GLIMPSE INTO THE HIDDEN ASPECTS OF URINARY TRACT INFECTION IN PATIENTS WITH DIABETES MELLITUS AND PROSTATOMEGALY

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ABSTRACT

BACKGROUND

The worldwide prevalence of diabetes has risen dramatically over the past two decades from 30 million cases in 1985 to 382 million in 2013. Infections are of particular concern in diabetics. Benign prostatic hyperplasia and benign prostatic enlargement are the most common diseases in aging men which can lead to lower urinary tract symptoms.

AIMS AND OBJECTIVE

The objective of this study.
1. To study various risk factors associated with Urinary tract infections in Diabetes with prostatomegaly.
2. To study causative microorganisms and their drug susceptibility in diabetics with Urinary tract infections having prostatomegaly.

MATERIALS & METHODS: STUDY SETTING

A hospital based prospective observational study conducted for a period of 1 year. 50 indoor cases meeting inclusion criteria were selected.

INCLUSION CRITERIA

Diabetics having prostatomegaly presenting with urinary tract infection or positive urine culture were included.

RESULTS

Out of 50 patients 46% had bacteriuria, 82% were above 50 years. Longer duration of diabetes >6years were associated with bacteriuria in 59.37% in contrast to <6 years in 22.22% of cases.

Significant higher bacteriuria was seen in group noncompliant to treatment than those of compliant group, 64% vs 28%.

Association of bacteriuria were lower in patients with HbA_1C <7% whereas no difference was observed in relation to fasting and postprandial blood sugar levels. Bacteriuric patients also had significantly high post voidal residue >150 ml in contrast to those with <150ml (56.75% vs. 38%) and greater size of prostate volume >40cc in comparison with volume <40 (57.57% vs 23.53%).

E. coli was the commonest organism followed by klebsiella in 56.52% and 17.39% respectively and were sensitive to imipenem, cefepime, aminoglycoside, fluoroquinolones and nitrofurantoin.

CONCLUSION

Urinary tract infection is frequently encountered in diabetics with prostatomegaly. Elderly patients aged >50 years, longer duration of diabetes, non-adherence to treatment, insulin therapy and prostate volume >40cc could be considered as significant risk for bacteriuric urinary infection. Uncontrolled blood glucose with $HbA_1 C$>7%, post void residue >150 ml and prostate volume >40 cc are associated with bacteriuria. E. coli is the commonest organism and imipenem, cefepime, aminoglycosides, fluoroquinolones and nitrofurantoin showed favourable response.

KEYWORDS

Diabetes mellitus, Prostatomegaly, UTI, Bacteriuria, HbA1c.

INTRODUCTION: Diabetes is growing alarmingly in India, home to more than 65.1 million people with the disease according to data of 2013, compared to 50.8 million in 2010. India's economic boom has been accompanied by a meteoric increase in the number of people with diabetes and those at risk for the disease. Prevalence rates are up to 20% in some cities, and recent figures showed surprisingly increased rates in rural areas.[1]

Infections are of particular concern for diabetic patients. Diabetics are especially prone to foot infections, surgical site infections and urinary tract infections (UTI). Studies have shown that diabetics experience worse outcomes with infections. Though hospitalized patients do not have a high mortality rate they do face longer hospitalization and recovery time.[2]

Benign prostatic hyperplasia (BPH) and benign prostatic enlargement (BPE) are one of the most common diseases in aging men which can lead to lower urinary tract symptoms (LUTS). The relation between BPH, BPE and LUTS though is complex, because not all men with BPE develop LUTS and not all men with LUTS have BPE.[3] With a changing demographic profile and an increasingly aging population in almost all societies, it is inevitable that this disorder will become even more prevalent and inflict a major challenge for all health care systems in the future. The enlarged prostate results in urethral compression which significantly contributes to bladder dysfunction and LUTS. The bladder wall becomes thickened, trabeculated, and irritable when it is forced to hypertrophy and increase its own contractile force.[4]

UTI may be asymptomatic (subclinical infection) or symptomatic (disease) which encompasses a variety of clinical entities, including asymptomatic bacteriuria (ABU), cystitis, prostatitis, and pyelonephritis. In the pre-antibiotic era, UTI caused significant morbidity. By definition UTI means a bacterial / nonbacterial invasion of the urinary tract that can occur anywhere between the urethra and the kidney. UTIs can be divided anatomically into upper and lower tract infections.[5]

Lower UTI includes Prostatitis, Epididymitis, Cystitis, and Urethritis whereas upper tract disease includes Pyelonephritis and pyelitis. Pyelitis is infection restricted to renal pelvis and pyelonephritis is infection involving both kidney and pelvis. The anatomical distribution of upper urinary tract infection is same in male and female. The term "significant bacteriuria" is sometimes used to emphasize that the number exceeds that which might be caused by contamination during the collection of the specimen.[6]

METHODS: Patients of age group >30 years, a detailed history was obtained after taking consent from the patient, with special reference to duration and type of diabetes, treatment taken and adherence, symptoms related to diabetes and its complications.

History in relation to UTI like burning micturition, frequency, urgency, dysuria, suprapubic pain, haematuria and any symptoms suggestive of acute pyelonephritis like fever, chills, nausea, vomiting and diarrhoea were noted. Past history of urinary tract instrumentation or catheterization were also asked.

A detailed examination of all systems with special emphasis on temperature, pulse rate, blood pressure, suprapubic tenderness, costovertebral angle tenderness, tenderness/ mass on deep abdominal palpation were carried out.

1. **Ultrasonography:** USG was done in the radiology department by a senior radiologist using 3.5 MW Mechanical Probe USG machine for radiological diagnosis of various pathological conditions causing prostatic hypertrophy (like BPH, prostatic abscess, prostatitis etc) with special emphasis on radiological grading of prostatomegaly, pyelonephritis [particulate matter in the collecting system, reduced areas of cortical vascularity by using power Doppler, gas bubbles (emphysematous pyelonephritis), abnormal echogenicity of the renal parenchyma], cystitis [thickening of bladder wall as a result of oedema] and estimating volume of residual urine
2. Collection of mid-stream urine were done as per protocol. Routine urine examination and culture sensitivity were carried out in each case.

In case of patients with sterile pyuria with clinical and radiological features of genitourinary tuberculosis (e.g. thickened wall of bladder and ureter, multifocal strictures and hydronephrosis, mural thickening and enhancement.) were screened by DNA PCR of urine for mycobacterium tuberculosis.

Other investigations carried out were fasting blood sugar (FBS), postprandial blood sugar (PPBS), HbA_1C, Complete blood count, serum creatinine etc.

STATISTICAL METHODS: The collected data was compiled, tabulated and analysed in terms of descriptive statistics using SPSS version 17.0 software. Continuous variables were presented as mean±SD and categorical variables were expressed as frequencies and percentages. Nominal categorical data between the groups were compared using Chi-squared test or Fisher's exact test as appropriate. $p < 0.05$ was considered statistically significant.

RESULTS: Out of total 50 patients, 23(46%) were found to be bacteriuric whereas 27(54%) were non bacteriuric (Figure 1).
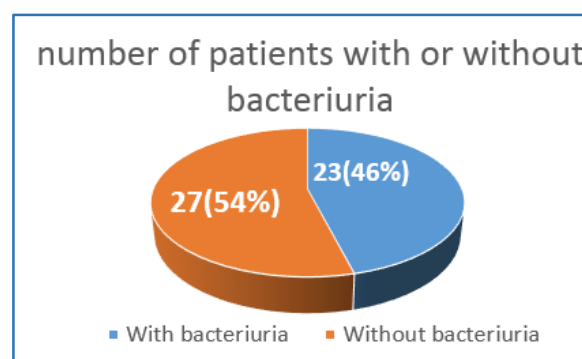

Fig. 1: Distribution of patients with or without bacteriuria

41(82%) of the total patients were more than 50 years (most of them were in the age group of 51 to 60 years) and only 9(18%) were less than 50 years (Table1).

Age group (years)	Number of patients
30-39	01
40-49	08
50-59	29
≥60	12
Table 1: Age distribution of cases	

When evaluated on the basis of type of diabetes, majority i.e. 46(92%) were type 2 diabetics and 4(8%) were type 1 diabetics. 20(43.48%) of type 2 diabetics and 03(75%) of type 1 diabetics were bacteriuric (p>0.05). [Table 2]

Among the 32 patients who were diabetics for >6 years, 19(53.38%) had bacteriuria in contrast to only 04(22.22%) of 18 with duration of diabetes less than 6 years (p< 0.05). Out of 16 diabetics using insulin as modality of treatment either as sole treatment or in combination with oral anti-diabetic agents, 11(68.75%) were bacteriuric while only 12(35.29%) of 34 diabetics who used treatment modality other than insulin were found to have bacteriuria (p<0.05). [Table 2]

When evaluated on the basis of compliance to treatment and follow up, only 7(28%) out of 25 diabetics with prostatomegaly with compliance to treatment (antidiabetic and BPH treatment) had bacteriuria whereas 16(64%) of 25 who were non-compliant were found to be bacteriuric (p<0.05). [Table 2]

Patients complicated with diabetic neuropathy (n=14), 6(42.86%) had bacteriuria and 17(47.22%) out of 36 without diabetic neuropathy had bacteriuria (p>0.05). [Table 2]

Leucocytosis were observed in 13(48.14%) of 27 non bacteriuric patients in contrast to 9(39.13%) out of 23 patients with bacteriuria (p>0.05). [Table 2]

Although 37 cases had FBS >200mg/dl, only 16(43.24%) were bacteriuric in comparison to 7(53.85%) out of 13 with FBS <200, the difference was not statistically significant (p >0.05). Similarly 35 cases with PPBS >250, 18(51.43%) were bacteriuric while 5(33.33%) out of 15 patients with PPBS <250 had bacteriuria (p >0.05). [Table 2]

19(59.38%) of 32 patients with HbA$_1$C levels >7% were bacteriuric as compared to 4(22.22%) out of 18 patients with HbA$_1$C levels <7% (p < 0.05).

21(56.76%) patients out of 37 with Post voidal residual volume (PVR)> 150ml were bacteriuric whereas only 2(15.38%) out of 13 with PVR <150ml had bacteriuria. (p<0.05). [Table 2]

Out of 33 patients who had prostate volume >40cc, 19(57.58%) were bacteriuric whereas 4(23.53%) out of 17 patients with prostate volume <40cc were found to be bacteriuric. (p<0.05). [Table 2]

Sl. No.	Variables	With bacteriuria	Without bacteriuria	P value
1	No. of patients	23	27	
2	Age			
	>50 years	20	21	0.479
	<50 years	3	6	
3	Type of diabetes			
	Type 1	3	1	0.322
	Type 2	20	26	
4	Duration of diabetes			
	< 6 years	4	14	0.017
	>6 years	19	13	
5	Treatment taken for diabetes			
	Regimen containing insulin	11	5	0.036
	Regimen without insulin	12	22	
6	Adherence to follow up			
	Yes	7	18	0.022
	No	16	9	
7	Diabetic neuropathy			
	Yes	6	8	1
	No	17	19	
8	Leukocytosis			
	Yes	9	13	0.577
	No	14	14	
9	HbA1C			
	<7%	4	14	0.017
	>7%	19	13	
10	Fasting blood sugar			
	<200 mg/dl	7	6	0.536
	>200 mg/dl	16	21	
11	Post prandial sugar			
	<250 mg/dl	5	10	0.349
	>250 mg/dl	18	17	
12	Post void residual volume			
	>150 ml	21	16	0.011
	<150 ml	2	11	
13	Size of prostate			
	>40 cc	19	14	0.035
	< 40 cc	4	13	
Table 2: Showing different variables in the series				

Most common bacteria isolated was E. Coli (n=13) followed by Klebsiella (n=4). Other organisms isolated included were Proteus (n=2) Enterococci (n=2), Pseudomonas (n=1) and staphylococci (n=1).

Most of the organisms were susceptible to antimicrobials like Imipenem, Aminoglycosides and Fluoroquinolones. E. coli isolates in majority of the patients were sensitive to both Imipenem and fluoroquinolones like ciprofloxacin and aminoglycosides like amikacin.

Micro organism	IE*	CPM#	AMC©	CIPRO**	AMIKA§	GENTAθ	LEVOє	NTΔ
E.coli (13)	13(100%)	09(69.23%)	07(53.84%)	07(53.84%)	08(61.53%)	08(61.53%)	04(30.76%)	08(61.53%)
Klebsiella (04)	03(75%)	-	-	03(75%)	01(25%)	03(75%)	-	-
Proteus (02)	02(100%)	-	-	02(100%)	03(100%)	03(100%)	-	-
Enterococci (02)	02(100%)	-	0	02(100%)	02(100%)	02(100%)	-	02(100%)
Pseudomonas (01)	01(100%)	-	-	01(100%)	01(100%)	01(100%)	-	-
Staphylococci (01)	01(100%)	-	-	01(100%)	-	-	01(100%)	-
Table 3: Showing sensitivity of different organisms for antibiotics								

[*IE-imipenem; #CPM-Cefepime; ©AMC-amoxiclav; **CIPRO-Ciprofloxacin; §AMIKA-Amikacin; θGENTA-Gentamycin; єLEVO-Levofloxacin; ΔNT-Nitrofurantoin]
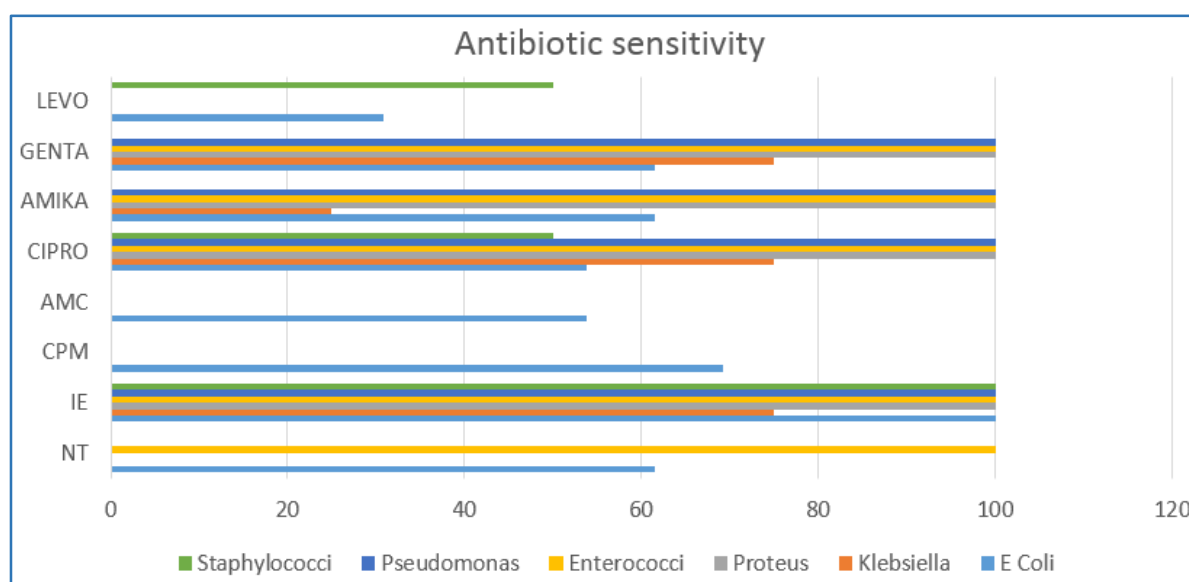

Fig. 2: Antibiotic sensitivity of different organisms

DISCUSSION: The study assessed the probable risk factors for UTI in general and bacteriuria in particular in diabetic patients with prostatomegaly. There is paucity of study with similar study profile and similar variables especially in north eastern part of India.

As it is a hospital based study, true prevalence and incidence of UTI in patients with diabetes and prostatomegaly is difficult to predict. As asymptomatic bacteriuria is difficult to define in general population, incidence of bacteriuria varied greatly in different studies conducted earlier. In present study, 50 indoor patients were diagnosed to have diabetic prostatomegaly with UTI. Diabetics with bacteriuria among these patients constituted 46% of population. In similar study done by Chaudhary BL et al[7] 2014 found prevalence of bacteriuria to be 32% while according to Huvos et al[8] 1959 prevalence was 26%.

Prostatomegaly with UTI was found to be more prevalent in the age group of 50 to 60 years in the present series. The observations made by Ross C[9] 2012 and Vesely S et al[10] 2003 reported prostatomegaly as common in 45-71 years and 45-91 years respectively in their series. Also size of the prostate (more than 40cc) constitutes a significant risk factor in present study. Similar results were noted by Ross C[9] 2012 and Vesely S et al[10] 2003.

Present study did not find any relation between type of diabetes and risk of bacteriuria. This was in concordance with the study done by Geerlings SE[11] 2008 and Yismaw G

& Asrat[12] 2012 who didn't observe any statistical significance when patients with UTI and diabetes were compared on the basis of type of diabetes.

Present study showed positive correlation between duration of diabetes (more than 6 years) and chances of having bacteriuria. This was similar to studies done by Yismaw & Asrat[12] 2012 and Gorter KJ et al[13] 2010 who found duration of diabetes more than 5 years as a risk factor for bacteriuric UTI. But Hamdan HZ et al[14] 2015 didn't find any association of duration of diabetes with bacteriuric UTI.

In present study diabetics who used insulin as modality of treatment were found prone to develop bacteriuric UTI. Al-Rubeaan KA et al[15] 2012 [with odds ratio and 95% CI 4.69 and (4.28-5.14)] in Saudi Arabia and Boyko EJ et al[16] 2005 (RR=3.7, 95% CI:1.8, 7.3) in USA noted increased incidence of bacteriuric UTI in patients taking insulin as treatment modality in comparison to patients on oral antidiabetic agents and those who were on lifestyle modification.

In the present study non-compliance with treatment emerged as risk factor for bacteruric UTI. No supporting studies were found for this result.

Brauner, A et al[17] 1993 and Papazafiropoulou A et al[18] 2010 found no significant association between complications of diabetes and bacteriuric UTI. Present study did not find any relationship between complication of diabetes like neuropathy and bacteriuric UTI.

Absence of significant leucocytosis among bacteriuric patients as compared to patients without bacteriuria was noted in present study. Nancy C. McGuire et al[19] 2002 in their study found similar results in diabetic dogs. Similar studies in human comparing bacteriuric and non bacteriuric diabetics are lacking.

Present study got high prevalence of bacteriuria among the diabetics with HbA$_1$c levels >7%. Srinivas A[20] 2014 found positive correlation between high levels of HbA$_1$c and increased risk of bacteriuric UTI [Mean HbA$_1$c in diabetics with recurrent UTI was 9.26 ± 3.83 (i.e. > 8.0)]. Bonadio M et al[21] 2001 also got similar results with significant association at HbA$_1$c more than or equal to 7% (mean HbA$_1$c 9.2%±1.9%).

Post prandial sugar level(>250mg/dl) and fasting sugar level(>200mg/dl) were high 68% and 76% of UTI patients irrespective of presence or absence of bacteriuria but this factor was not found to influence incidence of bacteriuria in diabetic population in present study. Simkhada R[22] 2013 in a study conducted in Nepal found no significant correlation between the degree of sugar control and growth of organism with p=0.055 and 0.16 respectively for fasting and PP which supports finding in the present study.

A statistical association is observed between bacteriuria and increased PVR in the present study. Simsir A et al[23] 2011 indicated a direct proportion between the incidence of bacteriuria and increased post-void residual volume >150ml (P < 0.0001). Ellenberg M[24] 1980 demonstrated increase in frequency of UTI with increase in urinary bladder residual volume but Boyko EJ et al[16] 2005 did not found any association of bacteriuric UTI and PVR.

Most common bacteria isolated was E. coli (n=13) and the next common being Klebsiella (n=4). Studies done by Bonadio M et al[21] 2006 had found an increased incidence of E-coli 54.1% in diabetic patients with bacteriuria, the next prevalent organism being Enterococcus spp:8.3%. O'Sullivan et al[25] 1951 reported E. coli and streptococcus faecalis as most common uropathogen. Similar results with this study were seen with studies done by Shah B. V et al[26] 1948, Zhanel et al[27] 1991 and Huvos et al[8] 1959.

CONCLUSION: UTI is frequently encountered in diabetics with prostatomegaly. Factors like age (i.e. age >50 years), volume of prostate, prostate size more than 40cc, non-adherence to treatment and insulin therapy could be considered as significant risk for bacteriuric UTI among diabetics.

Patients with diabetes more than 6 years duration were found to be associated with higher prevalence of UTI (but not for bacteriuria). Uncontrolled blood sugars for longer duration suggested by HbA$_1$c >7% in diabetic patients and post voidal residue >150 ml did show an increased propensity for developing bacteriuric urinary tract infections. Type of diabetes and associated diabetic complication does not seem to have any impact on risk of developing bacteriuric UTI.

E. coli was the most common organism isolated in patients. Klebsiella, Proteus and Enterococci were other common organisms isolated. Imipenem, fluoroquinolones and aminoglycosides emerged as most effective antimicrobials.

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