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Original Research Article

Spectrum of uropathogens and their antibiotic sensitivity pattern in diabetes mellitus patients at a tertiary care hospital in Odisha, India

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ABSTRACT

Background: Diabetes Mellitus is the most common endocrine disorder involving almost all systems of body. Untreated or poorly treated Diabetics are susceptible to develop a series of complications responsible for raised morbidity and mortality. Diabetes Mellitus has a number of long term effects on the Genitourinary system. Urinary tract infections have long been recognised as a significant problem in patients with Diabetes Mellitus.
Methods: Prospective observational study. Diabetic patients with culture positive UTI were included. Gestational diabetes, Immunocompromised patients and patients with congenital renal anatomical abnormalities were excluded.
Results: Authors included 211 numbers of culture positive UTI among diabetic patients. Out of which, 65 were male and 146 were female. Maximum number of patients belong to 56-65 years age group. *Escherichia coli* was the predominant organism isolated. Gram positive organisms showed 100% sensitivity to Vancomycin and Linezolid. Gram negative organisms showed 100% sensitivity to Polymyxin B.
Conclusions: Genitourinary tract infection is not an infrequent complication seen in diabetes patients. Most common causative organism and their antibiotic sensitivity pattern should be done in tertiary care hospital for a better antibiotic policy.

Keywords: Antibiotic sensitivity, Diabetes Mellitus, Urinary tract infection, Uropathogen

INTRODUCTION

Incidence of infection is higher in diabetes and such infection results in complications. Diabetic patients tolerate infection poorly. Infections and diabetic control adversely affect each other. The diabetic has an altered response to infection as these patient's inherent susceptibility to infection as well as the potential to mount a normal inflammatory response.[1]

The complement system is one of the main mechanisms responsible for the humoral immunity. It consists of serum and surface proteins whose main functions are to promote the opsonisation and phagocytosis of microorganisms through macrophages and neutrophils and to induce the lysis of these microorganisms. Moreover, complement activation products provide the second signal for B-lymphocyte activation and antibody production. Although some studies have detected a deficiency of the C4 component in DM, this reduction of C4 is probably associated with polymorphonuclear leucocyte dysfunction and reduced cytokine response.[2,3]

Mononuclear cells and monocytes of persons with DM secrete less interleukin-1 (IL-1) and IL-6 in response to

stimulation by lipopolysaccharides.[4] It appears that the low production of interleukins is a consequence of an intrinsic defect in the cells of individuals with DM.[5] However, other studies reported that the increased glycation could inhibit the production of IL-10 by myeloid cells, as well as that of interferon gamma (IFN-γ) and tumor necrosis factor (TNF-α) by T cells. Glycation would also reduce the expression of class I major histocompatibility complex (MHC) on the surface of myeloid cells, impairing cell immunity.[6]

Decreased mobilization of polymorphonuclear leukocytes, chemotaxis, and phagocytic activity may occur during hyperglycemia.[7] The hyperglycemic environment also blocks the antimicrobial function by inhibiting glucose-6-phosphate dehydrogenase (G6PD), increasing apoptosis of polymorphonuclear leukocytes, and reducing polymorphonuclear leukocyte transmigration through the endothelium.[8] In tissues that do not need insulin for glucose transport, the hyperglycaemic environment increases intracellular glucose levels, which are then metabolized, using NADPH as a cofactor. The decrease in the levels of NADPH prevents the regeneration of molecules that play a key role in antioxidant mechanisms of the cell, thereby increasing the susceptibility to oxidative stress.

Regarding the mononuclear lymphocytes, some studies had demonstrated that when the glycated hemoglobin (HbA_{1c}) is <8.0%, the proliferative function of CD4 T lymphocytes and their response to antigens is not impaired.[9] Glycation of immunoglobulin occurs in patients with diabetes in proportion with the increase in HbA_{1c}, and this may harm the biological function of the antibodies.[4] However, the clinical relevance of these observations is not clear, since the response of antibodies after vaccination and to common infections is adequate in persons with DM. A significantly lower chemotaxis has been found in polymorphonuclear leucocytes of diabetic patients (type 1 and type 2) than in those of controls.[10] Studies also showed both impaired chemotaxis and phagocytosis of the monocytes of diabetic patients.[11]

Aims and objectives of this study was to observe the clinical and laboratory profile of genitourinary tract infection in diabetes patients. To observe the yield of urine culture, discharge culture and microscopic examination in diabetic UTI patients and the common causative organism isolated in culture and their antibiotic sensitivity pattern.

METHODS

The present study was under taken in the Department of Medicine with the assistance of Department of Microbiology at VSS.I.M.S.A.R, Burla during the period December 2015 to November 2017. All the patients of diabetes mellitus with symptomatology of genitourinary tract infection admitted to medical ward and urine culture being positive to microorganisms were included in this study. Diabetes mellitus was diagnosed as per the diagnostic criteria.

Diabetics who were excluded from the study are gestational diabetes mellitus, Congenital renal anatomical abnormalities, Immuno-compromised state: HIV, patients on steroid, malignancy, transplant recipients.

Initially all the patients were screened for genitourinary tract infection by culture of urine and discharge. Each of these patients with positive culture were enquired as regards to their age, sex, about their presenting complaints, duration of symptoms, history of treatment with respect to urinary tract infection and glycemic control, history of similar attack, or history of any instrumentation of urinary tract. The patients were examined in detail. General examination, systemic examination were carried out. The history and examination finding were recorded in the proforma.

All the routine investigation like Hb%, DC, TLC, Fasting Blood Sugar, HbA_{1c}, blood urea and serum creatinine were carried out. Ultrasonography was done. Straight X-ray abdomen and CT scan of abdomen were done in selected cases. Routine and microscopic examination of urine and discharge, culture and antibiotic sensitivity of urine and discharge were done.

Culture of urine**:** Mid-stream urine was collected and sample sent to department of microbiology, was cultured within two hours. The urine was mixed thoroughly before the inoculation into culture plates. The inoculation was done into the surface of the agar plates (MacConkey and blood agar) by means of sterile calibrated platinum loop to deliver 0.01 or 0.001 ml of urine. Then the plates were incubated at 37ºC for 24 hours aerobically. Colonies were counted on each plate. The number of colony forming unit (CFU) is multiplied by 1000 if 0.001 ml loop was used or by 100 if 0.01 ml loop was used to determine the number of microorganisms per ml in the original specimen.

Culture with colony counts $\geq 10^5$/ml were considered significant bacteriuria. Organisms were identified by their colonial characteristics and different biochemical methods. Antibiotic sensitivity pattern was tested by disc diffusion method using multidisc.

RESULTS

In this present study, authors included 211 culture positive UTI among diabetic patients of age more than 14 years from December 2015 to November 2017 at VSS Institute of Medical Sciences and Research, Burla, Odisha. Out of 211 diabetic patients, 65 were male and 146 were female. Maximum number of patients belong to the age group of 56-65 years, followed by 46-55 years age group. Least number of patients were seen in the age group of 26-35 years. Table 1 is showing age and sex wise distribution of diabetic patients with UTI.

Table 1: Age and sex wise distribution of diabetic patients with genitourinary tract infection.

Age group	Male (%)	Female (%)	Total (%)
15-25 years	13 (6.1%)	23 (10.9%)	36 (17%)
26-35 years	4 (1.8%)	14 (6.7%)	18 (8.5%)
36-45 years	5 (2.3%)	18 (8.5%)	23 (10.8%)
46-55 years	15 (7.2%)	34 (16.1%)	49 (23.3%)
56-65 years	18 (8.7%)	40 (18.9%)	58 (27.6%)
>65 years	10 (4.8%)	17 (8%)	27 (12.8%)
Total	65 (30.9%)	146 (69.1%)	211 (100%)

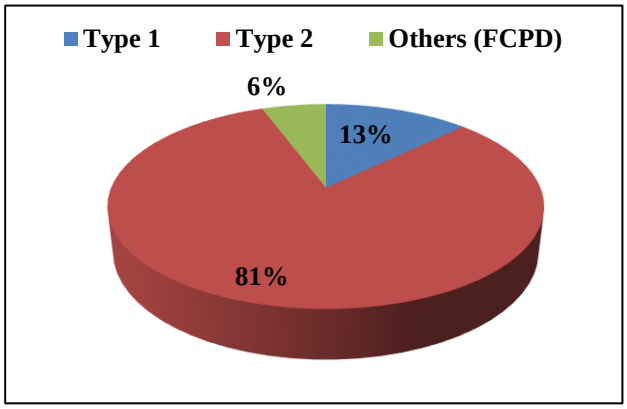

Figure 1: Percentage contribution of various types of diabetes with genitourinary tract infection in the study.

In this study, type 2 diabetes patients were maximum in number. FCPD contributed least number of cases. Figure 1 is showing percentage contribution of various types of diabetes in this study. Dysuria, increased frequency of micturition and fever were the predominate presenting symptoms found in present study. Table 2 is showing various symptoms and signs observed in this study group.

Table 2: Various presenting symptoms and signs in patients of genitourinary tract infection with diabetes in the study.

Signs and Symptoms	No. of cases	Percentage (%)
Fever	130	61.6
Dysuria	159	75.3
Increase frequency of micturition	140	66.3
Itching	55	26
Urethral discharge	50	23.7
Supra pubic tenderness	45	21.3
Renal angle tenderness	59	27.9

Microorganisms isolated from urine sample of diabetic patients were *Escherichia coli* 67 (31.75%) which was most prevalent followed by *Klebsiella* 53 (25.1%), *Pseudomonas species* 30 (14.2%), *Staphylococcus species* 16 (7.5%), *Streptococcus* 6 (2.8%). *Candida species* were isolated in 39(18.4%) and mixed growth were seen in 4 (1.8%). Table 3 is showing microorganisms isolated among patients of genitourinary tract infection. *Staphylococcus* and *Streptococcus* were found to be 100% sensitive to Vancomycin and linezolid. In addition to this, Streptococcus was 100% sensitive to Nitrofurantoin. Table 4 is showing Gram positive bacteria and their sensitivity to antibiotics.

Table 3: Microorganisms cultured from patients of genitourinary tract infection with diabetes in the study.

Microorganisms	No. of positive cases	Percentage (%)
E. coli	67	31.75
Klebsiella	53	25.1
Pseudomonas	30	14.2
Streptococcus	6	2.8
Staphylococcus	16	7.5
Candida	39	18.4
Mixed	4	1.8

Table 4: Gram positive bacteria cultured and their sensitivity to antibiotics in the study.

Antibiotics	*Staphylococcus* (%)	*Streptococcus* (%)
Ampicillin	5 (31.25)	5 (83.3)
Nalidixic acid	6 (37.5)	3 (50)
Nitrofurantoin	11 (68.75)	6 (100)
Ciprofloxacin	8 (50)	2 (33.3)
Norfloxacin	3 (18.75)	1 (16.66)
Cotrimoxazole	6 (37.5)	2 (33.3)
Amikacin	9 (56.25)	3 (50)
Vancomycin	16 (100)	6 (100)
Linezolid	16 (100)	6 (100)

All the gram negative organisms were found to be 100% sensitive to Polymyxin B. *E. coli* was least sensitive to Norfloxacin. Klebsiella was least sensitive to cefotaxime and cotrimoxazole. Pseudomonas was least sensitive to Norfloxacin. Table 5 is showing Gram negative bacteria and their sensitivity to antibiotics. Cumulative antibiotic sensitivity was highest for nitrofurantoin, followed by amikacin. It was found to be very less for cefotaxime and norfloxacin. Table 6 is showing cumulative antibiotic sensitivity of all the bacteria isolated from culture.

DISCUSSION

The present study included 211 patients of Diabetes Mellitus with UTI admitted to general medicine ward.

Among them 65 were male and 146 were female patients. Our study correlates well with studies by J Janifer, S Geethalakshmi et al, also found that women had a significantly higher prevalence of UTI than men.[12]

Table 5: Gram negative bacteria cultured and their sensitivity to antibiotics in the study.

Antibiotics	*E. coli*	*Klebsiella*	*Pseudomonas*
Ampicillin	33 (49.25)	27 (51)	12 (40)
Nalidixic acid	30 (44.7)	14 (26.4)	12 (40)
Nitrofurantoin	64 (95.5)	51 (96.2)	23 (76.6)
Ciprofloxacin	13 (19.4)	14 (26.4)	10 (33.3)
Gentamicin	19 (28.35)	18 (33.9)	7 (23.3)
Norfloxacin	12 (17.9)	16 (30.18)	5 (16.6)
Cefotaxime	15 (22.38)	11 (20.75)	10 (33.3)
Cotrimoxazole	24 (35.8)	11 (20.75)	6 (20)
Amikacin	63 (94)	46 (86.8)	19 (63.3)
Polymyxin	67 (100)	53 (100)	30 (100)

Table 6: Cumulative antibiotic sensitivity of all the bacteria isolated from culture in the study.

Antibiotics	No. isolate sensitive	% Sensitive
Ampicillin	82	38.8
Nalidixic acid	65	30.8
Nitrofurantoin	155	73.4
Ciprofloxacin	47	22.2
Gentamicin	44	20.85
Norfloxacin	37	17.53
Cefotaxime	36	17.06
Cotrimoxazole	49	23.22
Amikacin	140	66.3

Maximum number of cases were having type 2 diabetes mellitus (172 cases), followed by type 1 DM (27 cases) and FCPD (12 cases). Similar observation was made by Kayima JK in their study.[13]

In this study authors found that most common presenting symptom of urinary tract infections is dysuria (75.3%), followed by increased frequency of micturition (66%), fever (61%). Authors have found that fever was the most common presenting symptoms (57.4%), followed by dysuria (41.4%), increase frequency of micturition (27.3%).[14]

Out of 211 cases, Gram positive organisms were isolated in 22 cases, Gram negative organisms were isolated in 150 cases, Candida species were isolated in 39 cases and 4 cases had mixed species on culture. J Janifer, S Geethalakshmi et al, also found maximum cases with Gram negative organisms followed by Gram positive organisms and candida species in that order.[12]

The contribution of *E. coli* was 31.7%, *Klebsiella species* 25.1%, *Pseudomonas* 14.2%, *Staphylococcus* 7.5%, *Streptococcus* 2.8%, *Candida species* 18.4%. This study correlates with Manik C Shill and Naz H Huda et al, who found that *E. coli* was the predominant organism isolated.[15]

Gram positive organisms were showing 100% sensitivity to both Vancomycin and linezolid, least sensitivity was shown to Norfloxacin. Gram negative organisms were showing 100% sensitivity to Polymyxin B, least sensitivity was shown to Norfloxacin. Antibiotic sensitivity pattern of organisms isolated showed that Nitrofurantoin and Amikacin were having highest cumulative antibiotic sensitivity, 73.4% and 66.3% respectively. Least sensitive antibiotic was found to be Cefotaxime. Aswani SM et al, found that the isolated *E. coli* strains showed an increased sensitivity to carbapenems in both diabetics (93.8%) and non-diabetics (95.1%) and decreased susceptibility to ampicillin (diabetics 16.7 per cent vs. non-diabetics 17 per cent).[14] Manik C Shill and Naz H Huda et al, found that the most effective antibiotic overall was meropenem followed by amikacin.[15]

CONCLUSION

Genitourinary infection is more common among diabetic females as compared to diabetic males. The common mode of presentation was dysuria, increased frequency of micturition and fever. Probably high sugar level is the main cause of increased frequency of urinary tract infection among the diabetic patients, so tight glycaemic control is required to reduce the occurrence of urinary tract infection in diabetic patients.

Antibiotic sensitivity varies among gram positive and gram negative organisms. Antibiotic sensitivity pattern of Gram positive bacteria was more sensitive to Vancomycin, Linezolid followed by Nitrofurantoin, Amikacin and Ampicilin. On the other side, the Gram-negative bacteria were more sensitive to Polymyxin B, followed by Nitrofurantoin, Ampicillin and Gentamycin. So, we need a proper antibiotic policy in tertiary care hospitals to provide effective treatment as well as prevent the misuse of Antibiotics. However further studies with large sample size is highly recommended to further support the findings from this study

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