Effect of Glycemic Control on the Clinical and Laboratory Profile of UTI in Patients with Diabetes Mellitus

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ABSTRACT

Introduction: Urinary Tract Infection is the commonest infection in the patients of Diabetes Mellitus. Glycemic control, which is a major goal in the management of DM, may have an effect on their clinical profile and investigations. In this study, we compared the clinical and laboratory profile of UTI in patients of DM having good glycemic control with those having poor glycemic control.

Material and Methods: This was a prospective observational study in the patients admitted in Department of General Medicine in a tertiary care centre in Central India between January 2017 and September 2018. A total of 100 consecutive patients of DM with culture positive UTI were included in the study.

Results: Out of the 100 patients, 44% were males and 56% were females; 10% had Type 1 DM and 90% had Type 2 DM; and 57% had good glycemic control, whereas 43% had poor glycemic control. Patients on Oral Hypoglycemic Agents had better glycemic control (68.1%) than those on Insulin (26.3%) [P = 0.002]. 'Adherence to treatment' (85.9%) and 'regular follow up' (71.9%) were attributes of patients with good control [P < 0.001]. Commonest symptom seen was Dysuria (62%). Urinary incontinence (15%) [P = 0.001] and renal angle tenderness (14%) [P = 0.03] were significantly commoner in the poor glycemic control group. Escherichia coli was the commonest isolate in urine culture (70%). E.coli and other Gram Negative Bacilli were most susceptible to Aminoglycosides (72% and 83%) whereas Gram Positive Cocci were most susceptible to Nitrofurantoin (100%). Resistance to Ampicillin was uniformly high.

Conclusion: Glycemic control was better in those patients who adhered to treatment and had regular follow-up. Urinary incontinence and renal angle tenderness were associated with poor glycemic control. E.coli was the commonest isolate and Amikacin, Ceftriaxone and Nitrofurantoin were the most useful antibiotics.

Keywords: Diabetes Mellitus, DM, Urinary Tract Infections, UTI, Glycemic Control

INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in either insulin secretion or insulin action, or both. Immune dysfunction is a major problem seen in the disease course and can be in the form of either autoimmune disease or poor immune response, the latter leading to a higher incidence of infections.

Urinary tract is the commonest system to be affected by infections in DM. Indeed cystitis is the commonest infection in DM, surpassing even respiratory tract infections like acute rhinolaryngitis and acute bronchitis, and skin infections like dermatomycoses.[1] The correlation between higher incidence of Urinary Tract Infections (UTI) and diabetic patients[2] has been attributed to various impairments in the immune system, poor metabolic control of diabetes, and incomplete bladder emptying due to autonomic neuropathy. Further factors that were found to increase the risk for UTI in diabetics include age, glycemic control, and long term complications, primarily diabetic nephropathy and cystopathy.[3] Poor glycemic control may predispose to more severe UTI and greatly increase the risk of complications in UTI.[4] Invariably, *E.coli* is the most common isolate in UTI in DM. Other pathogens commonly isolated include *Klebsiella*, *Proteus*, and *Staphylococcus aureus*.[5] The high rates of antibiotic prescription for UTI in these patients may further induce the development of antibiotic-resistant urinary pathogens.[6]

In this study, we profiled the differences in clinical and laboratory findings of Urinary Tract Infections (UTIs) in patients of Diabetes Mellitus, based on their glycemic control.

MATERIAL AND METHODS

The present study was a prospective observational study conducted in the Department of General Medicine in a tertiary care centre in Central India between January 2017 and September 2018.

Inclusion Criteria

- All patients of Diabetes Mellitus with urine culture showing growth of pathogens > 10^5 cfu/ml.

Exclusion Criteria

- Age < 18 years,
- Immunocompromised states like HIV and those patients who are on steroids or immunosuppresants,
- Patients with a history of having received antibiotics within two weeks prior to culture,
- Patients who were on continuous indwelling catheter,
- Gestational Diabetes Mellitus and Menstruating women.

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- Patients who did not give informed consent for the study.

Methodology

All patients who were known cases of DM and were on treatment and/or had a Fasting Blood Glucose (FBG) ≥ 126 mg/dL, or a 2 hour Postprandial Glucose ≥ 200 mg/dL, or a HbA1C value ≥ 6.5% were eligible for the present study. A total of 100 consecutive adult in-patients of DM, as per the inclusion and exclusion criteria, were included in the study. A detailed history was taken and a detailed examination of all systems was done.

Mid stream urine was collected by clean catch technique, in the overwhelming majority, and the urine sample was obtained by puncturing the Foley's catheter with a needle in a very small proportion of patients, who had to be catheterized during the course of their illness. Urine samples were sent to the laboratory immediately for routine evaluation and for culture and antibiotic sensitivity.

Other investigations included CBC, FBG 2hour PG, HbA1C and USG abdomen for evaluating urinary tract.

HbA1C values, in particular, were used as a measure of the glycemic control. A value of ≤8.5% was taken as good (or intermediate) control and a value >8.5% was taken as poor control (As per American Diabetes Association recommendations, 2015).

STATISTICAL ANALYSIS

Data was analysed using IBM SPSS software version 20. Chi-square test / Fisher's exact test was used to determine significance of the study parameters. *P* value <0.05 was considered to be statistically significant.

RESULTS

Throughout this study "good control" stands for "good or intermediate glycemic control" and "poor control" stands for "poor glycemic control".

Out of the 100 patients selected for this study, 57% had good control and 43% had poor control of their DM with no significant discordance among the sexes (*P* = 0.7). Also,

Sex	Male		Female	
	No.	%	No.	%
Good control	26	59	31	55
Poor control	18	41	25	45
Total	44	100	56	100

Table-1: Sex distribution and Glycemic control

Duration in years	< 1 year		1-10 years		> 10 years		Total
	No.	%	No.	%	No.	%	
Good control	11	52.3	38	61.2	8	47	57
Poor control	10	47.7	24	38.8	9	53	43
Total	21	100	62	100	17	100	100

Table-2: Duration of Diabetes Mellitus

Treatment taken	Insulin therapy		OHA		No treatment	
	No.	%	No.	%	No.	%
Good control	5	26.3	47	68.1	5	41.6
Poor control	14	73.7	22	31.9	7	58.4
Total	19	100	69	100	12	100

Table-3: Treatment taken for Diabetes Mellitus

Treatment	Good control (n = 57)		Poor control (n = 43)		P
	No.	%	No.	%	
Adherence to treatment	49	85.9	9	20.9	<0.001
Follow-up	41	71.9	7	16.3	<0.001

Table-4: Adherence to treatment and follow-up

Symptom	Good control		Poor control		Total
	No.	%	No.	%	
Asymptomatic	8	66.7	4	33.3	12
Fever	34	58.6	24	41.4	58
Dysuria	32	51.6	30	48.4	62
Frequency	24	52.1	22	47.9	46
Urgency	18	54.5	15	45.5	33
Hematuria	2	33.3	4	66.7	6
Pyuria	9	45	11	55	20
Suprapubic pain	25	50	25	50	50
Flank pain	8	42.1	11	57.9	19
Incontinence	3	20	12	80	15

Table-5: Symptoms of UTI

Sex	Good control		Poor control		Total
	No.	%	No.	%	
Male	1	25	3	75	4
Female	7	87.5	1	12.5	8

Table-6: Asymptomatic bacteriuria

Examination	Good control		Poor control		Total
	No.	%	No.	%	
Suprapubic tenderness	36	63.1	26	60.4	62
Renal angle tenderness	4	7	10	23	14
Normal	17	29.9	7	16.6	24
Total	57	100	43	100	100

Table-7: Evaluation of tenderness

Urine pus cells	Good control		Poor control	
	No.	%	No.	%
< 11	4	7	2	4.6
11-100	46	80.7	33	76.7
>100	7	12.3	8	18.7
Total	57	100	43	100

Table-8: Pus cells in urine

Organism	Good control		Poor control		Total
	No.	%	No.	%	
E. coli	40	70.2	30	69.8	70
Klebsiella	3	5.3	3	7	6
Enterococcus	0	0	6	14	6
Coagulase negative Staphylococcus	2	3.5	2	4.7	4
Proteus	2	3.5	1	2.3	3
Pseudomonas	2	3.5	1	2.3	3
Staphylococcus aureus	2	3.5	0	0	2
Streptococcus	2	3.5	0	0	2
Candida	4	7	0	0	4
Total	57	100	43	100	100

Table-9: Organism isolated in Urine Culture

Organism (Numbers)	Ampi-cillin	Amoxy-cillin	Ceftria-xone	FQs	Amino-glycosides	Nitro- furantoin
E. coli (70)	14(20%)	24 (34%)	47 (67%)	20(28%)	51 (72%)	48 (68%)
Other GNBs (12)	3 (25%)	6 (50%)	7 (58%)	9 (75%)	10 (83%)	6 (50%)
GPCs (14)	4 (28%)	10 (72%)	6 (42%)	7 (50%)		14 (100%)

Table-10: Antibiotic sensitivity of various organisms isolated

10% of patients had Type 1 DM and 90% had Type 2 DM (table-1).

It was observed that patients with duration < 1 year (Newly diagnosed cases) and those with duration > 10 years (Long standing cases) had poorer control (47.7% and 53% respectively) than those who had duration of DM between 1-10 years (only 38.8%). ($P = 0.51$) (table-2).

Of the 100 patients, 19 were on Insulin therapy, 69 were on OHAs and12 were not on any drugs. Most of the patients on OHAs (68.1%) were found to have Good control, but much lesser number of patients on Insulin (26.3%) were having Good control ($P = 0.002$) (table-3).

88% of the patients had symptomatic UTI. 15% of the patients had Urinary incontinence, and this was found to be much more common in patients with poor control ($P = 0.001$). No significant statistical difference was seen between the groups for all the other symptoms (table-4,5).

12% of the patients had ASB: 8 Females and 4 Males ($P = 0.42$). Also, 8 of the patients had Good control, whereas 4 had Poor control (table-6).

During examination of the patients, 62% and 14% had suprapubic and renal angle tenderness respectively. Renal angle tenderness was seen more often in the poor control group ($P = 0.03$) (table-7).

94% of the patients had pyuria, and 15% had gross pyuria ($P = 0.6$) (table-8).

8 different bacterial species were isolated. Candida was also isolated in 4 of the patients. *E.coli* was the most common pathogen seen with 70% of the cases isolating it (table-9).

Antibiotic susceptibility testing showed that *E.coli* and other

GNBs were maximally susceptible to Aminoglycosides (72% and 83%). Among GPCs, susceptibility to Nitrofurantoin was 100% and to Amoxycillin was 72%. Uniformly, resistance to Ampicillin was high among all isolates (table-10).

DISCUSSION

It is a well known fact that UTI is much more common in DM than in general population. However, the role of glycemic control in UTI and its complications is not very clear.

In our study comprising of 100 consecutive patients with culture positive UTI and DM, females were more in number than males. The greater incidence of UTI in females is recognised universally. While the study on diabetic UTI in India by Abdulla MC et al.[7] had documented 64.9% females and 35.1% males and Aswani SM et al.[8] had documented 54.2% females and 45.8% males, studies outside India too have documented this greater incidence (Geerlings SE et al.[9], Boyko EJ et al.[10]). Our study too had a similar sex distribution with 56% females and 44% males.

Most of the studies on UTI in DM has been on T2DM alone. In our study 10% of the patients had Type 1DM and 90% had Type 2DM. Glycemic control was poorer in patients of Type 1DM (70%) than Type 2 DM(40%). LMAJ Muller et al. (2005)[1] had found a similar distribution of types of DM in UTI with T1DM in 12.5% and T2DM in 87.5% patients.

In our study, 21% of the patients had newly or recently diagnosed DM, 62% had DM between 1 to 10 years, and 17% had long standing DM of longer than 10 years duration. The glycemic control was better in the middle group (61.2%) compared to the group with new/recent DM (52.3%), which in turn, was better than group with long standing DM (47%). The probable reason for this seems to be higher HbA1C in undiagnosed diabetics and inadequate OHA dose titration in recently diagnosed cases, and the rising insulin requirements and worsening insulin resistance in the older population. Patients with duration of DM between 1- 10 years seem to have been titrated to adequate dosing of drugs and also seem to be better educated about need for adherence to treatment and follow-up. Aswani SM et al.[8] has found a similar distribution with majority of patients in the middle duration group (60%). While Boyko et al.[11] concluded that the risk of UTI was not related to the duration of DM, Janifer J et al.[12] had found association between longer duration of DM and UTI.

In our study, 19 were on Insulin therapy, 69 were on OHAs and12 were not on any drugs. Patients receiving OHAs had better glycemic control than the patients on insulin. While 68.1% of patients on OHAs had a good control, only 26.3% of the patients on insulin had good control (p = 0.002). A study by Joshi SR et al.[13] in diabetic subjects of Madhya Pradesh found that 72% had suboptimal glycemic control; Further, 95% were on OHAs, 3% were on insulin and 2% patients took both OHAs and insulin. Cramer et al.[14] had shown that adults on insulin therapy averaged only 77% of prescribed doses, and had poorer glycemic control. Al-Rasheedi AA[15] too found poorer glycemic control among patients with combined OHAs and insulin than OHAs alone. Factors for poorer glycemic control in patients on insulin include, poor compliance and adherence to insulin (due to cost, technique and lower educational status) and the advanced state of DM in these patients which necessitated insulin therapy in the first place. All these factors are valid in our study too due to the lower educational and socioeconomic status in general in our study population.

Helgeson VS et al.[16] and García-Pérez L-E et al.[17] have shown inverse relation between rising adherence to treatment and poor glycemic control in DM, as might be expected. In our study too, patients who did not adhere to treatment had poor glycemic control (80.9%, $P < 0.001$). Similar overwhelming evidence was there in our study for poorer glycemic control in patients with poor follow-up (69.2%, $P < 0.001$).

Symptoms of UTI most commonly seen were dysuria (57.4%), fever(41.4%) and frequency(23.7%) in a study by Aswani SM et al.[8] Our study concurred with these - Dyuria (62%), fever (58%) and frequency (46%) were the commonest symptoms in our study also. Incontinence was seen much more commonly in patients who had poor glycemic control. (P =0.001). A study by Jackson SL et al[18], concluded that women with DM (as compared to men) and those with complications like peripheral neuropathy, and retinopathy were significantly associated with severe incontinence (P = 0.01–0.06)

The prevalence of asymptomatic bacteriuria (ASB) in diabetic patients varies from 9-27% in various studies. Meta-analysis of studies since 1966 by Renko M et al.[19] has shown a prevalence of 14.2% and 2.3% in diabetic women and men respectively. ASB was seen in 12% of the UTIs in the present study which is comparable to those of other studies. ASB was seen more in females (66.7%) than males (33.3%) but was not significant (p = 0.42). While studies by Bonadio M et al.[20], Geerlings SE et al.[21], and Sotiropoulos A et al.[22] found increased incidence of ASB in poorer glycemic control, Renko M et al.[19], and Boyko et al.[11] failed to show any relation between them. In our study too, rates of ASB did not vary significantly with glycemic control.

Tenderness on abdominal examination was found more in group with poor glycemic control (83.4%) than in group with good glycemic control (70.1%) [P = 0.03]. Reasons may be due to the greater prevalence of severe cystitis and pyelonephritis in the poor glycemic control group.

Pyuria was seen in 94% of the patients with gross pyuria occuring more often in the group with poor glycemic control. In concordance with other studies, including Geerlings SE et al.[23], Aswani SM et al.[8], Janifer J. et al[12], and Goswami R et al.[5], *E.coli* was the commonest organism encountered with isolation in 70% of the urine culture specimens, followed by *Klebsiella* and *Enterococcus* (6% each). *Candida* was isolated in 4% of the specimens. Glycemic control and gender had no role to play in the bacteria isolated.

Antibiotic sensitivity showed maximal overall susceptibility to Nitrofurantoin (68% of all pathogens), followed by Amikacin (61%) and Ceftriaxone (60%). In studies by Aswani et al.[8] and Janifer J et al.[12], maximal susceptibility was noted to Cefaperazone/Sulbactam, Piperacillin/ Tazobactam and Meropenem and maximum resistance was

to Ampicillin. In our study too, maximal antibiotic resistance was noted against Ampicillin (79% of the pathogens were resistant), followed by Ciprofloxacin (64% resistance) and Amoxycillin (60% resistance).

CONCLUSION

There is increased risk of Urinary Tract infection in the Diabetic population. In this study, Urinary Tract infection was seen more often in females than in males. Glycemic control in UTI patients was seen to be better in those whose drug dosages had been titrated over time and those who had been educated about need for adherence to treatment and follow-up.

As in the general population, clinical presentation most often included symptoms like dysuria, fever and frequency of micturition and signs like suprapubic tenderness. Urinary incontinence and renal angle tenderness were associated with poor glycemic control.

Pyuria is a good indicator of urinary tract infection and had no relation to glycemic control. *E.coli* was the most common organism isolated and the majority of the infections were by Gram negative bacilli. *Enterococcus* was commonest among Gram positive cocci. Nitrofurantoin, Amikacin and Ceftriaxone were good candidates for empirical treatment, while Ampicillin and Ciprofloxacin should probably be avoided till culture sensitivity results were available.

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