

Original Research Article

A clinical and microbiological study of urinary tract infections in diabetes mellitusMavuluri Chaitanya ¹, Atluri Pavan Rajesh ², Kota Lakshmi Narayana ³, Kamal Kiran ⁴¹Assistant Professor, Department of Family Medicine, NRI Medical College/General Hospital, Chinakakani, Guntur, AP, India²Final Year Post Graduate, Department of Family Medicine, NRI Medical College/General Hospital, Chinakakani, Guntur, AP, India³Professor &HOD, Department of Family Medicine, NRI Medical College/General Hospital, Chinakakani, Guntur, AP, India⁴Senior Consultant Nephrologist, Department of Nephrology, Kamineni Hospitals, LB Nagar, Telangana, India.

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Abstract

Aim & Objective: To study clinical and microbiological profile of urinary tract infections and also to determine antibiotic sensitivity pattern for isolated organisms in patients with diabetes mellitus. **Methodology:** It was a prospective and observational study. The present study to be conducted on diabetic patients who had pus cells of more than 10 per high power field on complete urine examination who attending general medicine OPD or admitted as in patients in Kamineni hospitals, LB Nagar, Hyderabad. **Results:** In our study prevalence of culture positive urinary tract infection is 44%. In our study there is higher prevalence of culture positive UTI in females (46%) compared to male patients (44%). In our study age of the patient did not show any association with culture positive UTI. In our study we found that symptoms urgency, frequency, supra pubic pain had significant association with culture positive urinary tract infection. In present study there is no association of culture positive UTI with type of diabetes, duration of diabetes and treatment modality for diabetes. Elevated HbA1c correlates with occurrence of UTI and the predisposition of the diabetic to UTI depends on the degree of glycemic control over a period of weeks to months. Achieving an HbA1c <7.0 percent appears to protect those diabetics who do not have other underlying predisposing factors for UTI. An HbA1c >8.0 percent in patients with diabetes mellitus increase the chance of developing UTI. Leucocytosis, anemia was observed significantly in the culture positive group. **Conclusion:** In present study there is no association of culture positive UTI with type of diabetes, duration of diabetes and treatment modality for diabetes

Keywords: Diabetes, UTI, Leucocytosis, Culture positive, Microbiological profile.

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Introduction

Diabetes mellitus is leading cause Of death and disability worldwide. [1;2] Its global prevalence was about 8% in 2011 and is predicted to rise to 10% by 2030. [3] Infections are of particular concern for diabetic patients. Diabetes can slow down the body's ability to fight infections by weakening the immune system. People with diabetes are especially prone to foot infections, yeast infections, surgical site infections and urinary tract infections. Studies have shown that diabetes experience worst outcomes with infections. Though hospitalized patients do not have a high mortality rate they do face longer hospitalization and recovery time. [4-6] Urinary tract infections (UTI) are the second most common infectious complaint in outpatient primary care clinics. By definition it means a bacterial/nonbacterial invasion of the urinary tract that can occur anywhere between the urethra and the kidney. UTI are common in young children and sexually active women. UTIs can be divided anatomically into upper and lower tract infections. [7]

It has been estimated that UTI account for 7 million hospital visits per year with 1 million visits to the emergency department⁷. Urine is a good culture medium for the growth of bacteria By far the most common mechanism by which bacteria enter the urinary tract is by ascending from the peri urethral area. It is hypothesized that women are more prone to UTI than men because their urethra is shorter and is in close proximity to the anus. An uncomplicated

UTI is generally defined as one occurring in a healthy, young, non pregnant women. Complicated UTIs are those associated with bladder or that are secondary to anatomic or functional abnormalities that impair urinary tract drainage. Most complicated UTIs are nosocomial in origin. [8]

Diabetes affects many systems that protect against infection in general and against urinary tract infection specifically. Poor circulation in diabetes, reduced ability of white blood cells to fight infection, dysfunctional bladder that contract poorly all contribute to increased prevalence of UTI in diabetics. [9] Asymptomatic bladder infections detected by a positive urine culture are also common among diabetics without any clinical evidence of UTI.

Empirical antibiotic therapy is usually applied in UTI as it is one of the most common infection and for this, knowledge of the common uropathogens and their susceptibility to commonly used antibiotics is needed. Treatment becomes even more challenging in the presence of risk factors such as higher age, comorbidity, and immunosuppression. Various studies done worldwide have shown changing patterns in the etiology of UTIs. [10] However, studies on UTI and the pattern of antibiotic resistance in India are few. [11] The present trends of the uropathogens and their susceptibility to various antibiotics are essential to formulate guidelines for the empirical treatment of UTIs while awaiting the culture sensitivity. This present study is in endeavour to assess the prevalence, risk factors associated with, microorganisms associated with and their antimicrobial sensitivity pattern in diabetics with urinary tract infections in a South Indian tertiary hospital setup.

Aims and objectives

1. To study clinical and microbiological profile of urinary tract infections in patients with diabetes mellitus.

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2. To determine antibiotic sensitivity pattern for isolated organisms.

Materials and Methods

Study Group

The present study to be conducted on diabetic patients who had pus cells of more than 10 per high power field on complete urine examination who attending general medicine OPD or admitted as in patients in Kamineni hospitals, LB nagar, Hyderabad.

Study Period

December 2012 — September 2014

STUDY DESIGN

Prospective, Observational study

Data Analysis

Statistical analysis was performed using Medcalc software version 14.12.0. The statistical significance of relationship between variables under study and outcome was determined using Fisher's exact test, Chi square test. To determine effect of variables under study on outcome, Multivariate analysis using Logistic regression model was done. $P < 0.05$ was considered to be statistically significant.

Inclusion Criteria

Diabetic patients who had history of diabetes or with fasting venous blood glucose value equal, or more than 126mg/dl and post prandial blood sugar more than or equal to 200mg/dl or glycated hemoglobin more than or equal to 6.5%. And with pus cells of more than 10 per high power field in complete urine examination with or without clinical features of urinary tract infection were included in the study.

Both Type I and Type II diabetics were included in the study. Irrespective of their sex, duration of diabetes, treatment taken, adherence to treatment, all patients above age of 20 years were included in the study.

Exclusion Criteria

- Patients who received antibiotics within two weeks prior to urine culture

- Patients on continuous indwelling urine catheter
- Patients with other diagnosed renal diseases such as anatomical renal defects (horse shoe kidney, duplicated ureters etc.), renal calculi, and cystic renal diseases are excluded.

Methods

All the patients included in the study group underwent a complete clinical and laboratory evaluation.

The clinical evaluation consisted of:

1. A detailed history was taken after taking consent from the patient, with special reference to duration of diabetes, type, treatment taken and adherence
2. History in relation to Urinary tract infection like burning micturition, frequency, urgency, dysuria, suprapubic pain, hematuria and fever were noted.
3. Past history of urinary tract instrumentation or catheterization were also asked.
4. A detailed examination of all systems with special emphasis on suprapubic tenderness, costovertebral angle tenderness and tenderness/mass on deep abdominal palpation were carried out.

The laboratory evaluation consisted of:

1. Complete urinary examination (CUE)
2. Urine culture
3. Glycated hemoglobin (HbA1c) fasting blood sugar (FBS), Post prandial Blood sugar (PLBS)
4. Serum creatinine
5. USG abdomen for evaluating urinary tract
6. Complete blood picture (CBP)

Ethics committee approval

Ethics committee of our institution has reviewed the protocol and approved the study. Informed consent was taken from all the patients in the study group.

Results

The present study was conducted on 257 subjects with diabetes mellitus with evidence of pus cells more than 10 per high power field in complete urine examination attending general medicine OPD or admitted as in patients in Kamineni hospitals, L.B nagar, Hyderabad.

Throughout the study 'culture positive' means growth of organism after 24 hrs of culture with a colony count $> 10^5$ cfu/ml. And the term 'culture negative' means urine culture showing no growth or colony count with $< 10^5$ cfu/ml.

Table 1: Frequencies of culture positive and culture negative

Cases	Frequency	Percent
Culture Positive	114	44%
Culture Negative	143	56%
Total	257	100%

Out of 257 subjects 114 (44%) subjects were culture positive and 143 (56%) subjects were culture negative.

Gender Distribution

Table 2: Gender distribution

Gender	Culture Positive	Culture Negative	P = 0.8
Males (n=147)	64(44%)	83(56%)	
Females (n=110)	50(46%)	60(54%)	

In our study group out of 147 male patients 64 (44%) were culture positive 83 (56%) were culture negative. Amongst 110 female patients 50 (46%) were culture positive and 60 (54%) were culture negative. There is increased prevalence of culture positive UTI in female patients compared to male patients. However the association is not statistically significant ($p=0.8$, chi square-0.03).

Age Distribution

Table 3: Age Distribution

Age (years)	Culture Positive (n=114)	Culture Negative (n=143)	P = 0.8
21-40	1(1%)	4(3%)	
41-60	46(40%)	59(41%)	
61-80	58(51%)	68(48%)	
81-100	9(8%)	12(8%)	

Mean Age	63.08±10.9	62.75±12.56	
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Chi square for trend

The maximum number of patients in culture positive group belonged to 61-80 years age group (51%) followed by 41-60 years age group (40%), 81-100 years age group (8%) and 21-40 years age group (1%). The mean age of culture positive group was 63.08±10.9 years and mean age of culture negative group was 62.75±12.56 years.

There was no significant difference between age groups between culture positive and culture negative groups.

Type of Diabetes

Table 4: Type of DM

Type of DM	Culture Positive	Culture Negative	Total	P = 0.7
Type 1 (n=9)	3(3%)	6(4%)	9	
Type 2(n=248)	111(97%)	137(96%)	248	

In our study group out of 257 subjects 9(4%) patients were Type 1 diabetes and 248(96%) patients were Type 2 diabetes. There was no statistically significant (p=0.7) association between type of diabetes and culture positive and culture negative group.

Duration of Diabetes

Table 5: Duration of DM

Duration of DM in years	CulturePositive	CultureNegative	P = 0.7
<1 yr	9(8%)	12(8%)	
1-5 yrs	37(32%)	47(33%)	
6-10yrs	41(36%)	53(37%)	
11-15 yrs	15(13%)	20(14%)	
<15 yr	12(11%)	11(8%)	

The maximum number of culture positive patients had diabetes for duration of 6-10 years (36%). The mean duration of diabetes in culture positive group is 7.92±5.92 years and culture negative group is 7.76±6.33 years. There was no statistically significant difference in relation to duration of diabetes and urine culture result with p value=0.7.

Treatment Modality For Diabetes

Table 6: Treatment modality for diabetes mellitus

Type of DM	Culture Negative(n=143)	Culture Positive (n=114)	Total	P = 0.9
Insulin(%)	50(38%)	43(38%)	93	
Oral(%)	60(45%)	49(43%)	109	
Both(%)	20(15%)	19(17%)	39	
No treatment(%)	3(2%)	3(2%)	6	

The maximum number of patients in culture positive group were on oral hypoglycemic medications (45%) followed by insulin (38%). Patients receiving both oral hypoglycemic medications and insulin constituted 15% of the population and those not receiving medical management constituted 2% of the study population, there is no significant difference with regards to type of treatment they are receiving among culture positive and culture negative groups.

Symptoms and Signs of Urinary Tract Infection

Table 7: Symptoms of urinary tract infection

Presentation	Culture Positive(n=114)	Culture Negative(n=143)	P Value
Asymptomatic	26(8%)	46(14%)	
Fever	69(21%)	79(25%)	0.3
Dysuria	42(13%)	44(14%)	0.3
Frequency	65(20%)	55(17%)	0.02
Urgency	67(20%)	48(15%)	<0.0001
Super Pubic Pain	52(16%)	42(13%)	0.004
Flank Pain	7(2%)	8(2%)	0.4

In our study group, out of 114 culture positive patients most common complaint was fever (21%) followed by urgency (20%), increased frequency of urination (20%), supra pubic pain (16%), dysuria (13%) and flank pain (2%). The symptoms urgency (p<0.0001), frequency (p=0.002), supra pubic pain (P=0.004) showed significant positive association with culture positive patients

Evaluation of Tenderness

Table 8: Evaluation of tenderness

Examination	Culture Positive	Culture Negative	P Value
Supra Pubic Tenderness(n=105)	60(57%)	45(43%)	0.0006
Renal angle Tenderness (n=14)	7(50%)	7(50%)	0.66

Out of 105 patients who had supra pubic tenderness on examination 60 patients (57%) were culture positive and 45 patients were culture negative. There is statistically significant correlation between supra pubic tenderness and culture positivity ($p=0.004$).

Asymptomatic Bacteriuria

Table 9: Asymptomatic bacteriuria

Gender	Symptomatic	Asymptomatic	P Value
Men (n=64)	47(73%)	17(26%)	0.3
Women (n=50)	41(82%)	9(18%)	

In present study out of 114 cultures positive patients 26 (8%) patients are asymptomatic. Out of 50 culture positive females 9 (18%) are symptomatic and among 64 culture positive males 17 (26%) are symptomatic. There is no significant association between asymptomatic bacteriuria in relation to gender.

Blood Investigations

Glycated Hemoglobin (HbA1c)

Table 10: Evaluation of HbA1c

HbA1C(%)	Culture Positive(n=114)	Culture Negative(n=143)	P Value
<7	1(1%)	53(37%)	<0.0001
>7	113(99%)	90(63%)	
Mean	8.18±1.09	7.47±1.17	

The evaluation of HbA1c among culture positive and culture negative group showed that maximum number of patients (99%) in culture positive group had HbA1c >7%. There is statistically significant correlation between HbA1c and culture positive

patients ($p<0.0001$). Mean HbA1c of culture positive group was 8.18±1.09 and mean HbA1c of culture negative group was 7.47±1.17.

Total Leucocyte Count

Total leucocyte count: Leucocytosis (>11,000 cells/cumm) was present in 70 patients (61%) of culture positive group and 48 patients (34%) of culture negative group. There is statistically significant correlation between leucocytosis and culture positive group ($p=0.002$).

HEMOGLOBIN (Hb): Anemia according to present study is defined as Hb less than 12 g/dl. Accordingly 82 patients (72%) in culture positive group had anemia and 80 patients (56%) in culture negative group had anemia there is statistically significant correlation between anemia and culture positivity ($p=0.02$).

Urine Culture

Table 11: Organisms isolated

Organism	Number	Percentage
E.coli	79	69%
Klesiella	18	16%
Pseudomonas	12	10%
Proteus	3	3%
E.fecalis	1	1%
Citobacter	1	1%

In our study most common organism isolated in urine culture is E.coli (69%) followed by Klesiella (16%), Pseudomonas (10%), Proteus (3%), E.fecalis (1%) and Citobacter(1%).

Antibiotic Sensitivity Pattern

Table 12: Antibiotic sensitivity pattern to isolated organisms

Antibiotics tested	E.coli(n=79)sensitivity	Klebsiella(n=18)sensitivity	Pseudomonas(n=12)sensitivity	Proteus(n=3)sensitivity	E.fecalis(n=1)sensitivity	Citobacter(n=1)sensitivity
Nitrofurantoin	55(69%)	2(11%)	0	0	1(100%)	1(100%)
Amikacin	61(77%)	10(83%)	3(25%)	2(66%)	0	0
Co-trimoxazole	29(36%)	4(22%)	0	1(33%)	0	0
Ciprofloxacin	16(20%)	5(27%)	5(41%)	1(33%)	0	0
Ofloxacin	17(21%)	5(27%)	4(33%)	1(33%)	0	0
Norfloxacin	14(17%)	2(11%)	3(25%)	1(33%)	0	0

Cefotaxime	9(11%)	1(5%)	1(8%)	1(33%)	0	0
Ceftriaxone	6(7%)	2(11%)	0	0	0	0
Cefoperazone+sulbactam	52(65%)	9(50%)	3(25%)	2(66%)	0	0
Piperacillin+tazobactam	51(64%)	9(50%)	5(41%)	2(66%)	0	0
Imepenem	69(87%)	13(72%)	5(41%)	2(66%)	0	1
Meropenem	61(77%)	13(72%)	5(41%)	2(66%)	0	1
Ertapenem	36(45%)	4(22%)	1(8%)	0	0	0
Gentamicin	1(1%)	2(11%)	2(16%)	1(33%)	0	0
Colistin	2(2%)	6(33%)	7(58%)	0	0	0
Polymixin	2(2%)	6(33%)	7(58%)	0	0	0

Maximum number of E.coli isolates were found to be sensitive to imepenem (87%) followed by meropenem(77%), amikacin(77%) , nitrofurantoin(69%), cefoperazone+sulbactam(65%), piperacillin+tazobactam(64%).

E.coli-showed less sensitivity To of loxacin (21%), norfloxacin (17%), ciprofloxacin(20%), cefotaxime (11%), ceftriaxone(7%). Klebsiella isolates were found to be maximally sensitive to amikacin with 83% of growth cultures showing in vitro sensitivity. Imepenem and meropenem were found to be sensitive in 72% of Klebsiella isolates. Piperacillin-tazobactam and cefoperazone-sulbactam showed sensitivity in 42% of Pseudomonas isolates.

Discussion

The aim of the present study is to study the clinical and microbiological profile of urinary tract infections in diabetes mellitus and to determine the antibiotic sensitivity pattern for isolated organisms

Prevalence

In the present study out of 257 patients studied 114 patients (44%) were culture positive. This result was comparable with the study done by Saber M et al. [12] with prevalence of culture positive UTI to be 45.6% between age group of 20-60 yrs and prevalence of culture positive UTI above age of 60 years was 42.1%. The study done by Visvanathan V et al [13] found similar prevalence (42.8%) of culture positive UTI.

The study done by Saleem M et al [14] found slightly higher prevalence of urinary tract infection compared to our study. They found prevalence of about 56.4% in diabetic patients belonging to lower socioeconomic status and prevalence of 51.6% in the diabetic patients belonging to higher socio economic status.

Sex Distribution

In the present study out of 110 female patients studied 50 (46%) had culture positive urinary tract infection and out of 147 male patients studied 64 (44%) had culture positive urinary tract infection.

There is female predilection of urinary tract infection in our study this is in concordance with previous studies by Visvanathan V et al, [13] Baloch GH et al, [14] who found higher prevalence of urinary tract infection in female diabetics compared to male diabetic patients. However the association is not statistically significant. [15]

Age Distribution

In our study the mean age of culture positive group was 63.08±10.9 years and mean age of culture negative group was 62.75±12.56 years. There is no significant correlation between age of the patient and incidence of culture positive urinary tract infection in our study. Aswani SM et al [16] and BonadioM et al [21] also made similar observation in their study.

Type of Diabetes

There is no significant difference in the prevalence of urinary tract infection in relation to type of diabetes (1 or 2) this was in concordance with the studies done by Milford H et al [17], C. R. Cardwell⁹¹ et al and D M Fleming. [18]

Duration of Diabetes

In our study mean duration of diabetes in culture positive group is 7.92±5.92 years and culture negative group is 7.76±6.33 years.

There is no significant correlation between duration of diabetes and prevalence of urinary tract infection. Similar observation was made by Aswani SM et al [16]

Visvanathan V et al [13] in their study found increased prevalence of urinary tract infection with increased duration of diabetes. This is probably due to higher prevalence of diabetic neuropathy and subsequent incomplete bladder emptying in long standing diabetes. However no such association was observed in our study.

Treatment Received For Diabetes

In the present study there is no significant association between the incidence of culture positive urinary tract infection with type of treatment received for diabetes. This was in concordance with the study done by Aswani SM et al. [16]

Syptoms and Signs of Urinary Tract Infection

In the present study, fever (21%) was the most common clinical presentation followed by urgency (20%), frequency (20%), supra pubic pain (16%) and dysuria (13%). This was in contrast with a previous study done by Aswani SM et al [16] where the common clinical presentation was fever (57.4%) followed by dysuria (41.4%). In present study there is positive association between lower urinary tract symptoms such as urgency (p<0.0001), frequency (p=0.002), supra pubic pain (p=0.004) and prevalence of urinary tract infection.

In our study evaluation of supra pubic tenderness showed statistically significant association (p=0.004) with prevalence of culture positive urinary tract infections.

Asymptomatic Bacteruria

In the present study, prevalence of asymptomatic bacteruria was 8%. A similar prevalence was observed in a study done by Chitā T et al [19] (8.4%). Among the culture positive females (n=50) 9 (18%) were asymptomatic and among the culture positive males (n=64) 17 (26%) were asymptomatic. This observation is in contrast with previous studies done by Chitā T et al [19] where prevalence of asymptomatic bacteruria is higher in females (12.2%) than in men (3.2%).The study done by Greerlings SE et al [20] found higher prevalence of asymptomatic bacteruria in diabetic woman (26%) compared to non-diabetic woman (6%).

Glycemic Control

In the present study 91% of patients had HbA1c (>7% and 8% of patients had HbA1c > 10%.Mean glycated hemoglobin was 8.18±1.09 in culture positive group and mean glycated hemoglobin in culture negative group was 7.47±1.17. This showed statistically significant positive association (p<0.0001) (OR-1.60) with prevalence of urinary tract infection. The previous studies

done by Arul prakasam K.C. et al, Viswanathan V et al [13] showed increased prevalence of urinary tract infection with poor glycemic control. Bonadio M et al [21] found mean HbA1c to be 7.8 ± 1.6 SD in patients with urinary tract infection. Tseng CC et al [22] noted that a HbA1c >8.1% was associated with an increased risk of urinary tract infection and the presence of HbA1c <6.5% significantly ($p=0.026$) decreased the risk of urinary tract infection irrespective of whether there was underlying predisposing factors or not.

Anemia and Leucocytosis

The prevalence of anemia was significantly higher in the culture positive group ($p=0.02$). Leucocytes count was significantly higher in the culture positive group ($p=0.002$). Huvos et al [23] had also noticed leucocytosis in 8% of culture positive patients in his study.

Prevalence of Isolated Organisms

In the present study the most common organism isolated was E.coli (69%) followed by Klebsiella (16%), Pseudomonas (10%), Proteus (3%), E.fecalis (1%), Citobacter (1%). This result is comparable with the previous studies. The study done by Viswanathan V et al [13] showed similar results E.coli (71%) is predominant organism isolated followed by Klebsiella (13.5%), pseudomonas(9%). In our study Klebsiella was the second common organism isolated where in some studies showed proteus and staphylococcus aureus as second common organism. The studies done by Baloch GH et al [15] showed isolation of E.coli (65%) followed by Proteus spp (13%) .

Antibiotic Sensitivity Pattern

In present study E.coli showed sensitivity to

- carbapenems (87%),
- amikacin (77%)
- nitrofurantoin (69%),
- cefoperazone+sulbactam (65%),
- piperacillin+tazobactam(64%).

This is correlating with previous studies done by Arul prakasam K.C et al [24] showed E.coli is more sensitive to carbapenems(93.8%) and Saber MH et al. [12] (2010) demonstrated that E.coli sensitivity to carbapenems was 100% in diabetics.

E.coli showed less sensitivity to commonly used

- Fluoroquinolones [ofloxacin(21%), norfloxacin(17%), ciprofloxacin(20%)]
- cephalosporins which include efotaxime(11%), ceftriaxone(7%) similar resistance pattern was found in previous studies Arul prakasam K.C et al, [97] Bonadio M et al. [21]

Conclusions

1. In present study there is no association of culture positive UTI with type of diabetes, duration of diabetes and treatment modality for diabetes
2. Elevated HbA1c correlates with occurrence of UTI and the predisposition of the diabetic to UTI depends on the degree of glycemic control over a period of weeks to months. Achieving an HbA1c <7.0 percent appears to protect those diabetics who do not have other underlying predisposing factors for UTI. An HbA1c >8.0 percent in patients with diabetes mellitus increase the chance of developing UTI.
3. Leucocytosis, anemia was observed significantly in the culture positive group.
4. E .coli was the commonest organism isolated in urine culture and Klebsiella was the second common organism isolated.
5. E.coli showed sensitivity to carbapenems, nitrofurantoin, amikacin followed cefoperazone/sulbactam, piperacillin/tazobactam.
6. E.coli showed less sensitivity to commonly used cephalosporins and fluoroquinolones.

Recommendations

1. Achieving good glycemic control in diabetic patients decreases the prevalence of urinary tract infections.
2. Diabetics should not be treated for urinary tract infection on the basis of leucocyturia and urine culture should be advised.
3. The pattern of bacterial resistance is constantly changing over years, it is important to monitor the antibiotic susceptibility patterns of isolated organisms to ensure rational use of antibiotics for empirical and definitive treatment of urinary tract infections in the patients with diabetes mellitus.

Limitations

1. Control group comprising of non diabetics was not included for the comparison
2. Samples at tertiary health care hospital are not representative of the whole population

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