

## Genitourinary infection in diabetes

**Sandeep Julka**

Director Endocrinology, Synergy Multispeciality Hospital, Indore, Madhya Pradesh, India

### ABSTRACT

Diabetes is known to increase the risk of infection and the commonest amongst them are the ones involving the genitourinary tract. The infections in a diabetic patient are unique in that they are recurrent, more severe, requiring hospitalization, and also have higher mortality than nondiabetics. Some infections are exclusively found in diabetics like the emphysematous pyelonephritis while others have their natural history complicated due to hyperglycemia. Asymptomatic bacteriuria may lead to albuminuria and urinary tract infection and may need to be treated in diabetics. Not just this certain organisms have a predilection for the genitourinary tract of the diabetic patient. All of the above makes the diabetic patient vulnerable to infections and therefore early diagnosis and appropriate treatment is mandatory.

**Key words:** Asymptomatic bacteriuria, diabetes, genitourinary infection

### INTRODUCTION

It is known that diabetes doubles the risk of various vascular diseases. On an average a 50-year-old diabetic with no history of vascular disease is 6 years younger at the time of death as compared to a nondiabetic. What is interesting to know is that 40% of the years of life lost can be attributed to nonvascular conditions like cancers, infections, and neurodegenerative disorders.<sup>[1]</sup>

Amongst the infections affecting the diabetic patient those affecting the genitourinary tract are commonest. There is 60% increase in the risk of urinary tract infection (UTI) and a two- to four-fold increase in genital tract infections.<sup>[2,3]</sup> UTI in diabetes have certain unique features in that they involve the upper tract in 80%, are bilateral in most cases and are more prone for complications.<sup>[4]</sup>

Recurrence rates are 25-45% which are significantly higher

than in nondiabetic, this despite the fact diabetics tend to receive longer and more potent initial treatment.<sup>[5]</sup>

The more complicated UTI and the recurrent nature increase the risk of hospitalization by two-folds leading to economic stress on the patient.<sup>[6]</sup> There is also an associated increase in morbidity and mortality. In a country like ours where health-related spending is a major limiting factor for access to good healthcare, it is important that a physician in the primary care needs to have a level of awareness regarding diagnosis treatment and prevention of UTI in this high risk group.

### FACTORS PREDISPOSING DIABETES TO INFECTIONS

Several aspects of immunity are altered in patients with diabetes. Polymorpholeukocyte function is depressed particularly when acidosis is present. Leukocyte adherence, chemotaxis, and phagocytosis may be affected. Antioxidant systems involved in bactericidal activity may also be impaired. The humoral activity appears to be normal as responses to vaccines appear to be normal.<sup>[3]</sup>

#### Factors predisposing and complicating genitourinary infections

- Hyperglycemia
- Acidosis

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**Corresponding Author:** Dr. Sandeep Julka, Scheme No. 74 Sector C, Vijay Nagar, Indore-452 010, Madhya Pradesh, India.

E-mail: sandeep\_julka@yahoo.com

- Obstruction like calculus, papillary necrosis, fungal balls, instrumentation, vesicouretric reflux and cystopathy with increased post void residue
- Organisms like *E. coli*/Candida which have predilection for the diabetic patient
- Miscellaneous.

Microcirculatory abnormalities (decreased tissue perfusion), sensory and autonomic neuropathy, and skin and mucosal colonization with *Staphylococcus aureus* and Candida.

## TYPES AND SITES OF INFECTIONS

Infections more commonly found in diabetes:

- Emphysematous pyelonephritis (EPN)
- Emphysematous cystitis
- Prostatic abscess.

Common infections but complicated by diabetic status:

- Asymptomatic bacteriuria
- Acute pyelonephritis
- Perinephric and renal abscess
- Fournier's gangrene
- Papillary necrosis
- Balanitis
- Vulvovaginal candidiasis
- Fungal pyelonephritis and fungal cystitis.

## URINE SAMPLE COLLECTION

- Midstream clean voided (after cleaning genitals with betadine)
- Aseptic bladder puncture
- Catheter tip culture (controversial)
- A colony counts more than  $10^5$  colony forming unit (cfu)/ml of one or two organism is considered significant.

### Organisms isolated in Indian diabetics

Of the 533 pathogens isolated from 495 diabetic subjects with UTI, 362 were gram -ve, 100 gram +ve cocci, and 71 were Candida.

Amongst the gram -ve pathogens *E. coli* was most common (71%). Then Klebsiella 13% and then Pseudomonas 8%, and Proteus only 1%.

In gram +ve 59% were enterococci, 25% coagulase negative staph, 8% beta-hemolytic streptococci and 2% *S. aureus*.

In Candida species 80% were Candida spp and 20% *Candida albicans*.<sup>[7]</sup>

Similar uropathogens were grown in other Indian studies.<sup>[8,9]</sup>

## SENSITIVITY PATTERN

The alarming increase in antibiotic resistance is a worldwide phenomenon, two-third of *E. coli* isolated in Indian subjects are extended spectrum beta-lactamase (ESBL) positive, that is, they will not respond to the usual antibiotics. Resistance for the most commonly used antibiotics for uncomplicated UTI in outpatient department (OPD) settings such as fluoroquinolones is significant (74%).<sup>[9]</sup> Gram negative bacilli are highly sensitive to salbactam/cefoparazone (90%) and piperacillin/tazobactam (83%). Both antibiotics are relatively expensive taking in to account 2 weeks duration of therapy, sometimes even longer.

Similarly gram positive cocci were sensitive to these drugs to the tune of 70%.

Gram negative were more sensitive to amino glycosides.

Gram positive cocci were more sensitive to ofloxacin and gram negative bacilli to ciprofloxacin (approximately 60%).

Recently there is news of the gram negative Enterobacteriaceae with resistance to carbapenam, thought to be our last resort to complicated UTI, conferred by New Delhi metallo-beta-lactamase-1 (NDM1).

If this spreads, which it eventually will due to intercontinental travel, it will be a worldwide public health disaster.<sup>[10]</sup>

The antifungal drugs fluconazole and amphotericin B retain sensitivity and are effective in treatment of symptomatic fungal UTI.<sup>[11]</sup> Non-albicans Candida may have increased resistance to azoles and systemic amphotericin B may be necessary to treat infections with some of the species. Therefore, early diagnosis and initiation of definitive therapy after sensitivity reports will not only help eradicate infection, but also prevent emergence of resistance.

### Asymptomatic bacteriuria

ASB is the presence of bacteria in bladder urine in a asymptomatic individual. Two consecutive samples should show the same uropathogens to prove it.

Complications of pregnancy associated with ASB are well-documented, such as pyelonephritis and premature birth.<sup>[12]</sup>

In a recent meta-analysis, ASB was found to be three times higher in patient with diabetes which included woman, men,

and adolescents. Also they are more often presented with albuminuria and symptomatic UTI.<sup>[13]</sup>

Taking the recent studies into consideration it seems prudent to treat ASB in these high risk patients.

## EPN

It is a necrotizing infection of the renal parenchyma and its surrounding areas that results in the presence of gas in the renal parenchyma, collecting system or the perinephric tissue. Between 85 and 100% are diabetics, approximately 40% have obstruction most commonly calculus, and in 10% it is bilateral.<sup>[14]</sup>

### Presentation

Fever, flank pain, pyuria similar to any pyelonephritis, but can also present as shock and altered sensorium. Therefore, in a patient with UTI if the fever does not subside after 3-4 days of antibiotics think of papillary necrosis or renal abscess or EPN.

### Poor prognostic indicators

Acute renal failure, shock, thrombocytopenia, altered sensorium, and severe proteinuria.

### Diagnosis

CT abdomen is diagnostic

A radiologic classification<sup>[15]</sup> has been proposed which helps in planning management appropriately.

- Class 1: Gas in the collecting system
- Class 2: Gas in the renal parenchyma
- Class 3a: Gas in perinephric space
- Class 3b: Gas in the pararenal space
- Class 4: Bilateral or EPN in solitary kidney.

### Organisms

*E. coli*, *Klebsiella*, and *Proteus* in that order of prevalence.

### Management

Broad spectrum antibiotics, aggressive glycemic control, and hydration. Antibiotics like cefoparazone salbactam or piperacillin tazobactam and if ESBL suspected start carbapenem.

For glycemic control intravenous insulin is ideal and at times rates of up to 20 to 30 units of regular insulin hourly may have to be required by the patient in sepsis.

### Surgical interventions

It is of utmost importance to decide the appropriate time of surgical interventions. The urologist and the endocrinologist have to be in constant touch for the

day-to-day progress of the conservatively managed patient so that when desired the urologist can intervene.

- The class 1 and 2 can be managed conservatively and may require percutaneous drainage (PCD) in some cases
- Class 3a and b PCD and if poor prognostic factors nephrectomy
- Class 4 bilateral PCD and if not controlled think of nephrectomy.

### Renal and perinephric abscess

The renal abscess develops in two ways, the renal cortical abscess or the carbuncle and the renal corticomedullary abscess.

The patients present with fever and flank pain and mass.

Diagnosis by computed tomography (CT) scan or ultrasonography (USG).

Treatment includes antibiotics and PCD and occasionally nephrectomy.<sup>[16]</sup>

### Renal papillary necrosis

This condition should be suspected in patients who have frequently relapsing or difficult to treat pyelonephritis and also in those with a fulminant presentation with hematuria. There may be renal colic due to passage of renal papillae. Women account for almost 80% of the cases.

Diagnosis depends on the demonstration of papillary/caliceal abnormalities without focal renal loss.

Treatment includes eradication of infection and catheter drainage or PCD may be required<sup>[16]</sup> [Figures 1-3].

### Prostatic abscess

Prostatic abscess is a rare condition, but is found almost exclusively in diabetics and those with prolonged catheterization. It should be suspected when there are recurrent and persisting symptoms of fever dysuria and urethral discharge despite adequate antibiotics.<sup>[17]</sup>

### Diagnosis

Digital rectal examination may show fluctuation, if not then transrectal ultrasound (TRUS) helps.

### Treatment

Appropriate antibiotics and drainage.

### Renal tract candidiasis

*Candida albicans* and less commonly *Candida glabrata* infection is seen in diabetics especially with use of broad spectrum antibiotics or indwelling catheters. They may be

asymptomatic or may present with cystitis, pyelonephritis, or fungal ball obstruction.

Diagnosis is by a urine culture with  $10^5$  cfu/ml of *Candida*.

Treatment is by fluconazole or parenteral Amphotericin B. A fungal ball needs removal by cystoscope or an ureteroscopy or occasionally an open procedure may be required (11/14).

### Fournier's gangrene

It is a necrotizing fasciitis that occurs around male genitalia. The patient presents with pain swelling erythematous crepitation and possible skin breakdown with overlying bullae along with signs of toxicity.

Testicles are spared because of the separate blood supply.

Treatment includes antibiotics and wide surgical debridement of devitalized tissue. Orchiectomy is not required. The bacteriologic finding is mixture of gram negative bacteria and anaerobes and occasionally streptococci.

Mortality is high, 40-50% even with aggressive management.

### Vulvovaginal candidiasis

Diabetic women are predisposed to this infection. Vaginal epithelial cells bind to *Candida albicans* with greater propensity in diabetics than in nondiabetics.

Treatment includes topical and oral azoles. Topical is the first choice of therapy. Oral antimycotics are known to potentiate the hypoglycemic effect of several sulfonylureas and may precipitate hypoglycemia.

### Balanitis

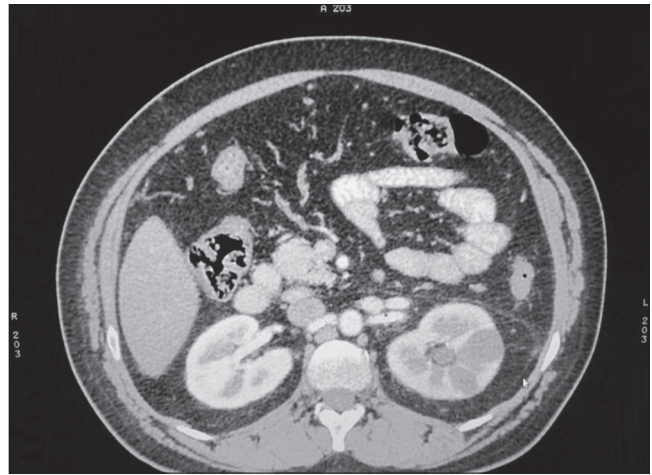
It is the inflammation of the glans and often involves the prepuce (balanoposthitis). Commonest organism is *Candida* spp. Therefore, an antifungal should always be prescribed to the patients having balanitis and balanoposthitis.<sup>[18]</sup>

### Tuberculosis

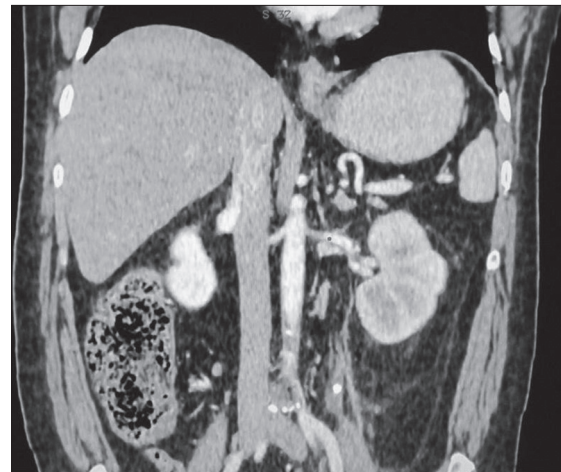
Genitourinary urinary tuberculosis (GUTB) is still found in our country and has significant complications in terms of scarring of the genitourinary tract. Genital tract tuberculosis accounts for 18% of the disease burden in India and 18% of infertile women suffer from it. The urinary tract tuberculosis accounts for 4% of all infections of the urinary tract in India.<sup>[19]</sup>

### Principles of management

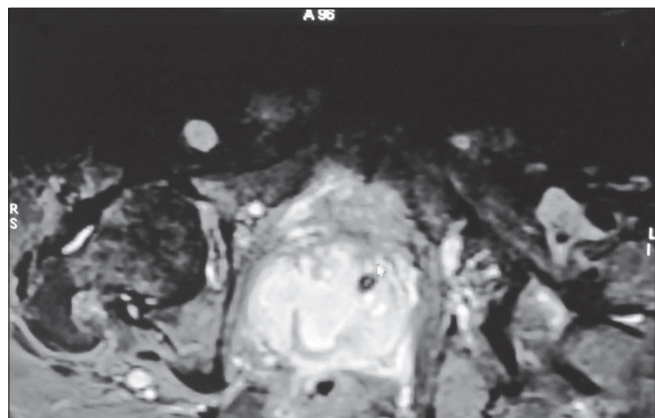
They are similar to those in pulmonary tuberculosis. GUTB is to be considered a severe form of TB for two reasons. First, in renal TB the size of the bacillary population is



**Figure 1:** A 45-year-old diabetic male presented with high grade fever flank pain and dysuria. He was found to have pyelonephritis and impending abscess and an uretric stone



**Figure 2:** A 45-year-old diabetic male presented with high grade fever flank pain and dysuria. He was found to have pyelonephritis and impending abscess and an uretric stone



**Figure 3:** A 63-year-old diabetic male presented with paraparesis, high grade fever and dysuria. magnetic resonance imaging done for evaluation of paraparesis also revealed a prostatic abscess. The patient's insulin requirements reduced drastically after the abscess drainage

similar to that of cavitary pulmonary TB ( $10^7$ - $10^9$ ). Second, if not aggressively treated, GUTB could potentially result in irreversible structural and functional damage.

Another aspect to be kept in mind is that the newer fluoroquinolones such as levofloxacin and gatifloxacin are used in the community setting for the empirical treatment of presumed UTIs. These drugs have excellent antimycobacterial activity and hence may mask the presentation of GUTB, thereby delaying the diagnosis and also may result in emergence of resistance.<sup>[20]</sup>

### Duration of therapy

The optimal duration of antimicrobial therapy has not been studied systematically. Although the importance of giving the appropriate antimicrobial therapy for the appropriate time is essential to eradicate the infection and also prevent relapse and resistance.

A 7-day regimen for patients with lower UTI is suggested and a 10-14 day course for those presenting with fever, bacteremia, or hypotension.

Long-term suppressive therapy may be considered for patients with frequent recurrent symptomatic infection in whom the underlying genitourinary abnormality cannot be corrected. Norfloxacin may be given in a dose of 400 mg twice a day for a month and then 400 mg once a day for additional 2 months (18 Canadian).

### Prevention

Studies have shown if practitioners discuss and educate the patients regarding infections on regular follow-up visits it increases the awareness and an early health seeking behavior.<sup>[21]</sup> Early reporting of symptoms help in early cure and just a little effort on the part of the care giver can significantly reduce the burden of infections and the related morbidity and mortality.

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