Journal of Advances in Medical and Pharmaceutical Sciences
9(4): 1-10, 2016, Article no.JAMPS.28241
ISSN: 2394-1111

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Urinary Tract Infections in Adult Women: Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2016/28241
Editor(s):
(1) Costas Fourtounas, Faculty of Medicine, School of Health Sciences, University of Thessaly, Greece.
Reviewers:
(1) Ana Paosinho, Egas Moniz Hospital, Lisbon, Portugal.
(2) Akobi Oliver Adeyemi, Federal Medical Centre, Bida, Niger State, Nigeria.
Complete Peer review History: http://www.sciencedomain.org/review-history/16011

Review Article

Received 10th July 2016
Accepted 7th August 2016
Published 1st September 2016

ABSTRACT

Urinary tract infections occur more frequently in women than in men. *Escherichia coli* and *Staphylococcus saprophyticus* are the most common causatives of urinary tract infections in women. The severity of urinary tract infection is determined by the innate defense mechanisms of the host and by the virulence of the infecting agents. There are factors that make females prone to urinary tract infections as anatomical structure, alterations in vaginal flora, use of indwelling catheters, sexual activity, and advance in age, genetic factors, pregnancy, dysfunctional voiding and diabetes mellitus. Acute phase response alters the concentrations of a number of proteins. A series of changes in lipid metabolism occurs during acute phase response. As a result, plasma triglycerides (TG) and very low density lipoproteins (VLDL) levels increase, while high density lipoproteins (HDL), low density lipoproteins (LDL) and total cholesterol (TC) levels decrease. Patients with urinary tract infections have significant increase of blood urea with slight increase in serum creatinin.

Keywords: UTI; Immune response; Escherichia coli; predisposing factors; blood biochemical measurements.

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1. INTRODUCTION

Urinary tract infections occur more frequently in women than in men [1]. Approximately half of all women have at least one symptomatic urinary tract infection (UTI) during their lifetime [2,3]. Asymptomatic urinary tract infection is common in women and its prevalence increases with advancing age. Treatment for this condition is not always considered necessary but, in women, the possibility of pregnancy makes evaluation worthwhile, because asymptomatic bacteriuria is associated with an increased risk of pyelonephritis and adverse outcomes of pregnancy [4]. Many women experience relapses or re-infections of the lower urinary tract even after treatment with broad-spectrum antibiotics [5,6]. Urinary tract infections have important health impacts on individuals suffering from them because of their effects on certain biochemical parameters in blood [7]. If predisposing factors are not identified and removed, urinary tract infection can lead to more serious consequences, in particular kidney damage and renal failure [4].

2. ETIOLOGY

Escherichia coli and *Staphylococcus saprophyticus* account for about 80% of community- acquired uncomplicated urinary tract infections, particularly in women under 50 years of age [8,9]. The source of the *Escherichia coli* that causes urinary tract infections is the patient's own colonic flora that colonizes the urogenital area [10]. The pathogenicity of *Escherichia coli* is mainly related to mechanisms of colonization and invasion of the bladder epithelium and the ability to form intracellular bacterial communities [4]. Certain O serotypes of *Escherichia coli* preferentially cause urinary tract infections. These uropathic strains are characterized by Ppili with adhesion proteins that bind to specific receptors on the urinary tract epithelium [10]. The adhesion P pili bind to glycolipids found on mucosal surfaces in the urinary tract [1]. Another important virulence factor is type 1 fimbriae. These are very important in the mechanism of bacterial adhesion to the uroepithelium. They are comprised of several subunits, the most important of which is an adhesion protein known as Fim H which mediates both cellular invasion of *Escherichia coli* and adhesion to mannose- containing glycoproteins [4]. Uropathogenic *Escherichia coli* are better adapted to the urethra, periurethra and vagina than other *Escherichia coli* [1]. The motility of *Escherichia coli* may aid its ability to ascend the urethra into the bladder and ascend the ureter into the kidney [10].

Staphulococcus saprophyticus occurs in the periurethral and urethral flora but transiently and in small numbers. *Staphylococcus saprophyticus* shows a tropism for the epithelial lining of the urinary tract, the only organ system in which it causes disease [11]. It is an important opportunistic pathogen and is a common cause of urinary tract infection in sexually active young women [12]. It is second only to *Escherichia coli* as most frequent causative of community-acquired urinary tract infections in young women [11,12]. Urinary tract infection caused by *Staphylococcus saprophyticus* is usually symptomatic and in approximately one half of all cases the upper urinary tract is involved [11]. *Staphylococcus saprophyticus* accounts for 10-15% of acute symptomatic urinary tract infections in young females [13]. Gastrointestinal tract is one of the dominant sources of urinary tract infections [14,15]. Urinary tract infections due to *Enterococci* are quite common, particularly in patients who have received antibiotic treatment or who have undergone instrumentation of the urinary tract [16]. *Enterococcus faecalis* causes urinary tract infections [10]. Urinary tract infections have been reported as a frequent focus of infection for enterococcal bacteremia [17,18].Gram-negative bacilli such as *Proteus mirabilis* and *Klebsiella pneumonia* can be cultured. *Proteus, Klebsiella* and most *Enterobacteriaceae* species show urease activity and form urinary calculi, which can act as reservoirs of infection [17]. Colonization of the introitus with *Enterobacteriaceae* species is a predisposing factor for urinary tract infection in women [19].

Escherichia coli is the main organism responsible for nosocomial urinary tract infections, but other Gram-negative pathogens, including *Pseudomonas spp., Enterobacter spp., Serratia spp., Citrobacter spp.,* and urease-producing *Klebsiella spp*., *Proteus spp*., *Corynebacterium urealyticum ,* and *Providencia spp*. is also involved in this type of infection [20]. They are commonly involved in nosocomial urinary tract infections due to the inability of antibiotics to penetrate into the biofilm formed around and within the infectious stone [21]. *Staphylococcus aureus*, *Staphylococcus haemolyticus* and Group B haemolytic

Streptococci are implicated in urinary tract infections [17].

The numbers of fungal urinary tract infections are increasing particularly those caused by *Candida spp.,* and, to a lesser extent, by *Aspergillus spp.* and Gram-positive bacteria, including *Enterococcus spp*. and *Staphylococcus spp.*, can cause nosocomial urinary tract infections due to selective pressure from the antimicrobial agents used in hospitalized patients [4]. Candiduria is a condition most often found in elderly, hospitalized or immunocompromised patients [22]. *Candida albicans* is the most common species isolated followed by *Candida glabrata* and other *Candida spp*. [23,24]. The bacteria causing urinary tract infections during pregnancy mirror those in non-pregnant patients. During pregnancy, nonbacterial causes include *Chlamydia* species and fungal infections, such as *Candida albicans*. Medical interventions during pregnancy can result in nosocomial infections; for example, urethral instrumentation and catheterization predispose to ascending bacteria [17].

3. IMMUNE RESPONSE

The first protection against urinary tract infection involves physical barriers (unidirectional urinary flow), epithelial cells and the production of proteins that hinder bacterial adhesion [25]. The structural variability of host cell glycoconjugates characterizes pathogen recognition at mucosal sites. Subsequently, the oncoming inflammation activates the uroepithelial cells, which produce mediators of inflammation, until the pathogens are destroyed and eliminated. The functional chemokines and chemokine receptors are crucial for neutrophil recruitment and for neutrophil dependent bacterial clearance. The neutrophil- mediated defense is essential for resistance to urinary tract infections [26]. The neutrophil and local environment of cytokine/chemokine/cell adhesion molecules governs the intensity and persistence of the host response [27]. The binding of antigenic determinants of pathogenic strains activates a signaling cascade, leading to the production of cytokines, including IL-6, IL-8, and TNF [28].

Susceptibility to urinary tract infections is caused by inefficient bacterial clearance due to an impairment of the innate host defense [29]. The severity of urinary tract infection is determined by the innate defense mechanisms of the host and by the virulence of the infecting agents. The pathogenesis of the inflammation involves the recruitment of neutrophils into the urinary tract and chemokine-chemokine receptor interactions [26]. With regard to recurrence of urinary tract infection, a subgroup of toll-like receptors, i.e., TLR-4 was shown to play an important role in the host response to uropathogens. After binding of uropathogens to the receptor, the main cytokine involved in the response is IL-8, which binds to the CXCR-1 receptor on the neutrophil plasma membrane. CXCR-1 mediates the migration of uropathogens through the urothelial wall, leading to pyuria, i.e., the macroscopic presence of pus in the urine [4]. An inhibition of mucosal signaling creates a state of asymptomatic bacterial carriage (asymptomatic bacteriuria) [26]. It has been recognized that the adipose tissue participates actively in inflammation and immunity, producing and releasing a variety of pro-inflammatory and anti-inflammatory factors [30].

During pregnancy, maternal immunity undergoes modification, favoring the implantation and development of the embryo. Research suggests that the immune response is modulated from a cell-mediated to a humoral response. This mechanism does not solely rely on the recognition of cell-surface major histocompatibility complex (MHC) proteins, resulting in less efficient responses to the bacterial cell surface proteins and possibly facilitating pathogenicity. These changes allow uropathogens to infiltrate, proliferate and ascend proximally [17].

4. PREDISPOSING FACTORS

There are factors that make females prone to urinary tract infections. We'll focus on the important factors that predispose women to urinary tract infections.

4.1 Anatomical Structure

Urinary tract infections occur more frequently in women than in men [1]. The gender difference in the incidence of symptomatic infection is attributed in part to the shorter urethra of women and the proximity of the urethra to the anal opening and vaginal introitus [31,10,4]. In women, fecal-perineal-urethral contamination is the most probable

explanation for urinary tract infections caused by enteric bacteria [4].

4.2 Altered Vaginal Flora

Lactobacilli are the dominant bacteria in the vaginal flora [4]. The vagina of women in the reproductive age is highly acidic (pH=3.8-4.2) [32]. This acidity is thought to be as a result of breakdown of glycogen present in the vaginal mucosa to lactic acid by *Lactobacillus* species [32]. Low vaginal pH inhibits the growth of pathogens [33,34]. Additionally, Lactobacilli produce hydrogen peroxide [4]. Cell wall fragments of *Lactobacillus* species could block attachment of bacterial uropathogens to uroepithelial cells [19]. The amount of glycogen liberated from vaginal cells is influenced by fluctuation in the estrogen concentration and estrogen is almost none existent after menopause, thus accounting for the reduced acidity of vaginal fluid at these times [33]. After menopause vaginal pH will be 6.0 to 8.0 [35]. This alteration in vaginal pH causes alteration in vaginal flora and may cause urinary tract infection. Incomplete cure and recurrence of genitourinary tract infection leads to a shift in the local flora from predominance of lactobacilli to coliform uropathogens facilitating urinary tract infections by these microorganisms [4].

4.3 Use of Undwelling Catheters

The majority of urinary tract infections are related to indwelling urinary catheters [36]. Most urinary tract infections caused by *Candida spp.* are associated with the use of indwelling urinary devices [4]. Coagulase-negative staphylococci involve patients with chronic indwelling catheters [37]. Biofilms surround indwelling catheters in long-term catheterized women. Bacteria become highly resistant to most antibiotics via biofilms, which prevent antibiotics reaching the pathogenic microorganisms [4]. In older women, the main factors for development of recurrent urinary tract infections are urethral catheterization [38].

4.4 Sexual Activity

Sexual activity in women has been established as a significant risk factor for urinary tract infections [17]. In young sexually active women, sexual activity is the cause of 75-90% of bladder infections, with the risk of infection related to the frequency of sex [39]. Intercourse can traumatize the urothelium of the distal urethra, resulting in increased bacterial invasion [17]. The incidence of symptomatic urinary tract infection is associated with vaginal intercourse, spermicide, diaphragm, and recentness of forming a relationship. Condom use has been associated with increased risk of urinary tract infection, but this effect may be due to trauma. Uropathogenic *Escherichia coli* are transmitted between persons during sexual activity [1]. Re-infection by coliform bacteria from the vaginal reservoir can occur as a result of sexual activity. Urinary tract infections recur in 4-5% of pregnancies [17].

4.5 Advanced Age

Estrogen stimulates proliferation of *Lactobacillus* in the vaginal epithelium causing reduction of vaginal pH, thereby preventing vaginal colonization by Enterobacteriaceae [4]. Vaginal atrophy is a condition that most women experience much later in life [40]. It is defined as an irreversible involution of the mucous membranes and tissues of the vagina following the drop in estrogen that commonly occurs in women during menopause [40,41,42]. The vaginal pH during menopause tends toward values considerable higher than those observed during fertility [41]. This is attributed to low estrogen levels [34,43]. Alkalinization of the vagina leads to the colonization by enteric organisms facilitating urinary tract infections [34,43].

In addition, in older women, the absence of estrogens decreases the volume of vaginal muscles, resulting in slackness of the ligaments holding the uterus, pelvic floor, and bladder, resulting in prolapsed of the internal genitalia increasing the risk for urinary tract infections [4]. In older women, the deterioration in the functional status is the main factor for the development of recurrent urinary tract infections [38].

4.6 Genetic Factors

Urinary tract infections are more prevalent in female relatives of women with recurrent urinary tract infections, which suggest a familial genetic predisposition to the disease [44,45]. Patients with recurrent urinary tract infections showed a high prevalence of the HSPA1B1267G allele [46]. Premenopausal women with recurrent urinary tract infections have lower CXCR2 expression (26). Because CXCR1 gene encodes a human chemokine receptor gene for

IL-8 chemokine, a reduced CXCR1 expression is observed in adults with recurrent urinary tract infections [26,47].

Polymorphism of receptors involved in the inflammation process seems to be involved in the degree of susceptibility to developing symptomatic urinary tract infection [4]. Some authors have studied genetic polymorphism in asymptomatic bacteriuria, a condition considered to be a risk factor for symptomatic urinary tract infections [48]. Toll like receptors are a family of receptors that recognize pathogen-associated molecules, and whose activation leads to the transcription of appropriate host-defense genes and to the recruitment of leukocytes [49]. Studies found an association between urinary tract infections in adults and TLR1, TLR4, and TLR5 polymorphism [49]. Polymorphism of HSPA1B gives susceptibility to urinary tract infections [26].

4.7 Pregnancy

Urinary tract infections during pregnancy are common and are associated with significant maternal and perinatal morbidity and mortality [17]. During pregnancy, development of urinary tract infection is correlated with stasis of urine in the ureters, which impairs emptying of the bladder, with an increased postvoid residual urine volume, vesicoureteral reflux, and increased urinary pH [50]. Seventy percent of pregnant women develop glycosuria and this, in combination with physiological amino acid urea of pregnancy and a fall in urine osmolality, favor bacterial proliferation [17].

Pyelonephritis is more common during the second half of pregnancy [51]. This results from increasing mechanical compression by the enlarging uterus [4]. A history of recurrent urinary tract infection, diabetes, and anatomical abnormalities of the urinary tract increase the risk of developing a urinary tract infection during pregnancy [52].

4.8 Dysfunctional Voiding

Dysfunctional voiding is defined as abnormal bladder emptying in neurologically normal individuals, especially young women in whom there is increased external sphincter activity during voluntary voiding [4]. A study of 49 women with recurrent urinary tract infections found that 76% had dysfunctional voiding [53]. Dysfunctional voiding may disrupt laminar urine flow through the urethra, causing urinary tract infection as bacteria are transferred back from the meatus to the bladder as a result of the "milk-back" phenomenon [54].

4.9 Diabetes Mellitus

The urinary tract is the principal site of infection in diabetes [55]. Adults with diabetes are more susceptible to developing lower urinary tract infection and genital infections due to various predisposing factors, such as hyperglycemia-related impairment of the immune response and glucoseuria. Anatomic and functional abnormalities of the urinary tract are also associated with diabetes, and these abnormalities complicate urinary tract infection [56]. Changes in host defense mechanisms, the presence of diabetic cystopathy and of microvascular disease in the kidneys may play a role in the higher incidence of urinary tract infections in diabetic patients [57]. The high level of infection in the urinary tract of diabetic women may be determined by the number of microorganisms located in the vagina. Age, longer duration of diabetes, and poor glycemic control were significantly associated with urinary tract infection among subjects with diabetes [55]. A Dutch study showed that despite the fact that patients with diabetes more often received longer and more potent initial treatment than patients without diabetes, women with diabetes more often had recurrences of the urinary tract infections [58].

4.10 Obesity

The obese are significantly more likely to be diagnosed with a urinary tract infection or pyelonephritis than non-obese patients [59]. Overall, the incidence of urinary tract infections and pyelonephritis were 2-5 and 5-fold higher among obese individuals (body mass index ≥30 Kg/m^2) than among non-obese individuals. Women had a higher risk for obesity- associated pyelonephritis than men [60]. A cohort study indicated that obesity was a risk factor for urinary tract infections and the obese females were at particularly higher risk for pyelonephritis [59]. Studies on pregnant and postpartum women showed increased risk of urinary tract infections in obese women [61,62]. The association between obesity and urinary tract infections may be due to some confounders

such as diabetes mellitus and other co-morbidity associated with obesity [63].

5. EFFECT OF URINARY TRACT INFECTIONS ON BLOOD BIO-CHEMICAL MEASUREMENTS

Inflammation is a process of a series of changes in the area of or away from the inflammation in the case of an inflammatory disease, or such cases as a response to the inflammation and tissue damage of an organism [64]. These changes are common reactions and not specific to a disease, which are called acute phase reactions [65]. Acute phase response includes neutroendocrine, hematopoietic and metabolic changes, including increased cortisol, leukocytosis and enhanced protein catabolism. Acute phase response alters the concentrations of a number of proteins. These proteins are called acute phase proteins. The proteins increasing in amount (such as C-reactive protein, serum amyloid A, ceruloplasmin, complement, haptoglobin, and fibrinogen) are called positive acute phase proteins, while proteins ecreasing in amount (such as albumin, transferrin, α-2 HS glycoprotein, α- fetoprotein, factor XII) are called negative acute phase proteins. Changes occurring during acute phase are intended to combat against infections and/or to facilitate tissue repair [64].

There are changes in lipids and lipoproteins in the course of many disorders characterized by infection and inflammation. Vanleuwen et al. 2003 stated that increased cytokines caused decreased levels of cholesterol in acute illness [66]. Al-Hadraawy et al. [7] found significant decrease in serum levels of total cholesterol, triglycerides, low-density lipoprotein, and very-low density lipoprotein. A study showed that urinary tract infections caused significant decrease in serum levels of total cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein [67]. Nassaji and Ghorbani [68] revealed that among patients with acute bacterial infections there were lower serum levels of total cholesterol and high-density lipoprotein and non-significant differences in triglycerides and low-density lipoprotein when compared with the control. Gordon et al. (1996) mentioned that in critically ill patients serum triglyceride concentration was higher in patients with an infection compared to patients without infection, but these differences were statistically non-significant [69]. Bacterial infections cause profound effects on different types of lipid concentration via formation of free radicals, these radicals cause lipid peroxidation [70]. Infections facilitate cytokine-induced alterations in lipid and lipoprotein metabolism leading to decreased serum levels of total cholesterol, high-density lipoprotein, and low- density lipoprotein [71]. The increased level of cytokines during urinary tract infections probably play a role in decrease the level of low density lipoprotein, or the level of low density lipoprotein decreases due to the host immune response toward microorganisms causing urinary tract infections which could induce low density lipoprotein oxidation leading to reduced level of low density lipoproteins [67]. Alvarez and Romas, 1986 stated high density lipoproteins decrease during sepsis [7]. Inflammation decreases the levels of high density lipoproteins by increasing the activity of endothelial lipase and soluble phospholipase A2 and replacing the Apo-A1 in the high density lipoproteins with serum amyloid A [64]. Triglycerides significantly decrease in urinary tract infections and this is due to the alteration in the function and composition of the lipoproteins. Patients with urinary tract infections have significant increase of blood urea with slight increase in serum creatinin [7].

6. CONCLUSION

Female's own colonic flora is the major cause of urinary tract infections in women. There are many factors that make women more susceptible to urinary tract infections. The susceptibility to urinary tract infections could be attributed to inefficient innate host defense. Urinary tract infections cause considerable alterations in various biochemical blood components. If not treated, urinary tract infections might cause adverse effects on female health and even could lead to death.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Foxman B, Manning S, Tallman P, Bauer R, Zhang L, Koopmn J, Gillespie B, Sobel J, Marrs C. Uropathogenic *Escherichia coli* are more likely than commensal *E. coli* to be shared between heterosexual sex partners. Am J Epidemiol. 2002;156: 1133-1140.
2. Kunin CM. Urinary tract infections in females. Clin Infect Dis. 1994;18:1-10.
3. Engel JD, Schaeffer AJ. Evaluation of and antimicrobial therapy for recurrent urinary tract infections in women. Urol Clin North Am. 1998;25:685-701.
4. Minardi D, D'anzeo G, Cantoro D, Conti A, Muzzonigro G. Urinary tract infections in women: Etiology and treatment options. Int J Gen Med. 2011;4:333-343.
5. Norinder BS, Norrby R, Palmgren AC, Hollenberg S, Eriksson U, Nord CE. Microflora changes with norfloxacin and pivmecillinam in women with recurrent urinary tract infection. Antimicrob Agents Chemother. 2006;50:1528-1530.
6. Uehara S, Monden K, Nomoto K, Seno Y, Kariyama R, Kumon H. A pilot study evaluating the safety and effectiveness of *Lactobacillus* vaginal suppositories in patients with recurrent urinary tract infection. Int J Antimicrob Agents. 2006; 28(1):530-534.
7. Al-Hadraawy S, Al-Hadraawy M, Mohamed K. Study effect of urinary tract infection on some biochemical profile among patients in al-najaf government, Iraq. World Journal of Pharmaceutical Research. 2015;4(8):134-141.
8. Ronald A. The etiology of urinary tract infection: Traditional and emerging pathogens. Dismon. 2003;49(2):71-82.
9. Hummers-Pradier E, Kochen MM. Urinary tract infections in adult general practice patients. Br J Gen Pract. 2002; 52(482):752-761.
10. Levinson W. Review of medical microbiology and immunology. 11ed. Mcgraw-Hill Companies. Usa; 2010.
11. Joklik W, Willett H, Amos B, Wilfert C. Zinsser Microbiology. 20th Ed. Appleton & Lange. Usa; 1992.
12. Murray P, Baron E, Pfaller M, Tenover F, Yolken R. Manual of clinical microbiology. 7th Ed. Asm Press. Washington; 1999.
13. Walter Es, Braunwald E. Urinary tract infection and pyelonephritis. Harrison's Principles of Internal Medicine. 15th Ed. 2001;2:1620-1626.
14. Graninger W, Ragette R. Nosocomial bacteremia due to *Enterococcus faecalis* Without Endocarditis. Clin. Infect. Dis. 1992;15:49-57.
15. Maki DG, Agger WA. Enterococcal bacteremia: Clinical features, the risk of endocarditis, and management. Medicine (Baltimore).1988;67:248-269.
16. Wessels MR, Wilson JD. streptococcal and enterococal infections. Harrison's Principles of Internal Medicine. 12th Ed. 1991;1:901-909.
17. Mccormick T, Ashe G, Kearney M. Urinary tract infection in pregnancy. The Obstetrician & Gynaecologist. 2008; 10(3):156-162.
18. Klevens RM. Dialysis surveillance report: National Healthcare Safety Network (NHSN)- data summary for 2006. Semin. Dial. 2006;21:24-28.
19. Larsen B, Monif G. understanding the bacterial flora of the female genital tract. Clinical Infectious Diseases. 2012;55(11): 69-77.
20. Wagenlehner FM, Niemetz AH, Weidner W, Naber Kg. Spectrum and antibiotic resistance of uropathogens from hospitalized patients with urinary tract infections: 1994-2005. Int J Antimicrob Agents. 2008;31(1):25-34 (Pubmed).
21. Marcus RJ, Post JC, Stoodley P, Hall-Stoodley L, Mcgill Rl, Sureshkumar KK, Gahlot V. Biofilms in nephrology. Expert Opin Biol Ther. 2008;8(8):1159-1166.
22. Carvalho M, Guimaraes CM, Mayer JR, BORDIGNON GP, Queiroz-Telles F. Hospital- associated funguria: Analysis of risk factors, clinical presentation and outcome. Braz J Infect Dis. 2001;5(6): 313-318.
23. Kauffman CA, Vazquez JA, Sobel JD, Gallis HA, Mckinsey DS, Karchmer AW, Suqar AM, Sharkey PK, Wise GJ, Mangi R, Mosher A, Lee JY, Dismukes WE. Prospective multicenter surveillance study of funguria in hospitalized patients. The National Institute for Allergy and Infectious Diseases (Niaid) Mycoses Study Group. Clin Infect Dis. 2000;30(1):14-18.
24. Chen SC, Tong ZS, Lee OC, Halliday C, Playford EG, Widmer F, Kong Fr, Wu C, Sorrell TC. Clinician response to Candida

organisms in the urine of patients attending hospital. Eur J Clinmicrobiol Infect Dis. 2008;27(3):201-208.

25. Mak RH, Kuo H-J. Pathogenesis of urinary tract infection: An update. Current Opinion In Pediatrics. 2006;18(2):148-152.
26. Zaffanello M, Malerba G, Cataldi L, Antoniazzi F, Franchini M, Monti E, Fanos V. Genetic risk for recurrent urinary tract infections in humans: A symptomatic review. Journal of Biomedicine and Biotechnology; 2010.
27. Webb NJ, Brenchley PE. Cytokines and cell adhesion molecules in the inflammatory response during acute pyelonephritis. Nephron Experimental Nephrology. 2004;96(1):1-6.
28. Fischer H, Yamamoto M, Akira S, Beutler B, Svanborg C. Mechanism of pathogen-specific Tlr4 activation in the mucosa: Fimbriae, recognition receptors and adaptor protein selection. Eur J Immunol. 2006;36(2):267-277.
29. Frendeus B, Godaly G, Hang L, Karpman D, Lundstedt AC, Svanborg C. Interleukin 8 receptor deficiency confers susceptibility to acute experimental pyelonephritis and may have a human counterpart. Journal of Experimental Medicine. 2000;192(6):881-890.
30. Falagas Me, Kompoti M. Obesity and infection. Lancet Infect Dis. 2006; 6(7):438-446.
31. Hooton TM, Stapleton AE, Roberts P, Winter C, Scholes D, Bavendam T, Stamm We. Perineal anatomy and urine-voiding characteristics of young women with and without recurrent urinary tract infections. Clin Infect Dis. 1999;29:1600-1601.
32. Ekanom EI, Efiok EE, Udoh AE, Inyang-Out A. Study of the bacterial flora of the vagina and cervix in women of childbearing age in rural community of Niger Delta Region, Nigeria. Gynecol Obstetric. 2012;2(1).
33. Al-Saadi M, Al-Windawi S. changes of vaginal ph in correlation with serum Fsh, Estradiol and vaginal bacterial culture in premenopausal and postmenopausal women. The Iraqi Journal of Medical Sciences. 2003;2(3):370-375.
34. El-Nahi S. Distribution of vaginal microbial infections of iraqi infertile females according to age, body mass index and menstrual cycle. I.J.S.N. 2012;3(1):147-152.
35. Caillouette J, Sharp C, Zimmerman G, Roy S. Vaginal Ph as a marker for bacterial pathogens and menopausal status. Am J Obstet Gynecol. 1997; 176:1270-1277.
36. Burton DC, Edwards JR, Srinivasan A, Fridkin SK, Gould CV. Trends in catheter associated urinary tract infections in adult intensive care Units-United States, 1990-2007. Infect. Control Hosp. Epidemiol. 2011;32:748-756.
37. O'gara J, Humphreys H. Staphylococcus Epidermidisbiofilms: Importance and implications. J. Med. Microbiol. 2001; 50:582-587.
38. Nicolle LE. Asymptomatic bacteruria in the elderly. Infect Dis Clin North Am. 1997;11(3):647-662.
39. Nicolle LE. Uncomplicated urinary tract infection in adults including uncomplicated pyelonephritis. Urol Clin North Am. 2008; 35(1):1-12.
40. Cenzonl M. Vaginal atrophy; 2012 (Internet).
41. Freedman MA. Vaginal Ph, estrogen and genital atrophy; 2008(Internet).
42. Goh PSC. An Outpatient Approach to vaginal discharge; 2010 (Internet).
43. Miller Ke. Vaginal Ph for diagnosis status of menopause. Am Fam Physician. 2005;71:979.
44. Hopkins WJ, Uehling DT, Wargoski DS. Evaluation of a familial predisposition to recurrent urinary tract infections in women. American Journal of Medical Genetics. 1999;83(5):422-424.
45. Scholes D, Hooton TM, Roberts PL, Stapleton AE, Gupta K, Stamm WE. Risk factors for recurrent urinary tract infection in young women. Journal of Infectious Diseases. 2000;182(4):1177-1182.
46. Karoly E, Fekete A, Banki NF, Szebeni B, Vannay A, Szabo AJ, Tulassay T, Reusz GS. Heat shock protein 72 (Hsoa1b) gene polymorphism and toll-like receptor (Tlr)4 mutation are associated with increased risk of urinary tract infection in children. Pediatric Research. 2007; 61(3):371-374.
47. Lundstedt A-C, Mccarthy S, Gustafsson Mcu, Godaly G, Jodal U, Karpman D,

Leijonhufvud I, Linden C, Martinell J, Ragnarsdottir B, Samuelsson M, Truedsson L, Andersson B, Svanborg C. A genetic basis of susceptibility to acute pyelonephritis. Plos One. 2007;2(9).

48. Hooton TM, Scholes D, Stapleton AE, Roberts PL, Winter C, Gupta K, Samadpour M, Stamm WE. A prospective study of asymptomatic bacteruria in sexually active young women. N Engl J Med. 2000;343(14):992-997.
49. Hawn TR, Scholes D, Li SS, Wang H, Yang Y, Roberts PL, Stapleton AE, Janer M, Aderem A, Stamm WE, Zhao LP, Hooton Tm. Toll-like receptor polymorphisms and susceptibility to urinary tract infections in adult women. Plosone. 2009;4(6).
50. Krcmery A, Hromec J, Demesova D. Treatment of lower urinary tract infection in pregnancy. Int J Antimicrob Agents. 2001; 17(4):279-282.
51. Hill JB, Sheffield JS, Mcintire DD, Wendel GD. Acute pyelonephritis in pregnancy. Obstet Gynecol. 2005;105(1):18-23.
52. Golan A, Wexler S, Amit A, Gordon D, David MP. Asymptomatic bacteruria in normal and high-risk pregnancy. Eur J Obstet Gynecol Reprod Biol. 1989; 33(2):101-108.
53. Akkad T, Pelzer AE, Mitterberger M, Rehder P, Leonhartsberger N, Bartsch G, Strasser H. Influence of intravesical potassium on pelvic floor activity in women with recurrent urinary tract infections: comparative urodynamics might lead to enhanced detection of dysfunctional voiding. Blu Int. 2007; 100:1071-1074
54. Yagci S, Kibar Y, Akay O, Kilics S, Erdemir F, Gok F, Daynacm. The effect of biofeedback treatment on voiding and urodynamic parameters in children with voiding dysfunction. J Urol. 2005;174(5): 1994-1997
55. Janifer J, Geethalakshmi S, Satyavani K, Viswanathan V. Prevalence of lower urinary tract infection in South Indian type 2 diabetic subjects. Indian J Nephrol. 2009;19(3):107-111.
56. Grandy S, Kathleen M, Hardy E. Prevalence and recurrence of urinary tract and genital infections among adults with and without type 2 diabetes mellitus in the general population: A longitudinal cohort study. Journal of Diabetes Research & Clinical Metabolism; 2013 (Internet)
57. Sridhar CB, Anjana S, Mathew JT. Acute infections. In: MMS Ahuja, BB Tripathy, GP Sam Moses, HB Chandalia, AK Das, PV Rao, Editors. Rssdi text book of diabetes mellitus. Hyderabad, India. 2002;471-478.
58. Schneeberger C, Stolk RP, Devries JH, Schneeberger PM, Herings RM, Geerlings SE. differences in the pattern of antibiotic prescription profile and recurrence rate for possible urinary tract infections in women with and without diabetes. Diabetes Care. 2008;31: 1380-1385.
59. Semins M, Shore A, Makary M, Weiner J, Matlaga B. The impact of obesity on urinary tract infection risk. Urology. 2011; 79(2):266-269.
60. Barber J. Obesity linked with increased risk for urinary tract infections; 2013 (Internet).
61. Basu JK, Jeketera CM, Basu D. Obesity and its outcomes among pregnant South African women. Int J Gynaecol Obstet. 2010;110(2):101-104.
62. Ushakiran TS, Hemmadi S, Bethel J, Evans J. Outcome of pregnancy in a woman with an increased body mass index. Bjog. 2005;112(6):768-772.
63. Nassaji M, Ghorbani R, Tamadon M, Masomeh. Association between body mass index and urinary tract infection in adult patients. Nephrourol Mon. 2015;7(1) (Internet).
64. Balci B. The modification of serum lipids after acute coronary syndrome and importance in clinical practice. Curr Cardiol Rev. 2011;7(4):272-276.
65. Feingold KR, Grunfeld C. The acute phase response inhibits reverse cholesterol transport. J Lipid Res. 2010; 51:682-684.
66. Vanleeuwen HJ, Heezius EC, Dallinga GM, Vanstrijp JA, Verhoef J, Vankessel KP. Lipoprotein metabolism in patients with severe sepsis. Crit Care Med. 2003; 31:1359-1366.
67. Johnkennedy N, Chinedu O, Richard N, Chinedu I, Chinyere O, Ukamata E. Investigations on serum lipid profile in patients with urinary tract infections. Global Journal of Scientific Researches. 2013;1(3):68-70.

68. Nassaji M, Ghorbani R. Plasma lipid levels in patients with acute bacterial infections. Turk J Med Sci. 2012;42(3): 465-469.

69. Luthold S, Berneis K, Bady P, Muller B. effects of infectious disease on plasma lipids and their diagnostic significance in critical illness. Eur J Clininves. 2007; 37:573-579.

70. Nnodim Jk, Ihim A, Uduji Hi. Attenuation of chloroquine-induced hepatoxicity and renaldamage by gnetumbucholzianum leaf extract. New Zealand Journal of Medical Laboratory Science. 2012;66:46-47

71. Gazi I, Elisaf M. Effect of infection on lipid profile: Focus on epstein-barr virus. Clin. Lipidol. 2010;5(5):607-610.

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