Indian Journal of Basic and Applied Medical Research; September 2018: Vol.-7, Issue- 4, P . 359 - 366

Original research article

Prevalence of UTI among diabetic patients–a prospective study

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ABSTRACT

The aim of the study was to compare the epidemiological, microbiological and clinical features of diabetic patients with urinary tract infection (UTI) .

Materials & Methods: A prospective study was performed on 490 consecutive patients with proven UTI with diabetics this study is conducted in various Medical Colleges in Tamil Nadu. The patients were studied on the basis of a specific questionnaire.

Results: Of 490 enrolled patients. The most frequent causative agents of UTI in diabetics were: E.coli (respectively, 51%), klebsiella sp. (26%) Proteus sp. (7%), Pseudomonas sp. (6%), citrobacter(4%) acinobacter(7%). More than 50% of the isolated strains were resistant to gentamicin, piperacillin and norfloxacin.

Conclusion: Urinary tract infection occurs with increased frequency and severity in patients with diabetes mellitus. General host factors enhancing risk for urinary tract infection in diabetics include age, metabolic control, and long term complications, primarily diabetic nephropathy and cystopathy. Alterations in the innate immune system have been described and may also contribute. Early diagnosis and prompt intervention is recommended to limit morbidity 77 and mortality of symptomatic infection.

Introduction

Type 2 diabetes mellitus is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Patients with type 2 diabetes mellitus are at increased risk of infections, with the urinary tract being the most frequent infection site. Various impairments in the immune system, in addition to poor metabolic control of diabetes, and incomplete bladder emptying due to autonomic neuropathy may all contribute in the pathogenesis of urinary tract infections (UTI) in diabetic patients. Factors that were found to enhance the risk for UTI in diabetics include age, metabolic control, and long term complications, primarily diabetic nephropathy and cystopathy.

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The spectrum of UTI in these patients ranges from asymptomatic bacteriuria (ASB) to lower UTI (cystitis), pyelonephritis, and severe urosepsis. Serious complications of UTI, such as emphysematous cystitis and pyelonephritis, renal abscesses and renal papillary necrosis, are all encountered more frequently in type 2 diabetes than in the general population. Type 2 diabetes is not only a risk factor for community-acquired UTI but also for health care-associated UTI, catheter-associated UTI, and post-renal transplant-recurrent UTI. In addition, these patients are more prone to have resistant pathogens as the cause of their UTI, including extended-spectrum β-lactamase-positive Enterobacteriaceae, fluoroquinolone-resistant uropathogens, carbapenem-resistant Enterobacteriaceae, and vancomycin-resistant Enterococci. Type 2 diabetes is also a risk factor for fungal UTI, mostly caused by *Candida*. Diabetes is also associated with worse outcomes of UTI, including longer hospitalizations and increased mortality.

The increased risk of UTI among diabetic patients, coupled with the increase in the incidence of type 2 diabetes mellitus worldwide in recent years, may impose a substantial burden on medical costs. In addition, the high rates of antibiotic prescription, including broad-spectrum antibiotics, for UTI in these patients may further induce the development of antibiotic-resistant urinary pathogens.

All types of UTI are more frequent in patients with type 2 diabetes. Various studies have reported the overall incidence of UTI among these patients. An observational study of all patients with type 2 diabetes in the UK general practice research database found that the incidence rate of UTI was 46.9 per 1,000 person-years among diabetic patients and 29.9 for patients without diabetes. Women with previously diagnosed diabetes had a higher risk of UTI than those with recently diagnosed diabetes (within 6 months) (91.9/1,000 person-years; 95% confidence interval [CI] 84.3–99.4, vs 70.5/1,000 person-years; 95% CI 68.2–72.8). A cohort study of over 6,000 patients enrolled in ten clinical trials found an incidence rate of 91.5 per 1,000 person-years in women and 28 per 1,000 person-years in men, and a cumulative incidence of 2% during 6 months. A recent American study performed on a health service data base with more than 70,000 patients with type 2 diabetes found that 8.2% were diagnosed with UTI during 1 year (12.9% of women and 3.9% of men, with incidence increasing with age). Another American database study from 2014 found that a UTI diagnosis was more common in men and women with diabetes than in those without diabetes (9.4% vs 5.7%, respectively) among 89,790 matched pairs of patients with and without type 2 diabetes mellitus.

ASB is more prevalent in women, due to a short urethra that is in proximity to the warm, moist, vulvar, and perianal areas that are colonized with enteric bacteria. ASB increases with age, and is also associated with urinary tract abnormalities or foreign bodies (urethral catheters, stents, etc). Many studies have reported an increased prevalence of ASB in diabetic patients, with estimates ranging from 8%–26%. A meta- analysis of 22 studies, published in 2011, found a point prevalence of 12.2% of ASB among diabetic patients versus 4.5% in healthy control subjects. The point prevalence of ASB was higher both in women and men, was higher in patients with a longer duration of diabetes, and was not associated with glycemic status, as evaluated by glycosylated hemoglobin A_{1c} (HbA_{1c}). A recent prospective study of inpatients at an Indian hospital found a 30% prevalence rate of ASB among diabetic patients.

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Pyelonephritis was found to be 4.1 times more frequent in pre-menopausal diabetic women than in women without diabetes in a case control study of a Washington State health group. In a Canadian study, diabetic women (type 1 and 2, identified by receipt of oral hypoglycemic or insulin therapy) were 6–15 times more frequently hospitalized (depending upon age group) for acute pyelonephritis than non-diabetic women, and diabetic men were hospitalized 3.4–17 times more than non-diabetic men. A Danish study reported patients with diabetes mellitus were 3 times more likely to be hospitalized with pyelonephritis, as compared to subjects without diabetes.

In men, risk of acute bacterial prostatitis, prostatic abscess, progression to chronic prostatitis, and infections following prostatic manipulations, such as trans-rectal prostate biopsy, is increased in patients with diabetes mellitus.

Multiple potential mechanisms unique to diabetes may contribute to the increased risk of UTI in diabetic patients. Higher glucose concentrations in urine may promote the growth of pathogenic bacteria. However, several studies did not find an association between HbA_{1c} level, which serves as a proxy for glycosuria, and risk of UTI among diabetic patients; also, sodium glucose cotransporter 2 inhibitors, which increase glycosuria, were not found to increase the rate of UTI. High renal parenchymal glucose levels create a favorable environment for the growth and multiplication of microorganisms, which might be one of the precipitating factors of pyelonephritis and renal complications such as emphysematous pyelonephritis. Various impairments in the immune system, including humoral, cellular, and innate immunity may contribute in the pathogenesis of UTI in diabetic patients. Lower urinary interleukin-6 and -8 levels were found in patients with diabetes with ASB, compared to those without diabetes with ASB. Autonomic neuropathy involving the genitourinary tract results in dysfunctional voiding and urinary retention, decreasing physical bacterial clearance through

h micturition, thereby facilitating bacterial growth. Bladder dysfunction occurs in 26%–85% of diabetic women, depending on age extent of neuropathy and duration of diabetic disease, and thus should be considered in all diabetic patients with UTI.

A paper from Saudi Arabia found the following factors to be associated with an increased risk of UTI among patients with diabetes: female sex (relative risk [RR] 6.1), hypertension (RR 1.2), insulin therapy (RR 1.4), body mass index (BMI) >30 kg/m^2 (RR 1.72), and nephropathy (RR 1.42). The release of new anti-diabetic sodium glucose cotransporter 2 inhibitors, which increase glycosuria, caused concern of a possible increase in UTIs, though a recent meta-analysis found similar incidences of UTI in patients treated with canagliflozin as compared with control groups. Dapagliflozin was associated with a slight increase in UTI (4.8% vs 3.7%), though no increase in pyelonephritis was found.

The most common pathogens isolated from urine of diabetic patients with UTI are *Escherichia coli*, other Enterobacteriaceae such as *Klebsiella* spp., *Proteus* spp., *Enterobacter* spp., and Enterococci. Patients with diabetes are more prone to have resistant pathogens as the cause of their UTI, including extended-spectrum β-lactamase-positive Enterobacteriaceae, fluoroquinolone-resistant uropathogens, carbapenem-resistant Enterobacteriaceae, and vancomycin-resistant Enterococci. This might be due to several factors, including multiple courses of antibiotic therapy that are administered to these patients, frequently for asymptomatic or only mildly

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symptomatic UTI, and increased incidence of hospital-acquired and catheter-associated UTI, which are both associated with resistant pathogens. Type 2 diabetes is also a risk factor for fungal UTI.

The diagnosis of UTI should be suspected in any diabetic patient with symptoms consistent with UTI. These symptoms are: frequency, urgency, dysuria, and suprapubic pain for lower UTI; and costovertebral angle pain/tenderness, fever, and chills, with or without lower urinary tract symptoms for upper UTI. Diabetic patients are prone to have a more severe presentation of UTI, though some patients with diabetic neuropathy may have altered clinical signs. A recent multi-center study from South Korea of women with community-acquired acute pyelonephritis found that significantly fewer of the diabetic patients had flank pain, costovertebral angle tenderness, and symptoms of lower UTI as compared to non-diabetic women. Patients with type 2 diabetes and UTI might present with hypo- or hyperglycemia, non-ketotic hyperosmolar state, or even ketoacidosis, all of which prompt a rapid exclusion of infectious precipitating factors, including UTI

Once the diagnosis of UTI is suspected, a midstream urine specimen should be examined for the presence of leukocytes, as pyuria is present in almost all cases of UTI. Pyuria can be detected either by microscopic examination (defined as ≥10 leukocytes/mm^3), or by dipstick leukocyte esterase test (sensitivity of 75%–96% and specificity of 94%–98%, as compared with microscopic examination, which is the gold standard). An absence of pyuria on microscopic assessment can suggest colonization, instead of infection, when there is bacteriuria. Microscopic examination allows for visualizing bacteria in urine. A dipstick also tests for the presence of urinary nitrite. A positive test indicates the presence of bacteria in urine, while a negative test can be the product of low count bacteriuria or bacterial species that lack the ability to reduce nitrate to nitrite (mostly Gram-positive bacteria). Microscopic or macroscopic hematuria is sometimes present, and proteinuria is also a common finding.

A urine culture should be obtained in all cases of suspected UTI in diabetic patients, prior to initiation of treatment. The only exceptions are cases of suspected acute cystitis in diabetic women who do not have long term complications of diabetes, including diabetic nephropathy, or any other complicating urologic abnormality. However, even in these cases, if empiric treatment fails or there is recurrence within 1 month of treatment, a culture should be obtained. The preferred method of obtaining a urine culture is from voided, clean-catch, midstream urine. When such a specimen cannot be collected, such as in patients with altered sensorium or neurologic/urologic defects that hamper the ability to void, a culture may be obtained through a sterile urinary catheter inserted by strict aseptic technique, or by suprapubic aspiration. In patients with long-term indwelling catheters, the preferred method of obtaining a urine specimen for culture is replacing the catheter and collecting a specimen from the freshly placed catheter, due to formation of biofilm on the catheter.

The definition of a positive urine culture

The definition of a positive urine culture depends on the presence of symptoms and the method of urinary specimen collection, as follows and as depicted in Figure 1 For the diagnosis of cystitis or pyelonephritis in women, a midstream urine count ≥10^5 cfu/mL is considered diagnostic of UTI. However, in diabetic women with good metabolic control and without long-term complications who present with acute uncomplicated cystitis, quantitative counts <10^5 colony-forming units [cfu]/mL are isolated from 20%–25% of premenopausal women and about 10% of

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postmenopausal women. Only 5% of patients with acute pyelonephritis have lower quantitative counts isolated. Lower bacterial counts are more often encountered in patients already on antimicrobials and are thought to result from impaired renal concentrating ability or diuresis, which limits the dwell time of urine in the bladder. Thus, in symptomatic women with pyuria and lower midstream urine counts ($\geq 10^2$ cfu/mL), a diagnosis of UTI should be suspected.

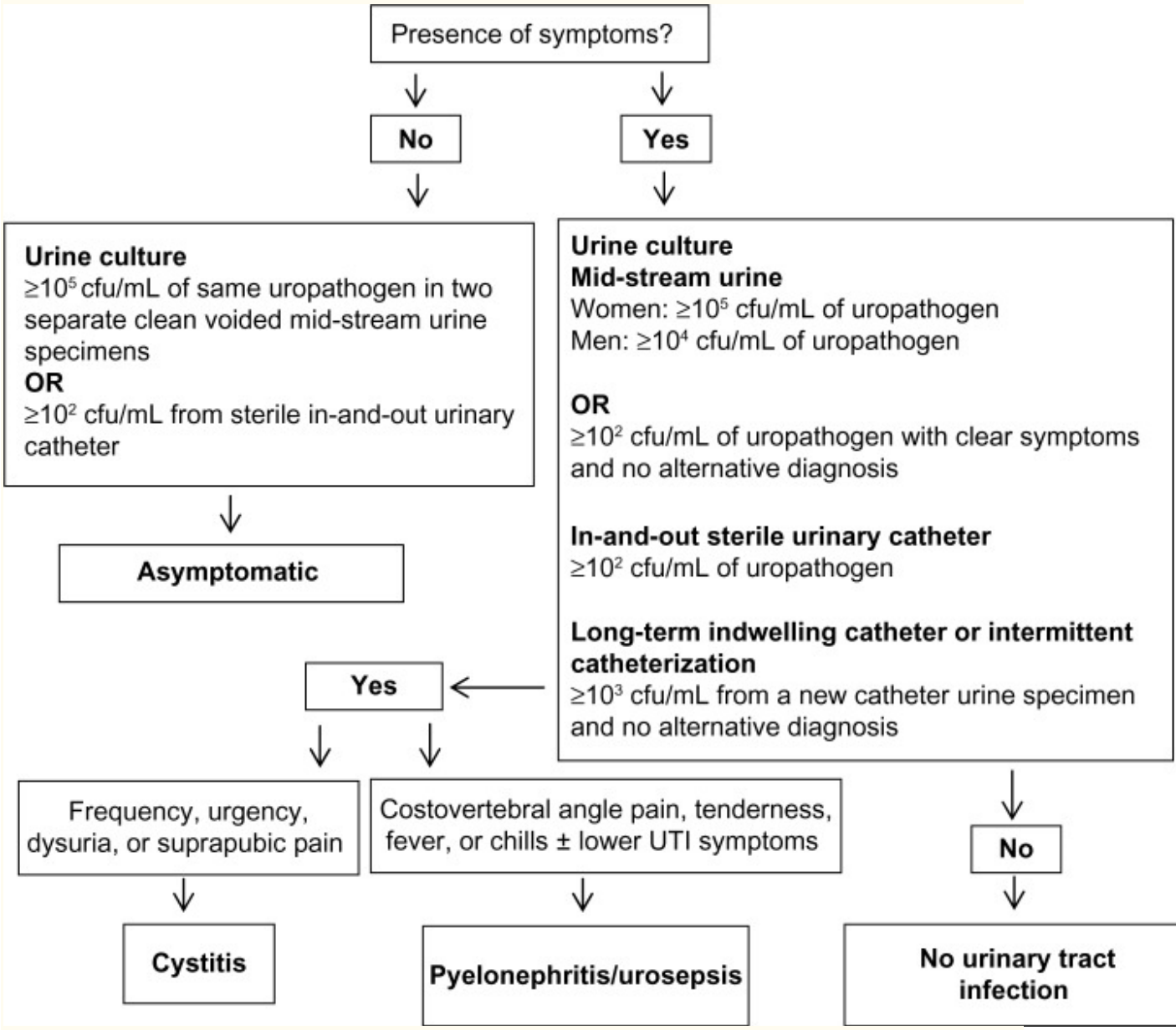

Figure 1

Flow chart for the diagnosis of urinary tract infection in patients with type 2 diabetes mellitus.

Abbreviations: cfu, colony-forming units; UTI, urinary tract infection.

For the diagnosis of UTI in men, a midstream urine colony count of $\geq 10^4$ cfu/mL is indicative. However, when coliform bacteria (eg, *E. coli*) are isolated, lower colony counts might also represent significant bacteriuria.

From an in-and-out catheter specimen, growth of $\geq 10^2$ cfu/mL, in the presence of urinary symptoms, is diagnostic of UTI. In patients with long-term indwelling catheters or intermittent catheterization, growth of $\geq 10^3$ cfu/mL from a single new catheter urine specimen indicates UTI; in a midstream voided urine specimen from a patient whose urethral, suprapubic, or condom catheter that has been removed within the previous 48 hours, and has no other identified source of infection, similar numbers would also indicate UTI.

The diagnosis of ASB can be made based on a growth of $\geq 10^5$ cfu/mL of the same uropathogen (up to two pathogens) in two consecutive clean voided mid-stream urine specimens, or $\geq 10^2$ cfu/mL in a specimen collected through a sterile in-and-out urinary catheter, in the absence of signs or symptoms of urinary infection. As many as 70% of diabetic women with ASB have accompanying pyuria. Thus, the presence of pyuria is not useful for differentiating between symptomatic or asymptomatic UTI.

RESULTS

AGE MALE	NUMBER	PERCENT	FEMALE	NUMBER	PERCENT	TOTAL
Lessthan 30 yrs	29	5.9		20	4.08	
31-40 yrs	94	19.1		108	22	
41-50 yrs	55	11.2		42	8.5	
51-60 yrs	42	8.5		45	9.1	
Above 60	30	6		25	5	
	250			240		490

Frequency of uti	Male	female	total
Less than 5 /yr	181	193	374
More than 5/yr	69	47	116
	250	240	490

symptoms	Male	percent	female	percent
Urgency,precipi, dysuria,fever with chills	114	23.2	81	16.5
Supra.pubic tender	56	11.4	96	19.5
Loin pain	18	3.6	33	6.7
A symptomatic	62	12.6	30	6.1

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ORGANISM	PERCENT	HIGHLY SENSITIVE	MODERATELY SENSITIVE	RESISTANT
E.COLI	51	CFS.PIT,MRP	AK NIT	G,CIP,COT,NX,CTX
KLEBSIELLA	26	CFS.PIT,MRP	AK NIT	G,CIP,COT,NIT,CTX,NX
PSEUDOMONAS	6	CFS.PIT,MRP	TOB,AK NX	G,CIP,CAZ,CTX
ACINOBACTER	7	CFS.PIT,MRP		AK,G,COT,NX,NIT CTX
PROTEUS	7	CFS.PIT,MRP	AK,NIT	G,CIP,CAZ CTX
CITROBACTER	4	CFS.PIT,MRP	COT	AK,G,CIP.NIT,CTX

CFS-CEFOPERAZONE SULBACTUM ,PIT-PIPERCILLIN TAZOBACTUM MRP-MEROPENUM G-GENTAMYCIN ,AK-AMIKACIN, COT-COTRIMOXAZOLE, NX-NALIDIXICACID, NIT-NITRO FURONTOIN,CIP=CIPROFLOXACIN CTX-CEFATOXIDINE,CAZ-CEFAZOLINE

Results:

Of 490 enrolled patients. The most frequent causative agents of UTI in diabetics were: E.coli (respectively, 51%), klebsiella sp. (26%) Proteus sp. (7%), Pseudomonas sp. (6%), citrobacter(4%) acinobacter(7%). More than 50% of the isolated strains were resistant to gentamicin, piperacillin and norfloxacin.

Conclusion:

Urinary tract infection occurs with increased frequency and severity in patients with diabetes mellitus. General host factors enhancing risk for urinary tract infection in diabetics include age, metabolic control, and long term complications, primarily diabetic nephropathy and cystopathy. Alterations in the innate immune system have been described and may also contribute. Early diagnosis and prompt intervention is recommended to reduce morbidity and mortality of UTI. Other than strict diabetic contol ,Hand,genital hygiene, correct washing techniques in female,barriers during sex and plenty of oral fluids can prevent UTI

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