

## Original Article

# Bacterial agents of Urinary tract infection in renal allograft recipients and their antimicrobial resistance pattern.

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Submitted on: 12 July, 2014. Accepted on: 10 October, 2014

### Abstract:

Urinary tract infection (UTI) is the most common infectious complications after renal transplantation. Recently many researchers reported that the bacterial agents of UTI in renal allograft recipients changed and demonstrated increased antimicrobial resistance to commonly used cephalosporins. This study was undertaken to isolate the bacteria which are responsible for UTI and their susceptibility pattern for appropriate antibiotic therapy in renal allograft recipients. This was an observational study conducted in the Department of Microbiology Bangabandhu Sheikh Mujib Medical University (BSMMU) from December 2010 to 2011. Twenty one renal allograft recipients from Department of Nephrology were evaluated for UTI after surgery up to six weeks. Microscopic examination, culture and sensitivity of urine specimen were performed. Out of 21 renal allograft recipients, 13(61.90%) patients developed UTI during initial post transplant period. Of 69 urine specimens collected from them 22(31.88%) yielded positive results for culture. *Enterococcus spp.* (50%) was the major bacterial pathogen isolated and showed 100% resistance to Cefuroxime, Ceftriaxone and Ceftazidime. *Enterococcus spp.* is an emerging pathogen responsible for development of UTI in renal allograft recipients which showed 100% resistance to 2nd and 3rd generation cephalosporin group.

**Key words:** Cephalosporins, Cephalosporins, *Enterococcus spp.*

### Introduction:

Urinary tract infection (UTI) is the most common infection following renal transplantation<sup>1</sup>. The reported incidence of post transplantation UTI varies considerably from 10 to 98%<sup>2</sup>. Differences in the definition of UTI, follow-up period, time of testing and the use of antimicrobial prophylaxis may explain this wide range<sup>3</sup>. Previously bacterial agents isolated from renal transplant recipients with UTI were almost similar to those causing UTI in the general population<sup>4</sup>. In Bangabandhu Sheikh Mujib Medical University (BSMMU) over a period of 2 years from January 2002 to December 2003 Islam et al<sup>5</sup> studied 31 post renal transplant patients of

which 51 episodes of bacterial infection occur. Among them UTIs account for 49 episodes (96%) and most of the isolated organism were Gram negative *Escherichia coli* (88%)<sup>5</sup>. Iqbal et al<sup>6</sup> in Karachi 2010 reported 51(77%) patients suffered from UTIs among 66(33%) renal transplant recipients and gram negative bacilli were the principal isolates. *Enterococcus spp.* is gram positive cocci that have emerged, over the last decades, as very important nosocomial pathogen causing UTIs<sup>7</sup>. Their ability to form biofilm is of particular importance in the development of UTI especially in catheterized patients<sup>8</sup>. *Enterococcus spp.* was found as the leading uropathogen responsible for 33 to 47% of UTI in transplant recipients<sup>1,9,10</sup>. Alangaden et al<sup>1</sup> found UTI(47%) among 65 patients from 2001 to 2004 and *Enterococcus spp.*(33%) and *Escherichia coli* (21%) were the most prevalent uropathogen. Most of the enterococcal UTIs occurred in the early post-transplant period<sup>1</sup>. Due to consequence of prophylactic therapy in renal allograft recipients multidrug resistant bacteria were emerging. So

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susceptibility pattern of the infecting microorganisms have been suggested to guide an appropriate antibiotic therapy in post renal transplant patients<sup>10</sup>. The prevalence of drug resistance varies considerably by region and country, thus awareness of local and regional antibiotic susceptibility among uropathogen is recommended to optimize empiric treatment<sup>11</sup>. We assume that, due to social, financial and environmental differences between countries and different transplant centre, the post transplant infectious pattern may be different too; so aims of this study was to find out bacterial agents of UTI and their antimicrobial resistance pattern in post renal transplant patients. The outcome of the study could help in the treatment of post transplant UTIs in our community and that may help to increase the chance of graft survival.

**Methods:**

This was an observational study carried out in the Department of Microbiology BSMMU, Shahbagh, Dhaka, Bangladesh from December 2010 to December 2011. A total 21 renal allograft recipients from the department of Nephrology, BSMMU were evaluated for UTI and their antimicrobial resistance pattern were determined. First urine specimens were taken from each patient in preoperative period for screening. Second and third specimens were directly taken from the catheter on 3rd and 7th post operative day & fourth specimens were taken within six weeks.

**Urinary studies:** Clean catch midstream urine in pre operative patients and with proper aseptic preparation from catheterized patients were collected for study. Urinary quantitative culture was performed on Chromoagar media. It was considered a positive result for urinary tract infection (UTI) when bacterial counts were recorded up to 10<sup>3</sup> or more per ml of urine<sup>12,13</sup>. Isolated Gram negative and Gram positive organisms were identified by standard phenotypic detection methods.

**Antibiotic susceptibility testing**

Antibiotic susceptibility testing was done by Kirby- Bauer disc diffusion method<sup>14</sup> on Mueller-Hinton agar (HiMedia laboratories, India) and in order to standardize the potency of the disc prepared, a representative disc from each batch was tested against reference strain of *Staphylococcus aureus* ATCC 25923. *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853. Results were interpreted as per National Committee for Clinical laboratory Standards (NCCLS) guidelines<sup>15</sup>.

**Results**

Twenty one renal allograft recipients were evaluated for UTI.

A total 69 urine specimens were collected in which 22(31.88%) were culture positive. Out of 21 renal allograft recipients 13(61.90%) recipients developed UTI. *Enterococci spp.* (50%) was the most common pathogenic organism isolated from urine specimen followed by *Escherichia coli* (18.18%), *Enterobacter spp.* (9.09%) & *klebsiella spp.* (9.09%), *Acinetobacter spp.* (4.54%) *Pseudomonas spp.*(4.54%) & *Staph. epidermidis* were (4.54%) (Table- 1). *Enterococcus spp.* were 100% resistant to ceftriaxone, ceftazidime, cefuroxime and amikacin. *Enterococcus spp.* showed 90%, 27% and 9% resistance against gentamicin, netilmicin and imipenem respectively (Figure -1). *Escherichia coli*, *Klebsiella*, *Enterobacter spp.* all showed 100% resistance to cephalosporin and ciprofloxacin except *Klebsiella* which was 50% resistant to ciprofloxacin (Table-2). *Pseudomonas*, *Acinetobacter spp.* also showed resistance to cephalosporin and ciprofloxacin but sensitivity showed against amikacin, imipenem and piperacillin/tazobactam. *Staph. epidremidis* was sensitive to vancomycin and showed resistance to co-trimoxazole, cephradine and amoxycillin.

Table 1: Bacterial agents of UTI in renal transplant recipients (n=22).

Microorganism	N(%)
<i>Enterococci spp.</i>	11 (50)
<i>Escherichia coli</i>	04 (18.18)
<i>Enterococci spp.</i>	02 (9.09)
<i>Klebsiella spp.</i>	02 (9.09)
<i>Acinetobacter spp</i>	01 (4.54)
<i>Pseudomonas spp.</i>	01 (4.54)
<i>Staph. epidermidis</i>	01 (4.54)

Table 2: Antibiotic resistance pattern of isolated *Escherichia colim*, *Enterobacter spp.* *Klebsiella spp.*

Antimicrobial agents	Name of Resistant oranisms (%)		
	<i>Escherichia coli</i> N=04	<i>Enterobacter spp.</i> N=02	<i>Klebsiella spp.</i> N=02
AMX	(100)	(100)	(100)
CH	(100)	(100)	(100)
COT	(50)	(100)	(100)
CIP	(100)	(100)	(50)
CTR	(100)	(100)	(100)
AMC	(100)	(100)	(100)
CAZ	(100)	(100)	(100)
AK	(00)	(100)	(50)
IPM	(25)	(50)	(50)
NET	(00)	(50)	(50)
TZP	=	(50)	(50)
GEN	(25)	(100)	(100)
CXM	(100)	(100)	(100)

Figure within Parenthesis indicate percentage

Amx= Amoxycillin    AMC= Amoxyclave    NET= Netilmycin  
 CH=Cephadrine(1st)    CAZ= Cefazidine(3rd)    GEN=Gentamicin  
 Cot= Co-trimoxazole    AK= Amikacin    CXM=Cefuroxime(2nd)  
 CIP= Ciprofloxacin    IPM= Imipenem  
 CTR= Ceftriaxone(3rd)    TZP=Piperacillin/Tazobactum

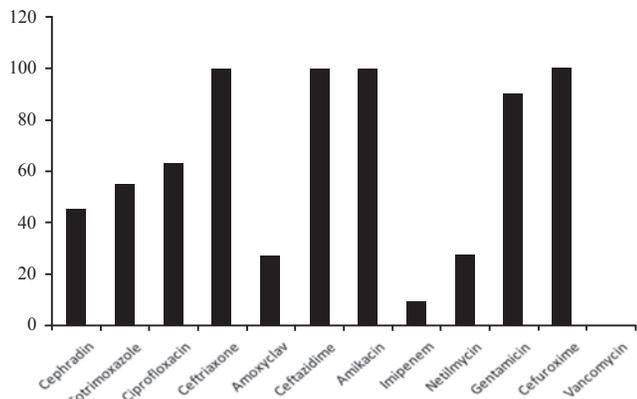


Figure 1: Antibiotic resistance pattern of *Enterococcus spp.*

**Discussion:**

Infections are the major determinant of the outcome of renal transplantation<sup>16</sup>. In this observational study, UTI developed in most of the patients (61.90%) within 6th weeks of renal transplantation. This finding was in almost consistent with the findings of the studies by Iqbal et al<sup>6</sup> in Karachi who have reported UTI to be 77% in renal transplant patients whereas Alangaden et al<sup>1</sup> found 47% UTI from 65(51%) patients among 127 adult renal allograft recipients from 2001 to 2004. This may be due to geographical variation and length of study. In this study, major isolated pathogen causing UTI was *Enterococcus spp.* (50%). These observations are also in accordance with the data by Sanchez et al<sup>10</sup>. They showed *Enterococcus spp.* (47%) to be the major bacterial pathogen of UTI as an emerging bacterium responsible for symptomatic infections in renal allograft recipients. Alangaden et al<sup>1</sup> and Schieszer et al<sup>9</sup> found *Enterococcus spp.* causing 33% and 40% in UTI in transplanted patient respectively. Mathe et al<sup>17</sup> also reported *Enterococcus spp.* as the leading uropathogen causing UTI after renal transplantation. Newer immunosuppressive agents in recent years is associated with some changes in the epidemiology of post transplant infection<sup>1</sup>. In this study, other pathogens besides *Enterococcus spp.* were *Escherichia coli* (18.18%) *Enterobacter spp.* (9.09%) *Klebsiella spp.* (9.09%), *Acinetobacter spp.*(4.50%) *Pseudomonas spp.*(4.50%) and *Staph. epidermidis* (4.50%). Islam et al<sup>5</sup> in their study observed *Escherichia coli* (88%) and *Klebsiella spp* (6%), *Pseudomonas spp* (3%) *Enterococcus spp* (3%) in renal allograft recipients. This indicates the changing pattern of etiological agents in renal allograft recipients in BSMMU probably due to invasive device, hospital acquired infection, immunosuppressive therapy and prolongs hospital stay as *Enterococcus* are the predominant inhabitants of gastrointestinal tract and act as an opportunistic pathogen.

Whereas Iqbal et al<sup>6</sup> found besides *Escherichia coli* (51%) other pathogen were *Pseudomonas aeruginosa* (18%), *Klebsiella spp.*(14%), *Morganella morgani*(8%), *Enterobacter spp.*(5%), *Enterococcus. spp.*(3%), MRSA(1%). Chuang et al<sup>18</sup> in 2005 in US transplant centre reported *E. coli* (29%) to be the major uropathogen, followed by *Enterococcus spp* (24%), *Staphylococcus* (12%) and *Klebsiella spp.*(10%). Many reasons may contribute to the variation in bacterial agents of UTI in renal allograft recipients like hospital acquired infections, bacterial agents vary from hospital to hospital and infection control program.

In the present study, *Enterococcus spp.* was 100% resistant to ceftriaxone, ceftazidime, cefuroxime and amikacin. *Enterococcus spp.* also showed 90%, 63%, & 55% resistance against gentamicin, ciprofloxacin & Cotrimoxazole respectively. The least resistant drugs against *Enterococcus spp* were imipenem (9%) and netilmycin(27%). This finding was consistent with the study by Sanchez et al<sup>10</sup> except one multidrug resistant *Enterococcus spp* detected in their study which was sensitive only to vancomycin. In this study no vancomycin resistant Enterococci (VRE) was detected. In recent studies, *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Pseudomonas*, *Acinetobacter spp.* all showed 100% resistance to cephalosporin and ciprofloxacin except *Klebsiella* which was 50% resistant to ciprofloxacin. Sanchez et al<sup>10</sup> in Brazil in 2010 observed 20% resistant against ciprofloxacin in *Escherichia coli* cases. *Staph. epidermidis* was sensitive to vancomycin and showed resistance to cotrimoxazole, cephradine and amoxyclave in this study. Islam et al<sup>5</sup> in 2011 found that all isolates were sensitive to ceftriaxone, ceftazidime and ciprofloxacin which was not consistent with present study. This marked variation in the sensitivity pattern between these studies might be due to difference in antibiotic prescription pattern. On the other hand Imipenem, netilmicin, and piperacillin / tazobactam have shown better sensitivity in almost all organisms in present study because these antibiotics are costly and used less frequently. In our hospital ( from where have recruited out study population) 3rd generation cephalosporins are the most commonly used antibiotic. *Enterococcus spp.* (50%) has emerged as the major pathogen responsible for UTI in renal transplanted patient which showed resistance to 2nd and 3rd generation cephalosporin group. Imipenem and netilmicin is the choice of therapeutic alternative.

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