Comparison of Clinical Presentation and Risk Factors in Diabetic and Non-Diabetic Females with Urinary Tract Infection Assessed as Per the European Association of Urology Classification

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ABSTRACT

Introduction: Diabetes has been known to cause severe complicated UTI as a result of its various changes in the genitourinary system. This study of UTI in diabetic females enables us to know the pattern of infections, their causative organisms and severity, particularly with reference to European Association of Urology (EUA) guidelines for UTI 2015.

Materials and Methods: This is a prospective single centre study done over a period of one year at Dayanand Medical College and Hospital on a total of 151 diabetic (Group A) and non-diabetic (Group B) female patients with diagnosis of UTI. A thorough history of the patients was taken which included looking for the anatomical level of infections, host risk factors; extra urogenital risk factors and nephropathy disease were assessed. All patients were adequately investigated. The UTI was classified according to the EAU classification for UTI, and an effort was made to find out the frequent class of UTI in this study group.

Results: A total of 151 females which included 70 diabetic (Group A) and 81 non diabetic (Group B) females were studied. The most common symptom was fever in both the groups. UTI was classified as per the EAU grades of UTI. In group A, the number of patients having severity grade from 1 to 6 were 47, 9, 4, 2, 4, and 4 respectively. The most common clinical presentation in both the groups was cystitis followed by pyelonephritis and urosepsis. In group B, the number of patients having severity grade from 1 to 6 were 66, 4, 5, 5, 0 and 1 respectively. Most common organism was *E-coli*, which was susceptible to most of the antibiotics.

Conclusion: UTI in diabetic and non-diabetic female patients have different patterns. Uncontrolled diabetes was more commonly associated with severe UTI like pyelonephritis and emphysematous pyelonephritis. *E. coli* was most common isolate in either group, followed by *klebsiella* and *Pseudomonas*. *Candida* was isolated only from the diabetic population. Therefore, the most common type of UTI as per the EAU classification in both diabetic and non diabetic female was CY-1R: *E. coli* (a): 'simple cystitis but recurrent with susceptibility to standard antibiotics', in our study.

INTRODUCTION

India is considered the diabetic capital of the world. The urinary tract is the most common site of infection in diabetic patients. The urinary tract infections (UTIs) in diabetic patients may lead to severe kidney damage and renal failure. Improved control of the diabetes mellitus (DM) can prevent damage to organs in urinary tract. Microorganisms become more virulent in a high glucose environment [1]. DM has been known to cause severe complicated UTI as a result of its various changes in the genitourinary system. The morbidity of UTI is more in diabetic women as a result of altered immunity [2]. Therefore, this study enables us to know the pattern of urinary infections, causative organisms and severity, particularly with reference to European Association of Urology (EAU) guidelines for UTI 2015 [3].

MATERIALS AND METHODS

This is a prospective single centre study done over a period of one year at Dayanand Medical College and Hospital. A total of 151 female patients with diagnosis of urinary tract infection were included in this study. Female patients with diabetes were assigned group A and non-diabetics were assigned group B. A thorough history of the patients was taken which included looking for the anatomical level of infections like urethritis, cystitis and pyelonephritis. Host risk factors for recurrent UTI like postmenopausal status and status

of diabetes control were noted. Extra urogenital risk factors like pregnancy and poorly controlled diabetes were included. History of nephropathy disease like renal insufficiency was taken. History of stone disease, neurogenic bladder and previous urological surgery was also taken. All patients underwent complete blood count, renal function tests, urine microscopy, urine culture and ultrasonography. For urine microscopy, 5ml of clean catch midstream urine was centrifuged at 3000 rpm for five minutes, the centrifuged urine was viewed under microscope, and more than five WBC per high power field was considered significant. A fasting sugar, postprandial sugar and HbA1c were done. The UTI was classified according to the European association of urology classification for UTI, and an effort was made to find out the frequent class of UTI in our group.

RESULTS

A total of 151 females who enrolled for the study were evaluated. Seventy patients were diabetic (Group A). Eighty one females were non diabetic (Group B). The mean age of study population was 47.79 years. Mean age of females in group A was 53.23 years and in group B was 41.23 years. When the symptoms were evaluated in the two groups we found that fever was present in 31 and 52 females in Group A and Group B respectively. Dysuria was present in 33 and 18 females, storage Lower Urinary Tract Symptoms (LUTS) like frequency, urgency and nocturia was present in 37

and 27 females in Group A and B respectively. Voiding LUTS like poor urinary stream, dribbling were present in 20 and 14 patient; pain abdomen was present in 39 and 17 patients in Group A and Group B respectively. Vomiting was present was in 13 and 28 patients. Haematuria was present in 8 and 9 females of Group A and Group B respectively in Group A and Group B respectively. The occurrence of dysuria, storage LUTS, voiding LUTS, and pain abdomen was more in Group A, however only the frequent occurrence of dysuria was statistically significant (p-value<0.001) [Table/Fig-1]. The predisposing factors [Table/Fig-2] were evaluated like pregnancy, (5.7% in group A versus 9.8% in group B), presence of renal or ureteric calculi (22.85% in Group A and 30.8% of group B), neurogenic bladder (11.4% in Group A and 8.6% of Group B) and prior instrumentation in (5.7% in Group A and 7.4% of Group B). None of the risk factors had any statistical significance in either group.

Amongst the organisms isolated after urine culture, the most common organism was *E. coli* present in 36 and 52 females in group A and B respectively. *Klebsiella* was the second common amongst the organism isolated which was seen in 13 and 18 females; *Enterococcus* was seen in 7 and 1; *Pseudomonas* in 9 and 8 females; *Staphylococcus aureus* in 1 and 4 females of group A and B respectively. The occurrence of *Candida* infection was statistically significant in diabetic females [Table/Fig-3]. Pyelonephritis was found in 22 of diabetic females and 17 in non diabetic females. This association was however not statistically significant. Ten of the diabetic cases had gas on imaging and was diagnosed to have emphysematous pyelonephritis. The occurrence of emphysematous pyelonephritis was statistically higher in diabetic female patients. Only one female in Group B had emphysematous pyelonephritis. Twenty of the diabetic females had pre-existing chronic kidney disease and 11 of non-diabetic females had Chronic Kidney Disease (CKD). Although CKD was more in diabetic group but this association was statistically not significant [Table/Fig 4]. Using

Symptoms	Group A	Group B	p-value
Fever	31(44.28%)	52(64.19%)	0.01
Dysuria	33(47.1%)	18(22.22%)	0.001
Storage LUTS	37(52.8%)	27(33.33%)	0.015
Voiding LUTS	20(28.57%)	14(17.2%)	0.09
Pain Abdomen	39(55.7%)	17(20.98)	0.001
Vomiting	13(18.5%)	28(34.56%)	0.027
Haematuria	8(11.4%)	9(11.11%)	0.095

[Table/Fig-1]: Distribution of clinical symptoms in both groups and their statistical significance

Risk Factors	Group A	Group B	p-value
Pregnancy	4(5.7%)	8(9.8%)	0.34
Calculus	16(22.85%)	25(30.8%)	0.26
Neurogenic Bladder	8(11.4%)	7(8.6%)	0.56
Recent Instrumentation	4(5.7%)	6(7.4%)	0.56

[Table/Fig-2]: Distribution of risk factors in either groups and their statistical significance

Organism	Group A	Group B	p-value
E. Coli	36(51.4%)	52(64.19%)	0.11
Kliebsiella	13(18.57%)	18(22.22%)	0.57
Enteococcus	7(10%)	1(1.2%)	0.01
Pseudomonas	9(12.8%)	8(9.8%)	0.56
Acinetobacter	3(4%)	0(0%)	0.53
Proteus	2(2.8%)	2(2.4%)	0.88
Staphylococcus aureus	1(1.4%)	4(4.9%)	0.22
Candidia	8(11.4%)	0(0%)	0.001

[Table/Fig-3]: Distribution of organisms in either groups and their statistical significance

Complication	Group A	Group B
Pyelonephritis	22	17
Emphysematous Pyelonephritis	10	1
Sepsis	6	9
CKD	20	11

[Table/Fig-4]: Complication in either group

Clinical presentation	Grade of severity	Risk factors (RF)	Pathogens
UR: Urethritis CY: Cystitis PN: Pyelonephritis US: Urosepsis MA: Male genital glands	1: Low, cystitis 2: PN, moderate 3: PN, severe, established 4: US: SIRS 5: US: Organ dysfunction 6: US: Organ failure	O: No RF R: Recurrent UTI RF E: Extra urogenital RF N: Nephropathic RF U: Urological RF C: Catheter RF	Species Susceptibility Grade • Susceptible • Reduced susceptibility • Multi-resistant

[Table/Fig-5]: UTI classification and severity assessment as proposed by European Association of Urology (EAU guidelines for UTI 2015)

	Patients in Group A	Patients in Group B
Clinical presentation		
Cystitis (CY)	47	67
Pyelonephritis (PN)	13	8
Urosepsis (US)	10	6
Clinical severity		
Grade 1	47	66
Grade 2	9	4
Grade 3	4	5
Grade 4	2	5
Grade 5	4	0
Grade 6	4	1

[Table/Fig-6]: Clinical Presentation in our study as per by European Association of Urology (EAU guidelines for UTI 2015)

the latest European association of Urology classification of UTI, we classified the grades of UTI as per the severity grade [Table/Fig-5]. In group A, the number of patients having severity grade ranging from 1 to 6 were 47, 9, 4, 2, 4, and 4 females respectively. The most common clinical presentation was cystitis (CY) seen in 47 patients followed by pyelonephritis (PN) seen in 13 and urosepsis (US) found in 10 of the female patients. Diabetes itself is risk factor so all the females in this group had this risk factor. In group B, the number of patients having severity grade ranging from 1 to 6 were 66, 4, 5, 5, 0 and 1 respectively. The most common clinical presentation was cystitis (CY) seen in 67 females, followed by pyelonephritis (PN) seen in 8 females and urosepsis (US) seen in 6 females [Table/Fig-6].

DISCUSSION

Our study group included 151 females who were diagnosed to have urinary tract infection. An analysis of the symptoms revealed that fever was the most common presenting symptom in both group A and Group B. This appeared to be more common in group B but this value was not significant (p-value>0.01). The occurrence of dysuria was second most common presenting symptom in our study group. This was more in Group A of diabetic females (p-value<0.001). Storage and Voiding LUTS appeared to be more in group A as compared to Group B. These finding were not statistically significant. Similarly, pain abdomen was more in group, A which was also not statistically significant. This could be explained by occurrence of more severe infection and inflammation in diabetic patients. Occurrence of neuropathy may add to occurrence of such LUTS. However, the neuropathy component was not evaluated in our study group. The most common symptom associated with UTI in both diabetics and non-diabetics in our study was fever. Fever generally indicates an evident or a smouldering infection which is more commonly a UTI in females. Bonadio M et al., also found

higher incidence of fever in diabetic females as compared to non-diabetic (14.9 % vs. 13.1 % respectively) [4]. Several studies on the prevalence of asymptomatic bacteriuria also showed higher incidence of asymptomatic bacteriuria in diabetic females as compared to non-diabetic females (26 % vs. 6 % respectively) [5]. The most common risk factor in our study group was obviously the diabetes mellitus. The second common risk factor was calculus disease, which was present in 22.85 % patients in group A and in 30.8 % in group B. The occurrence of calculus is more common in non diabetic group. Hence, it appeared that calculus increasing the chances of infection in non diabetic patients. However, this association was not statistically significant. The occurrence of neurogenic bladder and history of recent instrumentation was marginally higher in the diabetic group. Pregnancy as a risk factor was more common in nondiabetic group. However, none of the risk factor has any statistically significant association. Out of the 70 diabetic females 23 had, uncontrolled diabetes as measured by raised HB1Ac levels. The most common organism isolated in our study was *E. coli* which was isolated in 51.4% in Group A and in 64.19 % females in Group *B. Klebsiella* was the second most common isolate and was present in 18.57 % of group A and in 22.22% of Group *B. Pseudomonas* was the third most common isolate was isolated in 12.8% and 9.8% of group A and group B respectively. *Candida* was isolated in only in 11.4 % of diabetic females and none in group B. Bonadio M et al., in their study have shown *E. coli* as the commonest organism isolated in diabetics (males 32.5 per cent vs. females 54.1 per cent) and non-diabetics (males 31.4 % vs. 58.2%) [4]. In our study eight patients had UTI due to *Candida* and all of these were diabetic. The prevalence of ESBL *E. coli* was significantly higher in diabetics (78.6 %) than in non-diabetics. The isolation rates of ESBL *E. coli* in diabetics (47.8 per cent) vs. non-diabetics were also found to be higher in this study compared to a study conducted by Saber MH et al., [6]. Apart from diabetes the risk of fungal UTI increases with indwelling urethral catheters, hospitalization and antibiotics [7]. Sepsis was more in group B (11%) as compared to group A (8.5%). However, this was also not statistically significant. In a study done by Saleem M et al.,[8] diabetic patients in the lower socioeconomic status, *E. coli* was isolated from 32.9% diabetic males and 25.5% from female diabetic patients. *Pseudomonas* sp was prevalent in. 1.4% males and 9.1% females. The incidence of *P.aeruginosa* in diabetic patients clearly indicates immune suppression by this opportunistic uropathogen, which never causes any symptoms of UTI in the non diabetic subjects [9]. *Enterococci* could be a consequence of nosocomial UTI [6]. *Enterococcus* feacalis was found to be the cause of 35% of UTI in hospitalized patients [10,11].

When the UTI was classified according to the EAU classification, we found that the most common site of the infection was localized to the bladder and most common presentation of females in both

Group A and B was due to cystitis (CY). Group A had diabetes as a risk factor and second being calculus. In group, B the most common risk factor was calculus. So, as per the EAU classification at least one risk factors (1R) and most common organism was *E. coli* which was susceptible to most of the antibiotics. Therefore, the most common type of UTI in diabetic and non diabetic females was CY-1R: *E. coli* (a): 'simple cystitis but recurrent with susceptibility to standard antibiotics', in our study group.

CONCLUSION

Urinary tract infections in diabetic and non-diabetic female patients behave differently. The clinical symptoms of dysuria and pain abdomen were more significant in diabetic females. Both diabetic and non-diabetic patients have similar risk factors. Uncontrolled diabetes was more commonly associated with severe UTI like pyelonephritis. *E. coli* was most common isolate in either group, followed by *Klebsiella* and *Pseudomonas*. *Candida* was isolated only from the diabetic population. Emphysematous pyelonephritis was more common in diabetic females. A thorough watch and aggressive management of a diabetic patient who presents with simple UTI can prevent progression to more dreaded complications and associated morbidity and mortality.

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