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BK Virus Infection and Risk Factors in Kidney Transplant Recipients

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ABSTRACT

Objective: BK virus (BKV) infection is a significant concern for kidney transplantation (KT) recipients, potentially leading to nephropathy and graft loss, particularly under intensive immunosuppression. This study investigates the prevalence of BKV infection and its associated risk factors following KT.

Materials and Methods: We conducted a retrospective cohort study on 322 KT recipients undergoing routine follow-up in our unit. BKV infection was defined as either high-level BK viruria (BKV DNA load in urine ≥10^7 copies/mL) or BKV-associated nephropathy. Risk factors were assessed using univariate and multivariate Cox regression analyses.

Results: BKV infection was diagnosed in 9.6% (n=31) of patients, with a median onset of 8.7 months (range: 3.02–31.4). Recipients with BK virus infection were more likely to have received kidneys from non-relative living donors (p=0.005). Smoking and calcineurin inhibitor treatment were more prevalent among infected patients compared to those without BKV infection (p=0.015 and p=0.034, respectively). Additionally, BKV-infected patients experienced higher rates of acute rejection episodes (p=0.009) and all-cause allograft loss (p=0.009). In univariate analysis, smoking (hazard ratio [HR]: 2.697, p=0.007), diabetes mellitus (HR: 2.207, p=0.082), non-relative living donors (HR: 4.355, p=0.001), and induction therapy with anti-thymocyte globulin (ATG) (HR: 2.146, p=0.082) were identified as potential risk factors for infection. Smoking and non-relative living donors were independent risk factors for BKV infection (HR: 2.100, p=0.046 and HR: 4.243, p=0.019, respectively).

Conclusion: While immunosuppressive therapy is a well-recognized risk factor for BKV infection, our study highlights smoking and non-relative living donors as independent risk factors. Close monitoring of high-risk recipients and smoking cessation counseling should be prioritized to mitigate BKV infection risk.

Keywords: BK viruria, non-relative living donors, rejection, renal transplantation, smoking.

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INTRODUCTION

BK virus (BKV) infection represents a significant and persistent challenge for patients undergoing kidney transplantation (KT), particularly those receiving intensive immunosuppressive treatment.[1] BKV remains latent in immunocompetent individuals following initial infection, but in transplant recipients, immunosuppression leads to viral reactivation, often resulting in nephropathy. Therefore, BK virus-associated nephropathy (BKVAN) is a substantial factor in the development of allograft failure and kidney dysfunction in KT recipients.[2] In the first year after KT, the prevalence of BKVAN ranges from 1% to 10%, with graft loss rates in affected patients reaching up to 50%.[3,4]

BKV, a double-stranded DNA virus from the Polyomavirus family, is non-enveloped with an icosahedral structure and shares 70% genomic homology with simian virus 40 (SV40), for which immunohistochemical staining aids in diagnosing BKVAN.[5] Typically contracted during childhood, the virus has a seroprevalence of 90% in adults and remains latent in renal urothelial and tubular epithelial cells. In KT recipients, BKV infection follows a sequential progression from viruria to viremia, usually emerging within six weeks.[6] Approximately 50% of patients with viremia develop BKVAN, typically within the first year post-transplant, with the highest incidence occurring between three and six months following KT. Thus, current guidelines emphasize the importance of ongoing monitoring and management of BKV infection after transplantation to minimize long-term complications and improve patient outcomes.[7]

Effective antiviral therapies for BKV infection are currently unavailable beyond reducing immunosuppressive drugs. The most effective strategy for preventing graft loss involves implementing screening protocols for early diagnosis and appropriate reduction of immunosuppression. This approach allows BKV-specific T cell-mediated immunity to be restored in recipients with persistent or increasing BK viremia, thereby preventing nephropathy.[8] Recommended strategies prioritize reducing the dosage of calcineurin inhibitors (CNI) or antiproliferative drugs.[9] However, minimizing immunosuppression increases the likelihood of donor-specific antibody formation and elevates the risk of both acute and chronic rejection. While treatments such as intravenous immunoglobulin (IVIG), quinolones, cidofovir, and leflunomide have shown varying levels of effectiveness in managing BKV infection, their therapeutic benefits remain a subject of debate.[10]

Recipient, donor, and immune system-related factors play a crucial role in the development of BK viremia. Additionally, intensive immunosuppressive therapy is a well-established risk factor for BKVAN.[11] This study aimed to assess the prevalence of BKV infection at our center, explore the therapeutic strategies used, and identify risk factors associated with BKV infection in KT recipients.

KEY MESSAGES

- In the long-term follow-up, KT recipients with BKV infection experienced higher rates of acute rejection episodes and all-cause allograft loss.
- Smoking and non-relative living donors were identified as independent risk factors for BKV infection.
- All KT recipients who smoke should be encouraged to quit smoking.

MATERIALS AND METHODS

Study Population and Data Collection

We conducted a retrospective cohort study that included 322 KT recipients from our transplantation unit, all undergoing routine follow-up. The demographic and clinical data collected included sex, age, comorbidities (such as hypertension, diabetes mellitus, and new-onset diabetes post-transplantation), smoking status, causes of end-stage renal disease (ESRD), transplantation date, donor type (living or cadaveric), induction treatment, delayed graft function (defined as the need for dialysis within the first week of KT), immunosuppressive regimens, rejection episodes, and allograft loss. Additionally, laboratory parameters were assessed, including proteinuria, estimated glomerular filtration rate (eGFR), and urine BKV viral loads. Laboratory values obtained at the third month post-transplant were considered baseline values for KT recipients. The estimated glomerular filtration rate was calculated using the creatinine-based formula from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).[12] The institutional review board approved the study design and procedures in accordance with the principles of the Declaration of Helsinki and ethical standards for human research (Gazi University Ethics Committee, Protocol ID: 2021/979, Date: 02.11.2021). As this was a retrospective study and all procedures were part of standard care, informed consent was not required.

Immunosuppression Treatments

The decision on induction therapy (none, basiliximab, or anti-thymocyte globulin) was based on the immunological risk of the recipients. In our unit, induction therapy with basiliximab was administered at a dosage of 20 mg on days 0 and 4, while the standard regimen for anti-thymocyte globulin (ATG) was 1.5 mg/kg for 4–7 days. All patients received 500 mg of intravenous methylprednisolone on the day of surgery. The

dose was halved on subsequent days and then switched to 20 mg of oral prednisolone daily. The prednisolone dose was gradually reduced by 5 mg every two weeks until a maintenance dose of 5–10 mg was reached. Unless contraindicated, all patients continued to receive at least 5 mg of prednisolone during routine follow-up. Maintenance therapy consisted of a combination of prednisolone and a CNI, such as tacrolimus or cyclosporine, along with an antimetabolite, either mycophenolate mofetil (MMF) or azathioprine. In cases of intolerable side effects, mammalian target of rapamycin inhibitors (mTORi) were used.

Definition and Screening of BKV Infection

At our institution, BKV-DNA levels in urine were monitored using quantitative polymerase chain reaction (qPCR) at systematically scheduled intervals. Monitoring was performed monthly during the first three months post-transplant and then every three months until the end of the first year. Additionally, measurements were taken when an allograft biopsy was warranted or when kidney allograft dysfunction was suspected.

BKV infection was defined by the presence of high-level BK viruria in urine or the occurrence of BKVAN. High-level BK viruria was characterized by a BKV DNA load in urine of $\geq 10^7$ copies/mL. Kidney biopsies were performed to diagnose BKVAN if a persistent increase in urine BKV DNA levels of $\geq 10^7$ copies/mL was detected in two readings at least two weeks apart. The diagnosis of BKVAN was confirmed through histopathological examination and positive immunohistochemical staining using immunoperoxidase for SV40 antigen.

Statistical Analysis

KT recipients were categorized into two groups based on the presence or absence of BKV infection. Demographic data, laboratory parameters, and transplantation-related factors were then compared between these groups. Numerical data were summarized using descriptive statistics according to their distribution. Variables with a normal distribution are presented as means with standard deviations, while those without a normal distribution are reported as medians with interquartile ranges. Nominal data are described using counts (n) and percentages (%). The Mann-Whitney U test was applied to numerical variables that did not follow a normal distribution, while the independent samples t-test was used for normally distributed variables to compare the groups. For nominal variables, the Chi-square or Fisher's exact test was utilized. Cox regression analyses were conducted to identify independent risk factors associated with BKV infection. When selecting variables for the Cox regression analysis, their clinical significance regarding BKV infection was carefully assessed. Potential risk factors were identified by reviewing previous studies and relevant literature. Variables with a p-value of less than 0.1 in the univariate analysis were selected for inclusion in the multivariate analysis. A p value of <0.05 was considered the threshold for statistical significance. All statistical analyses were conducted using SPSS software, version 20.0 (IBM Corp., Chicago, IL, USA).

RESULTS

A total of 322 patients were included in this analysis, with a median follow-up duration of 116 (78–169) months. During routine follow-up, 9.6% (n=31) of participants developed BKV infection. The study cohort comprised 35% female participants, with a median age of 45 (37–56) years. The use of ATG for induction therapy was more common in recipients who developed BKV infection (64% vs. 40%, p=0.007). Relative living donors were more prevalent among patients without BKV infection (59% vs. 29%, p=0.001), while non-relative living donors were more common among recipients with BKV infection (39% vs. 18%, p=0.005). Furthermore, recipients with BKV infection demonstrated a higher prevalence of smoking (42% vs. 22%, p=0.015) and CNI treatment (100% vs. 87%, p=0.034). KT recipients with BKV infection experienced higher rates of rejection episodes (32% vs. 14%, p=0.009) and all-cause graft failure (29% vs. 12%, p=0.009) during routine follow-up. Additionally, the eGFR of recipients with BK virus infection were 48 (10–59), compared to 66 (44–83) mL/min/1.73 m^2 in those without infection at the last follow-up (p=0.002). Other demographic characteristics remained comparable across the study population, as detailed in Table 1.

The median urine BK virus polymerase chain reaction (BKV-PCR) level at diagnosis was 1.8 x 10^8 copies/mL (2.2 x 10^7 – 7.6 x 10^8). The median time to BKV infection was 8.7 (3.02–31.4) months, with 55% (n=17) of cases emerging within the first year post-transplant. The median time for urine BK viruria to become negative was 4 (3–8) months. A total of six (19%) recipients with BKV infection lost their allograft function. Immunosuppressive doses were reduced in 26 (84%) patients, while in five (16%) patients, antimetabolite treatment was switched to mTORi. Additionally, six (19%) patients received fluoroquinolones, six (19%) were treated with IVIG, one (3%) received leflunomide, and one (3%) was given cidofovir. Immunosuppressive management and therapeutic approaches for BKV infection in KT recipients are shown in Figure 1.

Possible risk factors for BKV infection in KT recipients, including male sex, age, smoking, diabetes mellitus, preemptive transplantation, delayed graft function, donor source, induction therapy, maintenance immunosuppressive

Table 1. Demographic characteristics and clinical outcomes of patients with BK virus infection

	Total n=322	No BKV infection n=291 (90.4%)	BKV infection n=31 (9.6%)	p*
Age at transplantation (years)	45 (37–56)	45 (37–56)	49 (34–55)	0.943
Female sex, n (%)	114 (35)	107 (37)	7 (23)	0.116
DM, n (%)	35 (11)	29 (10)	6 (19)	0.126
HT, n (%)	231 (72)	207 (71)	24 (77)	0.535
CAD, n (%)	35 (11)	30 (10)	5 (16)	0.322
NODAT, n (%)	56 (17)	52 (18)	4 (13)	0.488
Smoking status, n (%)	78 (24)	65 (22)	13 (42)	**0.015**
Cause of ESRD, n (%)				
HT	30 (9)	27 (9)	3 (10)	1.000
DM	21 (7)	17 (6)	4 (13)	0.130
Glomerulonephritis	68 (21)	65 (22)	3 (10)	0.111
Urological abnormalities	24 (8)	22 (8)	2 (6)	1.000
Other causes	104 (32)	93 (32)	11 (35)	0.690
Unknown etiology	75 (23)	67 (23)	8 (26)	0.728
Dialysis duration (years)	3 (1.5–7)	3 (1.5–7.5)	5 (2.5–10)	0.136
Donor type, n (%)				
Living-related	181 (56)	172 (59)	9 (29)	**0.001**
Living-unrelated	63 (20)	51 (18)	12 (39)	**0.005**
Deceased donor	78 (24)	68 (23)	10 (32)	0.275
Induction therapy, n (%)				
No induction	100 (31)	93 (31)	7 (23)	0.283
Basiliximab	87 (27)	83 (29)	4 (13)	0.087
ATG	135 (42)	115 (40)	20 (64)	**0.007**
Preemptive transplantation, n (%)	86 (27)	76 (26)	10 (32)	0.463
Delayed graft function, n (%)	34 (11)	30 (10)	4 (13)	0.552
IS therapy, n (%)				
CNI	285 (88)	254 (87)	31 (100)	**0.034**
Antimetabolites	276 (86)	248 (85)	28 (90)	0.593
mTORi	61 (19)	58 (20)	3 (10)	0.228
eGFR at baseline (mL/min/1.73 m^2)	73 (59–91)	73 (58–92)	66 (57–85)	0.430
Proteinuria at baseline (mg/24h)	250 (172–430)	241 (170–408)	321 (181–430)	0.275
Rejection episode, n (%)	51 (16)	41 (14)	10 (32)	**0.009**
eGFR at last follow-up (mL/min/1.73 m^2)	63 (40–82)	66 (44–83)	48 (10–59)	**0.002**
Allograft loss, n (%)	44 (14)	35 (12)	9 (29)	**0.009**
Follow-up duration (months)	116 (78–169)	118 (80–179)	79 (45–121)	**0.001**

ATG: Anti-thymocyte globulin; CAD: Coronary artery disease; CNI: Calcineurin inhibitors; DM: Diabetes mellitus; ESRD: End-stage renal disease; HT: Hypertension; IS: Immunosuppressive treatment; eGFR: Estimated glomerular filtration rate; mTORi: Mammalian target of rapamycin inhibitors; NODAT: New-onset diabetes after transplantation; *: The p-values indicate statistical comparisons between the "No BKV Infection" and "BKV Infection" groups.

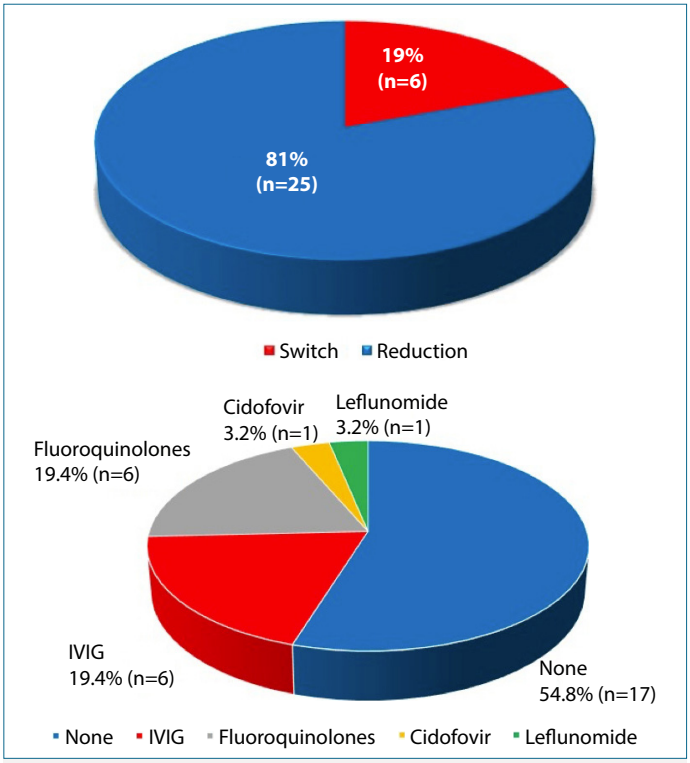

Figure 1. Immunosuppressive management and therapeutic approaches for BK virus (BKV) infection in kidney transplant recipients.

treatments (CNI and antimetabolites), and rejection episodes in the first six months post-transplant, were analyzed using Cox regression analysis. Univariate analysis identified several potential risk factors, including smoking (hazard ratio [HR]: 2.697, 95% confidence interval [CI]: 1.320–5.514), diabetes mellitus (HR: 2.207, 95% CI: 0.904–5.390), use of non-relative living donors (HR: 4.355, 95% CI: 1.831–10.360), and induction therapy with ATG (HR: 2.146, 95% CI: 0.907–5.077). However, in the multivariate analysis, only smoking and the use of non-relative living donors remained statistically significant. The respective HRs for these factors were 2.100 (95% CI: 1.012–4.360; p=0.046) and 4.243 (95% CI: 1.264–14.239; p=0.019) (Table 2).

DISCUSSION

In our study, the prevalence of BKV infection among KT recipients was 9.6%. Patients with BKV infection had shorter follow-up periods compared to those without infection. Moreover, these patients experienced higher rates of rejection episodes and allograft failure in long-term follow-up. Additionally, our study identified non-relative living donors and smoking habits as independent risk factors for BKV infection. These findings highlight the association between specific donor types and lifestyle factors, such as smoking, with an increased risk of BKV infection in KT recipients.

This study revealed that 9.6% of KT recipients developed BKV infection, with a median diagnosis time of 8.7 months. Notably, previous studies by Chan et al. (20.9%), Dogan et al. (15.8%), and Skulratanasak et al. (30%) have reported a higher prevalence for BKV infection than our study.[13–15] These disparities across different centers may be attributed to variations in the definitions of infection used in these studies. For instance, the inclusion of patients with low urine BKV levels in the study by Skulratanasak et al. may have contributed to the higher reported BKV infection rates among their patients. Additionally, differences in immunosuppressive protocols among medical centers may explain the variability in prevalence. In the TRANSFORM study (Trial to Reduce Immunosuppression Following Living Donor Kidney Transplantation), researchers found lower rates of cytomegalovirus (CMV) and BK virus infections in recipients treated with everolimus combined with reduced exposure to CNI compared to standard therapy.[16] The immune status of KT recipients plays a crucial role in the development of BKV infection.

Potent immunosuppressive regimens used post-transplant are believed to contribute to BKVAN and allograft kidney damage.[17] In the mid-1990s, new immunosuppressive agents such as tacrolimus and mycophenolate were introduced, and the frequency of BKVAN, previously a rare clinical problem in KT, began to rise. Over the years, it has become increasingly clear that immunosuppressive treatment regimens play a critical function in the emergence of BKVAN. Therefore, the American Society of Transplantation recommends reducing immunosuppressive treatment in KT recipients with two approaches for managing BKV infection. One approach involves initially decreasing the dose of CNI by 25% to 50%, followed by a 50% reduction in MMF until discontinuation. The other approach suggests initially reducing MMF by 50%, followed by a 25% to 50% reduction in CNI, with eventual discontinuation of MMF.[6] We found that ATG treatment for induction and CNI treatment post-transplant were more prevalent in patients with BKV infection. Consistent with these guidelines, our primary approach to managing BKV infection was adjusting immunosuppressive medication doses in affected patients.

Additionally, allograft loss was observed in 29% of our patients during long-term follow-up. Similarly, Gras et al.[18] reported that 34% of patients lost their allograft, mainly due to BKV-induced graft dysfunction or chronic humoral rejection during follow-up. They also found that after reducing immunosuppressive therapy, the acute rejection rate was higher than that of matched controls (13.8% vs. 3%, p=0.003). The increase in acute rejection and allograft loss observed in

Table 2. Univariate and multivariate analysis of risk factors for BK virus infection

	Univariate analysis (HR, 95% CI)	p	Multivariate analysis (HR, 95% CI)	p
Male sex	1.911 (0.823–4.434)	0.132		
Age	0.994 (0.967–1.022)	0.677		
Smoking status	2.697 (1.320–5.514)	0.007	2.100 (1.012–4.360)	**0.046**
DM	2.207 (0.904–5.390)	0.082	1.893 (0.768–4.664)	0.166
Preemptive transplantation	1.496 (0.703–3.183)	0.296		
Delayed graft function	1.114 (0.389–3.188)	0.840		
Donor type				
Living-related				
Living-unrelated	4.355 (1.831–10.360)	0.001	4.243 (1.264–14.239)	**0.019**
Deceased donor	2.247 (0.912–5.540)	0.079	1.745 (0.460–6.624)	0.413
Induction therapy				
No induction				
Basiliximab	0.576 (0.168–1.968)	0.379	0.300 (0.073–1.236)	0.095
ATG	2.146 (0.907–5.077)	0.082	0.950 (0.253–3.568)	0.939
CNI treatment	24.936 (0.252–2470.208)	0.170		
Antimetabolite therapy	1.757 (0.533–5.791)	0.355		
Rejection episode (first 6 months post-transplantation)	2.007 (0.609–6.618)	0.252		

HR: Hazard ratio; CI: Confidence interval; ATG: Anti-thymocyte globulin; CNI: Calcineurin inhibitors; DM: Diabetes mellitus.

patients with BKV infection in our study may be attributed to this phenomenon. Although immunosuppression was reduced to prevent allograft loss due to BKV infection, the risk of rejection episodes and allograft failure during long-term follow-up may have increased. These findings highlight the potential for acute allotransplant rejection, which should be carefully considered during follow-up. In particular, patients with increasing serum creatinine levels despite a decreasing viral load should be evaluated for a renal biopsy.

Our analysis identified non-relative living donors and smoking as independent risk factors for BKV infection. These findings may be linked to greater human leukocyte antigen (HLA) incompatibility in transplants from unrelated donors. Previous studies have demonstrated that HLA mismatching increases the likelihood of developing BKVAN.[19,20] Schnitzler et al.[21] reported similar findings for CMV, showing that kidney transplant recipients with HLA-DR mismatches had a higher incidence of CMV disease. This suggests that the degree of HLA compatibility could be a crucial factor in susceptibility to viral infections post-transplantation. On the other hand, patients with better HLA compatibility may have an advantage, as they are less likely to require intensive immunosuppressive treatment.

The harmful effects of smoking are well-documented in individuals with chronic kidney disease, including KT recipients.[22] Research has shown that smoking directly damages the kidneys through oxidative stress-induced nephrotoxicity and indirectly contributes to kidney injury by exacerbating risk factors such as hypertension and diabetes.[23, 24] Smoking is widely recognized as a contributing factor to numerous infectious diseases, particularly those affecting the respiratory system.[25] Moreover, smoking has been identified as a risk factor for urinary tract infections, especially those associated with catheter use and pregnancy.[26,27] Ma et al.[28] previously reported that tobacco smoking significantly alters the composition of the urinary tract microbiome, with a more pronounced effect in patients with bladder cancer. Thus, it is plausible to suggest that these microbiome changes could potentially facilitate BKV infection in the immunosuppressed environment of KT recipients. To the best of our knowledge, this is the first study to identify smoking as a risk factor for BKV infection.

The main limitations of this study stem from its retrospective and single-center design, which inherently limits the generalizability of the findings. The sample size was restricted to patients from a single institution, resulting in a relatively small cohort that may not fully represent the broader patient

population. Moreover, the study's ability to comprehensively evaluate patients was limited by the small number of allograft biopsies, which were only performed in patients with clinically significant BKVAN and rejection. This approach may have overlooked subtle or less severe cases of rejection or BKVAN that with a more comprehensive biopsy protocol could have detected. Furthermore, the absence of routine serum BKV-DNA testing by PCR at our institution prevented consistent viral load monitoring across all patients. Routine testing could have provided valuable data for assessing the relationship between viral activity and graft outcomes. Finally, some missing HLA data prevented a thorough analysis of potential correlations between HLA mismatches and the development of BKV infection, further limiting the depth of our analysis.

CONCLUSION

In conclusion, balancing immunosuppressive therapies with the risk of allotransplant rejection and BKV infection is essential for the management of KT recipients. Regular monitoring and adjusted immunosuppression are crucial to preventing BKV infection after transplantation. Non-relative living donors and smoking are significant determinants of BKV infection. All KT recipients who smoke should be encouraged to quit smoking.

Ethics Committee Approval: The Gazi University Clinical Research Ethics Committee granted approval for this study (date: 02.11.2021, number: 2021/979).

Author Contributions: Concept – OFA, AD, SY; Design – OFA, SY, CC; Supervision – OFA, OH; Resource – YE, GG; Materials – AD, CC, HSY; Data Collection and/or Processing – AD, CC, HSY; Analysis and/or Interpretation –OFA, OH, GG; Literature Search – OFA, SY, YE; Writing – OFA; Critical Reviews – OFA, YE, GG.

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REFERENCES

1. Nourie N, Boueri C, Tran Minh H, Divard G, Lefaucheur C, Salmona M, et al. BK Polyomavirus Infection in Kidney Transplantation: A Comprehensive Review of Current Challenges and Future Directions. Int J Mol Sci 2024;25(23). [CrossRef]
2. Fernández-Ruiz M. BK polyomavirus-associated nephropathy, graft inflammation, and immunosuppression: Shedding light on the conundrum. Transpl Infect Dis 2024;26(2):e14272. [CrossRef]
3. Hassan S, Mittal C, Amer S, Khalid F, Patel A, Delbusto R, et al. Currently recommended BK virus (BKV) plasma viral load cutoff of ≥4 log10/mL underestimates the diagnosis of BKV-associated nephropathy: a single transplant center experience. Transpl Infect Dis 2014;16(1):55-60. [CrossRef]
4. Borriello M, Ingrosso D, Perna AF, Lombardi A, Maggi P, Altucci L, et al. BK Virus Infection and BK-Virus-Associated Nephropathy in Renal Transplant Recipients. Genes (Basel) 2022;13(7):1290. [CrossRef]
5. Kotla SK, Kadambi PV, Hendricks AR, Rojas R. BK polyomavirus-pathogen, paradigm and puzzle. Nephrol Dial Transplant 2021;36(4):587-93. [CrossRef]
6. Rinaldo CH, Tylden GD, Sharma BN. The human polyomavirus BK (BKPyV): virological background and clinical implications. Apmis 2013;121(8):728-45. [CrossRef]
7. KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant 2009;9 (Suppl 3):S1-155. [CrossRef]
8. Parajuli S, Jorgenson M, Meyers RO, Djamali A, Galipeau J. Role of Virus-Specific T Cell Therapy for Cytomegalovirus and BK Infections in Kidney Transplant Recipients. Kidney360 2021;2(5):905-15. [CrossRef]
9. Kotton CN, Kamar N, Wojciechowski D, Eder M, Hopfer H, Randhawa P, et al. The Second International Consensus Guidelines on the Management of BK Polyomavirus in Kidney Transplantation. Transplantation 2024;108(9):1834-66. [CrossRef]
10. Santeusanio AD, Lukens BE, Eun J. Antiviral treatment of BK virus viremia after kidney transplantation. Am J Health Syst Pharm 2017;74(24):2037-45. [CrossRef]
11. Beimler J, Sommerer C, Zeier M. The influence of immunosuppression on the development of BK virus nephropathy-- does it matter? Nephrol Dial Transplant 2007;22 (Suppl 8):viii66-viii71. [CrossRef]
12. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150(9):604-12. [CrossRef]
13. Skulratanasak P, Mahamongkhonsawata J, Chayakulkeereeb M, Larpparisutha N, Premasathiana N, Vongwiwatana A. BK Virus Infection in Thai Kidney Transplant Recipients: A Single-Center Experience. Transplant Proc 2018;50(4):1077-9. Erratum in: Transplant Proc 2019;51(9):3191. [CrossRef]
14. Chan BD, Wong G, Jiang Q, Lee MM, Wong WY, Chen F, et al. Longitudinal study of BK Polyomavirus outcomes, risk factors, and kinetics in renal transplantation patients. Microb Pathog 2020;142:104036. [CrossRef]

15. Dogan SE, Celebi ZK, Akturk S, Kutlay S, Tuzuner A, Keven K, et al. Prevalence and Risk Factors of BK Viremia in Patients With Kidney Transplantation: A Single-Center Experience From Turkey. Transplant Proc 2017;49(3):532-6. [CrossRef]
16. Berger SP, Sommerer C, Witzke O, Tedesco H, Chadban S, Mulgaonkar S, et al; TRANSFORM investigators. Two-year outcomes in de novo renal transplant recipients receiving everolimus-facilitated calcineurin inhibitor reduction regimen from the TRANSFORM study. Am J Transplant 2019;19(11):3018-34. [CrossRef]
17. Jamboti JS. BK virus nephropathy in renal transplant recipients. Nephrology (Carlton) 2016;21(8):647-54. [CrossRef]
18. Gras J, Le Flécher A, Dupont A, Vérine J, Amara A, Delaugerre C, et al. Characteristics, risk factors and outcome of BKV nephropathy in kidney transplant recipients: a case-control study. BMC Infect Dis 2023;23(1):74. [CrossRef]
19. Patel H, Rodig N, Agrawal N, Cardarelli F. Incidence and risk factors of kidney allograft loss due to BK nephropathy in the pediatric population: A retrospective analysis of the UNOS/OPTN database. Pediatr Transplant 2021;25(5):e13927. [CrossRef]
20. Awadalla Y, Randhawa P, Ruppert K, Zeevi A, Duquesnoy RJ. HLA mismatching increases the risk of BK virus nephropathy in renal transplant recipients. Am J Transplant 2004;4(10):1691-6. [CrossRef]
21. Schnitzler MA, Lowell JA, Hmiel SP, Hardinger KL, Liapis H, Ceriotti CS, et al. Cytomegalovirus disease after prophylaxis with oral ganciclovir in renal transplantation: the importance of HLA-DR matching. J Am Soc Nephrol 2003;14(3):780-5. [CrossRef]
22. Lo R, Narasaki Y, Lei S, Rhee CM. Management of traditional risk factors for the development and progression of chronic kidney disease. Clin Kidney J 2023;16(11):1737-50. [CrossRef]
23. Messner B, Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. Arterioscler Thromb Vasc Biol 2014;34(3):509-15. [CrossRef]
24. InterAct Consortium; Spijkerman AM, van der A DL, Nilsson PM, Ardanaz E, Gavrila D, Agudo A, et al. Smoking and long-term risk of type 2 diabetes: the EPIC-InterAct study in European populations. Diabetes Care 2014;37(12):3164-71. [CrossRef]
25. Arcavi L, Benowitz NL. Cigarette smoking and infection. Arch Intern Med 2004;164(20):2206-16. [CrossRef]
26. Wallin HP, Gissler M, Korhonen PE, Ekblad MO. New insights into smoking and urinary tract infections during pregnancy using pregnancy-pair design: A population-based register study. Acta Obstet Gynecol Scand 2023;102(1):25-32. [CrossRef]
27. Mercadel AJ, Holloway SB, Saripella M, Lea JS. Risk factors for catheter-associated urinary tract infections following radical hysterectomy for cervical cancer. Am J Obstet Gynecol 2023;228(6):718.e1-718.e7. [CrossRef]
28. Ma W, Zhang W, Shen L, Liu J, Yang F, Maskey N, et al. Can Smoking Cause Differences in Urine Microbiome in Male Patients With Bladder Cancer? A Retrospective Study. Front Oncol 2021;11:677605. [CrossRef]