*Original Article*

# Detection of BK virus by PCR in Suspected Graft Dysfunction in Renal Transplant Recipients and Cystitis in Bone Marrow Transplant Recipients

*Abu Hasan[1#], Rummana Rahim[2#], Nazmul Hasan[3], Quazi Smita Haq[4], Fahmida Begum[5], Ebadur Rahman[6], Abu Jafar Mohammed Saleh[7], Mizanur Rahman[8]* *( # Abu Hasan & Rummana Rahim contributed equally to this work.)*

1. Chief Scientific Officer, Molecular Diagnostics Lab, Evercare Hospital Dhaka
2. Associate Consultant, Molecular Diagnostics Lab, Evercare Hospital Dhaka
3. Scientific Officer, Molecular Diagnostics Lab, Evercare Hospital Dhaka
4. Associate Consultant, Department of Hematology, Evercare Hospital Dhaka
5. Senior Consultant, Department of Nephrology, Evercare Hospital Dhaka.
6. Senior Consultant & Coordinator, Department of Nephrology, Evercare Hospital Dhaka.
7. Senior Consultant & Coordinator, Department of Hematology, Evercare Hospital Dhaka.
8. Senior Consultant, Molecular Diagnostics Lab, Evercare Hospital Dhaka.

***Address for Correspondence:***
Dr. Mizanur Rahman
Senior Consultant,
Molecular Diagnostics Lab,
Evercare Hospital Dhaka
mizanur.rahman@evercarebd.com

***Submitted:*** *05 – Jul - 2024*
***Accepted:*** *28 – Dec - 2024*

**ABSTRACT**

BK virus (BKV) is a prevalent infectious agent known to be a leading cause of nephropathy and graft loss among kidney transplant recipients. Furthermore, it has emerged as a significant concern for individuals undergoing hematopoietic stem cell transplantation, often presenting as hemorrhagic cystitis. However, the incidence of BK virus infection among transplant recipients in Bangladesh is unknown. Routine BKV PCR data were analyzed from hospital record from a total of 95 renal transplant recipients who were suspected of experiencing graft dysfunction, and 16 bone marrow transplants patients who developed cystitis and/or hematuria between October 2021 and December 2024. BKV was detected in 17 (17.89%) out of the 95 renal transplant recipients and in 11 (68.75%) of the 16 bone marrow transplant recipients. Co-infection with cytomegalovirus (CMV) was observed in 2 out of the 17 renal transplant recipients and in 5 out of the 11 bone marrow transplant recipients. Thus, prompt BKV identification by PCR may be important to decrease the likelihood of BKV associated nephropathy induced graft dysfunction and cystitis in bone marrow transplant.

**Keywords:** *BK virus, Renal transplant, Bone marrow transplant, Cystitis.*

## INTRODUCTION

BK virus (BKV) is a double stranded DNA virus, member of the Betapolyomavirus genus in the Polyomaviridae family[1]. BKV has a small, nonenveloped, icosahedral capsid with a diameter of 40 to 44 nm comprised of the virus-encoded capsid proteins VP1, VP2, and VP3[2]. VP1 is the sole viral protein that is externally exposed on the virion's surface, and it plays a crucial role in attaching the virus to host cell receptors, facilitating the virus's entry into the host cell. Furthermore, VP2 and VP3 have specific binding sites that interact with histones and genomic DNA[3].

BKV is widely prevalent in general population with over 80% individuals having antibodies against BK virus[4,5]. Usually, primary BKV infection occurs during childhood and then the virus remains dormant throughout life, especially in the kidneys and urinary system. It does not cause significant morbidity in healthy individuals[6,7]. The most common mode of transmission is through respiratory secretions or urine since infected individuals periodically excrete virus in the urine. Viral spread to other organs is believed to be via bloodstream and in immunocompetent individuals, it remains clinically silent in renal tubular epithelium[8]. Latent BKV becomes reactive in immunosuppressed individuals, such as pregnancy, HIV infection or transplantation; in such patients BKV develops BKV-related renal failure, known as BK virus-associated nephropathy (BKVAN). It is reported that BKV became reactivated in 10-60% of the cases of renal transplant patients from which 1-5% would undergo nephropathy; half of the patients with nephropathy rejected their transplanted kidney. Risk factors of BKV-induced nephropathy are not well-known. However,

immunosuppressant drugs, transplantation and BKV itself account as the major risk factors[9-12].

On the other hand, hemorrhagic cystitis (HC) is a well-recognized BKV associated complication in hematopoietic stem cell transplant (HSCT) or bone marrow transplant (BMT) recipients[13]. However, as of now, there have been no reported cases of BKV association with bone marrow transplant patients in Bangladesh since its initiation from 2014.

There have been very few studies conducted in our country pertaining to BKV. A study conducted by Nessa et al. in Bangladesh focused on renal transplant recipients. The study revealed that 26.6% of randomly selected renal transplant patients were infected by BKV, while there was no indication of BKV infection in the healthy control group[14]. This finding underscores the prevalence of BKV infection among renal transplant recipients in the region, highlighting the importance of monitoring and managing this viral infection in this vulnerable population[14].

Considering the high prevalence of renal failure and the role of BKV in graft rejection, this study aimed to determine the incidence of BKV infection in suspected graft disfunction in renal transplant and allogenic bone marrow transplant recipients referred to our hospital.

## MATERIAL AND METHODS

### Patient Population and Data Collection

The data of the patients were taken from hospital information system of Evercare Hospital Dhaka, situated at Bashundhara Residential Area, Dhaka, Bangladesh and the study period was October 2021 to December 2024. We included a total of 111 cases who underwent renal or bone marrow transplantation. Patients lacking any history of bone marrow or renal transplantation were excluded from this study. As it is a data based retrospective study, patient consent is not required in these cases.

### Viral nucleic acid extraction and purification:

Urine or blood samples were collected for BK virus isolation. DNA mini kit, Qiagen, Germany was used for viral DNA extraction. DNA was extracted from 200 µl of urine/serum sample following kit manufacturer's protocol and stored at -80˚C.

### PCR protocol

CE-IVD approved commercial real time PCR kit from GeneProof (BK Virus PCR Kit) was used for the detection of BK virus. 30 µl PCR master mix was added with 10 µl of each isolated nucleic acid sample, negative control and positive control in 0.2ml PCR tube (nuclease free water as negative and synthetic DNA as positive control was used). QuantStudio 5 Dx platform (Applied Biosystems, USA) was used for PCR amplification according to kit manufacturer's instruction which was programmed as follows: 37 °C for 2 min, 95 °C for 10 min, 45 cycles of 95°C for 5 s, 60°C for 40 s and 72°C for 20 s. Signal was acquired at 60˚C, and analysis was performed on the linear scale. Thresholds were set manually on each run. Fluorescence detected in FAM channel was for amplification of BK virus and HEX channel was for amplification of internal control.

## RESULT

### Demography

In a cohort of 111 transplant recipients, males constituted the majority 68(61.26%), outnumbering females. The median age of the study population was 40 years. Among the 111 cases, 95 (85.59%) had undergone renal transplantation, while 16 (14.41%) had received bone marrow transplants. The larger proportion of renal transplant recipients falls within the age group of over 45 years (40%; 38 out of 95), while in bone marrow transplant cases, half of the population are below 30 years of age (50%; 8 out of 16) (Table-1).

**Table1:** Demographics of study population

| Age | Total cases, (%) (n=111) | Renal transplanted, (%) (n=95) | | Bone marrow transplanted, (%) (n=16) | |
|---|---|---|---|---|---|
| | | Male | Female | Male | Female |
| Below 30yrs | 30 (27.03) | 16 (16.84) | 6 (6.32) | 6 (37.5) | 2 (12.5) |
| 30-45yrs | 36 (32.43) | 19 (20) | 13 (13.68) | 3 (18.75) | 1 (6.25) |
| >45yrs | 45 (40.54) | 23 (24.21) | 18 (18.95) | 1 (6.25) | 3 (18.75) |
| BKV positive | 28 (25.23) | 12 (12.63) | 5 (5.26) | 7 (43.75) | 4 (25) |
| BKV negative | 83 (74.77) | 47 (49.47) | 31 (32.63) | 3 (18.75) | 2 (12.5) |

**BKV detection in renal transplant recipients**

Virological analysis of plasma or urine samples by PCR showed the presence of detectable BKV DNA in 17 (17.89%) of the post-transplantation patients out of a total of 95 renal transplant cases having suspicion of graft disfunction. Of them, 74 were blood samples as preferred by the clinician and the positivity rate was 9.46% (7/74). The remaining 21 samples were urine specimens as preferred by the clinician and out of them 9 (42.86%) were tested positive for BKV. Kidney transplant recipients with BKV positivity had elevated serum creatinine levels, with a median value of 1.8 mg/dl (IQR: 1.56-3.0). All renal transplant recipients who tested positive for BKV exhibited graft dysfunction.

**BKV and CMV/EBV/HHV-6 co-infection in renal transplanted cases**

As transplant patients often got infection with CMV, EBV, HHV [15] along with BKV 15 renal transplant recipients' sample were further evaluated for CMV, EBV, and HHV6. We found 7 positives for CMV and 1 showed co-infection with CMV and EBV (Table-2).

**BKV detection in bone marrow transplant recipients**

Out of 16 BMT recipients with suspected cystitis, 11 (68.75%) tested positive for BKV. Majority cases were tested positive (~91.67%; 11/12) using urine specimens, while the remaining 4 were diagnosed through blood specimens. Among the BMT recipients with BKV positivity, their serum creatinine levels were within the normal range, with a median value of 0.77 mg/dl (IQR: 0.65-1.0). All bone marrow transplant recipients who tested positive for BKV exhibited hemorrhagic cystitis (Table-3).

**Table 2:** Viral load and serum creatinine correlation in renal transplant recipients

| Sl. no | Highest level of BKV viral load | | Serum creatinine | Corresponding CMV/EBV/HHV6 infection | Clinical Diagnosis | Transplant type (years) |
|---|---|---|---|---|---|---|
| | Blood | Urine | | | | |
| 1 | | 1x108 | 4.26 | CMV & EBV positive | Chronic graft rejection | Kidney (2020) |
| 2 | | 1x105 | 1.32 | | Graft dysfunction | Kidney (2021) |
| 3 | 1.5x105 | | 1.79 | | Graft dysfunction | Kidney (2021) |
| 4 | 4.9x103 | | 2.01 | | Graft dysfunction | Kidney (2021) |
| 5 | 650 | | 1.8 | | Graft dysfunction | Kidney (2022) |
| 6 | 943 | | 2.84 | | Graft dysfunction | Kidney (2021) |
| 7 | | 1x107 | 8.43 | | Graft dysfunction | Kidney (2022) |
| 8 | 950 | | 3.0 | | Graft dysfunction | Kidney (2022) |
| 9 | 3.3x106 | | 1.56 | CMV positive | Graft dysfunction | Kidney (2022) |
| 10 | | 2.1x107 | 1.6 | | Graft dysfunction | Kidney (2022) |
| 11 | | 1.2x109 | 1.45 | | Graft dysfunction | Kidney (2022) |
| 12 | | 1x109 | 1.37 | | Graft dysfunction | Kidney (2022) |
| 13 | | 2.8x108 | 2.14 | | Graft dysfunction | Kidney (2023) |
| 14 | | 1.8x108 | 1.6 | | Graft dysfunction | Kidney (2023) |
| 15 | | 1x104 | 16.18 | | Graft dysfunction | Kidney (2022) |
| 16 | | 1.1x104 | 3.9 | | Graft dysfunction | Kidney (2022) |
| 17 | 2.6x104 | | 1.7 | | Graft dysfunction | Kidney (2022) |

**Table3:** Viral load and serum creatinine correlation in bone marrow transplant recipients

| Sl. no | Highest level of BKV viral load | | Serum creatinine | Corresponding CMV/EBV/HHV6 6 infection | Clinical Diagnosis | Transplant type (years) |
|---|---|---|---|---|---|---|
| | Blood | Urine | | | | |
| 1 | | 7.4x108 | 0.77 | CMV, EBV & HHV6 positive | Hemorrhagic cystitis | Bone marrow (2020) |
| 2 | | 2.5x107 | 0.82 | Negative | BKV cystitis | Bone marrow (2021) |
| 3 | | 4.7x108 | 1.1 | CMV positive | Hemorrhagic cystitis | Bone marrow (2022) |
| 4 | | 7.9x106 | 1.0 | CMV positive | BKV cystitis | Bone marrow (2021) |
| 5 | | 1.8x104 | 0.79 | Negative | BKV cystitis | Bone marrow (2023) |
| 6 | | 7.1x108 | 0.35 | CMV positive | Hemorrhagic cystitis | Bone marrow (2023) |
| 7 | | 4.1x107 | 0.57 | CMV positive | Hemorrhagic cystitis | Bone marrow (2023) |
| 8 | | 6.3x106 | 1.1 | Negative | Hemorrhagic cystitis | Bone marrow (2023) |
| 9 | | 2.5x109 | 0.69 | HHV6 positive | Hemorrhagic cystitis | Bone marrow (2023) |
| 10 | | 4.9x104 | 0.65 | Negative | Hemorrhagic cystitis | Bone marrow (2023) |
| 11 | | 1x103 | 0.7 | Negative | Hemorrhagic cystitis | Bone marrow (2023) |

**BKV and CMV/EBV/HHV-6 co-infection in bone marrow transplanted cases**

BKV positive BMT recipients underwent evaluation for CMV, EBV, and HHV6. In terms of co-infections, 4 cases displayed positivity for both CMV and BKV, 1 case BKV and HHV6 positive while 1 case exhibited co-infection involving CMV, EBV, HHV6, and BKV. BKV viral load was found higher in most of the co-infection cases (Table-3).

## DISCUSSION

Renal transplantation, an advanced form of renal replacement therapy, has emerged as the preferred approach for managing patients with end-stage renal disease[16].The BK virus constitutes a significant risk factor for graft dysfunction and potential graft loss following kidney transplantation[17,18]. Renal allograft recipients rely on ongoing immunosu-ppressive treatment, and advancements in immunosuppressive medications have notably diminished complications associated with rejection in these recipients[19,20]. Effective immunosupp-ression has been associated with a higher occurrence of BK viral infection in this population, ultimately resulting in the development of BKV nephropathy[21,22].

Prompt identification of BKV reactivation in both urine and plasma serves as a valuable clinical resource for pinpointing individuals at risk of BKVAN and for tracking their response to Treatment[23,24]. BK viremia load > 1,85, 000 copies/ml at the time of first positive BKV diagnosis - to be the strongest predictor for BKVAN. In addition, the BKV peak viral loads in blood reaching 2,23,000 copies/ml at any time was found to be predictive for BKVAN [25]. BKVAN is defined as persistently high BK viral load in plasma >10,000 copies/mL for four weeks[26]. BKV shedding in the urine is common and can occur in up to 30% of renal transplant recipients. Urine can be screened for BKV by quantification of urine BKV DNA by PCR. If only urine BK screening is to be performed, urine BKV PCR will be considered as the superior assay, using the threshold of >1 × 107 copies/mL as suggestive of BKVAN[27]. The excretion of BK virus in urine is observed in 20-60% of kidney transplant patients. The occurrence of BK viremia is approximately 13%, and post-transplant nephropathy is reported in roughly 8% of cases. Nephropathy can ultimately

lead to graft loss[28-33]. In our study, renal transplant recipients' BKV shedding rate was 47.62% (10/21) and viremia rate was 9.46% (7/74) which is similar to the above findings. Another study from Greece reported dissimilar findings where patients with high plasma and/or urine viral load had stable renal function with no sign of graft failure[34].

Hemorrhagic cystitis (HC) poses a significant health risk for patients undergoing hematopoietic stem cell transplantation (HSCT). The connection between BK virus (BKV) and HC was initially identified in the 1980s when substantial quantities of BKV were found in the urine samples of individuals who had received HSCT[35,36]. The incidence of BKV-associated HC in individuals undergoing HSCT is approximately 10%, often occurring around 2 weeks following the transplantation procedure[37]. BKV viruria is detected in roughly 50% of patients undergoing bone marrow transplantation, and increased viruria levels are linked to an elevated risk of developing HC[38–40].

In our study population, BKV viruria was detected in 68.75% (11/16) of bone marrow transplant cases and ultimately developed hemorrhagic cystitis which corresponds to the above findings. Common symptoms of HC patients were dysuria, frequent urination, urinary urgency, suprapubic discomfort, and the presence of blood in the urine (hematuria)[41-45].

BK virus (BKV), Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) reactivations are common after kidney transplantation and associated with increased morbidity and mortality[46]. In our study, we found co-infections of CMV, EBV and BKV in 2 renal transplant and 6 bone marrow transplanted cases. A single case of bone marrow transplant was noted with CMV, EBV, HHV-6 and BKV infection. The effects of combined reactivations are unknown and co-infection related scientific research and case reports published worldwide[47-49]. Early diagnosis is the key to prevent graft loss.

Serum creatinine level within normal range (0.5-1.2 mg/dl) is the most important marker of normal functioning kidney. In renal transplant patients, allograft dysfunction is presented with elevation of serum creatinine. The main presenting indicator for graft dysfunction is elevated level of serum creatinine in renal transplant patient. Kidney transplant recipients with BKV positivity had elevated serum creatinine levels (median 1.8 mg/dl) whereas BKV positivity in bone marrow transplant recipients had normal creatinine levels (median 0.77 mg/dl) as expected.

BK virus infections are common childhood infections; in immunocompetent individuals the virus remains latent in the kidneys, central nervous system, and B lymphocytes. In immunocompromised patients, the infection reactivates and spreads to other organs and causes significant morbidity, in particular BKVAN in renal transplant recipients and hemorrhagic cystitis in hematopoietic stem cell recipients[3,7]. Since the discovery of the clinical significance of BK virus infection in renal and bone marrow transplant recipients, a great amount of scientific research has taken place worldwide. However, there are limited published data regarding BK virus nephropathy in renal transplant recipients or there is no data of BK hemorrhagic cystitis infection in bone marrow transplant recipients in Bangladesh. Kidney transplant has been started in Bangladesh since 1982[50,51] and bone marrow transplant since 2014[52], but screening for BKV infection is not initiated yet for donor or recipients.

The present study has several limitations. It is worth noting that this research is single-centered and based on a relatively small sample size, which may restrict the applicability of its findings to a broader population. Additionally, the retrospective study design adds to the study's constraints. Therefore, it is strongly advisable to pursue a larger-scale, multi-centric study for more comprehensive and in-depth examination of BKV-associated nephropathy (BKVAN) and BKV-induced hemorrhagic cystitis in transplant recipients.

## CONCLUSION

BK virus infection poses a significant and global concern for individuals who have undergone renal and bone marrow transplants. Early detection and appropriate management such as reduction of immunosuppression may significantly lower the

risk of BKV infection-induced graft failure. The findings from this research underscore the prevalence of BK virus infection among recipients of renal and bone marrow transplants in our country. Therefore, heightened vigilance is warranted for these patients, with a particular focus on monitoring for the development of BK virus nephropathy or hemorrhagic cystitis, as there are currently no known antiviral treatments proven effective in clearing the virus.

## REFERENCES


1. Johne R, Buck CB, Allander T, Atwood WJ, Garcea RL, Imperiale MJ, Major EO, Ramqvist T, Norkin LC. Taxonomical developments in the family Polyomaviridae. Arch Virol. 2011 Sep;156(9):1627-34. DOI: 10.1007/s00705-011-1008-x. Epub 2011 May 12. PMID: 21562881; PMCID: PMC3815707.
2. Imperiale, MJ.; Major, EO. Polyomaviruses. In: Knipe, DM.; Howley, PM.; Griffen, DE.; Lamb, RA.; Martin, RA.; Roizman, B.; Straus, SE., editors. Fields virology. 4th edn. Philadelphia: Lippincott Williams and Wilkins; 2007. p. 2263-2298.
3. Ambalathingal GR, Francis RS, Smyth MJ, Smith C, Khanna R. BK Polyomavirus: Clinical Aspects, Immune Regulation, and Emerging Therapies. Clin Microbiol Rev. 2017 Apr;30(2): 503-528. DOI: 10.1128/ CMR. 00074-16. PMID: 28298471; PMCID: PMC5355639.
4. Flaegstad T, Ronne K, Filipe AR, et al. Prevalence of anti BK virus antibody in Portugal and Norway. Scan J Infectious Dis. 1989;21 (2): 145–147. DOI: 10.3109/ 00365548909039961
5. Stolt A, Sasnauskas K, Koskela P, Lehtinen M, Dillner J. Seroepidemiology of the human polyomaviruses. J Gen Virol. 2003 Jun;84(Pt 6):1499-1504. DOI: 10.1099/ vir.0.18842-0. PMID: 12771419.
6. Gardner SD, Field AM, Coleman DV, Hulme B. New human papovavirus (B.K.) isolated from urine after renal transplantation. Lancet. 1971;1(7712):1253–7.
7. Boukoum H, Nahdi I, Sahtout W, Skiri H, Segondy M, Aouni M. 2016. BK and JC virus infections in healthy patients compared to kidney transplant recipients in Tunisia. Microb Pathog 97:204 –208. https://doi.org/ 10.1016/j.micpath.2016.06.015.
8. Moens U, Rekvig OP. Human Polyomaviruses: Molecular and Clinical Perspectives. 2001. pp. 359–408.
9. Dei R, Marmo F, Corte D, Sampietro MG, Franceschini E, Urbano P. Age-related changes in the prevalence of precipitating antibodies to BK virus in infants and children. J Med Microbiol. 1982;15(3):285–91.
10. Knowles WA, Gibson PE, Gardner SD. Serological typing scheme for BK-like isolates of human polyomavirus. J Med Virol.1989;28(2):118–23.
11. Knowles WA. Human Polyomaviruses: Molecular and Clinical Perspectives. Wiley Online Library; 2001. pp. 527–59.
12. Ramos E, Drachenberg CB, Wali R, Hirsch HH. 2009. The decade of polyomavirus BK-associated nephropathy: state of affairs. Transplantation 87:621– 630. https://doi.org/10.1097/ TP.0b013e318197c17d]
13. Erard V, Storer B, Corey L, Nollkamper J, Huang ML, Limaye A, Boeckh M. 2004. BK virus infection in hematopoietic stem cell transplant recipients: frequency, risk factors, and association with post engraftment hemorrhagic cystitis. Clin Infect Dis 39:1861–1865. https://-doi.org/10.1086/426140.
14. Nessa A, Mannan N, Tabassum S, Sultana S, Islam SMR. BK Virus Infection: A Hidden Threat for Renal Transplant Recipients. April 2018Bangladesh Medical Research Council Bulletin 43(3):101. DOI: 10.3329/ bmrcb.v43i3.36400.
15. Cukuranovic J, Ugrenovic S, Jovanovic I, Visnjic M, Stefanovic V. Viral infection in renal transplant recipients. ScientificWorldJournal. 2012;2012:820621. DOI: 10.1100/2012/820621. Epub 2012 May 2. PMID: 22654630; PMCID: PMC3357934.
16. Tonelli M, Wiebe N, Knoll G, Bello A, Browne S, et al. (2011) Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant 11: 2093-2109. Link: http://bit.ly/ 2lYFYuw
17. Hariharan S (2006) BK virus nephritis after renal transplantation. Kidney Int 69: 655-662. Link: http://bit.ly/2lBmj3o
18. Hirsch HH, Knowles W, Dickenmann M, Passweg J, Klimkait T, et al. (2002). Prospective study of polyomavirus type BK replica on and nephropathy in renal-transplant recipients. N Engl J Med 347: 488-496. Link: http://bit.ly/2ks7Ab0
19. Szumilas K, Wilk A, Wiśniewski P, Gimpel A, Dziedziejko V, Kipp M, Pawlik A. Current Status Regarding Immunosuppressive Treatment in Patients after Renal Transplantation. Int J Mol Sci. 2023 Jun 18;24(12):10301. DOI: 10.3390/ijms241210301. PMID: 37373448; PMCID: PMC10298917.
20. Cheung CY, Tang SCW. Personalized immunosuppression after kidney transplantation. Nephrology (Carlton). 2022 Jun;27(6):475-483. DOI: 10.1111/nep.14035. Epub 2022 Mar 9. PMID: 35238110.
21. Badwal S, Chopra GS, Varma PP, Hooda AK. BK polyoma viral infection in renal allograft recipients. Med J Armed Forces India. 2011; 67: 122-30.
22. Hirsch H.H., Randhawa P.S., AST Infectious Diseases Community of Practice BK polyomavirus in solid organ

transplantation—Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin. Transplant. 2019;33:e13528. DOI: 10.1111/ctr.13528.

23. Bechert CJ, Schnadig VJ, Payne DA, Dong J. Monitoring of BK Viral Load in Renal Allograft Recipients by Real-Time PCR Assays. Am J Clin Pathol. 2010; 133: 242-50
24. Saundh BK, Baker R, Harris M, Welberry Smith MP, Cherukuri A, Hale A. Early BK polyomavirus (BKV) reactivation in donor kidney is a risk factor for development of BKV-associated nephropathy. J Infect Dis. 2013 Jan 1;207(1):137-41. DOI: 10.1093/ infdis/jis642. Epub 2012 Oct 24. PMID: 23100561.
25. Elfadawy, NS; Flechner, SM; Xiaobo, L; Schold, J; Tian, D; Srinivas, TR; Poggio, E; Fatica, R; Avery, R; Mosaad, SB (2013). "The impact of surveillance and rapid reduction in immunosuppression to control BK virus-related graft injury in kidney transplantation". Transplant International. 26 (8): 822–32. DOI:10.1111/tri.12134. PMID 23763289
26. Drachenberg CB, Papadimitriou JC, Hirsch HH, et al. Histological patterns of polyomavirus nephropathy: correlation with graft outcome and viral load. Am J Transplant. 2004;4(12):2082–2092. DOI:10.1046/ j.1600-6143.2004.00603.x
27. Wiseman AC. Polyomavirus Nephropathy: a current perspective and clinical considerations. Am J Kidney Dis 2009; 54: 131–142
28. Brennan DC, Agha I, Bohl DL, Schnitzler MA, Hardinger KL et al. (2005) Incidence of BK with tacrolimus versus cyclosporine and impact of preemptive immunosuppression reduction. Am J Transplant 5: 582-594. Link: http://bit.ly/2kiej7t
29. Hirsch HH (2005) BK virus: opportunity makes a pathogen. Clin Infect Dis 41: 354-360. Link: http://bit.ly/ 2lwwLJC
30. Boothpur R, Brennan CD (2010) Human polyoma viruses and disease with emphasis on clinical BK and JC. J Clin Virol 47: 306-312. Link: http://bit.ly/2lQMYtc
31. Ramos E, Drachenberg CB, Wali R, Hirsch HH (2009) The decade of polyomavirus Bkassociated nephropathy: state of affairs. Transplantation 87: 621-630. Link: http://bit.ly/2lVQ9zT
32. Wojciechowski D, Chanda R, Chandran S, Lee B, Webber A, et al. (2012) Ciprofl oxacin prophylaxis in kidney transplant recipients reduces BK virus infection at 3 months but not at 1 year. Transplantation 94: 1117-1123. Link: http://bit.ly/2lwwXZm
33. Randhawa P, Brennan CD (2006) BK virus infection in transplant recipients: an overview and update. Am J Transplant 6: 2000-2005. Link: http://bit.ly/2lRxG7x.
34. Koukoulaki M, Grispou E, Pistolas D, Balaska K, Apostolou T, Anagnostopoulou M, Tseleni-Kotsovili A, Hadjiconstantinou V, Paniara O, Saroglou G, Legakis N, Drakopoulos S. Prospective monitoring of BKvirus replication in renal transplant recipients. Transpl Infect Dis. 2009; 11: 1-10.
35. O'Reilly RJ, Lee FK, Grossbard E, Kapoor N, Kirkpatrick D, Dinsmore R, Stutzer C, Shah KV, Nahmias AJ. 1981. Papovavirus excretion following marrow transplantation: incidence and association with hepatic dys function. Transplant Proc 13:262–266.
36. Arthur RR, Shah KV, Baust SJ, Santos GW, Saral R. 1986. Association of BK viruria with hemorrhagic cystitis in recipients of bone marrow transplants. N Engl J Med 315:230–234. https://doi.org/10.1056/NEJM 198607243150405.
37. Dropulic LK, Jones RJ. 2008. Polyomavirus BK infection in blood and marrow transplant recipients. Bone Marrow Transplant 41:11–18. https://doi.org/ 10.1038/ sj.bmt.1705886.
38. Erard V, Kim HW, Corey L, Limaye A, Huang ML, Myerson D, Davis C, Boeckh M. 2005. BK DNA viral load in plasma: evidence for an associ ation with hemorrhagic cystitis in allogeneic hematopoietic cell trans plant recipients. Blood 106:1130–1132. https:// doi.org/10.1182/blood-2004-12-4988.
39. Pavlakis M, Haririan A, Klassen DK. 2006. BK virus infection after non renal transplantation. Adv Exp Med Biol 577:185–189. https://doi.org/10.1007/0-387-32957-9_13.
40. Bogdanovic G, Priftakis P, Giraud G, Kuzniar M, Ferraldeschi R, Kokhaei P, Mellstedt H, Remberger M, Ljungman P, Winiarski J, Dalianis T. 2004. Association between a high BK virus load in urine samples of patients with graft-versus-host disease and development of hemorrhagic cysti tis after hematopoietic stem cell transplantation. J Clin Microbiol 42: 5394–5396. https://doi.org/10.1128/JCM.42.11.5394-5396.2004.
41. Kwon HJ, Kang JH, Lee JW, Chung NG, Kim HK, Cho B. 2013. Treatment of BK virus-associated hemorrhagic cystitis in pediatric hematopoietic stem cell transplant recipients with cidofovir: a single-center experience. Transpl Infect Dis 15:569–574. https://doi.org/ 10.1111/tid.12136.
42. Savona MR, Newton D, Frame D, Levine JE, Mineishi S, Kaul DR. 2007. Low-dose cidofovir treatment of BK virus-associated hemorrhagic cystitis in recipients of hematopoietic stem cell transplant. Bone Marrow Transplant 39:783–787. https://doi.org/ 10.1038/ sj.bmt.1705678.
43. Josephson MA, Gillen D, Javaid B, Kadambi P, Meehan S, Foster P, Harland R, Thistlethwaite RJ, Garfinkel M, Atwood W, Jordan J, Sadhu M, Millis MJ, Williams J. 2006. Treatment of renal allograft polyoma BK virus infection with leflunomide. Transplantation 81:704–710.

https://doi.org/10.1097/01.tp.0000181149.76113.50.

44. Randhawa PS. 2005. Anti-BK virus activity of ciprofloxacin and related antibiotics. Clin Infect Dis 41:1366–1367. https://doi.org/10.1086/497080.
45. Leung AY, Chan MT, Yuen KY, Cheng VC, Chan KH, Wong CL, Liang R, Lie AK, Kwong YL. 2005. Ciprofloxacin decreased polyoma BK virus load in patients who underwent allogeneic hematopoietic stem cell transplantation. Clin Infect Dis 40:528–537. https://-doi.org/10.1086/427291.
46. Blazquez-Navarro A, Dang-Heine C, Wittenbrink N, Bauer C, Wolk K, Sabat R, Westhoff TH, Sawitzki B, Reinke P, Thomusch O, Hugo C, Or-Guil M, Babel N. BKV, CMV, and EBV Interactions and their Effect on Graft Function One Year Post-Renal Transplantation: Results from a Large Multi-Centre Study. EBioMedicine. 2018 Aug;34:113-121. DOI: 10.1016/j.ebiom.2018.07.017. Epub 2018 Jul 30. PMID: 30072213; PMCID: PMC6116415.
47. Egli A, Binggeli S, Bodaghi S, Dumoulin A, Funk GA, Khanna N, Leuenberger D, Gosert R, Hirsch HH. Cytomegalovirus and polyomavirus BK posttransplant. Nephrol Dial Transplant. 2007 Sep;22 Suppl 8:viii72-viii82. DOI: 10.1093/ndt/gfm648. Erratum in: Nephrol Dial Transplant. 2008 Jan;23(1):426. PMID: 17890268.
48. Herrera S,Bernal-Maurandi J, Cofan F, Ventura P, Marcos MA, Linares L, Cuesta G, Diekmann F, Moreno A, Bodro M. BK Virus and Cytomegalovirus Coinfections in Kidney Transplantation and Their Impact on Allograft Loss. J Clin Med. 2021 Aug 24;10(17):3779. DOI: 10.3390/jcm10173779. PMID: 34501226; PMCID: PMC8432040.
49. Rudreshwar P, Georgi A, Milly M, Rajeevalochana P, Priyanka1 K, Anusha R. Coinfection of BK Virus and Cytomegalovirus in Renal Transplant Recipients. Indian Journal of Transplantation 11(4):p 204-207, Oct–Dec 2017. | DOI: 10.4103/ijot.ijot_54_17
50. Sanwar SM. Organ Donation for Transplantation in Bangladesh. Saudi Journal of Kidney Diseases and Transplantation 32(5):p 1441-1449, Sep–Oct 2021. | DOI: 10.4103/1319-2442.344765
51. Rahman M; Mahmood S. Status of Organ Donation and Transplantation in Bangladesh. Transplantation 101:p S30, August 2017. | DOI:

    10.1097/01.tp.0000525017.89355.
52. Akter M, Saleh AJM, Uddin CMM, Karim CMM, Haq QS, Khan MA. Hematopoietic Stem Cell Transplantation in Bangladesh: Activity and Outcome Update. Blood 2022; 140 (Supplement 1): 4853–4854. DOI: https://-doi.org/10.1182/blood-2022-168388.