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Original Article

KIDNEY TRANSPLANT

Viral infections and clinical outcomes in kidney transplant recipients in Northern Brazil

Infecções virais e seus desfechos clínicos em receptores de transplante renal no Norte do Brasil

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Summary **Purpose:** To identify the occurrence of opportunistic viral infections and analyze their association with sociodemographic, clinical, and therapeutic variables in kidney transplant recipients at a referral hospital in Northern Brazil. **Methods:** This cross-sectional, analytical, descriptive, and retrospective study included 78 kidney transplant recipients followed between January 2022 to June 2025. Sociodemographic, clinical, laboratory, and therapeutic data were collected. Statistical analyses included absolute and relative frequencies, Fisher's exact test, and binomial logistic regression, adopting a significance level of $p<0.05$. **Results:** Viral infection prevalence was 71.8%, with Cytomegalovirus being the most frequent pathogen. No significant association was found between sociodemographic variables and viral infection occurrence ($p>0.05$). A significant association was observed between immunosuppressive regimens and viral coinfection ($p=0.006$). The presence of viral infection was the only factor significantly associated with hospitalization ($p<0.001$), whereas sex, age, and immunosuppressive regimen showed no significant association. **Conclusion:** Opportunistic viral infections are highly prevalent among kidney transplant recipients, with Cytomegalovirus as the predominant agent. Viral infection was associated with adverse clinical outcomes, particularly hospitalization, highlighting the importance of early monitoring and management in this population.

Keywords: cytomegalovirus; immunosuppressive agents; viral infections; kidney transplantation; coinfection.

Resumo **Objetivo:** Identificar a ocorrência de infecções virais oportunistas e analisar sua associação com variáveis sociodemográficas, clínicas e terapêuticas em receptores de transplante renal em um hospital de referência no Norte do Brasil. **Método:** Estudo transversal, analítico, descritivo e retrospectivo, realizado com 78 pacientes transplantados renais acompanhados entre janeiro de 2022 a junho de 2025. Foram coletados dados sociodemográficos, clínicos, laboratoriais e terapêuticos. As análises estatísticas incluíram frequências absolutas e relativas, teste exato de Fisher e regressão logística binomial, adotando-se $p<0,05$. **Resultados:** Observou-se prevalência de infecção viral em 71,8% dos pacientes, com predomínio do citomegalovírus. Não houve associação significativa entre variáveis sociodemográficas e ocorrência de infecção viral ($p>0,05$). Verificou-se associação significativa entre regimes imunossupressores e coinfecção viral ($p=0,006$). A presença de infecção viral foi o único fator associado à hospitalização ($p<0,001$), enquanto sexo, idade e regime imunossupressor não apresentaram associação significativa. **Conclusão:** As infecções virais oportunistas apresentam alta frequência em receptores de transplante renal, destacando-se o citomegalovírus. A infecção viral mostrou-se associada a desfechos clínicos adversos, especialmente hospitalização, reforçando a importância do monitoramento e manejo precoce desses pacientes.

Descritores: citomegalovírus; agentes imunossupressores; infecções virais; transplante renal; coinfecção.

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Introduction

Kidney transplantation is currently the main treatment for patients with end-stage chronic kidney disease. Compared to hemodialysis, it provides better quality of life and increased survival expectancy[1]. Globally, Brazil stands out for having the largest public transplant program, funded by the Unified Health System (SUS), and ranks as the third country in the number of kidney transplants performed annually[2]. Despite technical and surgical advances, post-transplant infections remain one of the major challenges for graft maintenance and patient survival[3].

Immunosuppression is an essential component of kidney transplantation, as it aims to prevent graft rejection and ensure long-term survival. Immunosuppressive regimens typically combine drugs with different mechanisms of action, such as calcineurin inhibitors (tacrolimus and cyclosporine), antimetabolites (mycophenolate mofetil and azathioprine), corticosteroids, and, in some cases, mTOR inhibitors (everolimus and sirolimus)[1,4]. Although effective, these drugs increase susceptibility to opportunistic infections, neoplasms, and metabolic complications[5]. The risk is higher in the first months after transplantation, when immunosuppression is more intense, favoring complications caused by opportunistic viruses that impact graft survival[6,7].

Among these viruses, Cytomegalovirus (CMV), BK Polyomavirus (BKV), and Epstein–Barr Virus (EBV) are particularly notable. CMV is the most prevalent agent in solid organ transplantation. According to CONITEC report no. 487/2024, annual CMV infection rates range from 10.3% to 63.2%, depending on population profile, type of transplant, laboratory surveillance, and prophylactic strategies[8]. In Salvador, Bahia, a study found that 63.2% of kidney transplant recipients developed CMV infection, with 75% of cases occurring within the first 100 days after the procedure, highlighting the high incidence of the virus in the national context[9]. This condition is associated with graft rejection, increased mortality, and higher hospital costs[10].

BKV, in turn, is characterized by its renal tropism and its potential to cause direct graft injury. A study conducted at Walter Cantídio University Hospital in Fortaleza, Ceará, involving 187 recipients, reported a prevalence of 55.6%, associated with the intensity of immunosuppression and longer hospital stays in patients with comorbidities[11].

EBV is directly linked to the development of post-transplant lymphoproliferative disease (PTLD), an uncommon but highly morbid and potentially fatal complication. A Brazilian study conducted between 2018 and 2020 showed that among 1,625 monitored kidney transplant recipients, 14.6% presented EBV viremia, and 17.2% of these progressed to PTLD. Overall survival was 60.4% at 1 year and 46.8% at 2 years, demonstrating the clinical impact of this infection[12].

However, in Northern Brazil, there is still a scarcity of epidemiological data, which hinders the development of protocols adapted to local particularities. The analysis conducted in this study aims to identify the occurrence of viral infections in kidney transplant recipients, relate them to clinical factors such as immunosuppressive regimens and sociodemographic variables, and understand their clinical outcomes, contributing to more effective prevention and treatment strategies.

This study aimed to identify the occurrence of opportunistic viral infections and analyze their association with sociodemographic, clinical, and therapeutic variables in kidney transplant recipients at a referral hospital in Northern Brazil.

Methods

Study Design

This is a cross-sectional, analytical, descriptive, and retrospective study conducted at Ophir Loyola Hospital (HOL), located in Belém, Pará, in the Northern region of Brazil. Data were obtained from the institution's Medical Records and Statistics Coordination (CAME).

Study Population and Setting

The study population consisted of patients who underwent kidney transplantation at HOL between January 2022 and June 2025.

HOL is a reference center for specialized care in the state of Pará, receiving patients referred from primary care, outpatient, and hospital services, with care fully provided through the Brazilian Unified Health System (SUS). The institution was a pioneer in kidney transplantation in the Northern region, initially with living donors and later with deceased donors. Currently, the Kidney Transplant Program at HOL is nationally and internationally recognized, presenting outcomes comparable to leading centers worldwide, supported by a multidisciplinary team that follows patients from the pre-transplant phase to postoperative follow-up.

Data Collection and Processing

The study was conducted in accordance with Resolution No. 466/2012 of the Brazilian National Health Council, following approval by the Research Ethics Committee (REC) of HOL (approval no. 7,561,846; CAAE 8850525.0.0000.5550). Data collection occurred between July and August 2025 and included patients who underwent kidney transplantation between January 2022 and June 2025, regardless of clinical indication.

Inclusion criteria were adult patients (≥18 years), residents of the state of Pará, who underwent kidney transplantation at HOL and had post-transplant follow-up at the same institution during the study period. Eligibility required the availability of medical records containing information on immunosuppressive regimen, clinical outcomes, and at least one documented qPCR result for CMV, BKV, EBV, or other opportunistic viruses investigated during follow-up.

Exclusion criteria included patients under 18 years of age, recipients of other types of transplants, individuals without post-transplant follow-up at the institution, patients diagnosed with oncological or neurological diseases, and medical records lacking essential clinical or laboratory data for analysis.

As this was a retrospective study using secondary data, viral monitoring was analyzed according to the information available in medical records, and it was not possible to confirm uniformity in the timing of laboratory tests for all patients. Only patients with sufficient laboratory records to determine the presence or absence of viral infection during the study period were included.

Statistical Analysis

Data were organized using Microsoft Excel® (version 2309), and statistical analyses were performed using Jamovi software (version 2.6.44). Descriptive statistical analysis was conducted, including absolute (n) and relative (%) frequencies for categorical variables.

The variables were organized into four groups. Sociodemographic variables included gender, age group, color/race, and place of residence. Clinical and laboratory variables included the presence of opportunistic viral infection, the type of virus identified, the occurrence of viral coinfection, and clinical outcomes. Therapeutic variables included the immunosuppressive regimen and the antiviral treatment administered.

To analyze the associations between categorical variables, including immunosuppressive regimens and therapeutic strategy in relation to the risk of coinfection, as well as the association of other variables with a positive clinical diagnosis of viral infection, Fisher's exact test was used. A significance level of 5% ($p<0.05$) was adopted.

In addition, binary logistic regression was performed to assess the association between independent variables (gender, age group, immunosuppressive regimen, and occurrence of viral infection) and hospitalizations. The results were expressed as odds ratios (OR) with corresponding 95% confidence intervals (95%CI).

For the analysis of viral coinfection, only patients with positive results for viral infection were considered. All other analyses, including associations with viral occurrence and binary logistic regression, were performed using the total study population to ensure greater statistical robustness and accuracy.

Results

Initially, 80 medical records of kidney recipient patients followed at Ophir Loyola Hospital were evaluated, from January 2022 to June 2025. Of these, two were excluded for not meeting the eligibility criteria, totaling 78 included in the analysis. Predominance of positive results for viral infections was observed in 56 patients (71.8%), while 22 (28.2%) presented negative results. Among the positive cases, two deaths (3.6%) were recorded (Table 1).

Table 1. Viral infection profile of kidney transplant recipients followed at Ophir Loyola Hospital (Jan 2022 – Jun 2025).

Variables	n (%)
All analyzed records	78 (100)
Positive for any virus	56 (71.8)
Negative for viral tests	22 (28.2)

Source: Study data. Analyzed in Jamovi (version 2.6.44).

Regarding the sociodemographic profile of the patients, a predominance of males was observed (64.3%), while females accounted for 35.7% of the cases. The most prevalent age group was 40 to 49 years (30.4%), followed by 50 to 59 years (23.2%), indicating a higher concentration of recipients in adulthood. Regarding self-reported color/race, there was a predominance of brown patients (80.4%). Concerning place of residence, most patients were from the Metropolitan Region of Belém (67.9%), followed by Northeast Pará (12.5%) and Southeast Pará (7.1%). No statistically significant association was observed between sociodemographic variables and the occurrence of viral infection, according to the analyses performed using Fisher's exact test (Table 2).

Table 2. Sociodemographic profile of kidney transplant recipients followed at Ophir Loyola Hospital (Jan 2022 – Jun 2025).

Variables	Characteristic	Positive n (%)	Negative n (%)	*p-value
Gender	Male	20 (25.6)	7 (9.0)	0.797
	Female	36 (46.2)	15 (19.2)	
Age group	20 to 29 years	10 (12.8)	5 (6.4)	0.872
	30 to 39 years	10 (12.8)	2 (2.6)	
	40 to 49 years	16 (20.5)	8 (10.3)	
	50 to 59 years	13 (16.7)	5 (6.4)	
	60 to 69 years	7 (9.0)	2 (2.6)	
Color/Race	Brown	45 (57.7)	16 (20.5)	0.425
	Yellow	2 (2.6)	0 (0.0)	
	White	5 (6.4)	2 (2.6)	
	Black	4 (5.1)	4 (5.1)	
Region of residence	Metropolitan Region	38 (48.7)	14 (17.9)	0.811
	Northeast Pará	7 (9.0)	2 (2.6)	
	Southeast Pará	4 (5.1)	3 (3.8)	
	Not informed	7 (9.0)	3 (3.8)	

*Reference value $p<0.05$. Higher values indicate statistical insignificance.
Source: Study data. Analyzed in Jamovi (version 2.6.44).

Regarding opportunistic infections, CMV was the most prevalent agent, present in approximately 83.9% of isolated infection cases, with its prevalence increasing to 96.4% when associated with other viruses. BKV was the second most frequent (7.1%), followed by EBV, hepatitis B, genital herpes, herpes zoster, anal herpes, and hepatitis A, each accounting for 1.8% of cases. These findings highlight the predominance of CMV in opportunistic infections after kidney transplantation. Coinfection was observed in 12.5% of patients.

Regarding treatment, ganciclovir was the most commonly used antiviral (89.3%), followed by acyclovir in a smaller proportion, in addition to combined regimens in specific cases. The most frequently observed adverse clinical outcomes were hospitalization (53.8%), graft loss (10.3%), graft complications (2.6%), and death (3.6%). A statistically significant association was observed between the occurrence of viral infections and adverse clinical outcomes, as determined by Fisher's exact test (p=0.01) (Table 3).

Table 3. Frequency of detected viruses, treatment, coinfection, and clinical outcomes in kidney transplant recipients followed at Ophir Loyola Hospital (Jan 2022 – Jun 2025).

Variables	Characteristic	Positive n (%)	Negative n (%)	*p-value
Detected Viruses	CMV	47 (83.9)	-	-
	CMV + BKV	4 (7.1)	-	
	CMV + EBV	1 (1.8)	-	
	CMV + Herpes Zoster	1 (1.8)	-	
	CMV + Genital Herpes + Hepatitis B	1 (1.8)	-	
	Anal Herpes	1 (1.8)	-	
	Hepatitis A	1 (1.8)	-	
Treatment	Ganciclovir	50 (89.3)	-	-
	Acyclovir	2 (3.6)	-	
	Acyclovir + Ganciclovir	3 (5.4)	-	
	Ganciclovir + Methylprednisolone Pulse Therapy	1 (1.8)	-	
Infection/Coinfection Frequency	No coinfection	48 (87.5)	-	-
	Coinfection	8 (12.5)	-	
Clinical outcomes	Hospitalization	42 (53.8)	-	0.01
	Graft loss	8 (10.3)	1 (1.3)	
	Graft complications	2 (2.6)	0 (0.0)	
	Graft rejection	1 (1.3)	0 (0.0)	
	Death	2 (3.6)	0 (0.0)	
	No hassle	1 (1.3)	20 (25.6)	

CMV: Cytomegalovirus; BKV: BKV Polyomavirus; EBV: Epstein–Barr Virus; *reference value p<0.05. Higher values indicate statistical insignificance.
Source: Study data. Analyzed in Jamovi (version 2.6.44).

An analysis of the immunosuppressive regimens used by patients who tested positive for viral pathogens revealed that the antimetabolites azathioprine (44.6%) and mycophenolate sodium (41.1%) were the most commonly used drugs. Approximately 41.1% of patients received combination drug therapy, reflecting different clinical strategies based on the patient's profile. A statistically significant association was observed, using Fisher's exact test, between regimens that included mycophenolate sodium and the presence of coinfections (p=0.006) (Table 4).

Table 4. Immunosuppressive regimens and therapeutic strategies used in kidney transplant recipients followed at Ophir Loyola Hospital (Jan 2022 – Jun 2025).

Variables	Characteristic	n (%)	No coinfection(n)	coinfection (n)	*p-value
Immunosuppressive regimens	Azathioprine	25(44.6)	25	0	0.006
	Mycophenolate sodium	23(41.1)	16	7	
	Others	8(14.3)	7	1	
Therapeutic strategy	Monotherapy	33(58.9)	28	5	1.000
	Combination therapy	23(41.1)	20	3	

*Reference value p<0.05. Higher values indicate statistical insignificance.
Source: Study data. Analyzed in Jamovi (version 2.6.44).

In the binomial logistic regression analysis, the presence of viral infection was the only factor significantly associated with hospitalization and other adverse clinical outcomes (p<0.001). Patients with positive test results were more likely to be adverse clinical outcomes compared to uninfected individuals. Other variables, including gender, age, and immunosuppressive regimen, were not significantly associated with the clinical outcomes in question (p>0.05) (Table 5).

Table 5. Binomial logistic regression analysis of factors associated with hospitalization and other adverse clinical outcomes in kidney transplant recipients followed at Ophir Loyola Hospital (Jan 2022 – Jun 2025).

Variables	Characteristic	OR	95%CI	*p-value
Gender	Female (ref)	1.00	–	–
	Male	0.17	0.02–1.31	0.174
Age group	20 to 29 years (ref)	1.00	–	–
	30 to 39 years	6.10	0.70–52.90	0.396
	40 to 49 years	1.32	0.15–11.80	0.893
	50 to 59 years	1.07	0.12–9.60	0.976
	60 to 69 years	7.64	0.89–65.50	0.343
Immunosuppressive regimens	Mycophenolate sodium (ref)	1.00	–	–
	Azathioprine	3.08	0.35–27.50	0.485
	Others	4.57	0.51–40.90	0.464
Viral infection	Positive (ref)	1.00	–	–
	Negative	1,245.00	Wide CI	<0.001

OR: odds ratio; 95%CI: 95% confidence intervals; ref: reference Characteristic (OR=1.00); *reference value p<0.05. Higher values indicate statistical insignificance.
Source: Study data. Analyzed in Jamovi (version 2.6.44).

Discussion

The present study demonstrated a high frequency of viral infections in kidney transplant recipients, reinforcing the vulnerability of this population, particularly among adult and male individuals, indicating a higher occurrence of kidney transplantation in middle-aged adults, a group more prone to the development of chronic diseases.

Most patients self-identified as brown and were residents of the Metropolitan Region of Belém. These findings reflect the predominant ethnic profile in the state of Pará[13] and also indicate a concentration of healthcare services in the capital, which may highlight regional disparities in access to post-transplant follow-up. Patients from more remote areas may face greater difficulty in maintaining clinical follow-up and undergoing routine examinations, which can increase the risk of complications and compromise treatment success.

Cytomegalovirus stood out as the main viral pathogen, reinforcing its role as the leading viral agent in the post-kidney transplant period, as widely described in the literature[14,15]. In contrast, a low prevalence of BK Polyomavirus infection was observed, differing from previous studies. Blazquez-Navarro et al.[7] identified BKV as the most prevalent viral infection, reaching up to 80% of kidney transplant recipients and being associated with complications such as nephropathy. Similarly, Oliveira et al.[11] reported a positivity rate of 52.6% in these patients. Only one patient (1.8%) tested positive for Epstein–Barr virus (EBV), which, despite its low prevalence, remains clinically relevant due to its oncogenic potential in immunosuppressed individuals[16]. These differences may be related to incomplete medical records and the absence of specific diagnostic tests, particularly molecular methods capable of detecting latent or low viral load infections.

The predominant use of ganciclovir reflects its importance in the management of these infections. However, its effectiveness may be compromised by mutations in the viral genes UL97 and UL54 of CMV, which confer resistance to the drug. In a study conducted at Ophir Loyola Hospital, resistance-associated mutations were detected in approximately 22.72% of CMV-positive samples, reducing the effectiveness of ganciclovir and leaving patients more susceptible to viral infections[17]. In cases of refractory or treatment-resistant infections, alternative strategies have been explored, such as the use of maribavir, letermovir, and virus-specific cellular therapy[18,19].

The association between viral infections and adverse clinical outcomes indicates increased susceptibility of infected patients to complications in the post-transplant period. This finding reinforces that the presence of agents such as CMV and BKV is associated with hospital morbidity, including nephropathy, interstitial fibrosis, tubular atrophy, and graft rejection[6,20]. The observed statistical significance supports this relationship and highlights the importance of early monitoring of these infections. The consistency between these findings and the literature underscores the clinical relevance of viral infections in compromising renal function and the need for early interventions in immunosuppressed patients.

The association observed between the use of mycophenolate sodium and coinfection may be related to the drug's mechanism of action, which inhibits lymphocyte proliferation, contributing to greater immunosuppression and, consequently, increased susceptibility to opportunistic infections[21,22].

This study has some limitations that should be considered when interpreting the results. Due to its cross-sectional and retrospective design, it is not possible to establish causal relationships between the analyzed variables. In addition, the small sample size may have limited the statistical power of the analyses, particularly in multivariate evaluations, contributing to imprecise estimates and wide confidence intervals. Therefore, multicenter studies with greater population diversity and longitudinal follow-up are recommended to strengthen the findings.

Furthermore, the possibility of selection bias should be considered, as only patients with complete laboratory data were included, which may not fully represent the studied population. Additionally, relevant clinical information, such as comorbidities, time since transplantation, and donor type, was not consistently available in all medical records, preventing their inclusion in the analyses and potentially influencing the observed results.

Conclusion

This study demonstrates a high prevalence of opportunistic viral infections in kidney transplant recipients in Northern Brazil, with a predominance of Cytomegalovirus. The findings may support the development of more effective protocols for monitoring, prevention, and treatment, contributing to the reduction of morbidity and mortality and to the improvement of patients' quality of life, while balancing graft rejection control with the prevention of infectious complications. Considering the current scenario of opportunistic viral infections in kidney transplant recipients, it is essential to better understand how the state of immunosuppression influences viral susceptibility and the clinical course of these individuals.

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