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Etiological Agents of Urinary Tract Infection (UTI)

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ABSTRACT

Urinary tract infection is one of the most common infectious diseases and has a high financial burden on society. The occurrence of urinary tract infection acquired by the population is higher in young women, almost half of all women will have at least one UTI episode during their lifetime, and about 1 in 3 women will have at least one UTI episode at the age of 24 years. Urinary tract infection increases with age for both sexes. It is estimated that 10 percent of men and 20 percent of women over 65 years of age have bacterial symptoms. Worldwide, Community-associated UTI (CAUTI) prevalence is 0.7% and the main risk factors are age, sexual activity, history of urinary tract infection, and diabetes. UTI is caused by Gram-negative and Gram-positive bacteria, where more than 95 % of UTI cases are caused by bacteria. Gram-negative organisms, primarily from the Enterobacteriaceae family, are responsible for UTI. It includes Escherichia coli (74.20 %), Enterococcus spp (5.30 %), Staphylococcus saprophyticus (1.40 %) Pseudomonas spp. (3.20 %), Klebsiella pneumoniae (6.20 %), and Proteus mirabilis (2.00 %) are among the bacteria that cause UTIs, with other bacteria accounting for 8.70 % .The aim of this review is to provide a summary and critical evaluation of the published evidence about the etiological agents of urinary tract infection.

Keywords : Urinary Tract Infection (UTI), UTI Etiological, Gram Negative Uropathogens, Gram- Positive Uropathogens.

I. INTRODUCTION

Urinary tract infection (UTI) is a bacterial infection that affects any region of the urinary tract. Urine normally does not include bacteria, although the fact that it contains a range of fluids, salts, and waste products. When bacteria enters the bladder or kidney and reproduces in the urine. The global incidence of urinary tract infections (UTI) is estimated to be over 150 million cases per year. Approximately 40% of women and 12% of men will have at least one symptomatic UTI in their lifetime, with 25% of affected women experiencing recurrent UTI (RUTI) [1]. Therefore, most UTI is caused by bacteria, and this condition is called asymptomatic bacteriuria when they occur in the urine without causing

symptoms; when bacterial development contributes to symptoms, this condition is referred to as symptomatic bacteriuria, and depending on localized or systemic extension, urinary tract infections can manifest as bacteriuria with limited clinical symptoms and sepsis [2]. According to studies from European countries and the USA, ca. For UTIs, 15% of all community-prescribed antibiotics are administered. Urinary tract infection is responsible for many annual hospitalizations, especially among the elderly; the number of emergency admissions of elderly people with a primary diagnosis of UTI in the United Kingdom saw a 200 percent rise from 2001/2002 to 2012/2013, in parallel with a similar increase in bedding days, which is the second highest increase (in absolute terms) among groups of conditions. It is suspected, however, that UTIs have been substantially over-coded in recent years: part of the increase could be due to improvements in coding practice, partly due to the increased production of antibiotic resistance. UTIs account for at least 40% of all hospital infections, however, and most of them occur after catheterization, which is known to be one of the key risk factors associated with the onset of UTI [3]. On the opposite side, Infectious disease outbreaks are a major public health concern, especially in developing countries, even though they are on the decline in developed countries. Infectious diseases account for about 40% of morbidity in developing countries, where about 75% of the world's population lives, while it is just 4% in developed countries [4]. Infectious diseases are now one of the leading causes of death worldwide, and attempts to prevent and monitor their spread account for the majority of US global health spending [5]. The bacteria that cause urinary tract infections typically enter the bladder via the urethra. However, infection can potentially spread through the blood or lymphatic system. It is believed that the bacteria are usually transmitted to the urethra from the bowel Figure (1) [6].

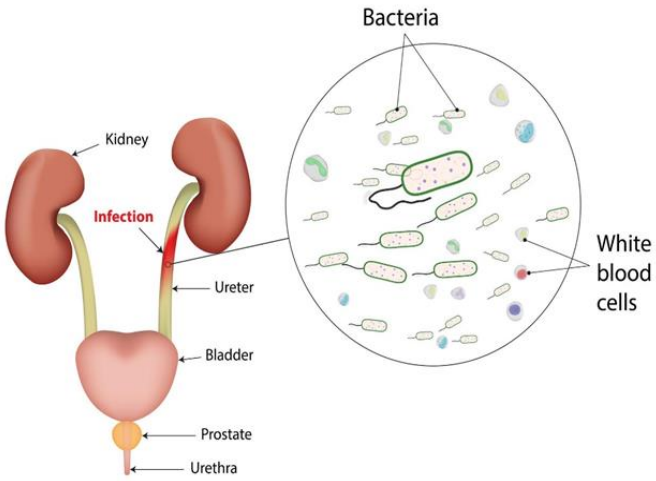

Figure [1] Urinary Tract Infection (UTI)

As shown, urinary tract infection causes the lining of the urinary tract to become red and irritated – inflammation [7]. Most infections involve the lowest urinary tract: the bladder and the urethra. Urinary tract infections do not always cause symptoms [8].

In all classes of age, these occur. Among infants and newborns, boys are more impacted than girls. Significant underlying congenital defects are usually present when the urinary tract is the source of neonatal sepsis [9 & 10]

II. Objective of the study

The aim of this review is to provide a summary and critical evaluation of the published evidence about the etiological agents of urinary tract infection with focusing on the most common cased Gram Negative and Gram- Positive bacteria that cause UTI.

III. Causes of Urinary Tract Infection UTI

Infection is the penetration of a pathogenic organism into the tissues of the host body, as well as the host's tissues' response to the pathogens and their toxins. Infectious diseases account for 3% of the top ten causes of death and 16% of all deaths per year. Infectious diseases are now one of the leading causes of death worldwide, and attempts to prevent and

monitor their spread account for the majority of US global health spending [5]. Infectious disease outbreaks are a major public health concern, especially in developing countries, even though they are on the decline in developed countries. Infectious diseases account for about 40% of morbidity in developing countries, where about 75% of the world's population lives, while it is just 4% in developed countries [11].

Urinary tract infections are caused by microorganisms; normally, dead bacteria penetrate the urethra and bladder, causing inflammation and infection. While urethral and bladder infections are the most common, bacteria may also pass through the ureters and invade the kidneys. Escherichia coli, a bacterium usually found in the intestine, is responsible for more than 85-90% of bladder infections –cystitis [12].

The urethra may be infected with Chlamydia and Mycoplasma bacteria, but not the bladder. UTIs are given different names depending on where they occur. For example:

- Cystitis is the medical term for a bladder infection.
- Urethritis is an inflammation of the urethra.
- Pyelonephritis is the medical term for a kidney infection.
- The ureters are very rarely the site of infection.

In 5–10% of cases, Staphylococcus saprophyticus is to blame [13].

Healthcare-related urinary tract infections (mostly related to urinary catheters) include a much broader range of pathogens including: E. coli (27 %), Klebsiella (11 %), Pseudomonas (11 %), Candida albicans (9 %), and Enterococcus (7%) among others (6,14 &15].

Infections of the urinary tract caused by Staphylococcus aureus typically occur as a result of infections spread through the blood [16].The urethra may be infected with Chlamydia trachomatis and genital mycoplasma, but not the bladder. Rather than a urinary tract infection, these infections are commonly known as urethritis [17].

IV. Classifications of UTI Clinically

UTI is classified on the basis of clinical symptoms, laboratory data, and microbiological findings and is usually divided into uncomplicated and complicated urinary tract infection and urosepsis. [18].

Traditionally, Urinary tract infection is classified into two groups as symptomatic and asymptomatic. An asymptomatic urinary tract or asymptomatic bacteriuria (ABU) is characterized by the presence of bacteria in the urine without clinical signs or symptoms of a host UTIs [13]. Based on the site of the infection, its severity, and / or the complexity of the infection, UTI symptoms are classified as follows:

Lower UTI: The lower urinary tract was defined as a urinary tract infection without involvement of the renal parenchyma and with normal renal scintigraphy. Lower UTI (cystitis) is an infection of the bladder usually caused by bacteria that travel into the urethra from the digestive system [19].

Upper UTI: Intra-renal abscess, pyelonephritis, perinephric abscess (usually late complications of pyelonephritis). Upper UTI or pyelonephritis is an invasive renal parenchyma infection with symptoms such as a triad of fever, kidney angle tenderness, nausea, and vomiting. It may or may not be a symptom of the upper urinary tract. These infections frequently cause urinary infection and common complications, including kidney failure, development of abscesses, and failure of the kidney. It is typically treated with intravenous antibiotics that treat the infection's urine and systemic components [20].

Uncomplicated & Uncomplicated UTI: This is a consequence of bacterial infection and its prevalence is higher among women than among men. This includes the prevalent type of infection that affects the lower and upper tracts, leading to bladder and

kidney infections, such as cystitis and kidney infection.

Uncomplicated UTI - a structurally and neurologically normal urinary tract infection. Simple cystitis of short duration (1-5 days). Structurally / functionally normal urinary tract infection. Uncomplicated infection is an episode of cystic urethritis after bacterial colonization of the mucous membrane of the ureter and bladder.

Complicated UTI – a functional or structural abnormalities (eg, indwelling catheters, renal stones). Patients with a structural or functional abnormality of the urinary tract. Complicated urinary tract infection (UTI) occurs in men and women at any point in their lives and has a tendency to have dangerous consequences leading to death in dangerous conditions.

These infections are very complex and difficult to treat and they are persistent. The complicated urinary tract infections can lead to results such as structural abnormalities that lesions that ability in the urinary tract to expel urine and this in turn provides a better range for bacterial growth as urine is considered to have an appropriate growth medium and leads to dire consequences. In addition, bladder and kidney malfunction and kidney transplantation are other factors of complicated urinary tract infection (10 & 21].

V. Symptoms of Urinary Tract Infection UTI

A urinary tract infection causes the lining of the urinary tract to become red and irritated – inflammation [22]. Most infections involve the lowest urinary tract: the bladder and the urethra. Urinary tract infections do not always cause symptoms. In all classes of age, these occur. Among infants and newborns, boys are more impacted than girls. Significant underlying congenital defects are usually present when the urinary tract is the source of neonatal sepsis. Frequent symptoms of an infection include:

- Strong, persistent urge to urinate.
- Dysuria (painful urination).
- Passing urine frequently in small amounts.
- Pelvic or rectal pain.
- Strong-smelling urine, [8 & 9].

More specific symptoms may be depending on the affected part of the urinary system:

Kidneys (pyelonephritis): These small organs are located on the back of the body. It is the body's filters that extract waste and water from the blood. These stools are converted into urine. It causes the following symptoms:

- Pain in the upper back and side (flank).
- A high fever.
- Chills and Trembling.
- Sickness and/or vomiting [9 & 22]

Bladder (cystitis): The urinary bladder is an organ that collects urine to be excreted through urination after filtering urine through the kidneys. This is commonly called as lower urinary tract infection or bladder infection and affects the bladder. It causes the following symptoms:

- Pressure or spasm in the groin or lower abdomen.
- Feeling the need to urinate despite an empty bladder
- Discomfort in the lower abdomen
- Frequent, painful urination
- Urine that is bloody or discolored [8 & 10].

Urethra (urethritis): Urethritis is an inflammatory disease that affects the male urethra and is commonly caused by an infectious pathogen that is sexually transmitted. Particularly chlamydia and gonorrhea, typically cause urethritis. However, other kinds of bacteria, can cause urethritis as well.

- Urination that is painful or burning
- Discharge caused by urethra

- Urethritis often has no noticeable symptoms [8, 23 & 24].

VI. Treatment of Urinary Tract Infection UTI

Traditionally, treatment for UTIs has consisted of antimicrobial therapy. Several antibiotics have been used in the treatment, including penicillins, sulfanilamide, nitrofurantoin, and cephalexin [13]. As well as a short course of antimicrobials, such as trimethoprim sulfamethoxazole, is used to treat urinary tract infections [25]. Fosfomycin can be used as an effective treatment for both UTIs and complex UTIs, including acute pyelonephritis [26].

In uncomplicated cases can be treated based on symptoms alone, UTIs are treated with a short course of antibiotics such as nitrofurantoin or trimethoprim / sulfamethoxazole [6]. Many of the antibiotics used to treat this condition are becoming increasingly resistant to. Usually a three-day treatment with trimethoprim / sulfamethoxazole or fluoroquinolone will suffice, while nitrofurantoin requires 5-7 days.Fosfomycin may be used as a single dose but it is not effective [27].

Complicated UTIs are more difficult to treat, with more intensive testing, therapy, and follow-up. It may be necessary to identify and treat the underlying problem. Antibiotic resistance is raising concerns regarding the treatment of difficult and recurrent UTIs in the future [28, 29 & 30]. In addition, in some circumstances, a lengthier course of antibiotics or intravenous antibiotics may be required. Further diagnostic testing may be required if symptoms do not improve in two or three days. Phenazopyridine may aid in the relief of symptoms. Antibiotics are rarely needed in people who have bacteria or white blood cells in their urine but no symptoms, with the exception of pregnancy [31]. In those with frequent infections, a brief course of antibiotics can be taken as soon as symptoms appear, while long-term antibiotics can be administered as a prophylactic precaution in those who get infections frequently [6].

Risk factors for UTI

Risk factors specific to women for UTIs include such as:

Pregnancy: The prevalence of bacteriuria increases by roughly 1% during pregnancy. They also confirmed that the risk of bacteriuria increases with the length of pregnancy, rising from 0.8 percent of bacteriuric women in the 12th gestational week to 2% at the end. The prevalence of asymptomatic bacteriuria in pregnancy ranges from 4-7 percent (range 2-11 percent) and is comparable to that of non-pregnant women [32].

Complication in Pregnant Women: The lack of treatment or improper treatment of UTI can lead to obstetric and neonatal complications, early rupture of membranes, premature delivery and labour, intrauterine growth restriction, low birth weight, abortion, and foetal death are among them. Hypertension, preeclampsia, anaemia, chorioamnionitis, endometritis, septicemias and impairment of renal function have all been linked to UTI [33].

Anemia: Bacteriuria in pregnancy was linked to maternal anaemia. On the other hand, found no link between bacteriuria and anaemia.

Diabetes: A study by Renko et al. which investigated whether asymptomatic bacteriuria (ASB) is more common in diabetic patients than in healthy people [34]. Geerlings et al., evaluated the prevalence of UTI and risk factors for asymptomatic bacteriuria (ASB) in women with and without diabetes, and reported that the prevalence of ASB is higher in all diabetic patients compared to control participants [35].

Sexual Activity: UTI has long been associated with sexual activity; hence, uncomplicated UTI has been dubbed honeymoon cystitis. UTIs are most common in women between the ages of 18 and 29, when they are most likely to initiate sexual activity. In this age group, recent, frequent vaginal intercourse is a considerable risk factor [36]. If a woman develops a UTI caused by UPEC, the same UPEC strain is twice as likely to be detected in a urethral or rectal specimen of her most recent sexual partner as an E.

coli strain isolated from her rectal specimen (IDSA, 1999). According to Buckley et al., (1978) 30% of women experience at least a one log rise in germs in the bladder after sexual intercourse. Women who have been sexually active in the last month are six times more likely to become infected, as are women who have a new sexual partner [37].

Contraception: Women who take spermicides for birth control have a higher vaginal pH and are more likely to be colonized by uropathogens, especially E. coli [38]. In comparison to women who do not use spermicide, these women have a five-fold increased risk of infection. The organisms produce hydrogen peroxide and keep the vaginal environment acidic, preventing colonization. The use of diaphragm may contribute to infection regardless of concurrent spermicide use, but because most diaphragm users also use spermicide, quantifying the increased risk owing to the diaphragm is challenging. The use of a spermicide-free birth control pill or condom is not linked to an increased risk of urinary infection [38].

Catheterization: A catheter-associated urinary tract infection (UTI) is a common nosocomial infection. UTIs are more common in those who can't urinate on their own and have to use a catheter [39]. This could include hospitalized people with neurological issues that make controlling their urination challenging [40]. The implantation of a catheter transports bacteria into the bladder and establishes an additional entry point for bacteria; catheter placement raises the risk of UTI by up to fourfold [41]. Urethral catheterization is responsible for 80% of nosocomial UTIs, while genitourinary manipulation is responsible for 5-10%. Catheters introduce germs into the bladder and promote colonization by providing a surface for bacterial adherence and irritating the mucosa [42].

Unhygienic Practices: One of the risk factors for UTI, according to studies, is widespread use of filthy absorbents and poor washing and drying of reused absorbents across Africa, Southeast Asia, and the Middle East. According to a study of Tanzanian women, only 18 percent of them use sanitary pads, with the rest utilising cloth or toilet paper [43]. Another study indicated that between 31 and 56 percent of Nigerian schoolgirls use toilet tissue or fabric to absorb their menstrual blood rather than period pads [44 & 45]. Only around a third of women in Gambia used sanitary pads on a regular basis [46]. In India, studies have indicated that between 43 percent and 88 percent of girls choose to wash and reuse cotton fabric over disposable pads [47].

7. Etiological Agents of Urinary Tract Infection

It is not surprising that many bacteria can grow in the urinary system, and do so frequently because urine is a good way for bacteria to grow. In most circumstances, bacteria that colonise the urinary tract do not cause disease because the host possesses a variety of quick and effective ways to remove bacteria from the urinary system. Urination, as well as the innate and adaptive immunological responses of the host, are examples of these methods. Bacteria that cause UTIs have specific characteristics that allow them to persist in the urinary system, or they live in a host that is weakened in some way, limiting their ability to remove bacteria.

UTI is caused by Gram-negative and Gram-positive bacteria, according to study by Davenport et al., 2017, more than 95 % of UTI cases are caused by bacteria. Gram-negative organisms, primarily from the Enterobacteriaceae family, are responsible for UTI. It includes Escherichia coli (74.20 %), Enterococcus spp. (5.30 %), Staphylococcus saprophyticus (1.40 %) Pseudomonas spp. (3.20 %), Klebsiella pneumoniae (6.20 %), and Proteus mirabilis (2.00 %) are among the bacteria that cause UTIs, with other bacteria accounting for 8.70 % [48]. Normally, dead bacteria penetrate the urethra and bladder, causing inflammation and infection. While urethral and bladder infections are the most common, bacteria may also pass through the ureters and invade the kidneys. Escherichia coli, a bacterium usually found in the intestine, is responsible for more than 85-90% of bladder infections –cystitis [49]. The urethra may be infected with Chlamydia and Mycoplasma

bacteria, but not the bladder. UTIs are given different names depending on where they occur. For example:

- Cystitis is the medical term for a bladder infection.
- Urethritis is an inflammation of the urethra.
- Pyelonephritis is the medical term for a kidney infection.
- The ureters are very rarely the site of infection.
- In 5–10% of cases, Staphylococcus saprophyticus is to blame [13].

Healthcare-related urinary tract infections (mostly related to urinary catheters) include a much broader range of pathogens including E. coli (27 %), Klebsiella (11 %), Pseudomonas (11 %), Candida albicans (9 %), and Enterococcus (7%) among others. Infections of the urinary tract caused by Staphylococcus aureus typically occur as a result of infections spread through the blood. The urethra may be infected with Chlamydia trachomatis and genital mycoplasma, but not the bladder. Rather than a urinary tract infection, these infections are commonly known as urethritis [15, 16, & 17].

A pathogen is usually defined as a microorganism causing disease to its host, and virulence refers to the severity of disease symptoms [50]. Pathogens are taxonomically varied and include bacteria, unicellular and multicellular eukaryotes. Pathogens have an impact on all living organisms. Bacteria abound on the planet, and they can be found in almost any environment. A kilogram of surface seawater contains over ten billion microorganisms on average [51]. Although the average human is made up of roughly 30 trillion cells, he or she also carries a similar amount of bacteria, the most of which are found in the intestines. The vast majority of bacteria we come into contact with have no negative effects and can even be useful, while a small percentage of them can be harmful to human health. A human pathogen is found in around one out of every billion microbial species. In fact, over 1400 human pathogens have been identified, while it is estimated that there are one trillion microbial species on the planet, the vast majority of them are unknown [52]. Bacterial pathogens are divided into two categories: main or primary pathogens and opportunistic pathogens.

Primary pathogens: are capable of infecting and causing disease in previously healthy people who have their immune systems intact. These bacteria, on the other hand, may be more likely to cause disease in people who have weakened immune systems.

Opportunistic infections: Individuals with healthy immune systems are rarely infected by opportunistic infections. Anatomical and immunological protections these bacteria can only cause disease when these defenses are damaged or degraded, as a result of congenital or acquired disease, immunosuppressive medication, or surgical methods.

Many opportunistic pathogens, such as coagulase-negative staphylococci and E. coli, are found in the normal human flora and are carried on the skin or mucosal surfaces, where they cause no harm and may even be useful by preventing the colonization of other pathogens. Furthermore, introducing these organisms into anatomical locations where they are not ordinarily prevalent, or removing competing bacteria with broad-spectrum antibiotics, could allow for limited proliferation and disease development. The abovementioned classification applies to the vast majority of diseases; nevertheless, within both groups of bacterial pathogens, there are exceptions and variances. The genetic makeup and pathogenicity potential of different strains of the same bacterial species can differ. The majority of Neisseria meningitides strains, are innocuous commensals and are classified as opportunistic bacteria, but some hyper virulent clones of the organism can cause disease in a previously healthy person. People's genetic makeup and susceptibility to invading microorganisms, on the other hand, differ. Mycobacterium tuberculosis, for example, is a main pathogen that does not infect all hosts [53].

7.1 Gram-Negative Uropathogens

7.1.1 Escherichia coli: is a member of Gram-negative rod in shape, facultative anaerobic and motile in

nature. Theodor Escherich was the first to describe this bacterium in 1885 (Lim, 2010). Escherichia coli cells are typically 1.1–1.5 μm wide by 2–6 μm long and occur as single straight rods [54]. E.coli is the normal intestinal flora in both a human being and warm-blooded animals. They are the most common urinary tract pathogens in both the community and hospitals.

In fact, carbapenem-resistant (ESBL) broad-spectrum beta-lactamase-producing strains are a critical priority by the World Health Organization (WHO) as a bacterial pathogen for which new antibiotics must be designed [55].

Urinary tract infection (UTI) bacterial infections present clinically with a variety of signs and symptoms and may be caused by a group of organisms such as the uropathogenic Escherichia coli being the main causative agent of UTI,It is responsible for more than 80% of all community acquired infections.

7.1.2 Klebsiella pneumonia: is a ubiquitous Gram-negative envelope bacterium that is found on the mucosal surfaces of mammals and the environment. After Escherichia coli, Klebsiella is the second most common cause of UTIs. It's an opportunistic bacterial pathogen linked to urinary tract infection [56]. It was identified in 1882 by Carl Friedlander as an encapsulated bacillus after extracting it from the lungs of people who had died of pneumonia [57].

Approximately 12%-15% of urinary tract infection UTI is caused by K. pneumoniae, and its prevalence is rising at an alarming rate all over the world, particularly in Asia [58].

7.1.3 Pseudomonas aeruginosa: is considered the third most prevalent bacteria linked to catheter-associated UTIs in hospitals. It is a human pathogen that can cause serious urinary tract infection (UTI). P. aeruginosa is a non-fermenter gram-negative bacillus with high intrinsic antibiotic resistance. This trait, combined with its rapid propensity to acquire new antibiotic resistance, makes this pathogen a major concern in infectious disease pathology, particularly when it is nosocomial [59].

Several factors have been associated with a reduced survival rate in patients with bacteremia due to P. aeruginosa: age, low functional status, central venous catheter, need for mechanical ventilation, resistance to carbapenems, APACHE score or high Pitt score, respiratory origin bacteremia, severe sepsis, respiratory failure, shock, thrombocytopenia, bedsores, polymicrobial infection, chronic kidney disease, cirrhosis, steroid use, cancer and AIDS. These factors have been linked to the pathogenesis of P. aeruginosa-induced diseases such as respiratory tract infections, burn wound infections, and keratitis [60].

Symptoms of P. aeruginosa vary based on the type of infection. Infection of the Urinary tract infection may cause: Urge to urinate on a regular basis, Urine that is cloudy or bloody, Urination that hurts, Urine has an unpleasant odour. Pelvic pain is a common ailment [61].

7.1.4 Proteus mirabilis: It's a gram-negative bacterium that belongs to the Enterobacteriaceae family. Proteus mirabilis is a frequent pathogen that causes bacteremia in patients with complicated urinary tract infections (UTIs) [62]. P. mirabilis is responsible for 1-10% of all urinary tract infections, depending on the study's geographic area and patient characteristics. This organism seems to be more common in complicated urinary tract infections (such as those in patients with spinal cord damage or structural abnormalities) and contributes significantly to catheter-associated urinary tract infections (CAUTI), accounting for 10-44 percent of long-term CAUTI [63].

A UTI is the most prevalent Proteus mirabilis infection. A UTI can cause the following symptoms: during urinating, you may experience pain or a burning sensation, urine that is cloudy, urination on a regular basis, pain in the abdomen, chills and fever and Fatigue. Furthermore, severe complications such as fever, discomfort, kidney damage, bacteremia, and death might occur.

7.1.5 E.aerogenes: is a Gram-negative, motile, straight rod bacterium that does not produce spores. Colonies

range in colour from beige to off-white and are often round, elevated, and wet with an entire edge. Enterobacter aerogenes has been described as a major opportunistic and multiresistant bacterial infection for humans during the last three decadesin Europe's hospital wards. Several outbreaks of hospital-acquired illnesses have largely documented this Gram-negative bacteria [64].

More than 90% of bacteria detected in cases of urinary tract infections are Enterobacter aerogenes. In addition, unlike other bacterial species and parasites, enterobacteria are found in humans' typical intestinal fora. Furthermore, enterobacteria have been linked to the majority of human illnesses in recent years, including UTIs. According to the National Nosocomial Infections Surveillance System, Enterobacter aerogenes was responsible for between 5% to 7% of hospital-acquired bacteremias in the United States.Enterobacter was shown to be the fifth most common pathogen in urinary tract infections among ICU isolates [65].

7.1.6 N.gonorrhoeae: N. gonorrhoeae was classified as a high priority pathogen. N. Infections with gonorrhoeae primarily affect the mucous membranes of the urethra and cervix, as well as the oropharynx, rectum, and conjunctivae. The incubation period is 1–14 days, but the sickness usually manifests itself in 2–5 days. Acute urethral infection is the most common simple infection in men. Urethral discharge and uncomfortable urination are common in male patients (dysuria).

The majority of infected women have lesser symptoms, and many are asymptomatic. Both sexes are susceptible to asymptomatic N. gonorrhoeae infections, which can go untreated. It's also to blame for a slew of difficulties and side effects that harm women's reproductive systems. The incidence of Neisseria gonorrhoeae infections has increased in recent years, as has its resistance profile to the various antibiotic classes available. According to the Center for Disease Control and Prevention (CDC), Neisseria Gonorrhoeae infection is one of the most important threats of antibiotic resistance in the United States and the world [66]. Infection with Neisseria gonorrhoeae has been more common in the last decade, especially among young people. According to the World Health Organization (WHO), the number of new cases of gonorrhoea has increased by 21% since 2005, with an estimated 78 million new cases per year. Prevalence and incidence estimates differed by location and gender. Direct approaches (direct examination, culture, molecular biology) are used to diagnose Neisseria gonorrhoeae infections, which are based on the presence of gonococci or their genomes in various places accessible for sample (urethra, cervix, vagina, rectum, pharynx, and urine [67]. The infection of N. gonorrhoeae begins with gonococci adherence to epithelial cells, followed by local cellular invasion. Gonorrhea possesses a number of surface proteins that help it stick together.

7.1.7 A.baumanni: is a Gram-negative bacteria that causes urinary tract infections. It is a member of the Moraxellaceae family. It's frequently linked to the use of urinary catheters or percutaneous nephrostomy tubes. The organism has the ability to accumulate a variety of resistance mechanisms, resulting in the establishment of strains resistant to all currently available antibiotics [68].

A. baumannii is still a prominent and difficult-to-treat pathogen with complex resistance patterns that present considerable hurdles to clinicians. Regarding the ubiquity and interest in A. baumannii infections, there is a scarcity of well-controlled scientific data to aid clinicians in selecting the best empirical and targeted therapy for a variety of infections [69]. A. baumannii is one cause of urinary tract infection. Accounting for only 1.6 percent of ICU-acquired UTIs. In most cases, this bacterium is linked to catheter-related infection or colonisation. In outpatients, A. baumannii rarely causes a serious UTI.

7.2 Gram- Positive Uropathogens

Gram-positive bacteria are a major cause of urinary tract infection (UTI), especially in the elderly, pregnant women, and those with other UTI risk

factors [70]. Gram-negative bacteria are responsible for 75 to 95% of uncomplicated urinary tract infection UTI. Complicated UTIs often occur in nosocomial settings, especially in people who have anatomical or functional changes in the urinary system, as well as underlying renal, metabolic, or immunological problems [71].

7.2.2 Staphylococcus Aureus (SA): is an uncommon isolate in urine cultures and only responsible for (0.5–6% of positive urine cultures), except in patients with risk factors for urinary tract colonization. It is a human pathogen as well as a commensal bacteria. S. aureus has colonised around 30% of the human population [72]. In the general population, Staphylococcus aureus is a relatively infrequent cause of urinary tract infection. Although S. aureus colonisation and infection of the ascending urinary tract is commonly subsequent to staphylococcal bacteremia emerging elsewhere, in some cases, S. aureus colonisation and infection of the ascending urinary tract is caused by S. aureus. Many types of Gram-positive bacteria have been linked to urinary tract infections. The most common human staphylococcal pathogen, Staphylococcus aureus, is a troublesome pathogen in human medicine. As end urology advances technologically, patients are more frequently fitted with various urinary catheters, increasing the risk of urinary tract infection. Gram positive bacteria, such as MRSA, are more common in complex urinary tract infections and hospitalized patients [73 & 74].

7.2.3 Staphylococcus epidermidis: Staphylococcus epidermis's a gram-positive facultative bacteria that formed slime for endocarditis and septicemia adhesions in humans. It is the most prevalent Staphylococcus species that reside on human skin and are coagulase-negative [75]. S. epidermis's currently accounts for nearly 22% of bloodstream infections in intensive care unit patients in the USA. In addition, infections caused by S. epidermis's prevalent in patients with indwelling central venous catheters. When S. epidermis's isolated from blood or body fluids in people who do not have any predisposing circumstances, it is frequently regarded as a contaminant. This bacterium has been linked to urinary tract infections in people who have indwelling urinary catheters or other urinary tract equipment [76].

While S. epidermidis has long been thought to be a urinary contaminant, this assumption should be approached with caution. The likelihood of a S. epidermidis UTI as the cause of the patient's symptoms should be investigated in a symptomatic patient with recurring positive urine cultures. In addition to antibiotic treatment, a thorough examination for underlying urinary tract problems is required [77].

7.2.4 Enterococcus faecalis: is a gram-positive, commensal bacteria that lives in the human digestive system. Most healthy people have E. faecalis, although it can cause endocarditis and sepsis, urinary tract infections (UTIs), meningitis, and other infections in humans [78]. E. faecalis was previously recognized as Streptococcus faecalis until 1984. Scientists previously classified the bacteria as belonging to the Streptococcus genus. E. faecalis is responsible for nearly 80% of human infections, according to the Centers for Disease Control and Prevention (CDC). When the bacteria gets into people's wounds, blood, or urine, it can cause infection. People with compromised immune systems are especially vulnerable, including those who: have a compromised immune system as a result of sickness or surgery are undergoing cancer treatment are on dialysis or having an organ transplant have HIV or AIDS have undergone a root canal [79].

VII. CONCLUSION

Infectious diseases are now one of the leading causes of death worldwide, and attempts to prevent and monitor their spread account for the majority of US global health spending (Infectious diseases, CSIS, May, 2021). Infectious disease outbreaks are a major

public health concern, especially in developing countries, even though they are on the decline in developed countries. Infectious diseases account for about 40% of morbidity in developing countries, where about 75% of the world's population lives, while it is just 4% in developed countries. Urinary tract infections are caused by microorganisms; normally, dead bacteria penetrate the urethra and bladder, causing inflammation and infection. While urethral and bladder infections are the most common, bacteria may also pass through the ureters and invade the kidneys. Clinically, Urinary tract infection (UTI) is a serious public health problem and is caused by a group of pathogens, but the most common by Escherichia coli, a bacterium usually found in the intestine, is responsible for more than 85-90% of bladder infections –cystitis.

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