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Review

Asymptomatic Bacteriuria in Apparently Healthy Individuals

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Abstract

Urinary tract infection (UTI) are the most common problem in healthy individuals, hospitalized and outdoor patients (Shahzad *et al.,* 2013) and it also has great socio-economic impacts on social aspects. The presence of bacteria in the urine is commonly known as bacteriuria (Nicolle, 1997). Symptomatic bacteriuria holds all symptoms like fever, pain and pressure in lower abdomen, irritating urination, dark bloody urine. Antibiotic treatments are given by medical personnel according to the guidelines by The Infectious Diseases Society of America (IDSA). In case of asymptomatic bacteriuria, they do not have any diagnostic symptoms but have quantitative count of ≥ 10^5 cfu organisms/mL of urine sample (warren *et al.,* 1999). Many factors affects Urinary Tract Infection including host factors like age, gender, diet, hormonal level and anatomical structures of any individuals. Females are more prone to asymptomatic bacteriuria due to the shortness of the urethra and closeness to anus, which enhance the entrance of fecal microflora to urinary tract (Shahzad *et al.,* 2013). In the current scenario, heavy use of antibiotics constitutes a global health problem and many UTI causing organisms to have become resistant to β-lactam antibiotics by producing extended spectrum β-lactamase (ESBL) enzymes. The production of ESBL by pathogenic bacteria poses a significant threat to public health issue in a community due to its dissemination in the environment through resistant genes. Especially with the emergence of pathogenic bacteria which are resistant (Multi, Extensive (XDR) and Pan-resistant) to multiple antimicrobial agents. Hence, diagnosis and treatment of asymptomatic UTIs has become a challenging task for researchers and medical practitioner. This review will cover the information about asymptomatic UTI causing agents, their antibiotic resistance and antibiotic treatment for this infection.

Keywords: Urinary tract infection, symptomatic bacteriuria, infectious diseases, antimicrobial agents.

Introduction

Urinary tract is a complex structure consists of kidney, urethra and bladder which are made up of sheet of urothelium. Muti-layered ciliated mucus epithelial cells present throughout the tract provide protection from microorganism but still some of the pathogens particularly bacteria cause infection. Urinary Tract Infections (UTIs) are of the most common diseases worldwide affecting all age groups, and can be defined as an inflammation of the tubular or parenchymal structures (Sauza, 2009; Heilberg and Schor 2003; Martins *et al*., 2010).

Types of Urinary Tract Infections

Urinary tract infection can be anatomically divided as upper UTI and lower UTI. Upper UTI involves acute pyelitis and acute pyelonephritis. Pyelitis is an infection of the pelvis region of kidney and pyelonephritis is the infection of parenchyma of the kidney. Lower UTI involves urethritis (infection of the urethra), cystitis (infection of the bladder), prostatitis (infection of the prostate).

Cystitis also referred as bladder infection. Most common symptoms of UTI are vaginal discharge, burning with urination, flank pain, fever, vomiting, urine with blood or pus. UTI may be divided as asymptomatic and symptomatic UTI. Complicated UTIs are more difficult to treat and usually requires more aggressive treatment and follow-up (Bryan and Charles, 2002). In case of asymptomatic, UTI bacteria present in the urine without showing any symptoms and generally not treated with general antibiotics (Ariathianto, 2011). Asymptomatic or uncomplicated infections can be diagnosed and treated based on symptoms alone. Antibiotics can be used by orally such as trimethoprim/ sulfamethoxazole (TMP/SMX), nitrofurantoin or fosfomycin are typically first line. Cephalosporins, amoxicillin/clavulanic acid, or a fluoroquinolone may also be used (Trestioreanu, 2010). Asymptomatic UTI majorly affects people who are otherwise healthy and having normal urinary tract and bladder. Treatment of this kind of infection is very important to control the aggressiveness of this infection.

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The upward movement of intestinal bacteria from the anus to the urinary opening is the main reason of colonization on the urethra, bladder, ureters and kidney. Though female urethra has its own, unique and balanced microbial ecosystem which control the entire vaginal environment (Pybus and Onderdonk, 1999) but still adult females are more prone to UTI due to some anatomical factors such as short and close structure of female urethra to the anus (Heilberg and Schor, 2003; Martins *et al*., 2010; Moura and Fernandes, 2010; Costa *et al*., 2010). Vaginal ecosystem is effective and influenced by age, gender, time of the menstrual cycle, pregnancy, infections, methods of birth control, frequency of sex, number of sexual partners (Schwebke *et al*., 1999; Burton and Reid, 2002; Clarke *et al*., 2002; Eschenbach *et al*., 2000; Ness *et al*., 2002) and sexual behaviors (Schwebke *et al*., 1999). In the past 100 years since the first microbiological study of the human vagina (Do¨derlein, 1892), *Lactobacilli* have been thought to be the predominant members of normal post pubertal vaginal microflora (Antonio *et al*., 1999). It plays a very important role to balance the normal vaginal ecosystem by preventing overgrowth of pathogens and other opportunistic organisms by producing lactic acid, hydrogen peroxide (H_2O_2), bacteriocins and other antimicrobial substances (Hillier, 1998).

Causing agents of Asymptomatic UTI

Staphylococcus, Corynebacterium, Peptostreptococcus, Gardnerella, Bacteroides, Mycoplasma, Enterococcus, Escherichia, Veillonella, Bifidobacterium and *Candida* sp. *are* (Redondo-Lopez *et al*., 1990; Larsen and Monif, 2001; Marrazzo *et al*., 2002) also present but in much lower numbers in urine of asymptomatic individuals. The most common organisms isolated in children with uncomplicated UTI are Enterobacteriaceae. The most common uropathogen, are *E. coli,* urease producing *Klebsiella* sp., *Pseudomonas aeruginosa, Serratia* sp., *Citrobacter* sp., *Corynebacterium urealyticum, Providencia* sp., *Proteus* sp. and also Gram positive bacteria like *Staphylococcus aureus, S. saprophyticus* and *Enterococcus sp.* According to Ronald (2002) *E. coli* remains the predominant uropathogen (80%) isolated in acute community acquired uncomplicated infections, followed by *Staphylococcus saprophyticus* (10-15%), *klebsiella, Enterobacter* and *Proteus* species and *Enterococcus* species infrequently causing uncomplicated cystitis and pyelonephritis. Consequently, complicated UTI has a more diverse etiology than uncomplicated UTI. The majority of symptomatic UTIs are seen in elderly women are caused by *E. coli*. Etiologic pathogens associated with uncomplicated UTI among patient with diabetes include *Klebsiella* sp., group B *Streptococci, Enterococci* sp. and *E. coli* (Ronald, 2002). Diabetic patients are particularly more susceptible to fungal UTI (Mindari *et al*., 2011).

Some fungal pathogen like *Candida* sp., *Aspergillus* sp. and *Cryptococcus neoformans* are the causative agents of asymptomatic UTI. Most UTI are caused by *Candida* sp. are associated with indwelling catheters and internal stents. In 2011, 500 urine samples were collected from healthy subjects by Onifade *et al*. (2011). In his findings, 27.2% of volunteers were positive for asymptomatic UTI and *E. coli* (66.18%) was the most predominant pathogen. In another study carried out by Adedeji and Abdulkadir (2009), 150 urine samples were collected from students of three tertiary institutes and the predominant organisms were *Escherichia coli* (28.57%), *Staphylococcus saprophyticus* (23.81%), *Klebsiella aerogenes* (23.81%), *Staphylococcus aureus* (9.52%), *Pseudomonas aeruginosa* (6.35%), *Streptococcus faecalis* (6.35%) and *Proteus mirabilis* (1.59%).

Antibiotic resistance of all uropathogens

Asymptomatic UTI infections are generally treated with antibiotics but use of antibiotics for prevention and repetitive treatment it's become a global health problem. WHO defines antimicrobial resistance as a microorganism's resistance to an antimicrobial drug that was once able to treat an infection by that microorganisms. Antimicrobial overuse, misuse and under use, poor infection control strategies, insufficient sanitation and infrastructure, decreased access to clinical microbiology laboratory, increased immunocompromised states, globalization, increased travellers are the key factors for emerging resistance bacteria (Hassani, 2014). All uropathogens become superbugs in all environment and hard to handling. These resistant organisms develop resistant gens and transfer the resistance gens by horizontal gene transfer and other transformation method. There are several mechanisms used by bacteria for achieving antimicrobial resistance like drug inactivation or modification (production of beta lactamase to deactivate beta lactam antibiotics), alternation of binding site of antibiotics, mutation of specific resistance genes, alternation of metabolic pathway, decreasing drug permeability or increasing active efflux (Li and Nikaido, 2009).

Gram-negative bacteria producing extended-spectrum β-lactamase (ESBL) have emerged as a significant challenge to undertake with present antibiotic armamentarium, both in hospital settings and in the community (Pitout and Laupland, 2008). ESBLs are plasmid-mediated enzymes with capacity to hydrolyse and thus inactivate broad spectrum β-lactam antibiotics, which in turn confer a decreased susceptibility against commonly used antibiotic drugs, such as penicillin and extended spectrum cephalosporins (Bradford, 2001). Plasmid-encoded or chromosomally encoded β-lactamases showing activity against penicillin and cephalosporins by splitting the amide bond of β-lactam ring.

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ESBL encoded plasmids also carry other resistance genes which are active against aminoglycosides, sulphonamides and quinolones. CTX-M, bla TEM, bla SHV, OXA are ESBL encoding genes. XDR bacteria defined as isolates being no susceptible to at least one agent in all but 2 or fewer antimicrobial categories listed in the Clinical and Laboratory Standards Institute (CLSI) guidelines (Magiorakos *et al*., 2011). Diabetic patients are particularly more susceptible to fungal UTI (Mindari *et al*., 2011). Carbapenem-resistant *Klebsiella pneumoniae* (CR-Kp) bacteriuria is a frequently encountered clinical condition, but its clinical impact is unknown. A study carried out by Zubair in (2014), 28 positive urine cultures were classified as asymptomatic bacteriuria (ASB) and 29 symptomatic urinary tract infections. Among 105 patients with CR-Kp bacteriuria, 80% 30 (84/105) and 20% (21/105) had ASB and symptomatic UTI respectively. In a study carried out by Anibijuwon (2011), 136 isolates were found as MDR organisms. Resistance to antibiotics was generally high; Tetracycline (100%), Erythromycin, Cotrimazole and Streptomycin (83.3%), Safamycin and Oxacillin (66.7%), while Ciprofloxacine, Amoxycillin, Chloramphenicol, Cephaloridue, Nitro-furantoin and Vancomycin showed 50% resistance respectively.

Conclusion

Considering the growing health problem of asymptomatic UTI, this is our duty to control the environment and several factors in many aspects. It is also necessary to control pollution, over usage of antibiotics to prevent or decrease development of resistance organisms. To prevent the wide spreading of asymptomatic UTI, public education and good personal hygiene are highly recommended among all individuals especially women and young girls, as they are more susceptible to this infection.

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