

Clinico-Microbiological Profile of Urinary Tract Infections in Diabetic Patients in a Tertiary Centre in Kerala

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ABSTRACT

Published on 29th September 2016

Objectives: *Primary Objective:* To study the role of blood C-reactive protein in distinguishing upper & lower urinary tract infections in Diabetic Patients. *Secondary Objective:* (1) To study the clinical spectrum of urinary tract infections in Diabetic patients including common organisms involved in UTI in diabetic patients & their antibiotic sensitivity & resistance pattern. (2) To assess correlation between (a) duration of diabetes & UTI, (b) HbA1c values & UTI

Methods: A Cross sectional study was done on 73 cases of Diabetic patients with UTI at Amrita Institute of Medical Sciences, Edappally, Kochi from a period from December 2013 to January 2015. The subjects were included based on specific inclusion criteria. They were divided in 2 groups - Upper and Lower UTI. Detailed history and examination was done on all patients. CRP value was measured on presentation and compared among 2 groups. Along with that, the clinical spectrum, urine culture and antibiotic sensitivity of all the cases were studied. The correlation between duration of Diabetes with UTI and control of diabetes with UTI was also done.

Results: In our study we evaluated 73 cases of Diabetic patients with UTI at Amrita Institute of Medical Sciences, Edappally, Kochi for a period from December 2013 to January 2015. The patients were divided in 2 groups, upper and lower UTI. Demographically both groups were comparable in all aspects. CRP at the time of presentation in both the groups was compared. We found out that the mean CRP value in case of Diabetic upper UTI was 216.80mg/L which was very high compared to the mean CRP in lower UTI diabetics which was only 26.71mg/L, with a significant P value <0.0001. Also in our study clinical spectrum including symptoms was studied and it was found out that in case of upper UTI the predominant symptoms were fever and abdominal or flank pain followed by vomiting, while in case of lower UTI the predominant symptom were fever and dysuria. Also we studied the major organisms isolated in upper and lower UTI in diabetics and found that gram negative bacilli were the predominant isolate in both groups. Among gram negative bacilli, E coli (61% lower UTI and 68% in upper UTI) and Klebsiella (24 % in lower UTI and 16% in upper UTI) were the major organism isolated in both the groups. Also we studied the sensitivity and resistance pattern of the organisms isolated from both groups in our institution and found out very high resistance pattern to most of the commonly used first line medications for UTI such as fluoroquinolones, aminoglycosides and nitrofurantoin. As the secondary objective the correlation between duration of Diabetes and risk of getting upper and lower UTI was studied. The mean duration of Diabetes in lower UTI was 8.55yrs and mean duration of Diabetes in upper UTI was 11.47 yrs, but however P value was found to be insignificant (0.070). The correlation between control of diabetes and risk of getting upper and lower UTI was also studied by comparing the HbA1c levels and the mean HbA1c was 7.63 in lower UTI and in case of upper UTI the mean HbA1c was 9.40, showing significant statistical difference (p value <0.0001).

Conclusion: A cross sectional study was done at Amrita Institute of Medical Sciences, Edappally, Kochi in which 73 cases of Diabetic patients UTI were studied. The patients were included in the study according to the inclusion and exclusion criteria mentioned in the methodology. The Patients were divided into 2 groups - Upper and lower UTI. We found out that the CRP levels in Diabetic patients with upper UTI was significantly high compared to the lower UTI (p value <0.0001), suggesting that CRP can be used as an excellent bio-marker for distinguishing upper and lower UTI in diabetic individuals at the time of presentation itself along with clinical features. The clinical features of diabetic patients with UTI were the same as non-diabetic patients. Our study showed that gram negative bacilli were the predominant organism isolated in both the groups with E coli and Klebsiella being the predominant isolate among them. The culture sensitivity and resistance pattern showed that there was very high resistance pattern in the organisms isolated from patients when compared to any studies so far, suggesting antibiotics such as Piperacillin-Tazobactam or Cefoperazone sulbactam should be started empirically for treating Diabetic patients UTI. We also proved in our study that there was no relation between duration of Diabetes and risk of getting upper or lower UTI, but it was the control of Diabetes which was important, as patients with uncontrolled diabetes were more prone to upper UTI (p value < 0001).

Keywords: C Reactive Protein, Clinical Spectrum of UTI, Duration of Diabetes, HbA1c

*See End Note for complete author details

Cite this article as: Prabhu H, Oommen AT, Henry R. Clinico-Microbiological Profile of Urinary Tract Infections in Diabetic Patients in a Tertiary Centre in Kerala. Kerala Medical Journal. 2016 Sep 29;9(3):97-104.

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INTRODUCTION

Urinary tract infection (UTI) is defined as infection of any part of the urinary system – which includes kidneys, ureters, bladder and urethra. The term UTI encompasses a variety of clinical entities, including asymptomatic bacteriuria (ABU), cystitis, prostatitis, and pyelonephritis. It is the second most common infection in the world for which people attend primary health care after respiratory tract infections. It accounts to almost 7 million office visits, nearly 1 million emergency department visits and in 100,000 hospitalizations during a year. It is estimated that the annual cost of community acquired UTI is around \$ 1.6 billion. Diabetes represents a spectrum of metabolic disorders, characterized by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production. It is a pandemic in both developed and developing countries. In 2000, there were an estimated 175 million diabetes affected patients around the world and by 2030; the projected estimate of diabetes is 354 million. China tops the list of number of Diabetics with 90.0 million followed by India which has 61.3 million. In India it is expected to reach a massive 101.2 million in 2030. India is the diabetes capital of the world, according to Indian Heart Association. It has been shown that nearly 1 million Indians die due to Diabetes every year. The most serious complications associated with UTI or complicated UTI, such as emphysematous cystitis, pyelonephritis, renal abscesses and renal papillary necrosis, are all encountered more frequently in type 2 diabetes than in the general population. The complications and mortality rate of upper UTI is much more than lower UTI. Clinical failure is seen more in cases of upper UTI. So what we want is appropriate identification of UTI at the earliest and distinguishing into upper and lower UTI, so that appropriate treatment can be started. In our study done at Amrita Institute of Medical Sciences we tried to prove if there is a relationship between CRP values in upper & lower UTI so that it can be used along with clinical features to distinguish upper and lower UTI, thereby aggressive antibiotic coverage can be started for upper UTI which is a more dangerous condition compared to lower UTI, thus reducing the mortality and morbidity. CRP, which is easily available & takes less than 1 hr & is a less expensive test compared to USG or CT abdomen for which we require sophisticated machines & trained professionals –both of which are not always available. In our study we are also studied the common organisms involved in UTI in diabetic patients & their antibiotic resistance & sensitivity pattern. So that in

a tertiary centre like AIMS, knowing the resistance & sensitivity pattern helps in starting the treatment empirically. Urosepsis, a common cause of sepsis can be managed in a better way thereby reducing the mortality and morbidity.

MATERIALS AND METHODS

Study Design

A Prospective Cross Sectional Study was conducted at the Amrita Institute of Medical Sciences, Kochi, Kerala. The study was done on Diabetic patients with Urinary Tract Infection, who were evaluated both as out-patient and in-patient.

Setting

The study was done at 1200 Bedded Tertiary care Hospital, Amrita Institute of Medical Sciences, Edapally, Kochi, Kerala.

Study Patients

- Diabetic Patients with UTI who were evaluated in AIMS, Kochi from November 2013 to January 2015.
- *Inclusion criteria*
Diabetic patients
Symptoms/ signs/ proven case of UTI
Age group: 18yrs & above
Both males & female
- *Exclusion criteria*
Age < 18yrs
Urinary calculi
Catheterised patients
Congenital anomalies of urinary tract.
Any other foci of infection

Measurements

The following Measurements were done in all the patients who were included in the study purpose:

- Name:
- Age:
- Sex:
- MRD No:
- History:
- General Examination:
- Per abdomen examination:

- Per rectal examination:
- Other systems:
- CRP:
- Fasting blood sugar:
- HbA1C:
- Creatinine:
- Urine routine:
- Urine culture & sensitivity.
- USG abdomen:
- CT Abdomen (if required):

Study duration

- From November 2013 to January 2015 (table 1)

Statistical applications

To test the statistical significance of difference in the mean values of Blood C-reactive protein between upper & lower Urinary tract Infections – Student t test was used.

Sample Size

Based on the results on blood CRP in an earlier publication “Renal Bio-metry & C-reactive Protein in the evaluation of Urinary Tract Infections”¹¹⁴ and with 99% confidence & 99% power minimum sample size came to be 15 in both groups. A minimum of “15” in the upper UTI & “50” lower UTI was taken.

Costing

All the investigations are done routinely. No added special investigations.

Variable	Group 1 (54 cases)	Group 2 (19 cases)
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RESULTS

Based on the results of the Previous Study¹¹⁴ and with 99% confidence & 99% power a Minimum of 50 cases of Lower UTI and 15 cases of Upper UTI were needed for the Study based on the ratio 3:1.

In our study we took 73 Diabetic patients with UTI of which Upper UTI was 19 in number and 54 cases of Lower UTI. The sample size was constituted by Patients who were evaluated at Amrita Institute of Medical Sciences (AIMS), Edapally, Kochi both as out-patient and in-patient from November 2013 to January 2015. In the description part Lower UTI will be assigned as Group 1 and upper UTI as Group 2 (Group 1-Lower UTI and Group 2- Upper UTI).

Table 1. Main variables studied and compared between both the groups

	Mean	Standard Deviation	Median	Mean	Standard Deviation	Median	P- value
Age (yrs)	65.42	10.57	66.50 (62.54-68.31)	63.00	9.72	65.00 (58.31-67.68)	0.383
CRP (mg/L)	26.71	23.28	19.05 (20.35-33.07)	216.80	79.11	203.90 (178.67-254.93)	<0.0001
FBS (mg/dl)	117.00	28.42	111.00 (109.24-124.76)	158.63	45.33	147 (136.77-180.48)	<0.0001
Duration of Diabetes (yrs)	8.55	6.29	7.50 (6.83-10.27)	11.47	4.83	13.00 (9.14-13.80)	0.70
HBA1C (%)	7.63	1.80	7.00 (7.13-8.12)	10.29	2.76	9.40 (8.96-11.62)	<0.0001

To test the statistical significance of difference in Mean values of Age, FBS and HbA1c between the 2 groups Students t Test was done. And to determine the Statistical Difference of CRP and Duration of Diabetes between 2 groups Wilcoxn’s Rank-sum test was done, since the distribution of Values was not normal (figure 1)

Out of 73 cases taken in both Groups 49 were females and 24 were males. A total of 54 cases of Lower UTI were taken which included 38 females and 16 males. A total of 19 cases of Upper UTI were taken which included 11 females and 8 males. There was no significant Gender difference in both groups with P value 0.477. So both groups were comparable.

In case of Lower UTI the mean age was 65.42 yrs and in case of Upper UTI the mean age was 63.00 yrs. P value according to student’s t-test was 0.383 and was not significant. Therefore both the groups were comparable to each other with respect to age. (figure 2).

In case of Lower UTI the most common symptom was fever followed by dysuria. Almost 63.0 % of the cases

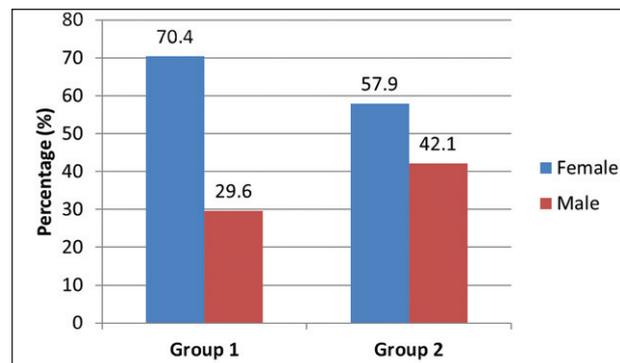


Figure 1. Gender distribution of cases in both groups

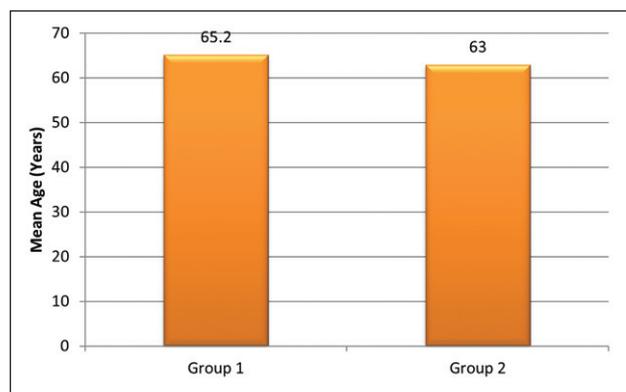


Figure 2. Age distribution

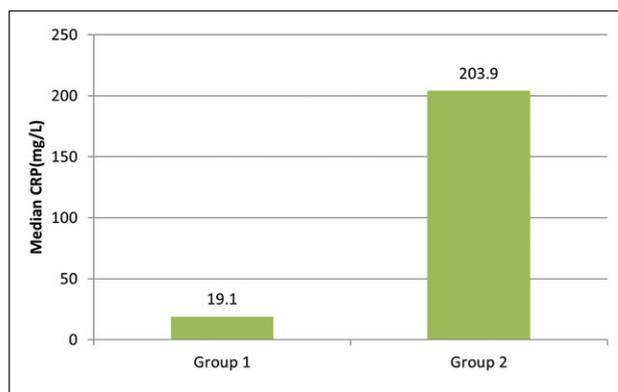


Figure 4. Comparison of CRP values in both groups

had fever and 42.5 % cases had dysuria. Only 25.9 % cases had vomiting with 14.8 % having pain abdomen or supra pubic pain. In case of Upper UTI the most common symptoms were fever and abdominal/Flank pain. Almost 90 % cases had fever and 73.7 % cases had flank pain. More than 50 % of the cases had vomiting. When common symptoms of both groups were compared those in the upper UTI had more fever, vomiting and flank Pain. In fact almost 90 % of cases of upper UTI has fever. Presence of Flank pain was present in almost 73.7 % of upper UTI cases (figure 3).

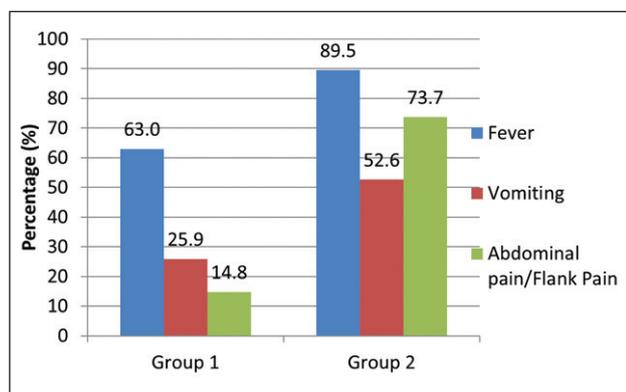


Figure 3. Symptom distributions in both groups

Comparison of the CRP was main variable in the study (figure 4). In case of Lower UTI the mean CRP value was 26.71 mg/L and in case of upper UTI the mean CRP was 216.80 mg/L. The statistical difference was done using Wilcoxon’s rank-sum test since the distribution of values was not within normal range. The median CRP Value was in Group 1 was 19.05 mg/L (20.35-33.07) and in group 2 it was 203.90mg/L (178.67-254.93). P- Value was found to be <0.0001 was very highly significant. In the graph below Median values of CRP are compared.

The mean duration of Diabetes in Lower UTI was 8.55yrs and mean duration of Diabetes in Upper UTI was 11.47 yrs. Statistical significance was done using Wilcoxon’s rank sum test since the distribution

of values was not within normal range and P value was found to be 0.070 which was not significant. The median duration of years in case of lower UTI was 7.5 yrs while in case of upper UTI it was 13.0 yrs. In case of lower UTI the mean Hba1c was 7.63% and in case of upper UTI the mean Hba1c was 9.40%. P value was calculated according to student’s t-test was <0.001 and was found to be significant. In case of lower UTI the mean FBS was 117mg/dl and in case of upper UTI mean FBS was 158.63 mg/dl. P value calculated according to student’s t-test was <0.001 and was significant. In case of lower UTI, among 54 cases the most common isolate was E-coli with 61% (33 cases). It was followed by Klebsiella 24% (13 cases)

Lower UTI - Organism	Frequency	Percentage
E-coli	33	61.0
Klebsiella	13	24.0
Pseudomonas	3	5.6
Enterococcus	2	3.7
Citro bacter	1	1.9
Enterobacter	1	1.9
Strenotrophomonas Maltophilia	1	1.9
Total	54	100.0

and Pseudomonas (3 cases). There were only 2 cases of Enterococcus (4%). Rest of 3 isolates was Citrobacter, Strenotrophomonas Maltophilia and Enterobacter each with 1 case each (table 2).

In case of upper UTI among the 19 cases, E coli were again the predominant isolate with 69% (13 cases). Followed by Klebsiella 19% (3 cases) and one case each of Pseudomonas, Chrysobacterium indolens and Enterococcus (table 3).

In our study the sensitivity & resistance pattern on isolated organisms was also studied. It was surprising to find very high resistance in both the groups in our institution. The isolated species from our study

Table 3. Isolated Organisms in Upper UTI

Upper UTI- Organism	Frequency	Percentage
E-coli	13	68.4
Klebsiella	3	15.7
Pseudomonas	1	5.3
Chrysobacterium indolens	1	5.3
Enterococcus	1	5.3
Total	19	100.0

showed very high ESBL positivity and MDR positivity. In case of lower UTI and upper UTI E-coli was the major Isolate. 61%(33 cases out of 54) in case of lower UTI and 69 % (13 cases out of 19) in case of upper UTI. ESBL positivity was found in 97 % (32 out of 33) of lower UTI and 84.6 % (11 out of 13) of upper UTI. The 2nd most common isolate in both Groups were Klebsiella, with a distribution of 24.1 % (13 out of 54) in lower UTI and 15.7% (3 out of 19) in upper UTI. In addition to E-coli and Klebsiella other gram negative organisms in group 1 included Pseudomonas, Stenotrophomonas Maltophilia and Citrobacter, while in group 2 it was Pseudomonas and Chrysobacterium Indologens. The total ESBL positivity among gram negative species was 92.3 % in Lower UTI and 83% in upper UTI-E coli which was the major isolate in both cases showed a high multidrug resistance also. In case of lower UTI it was 81.8% (27 out of 33) and upper UTI (9 out of 13) it was 69.2 %. Same as in the case of E-coli, ESBL positivity was very high for both groups Klebsiella with lower UTI having 84.6% (11 out of 13) and upper UTI 66.7% (2 out of 3). While in case of Klebsiella the MDR positivity was 69.2 % (9 out of 13) in lower UTI and 66.7 % (2 out of 3) upper UTI. The sensitivity of the major isolates in both groups was also studied. In Lower UTI E-coli which was the major species showed very high resistance to the commonly used fluoroquinolones, with only 21.20% sensitivity. E-coli showed very high resistance to Amoxicillin and Clavulanic acid and Ceftriaxone. The sensitivity to Cefoperazone - sulbactam and Piperacillin Tazobactam was both 69 %. The sensitivity to nitrofurantoin was 78 % while aminoglycosides was 69.30 %. In case of the next major isolate, Klebsiella showed better sensitivity when compared to E-coli, even though the resistance pattern was still very high. The sensitivity to Cefoperazone- sulbactam and Piperacillin-Tazobactam was 61.05 % each. Klebsiella showed severe resistance to both amoxicillin and Clavulanic acid. While the sensitivity to aminoglycosides was much better (69.20 %), whereas sensitivity to commonly used fluoroquinolones was only 38.80 %. In case of the next major isolate, Klebsiella showed better sensitivity when compared to

E-coli, even though the resistance pattern was still very high. The sensitivity to Cefoperazone- sulbactam and Piperacillin-Tazobactam was 61.05 % each. Klebsiella showed severe resistance to both amoxicillin and Clavulanic acid. While the sensitivity to aminoglycosides was much better (69.20 %), whereas sensitivity to commonly used fluoroquinolones was only 38.80 %. In case of the Upper UTI the second most common isolate was Klebsiella. Of 3 isolated Klebsiella, 2 were ESBL. Upper UTI had 1 case of Enterococcus. It was a MRSA Isolate and was sensitive to Vancomycin and linezolid.

DISCUSSION

Urinary Tract Infections is the second most common infection after infections of the respiratory tract.. Diabetes is one of the most common risk factor for UTI and the complicated forms of UTI such as pyelonephritis, renal abscesses and renal papillary necrosis was frequently seen more in diabetic individuals adding to very high mortality and morbidity among diabetic patients with UTI. In our study the main objective was the use of CRP, which is a cheap and commonly available laboratory investigation, as an early indicator for distinguishing between upper and lower UTI in Diabetic individuals. The data received from the previous studies have been very conflicting that, majority of the studies showing significant difference of CRP in upper and Lower Urinary Tract infections with some studies showing no significant difference at all. But interestingly most studies have been done on pediatric population with a handful of studies done in adult population. Our study primarily focus on adult population so that we can come up with an inexpensive early marker which is widely available all around so that differentiation between upper and lower UTI can be done at presentation of complaints.

In our study we had 73 cases Diabetic patients with UTI of which upper UTI were 19 in number and 54 cases were lower UTI. Among total of 73 cases 49 were female and 24 were males. In 54 cases of lower UTI, 38 were females and 16 were males, while in case of upper UTI 11 were females and 8 males. Comparison of CRP in both groups was the primary objective in our study. In case of diabetic Lower UTI a total of 54 diagnosed cases were taken. All the 54 cases were acute cystitis. The mean CRP value was 26.71mg/L with standard deviation of 23.23. While in cases of Diabetic Upper UTI, 19 diagnosed cases were taken. It included 17 cases of Pyelonephritis and 2 cases of renal abscess. The mean CRP was 216.80mg/L with

a standard deviation of 79.11. There was significant difference in case of CRP when compared both the groups. The P value calculated was <0.001 showing that the finding was very significant indicating CRP can be used as initial marker to distinguish upper and lower UTI in Diabetic individuals so that appropriate management can be started at the earliest. The organisms isolated from UTI have been a topic that has been widely studied both in India and outside India. But no major studies have been done in Kerala. By our study we are trying to see whether there is any significant variation in the organism isolated from UTI in Diabetic patients. Also we compared if there is any significant variation between upper and lower UTI isolates. In our Study among 54 cases of lower UTI the most common organism was E-coli— with 61% (33cases). It was followed by Klebsiella 24% (13 cases) and Pseudomonas (3 cases). There were only 2 cases of Enterococcus (4%). Rests of 3 isolates were Citrobacter, Stenotrophomonas Maltophilia and Enterobacter each with 1 case each.

In case of upper UTI among the 19 cases- E-coli was again the predominant isolate with 69%, followed by Klebsiella 19% and one case each of Pseudomonas, Chrysobacterium Indolens and Enterococcus. There wasn't a major difference among the isolates from both upper and lower UTI. Gram Negative species predominated both groups. Even among the major gram negative isolates E-coli and Klebsiella was the major isolate in both the groups. In case of gram positive organisms only 2 in lower uti and 1 in upper UTI was isolated.

All the studies, International, North Indian and South Indian Scenario, the isolates were the same all around. Even in our case the isolates were in agreement with all the above studies with gram negative species predominating with E- coli and Klebsiella leading. Only variation was that in case of our study gram positive isolates was very less compared to all the above studies and there were no Candida species isolated. In our study the sensitivity and resistance pattern on isolated organisms was also studied as a part of secondary objective, so that we could effectively use that information for empirically starting antibiotics for Diabetic UTI patients attending our Institution. It was very surprising to find very high resistance in both the groups in our Institution.

The isolated species from our study showed very high ESBL positivity and MDR positivity. In both groups the major Isolate was E-coli. But ESBL positivity was found to be 97% in case of lower UTI and 84.6 % in

case of upper UTI which was very high compared to the studies done so far. The case was the same with 2nd most common isolate that was Klebsiella with ESBL positivity of 84.6% in lower UTI and 66.7 % in upper UTI. The Total ESBL positivity among Gram Negative Species was 92.3 % in lower UTI and 83 % in upper UTI. The MDR species of both groups were also high with E-coli. In lower UTI it was 81.8% and in upper UTI it was 69.2 %, while in case of Klebsiella the MDR positivity was 69.2 % in case of Lower UTI and 66.7 % in case of Upper UTI

The sensitivity pattern was also extensively studied. In cases of sensitivity, lower UTI E-coli showed sensitivity of 78 % to nitrofurantoin and 69.30 % to aminoglycosides. It showed very high resistance to the commonly used fluoroquinolones and amoxicillin- Clavulanic acid. Only 21.2 % was sensitive to fluoroquinolones. Sensitivity to Cefoperazone-sulbactam and Piperacillin- Tazobactam was 69 % each. Klebsiella in lower UTI also showed almost same resistance pattern when compared to E-coli. It was 69.2% sensitive to Aminoglycosides and 61.05 % sensitive to both Cefoperazone sulbactam and Piperacillin-Tazobactam. Sensitivity to Nitrofurantoin was only 38.5 % which was very low compared to E-coli. Sensitivity towards fluoroquinolones was 69.2 %. Of the 2 Gram positive Isolate both were Enterococcus and both were MRSA positive.

Even in case of upper UTI sensitivity was similar to lower UTI. E coli showed only 23.1 % and 15.4% sensitivity to Fluoroquinolones and Amoxicillin- Clavulanic acid respectively. E-coli showed better sensitivity to Cefoperazone- Sulbactam and Piperacillin- Tazobactam with 61.5% and 76.0 % each. Sensitivity to Nitrofurantoin was 46.2 %. Of 3 isolates of Klebsiella 2 of them were ESBL. 1 Gram positive species isolated was Enterococcus and was MRSA. Even though the antibiotic sensitivity pattern is almost same everywhere, our study shows a very high percentage of resistance patterns with large number of ESBL isolates and MDR isolates in both groups suggesting higher antibiotics as empirical treatment for Diabetic UTI. In our study we studied whether there was any relation between duration of Diabetes and chances of getting upper and lower UTI.

The mean duration of Diabetes in Lower UTI was 8.55yrs and mean duration of Diabetes in upper UTI was 11.47yrs. P value was 0.070 and it was not significant indicating that duration of diabetes did not influence the upper or lower UTI.

HbA1c is the best marker for the control of diabetes. In

our study we compared whether there is any relation between control of diabetes and chances of UTI and also if it is equal for both groups in diabetic individuals. In case of lower UTI in our study the mean HbA1c was 7.63% and in case of Upper UTI the mean HbA1c was 9.40%, showing significant difference, suggesting that patient with poorly controlled Diabetes are more prone to upper UTI.

SUMMARY AND CONCLUSIONS

A Cross sectional Study was done at our hospital, Amrita Institute of Medical Sciences, Edapally, Kochi. The patients were included in the study according to the inclusion and exclusion criteria mentioned in the methodology. The study period was from November 2013 to January 2015.

The study consisted of 73 cases of Diabetic patients with UTI. Of them 54 were cases of lower UTI and 19 were cases of upper UTI.

The main objective of our study was to estimate the role of blood CRP in upper and lower UTI in diabetic individuals so that, whether it can be used as a tool to distinguish upper and lower UTI at the time of presentation along with clinical features.

Our study found out that the mean CRP level in upper UTI in diabetic Individuals was significantly high compared to lower UTI in diabetic individuals.

So we suggest CRP as an excellent bio-marker in distinguishing upper and lower UTI in diabetic patients along with clinical features at the time of initial presentation, so that appropriate empirical antibiotics can be started, thereby reducing the high mortality and morbidity associated the upper UTI in diabetic individuals.

Also as a part of our study we evaluated the clinical presentation, including the symptoms with which the patients presented. In upper UTI the major presentation was fever and abdominal or flank pain followed by vomiting, while in lower UTI the major symptoms were fever and dysuria followed by supra pubic pain and vomiting. Hence it was concluded that clinical presentation including symptoms and signs did not show significant difference between diabetic and non-diabetic individuals.

Also we found out that the isolated organisms for UTI in diabetic individuals was almost the same for both

upper and lower UTI. Gram negative species was the predominant isolate and among them E coli and Klebsiella were the most common ones. The most interesting, but unfortunate thing found in our study was the extensive resistance pattern to organisms isolated among diabetic UTI patients that came to our institution. Majority of the species were ESBL and MDR as described. And the resistance pattern was very high compared to any studies done so far in south and north India and even when compared with studies around the world. Our study suggests that higher spectrum antibiotics like Piperacillin-Tazobactam and Cefoperazone Sulbactam should be the 1st line drugs for empirical treatment, in both upper and lower UTI diabetic patients in order to reduce the high mortality and morbidity associated with Diabetic UTI. Our study shows that there is emergence of very high resistance organisms in community acquired UTI, suggesting the need to avoid abuse of antibiotics and need for completion of course of antibiotics to prevent emergence of drug resistance species.

We also concluded in our study that there was no relation between duration of diabetics and risk of getting upper and lower UTI infections. For both groups duration did not affect the chances of getting UTI. But it was the adequate control of diabetes which played the crucial role. It was found in our study that HbA1C levels were elevated in patients with upper UTI with a mean value of 9.4% compared to lower UTI patients where the mean value was 7.6% showing that patients with uncontrolled diabetes were more prone to upper UTI and than those with controlled diabetes. Thus we suggest that adequate control of diabetes is of utmost importance in preventing UTI especially upper UTI like pyelonephritis in diabetic patients.

END NOTE

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Conflict of Interest: None declared

REFERENCES

1. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med.* 2002 Jul 8;113 Suppl 1A:5S - 13S.
2. Orna Nitzan, Mazen Elias, Bibiana Chazan, Walid Saliba. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. *Diabetes Metab Syndr Obes.* 2015; 8: 129-136.
3. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025 -Prevalence, numerical estimates and projections. *Diabetes Care* 1998; 21: 1414-31.
4. F Khan, MA Malik, K Afzal, A Malik, M Khalid. Renal biometry and serum C - reactive protein levels in the evaluation of urinary tract infections. *Indian J Nephrol* 2004; 14: 10-14.
5. Agrawal P, Pandey A, Sompura S, Pursnani ML. Role of blood C - reactive protein levels in upper urinary tract infection and lower urinary tract infection in adult patients (>16 years). *J Assoc Physicians India.* 2013 Jul;61(7):462-3.
6. Parviz Ayazi, Abolfazl Mahyar, Hassan Jahani Hashemi, Mohammad Mahdi Daneshi1, Toktam Karimzadeh, Fatemeh Salimi. Comparison of Procalcitonin and C Reactive Protein Tests in Children with Urinary tract infection. *Iran J Pediatr* Dec 2009; 9(4):381-386.
7. Daniel Tsung-Ning Huang, Fu-Yuan Huang, Tsuen-Chiuan Tsai, Jeng-Daw Tsai, Nan-Chang Chiu, Chun-Chen Lin. Clinical differentiation of acute pyelonephritis from lower urinary tract infection in children *J Microbiol Immunol Infect.*2007;40:513-517.
8. Ayazi P, Mahyar A, Daneshi MM, Jahani Hashemi H, Pirouzi M, Esmailzadehha N. Diagnostic Accuracy of the Quantitative C-Reactive Protein, Erythrocyte Sedimentation Rate and White Blood Cell Count in Urinary Tract Infections among Infants and Children. *Malays J Med Sci.* 2013 Oct;20(5):40-6.
9. Al-Sayyad, Ahmed J,EL-Morshedy, Salah M, Abd Al Hamid, Ehab A, Karam, Nehad A, Imam, A. Basset A, Karam, Rehab. Evaluation of Biomarkers to Differentiate Upper from Lower Urinary Tract Infections in Children. *UroToday International Journal* 2011; 4(4): 1. [Source] <https://www.scribd.com/doc/292744990/Evaluation-of-Biomarkers-to-Differentiate-Upper-From-Lower-Urinary-Tract-Infection-in-Children>
10. Janifer, S. Geethalakshmi, K. Satyavani, V. Viswanathan. Prevalence of lower urinary tract infection in South Indian type 2 diabetic subjects. *Indian J Nephrol.* 2009; 19(3): 107-111.
11. Goswami R, Bal CS, Tejaswi S, Punjabi GV, Kapil A, Kochupillai. Prevalence of urinary tract infection and renal scars in patients with diabetes mellitus. *Diabetes Res Clin Pract.* 2001 ; 53(3): 181-6.
12. Akram M, Shahid M, Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India. *Ann Clin Microbiol Antimicrob.* 2007 6:4.
13. Tankhiwale SS, Jalgaonkar SV, Ahamad S, Hassani U. Evaluation of extended spectrum beta lactamase in urinary isolates. *Indian J Med Res.* 2004 Dec;120(6):553-6.
14. Dr Alka Nerurkar, Dr Priti Solanky, Dr Shanta S. Naik. Bacterial pathogens in urinary tract infection and antibiotic susceptibility pattern. *JPBMS* 2012; 21(12):1-3.
15. Sheung-Mei Lau, Ming-Yieh Peng, Feng-Yee Chang. Resistance rates to commonly used antimicrobials among pathogens of both bacteremic and non-bacteremic community-acquired urinary tract infection. *J Microbiol Immunol Infect* 2004; 37: 185-191.
16. Orret FA, Davis GK. A comparison of antimicrobial susceptibility profile of urinary pathogens for two years, 1999 and 2003. *West Indian Med J* 2006; 55: 95-9.
17. Gupta V, Yadav A, Joshi RM. Antibiotic resistance pattern in uropathogens. *Indian J Med. Microbiol.* 2002; 20: 96-8.
18. Finkelstein R, Kassis E, Reinhertz G, Gorenstein S, Herman P. Community-acquired urinary tract infection in adults: a hospital viewpoint. *J Hosp Infect* 1998; 38: 193-202.
19. Goldstein FW. Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infection in France. Multicenter study group. *Eur J Clin Microbiol Infect Dis* 2000;19:112-7
20. Gales AC, Jones RN, Gordon KA, Sader HS, Wilke WW, Beach ML, et al. Activity and spectrum of 22 antimicrobial agents tested against urinary tract infection pathogens in hospitalized patients in Latin America: report from the second year of the SENTRY antimicrobial surveillance program (1998). *J Antimicrob Chemother.* 2000 Mar;45(3):295-303.
21. Jones RN, Kugler KC, Pfaller MA, Winokur PL. Characteristics of pathogens causing urinary tract infections in hospitals in North America: results from the SENTRY Antimicrobial Surveillance Program, 1997. *Diagn Microbiol Infect Dis.* 1999 Sep;35(1):55-63.
22. Boyko EJ, Fihn SD, Scholes D, Chen C-L, Normand EH, Yarbrow P. Diabetes and the risk of acute urinary tract infection among postmenopausal women. *Diabetes Care.* 2002 Oct;25(10):1778-83.
23. Al-Rubeaan KA, Moharram O, Al-Naqeb D, Hassan A, Rafiullah MR. Prevalence of urinary tract infection and risk factors among Saudi patients with diabetes. *World J Urol.* 2013; 31(3): 573-8.
24. Sawers JS, Todd WA, Kellett HA, Miles RS, Allan PL, Ewing DJ, Clarke BF. Bacteriuria and autonomic nerve function in diabetic women. *Diabetes Care.* 1986; 9(5): 460-4.
25. Rayfield EJ, Ault MJ, Keusch GT, Brothers MJ, Nechemias C, Smith H. Am J Med. Infection and diabetes: the case for glucose control. 1982; 72(3): 439-50.
26. James R, Hijaz A. Lower urinary tract symptoms in women with diabetes mellitus: a current review. *Curr Urol Rep* 2014;15(10):440