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Review Article

Post Renal Transplant Infections: A Narrative Review

Najiya Mahamood*, Jayakrishnan S S, Amiya N T, Fasmia Thabassum, Keerthana K

Department of Pharmacy Practice, College of Pharmaceutical Sciences, Govt. Medical College, Kozhikode, Kerala, India.

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ABSTRACT

Kidney transplantation is the preferred treatment for patients with end-stage renal disease (ESRD) because it offers better survival and quality of life than dialysis. Infections, however, continue to be one of the most prevalent complications post-kidney transplantation, attributable to immunosuppressive therapy and various patient-specific risk factors. These infections significantly affect graft survival, patient morbidity, and mortality. Urinary tract infections are the most commonly reported infectious complications. Viral infections, particularly cytomegalovirus (CMV) and BK virus infections, are the next most frequently reported complications. To improve transplant outcomes, it is important to diagnose early, administer appropriate antimicrobial therapy, and implement preventive measures.

*Corresponding Author:

Najiya Mahamood

najiyamahamood8@gmail.com

1. INTRODUCTION

Compared with long-term dialysis, kidney transplantation is generally considered the best course of action for patients with end-stage renal disease (ESRD), providing better quality of life and greater

survival benefits (Fishman, 2007; Green, 2013; Patel et al., 1997). Infections continue to be a major source of morbidity and mortality among kidney transplant recipients, despite substantial breakthroughs in surgical methods, perioperative care, and immunosuppressive

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medication (Fishman, 2007; Kotton, 2010).

Globally, more than 100,000 kidney transplant procedures are performed annually, making kidney transplantation the most common solid-organ transplant procedure worldwide. According to recent global transplant registry data, kidney transplantation accounts for the majority of solid-organ transplants performed worldwide, highlighting the substantial clinical burden associated with post-transplant infectious complications. Despite advances in transplantation medicine, infectious complications remain among the leading causes of hospitalization, morbidity, and mortality, particularly during the first year after transplantation (Scemla & Manda, 2019).

Kidney transplant recipients are susceptible to a wide range of bacterial, viral, and fungal infections because lifelong immunosuppressive therapy is required to prevent graft rejection (Green, 2013; Rubin, 1993). The net level of immunosuppression affects the occurrence of these infections, which can result from endogenous flora, donor-derived sources, or environmental exposure (Rubin, 1993; Fishman & Rubin, 1998).

Reported infection rates among kidney transplant recipients range from 40% to 80%, reflecting differences in study populations, duration of follow-up, geographic variations in pathogen prevalence, immunosuppressive regimens, prophylactic strategies, and definitions used to classify infectious episodes (Patel et al., 1997; Rubin, 1993). Urinary tract infections (UTIs) are the most commonly reported of these, followed by viral infections such as BK virus (named after the initials of the first patient from whom the virus was isolated) and cytomegalovirus (CMV) (Julian & Parasuraman, 2013). Clinicians face a major problem in managing these infections due to the growing prevalence of antibiotic resistance (McAteer & Tamma, 2024).

Although several reviews have discussed specific infectious complications such as cytomegalovirus infection, BK virus nephropathy, and urinary tract infections in kidney transplant recipients, there remains a need for an updated narrative review integrating current epidemiological evidence, emerging antimicrobial resistance trends, risk factors, clinical outcomes, preventive approaches, and the role of multidisciplinary healthcare teams. This review aims to provide a comprehensive overview of post-renal transplant infections and their contemporary management strategies.

2. METHODOLOGY

This narrative review was conducted to

summarize current evidence regarding post-renal transplant infections, including epidemiology, risk factors, clinical consequences, prevention, and management strategies. A literature search was performed using PubMed, Scopus, Web of Science, and Google Scholar databases. Relevant articles published in English from 1993 to 2024 were reviewed.

The search strategy employed combinations of the following keywords and Medical Subject Headings (MeSH): “kidney transplantation,” “renal transplantation,” “post-transplant infections,” “urinary tract infections,” “cytomegalovirus,” “BK virus,” “fungal infections,” “opportunistic infections,” “immunosuppression,” “antimicrobial prophylaxis,” and “transplant outcomes.” Boolean operators (AND/OR) were used to refine searches.

Original research articles, review articles, clinical practice guidelines, meta-analyses, and landmark studies relevant to kidney transplant infections were included. Additional references were identified through manual screening of bibliographies from selected articles.

3. EPIDEMIOLOGY OF POST-RENAL TRANSPLANT INFECTIONS

Graft malfunction, hospitalization, and mortality are all greatly increased by infections, which remain one of the most frequent problems after kidney transplantation (Fishman, 2007; Green, 2013). The length of time following transplantation and the severity of immunosuppressive treatment affect the occurrence and kind of infections (Kotton, 2010; Rubin, 1993). Infection risk is highest in the first year after transplant, especially in the first six months when immunosuppression is at its peak (Kotton, 2010; Rubin, 1993). While opportunistic infections predominate between one and six months, early infections (within the first month) are typically associated with surgical operations and hospital-acquired pathogens (Rubin, 1993; Fishman & Rubin, 1998).

Urinary tract infections are the most frequent infectious complication among kidney transplant recipients, according to epidemiological studies and meta-analyses (Julian & Parasuraman, 2013; Hosseinpour et al., 2023). Reported rates of urinary tract infections vary widely across studies and patient populations, with some studies reporting incidences approaching 74% during the first year after transplantation (Bharuka et al., 2024; Pinchera et al., 2024). Pneumonia, bloodstream infections, and surgical site infections are additional frequently

reported infections (Husain & Camargo, 2019).

Viral infections, especially CMV, are still quite common and have serious side effects, including a higher risk of acute rejection and subsequent infections (Humar et al., 2009). Multidrug-resistant organisms are also on the rise, according to new evidence, which complicates treatment outcomes and raises the cost of healthcare (McAteer & Tamma, 2024).

4. RISK FACTORS FOR POST-RENAL TRANSPLANT INFECTIONS

Risk factors include immunosuppressive therapy, hospital-related factors and patient-related conditions (Table 1).

5. TYPES OF POST-RENAL TRANSPLANT INFECTIONS

5.1 Bacterial infections

Bacterial infections represent the most common infectious complications following kidney transplantation (Alangaden et al., 2006). Urinary tract infections are the most frequent and are commonly caused by gram-negative bacteria such as *Escherichia coli* (Julian & Parasuraman, 2013).

Recent studies highlighted the increasing antimicrobial resistance among pathogens causing UTIs in transplant recipients and complicating treatment strategies (McAteer & Tamma, 2024).

5.2 Viral infections

Viral infections are major contributors to morbidity among transplant recipients because immunosuppressive therapy may lead to viral reactivation (Rubin, 1993; Razonable & Eid, 2009).

5.3 Fungal infections

Fungal infections are less common but are associated with high mortality in immunocompromised patients. Common pathogens include *Candida*, *Aspergillus*, and *Cryptococcus* species (Pappas et al., 2010).

5.4 Cytomegalovirus (CMV)

Cytomegalovirus infection is one of the most significant viral infections in kidney transplant recipients. It is associated with systemic illness, graft dysfunction and an increased risk of acute rejection. (Humar et al., 2009; Kotton et al., 2013).

5.5 BK virus

BK virus (a polyomavirus named after the initials of the first patient from whom it was isolated)

infection may lead to BK virus-associated nephropathy, an important cause of graft dysfunction and graft loss in kidney transplant recipients (Hirsch & Randhawa, 2013; Sulaiman et al., 2024).

5.6 Epstein–Barr virus

Epstein–Barr virus infection is associated with post-transplant lymphoproliferative disorder (PTLD), particularly in patients receiving intense immunosuppressive therapy (Allen et al., 2009).

5.7 Urinary tract infections

Urinary tract infections are the most frequently reported infections among kidney transplant recipients. Gram-negative organisms, particularly *Escherichia coli*, are the most common causative pathogens (Julian & Parasuraman, 2013).

The most common risk factors for UTI are ureteral stents, urinary catheterization, female sex, diabetes mellitus and immunosuppressive therapy. Recurrent or untreated UTIs may lead to complications such as pyelonephritis, bacteremia and graft dysfunction.

5.8 Pneumonia

Pneumonia may occur due to bacterial or opportunistic pathogens. These infections are more common in patients receiving high-dose immunosuppressive therapy and may contribute to significant morbidity and mortality in transplant recipients (Husain & Camargo, 2019).

5.9 Surgical site infections

Surgical site infections typically occur within the first month after transplantation and are often associated with perioperative contamination or postoperative complications (Alangaden et al., 2006).

6. TIMELINE OF POST-TRANSPLANT INFECTIONS

Post-transplant infections generally follow a predictable timeline after kidney transplantation (Rubin, 1993; Fishman & Rubin, 1998).

■ First month after transplantation:

Infections during this period are typically related to surgical procedures or hospital exposure. Common infections include surgical site infections, catheter-associated infections and hospital-acquired pneumonia.

■ One to six months after transplantation:

During this phase, patients are highly susceptible to opportunistic infections due to intensive immunosuppressive therapy. Common infections

Table 1: Risk factors for post-renal transplant infections

CATEGORY	RISK FACTORS
Immunosuppressive therapy	Suppression of immune response leading to increased susceptibility to opportunistic infections (Fishman, 2007; Kotton et al., 2013).
Hospital-related factors	Prolonged hospitalization; urinary catheterization; invasive procedures (Alangaden et al., 2006).
Patient-related factors	Extremes of age (pediatric recipients and elderly recipients older than 65 years); Female sex; diabetes mellitus; structural urinary tract abnormalities (Julian & Parasuraman, 2013).

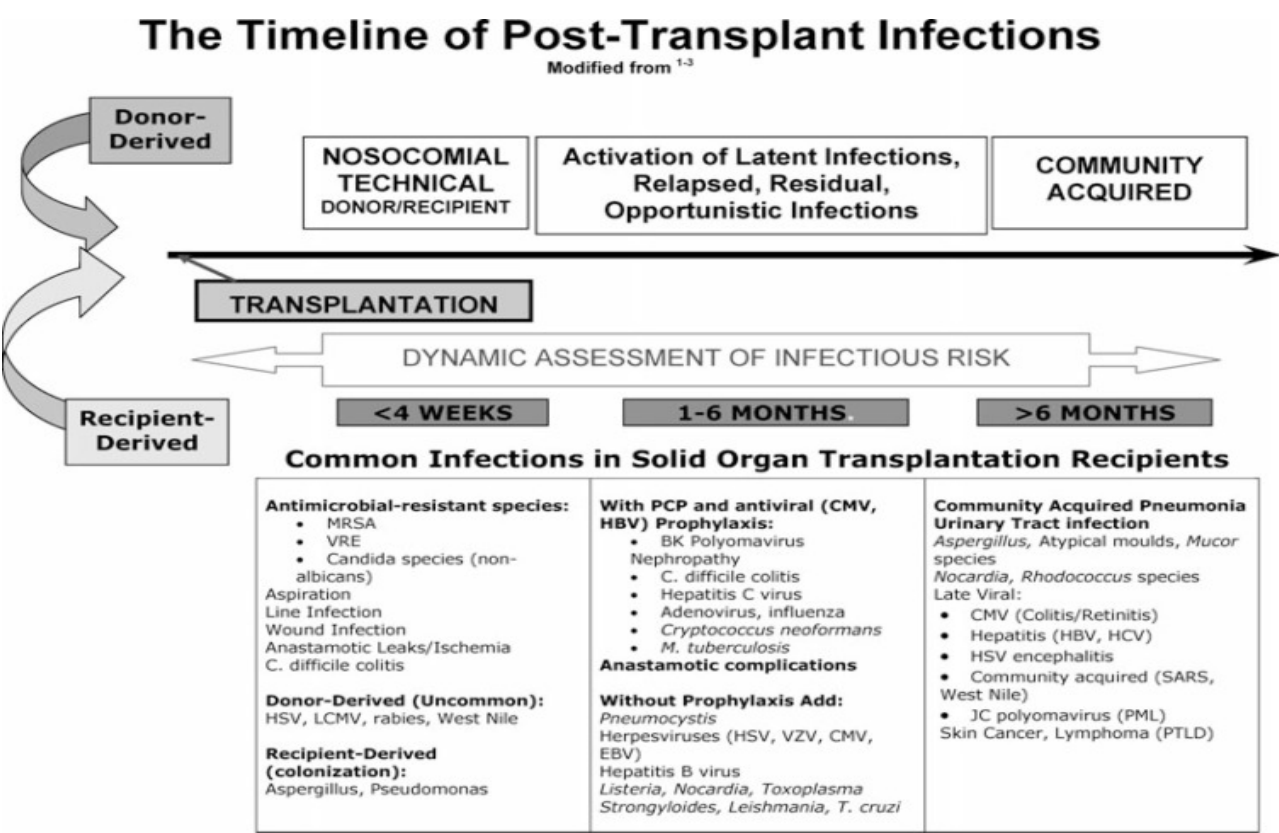


Figure 1: Timeline of post-transplant infections. Common patterns of opportunistic infection are observed following solid organ transplantation based on epidemiologic exposures and the ‘net state of immune suppression’. The timeline is altered based on the immunosuppressive regimen and prophylactic medications. The dynamic assessment of infectious risk represents assays that will measure an individual’s risk for infection due to specific pathogens or in general. (Adapted from Fishman JA, 2009).

include cytomegalovirus infection, fungal infections and *Pneumocystis pneumonia* (Rubin, 1993).

▪ After six months:
Late infections resemble community-acquired infections such as urinary tract infections and respiratory infections. Opportunistic infections may still occur in patients receiving prolonged immunosuppressive therapy (Rubin, 1993).
The timeline and pattern of post-transplant infections vary depending on the period after transplantation, as shown in Figure 1.

7. CLINICAL IMPACT

Infections following kidney transplantation have significant clinical and financial consequences. If not quickly detected and treated, these infections are a significant contributor to graft dysfunction and may eventually result in graft loss (Fishman, 2007; Kotton et al., 2013). Even though they are sometimes regarded as less serious, urinary tract infections can cause major side effects such as pyelonephritis, bacteremia, and recurring infections, all of which have a detrimental effect on graft function. CMV and other viral

infections are linked to long-term graft damage, acute rejection risk, and systemic disease (Humar et al., 2009). BK virus-associated nephropathy, a major contributor to transplant failure, can also result from BK virus infection (Kotton et al., 2013).

Infections place a significant pharmacoeconomic burden on patients and healthcare systems by increasing hospitalization rates, lengthening hospital stays, and raising healthcare expenditures (Kotton et al., 2013). Additionally, infections may necessitate lowering or changing immunosuppressive medication, which raises the possibility of graft rejection and presents a challenging therapeutic situation (Kotton, 2010).

All things considered, post-transplant infections negatively impact patient survival, quality of life, and long-term transplant results, underscoring the necessity of efficient prevention and therapeutic measures.

8. PREVENTION AND MANAGEMENT:

8.1 Antimicrobial Prophylaxis

Prophylactic antimicrobial therapy plays an important role in preventing opportunistic infections in transplant recipients. Trimethoprim-sulfamethoxazole is commonly used for the prevention of *Pneumocystis jirovecii* pneumonia and may also reduce the incidence of urinary tract infections (Martin et al., 2009).

8.2 Vaccination

Vaccination prior to transplantation is recommended to reduce the risk of infections. Vaccines against influenza, pneumococcal infection and hepatitis B are commonly recommended for transplant candidates (Danziger-Isakov et al., 2019).

8.3 Infection Control Measures

Strict infection control practices, regular monitoring, early diagnosis and prompt treatment are essential for preventing infectious complications and improving outcomes in renal transplant recipients. (Kidney Disease: Improving Global Outcomes [KDIGO], 2009).

9. STRATEGIES TO REDUCE DRUG COSTS

The high cost of medications can act as a barrier to transplantation. The following strategies may help reduce overall drug expenses:

- Recommend tactics that could lower drug costs like
 - restricting the use of biologic agents for induction therapy to patients at high risk of acute

rejection;

- minimizing the dose of CNI with a non-dihydropyridine CCB;
- substituting azathioprine for mycophenolate;
- utilizing bioequivalent generic medications that have undergone sufficient testing;
- long-term prednisone use.

➤ Generic medications should only be used if they meet established regulatory standards, including:

- contain the same active ingredient as the reference drug;
- are identical in strength, dosage form, and route of administration;
- has the same indications for use;
- is bioequivalent in suitable bioavailability investigations;
- satisfies the identical batch standards for quality, purity, strength, and identity;
- is produced in accordance with tight guidelines.

➤ Any modification to a prescribed immunosuppressive medication, including switching to a generic medication, should be communicated to the patient and the clinician in charge of their treatment.

➤ After switching to a generic drug that is tracked by blood levels, check the levels and modify the dosage as often as needed until a stable therapeutic goal is reached (KDIGO, 2009).

10. ROLE OF CLINICAL PHARMACISTS

Clinical pharmacists play an important role in identifying and resolving drug-related problems and optimizing patient outcomes. Their responsibilities include:

1. Obtaining and reviewing patient medication histories and clinical profiles.
2. Optimizing and adjusting medication therapy when clinically appropriate;
3. Analyzing test data, such as blood levels of immunosuppressive drugs;
4. Understanding drug-related problems and negative drug-related outcomes;
5. Providing pharmacotherapy-related information and counselling to patients and healthcare professionals;
6. Individual patient monitoring.

The most relevant adverse events after

transplantation are hepatotoxicity, CMV infection, neurotoxicity, and post-transplant diabetes. Two aspects were the main emphasis of the monitoring process:

- a) Efficacy as determined by laboratory tests and the frequency of allograft rejection or failure;
- b) Safety as determined by immunosuppressive blood levels (Gnatta et al., 2019).

Clinical pharmacists also play a pivotal role in therapeutic drug monitoring (TDM) of immunosuppressive agents such as tacrolimus, cyclosporine, sirolimus, and everolimus. Regular monitoring of drug concentrations assists in maintaining therapeutic efficacy while minimizing toxicity and reducing the risk of graft rejection.

In addition, pharmacists contribute significantly to the identification and management of drug–drug interactions. Antimicrobial agents frequently prescribed for transplant-related infections may alter immunosuppressant concentrations. For example, azole antifungals and macrolide antibiotics can increase calcineurin inhibitor levels, whereas rifampicin can substantially reduce their concentrations. Pharmacist-led monitoring and dose adjustments are therefore essential components of post-transplant care.

11. CONCLUSION

One of the biggest problems in the care of kidney transplant recipients is still post-renal transplant infections. Infections still have a major influence on graft survival, patient morbidity, and mortality despite advancements in transplantation therapy (Fishman, 2007; Kotton et al., 2013).

The most common infections are urinary tract infections, which are followed by viral infections like CMV and BK virus, each of which has a distinct impact on unfavorable clinical outcomes (Julian & Parasuraman, 2013; Humar et al., 2009). The intricacy of immunosuppressive regimens and growing antibiotic resistance both increase the burden of these illnesses (McAteer & Tamma, 2024).

Improving patient outcomes requires early diagnosis, effective antimicrobial therapy, and preventive measures such as vaccination, antimicrobial prophylaxis, and stringent infection-control procedures (Martin et al., 2009; Danziger-Isakov et al., 2019; KDIGO, 2009). To optimize treatment and reduce complications, a multidisciplinary strategy involving doctors, microbiologists, and clinical pharmacists is essential (Gnatta et al., 2019).

To lessen infection-related consequences, future studies should focus on identifying high-risk

individuals, understanding changing epidemiological trends, and developing targeted therapies. Ultimately, strengthening evidence-based practices will increase long-term graft survival and improve kidney transplant recipients' overall quality of life.

Emerging antimicrobial resistance and evolving immunosuppressive strategies necessitate continuous surveillance and individualized infection management in kidney transplant recipients.

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Conflict of Interest

None declared.

Ethical Statement

There is no ethical approval required.

Declaration of Generative AI

No artificial intelligence (AI) tools were used in the preparation of this manuscript

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