## **OP-06**

## Is There a Relationship Between BK Virus and Human Leukocyte Antigen Subtype in Kidney Transplant Patients: A Retrospective Study

Enes Altunay<sup>1,2</sup>, Miray Kavuzlu<sup>2</sup>, Bircan Kantaroğlu<sup>2</sup>, Hayriye Altunay<sup>3</sup>, Bilkay Baştürk<sup>2,4</sup>

<sup>1</sup>Başkent University Faculty of Medicine, Department of Medical Microbiology, Adana, Turkey

<sup>2</sup>Başkent University Faculty of Medicine, Tissue Typing and Transplantation Laboratory, Adana, Turkey

<sup>3</sup>Başkent University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Adana, Turkey

<sup>4</sup>Başkent University Faculty of Medicine, Department of Immunology, Ankara Turkey

**Objectives:** Renal transplantation is still recognised as the best treatment for patients with end-stage renal disease as it improves survival and quality of life (1). Human leukocyte antigen (HLA) compatibility plays a key role in the success of kidney transplantation (2). HLA consists of a 3.6 million base pair genomic region (6p21) located on the short arm of chromosome 6. In fact the HLA region is the most variable region of our DNA. HLA molecules are cell surface glycoproteins whose primary function is to present endogenous and exogenous antigens to T lymphocytes for recognition and response. Some HLA subtypes have been associated with various autoimmune, neurological, rheumatological and viral infections. HLA is also involved in the development of immune response against viral infections (3-5). The main target of the recipient immune system in renal transplantation is the HLA molecules on the surface of donor cells. Graft survival is better in transplants from full HLA-matched siblings than in transplants from less compatible living or cadaveric donors (5,6).

On the other hand, modern immunosuppressant therapies allow to increase graft survival in all cases. However, aggressive immunosuppressive therapies can cause increased opportunistic infections such as BK virus (BKV) infections (7). As with some viral infections, BKV has been associated with various HLA subtypes (8-11). In this study, the relationship between HLA subtype and BKV infections occurring due to immunosuppression in kidney transplant recipients was evaluated.

**Materials and Methods:** Our study was planned retrospectively and HLA A, B, C, DRB1, DQB1 and DQA1 tissue typing were studied before transplantation in the study group. DNA isolation was performed from whole blood samples taken from patients. Tissue typing tests were performed by sequence-specific oligonucleotides and/or sequence-specific priming method based on polymerase chain reaction (PCR). After transplantation, patients were tested for BKV. DNA was isolated from urine and/or plasma samples of patients. Isolated samples were quantitatively evulated for BKV by the real-time PCR method.

In our study, the data of 71 patients who underwent kidney transplantation between November 2018 and November 2024 were retrospectively analyzed. Statistical analyses were performed using the SPSS software version 24. The variables were investigated using visual and analytical methods to determine whether or not they are normally distributed. Since the HLA sub-groups numbers were not normally distributed; nonparametric tests were conducted to compare these parameters, as well as to compare the nominal variables. The Mann-Whitney U test used to compare HLA sub-groups and BKV condition between the groups. A p-value of less than 0.05 was considered to show a statistically significant result.

**Results:** Retrospectively analyzed 23 of 71 patients were found to be BKV positive. While HLA-A, HLA-B and HLA-DRB1 subgroups were analyzed in all patients, HLA-C and HLA-DQB1 subgroup analyses were performed in 17 BKV positive patients and 36 BKV negative patients. HLA-DQA1 subgroup analysis was performed in 13 BKV positive patients and 32 BKV negative patients. In our analysis, HLA-B\*55 (p=0.003), HLA-C\*03 (p=0.016), HLA-DRB1\*13 (p=0,006) alleles were found to be significantly higher in the BKV positive group, while no statistically significant difference was found between the BKV positive and negative groups in HLA-A, HLA-DQB1 and HLA-DQA1 alleles. On the other hand, no statistically significant relationship was found between the BKV positive and negative groups in gender, donor type, and age (Table 1).

**Conclusion:** Since the number of patients included in the study was relatively small and HLA-C subgroup analysis was not performed in all patients, studies involving a larger patient population are needed to establish a link between HLA-B\*55, HLA-C\*03, HLA-DRB1\*13 alleles and the risk of developing BKV disease.

## References

- 1. Jain P, Cockwell P, Little J, Ferring M, Nicholas J, Richards N, et al. Survival and transplantation in end-stage renal disease: a prospective study of a multiethnic population. Nephrol Dial Transplant. 2009;24:3840-6.
- Opelz G. Impact of HLA compatibility on survival of kidney transplants from unrelated live donors. Transplantation. 1997;64:1473-5.
- Nudel R, Allesøe RL, Thompson WK, Werge T, Rasmussen S, Benros ME. A largescale investigation into the role of classical HLA loci in multiple types of severe infections, with a focus on overlaps with autoimmune and mental disorders. J Transl Med. 2021;19:230.
- 4. Debebe BJ, Boelen L, Lee JC; IAVI Protocol C Investigators; Thio CL, Astemborski J, et al. Identifying the immune interactions underlying HLA class I disease associations. Elife. 2020;9:e54558.
- Mathieu A, Paladini F, Vacca A, Cauli A, Fiorillo MT, Sorrentino R. The interplay between the geographic distribution of HLA-B27 alleles and their role in infectious and autoimmune diseases: a unifying hypothesis. Autoimmun Rev. 2009;8:420-5.
- Miles CD, Schaubel DE, Liu D, Port FK, Rao PS. The role of donor-recipient relationship in long-term outcomes of living donor renal transplantation. Transplantation. 2008;85:1483-8.
- 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;25:12801.
- Masutani K, Ninomiya T, Randhawa P. HLA-A2, HLA-B44 and HLA-DR15 are associated with lower risk of BK viremia. Nephrol Dial Transplant. 2013;28:3119-26.
- 9. Wunderink HF, Haasnoot GW, de Brouwer CS, van Zwet EW, Kroes ACM, de Fijter JW, et al. Reduced Risk of BK polyomavirus infection in HLA-B51-positive kidney transplant recipients. Transplantation. 2019;103:604-12.
- Rohn H, Michita RT, Schramm S, Dolff S, Gäckler A, Korth J, et al. HLA-E polymorphism determines susceptibility to BK virus nephropathy after livingdonor kidney transplant. Cells. 2019;8:847.
- 11. Kavuzlu M, Baştürk B, Ataç FB, Alışkan HE, Kantaroğlu B. Investigation of the relationship between BK virus and human leukocyte antigens in kidney transplant recipients. Exp Clin Transplant. 2020;18:51-4.

 Table 1. Clinical characteristics of patients positive and negative for

 BKV

Parameter	BKV negative (n=48)	BKV positive (n=23)	P-value
Sex			0.113
Male (n=43)	32	11	
Female (n=28)	16	12	
Donor type			0.334
Living (n=51)	35	17	
Deceased (n=20)	13	6	
Age group			0.286
Pediatric (n=15)	10	5	
Adult (n=56)	38	18	
BKV: BK virus			

BKV: BK virus