Tripolitana Medical Journal; 2016,Vol. 5, No. 2, pp. 47 - 54

Research Article

ISSN 2077-5628

The Clinical Impact of Urinary Tract Infections on Graft Function among Kidney Transplant Recipients

Attiya Alatery[1@], Zaineb Elmahjoub[1], Hamza Benisa[2] and Najat Al-megrahi[1]

[1]Department of Microbiology and Immunology, Faculty of Pharmacy, University of Tripoli, Tripoli-Libya
[2]Department of Microbiology and Immunology, Faculty of Pharmacy, El mergib University, Alkhoms-Libya

Received 12 August 2016/Accepted 10 December

ABSTRACT

Urinary tract infection (UTI) is considered as one of the important bacterial infections seen among renal transplant recipients (RTR). In this study, 117 RTRs (73 males and 44 females) were examined for the bacterial UTIs from January to June 2014. UTIs were diagnosed in 33 patients [12 males (5 asymptomatic bacteriuria and 7 symptomatic UTI) and 21 females (7 asymptomatic bacteriuria and 14 symptomatic UTI). 42 bacterial strains belonging to 16 different species were isolated from urine samples and identified by conventional tests and analytical profile index (API) then confirmed by automated Phoenix system. The isolated bacteria were 76% (32/42) gram negatives and 24% (10/42) gram positives where gram negatives include *K. pneumonia* (43.8%), *E. coli* (18.8%), *E. cloacae* (12.5%), *K. oxytoca* (6.3%), *E. hermanni* (3.1%), *S. fonticola* (3.1%), *B. cepacia* (3.1%), *P. aerogenes* (3.1%), *Y. pseudotuberculosis* (3.1%), and *E. aerogenes* (3.1%) while gram positives include *S. aureus* (30%), *S. saprophyticus* (20%), and *S. porcinus* (20%), *S. kloosii* (10%), *S. agalactiae* (10%), and *E. faecalis* (10%). Notably, infection with *S. aureus* caused significant increase in serum creatinine and urea, whereas infection with *K. pneumonia* and *S. fonticola* cause significant decrease in blood hemoglobin. Patients should be evaluated for UTIs during routine outpatient follow-up, particularly female patients, considering the higher incidence of UTI in females.

Keywords- *UTIs, Urinary tract infection; RTRs, Renal transplanted recipients.*

INTRODUCTION

Urinary tract infection (UTI) is an infection that affects part of the urinary tract and remains one of the most serious complications after kidney transplantation that leads to graft damage and even death.[1,2] Generally, patients who have undergone renal transplantation are subjected to high doses of immunosuppressive therapy which renders the patients under several microbial infection , particularly UTI.[3,4] Clinically, significant bacteriuria or UTI infection has been designated as colony count of 10^5 colony forming unite per one ml urine sample(cfu.ml^{-1}).[5] The types of bacterial infections observed following solid organ transplantation vary considerably according to the following factors; bacterial infections related to the transplantation operation or to its technical complications; bacterial infections related to the prolonged hospitalization (nosocomial infections); bacterial infections related to the immunosuppressive treatment; and bacterial infection occurring months after the operation (e.g. community acquired infection).[6] However, prospective studies addressing and evaluating these factors in Libya are lacking, although remarkable and promising progress has been done in solid organ transplantation program. In this review we will focus on the frequency of UTIs in renal transport recipients (RTRs). Generally, bacterial infections have been reported to occur in 47% of RTRs where UTI is the most common form of bacterial infection in RTRs and represents the major clinical problem connected with the graft rejection. The prevalence of UTI in RTRs ranges from 40 to greater than 90% occurring after hospital discharge.[7,8]

Uropathogens differ in terms of virulence factors and pathogenic mechanisms that allow them to colonize and infect the urinary tract.[9] Bacteria are the primary organisms that cause UTI where gram negatives represents 80-85% and gram positives represents 15-20% of the cases.[10] Although the microbial spectrum causing UTIs in RTRs is similar to that in non RTRs, the clinical complications are more severe in RTRs. In RTRs, the severity of UTI is in the highest during the first year post-transplantation due to the higher dose of immunosuppressive medications which may result in acute graft rejection.[11,12] Several studies in has shown that the most common pathogens causing UTIs in RTR include *Enterobacteriaceae,* Enterococci*, Staphylococci*, *Methacill*in-Resistant *Staphylococcus aurous* (MRSA), and *Pseudomonas* whereas *Salmonella, Candida,* or *Corynebacterium urealyticum* are less frequent microorganisms.[13,14]

A retrospective study by Pelle *et al* has shown that UTI among RTRs was confirmed in 75% of the cases seen in transplantation clinic and occurred mainly during the first year after transplantation. Importantly, the risk of developing acute pyelonephritis was correlated with the frequency of recurrent UTIs and rejection episodes.[15] Unfortunately, 17(47.2%) of the infected patients died within 3 months, and for 12 (71%) of these patients, infection with this strain contributed to or directly caused death.[16] In related study in Pakistan, UTI

@ Author to whom correspondence should be addressed: *Dr. Attiya Alatery. Tel. +218918050599; E-mail: attiya2182000@yahoo.co.uk;*

caused by *E. coli* caused a remarkable elevation in serum creatinine level and the patients received broad spectrum antibiotics and started haemodialysis.[17]

The current study aimed to identify the bacterial isolates causing UTI and address the impact of such isolates on the graft function as a clinical predictor of graft rejection among the Libyan RTRs

MATERIALS AND METHODS

Study design and specimens collection

This study is a cross-sectional and cohort was conducted between January-June 2014 at the Organ Transplant Center, Tripoli Central Hospital, Tripoli-Libya. The study proposal was reviewed and approved by the department review committee. Furthermore, the study design was reviewed and approved by the committee of the center. All clinical information was collected under the supervision of nephrology clinic staff. In this study, clean catch midstream urine samples were collected from 117 RTRs whom attended the outpatient clinic at Libyan National Organ Transplantation Program in accordance to CLSI guidelines.[18] Based on the results, the data analysis was only focused on the 42 strains isolated from 33 UTI positive patients who underwent kidney transplantation. The specimens were subjected to microscopic examination, urine culture and antibiotic susceptibility testing. Peripheral blood samples were collected on ethylene diamine tetra-acetic acid (EDTA) for complete blood count (CBC) and Hb analysis by high-performance liquid chromatography (HPLC). For chemical analysis, clotted samples were obtained, and serum was separated by centrifugation for 15 min to evaluate different parameters of the transplanted renal function as creatinine and urea.

Isolation and identification of bacterial strains

Loopful of urine samples were inoculated on standard combination of none selective and selective plates [Blood agar, MacConkey agar, and Nutrient agar (Oxoid, UK)] for enumeration and identification of bacteria respectively (Appendix 2). All agar plates were incubated at 37°C under aerobic conditions for 18- 24 hr. On the second day, positive urinary cultures were defined as bacteriuria with more than 10^5cfu.ml^{-1} for collected samples. further, the individual colonies of bacterial isolates were inspected and identified initially by gram staining and biochemical tests including triple sugar iron agar, Indole test, oxidase test, and capsule staining for gram negative then confirmed by API E20 (BioMerieux, France)(Appendix3). On the other hand, Mannitol salt agar (Oxoid, UK) and Chromogenic MRSA agar (BioMerieux, France) were deployed for gram positive bacteria then confirmed by Analytical Profile Index strips (API Staph-BioMerieux, France) (Appendix3). Finally, stock cultures were maintained in glyceryl nutrient broth then kept at –30° C (deep freezer) until subjected to antibiotic sensitivity tests.[19-21] All the procedures were carried out according to CLSI.[22]

Routine microscopic examination of urine samples

The urine samples of sufficient volume (> 10 mL) were accepted. Samples were centrifuged at 2000 rpm in Urised (Budapest, Hungary) then collects the particles from the bottom of the basin. Collected particles were examined microscopically under 15 fields at 400 x magnification. Subsequently, the Urised machine takes photographs through a built in microscope at several stages of processing, and evaluates the data via image processing software that is able to detect and further classify particular urine particles as WBCs and bacteria.[23,24]

Biochemical and blood evaluation

Renal function tests was measured from a morning blood sample using an automatic analyzer (Cobas integra 400 plus, Roche, Basel, Switzerland) to measure serum creatinine, and urea. In analytical unit precise temperature controlled reaction rotor ensure stable test conditions and reliable result.[25] Complete blood count was measured by an automated hematology analyzer counter (Sysmex, Kobe, Japan) and hemoglobin analysis was also performed by using high-performance liquid chromatography (HPLC). It uses fluorescent flow cytometry and cell counting method to reliably detect abnormal samples and reduce false positive results.[26,27] Reading of at least three replicates were collected for each factor during the time of study. Graft dysfunction was defined as more than 20% rise in the Scr.[13,28]

Statistical analysis

All data were collected using questionnaires then were entered into Microsoft Access XP software and exported into Statistical Package for Social Science (SPSS 20.0). Categorical variables are summarized as frequency (percentage). Continuous variables are summarized as mean ± standard deviation. To analyze data, Chi square test was used for comparing categorical variables. Mann-Whitney test were used for testing differences between means for continuous variables. All tests were two-tailed and statistical significance was established at *P* values less than 0.05.

RESULTS

Causative microorganisms

Forty two bacterial strains belonging to 16 different species were isolated from urine samples collected from 33 RTRs confirmed as UTI positive. Table-1 shows that seventy six percent (76%) of total isolated organisms were found to be Gram negative, while remaining 24% were gram positive. The most frequently isolated gram negative organisms were *Klebseilla pneumonia* (33.3%), *Escherichia coli*(14.3%), *Enterobacter cloacae* (9.5%), *Klebseilla oxytoca* (4.8%), *Escherichia hermanni, Serratia fonticola, Burkholderia cepacia*, *Pasteurella aerogenes, Yersinia pseudotuberculosis,* and *Enterobacter aerogenes* (2.4% each). The most frequently gram positive isolated organisms are distributed in the following manner; *Staphylococcus aureus* (7.1%), *Staphylococcus saprophyticus* and *Streptococcus porcinus* (4.8% each), *Staphylococcus kloosii*, *Streptococcus agalactiae,* and *Enterococcus faecalis* (2.4 each %). Notably, five types of mixed pathogens were also found among total screened patients (Table 2).

Our results has found that *K. pneumonia* (33.3%) was the most prevalent UTI etiological agent followed by *E. coli* (14.4%), *E. cloacae* (10%), and *S. aureus* (7.1%).

E. coli and *K. pneumonia* were more frequent in females in our study. The prevalence of *K. pneumonia* was found to be significantly different between females than males (12/2 ; 95% CI: 0.06, 0.56; *P* =0.008). Even though *E. coli* (14%) was the second most common isolated organisms, it showed remarkable but insignificant difference between females and males (5/1; 95% CI -0.51,0.75; *P* = 0.102) (Table 1). Similarly, previous studies done by Magliano

et al [29], Gondos *et al*[30] and Kiffer *et al*[31] found higher difference in *E. coli* rates of isolation between males and females and confirm that *E. coli* was the most common uropathogen in females than males.

The prevalence of isolated bacteria causing UTI in relation to type of UTI are explained in Table 3. According to our study, 12 strains were isolated from cases of asymptomatic UTI and 30 strains related to symptomatic UTI. In contrast to the symptomatic UTI, asymptomatic UTI is defined as the isolation of bacteria in an appropriately collected urine specimen in the absence of symptoms or signs of urinary infection. According to our results, the asymptomatic and symptomatic UTI were not significantly different between both sexes (χ^2 0.259; $P = 0.434$), although females seemed to have high frequency rate of developing asymptomatic (7 versus 5 cases) and symptomatic (20 versus 10 cases) UTI episodes as compared to malesUltimately, we found that UTI, either symptomatic or asymptomatic was more prevalent at 6 months post transplant, and the asymptomatic and symptomatic UTI were significantly different at more than 6 months post transplant ($P = 0.003$) in our study as shown in Table 4. Similarly, previous study that found the risk of developing symptomatic UTI at 6 months after asymptomatic bacteriuria was significantly increased[32]. Further, Fiorante *et al* showed that 51% of the recipients develop asymptomatic bacteriuria during the 3 years following transplantation.[33] Other study which also detected UTI in 27(10%) patient undergone renal transplant after 6 -72 months where 5 of them had asymptomatic bacteriuria and 22 of them had symptomatic infection.[34]

Table 1: Revalence of bacterial isolates causing UTIs in RTRs according to patients'gender

Bacteria		All (%)	M	F	95% CI	*P**
G-ve bacteria 76%	*Klebseilla pneumonia*	14 (33.3)	2	12	0.06,0.56	0.008
	Escherichia coli	6 (14.3)	1	5	-0.51,0.75	0.102
	Enterobacter cloacae	4 (9.5)	2	2	-1.94,0.26	1.00
	Klebseilla oxytoca	2 (4.8)	2	0	-	-
	Escherichia hermannii	1(2.4)	0	1	-	-
	Serratia fonticola	1(2.4)	0	1	-	-
	Burkholderia cepacia	1(2.4)	1	0	-	-
	Pasteurella aerogenes	1(2.4)	0	1	-	-
	Yersinia pseudotuberculosis	1(2.4)	1	0	-	-
	Enterobacter aerogenes	1 (2.4)	1	0	-	-
G+ve bacteria 24%	*Staphylococcus aureus*	3 (7.1)	2	1	-0.37,0.19	0.564
	Staphylococcus saprophyticus	2 (4.8)	0	2	-	1.00
	Staphylococcus kloosii	1(2.4)	1	0	-	-
	Streptococcus agalactiae	1 (2.4)	0	1	-	-
	Streptococcus porcinus	2 (4.8)	1	1	-0.29, 0.23	1.00
	Enterococcus faecalis	1(2.4)	1	0	-	-
	Total	**42 (100)**	**15**	**27**		

*χ^2 test for comparison of bacterial isolates frequency between males and females.

Table 2: Prevalence of Mixed UTIs in RTRs.

Causative microorganisms	Number of cases	(%)
E. coli+ E. cloacae	1	20
K. oxytoca+ K. pneumonia	1	20
K. pneumonia+E. coli+ P. aerogenes	1	20
K. oxytoca+ E. aerogenes+ Y. pseudotuberculosis	1	20
S. porcinus+ K. pneumonia	1	20
Total	**5**	**100**

Table 3: Prevalence of the isolated bacteria causing UTI in relation to type of UTI

Bacteria	Type of UTI				Total
	Asymptomatic		Symptomatic		
	Male	Female	Male	Female	
K. pneumonia	-	3	2	9	14
E. coli	1	1	-	4	6
E. cloacae	1	1	1	1	4
K. oxytoca	-	-	2	-	2
Other gram negatives	-	-	3	3	6
S. aureus	1	1	1	-	3
Other gram positives	3	1	-	3	7
Total	**5**	**7**	**10**	**20**	**42**

Other gram negatives include *E. hermannii*, *S. fonticola*, *B.* cepacia, *P. aerogenes* , *Y. pseudotuberculosis,* and *E. aerogene.* Other gram positives include *S. saprophyticus, S. kloosii, S. agalactiae, S. porcinus,* and *E. faecalis* (χ^2 0.259; $P = 0.434$)

Table 4: Prevalence of UTI in relation to duration of transplant.

Duration (days)	Type of UTI		Total	χ^2	*P*
	Asymptomatic	Symptomatic			
1-30	2	3	5	.200	0.655
31-180	2	2	4	0.00	1.00
>180	8	25	33	8.75	0.003
Total	**12**	**30**	**42**		

There is significant difference between asymptomatic and symptomatic UTI at >180days post transplant ($P<0.05$) in contrast to other transplant periods.

The *relationship between results of urine analysis and urine culture:*

In this study, 126 urine samples were analyzed for presence or absence of pus cells in patients' urine samples using UriSed technique. For the purpose of analysis, the samples were categorized into 3 groups; no pyuria, mild pyuria and sever pyuria according to the number of pus cells detected in urine samples as shown in Table 5. Interestingly, out of 97 samples with insignificant pyuria (no pyuria; pus <5), 25 samples showed positive culture where a number of bacterial strains were isolated and 72 samples in this group had no bacterial growth in urine cultures. 18 samples had pus in urine and categorized as mild pyuria (mild pyuria; pus 5-40). Of these samples, 8 urine samples showed positive culture and 10 samples has no bacterial growth. In the similar manner, 11 urine samples were categorized as significant bacteriuria (sever pyuria; pus >40) with positive bacterial culture for 9 samples and negative bacterial culture for 2 samples.

The effect of isolates on graft function

To address the clinical consequence for types of urine isolates on the graft function, we used Mann-Whitney test for comparing mean values of 4 laboratory parameters (Scr, serum urea, WBC, and Hb) used to assess the graft performance. Figures 1-4 have shown only which urine isolates had significant effect on each laboratory parameter. In our study, the mean values of Scr (> 1.5g/ dL) and serum urea (> 50g/ dL) have increased significantly in UTI cases caused by *S. aureus* (U 45.00; $P = 0.019$ and U 36.00; $P = 0.014$ respectively) as shown in Figure 1 and 2, respectively. Importantly, out of 3 cases of UTI caused by *S. aureus*,1 patient was retransplant and had *M. tuberculosis*. Moreover, type of UTIs were symptomatic in 1 patient, and asymptomatic in 2 patients. On the contrary, our study found that Hb values (≤ 12mg/ dL) had decreased significantly with UTI mediated by *K. pneumonia* (U 291.500 ; $P = 0.024$) as shown in Figure 3 and *S. fonticola* (U 1.000; $P = 0.035$) as shown in Figure 4. Finally, WBC values had no significant difference among bacterial isolates causing UTI. Similarly, another study done by Naseri found the total leukocyte count as qualitative methods are not useful for diagnosis of UTI[35]. In contrast to other study done by Dotis *et al* that

demonstrate total WBC was statistically significant risk factor for UTI.[36]

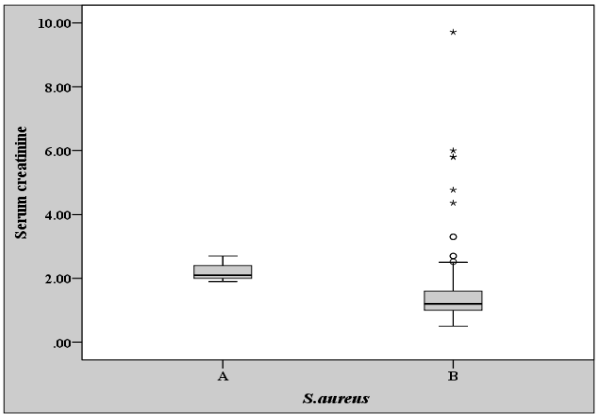

Figure 1: Significant changes in Scr among urinary isolates (A,B).

A: Cases infected with *S. aureus*. B. Other cases. By using Mann-Whitney test, Scr was significantly higher in cases infected with *S. aureus* than other cases (U 45.000; *P* 0.019).

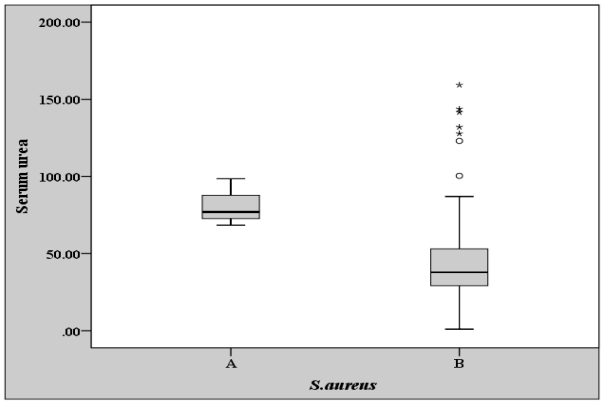

Figure 2: Significant changes in serum urea among urinary isolates (A, B).

A: Cases infected with *S. aureus*. B: Other cases. By using Mann-Whitney test, serum urea was significantly higher in cases infected with *S. aureus* than other cases (U 36.00; *P* 0.014).

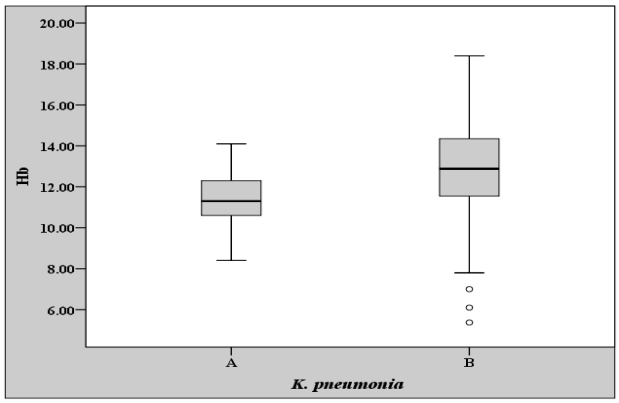

Figure 3: Significant changes in Hb among urinary isolates (A, B).

A: Cases infected with *K. pneumonia*. B Other cases. By using Mann-Whitney test, Hb was significantly less in cases infected with *K. pneumonia* than other cases (U291.500; *P* 0.024).

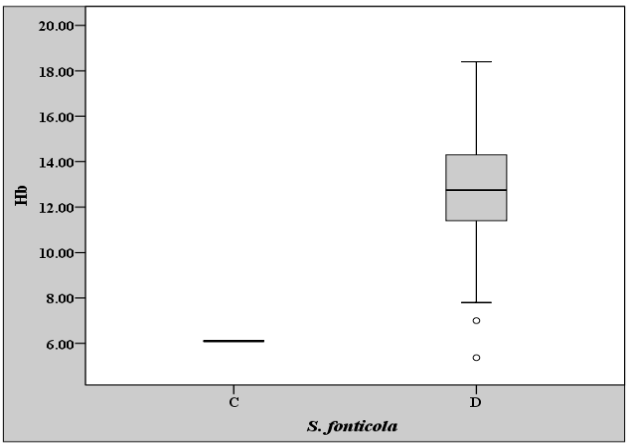

Figure 4: Significant changes in Hb among urinary isolates (C, D).

C: Case infected with *S. fonticola*. D: Other cases. By using Mann-Whitney test, Hb was significantly less in cases infected with *S. fonticola* than other cases (U 1.000; *P* 0.035)

DISCUSSION

Forty two bacterial strains belonging to 16 different species were isolated from urine samples collected from 33 RTRs confirmed as UTI positive. The identification procedures was carried out through conventional tests and analytical profile index (API) then confirmed by automated Phoenix system (Table 3.3). The total of bacterial species and strains isolated herein suggests that a broad range of microbial pathogens are associated with the infection of RTRs, as reported previously.[37,38] In close similarity to our observation, Takai *et al* has reported that the majority of organisms causing UTI following renal transplantation were gram negative isolates, while gram positive organisms are involved less frequently.[39] Generally, the most frequent pathogenic organisms demonstrated in transplant recipients were *E. coli* and other gram negative bacteria, such as *Klebsiella* spp, *Enterobacter* spp, and *P. aeruginosa*.[40-44] A regional study done in India by Sharma *et al* demonstrated *E. coli* as a common isolate followed by *Staphylococcus, Enterococus*, and *Pseudomonas*.[45]Another study by Igbal *et al* in Pakistan involved 200 adult live related renal transplant recipients has found that *E. coli* was the leading cause of UTI, followed by *Pseudomonas*, *Klebsiella*, and *M. morgagni*.[46] The present results agreed with a prospective study on 142 RTRs in Iran where UTI was the most prevalent infection among 59 cases (42%; 33 men, 26 women) and *K. pneumonia* was the most prevalent bacteria followed by *E. coli*, Enterococci, and *P. aeruginosa*.[47] Our results were further supported by a retrospective study analyzed files of 112 Libyan RTRs where the UTI was diagnosed in 33 patients (29.5%) and the major cause of UTI was *E. coli* followed by *Klebsiella* spp, and *Staphylococcus* spp.[48] Although other studies showed that major cause of UTI in RTRs was *Streptococci*[49], this was not the case in our study. The present results support the previous findings indicating that *E. coli, Enterobacter* spp, *Klebsiella* spp, and *Staphylococcus* spp are the principal etiological agents of UTI accounting for 80% of the screened cases.[30,50-53] Moreover, our result confirms and expands the previous findings that female transplant recipients have been

reported to be at a greater risk of developing UTI than males after renal transplantation.[42,44,52,54,55] Therefore, great deal of supporting data suggests direct correlation between prevalence of UTI and the gender of the recipient. This higher growth positivity seen in females is attributed to their anatomical structure (shorter urethra and proximity of the urethral opening to the vagina and anus) leading to easy access for coliform bacilli.

In agreement to our results, a previous studies done by Moradi *et al* found that the rate of asymptomatic bacteriuric episodes and symptomatic UTIs were not significantly different between males and females (*P* value >0.05).[56] Also, El Amari *et al* demonstrated that the asymptomatic bacteriuria in RTR was higher in females 45(58%) than in males 32(42%).[57] Similarly, Green *et al* noted that out of 112 RTR with asymptomatic bacteriuria, females 73(65%) were more prevalent than males 39 (35%).[32] Conversely, other study showed the males (65.0%) with renal transplants had higher frequency of asymptomatic UTIs than females (44.4%).[49] However, our results were further supported by a study done by Golebiewska *et al* who noted that no differenc8es in risk factors were seen for developing a symptomatic UTI versus an asymptomatic bacteriuria after renal transplant. Although asymptomatic bacteriuric episodes may be considered a risk factor for symptomatic infections, it remains to be determined if the treatment of asymptomatic UTI in renal transplant patients is in fact helpful or harmful in preventing symptomatic infections.[58,58] However, the causal link between asymptomatic and symptomatic episodes of UTI in kidney transplantation is questionable. Asymptomatic bacteriuria, which has been considered in the last decades as a risk factor for symptomatic UTIs in this population.[60] However, observational evidence indicates that asymptomatic bacteriuria may be associated with increased Scr and impaired renal function in according to study by Ciszek *et a1*[61] and asymptomatic bacteriuria can cause symptomatic infection in RTR.[59] In accordance to our results, a previous study has found that Scr was risk factor associated with *S. aureus* infection.[62-64] Also, other study has approved association between elevations in Scr and urea and existence of *Methicillin Resistant S. aureus* isolates.[65] Moreover The present results is similar to a study that reported anemia was significantly associated with increase prevalence of UTI mediated by *S. aureus*, *E. coli* and *P. aeruginosa*.[66] Furthermore, other study approved anemia probably due to *Klebsiella* infection in patient receive immunosuppressive therapy.[67] Collectively, the evolution in the management of transplantation has introduced routine perioperative prophylaxis, minimization of use of indwelling urethral catheters, and long term antimicrobial prophylaxis to prevent both asymptomatic bacteriuria and symptomatic urinary infection.[68]

Number of pus cells in urine has been used as an indication of UTI, but pyuria even can occur in the absence of bacterial growth due to antibiotic treatment prior to specimen collection and infection with organisms that do not grow on routine media for urine culture as mycobacterial, mycoplasmas, and anaerobic bacteria.[69] Our results agreed with previous study by Hashmi *et al* on 497 consecutive urine samples collected from 121 RTRs (75 males and 46 females). The study demonstrated that the isolates from the positive urine culture were independent on the presence or absence of WBCs. This might be strongly influenced by underlying clinical conditions and treatment, particularly immunosuppressive agents. RTRs are probably more likely to have urinary abnormalities than the random population, contributing to the poor specificity of their results.[70] This experience confirmed by ancient study.[71] Similarly, Faiman *et al* has concluded the presence of insignificant pyuria with positive culture indicate low risk of bacterial infections. This decreases the significance of pyuria as a screening tool in UTI due to leukocytosis as a side effect of adrenocorticoids.[72] Therefore, the method of urine analysis has a less reliable screening tool and should not be used to exclude UTI as a single test modality.[73] In a study to assess the diagnostic accuracy of urinalysis results from UriSed in predicting positive urine cultures, 384 urinary specimens were collected from 262 females and 122 males. Out of this number, 68 were positive for bacteriuria. Although the specificity of UriSed analyzer was within acceptable limits, and the sensitivity value was low. Thus, UriSed urinalysis results do not accurately predict the outcome of culture.[74]

Accordingly, UTI among RTRs should be monitored periodically and patients who are confirmed positive for bacterial culture must be considered under close control and started antibiotic treatment with the proper antibiotic regimen to avoid any chance of MDR emerging. Surveillance of UTIs for the first 3 months post-transplantation is a reasonable option for improving graft function and assuring the quality of life for the RTRs, especially for female patients. Furthermore, it is of great importance to document and analyse the data obtained from RTRs during UTI crises to build up clear and effective management protocols to fight any infections and correct the graft function.

REFERENCES

1. Foxman, B., (2002) Epidemiology of urinary tract infections: incidence, morbidity, and economic costs, *The American journal of Medicine* **113**(1), 5-13.

2. Gul, N., T.Y. Mujahid, and S. Ahmad (2004) Isolation, identification and antibiotic resistance profile of indigenous, *Pakistan Journal of Biological Sciences* **7**(12), 2051-2054.

3. Rivera-Sanchez, R., et al., (2006) Prospective study of urinary tract infection surveillance after kidney transplantation, *BMC Infectious Diseases* **10**(1), 245.

4. Melekos M.D. and K.G. Naber, (2000) Complicated urinary tract infections, *International Journal Of Antimicrobial Agents*. **15**(4), 247-256.

5. Forbes, B.A., et al., (2001) Bailey & Scott›s diagnostic microbiology, Mosby. Inc., St. Louis, 2002.

6. Soave, R., Prophylaxis strategies for solid-organ transplantation, *Clinical Infectious Diseases* **33**(1). S26-S31.

7. Rubin, R.H., (1993) Infectious disease complications of renal transplantation, *Kidney International* **44**(1), 221-236.

8. Wagener, M.M. and L.Y .Victor, (1992) Bacteremia in

transplant recipients: a prospective study of demographics, etiologic agents, risk factors, and outcomes, *American Journal of Infection Control* **20**(5), 239-247.
9. Ostergard, D.R., et al., (2008) Ostergard›s urogynecology and pelvic floor dysfunction. Lippincott Williams & Wilkins.
10. Gales, A.C., et al., (2002) Urinary tract infection trends in Latin American hospitals: report from the SENTRY antimicrobial surveillance program (1997-2000), *Diagnostic Microbiology and Infectious Disease* **44**(3), 289-299.
11. Venkat, K. and A. Venkat, (2004) Care of the renal transplant recipient in the emergency department, *Annals of Emergency Medicin* **44**(4), 330-341.
12. Bacheller CD , B.J., (1997) Urinary tract infections, *Med Clin North Am* .**81**719-30(3)
13. Munoz, P., (2001) Management of urinary tract infections and lymphocele in renal transplant recipients, *Clinical Infectious Diseases* **33**(1), S53-S57.
14. John, U., et al., (2006) High prevalence of febrile urinary tract infections after paediatric renal transplantation, *Nephrol Dial Transplant* **21**(11), 3269-3274.
15. Pelle, G., et al., (2007) Acute Pyelonephritis Represents a Risk Factor Impairing LongTerm Kidney Graft Function. *American Journal of Transplantation*, .7899-907(4)
16. Hota, S., et al., (2009) Outbreak of multidrug-resistant Pseudomonas aeruginosa colonization and infection secondary to imperfect intensive care unit room design, *Infection Control & Hospital Epidemiology* **30**(01), 25-33.
17. Suhail, M.A., M.S. Khaskeli, and A. Hamza, (2011) pattern, management and outcome of urological complications in first post-transplant year in 50 cases of renal transplant, *J Ayub Med Coll Abbottabad*. **23**(1).
18. Wayne, P., (2001) Clinical and Laboratory Standards Institute 2011. Performance standards for antimicrobial susceptibility testing: CLSI document M100-S21, *Clinical and Laboratory Standards Institute* **19**, 31.
19. Gul, N., T.Y. Mujahid, and S. Ahmad, (2004) Isolation, Identfication and Antibiotic Resistance Profile of Indigenous. *Pakistan Journal of Biological Sciences* **7**(12), 2051-2054.
20. Qin, X., et al., (2004) Kirby-Bauer disc approximation to detect inducible third-generation cephalosporin resistance in Enterobacteriaceae, *Annals of Clinical Microbiology and Antimicrobials* **3**(1), 1.
21. Kalsoom, B., et al., (2014) Patterns of antibiotic sensitivity of bacterial pathogens among urinary tract infections (UTI) patients in a Pakistani population, *African Journal of Microbiology Research* **6**(2), 420-414
22. Wayne, P., (2011) Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing: CLSI document M100-S21, *Clinical and Laboratory Standards Institute* **19**, 31.
23. Akin, O.K., et al., (2011) Evaluation of specimens in which the urine sediment analysis was conducted by full-automatic systems and a manual method together with urine culture results, *Afr J Microbiol Res*. **5**(15), 2145-2149.
24. Huysal, K., et al., (2014) Diagnostic accuracy of UriSed automated urine microscopic sediment analyzer and dipstick parameters in predicting urine culture test results, *Biochemia Medica* **23**(2), 211-217.
25. Becker-Cohen, R., et al., (2006) Risk factors for cardiovascular disease in children and young adults after renal transplantation, *Clin J Am Soc Nephrol.* **1**(6), 1284-1292.
26. Buttarello, M. and M. Plebani, (2008) Automated blood cell counts, *AmericanJournal of Clinical Pathology* 130(1), 104-116.
27. Adly, A.A., et al., (2014) Subclinical renal abnormalities in young thalassemia major and intermedia patients and its relation to chelation therapy, *Egyptian Journal of Medical Human Genetic* **15**(4), 369-377.
28. Iqbal, T., R. Naqvi, and S.F. Akhter, (2010) Frequency of urinary tract infection in renal transplant recipients and effect on graft function, *JPMA-Journal of the Pakistan Medical Association* **60**(10), 826.
29. Magliano, E., et al., (2012) Gender and age-dependent etiology of community-acquired urinary tract infections, *Scientific World Journal* 349597.
30. Gondos, A.S., et al., (2012) Urinary Tract Infection among Renal Transplant Recipients in Yemen, *PLoS One* **10**(12), . e0144266.
31. Kiffer, C.R., et al., (2007) Antibiotic resistance and trend of urinary pathogens in general outpatients from a major urban city. I*nt Braz J Urol.* **33**(1), 42-48.
32. Green, H., et al., (2013) Consequences of treated versus untreated asymptomatic bacteriuria in the first year following kidney transplantation: retrospective observational study. *European journal of clinical microbiology & infectious di*seases. **32**(1), 127-131.
33. Fiorante, S., et al., (2010) Systematic screening and treatment of asymptomatic bacteriuria in renal transplant recipients. *Kidney International* **78**(8), 774-781.
34. Lazinska, B., et al .(2005) ,Bacteriological urinalysis in patients after renal transplantation, *Polskie Towarzystwo Mikrobiology W Polish Society Of Microbiologists*. **500**(4), 317-321.
35. Naseri, M., (2008) Alterations of peripheral leukocyte count, erythrocyte sedimentation rate ,and C-reactive protein in febrile urinary tract infection, *Iran J Kidney Dis*. **2**(3), 137-142.
36. Dotis, J., et al., (2013) Urinary tract infections caused by extended-spectrum beta-lactamase-producing bacteria in children: a matched case-control study, *The Turkish Journal of Pediatrics* **55**(6), 571.
37. Ferraresso, M. and L. (2005) Berardinelli, Nosocomial infection in kidney transplant recipients: a retrospective analysis of a single-center experience, *Transplant Proc*. **37**(6), 2495-2496.
38. Kee, T., Y.M. Lu, and A. Vathsala, (2004) Spectrum of severe infections in an Asian renal transplant population, *Transplant* Proc. **36**(7), 2001-2003.
39. Takai, K., et al., (1998) Urinary tract infections following renal transplantation, *Transplant Proc*. **30**(7),.3140-3141
40. Ghasemian, S.M., et al., (1996) Diagnosis and management of the urologic complications of renal transplantation, *Clin Transplant* **10**(2), 218-23.
41. Viale, P. and L. Scudeller, (2004) [Infectious complications after renal transplantation, *G Ital Nefrol.* **21**(26), S48-52.
42. Maraha, B., et al., (2001) Infectious complications and antibiotic use in renal transplant recipients during a 1-year follow-up. *Clin Microbiol Infect.* **7**(11), 619-25.
43. Renoult, E., et al., (1994) Factors influencing early urinary tract infections in kidney transplant recipients. *Transplant Proc*. **26**(4), 2056-2058.
44. Takai, K., et al., (1998) Urinary tract infections following renal transplantation, *Clin Transplant.* **12**(1), 19-23.
45. Sharma, K.K., et al .(2007) Prevalence of infections in renal transplant recipients of north India, *Indian J Pathol Microbiol*. **50**(2), 453-457.
46. Iqbal, T., R. Naqvi, and S.F. Akhter, (2009) Frequency of

urinary tract infection in renal transplant recipients and effect on graft function, *J Pak Med Assoc*. **60**(10), 826-829.
47. Pourmand, G., et al., (2006) Posttransplant infectious complications: a prospective study on 142 kidney allograft recipients. *Urol J*. **3**(1), 23-31.
48. Elkehili, I., et al., (2010) Urinary tract infection in renal transplant recipients, *Arab Journal of Nephrology and Transplantation* **3**(2), 53-55.
49. Sinha, A.K., R. Ghacha, and I.A. Al-Khursany, (2000) Significant bacteriuria in renal transplant recipients, *Dialysis and transplantation* **29**(8), 477-480.
50. Kader, A.A., A. Kumar, and S.M. Dass, (2004) Antimicrobial resistance patterns of gram-negative bacteria isolated from urine cultures at a general hospital, *Saudi J Kidney Dis Transpl.* **15**(2), 135-9.
51. Alexopoulos, E., et al., (1985) Urinary tract infections after renal transplantation, *Drugs Exp Clin Res.* **11**(2), 101-105.
52. Domann, E., et al., (2003) Culture-independent identification of pathogenic bacteria and polymicrobial infections in the genitourinary tract of renal transplant recipients, *J Clin Microbiol* **41**(12), 5500-5510.
53. Al-Aasfari, R., S. Hadidy, and S. Yagan, (1999) Infectious complications of kidney transplantation, *Transplant Proc*. **31**(8), 3204.
54. Memikoglu, K.O., et al., (2007) Urinary tract infections following renal transplantation :a single-center experience. *Transplant Proc*. **39**(10), 3131-3134.
55. Schmaldienst, S., E. Dittrich, and W.H. Horl, (2002) Urinary tract infections after renal transplantation, *Curr Opin Urol.* **12**(2), 125-30.
56. Moradi, M., et al., (2009) Effect of antibiotic therapy on asymptomatic bacteriuria in kidney transplant recipients, *Urology Journal* **2**(1), 32-35.
57. El Amari, E.B., et al., (2011) Outcome of treated and untreated asymptomatic bacteriuria in renal transplant recipients. *Nephrology Dialysis Transplantation* **26**(12), 4109-4114.
58. Nicolle, L.E., et al, (2005) Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults, *Clinical Infectious Diseases* **40**(5), 643-654.
59. Gobiewska ,J., A. Debska-Slizien, and B. Rutkowski, (2014) Treated asymptomatic bacteriuria during first year after renal transplantation, *Transplant Infectious Disease* **16**(4), 605-615.
60. Coussement, J. and D. Abramowicz, (2013) Should we treat asymptomatic bacteriuria after renal transplantation? Nephrology Dialysis Transplantation: p. gft432.
61. Ciszek, M., et al., (2006) Urine cytokines profile in renal transplant patients with asymptomatic bacteriuria, *Transplantation* **81**(12), 1653-1657.
62. Adler, C., et al., (2001) Multiplicity distribution and spectra of negatively charged hadrons in Au+Au collisions at square root of (sNN) = 130 GeV., *Phys Rev Lett*. **87**(11), 112303.
63. Piercy, E., et al., (1989) Ciprofloxacin for methicillin-resistant *Staphylococcus* aureus infections. *Antimicrobial agents and chemotherapy* **33**(1), 128-130.
64. Castillo, J.S., et al., (2012) Mortality among critically ill patients with methicillin-resistant *Staphylococcus* aureus bacteremia: a multicenter cohort study in Colombia, *Revista Panamericana de Salud Publica* **32**(5), 343-350.
65. Sarapa, N., et al., (2014) Lack of effect of DX-619, a novel des-fluoro (6)-quinolone, on glomerular filtration rate measured by serum clearance of cold iohexol, *Antimicrobial agents and chemotherapy*, **20** (6) , 1912-1917.
66. Emiru, T., et al., (2013) Associated risk factors of urinary tract infection among pregnant women at Felege Hiwot Referral Hospital, Bahir Dar, *North West Ethiopia. BMC research notes* **6**(1), 292.
67. Jahan, A., E. Bhutia, and T.P. Yadav, (2013) *Klebsiella* infection-associated autoimmune haemolytic anaemia, *J Indian Acad Clin Med*. **14**, 190.
68. Yacoub, R. and N.K. Akl, (2011) Urinary tract infections and asymptomatic bacteriuria in renal transplant recipients. *Journal of global infectious diseases* **3**(4), 383.
69. Inglis, T., Microbiology and infection: (2007) a clinical core text for integrated curricula with self-assessment.: *Elsevier Health Sciences.*
70. Hashmi, P., et al., (1995) Routine urinalysis in renal transplant patients, *Journal of clinical pathology* **48**(4), 383-**384.**
71. Alwall, N. and Lohi, A (1973) Factors affecting the reliability of screening tests for bacteriuria, *Acta medica Scandinavica* **193**, 499-503.
72. Zitella, L., et al., (2006) Putting evidence into practice (PEP): Prevention of infection.
73. Yuen, S., F. Ng, and L. So, (2001) Evaluation of the accuracy of leukocyte esterase testing to detect pyuria in young febrile children: prospective study, *Hong Kong Medical Journal* **7**(1), 5-8.
74. Huysal, K., et al., (2013) Diagnostic accuracy of UriSed automated urine microscopic sediment analyzer and dipstick parameters in predicting urine culture test results, *Biochemia medica* **23**(2), 211-217.