A review on Causative Agents of Urinary Tract Infection and its Treatment

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ABSTRACT: Every step of disinfection and sterilisation is accompanied by cleanliness. Inadequate sanitation is the primary cause of infection. Urinary tract infection, one of the prevalent infectious diseases that increase the financial burden on society, is the infectious disease that affects the ureter, bladder, urethra, and kidneys most frequently. Urinary tract infections can be brought on by both Gram-positive and Gram-negative bacteria as well as certain fungi. Currently, the biological pathogen that is most common is uropathogenic Escherichia coli (UPEC). The other main pathogens that cause uncomplicated UTIs are Staphylococcus aureus, Klebsiella pneumoniae, Staphylococcus saprophyticus, Pseudomonas aeruginosa, Enterococcus faecalis, group B Streptococcus (GBS), Candida spp., and Proteus mirabilis. The majority of pathogens that cause UTI enter our bodies through the toilet seat. The traditional medical system employs a number of herbs, such as Nyctanthes arbor-tristis, Curcuma longa, Azadirachta indica, Terminalia chebula and Ocimum sanctum, etc. for the treatment of UTI. Additionally, there are other antimicrobials available for the treatment of UTI. However, sterilisation and disinfection using various chemical agents are included in the preventative measures. Among the disinfectants on the list are glutaraldehyde, ethyl alcohol, hydrogen peroxide, peracetic acid, formaldehyde, sodium hypochlorite, and quaternary ammonium compound, each of which has a unique minimum inhibitory concentration range against bacteria that cause UTIs. To effectively prevent UTIs, the usage of disinfectants might be promoted.

This review article presents an overview of various published articles in the aria of causative agents of urinary tract infection and its treatment.

Keywords: urinary tract, disinfectants, anti-bacterial, cystitis, pyelonephritis.

INTRODUCTION

To preserve the materials' predominance by lowering bacterial populations, cleanliness is a way of removing and minimizing dirtiness. Sterilization and disinfection are required for cleanliness (Mazzola et.al., 2009). Improper sanitation is the primary cause of illness. According to sanitation beliefs, illnesses spread through contact between healthy individuals and sick ones (Williams & Dye 2018). Infection comes from the compelled entry of pathogenic organisms into the host body, where they reproduce and then react with the tissues to produce poisons (Signore & Glaudemans 2011). Urinary tract infection is the most prevalent of the universal infectious illnesses that add to the cost to society's economy (Tandogdu et. al., 2016). An infection of the urinary tract (UTI) can damage the kidney, ureter, bladder, and urethra in addition to other urinary system organs. The urethra and bladder are parts of the lower urinary system, which is where most infections occur. Around 150 million people globally have UTIs each year (Stamm & Norrby 2001). Approximately 10.5 million persons in the United States visit hospitals for urinary tract infections, comprising 2.3 million emergency patients and 0.9% of ambulatory cases, according to a survey (Schappert & Rechtsteiner 2011; Foxman 2011; Foxman 2014).

URINARY TRACT INFECTION & ITS COMPLICATIONS

According to extensive and undisputed clinical and experimental evidence, urinary tract infections affect women four times more frequently than they do men. By way of the urethra, the blood, the lymph, or both, microorganisms can enter the renal system. But for intestinal bacteria (like Escherichia coli and microorganisms belonging to family Enterobacteriaceae), the introduction of microorganism through the urethra is the main cause of UTI. It rises the probability that women may develop UTIs. Additionally, the risk of infection is increased by bladder catheterization or instrumentation. Due to bacterial translocation inside the mucopurulent gap between the urethra and catheter, virtually all patients experience bacteriuria within 4 weeks following catheterization. The germs that cause the hematogenous infection first become infected elsewhere in the body. Additionally, the pathogenicity of UTI depends on the body's natural defence system (Tandogdu 2016).

CLASSIFICATIONS OF UTIs

According on the anatomy of the infected body parts (Table 1), the severity of the infections (Table 2), the risks associated with the infection (Table 3), and other microbiological results, urinary tract infections can be categorised.

According to microbiological findings it can further be classified as following (Tandogdu 2016).

a. Susceptible
b. Reduced susceptibility
c. Multi-resistant

Infected organ	Kind of disease
Urethra	Urethritis (UR)
Urinary bladder	cystitis (CY)
Kidney	pyelonephritis (PN)
Bloodstream	sepsis (US)

Table 1: Based on anatomy of part infected.

Grade of severity	Kind of disease
Low	Cystitis
Moderate	Pyelonephritis
Severe, established	Pyelonephritis
SIRS	Bloodstream sepsis (US)
Organ dysfunction	Bloodstream sepsis (US)
Organ failure	Bloodstream sepsis (US)

Table 2: Grade of severity of infection

Category risk factor	Type of infection
No Risk factor	O
Recurrent UTI Risk factor	R
Extra urogenital Risk factor	E
Nephropathic Risk factor	N
Urological Risk factor	U
Catheter Risk factor	C

Table 3: Risks associated with UTI

RISK FACTORS RELATING TO UTI

Some of the common risk factors associated with UTI include advanced age, an unsuitable diet, an exasperated immune response, smoking, diabetes mellitus, being overweight, concurrent infections in inaccessible places, a lack of regulation of risk factors, prolonged clinic visits prior to surgery—preferably while you're still in the hospital—a previous or persistent genitourinary infection, bowel surgery, colonisation with microbes, prolonged drainage, and urinary blundering. (Tandogdu 2016).

CAUSATIVE ORGANISMS OF UTI

Urinary tract infections can be brought on by both Gram-positive and Gram-negative bacteria as well as certain fungi. Currently, the biological pathogen that is most common is uropathogenic Escherichia coli (UPEC). UPEC is the bacteria most frequently found to cause simple UTIs, and it is followed by Klebsiella pneumoniae, Staphylococcus aureus, Pseudomonas aeruginosa, Staphylococcus saprophyticus, Enterococcus faecalis, group B Streptococcus (GBS), Candida spp., and Proteus mirabilis. (Foxman 2014; Najar et. al., 2009; Nielubowicz & Mobley 2010; Kline et. al., 2011; Ronald 2002).

Escherichia coli

The lower intestine of endotherms contains some gram-negative bacterium E. coli, which belongs to the Escherichia genus. These are the rod-shaped facultatively anaerobic bacteria (Bharadwaj 2016). The majority of E. coli strains are harmless, however certain serotypes cause severe food poisoning and occasionally cause product recalls due to food adulteration (Vogt 2002). E. colies are ejected into the the faecal content. The bacteria grows rapidly in fresh excrement under aerobic conditions for three days, but thereafter its concentrations decline (Russell & Jarvis 2001). Some E. coli variants can lead to meningitis in newborns, gastroenteritis, and urinary tract infections. Additionally, it causes severe stomach cramps, diarrhoea that typically becomes bloody in 24 hours, as well as sporadically elevated temperatures. In occasional situations, infectious strains are also responsible for gram-negative pneumonia, necrotizing enterocolitis (NEC), ongoing hemolytic anaemia, thrombocytopenia, inflammation of the peritoneum, and inflammation of the breast (Todar 2007).

Klebsiella pneumoniae

A widespread or pervasive bacterium, Klebsiella spp. may be found in two primary habitats: plants and surface water, sewage, and soil (Bagley et. al., 1978). Gram-negative K. pneumoniae bacteria live in the human body's nasopharynx and gastrointestinal system as saprophytes. The primary cause of nosocomial Klebsiella infections, UTIs, pneumonia, septicemia, wound infections, and neonatal septicemia is Klebsiella pneumoniae (Podschun & Ullmann 1988). The urinary system is where contamination typically occurs. Six to seventeen percent of nosocomial urinary tract infections (UTI) are caused by Klebsiella, and certain victim groups, such as those with neuropathic bladders or diabetes mellitus, are more likely to contract the infection (Bennett 1995).

Staphylococcus aureus

Staphylococcus aureus is a facultative aerobe that belongs to the gram-positive group of bacteria that may grow in the absence of oxygen by fermenting or using an alternate electron acceptor. Numerous studies suggest that S. aureus's pathogenicity depends on oxygen since this element is essential for the production of the virulence factor and the survival of the organism under harsh environmental circumstances (Bennett 1995). It frequently spreads across the person's skin and into their respiratory system. It is hopeful for the decrease of nitrate and catalase. S. aureus is usually the cause of food poisoning, sinusitis, and epidermal disorders like boils even though it is not necessarily harmful. Disease-associated strains usually encourage infections by producing powerful toxin from proteins and transmitting proteins of the surface of cell that adhere to and inactivate antibodies. The pathogenicity of S. aureus strains that produce Panton-Valentine leukocidin in their host phages is increased. Staff members with atopic dermatitis frequently have S. aureus infections (Masalha et. al. 2001). Staphylococcus aureus seldom causes urinary tract infections in the general population. S. aureus causes infection and colonisation of the ascending urinary tract in certain people. Urinary tract instrumentation and urethral catheterization both increase the risk of S. aureus contamination of the urinary system (Masalha et. al. 2001; Souri et. al. 2016; Murder 2006).

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Enterococcus faecalis

They are gram-positive, facultatively anaerobic, ovoid-shaped microorganisms. In each set, they emerge in minute chains or via various cells on the smear. Since E. faecalis lacks the cytochrome enzymes that streptococci have, even if certain strains do make pseudocatalase, it is catalase negative (Murray 1990). They can reproduce in 6.5% NaCl and at pH 9.6, grow at 10 and often at 45oC, and are designed to survive at 60oC for 30 minutes as their maximum temperature (Facklam 1985; Sahm and Torres 1988). Enterococci frequently cause UTIs, particularly in hospitalised patients. There have also been reports of perinephric abscess and enterococcal prostatitis. Healthy and young females who haven't had surgery or other procedures don't have frequent infections or structural issues. UTIs caused by enterococci account for 5% of cases (Murray 1990)

Pseudomonas aeruginosa

A widespread Gram-negative bacteria identified from soil, water, and plants is Pseudomonas aeruginosa. Additionally, it is an unscrupulous human pathogen cause to spreads illness to those with impaired immune systems or other health issues. P. aeruginosa possesses a amount of virulence issues, which include Exotoxin A, elastase, and phospholipase Care. These are categorised for the first time biochemically based on their cytotoxic action (Rahme et. al., 1997). Numerous virulence factors and cell-related characteristics of P. aeruginosa include extracellular enzymes or secretory virulence features such pyocyanin,elastase, phopholipase, protease, siderophores, hemolysins (rhamnolipids), and exotoxin A. These characteristics indicate a significant role in the development of illnesses such RTIs, burn wound infections, and keratitis brought on by P. aeruginosa (Mittal 2009). According to Woods et al., compared to isolates from other infection sites, strains from the site of urinary tract infections show enormous production of the enzymes elastase and protease (Woods 1986). P. aeruginosa is the third most familiar bacteria linked with UTIs caused by hospital-acquired catheters (Jarvis and Martone 1992).

Proteus mirabilis

Rod-shaped, negative for gramme Similar to E. coli, Proteus mirabilis is an Enterobacteriaceae family member. It generates hydrogen sulphide, is motile, lactose-negative, urease-positive, and indole-negative. It is a pathogen that is often found in the urinary system, mainly in individuals undergoing prolonged catheterization. P. mirabilis has the ability to start common urinary tract infections such pyelonephritis and cystitis. It is discovered in cases of asymptomatic bacteriuria, usually in elderly type 2 diabetic patients. These infections also cause bacteremia, which progressed to a potentially severe condition called urosepsis. Additionally, P. mirabilis infection causes urolithiasis, which is the construction of urinary stones. P. mirabilis is the cause of 1–10% of all urinary tract infections (Schaffer and Pearson 2015).

DISINFECTANTS EFFECTIVE AGAINST ORGANISMS CAUSING UTI

Disinfectants are antimicrobial compounds applied to the surface of inert materials to get rid of any germs that may be there. Below are the disinfectants that are very efficient against the bacteria that cause UTIs (McDonnell and Russell 1999).

Formaldehyde (CH_2CO)

A disinfectant and airborne sanitizer, formaldehyde has antimicrobial (virucidal, fungicidal and sporicidal) properties. It is a tasteless gas that has no colour. It is miscible with diethyl ether, benzene and acetone as well assoluble in water, ethanol, and chloroform. The gas is stable in a water absent environment and lacks compatibility with acids, urea, oxidizers, phenols, and alkalis. Marketable formaldehyde-alcohol solutions are stable. 0.5-1% formaldehyde solutions reduced 6–9 log10 in 8 hours after interaction (Mazzola et. al. 2009). The main drawbacks of formaldehyde are its potential carcinogenicity and lack of action in the presence of organic substances. It could also result in sensitivity and eczema (Penna et. al. 2001).

Gluteraldehyde ($C_2H_8O_2$)

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A crucial dialdehyde that is employed as a sterilant and disinfectant is glutaraldehyde. Its process entails cross-linking of proteins both outside and inside the cell, including the cell membrane. Because it lowers the growth of sporulated microorganisms, gluteraldehyde is a chemical substance that may be used for high level sterilisation. Detergents or synthetic compounds have no effect on it. It does not coagulate any proteins that could be on the outside of the object being sterilised and is nonhazardous. However, it is fatal and irritates the skin, eyes, and mucous membranes (Mazzola et. al., 2009).

Ethanol (C_2H_5OH)

Alcohol is a flammable, colourless liquid with a faint aroma. A flexible solvent, ethanol is also miscible with water and other organic solvents. However, they prevent spore germination and sporulation. The effectiveness of ethanol against viruses is greater. In general, it causes membrane dysfunction and quickly denaturing proteins that impede metabolism and result in cell death. This particular result is supported by denaturation of Escherichia coli dehydrogenase and an increased lag phase in Enterobacter aerogenes. It happens by blocking the metabolism needed for speedy cell multiplication (McDonnell and Russell 1999). Glycerin's (2% concentration) manifestation inhibits the action of ethanol in several strains, with the exception of E. cloacae and S. aureus, and prevents skin damage caused by alcohol. The MIC of ethanol is decreased by the addition of 10% iodine to 43750 mg/L for B. subtilis, E. cloacae, and 21870 mg/L for S. aureus. Alcoholic solutions are added to formaldehyde, chlorhexidine, and povidone iodine to prevent gram-negative bacteria that are common in the hospital environment from contaminating these chemicals. (Mazzola et. al., 2009). Pure ethanol will irritate both the skin and the eyes (LaGrega et. al., 2010). The signs of ingestion include nausea, vomiting, and inebriation. Chronic liver damage results from ingesting drugs over an extended period of time.

Hydrogen peroxide (H_2O_2)

The chemical agent hydrogen peroxide (H_2O_2) is frequently used for cleaning, sterilizing, and treating infections. It is sold as a clear, colourless fluid with varying concentrations on the market, ranging from 3 to 90%. Since hydrogen peroxide can easily break down into the non-toxic byproducts of water and oxygen, it is environmentally beneficial. Even though stabilisers are often added to pure solutions to prevent degradation, these solutions nonetheless maintained their stability. It demonstrates broad-spectrum action for bacteria, yeasts, viruses, and bacterial spores (Sagripanti and Bonifacino 1996). The impact often favours gram-positive bacteria over gram-negative ones. To have sporicidal effects, higher hydrogen peroxide concentrations (10–30%) and longer contact times may be required (Russell 2008). Populations higher than 8 log10 experienced decline in response to anordinary solution of 4% H_2O_2 (40k mg/L). The investigated residual strains shown reduced resistance, with MIC values which range from 469 to 1250 mg/L. It is a potent oxidant that is both safe and simple to use (Mazzola et. al., 2009). Although the presence of organic materials cannot reduce the sporicidal activity of 10% H_2O_2solution, Sagripanti and Bonifacino (1997) proved it. Lower concentrations have also demonstrated sporicidal activity after a longer duration of contact (Sagripanti and Bonifacino 1996).

Peracetic acid (CH_3COOOH)

It is a clear fluid without colour that smells strongly like acetic acid. It corrodes incredibly quickly. It possesses sporicidal, bactericidal, virucidal, and fungicidal effects at extremely low doses (0.3%) (Sagripanti and Bonifacino 1996). By disrupting sulfhydryl (TMSH) and sulphur (STMS) linkages, peracetic acid may destroy proteins and enzymes as well as increase the penetrability of cell walls (Sagripanti and Bonifacino 1996; Eissa and Nouby 2016). In addition to creating explosive mixes employing fast oxidizable metals, it is just annoying.

Sodium hypochlorite (NaOCl)

Solutions of sodium hypochlorite, also known as domestic bleach thatcommonly used assurface disinfectants. It can be used to clean plasma discharges that include the human immunodeficiency virus or HBV (McDonnell G, Russell 1992). The tested microorganisms may be found in the same MIC ranges

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when the initial free chlorine concentration is between 8000 and 9,000 mg/L. As the foundation of disinfectants, sodium hypochlorite offers a wide range of antibacterial actions at various temperatures. This substance is non-toxic, simple to handle, and compatible with detergents (Mazzola 2009)

Quaternary ammonium compounds

In addition to being excellent disinfectants, quaternary ammonium compounds (QACs) also have antiseptic properties (Frier 1971). These are occasionally identified as cationic detergents. QACs are used in a variety of medicinal contexts, including preoperative mucous membrane disinfection, usage on intact skin, and cleaning of unimportant surfaces. In addition, QACs have antibacterial properties, making them too powerful for deodorising and cleaning hard surfaces. They specifically target phospholipid bilayers as well as the cell's internal membrane. Small quantities impair the integrity of membranes, whereas larger doses cause cytoplasm to coagulate (Hugo and Frier 1969). The results are sporicidal. They prevent the growth of microorganisms and the germination of spores (McDonnell and Russell 1999).

Phenol (C_6H_5OH)

Depending on the composition, phenolic-type bactericidal chemicals have been used for a long time for their antiseptic, disinfecting, or preservation properties. In several cases, they were referred to as "general protoplasmic poisons". They possess membrane-active qualities that also contribute to their overall effectiveness (Denyer 1995).

HERBAL TREATMENT FOR UTI

Neem (Azadirachta indica)

It belongs to the Meloideae subfamily of the Meliaceae family and is more generally known as "India Lilac" or "Margosa". In our nation, the neem plant's many parts—including the areal parts, blossoms, seeds, fruits, oil, neem cake, and gum—are used as traditional Ayurvedic remedies. Neem oil leaf extracts and bark are traditionally used as medicines to treat respiratory problems, helminthiasis, leprosy, and as laxative. Additionally, it enhances human wellness. Neem oil is still effective at controlling several skin conditions. Together, the root, bark, flower, leaf, and fruit are used to cure phthisis, eczema, burning sensations, skin ulcers, and biliary illnesses (Girish and Shankara 2008; Kirtikar and Basu 1975). The following substances are among the active compounds that are water soluble and easily alcohol soluble: azardirachtin, nimbin, 1-maliantriol, nimbdin, and salannin (Kirtikar and Basu 1975). When compared to dried leaves, fresh leaves are more effective. Bark yields comparable outcomes (Francine et. al. 2015).

Tulsi (Occimum sanctum)

Tulsi is recognised as a medicinal plant having antibacterial properties that are effective against many microorganisms that are resistant to antibiotics. It also has anti-diabetic and anti-neoplastic properties.49 Both essential oils and aromatic composites are present. It is both a culinary herb and a striking, fragrant ornamental plant. Ocimum decrease lipid peroxidation and boost superoxide dismutase activity (Thaweboon and Thaweboon 2009). The Ocimum class's constituents include antibacterial, antifungal, antioxidant, and radioprotective properties (Kath and Gupta 2006; Ramesh and Satakopan 2010). Ocimum species can help in the treatment of central nervous system (CNS) illnesses like depression (Prasad et. al., 2012; Oliveira et. al., 2009). Ocimum is utilised as a medicinal plant since a phytochemical investigation shows that it contains phenolic chemicals, glycosides, flavonoids, tannins, and saponins. With a MIC of 20 mg/ml for E. coli, Vibrio cholera and Salmonella typhi the herb tulsi clearly has antibacterial activities. The plant showed improved antibacterial properties against all three pathogens after 30 minutes of engagement (Praveen 2010). In comparison to previous solvent extracts, isoamyl extract from 2012 exhibited greater and a wider spectrum of antibacterial activities, according to Prasad et al (Prasad et. al., 2012).

Turmeric (Curcuma longa L.)

Turmeric, a perennial rhizomatous shrub that belongs to the Zingiberaceae family, is mostly found in Southern Asia (Bisset 1994). It is widely cultivated throughout all of India and known as "Haldi" there

(Pharmacopoeia I, 1996). The shrub's creeping root stems are pear-shaped, oblongonate, and typically have little branches. Additionally, it is a commonly used drug in Nepal (Eigner and Scholz 1999). Additionally, it has impacts on digestion. Alkaloids, tannin, flavonoids, glycosides, and carbohydrates are all present in curcuma longa extract. Plants' antibacterial properties are due to alkaloids and flavonoids (Cordell 2001). Additionally, several extracts of the C. longa rhizome (petroleum ether, methanol, etc.) were more potent antibacterial agents than the raw extract of the plant Gupta et. al. 2015). According to research by Singh et al. from 2002, the essential oil component of turmeric has significant (P 0.001) antibacterial properties against the pathogenic Gram-positive S. aureus (CI) bacterium at low concentrations (20 mg/disc) (Singh et. al., 2002).

ANTI-BACTERIALS WIDELY USED IN TREATING UTI

Some of the anti-bacterial used systemically for treatment of UTI include Sulphonamides such as sulfamethoxazole in combination with Trimethoprim; Aminoglycosides such as Gentamycin, Amikacin; Beta-lactam antibiotics like Ceftizoxim, Ceftriaxone, Ceftazidime and Penicillin G; Quinolones and fluoroquinolones like Nalidixic acid, Norfloxacin, Ciprofloxacin; Miscellaneous: Nitrofurantoin, Vancomycin and Erythromycin etc., (Rang et. al. 2012).

CONCLUSION

With an extensive literature review, it was found that E. coli, S. aureus, Klebsiella, and other microorganisms the main contributors to urinary tract infections and various plants, including neem, tulsi, turmeric, parijat, etc., also have antibacterial properties. The disinfectants used most frequently to prevent UTI include phenol, formaldehyde, glutaraldehyde, quaternary ammonium compounds, hydrogen peroxide, etc.

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