

PREDISPOSING FACTORS FOR URINARY TRACT INFECTIONS

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ABSTRACT

The important predisposing factors for urinary infections in females are age, sex, pregnancy, sexual intercourse, menopause, use of birth control devices, catheterization, surgery, diabetes, use of calcium supplements, immuno-suppression, renal transplantation and spinal cord injury. Besides, UTI is also the most frequent medical complication in patients with neurologic bladder dysfunction leading to high morbidity, poor quality of life and limited life expectancy. Moreover, severe protein malnutrition, poor fluid intake, and poor hygiene resulting in decrease immunity are also associated with urinary tract infections.

Key-words: Urinary infection, predisposing factors, sex, sexual activity, birth control devices, diet, add & cancer

INTRODUCTION

A number of predisposing factors render individuals susceptible to urinary tract infections (UTIs). Any obstruction in normal urine flow or complete emptying of bladder facilitates the access of organisms to the bladder and, in turn, predisposes an individual to infection (Jackson *et al.*, 2000). There are numerous possible structural abnormalities of urinary tract that are associated with a 'residual urine' which increases the chances of infection and may become associated with repeated attacks of UTI. Some of these are renal calculi, tumors, and urethral stricture. All these factors cause obstruction to complete emptying of bladder (Shanson and Speller, 1999). Approximately 15% of the urinary stones diseases are infectious stones. These stones are composed of struvite and/or carbonate apatite. UTI caused by urease positive organisms is also a risk factor for the formation of infectious stones. If these infections are not treated and the stones are not removed, the kidney is damaged (Bichler *et al.*, 2002). Some important predisposing factors for urinary tract infections are:

1. SEX

An important predisposing factor for UTI is the sex of patient. It is evident from substantial research that UTIs are more common in females as compared to males (Mohsin and Siddiqui, 2010; Dielubanza and Schaeffer, 2011). Most infections in women are uncomplicated, whereas in men complicated infections predominate (Carlson and Mulley, 1985). Women are especially prone to UTIs probably because of the shortness of urethra and closeness of urethra to opening of genital and intestinal tract (Nester *et al.*, 2004). The shorter length of the female urethra allows uropathogens easier access to the bladder. Men are less prone to get UTI, possibly because of their longer urethra and the presence of antimicrobial substances in the prostatic fluid (Schaechter *et al.*, 1993). The relation of sex and incidence of UTI has been confirmed by the study of Laupland *et al.*, (2007). Laupland *et al.*, (2007) reported community onset of UTI among Canadian residents with the annual incidence of 1.75% and females were at significantly increased risk as compared to males (3% vs. 0.5%, RR 5.98; 95% CI, 5.81-6.15; P<0.001).

2. AGE

The incidence of UTIs in women tends to increase with increasing age. Symptomatic and asymptomatic UTIs are extremely common in the elderly population. The prevalence of bacteriuria in women is about 20% between ages 65 and 75, increasing to between 20-25% over the age of 80 years (Gray and Malone-Lee, 1995). Whereas, a significant number of infections occur in men only after the age of 50 years when prostatic hypertrophy or other urinary tract abnormalities occur. UTI in young men is unusual and requires further investigations (Shanson and Speller, 1999). The prevalence in men is 3% at age 65-70 years and about 20% at ages over 80 years (Gray and Malone-Lee, 1995). The geriatric (elderly) community is frequently affected by UTIs but these infections are usually asymptomatic. Approximately 25% of all infections in elderly are UTIs (Foxman, 2002). In a study (Buonanno and Damweber, 2006), it was documented that 50% of elderly women are affected by asymptomatic UTI. In many cases bladder catheterization is a contributing factor and causes increasing incidence of UTIs in elderly population. In another study (Rodhe *et al.*, 2006), it was reported that asymptomatic UTI was found in 14.8% of the overall individuals of ≥ 80 years of age. Of these, 19% were women and 5.8% were men. A woman over 80 years with urinary incontinence and needing support to walk has 50% risk of asymptomatic UTI. The majority of symptomatic

urinary tract infections occur in women after the age of 50 years (Shanson and Speller, 1999). In a study (Menon *et al.*, 1995), prevalence of symptomatic and asymptomatic UTI was evaluated in women between 57-97 years of age. It was found that symptomatic UTI occurred in 54% women and asymptomatic UTI occurred in 10% women. From these results it was concluded that asymptomatic UTI was common in elderly women while only a small percentage of women have symptomatic UTI. In another study, an increased prevalence of UTI among women aged 18-30 years was found associated with sexual intercourse and pregnancy (Cunha *et al.*, 2007). It has been reported that complicated UTIs were found most frequent among females aged between 40-59 years, while, in other age groups, uncomplicated UTIs were most frequent. It has also been noted that the isolation frequency of *E. coli* gradually decreases with increasing age with both complicated and uncomplicated UTIs (Kumamoto *et al.*, 2001).

UTIs are generally asymptomatic among apparently healthy, sexually active young women. In contrast, UTIs are more complicated among elderly individuals, infants and young children. UTI in children younger than 2 years has been associated with significant morbidity and long term medical consequences (Shortliffe, 2003). Winiecka *et al.*, (2002) evaluated the bladder instability in children with recurrent UTIs. It was found that the most common disturbance of lower urinary tract functioning in the children with recurrent UTI was instability of the detrusor muscles which occurred more often in children with vesicoureteral reflux.

The incidence of nosocomial UTIs has been found to be higher in age group of 53.6 ± 20 years than the patients in age group of 39.7 ± 22.2 years. However, all the UTIs are usually asymptomatic and develop in catheterized individuals (Parlak *et al.*, 2007). In contrast, Vessey *et al.* (1987) observed that the risk of UTI decreases with age.

3. SEXUAL ACTIVITY

Another predisposing factor, sexual intercourse, is also a common cause of UTIs among women because during sexual intercourse bacteria in the vaginal area could be messaged into the urethra. This problem can be avoided by urinating after sexual intercourse (Cornforth, 2002). Women who change sexual partners or have sexual intercourse more frequently may experience more frequent bladder infections (Kontiokari *et al.*, 2003). In a study (Scholes *et al.*, 2000), independent risk factors for recurrent UTI in young women included recent one month intercourse frequency (odds ratio (OR), 5.8; 95% confidence interval (CI), 3.1-10.6 for 4-8 episodes), 12 month spermicide use (OR, 1.8; 95% CI, 1.1-2.9), and new sex partner changing the past year (OR, 1.9; 95% CI, 1.2-3.2).

4. USE OF BIRTH CONTROL DEVICES

Several studies have shown that women who use a diaphragm are more likely to develop UTIs than women who use other forms of birth control (Strom *et al.*, 1987). More recently, investigators have demonstrated that women whose life partners use a condom with spermicidal foam also tend to have growth of *E.coli* in the vagina (Jancel and Dudas, 2002). Women with UTI are 2.7 times more likely to be current user of intra-uterine contraceptive device (IUCD)/condoms (95% CI, 1.3-5.6) and 1.6 times more likely to be housewives by occupation (95% CI, 1.0-3.0) as compared to women who did not have UTI. UTI among IUCD/condom users may reflect existence of unhygienic conditions during application of procedure or spread of infection by the thread of IUCD. UTI in these women may have serious consequences of developing renal damage (Bhurt *et al.*, 2000).

5. PREGNANCY

Pregnancy also acts as a risk factor for UTI as it causes anatomic and hormonal changes which favour development of UTI (Schlembach, 2006; Marinade *et al.*, 2009). A history of current UTI, diabetes mellitus, analgesic nephropathy, hyperuricaemia and Fanconi's syndrome are predisposing factors for UTI during pregnancy (Krcmery *et al.*, 2001). Dietary habits seem to be an important risk factor for UTI recurrence in fertile women, and dietary guidance could be a first step towards prevention (Kontiokari *et al.*, 2003). The physiological changes associated with pregnancy are the relaxation of ureter under the effect of hormones and increase urinary output. The chemical composition of urine is also affected and results in increased urinary substances e.g. glucose and amino acids, which may facilitate bacterial growth (Sheikh *et al.*, 2000). The pregnant women with kidney infection have a greater chance of delivering their babies prematurely with low weight (Mittal and Wing, 2005). Sometimes, it results in fetal and maternal morbidity (Lamyman *et al.*, 2005). Recently, the relationship of maternal UTIs in pregnancy with the rate of preterm birth was evaluated (Banhidy *et al.*, 2007). It was found that of 38,151 newborn infants, 5.7% had mothers with UTIs with pregnancy. Women with pregnancy also had somewhat shorter gestational age and a higher proportion of preterm birth. This preterm inducing effect of maternal UTI was preventable by antimicrobial therapy. In this connection, Hazir (2007) evaluated the frequency of asymptomatic UTI in pregnant women. Eleven hundred apparently healthy pregnant women were screened for significant bacteriuria. The prevalence of asymptomatic UTI was found to be 6.1%. However, asymptomatic UTI had no relationship with gestational age, parity, level of education, and body mass index. In a study (Al-Haddad, 2005) 500 pregnant women

were screened for asymptomatic UTI in their first and second trimester. Out of them 8.4% were positive for culture. A control group of non-pregnant women was also screened for asymptomatic UTI. The control group yielded 3% positive cultures. The frequency of UTI in pregnant women was observed 30% of the women suffered from UTI. Of these infected women, 53.7% were in the age group of 15-24 years and 48.8% were in the third trimester. Primigravida had highest percent culture positivity i.e. 66.6%. The incidence was higher in less than 20 years of age group i.e. 71.42%. The incidence of prematurity was 75% and that of low birth weight was 50% in untreated patients (Lavanya and Jogonalakshmi, 2002).

In a study (Hanif, 2006), it was observed that out of 1000 pregnant women, 42.6% complained one or more symptoms of UTI. The urine culture of symptomatic patients showed growth in only 8.69% cases. In another study carried out by Nath *et al.* (1996), 542 women were screened for UTI. Out of them, 9.04% had UTI. Of these, 35% had asymptomatic while remaining 65% had symptomatic UTI. Age-wise incidence of UTI in pregnancy was observed in the age groups of < 25 years, 25-29 years and ≥ 30 years as 5.26%, 10.36% and 12.43% respectively. Moreover, third trimester was associated with highest number of UTI cases (11.9%), followed by second (7.5%) and first (5.7%) trimester. Prevalence of asymptomatic UTI was 6.2% in pregnant women and 2.85% in non-pregnant women. However, it remained same statistically (P value > 0.05 by χ^2 test) (Khattak *et al.*, 2006).

Incidence of UTI during pregnancy among Pakistani women, was slightly low in pregnant women (28.5%) as compared to non-pregnant control subjects (30%). However, the difference was not significant. Symptomatic UTI was found in 22.4% pregnant and 20.0% non-pregnant subjects (Sheikh *et al.*, 2000). In a study conducted in Peshawar, Pakistan (Ahmad *et al.*, 2003) the prevalence of UTI was 29.57% in pregnant while 14% in non-pregnant control subjects.

In another study performed in Pakistan, 130 muslim women of child bearing age attending the outpatients clinic were interviewed in order to determine the frequency of cystitis and its associated risk factors including personal hygiene practices. Of these, 27% of the women experienced cystitis once in the past. About 63% women reported first UTI during pregnancy. A significant relationship was observed between parity and cystitis ($P < 0.001$). However, personal hygiene practices had no significant association with cystitis (Atiullah *et al.*, 1998). It is also evident from a study (Quiroga-Feuchter *et al.*, 2007) that among tested pregnant women, 16.7% developed symptomatic UTI and 25% had at least one UTI during four month follow-up. Symptomatic and asymptomatic UTIs are also significant risk factors for developing pyelonephritis in pregnant women (Macejko and Schaeffer, 2007). Approximately 20-40% women with asymptomatic UTIs develop pyelonephritis during pregnancy (Krcmery *et al.*, 2001). During pregnancy, the patients may also develop kidney abscess which is an extremely rare condition. In this connection, Santose *et al.* (2000) reported the case of a 35 years old pregnant woman with fever, nausea, vomits, right lumbar tenderness who was admitted in the urgency room. Clinical and diagnostic tests led to the development of kidney abscess.

During pregnancy symptomatic and asymptomatic UTI can trigger the development of serious complications affecting both the mother and the fetus. Thus, proper screening and treatment of bacteriuria is necessary to prevent complications during pregnancy. All women should be screened for bacteriuria in the first trimester. Women with a history of recurrent UTIs or urinary tract abnormalities should have repeated screening for bacteriuria during pregnancy (Macejko and Schaeffer, 2007).

6. MENOPAUSE

Postmenopausal women are also susceptible to UTI due to lack of estrogen which plays important role in pathogenesis (Hu *et al.*, 2004). The protective effect of estrogen replacement on ascending UTI is controversial. A study was designed using an experimental model of UTI. In that study surgically menopausal mice were supplemented with estrogen and the susceptibility of UTI was evaluated after experimental *E. coli* infection. Surprisingly, despite the hypothesis that estrogen would protect mice from infection, estrogen treatment significantly increased the susceptibility of the mice to ascending UTI (Curran *et al.*, 2007).

In postmenopausal women, sexual activity, history of UTI, treated diabetes and urinary incontinence are associated with a high risk of UTI. However, therapeutic role of oral estrogen remains uncertain. For instance, in a study (Hu *et al.*, 2004) which included the postmenopausal women aged between 55 and 75 years, development of UTI was noted in sexually active postmenopausal women (OR, 1.42; 95% CI, 1.07-1.87), with a history of UTI (OR, 4.20; 95% CI, 3.25-5.43), diabetes mellitus (OR, 2.78; 95% CI, 1.78-4.35) and urinary incontinence (OR, 1.36; 95% CI, 1.03-1.78).

7. CATHETERIZATION

Another common source of infection is catheter or tube placed in the bladder (Ribby, 2006; Warde, 2010). The use of vesical catheter over 5 days is the cause of UTI. Bacteria on the outside of the catheter can climb up the

device into the bladder and cause infection (Pawelczyk *et al.*, 2002). Infection associated with an indwelling catheter is a representative type of biofilm infection occurring in the urinary tract (Evans *et al.*, 2001). More than 90% of UTI in catheterized individuals are asymptomatic. These infections are rarely symptomatic and infrequently cause blood stream infection. (Tambyah and Maki, 2000).

Catheter associated UTI accounts for 40% of all nosocomial infections and are the most common source of Gram negative bacteremia in hospitalized patients. The risk of bacteriuria is approximately 5% per day in 10-20% of hospitalized patients who receive an indwelling foley catheter. With long term catheterization, bacteriuria is inevitable (Warren *et al.*, 1997). For example, the impact of urinary catheterization on 294 elderly (>65 years) inpatients with community acquired UTIs was studied (Kang *et al.*, 2007). Of 294, 144 subjects had urinary catheterization. Patients with urinary catheterization were found with significantly more advanced age, female predominance, frequent admission in hospital, longer hospital stay and higher pathogen isolation after culture than subjects without urinary catheterization ($P < 0.05$).

8. DIABETES

It is evident from literature that diabetic subjects are also at high risk of UTIs. For instance, in a study (Goswami *et al.*, 2001; Litza and Brill, 2010), the prevalence of UTI in diabetic subjects were found to be higher when compared with non-diabetic subjects (9% vs. 0.78%, $P = 0.05$). Symptomatic and asymptomatic UTIs occur more frequently in women with diabetes mellitus than women without diabetes mellitus (Daneshgari and Mooree, 2006). Women with diabetes who requires pharmacological treatment have approximately twice as high risk of cystitis as non-diabetic women (Boyko *et al.*, 2002) because of the changes in the immune system secondary to the high sugar concentration (Geerlings *et al.*, 2002). However, gestational diabetes mellitus was not associated with increased risk of UTIs (Rizk *et al.*, 2001). Although asymptomatic bacteriuria is not associated with serious health outcomes in healthy persons, further research needs to be undertaken regarding the impact of asymptomatic bacteriuria in patients with diabetes (Geerlings *et al.*, 2002). In another study, Geerlings *et al.* (2000) evaluated the characteristics associated with the development of UTI among diabetic subjects. It was found that 14% women with type 1 diabetes developed a symptomatic UTI. The most important risk factor for those women was sexual intercourse during the week before entry into the study (44% without vs. 53% with sexual intercourse). A total of 23% women with type 2 diabetes developed symptomatic UTI. The most important risk factor for those women was the presence of asymptomatic UTI at baseline (25% without vs. 42% with asymptomatic UTI). The risk of symptomatic and asymptomatic UTIs among diabetic and non-diabetic postmenopausal women was studied by Boyko *et al.* (2005). The incidences of symptomatic UTI in diabetic and non-diabetic women were recorded as 12.2% and 6.7% respectively. Whereas, the incidence of asymptomatic UTI was 6.7% for diabetic women and 3% for non-diabetic women. It was concluded that the increased UTI risk occurred mainly in diabetic women taking insulin and women with a longer diabetic duration (> 10 years) compared with non-diabetic women.

9. BLOOD TYPES

In addition to above mentioned predisposing factors, the literature has also documented that women with UTIs tend to have certain blood types (Jackson *et al.*, 2000). The presence or absence of blood group determinants on the surface of uroepithelial cells may influence an individual's susceptibility to UTIs. (Schaeffer *et al.*, 2001). Such as, as cited by Kinane *et al.* (1982), the blood groups AB or B, constitute independent risk factors in some but not all studies. Recently, Sakalliglu and Sakalliglu (2007) found the concordance of UTI with blood group A Rh positive. Infectious microorganisms interfere with specific molecules on epithelial cells. These specific molecules are antigens of the P and ABO system. Antigen structures on uroepithelial cells, for example, the glycolipids of the P antigen serves as receptors for adhesion of microorganisms. The proportion of persons with B phenotype was 23% and P1 antigen was found in 76% of patients suffering from chronic UTIs. In comparison with P1 negative individuals, P1 positive individuals has a longer disease history and more frequently suffered from symptomatic UTI as well as destructive renal changes. The Le (a) antigen and Le (b) antigen (Lewis phenotypes) were observed in 82% and 18% of the patients respectively (Ziegler *et al.*, 2004).

10. USE OF CALCIUM SUPPLEMENTS

The use of calcium supplements also increases the risk of UTI, since calcium ions significantly increase bacterial adherence to uroepithelial cells. Apicella and Sobota, (1990) demonstrated *in vitro* that as the concentration of calcium was increased to levels higher than normally found in the urine, there was a significant increase in bacterial adherence. It was also found that if the diet was supplemented with calcium there was an increase in the excretion of calcium in the urine and a corresponding increase in bacterial adherence when bacteria and uroepithelial cells were incubated in this urine.

11. SURGERY

Any surgery on the urinary tract increases the chances of UTI. Urological complications after renal transplantation are also frequently associated with UTIs (Senger *et al.*, 2007). UTI is also the most common bacterial infection occurring in the renal transplant recipients, particularly anatomic abnormalities of the native or transplanted kidneys and possible rejection and immunosuppression. The major risk factors for UTI in renal transplant recipients include indwelling bladder catheters, trauma to the kidney and ureter during surgery (Rubin, 1993; Wilson *et al.*, 2005). Steroids or cytotoxic drugs, as given to renal transplant recipients, greatly increase the chances of recurrent UTIs and infections of kidney in the first few months of post-transplant (Shanson and Speller, 1999). In a study (Senger *et al.*, 2007) it was observed that 13.3% episodes of UTI occurred in the first month to sixth month and 72% after the sixth month of transplantation. The most commonly isolated organism was *E. coli* (61.3%).

12. DIET

Frequent meat consumption appeared to be the predisposing factor for UTI. UTI were found significantly more common among the people consuming meat more frequently than once a week but not daily (Nayak *et al.*, 1999).

13. AIDS & CANCER

Certain diseases also predispose UTIs e.g. HIV patients are susceptible to acquire UTI (Padoveze *et al.*, 2002). Schonwald *et al.* (1999) performed a study to determine the relationship of UTI with AIDS. The analysis showed that patients with HIV had UTI more frequently than control (HIV negative) patients. Beside the difference in the frequency, it was also observed that *Enterococci* were the frequent isolates in patients with HIV disease, whereas, *E. coli* was most frequently isolated organism from control subjects. Cancer patients are also at high risk of UTI (Gerberding, 2002). In a study Munyis *et al.* (1998) determined the prevalence of UTI in children with cancer. The prevalence of UTI was 8.1% (CI = 6.1, 10.1). Out of 15, only 5 patients were symptomatic while remaining 10 were asymptomatic. *E. coli* and *Klebsiella* species were responsible for 93.4% of the infections.

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