

# Profile of infections in renal transplant recipients from India

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## ABSTRACT

**Background:** Infectious disorders are a major cause of concern in renal transplant recipients (RTRs) leading to considerable morbidity and mortality. We studied the profile and outcomes of infectious disorders in a cohort of RTR. **Materials and Methods:** In this prospective, observational study, we evaluated all RTR who presented with the features of infection. We also included asymptomatic patients with microbiological evidence of infection. We excluded patients with acute rejection, drug toxicity, and malignancy. Descriptive statistics were used to analyze the results. **Results:** The study population ( $n = 45$ , 35 male and 10 female) had a mean age of  $35.5 \pm 10.4$  years and follow-up after transplant was  $2.1 \pm 1.7$  years. Urinary tract infection (UTI,  $n = 15$ ) is the most common infection followed by tuberculosis (TB,  $n = 8$ ), cytomegalovirus ( $n = 6$ ), candidiasis ( $n = 7$ ), and hepatitis ( $n = 11$ ). Miscellaneous infections such as cryptosporidiosis and pneumocystis were seen in 10 patients. Simultaneous infections with two organisms were seen in 7 patients. Four patients succumbed to multiorgan dysfunction following sepsis, another 4 patients developed chronic graft dysfunction, while the remaining 35 RTR had a good graft function. **Conclusion:** Infectious complications are very common in the posttransplant period including UTI and TB. Further large scale studies are required to identify the potential risk factors leading to infections in RTR.

**Keywords:** India, infections, renal transplantation, tuberculosis, urinary tract infection

## Introduction

Kidney transplantation offers a better quality of life over hemodialysis in patients with end-stage renal disease (ESRD). The survival after transplantation is determined by multiple factors, including pretransplant co-morbidities, type of graft, and degree of immunosuppression.<sup>[1]</sup> The development of new immunosuppressive drugs leads to a reduction in the mortality of renal transplant recipients (RTRs). However, potent immunosuppression poses an additional risk of infectious disorders in the transplant recipients. One quarter of RTR

develop a serious infection in the posttransplant period that causes allograft dysfunction.<sup>[2]</sup> Infections occurring after transplantation account for half of the deaths and considerable morbidity in India.<sup>[3,4]</sup> Urinary tract infection (UTI) is the most common infection in the posttransplant period followed by candidiasis and tuberculosis (TB).<sup>[5]</sup> Hepatitis B and C viral (HBV and HCV) infection, cytomegalovirus (CMV), and pneumocystis are also common infections that are encountered in RTR.

The spectrum of posttransplant infections differs between the developed and developing nations. The risk factors prevalent in our country include tropical climate, poor hygiene and socioeconomic status, high rates of endemic infections, late

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presentation, poor diagnostic techniques, and lack of awareness in primary care physicians.<sup>[6]</sup> Renal transplantation centers are located in selected cities, which are unable to handle the volume of RTR.<sup>[7]</sup> Moreover, the transplant centers lay less emphasis on patients presenting with minor ailments such as fever and infection. Thus, more number of RTR will present to their local physicians for routine medical ailments.<sup>[8]</sup> It is essential for the local practitioners to identify the spectrum of infections that are common in RTR and direct appropriate therapy to improve the graft survival. The studies about the infectious complications in RTR are scanty from India.<sup>[9,10]</sup> Hence, we conducted this study to identify the profile of infectious disorders in RTRs.

## Materials and Methods

We conducted this prospective, observational study at a tertiary level nephrology center of the Armed Forces. All RTR who presented with features suggestive of underlying infection were included in this study conducted between June 2013 and June 2015. The requisite criteria were the presence of fever and features of the systemic inflammatory response syndrome (SIRS) with a suspected source of infection. Asymptomatic patients with microbiological evidence of infection either by culture or using serology were also included in the study. We excluded patients with acute rejection, drug toxicity, malignancy, and documented noninfectious etiologies of the SIRS such as pancreatitis.

This was a descriptive, observational study to analyze the risk factors leading to infectious complications after renal transplantation. We recorded the baseline data pertaining to the transplantation, the regime of immunosuppressive drugs used, episodes of graft rejection, co-morbid ailments, new onset diabetes after transplantation (NODAT), viral markers, and vaccination status. We also identified the episodes of infectious diseases that occurred prior to the transplantation. A detailed history was obtained from each patient regarding the suspected infectious complication and history of travel or exposure was noted. Clinical examination was done to localize the source of infection, and the graft kidney was palpated for any local tenderness or collection.

A detailed set of investigations, including the hematological and biochemical parameters, body fluid cultures, radiographs, and other imaging procedures was done in all patients to localize the source of infection. Invasive procedures such as lymph node biopsy, bronchoscopy, and kidney biopsy were done when indicated by the clinical profile. The diagnosis of any infectious disease is based on the standard guidelines using the clinical presentation and the investigation results. A clinical team analyzed each case with special reference to each infection, the duration after renal transplantation when it has appeared, the prevalence of the allograft dysfunction due to that infection and establishing a timetable of infection. The following risk factors are studied for the strength of association with infectious complication viz., age, sex, duration of dialysis prior to transplant, pretransplant infectious episode, posttransplant diabetes, rejection episodes, use

of antithymocyte globulin, CMV infection, co-morbid ailments prior to transplant, and protocol of immunosuppressive drugs.

The data collected was analyzed using SPSS Version 17 (SPSS Inc, Chicago, USA). Patterns of infection were further categorized with regard to the time interval after transplantation, the causative organism, and the site of infection. A minimum sample size of 20 was required assuming an Alpha error of 5% and the prevalence of posttransplant UTI among RTRs as 35%. This would give 80% power to our study in the estimation of the infection profile in RTR. The etiological association with risk factors is analyzed using Fisher's exact test and Student's *t*-tests.

## Results

A total of 45 patients (35 male and 10 female) were included in our study. The mean age of patients was  $35.5 \pm 10.4$  years and follow-up period after transplant was  $2.1 \pm 1.7$  years. Chronic interstitial nephritis, chronic glomerulonephritis, and diabetes were the three most common causes of the ESRD accounting for over 80% of cases in our study. All but one was live-related donor transplantation and majority of the donors were females. Pretransplant infections were documented in 33 (73.3%) patients, including UTI, pneumonia, TB, and hepatitis. All patients of hepatitis became seronegative with antiviral treatment prior to transplant. The majority of the study participants used basiliximab as part of induction therapy and mycophenolate in the maintenance immunosuppressive regimen. NODAT was seen in 20 patients and delayed graft function in 19 patients.

In our study, UTI is the most common posttransplant infection observed in 15 patients followed by TB in 8 (17.8%), CMV in 6 (13.3%), *Candida* in 7 (15.6%), HBV in 5 (11.1%), and HCV in 6 (13.3%) patients. Miscellaneous infections such as cryptosporidiosis, bacterial pneumonias, and cryptococcosis were seen in 10 patients. A total of 7 patients had multiple infections such as CMV with TB and candidiasis with TB. Majority of infectious episodes were after 1 year of transplant (77.77%), whereas 6 patients had an infectious episode between 6 months and 1 year (13.33%) and other 4 patients developed infection within 6 months of transplantation. Two-thirds of our patients presented with fever and systemic complaints suggestive of an infection, whereas asymptomatic identification was seen in one-third only. There were 4 deaths in our study group who developed multiorgan dysfunction as a result of sepsis and another 4 patients developed chronic graft dysfunction, while the rest of them (37 patients) recovered with good graft function.

## Discussion

Our results show that infectious disorders are a significant cause of morbidity and mortality in renal allograft recipients. There were 57 infectious episodes from 45 RTRs observed for a period of over 2 years. Postsurgical bacterial infections usually occur in the 1<sup>st</sup> month after transplantation; opportunistic infections (particularly CMV) are significant at 1–6 months

posttransplantation and a mixture of community acquired and opportunistic infections are usually identified in late posttransplant period in previous studies.<sup>[11,12]</sup> In our study, the infections were seen commonly after 1 year of transplantation. The immunosuppression-related TB and fungal infections predominate during this late period, accounting for the greater graft dysfunction, sepsis, and death.

UTI is the most common infection in RTRs, as was observed by other authors.<sup>[8,13]</sup> There was a male predominance (80%) in our study, which was contrary to the previous reports.<sup>[13,14]</sup> However, few authors have found no correlation between the gender and UTI, and male predominant subjects could explain their predominance in our study.<sup>[15]</sup> Eleven out of 15 patients of UTI had a history of pretransplant UTI ( $P < 0.001$ ) indicating the presence of pretransplant UTI as a risk factor for posttransplant UTI. In our study, *Escherichia coli* (33.3%) is the most common organism grown in culture followed by *Klebsiella* (20%), *Acinetobacter* (20%), *Proteus* (6.67%), and others such as *Staphylococcus* or *Pseudomonas* (6.67%). In a previous study, *E. coli* (31.5%), *Candida albicans* (21%), and *Enterococcus* spp. (10.5%) were the top three bacterial isolates in the culture.<sup>[16]</sup>

The reported prevalence of posttransplant TB varies between 2% and 15% in Asia and other countries.<sup>[17]</sup> In our study, the occurrence rate of posttransplant TB is 17.8%. The high prevalence of TB could be due to the fact that India is the world capital of TB with maximum risk of exposure. A similar observation was reported from Indian authors, who demonstrated a 51% of TB infection in RTR.<sup>[18]</sup> The use of modern, potent immunosuppressive agents such as tacrolimus or mycophenolate might increase the risk of TB, when compared to older immunosuppressant drugs such as azathioprine.<sup>[19]</sup> In our study, all patients of TB were using mycophenolate than azathioprine.

CMV infection continues to be a significant cause of morbidity and mortality in RTR.<sup>[20]</sup> Our data showed a 13% incidence of CMV infection, which was similar to other studies.<sup>[21]</sup> However, previous reports showed the occurrence of this infection in early posttransplant period, whereas our data suggest the presence in late period.<sup>[22]</sup> This could be due to the small number of cases which could induce a potential time bias in our study. Infection with hepatotropic viruses is a major problem in follow-up of RTR. Patients with HBV or HCV infection had significant graft dysfunction and mortality in our study. Similarly, Lee *et al.* have reported an inferior 10-year graft survival for HBV or HCV infected RTRs.<sup>[23]</sup> In the similar way, a 2005 meta-analysis has indicated that hepatitis B surface antigen positivity was associated with an increased risk of allograft loss.<sup>[24]</sup>

## Conclusion

There is a wide variety of infectious episodes in RTRs due to reduced immunity. The profiling of infections in renal allograft

recipients at our hospital provides relevant information to tropical countries, where the renal transplantation program is on the rise.

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## Conflicts of interest

There are no conflicts of interest.

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