

Bacterial profile of urinary tract infections in Diabetic postmenopausal women

Nedhal S. Ayoub*

Khalid Abdallah**

Safyia K. AL-Khazraji*

DMCAMB

FRCP, FACP

MSC

Summary:

Background: Urinary tract infection (UTI) is the most common bacterial infection in women in general and in postmenopausal women in particular. Bacteriuria occurs more often in elderly functionally impaired women but in general many of it are asymptomatic. However the risk factors associated with recurrent UTI in elderly women are not widely described. Bacteriuria in elderly women is associated with high mortality rates, however many of these bacteriuria are asymptomatic (Assel et al., 2009). The belief that diabetes, a common metabolic disorder is associated with a higher risk of UTI is widespread, diabetes results in several abnormalities of the host defense system that might result in a higher risk of certain infection.

Patient and Method: The prospective study included 200 cases of urinary tract infection with diabetes mellitus type 2 in postmenopausal women visiting Medicine out patients and in patients Clinic of Medical City Teaching Hospital in Baghdad city. This study period was from 15 November 2011 till 15 June 2012. Urine Samples were collected from women under supervision of the specialist's physicians. General urine examination was accomplished for each patient. For patients suspected with DM type 2 the Glycosylated haemoglobin (HbA1c) level was measured considering also the duration of diabetes. The urine samples were inoculated directly onto enrichment and selective media for the isolation of the causative bacteria. The isolates were identified using different microscopical, culture characteristics and biochemical testes.

Results: Totally in the four studied groups *E.coli* was the most common isolates bacteria 39(23.0%), followed by *Klebsiella* 26(15.3%), *Candida albicans* 25(14.7%), non hemolytic streptococcus 30(6.5%), *Moraxilla catarrhalis* 28(16.5%) and diaphtheroid 23(13.6%). Whereas *Staphylococcus aureus* comprised 13(7.7%). There was no significant relation shipe between type of uropathogenes and HbA1c level. However the relation was significant between uropathogenes and kind of diabetes treatment and duration of diabetes. *E.coli* and *klebsiella* growth isolated from diabetic cases was heavy rather than moderate growth.

Conclusion: In postmenopausal women the incidence of UTI in age group 50-60 yrs was higher than that of 61-70. However there was no significant difference between diabetic and non diabetic women groups. The risk of UTI was higher with longer duration of diabetes rather than degree of glycemc control (HbA₁C), women undergoing pharmacological treatment for diabetes were mainly at higher risk suggesting association between severity of diabetes and risk of UTI, *E.coli* was the most single isolated organism in all women as well as young women.

Keywords: Bacterial profile of urinary tract infections in Diabetic postmenopausal women

Introduction:

Urinary tract infection (UTI) is the most common bacterial infection in women in general and in postmenopausal women in particular. Bacteriuria occurs more often in elderly functionally impaired women but in general many of it are asymptomatic. However the risk factors associated with recurrent UTI in elderly women are not widely described. Bacteriuria in elderly women is associated with high mortality rates, however many of these bacteriuria are asymptomatic (1). The belief that diabetes, a common metabolic disorder is associated with a higher risk of UTI is widespread. Diabetes results in several abnormalities of the host defense system that might result in a higher risk of certain infection. These abnormalities include immunologic impairments, such as impaired migration, intracellular killing, phagocytosis, and chemotaxis in polymorphonuclear leukocytes from diabetic

Patients, and local complications related to neuropathy, such as impaired bladder emptying. Also, higher glucose concentration in urine may serve as a culture medium for pathogenic microorganisms (2). Diabetes may be associated with a higher risk of acute symptomatic UTI in postmenopausal women. Women undergoing pharmacologic treatment for diabetes were mainly at higher risk, suggesting an association between severity of diabetes and risk of UTI. One would expect a higher risk of UTI with longer duration of diabetes, as is the case with some diabetes complications, such as retinopathy or neuropathy. Association between degree of glycemc control as assessed by HbA₁c level and odds of UTI, although is possible. Another important factor in postmenopausal women is the potential role that estrogen deficiency plays in the development of bacteriuria. The alarming increase in multidrug-resistant uropathogenes makes it imperative that alternative strategies as the restoration of flora with lactobacilli that inhibits the

*Dept. of microbiology/ Baghdad Medical College.

**Dept. of Medicine, College of Medicine, University Of Baghdad.

attachment of uropathogens to the uroepithelial mucosa and thereby reduces the frequency of UTI (3).

Patients and Methods:

A total of 200 urine samples were obtained from postmenopausal and young women suffering from symptomatic and asymptomatic urinary tract infections (UTI) with and without diabetes mellitus type 2 visiting Medicine out patients and in patients Clinic of Medical City Teaching Hospital in Baghdad city. This study period was from 15

November 2011 till 15 June 2012. Urine Samples were collected from women under supervision of the specialists physicians. General urine examination was accomplished for each patient. For patients suspected with DM type 2 the Glycosylated haemoglobin (HbA1c) level was measured considering also the duration of diabetes. The urine samples were inoculated directly onto enrichment and selective media for the isolation of the causative bacteria. The isolates were identified using different microscopical, culture characteristics and biochemical tests.

Table (1) Uropathogenes isolated from each study group of women

UTI pathogens	Diabetic post-menopausal women with UTI n=50		post -menopausal women with UTI, no D.M n=50		post -menopausal women with Asymptomatic UTI, no D.M n=19		Young w UTI, no D.M n=50		Total n=169		P value	X ²
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%		
E.coli	15	30	15	30	2	10.5	7	14	39	23.0	0.08(Ns)	6.71
Klebsiella	10	20	8	16	3	15.7	5	10	26	15.3	0.5(Ns)	1.95
Staphylococcus aureus	4	8	4	8	3	15.7	2	4	13	7.7	0.4(Ns)	2.69
Beta-hemolytic streptococcus	1	2	0	0	0	0	0	0	1	0.6	0.4(Ns)	2.39
Candida albicans	10	20	5	10	2	10.5	8	16	25	14.7	0.5(Ns)	2.39
Enterobacter	2	4	1	2	1	5.2	0	0	4	2.3	0.4(Ns)	2.68
Proteus	0	0	0	0	1	5.2	0	0	1	0.6	0.4(Ns)	7.85
Pseudomonas aeruginosa	0	0	0	0	1	5.2	0	0	1	0.6	0.4(Ns)	7.85
Other bacteria												
Moraxilla catarrhalis	10	20	6	12	1	5.2	11	22	28	16.5	0.2(Ns)	4.03
Non hemolytic streptococcus	11	22	6	12	7	36.8	6	12	30	6.5	0.05(Ns)	7.61

X² = Chi -square , DF= degree of freedom

Table (2) Relationship of uropathogenes isolated from diabetic postmenopausal women with UTI with control, treatment, duration of diabetes

	<i>E.coli</i>		<i>Klebsiella</i>		Non hemolytic streptococcus		<i>Staphylococcus aureus</i>		<i>Staphylococcus epidermidis</i>		<i>Candidia albicans</i>		<i>Moraxilla catarrhalis</i>		Diphtheroids		Enterobacter	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
HbA1c > 7.5	7	14	2	4	1	2	5	10	4	8	5	10	5	10	4	8	1	2
7.6-8.5	3	6	1	2	1	2	4	8	2	4	2	4	2	4	0	0	0	0
>8.5	5	10	2	4	2	3	3	6	4	8	3	6	3	6	2	4	1	2
P value	0.4		0.8		0.7		0.7		0.6		0.4		0.4		0.1		0.6	
No meds-	1	2	0	0	1	2	0	0	0	0	0	0	1	2	0	0	1	2
Oral meds	4	8	2	4	1	2	5	10	4	8	5	10	7	14	4	8	0	0
Insuline -	10	20	5	10	2	4	7	14	6	12	5	10	2	4	2	4	1	2
P value	0.009		0.05		0.7		0.02		0.04		0.06		0.03		0.1		0.6	
Duration of diabetes < 10 y.	10	20	6	12	3	6	10	20	7	14	7	14	8	16	5	10	2	4
> 10 y.	5	10	1	2	1	2	2	4	3	6	3	6	2	4	1	2	0	0
P value	0.1		0.05		0.3		0.01		0.1		0.1		0.04		0.09		0.1	

Results:

Table (1) showed the uropathogens isolated from each study group. The total number of women in this table 169, including 19 with asymptomatic UTI. The most common isolated pathogens in postmenopausal women with UTI and diabetes were *E. coli* (30%), *Klebsiella* (20%), *Candida albicans* (20%), *Moraxilla Catarrhalis* (20%), nonhemolytic streptococcus (22%). In table (2) for patient with HbA1c >7.5 *E. coli* comprising the highest incidence of UTI isolates (14%). This was followed by *Staphylococcus aureus* (10%), *Candida albicans* (10%). Concerning patients administering oral hypoglycemic medication *Moraxilla catarrhalis* showed the highest incidence of UTI isolates (14%) followed by *staphylococcus aureus* (10%), *Candida albicans* (10%). Concerning patients administering insulin *E. coli* was the most frequent organisms (20%) followed with *Staphylococcus aureus* (14%), *Staphylococcus epidermidis* (12%), *Klebsiella* (10%), and *Candida albicans* (10%). Concerning patients with duration of diabetes <10 yrs *E. coli* and *staphylococcus aureus* were the most isolated UTI organisms (20% each) followed by *Moraxilla catarrhalis* (16%), *Staphylococcus epidermidis* (14%) and *Candida albicans* (14%). Concerning *E. coli* the P value in the groups of different hypoglycemic medication was 0.009 (significant difference) similarly the difference was significant concerning *staphylococcus aureus* and *Moraxilla catarrhalis* isolated in the groups of duration of diabetes (P value 0.01 and 0.04 respectively).

Discussion:

In this study, showed the distribution of bacteria isolated from urine culture from 169 cases. It showed *E. coli* in both P.M.W. with D.M and P.M.W. without D.M was (30%). In P.M.W. asymptomatic UTI was (10.5%) and in young women was (14%). These results were in accordance with the many previous results. *E. coli* is the single most common pathogen for all UTI syndrome/host group combination. Uncomplicated cystitis, the most common acute UTI syndrome caused by *E. coli* is characterized by dysuria, frequency and suprapubic pain fever and/or back pain suggests progression to pyelonephritis fever may take 5-7 days to resolve completely in appropriately treated patient with pyelonephritis persistently elevated or increasing fever and neutrophil count should prompt evaluation for intrarenal or perinephric abscess and/or obstruction renal parenchymal damage and loss of renal function during pyelonephritis occur primarily with urinary obstruction (4). *Klebsiella* In P.M.W. with D.M was (20%), in P.M.W. without D.M (16%), P.M.W. with asymptomatic UTI (15.7%) and young women (10%). These results were in accordance with previous results where *Klebsiella* account for only 1-2% of UTI episodes among otherwise healthy adults but for 5-17% of episodes of complicated UTI, including infection associated with diabetes (4). Ofek et al., (1993) (5) reported that

a good example in this respect is *Klebsiella* UTI in elderly individuals. Most cases of bacterial pyelonephritis are not caused by *Klebsiella* but by *E. coli* strains. However, although *Klebsiella* species are not a predominant cause of UTI, they can cause significant renal scarring even after a single episode of infection. Moreover, infections with these uropathogens are more likely to lead to death than are infections with most *E. coli* strains. The question whether a *Klebsiella* vaccine should be recommended for persons older than 60 years has to be clarified by cost-benefit analyses. Another point of interest is the possible eradication of *Klebsiella* in patients during their hospital stay. One of the new approaches is the use of cranberry juice. This juice shows a pronounced anti-adhesive effect on enterobacteria and therefore might prevent colonization of hospitalized patients or even eradicate these bacteria in colonized persons. Bonadio et al., (2001) Ronald et al., (1997) reported that the rate of *E. coli* isolation was found in both diabetic and non diabetic patients and that *Klebsiella* was much lower than that usually observed in community acquired UTI, thus suggesting that a significant part of his patients had nosocomial acquired UTI. Other studies have found that urinary *Klebsiella* is more frequent in patients with D.M than in non diabetic patients (4,6). *Staphylococcus aureus* in both P.M.W. with D.M and P.M.W. without D.M showed (8%), P.M.W. with asymptomatic UTI (10.5%) and young women (4%). These results were in accordance with a previous result reported that UTI are infrequently caused by *S. aureus* in contrast with that of most other urinary pathogens. The presence of *S. aureus* in urine suggests hematogenous dissemination ascending *S. aureus* infection occasionally. Beta-hemolytic streptococcus In P.M.W. with D.M and UTI was (2%) and P.M.W. without D.M and UTI. The organism was not isolated from the other groups. Walter, (2008) reported that the majority of beta hemolytic streptococcus infections in otherwise healthy adults are related to pregnancy and parturition, peripartum fever, the most common manifestation, is sometimes accompanied by symptoms and signs of endometritis or chorioamnionitis. Blood and vaginal swab cultures are often positive. Bacteremia is usually transitory but occasionally result in meningitis or endocarditis infection in adult that are not associated with peripartum period generally involve individuals who are elderly or have an underlying chronic illness, such as diabetes mellitus or malignancy. Among the infections that develop with some frequency in adult are cellulitis and soft tissue infection including infected diabetic skin ulcer, urinary tract and septic arthritis. *Candida albicans* In P.M.W. with D.M and UTI it was (20%) and P.M.W. without D.M and UTI (10%), P.M.W. no D.M and asymptomatic UTI (10%) and young women with UTI (16%) previous studies reported that the pathogenesis of retrograde infection of the urinary tract by *C. albicans* in most instances

begins in a predisposed patient such as a diabetic, a hospitalized individual, or a woman with vulvovaginal *Candida* infection (7,8). As common as these predisposing factors are, one would expect a greater frequency of candidal cystitis than occurs. *C. albicans* can colonize urothelial cells, although 50% less well than buccal epithelium, and this adherence, can be blocked by mannose. Nevertheless, candiduria remains rare in structurally and functionally normal urinary tracts even among prediabetic patients. The defenses operative near the portals of entry in males and females include normal flora, which may suppress *Candida* infection, as well as secretions from the female periurethral glands, which are reportedly fungistatic (9). Successful bladder colonization and infection with *Candida species* most likely requires a significant breach of these microbiologic and physiologic barriers, as occurs with urinary stasis or the presence of a foreign body. *Pseudomonas aeruginosa* was isolated only from one urine sample of P.M.W. with asymptomatic UTI. This proves that *Pseudomonas aeruginosa* is much less in community acquired infections than that in nosocomial infections. These were in accordance with previous results reported that UTI due *P. aeruginosa* in general occurs as colonization of a foreign body in the urinary tract, an obstruction in the genitourinary system, or urinary tract instrumentation or surgery. (10)

Other bacteria is the normal flora of the vagina, included (diphtheroid), *Moraxilla catarrhalis*, nonhemolytic streptococcus, coagulase negative staphylococcus, its presence in urinary tract is considered a contamination; however, their culture in table 1 appear in heavy growth so the data represent that they are opportunistic pathogens due to the heaviness of the growth. Vaginal flora is very important source in UTI since it may be ascending up to UTI in debilitated diabetic women.

1- Moraxilla catarrhalis In P. M.W. and UTI (20%), P.M.W. without D.M and UTI (5.2%), P.M.W. with no D.M and asymptomatic UTI (21%) and young women with UTI (22%). *Moraxilla catarrhalis* was formerly regarded as a common, essentially harmless inhabitant of the pharynx and women genital tract; however, during the past 2 decades, it has emerged as a significant pathogen to humans. Many microbiological and molecular diagnostic techniques have been developed, improving proper identification of this bacteria and allowing for the national and international distribution of *M. catarrhalis* strains to be characterized. Many studies have identified a number of virulence factors; however, their relationship to their actual role in infection and immunity has been established in only a few cases. (11,12)

2- Non hemolytic streptococcus In P.M.W. and UTI (22%), P.M.W. with out D.M and UTI (12%), P.M.W. with no D.M and asymptomatic UTI (36.8%) and young women with UTI (12%). Using Epi strept test; most of these isolates were *Enterococcus faecalis* which is a flora of intestine and vagina. The

pathogenesis of complicated and uncomplicated urinary tract infection (UTI) is complex and influenced by many host biological and behavioral factors and by properties of the infecting uropathogens. Leading etiological agents of UTIs include *Escherichia coli*, *Candida albicans*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, and *Proteus mirabilis* (13). The incidence of UTIs due to *E. faecalis* has risen steadily over the years, and infections due to multiple-drug-resistant strains present a significant medical problem (14,15). *Enterococcus* spp. rank third among the most common pathogens isolated from intensive care unit patients with UTIs and are a common cause of chronic or recurrent UTIs, especially those associated with structural abnormalities and instrumentation (Schaeffer et al., 1981). In spite of the role of *E. faecalis* as a leading cause of nosocomial UTI, little is known about the bacterial factors involved in such infections. The interaction between enterococci and uroepithelial tissue has been examined previously (16), with the goal of identifying a role for plasmid-encoded aggregation substance in the adhesion of enterococci to renal epithelial cells in vitro. In a study of *E. faecalis* isolates from patients with UTI and endocarditis, Guzman and coworkers (17) showed that UTI isolates adhered efficiently to urinary tract epithelial cells. The nature of the interaction of enterococci with uroepithelial tissue appears to be quite complex, with a role for bacterial cell surface carbohydrate and protein (17,18). About one-third of *E. faecalis* isolates from patients with bacteremia and UTIs express the Esp protein, compared to its rare occurrence in fecal isolates, suggesting that this surface protein may play an important role during these infections (19). Table (2) shows no significant relationships between microorganisms causing UTI and HbA_{1c}. This result is in accordance with previous results (29). This analysis found no significant association between degree of glycemic control as assessed by HbA_{1c} level and odds of UTI, although it is possible that the small sample size of diabetic women with this measurement may have resulted in insufficient power to detect a clinically meaningful difference. Table (2) shows significant relationships between microorganisms causing UTI and kind of treatment of the diabetes and duration of diabetes especially in those patients with diabetes more than ten years and on insulin treatment. These results were in accordance with previous results. The authors prospectively (1998-2002) followed 218 diabetic and 799 non-diabetic Washington State women aged 55-75 years for UTI and asymptomatic bacteria (AB). The baseline examination and two annual follow-up examinations included urine culture, measurement of hemoglobin A_{1c} and postvoid residual bladder volume, and a survey of diabetes and other characteristics. Surveillance for UTI included self-reports confirmed by microbiologic culture and medical record review. UTI incidence per 100 person-years was 12.2 for diabetic women

and 6.7 for nondiabetic women. Asymptomatic bacteriuria (AB) incidence per 100 person-years was 6.7 for diabetic women and 3.0 for nondiabetic women. In Cox models adjusted for multiple covariates, the increased UTI risk occurred mainly in women taking insulin and women with a longer diabetes duration (> or =10 years; compared with nondiabetic women. No clear linear trend between hemoglobin A1c and UTI or AB risk was seen. Postmenopausal women with diabetes have higher risks of UTI and AB in relation to diabetes duration and severity but not to recent glucose control (30).

Conclusion:

In postmenopausal women the incidence of UTI in age group 50-60 yrs was higher than that of 61-70. However there was no significant difference between diabetic and non diabetic women groups, The risk of UTI was higher with longer duration of diabetes rather than degree of glycemic control (HbA_{1c}), women undergoing pharmacological treatment for diabetes were mainly at higher risk suggesting association between severity of diabetes and risk of UTI, *E.coli* was the most single isolated organism in all women as well as young women. However there was significant difference in its incidence between postmenopausal and young women. The normal flora isolated in heavy growth from urine could be considered opportunistic pathogens, was higher, in addition to *E.Coli* and *Klebsiella*, UTI in diabetic women was more heavy and sever than in non diabetic showing a heavy growth of uropathogenes. all uropathogenes showed a multidrug resistance; and there was no obvious significant difference in susceptibility distribution of antibiotics between women groups. And susceptibility to the commonly effective nitrofurantion showed a decreased incidence in addition to ciprofloxacin and gentamycin.

Author Contributions:

Nedhal S.Ayoub: acquisition of data analysis, interpretation of data, study conception.
Khalid Abdallah: Study conception.

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