells and particles have been introduced for the analysis of urine Video camera and image-based analysis to capture and sort particles based on their dimensions, while others use the principles of flow cytometry. Several studies have shown that flow cytometry and image analysis can be used to detect bacteria in the urine ***(Huysal et al., 2013)***.

These methods have their various advantages; however, their costs make it virtually unaffordable in hospitals with poor resources in the tropics and other developing countries ***(Huysal et al., 2013)***.

Recently, in a study by Nnaemeka and his colleagues in 2014, modified methylene blue (MMB) test was used as a rapid screening test for significant bacteruria with high sensitivity (94.82 %) and specificity (97.17%) by using a colorimetric method. This method of screening can lead to a significant change in the number of culture requests and will save a lot of laboratory workloads regarding its low cost and feasibility ***(Nnaemeka et al., 2014)***.

Aim of The Work

The purpose of this study is to evaluate the use of modified methylene blue test as a rapid screening method for significant bacteriuria with resources that are easily affordable and commercially available.

URINARY TRACT INFECTION

Urinary tract infection is defined as microbial infiltration of the sterile urinary tract and is one of the most common bacterial infections worldwide. UTI encompass infection of the urethra (urethritis), bladder (cystitis), ureters (ureteritis) and kidney (pyelonephritis) ***(Barber et al., 2013)***.

Urinary tract infection is the second most common infection diagnosed in the acute hospital setting and accounts for almost 5% of all emergency department visits by adults aged 65 years and older. Although UTI is one of the most commonly reported infections in older adults, definitions for symptomatic UTI vary significantly across the literature, making the reported incidence and prevalence of symptomatic UTI in this population variable ***(Rowe et al., 2014)***.

A. Classification

Urinary tract infection is classified as community acquired and hospital acquired (Nosocomial UTI), Community acquired UTI is uncomplicated infection generally occurring in sexually active, non pregnant adult women who do not have structural or functional abnormalities of the urinary tract. Nosocomial UTI is that not present or incubating at the time of the hospital admission and developing 48-72 hours after hospital admission ***(Parvin et al., 2009)***.

Urinary tract infection is often divided into upper and lower UTI according to the clinical presentation. Lower UTI

refers to an infection of the bladder (cystitis) or the urethra (urethritis), while upper UTI refers to an infection of the kidney (pyelonephritis) ***(Malone, 2013)***.

Urinary tract infection can also be classified as complicated or uncomplicated. Uncomplicated UTI occurs in the absence of any anatomical or functional abnormality within the urinary tract and is the commonest type of infection. Complicated urinary tract infection (cUTI) occurs in the presence of an abnormal urinary tract or other factor that increases susceptibility to infection. Characteristics of patients with each type are shown in **Table (1)** ***(Colgan et al., 2011).***

Table (1): Characteristics of Patients with Uncomplicated & Complicated Urinary Tract Infection ***(Colgan et al., 2011)***.

Uncomplicated
▪ Immunocompetent. ▪ No known urologic abnormalities. ▪ Non pregnant. ▪ Premenopausal.
Complicated
▪ History of childhood UTI. ▪ Immunocompromised. ▪ Preadolescent or postmenopausal. ▪ Pregnant. ▪ Underlying metabolic disorder (e.g., diabetes mellitus). ▪ Urologic abnormalities (e.g., stones, stents, indwelling catheters, neurogenic bladder, polycystic kidney disease).

B. Causative organisms

Most urinary tract infections are monomicrobial; the most common pathogen is Escherichia coli, accounting for 70% to 95% cases of acute uncomplicated cystitis ***(Czaja et al., 2007)***.

The second most common pathogen is Staphylococcus saprophyticus, accounting for 5% to 15% of UTI, and occurs mainly in young women. Other less common pathogens include species of Enterobacteriaceae such as Klebsiella pneumoniae and Proteus mirabilis, Enterococcus faecalis, group B Streptococcus (GBS) and Staphylococcus aureus. Methicillin resistant Staphylococcus aureus (MRSA) in community-acquired uncomplicated UTI is rare ***(Grabe et al., 2013)***.

Group B Streptococcus causes UTI in the form of asymptomatic bacteriuria (ASB), cystitis, pyelonephritis, urethritis and urosepsis. GBS asymptomatic bacteriuria is particularly common among pregnant women; however, those most at risk for cystitis due to GBS are the elderly and immunocompromised individuals ***(Ulett et al., 2010)***.

The most common pathogens for cUTI are the same as uncomplicated, but Proteus mirabilis causes bacteremia more frequently in cUTI. Less common species can also occur in cUTI such as Serratia spp. and Providencia stuartii, as well as pathogens that also occur in catheter-associated urinary tract infection (CAUTI) such as Pseudomonas ***(Moore et al., 2014)***.

Antibiotic-resistant organisms that cause cUTI include Gram positive cocci such as MRSA, methicillin-resistant coagulase-negative staphylococci, vancomycin-resistant enterococci (VRE) and Gram negative organisms particularly those species that produce AmpC enzymes or extended-spectrum b-lactamase (ESBL). Urea-splitting organisms such as Proteus spp., Morganella morganii and Providencia stuartii are often found in patients with indwelling devices. Multidrug resistant Pseudomonas are difficult to treat. Candida spp. are frequently found as a colonizing organism and account for 5% of complicated UTI. There are few studies that detected other fungi as a causative organism ***(Pallett et al., 2010)***.

E. coli are the dominant species of CAUTI, complicated and uncomplicated. After E. coli, gram-negative bacilli, including Pseudomonas aeruginosa, Acinetobacter baumannii and Klebsiella ornithinolytica, are predominate in the biofilm that develops on catheters. The biofilms are difficult to be penetrated with antibiotics and also are difficult to be cultured with urine samples, leading to pockets of bacteria that can survive treatment and lead to seemingly recurrent infections. Common pathogens in uncomplicated, complicated and CAUTI are shown in **Table (2)** ***(Djeribi et al., 2012)***.

Table (2): Common pathogens in uncomplicated, complicated and catheter associated urinary tract infection ***(Djeribi et al., 2012)***.

Uncomplicated	Complicated	CAUTI
▪ E. coli ▪ Staphylococcus saprophyticus ▪ Klebsiella Spp. ▪ Proteus mirabilis ▪ Enterococcus faecalis ▪ Citrobacter ▪ Group B Streptococcus ▪ Staphylococcs aureus	▪ E coli ▪ Proteus mirabilis ▪ Enterococci ▪ Klebsiella Spp. ▪ Pseudomonas aeruginosa ▪ Enterobacter ▪ Staphylococcus aureus ▪ Staphylococci Coagulase-negative ▪ Providencia stuartii ▪ Serratia Spp.	▪ E coli ▪ Pseudomonas aeruginosa ▪ Acinetobacter baumannii ▪ Klebsiella ornithinolytica

Rare or Unusual Urinary Tract Pathogens

- **Corynebacterium urealyticum**

Corynebacterium urealyticum is a Gram-variable-staining rod, facultative anaerobic bacteria. It is an uncommon cause of UTI. The organism can be a catalyst for stone formation because of its strong urease activity and has been found associated with alkaline encrusted cystitis and pyelitis in children and adults with urinary tract symptoms and the formation of calculi. The main risk factors for these conditions were underlying urinary tract disease, antibiotic treatment, prolonged hospitalization, and urological manipulation. Renal transplant patients seem to be at particular risk for severe disease with Corynebacterium urealyticum ***(McCarter et al., 2009)***.

- **Yeast**

Detection of yeast, virtually always Candida Spp., in urine is uncommon in healthy individuals but is an increasingly important problem in hospitalized patients, particularly in intensive care units and long term care facilities (LTCFs). Candida albicans is the most frequently yeast isolated from urine. The primary risk factors for candiduria include diabetes mellitus, neoplasms, urinary catheterization, periodic use of broad-spectrum antibiotics or steroids, surgical procedures within the preceding month, female sex, increased age and hospitalization longer than 7 days. Diabetes and previous treatment with antifungals are independent risk factors for isolation of Candida species other than Candida albicans ***(Kauffman, 2005)***.

For many years Candida glabrata was considered a relatively nonpathogenic saprophyte of the normal flora of healthy individuals and certainly not readily associated with serious infection in humans. However, following the widespread use of immunosuppressive therapies together with broad-spectrum antibiotic treatment and increased incidence of human immunodeficiency virus (HIV) infection, the frequency of mucosal and systemic infections caused by Candida glabrata has increased significantly ***(Silva et al., 2012)***.

- **Mycobacteria**

Mycobacterial agents causing UTI are less frequent in immunocompetent individuals; they are more common and severe in immunocompromised individuals. The incidence of

tuberculosis nowadays is rising, particularly due to HIV infection. The most common causative organism of urinary tract tuberculosis is the Mycobacterium tuberculosis (MTB) and occasionally Mycobacterium bovis can also be detected. MTB has an important drawback on kidney transplant recipients, particularly during the first year after surgery ***(Ranjan et al., 2010)***.

- **Viruses and Parasites**

In general, viruses and parasites are not usually considered urinary tract pathogens. Trichomonas vaginalis may occasionally be observed in urinary sediment, and schistosoma haematobium can lodge in the urinary tract and release eggs into the urine. Adenoviruse types 11 and 21 have been implicated as causative agents in hemorrhagic cystitis in children ***(Forbes et al., 2007)***.

C. Route of Infection

Urinary tract infection occurs when virulent bacteria gain access to the normally sterile urinary tract, mostly by the ascending route. Hematogeneous spread may occur in neonates who have not developed a mature immune system yet and in immunocompromised children. Bacteria reaching the bladder multiply readily unless eliminated by defense mechanisms. Effective voiding washes out the bacteria, but some may be left in the film of the urine lining the bladder epithelium ***(Srivastava et al., 2011)***.

D. Risk Factors

In the majority of patients, UTI develops in the absence of any obvious structural abnormality (e.g. cystocele) or functional abnormality (e.g. vesicoureteric reflux [VUR]) within the urinary tract. Under normal circumstances, the urinary tract is sterile and infection develops only when bacterial virulence overcomes normal host defense mechanisms ***(Sheerin, 2011).***

The most important risk factor for bacteriuria is the presence of a catheter; CAUTI is the most common nosocomial infection; hospitalized patients have a risk of 5% per day while an indwelling catheter is in place ***(Malone, 2013)***.

Throughout childhood, having an anomaly of the urinary tract, such as urine reflux from the bladder back into the ureters, increases the risk of UTI. Boys who are younger than 6 months old who are not circumcised are at greater risk for UTI than circumcised boys of the same age ***(Tullus, 2012).***

For females, the lifetime risk of having UTI is greater than 50 %. Generally, the ascent of organisms into the bladder is easier in women than in men because of the relatively short urethra and absence of bactericidal prostatic secretions. Use of spermicide, low estrogen levels and new sexual partner within past year are risk factors ***(Guerra et al., 2012)***.

For males, 30% of those aged 50 or older suffer from UTI. The risk factors, beyond obstruction or stones, include

intercourse with infected female partners, lack of circumcision, and anal intercourse ***(Moore et al., 2014)***.

Pregnancy is one of the factors which increase the risk of UTI partly due to the pressure of gravid uterus on the ureters causing stasis of urine flow and is also attributed to the humoral and immunological changes during normal pregnancy ***(Jalali et al., 2014).***

Other risk factors include diabetes mellitus, renal failure, urinary tract obstruction (stenosis or stones), dehydration, stroke, multiple sclerosis, spina bifida, Alzheimer's disease, Parkinson's disease, kidney transplantation, instrumentation of the renal tract and immunosuppression ***(Sheerin, 2011)***.

E. Epidemiological Aspect

Urinary tract infection has become the most common hospital-acquired infection, accounting for as many as 35% of nosocomial infections ***(Kamat et al., 2009)***.

In Egypt, a study conducted on Theodor Bilharz Research Institute found prevalence of UTI to be 58% among males, and 46.7% among females; other studies on pregnant women in Egypt found that prevalence was within the range of 22-35 % ***(Sayed et al., 2007)***.

In the United States, UTI accounts for approximately 30% to 40% of all health care–associated infections. In community-dwelling older adults, the incidence and prevalence of UTI varies with age and gender. The incidence of UTI

ranges from 7% per year in postmenopausal women to 13% per year in adults older than 85 years. In men, the annual incidence of UTI ranges from 5% in men aged 65 to 74 years and is estimated to increase to 8% in men aged 85 years and older ***(Rowe et al., 2014)***.

Febrile UTI is the most common serious bacterial infection in childhood. In the first three months, UTI is present in 7.5% of females, 2.4% of circumcised males and 10% of uncircumcised males who present with a fever ***(Shaikh et al., 2008)***.

About 2-10% of young women are susceptible to ASB in pregnancy on routine screening and UTI complicates 1-3% of all pregnancies ***(Jalali et al., 2014)***.

The financial implications of UTI are quite high, predominantly as a result of the high incidence of UTI. The direct costs include the cost of outpatient doctor visits, antimicrobial prescription and hospital expenses as well as nonmedical cost associated with sick days and morbidity. The indirect cost of lost output should also be considered ***(Griebling, 2005)***.

F. Clinical Picture

1. Urethritis

Urethritis usually presents with dysuria and urethral discharge, although it is commonly asymptomatic. It is predominantly a sexually transmitted disease caused by Neisseria gonorrhoeae, Chlamydia trachomatis, Mycoplasma genitalium or Trichomonas vaginalis ***(Sheerin, 2011)***.

2. Cystitis

Cystitis or bladder infection is the most frequent type of UTI. It typically presents with dysuria, frequency, urgency, suprapubic pain, haematuria and offensive or cloudy urine. Systemic symptoms such as fever, nausea and vomiting, although rare, can also be present ***(Sheerin, 2011)***.

3. Pyelonephritis

Pyelonephritis can develop from uncomplicated UTI; however, it is more commonly seen in the setting of obstruction, urinary tract malformations, urolithiasis, or pregnancy. Typical symptoms include flank pain, chills, fever ≥ 38°C, nausea or vomiting and costovertebral angle tenderness. Common symptoms of cystitis also can be present, especially dysuria, increased frequency, and urgency ***(Litza et al., 2010)***.

4. Recurrent urinary tract infection

Recurrent UTI is a symptomatic infection that follows adequate treatment and proven resolution of a previous infection. It is considered recurrent if 2 uncomplicated infections occur within a 6-month period or 3 infections occur within the same year ***(Barber et al., 2013)***.

The pathogenesis of recurrent UTI involves bacterial reinfection or bacterial persistence, with the former being much more common. In bacterial persistence, the same bacteria may be cultured in the urine 2 weeks after initiating sensitivity-adjusted therapy. A reinfection is a recurrence with a different