Impact of BK polyomavirus origin in kidney transplant recipients

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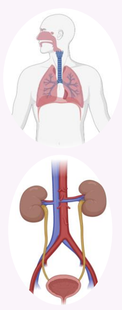
1 INTRODUCTION

BK polyomavirus (**BKPyV**) reactivation in the reno-urinary tract is a frequent complication in **kidney transplant recipients** and can progress to **BKPyV-associated nephropathy** (**BKPyVAN**). The classic disease sequence starts with asymptomatic viral detection in urine, followed by viremia in blood and worsening renal function. No antivirals targeting BKPyV are available. The post-transplantation management of patients includes frequent **screening for BKPyV** in plasma and preemptive **reduction in immunosuppressive medication** to restore the patient's cellular immunity. Previous studies have suggested the infection is most often transmitted by the kidney donor and that high donor IgG levels can increase the risk of disease. However, in Sweden, **recipient** or **donor** BKPyV status is not considered **before transplantation**.

Advancements in precision diagnostics and identifying the risk factors before transplantation could improve early diagnosis and enhance organ survival.

2 BACKGROUND

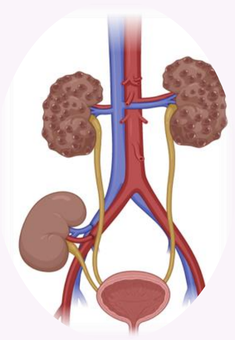
PRIMARY INFECTION
- Tonsils & **respiratory tract**
- Common cold-like, **subclinical**



70% infected by 10 years of age

KIDNEY TRANSPLANT
- Viral **reactivation** or **new** infection
- **1 in 3** patients affected
- Kidney infection leads to **nephropathy** & **graft loss**

SECONDARY SITE
- **Kidney**, urothelial, bladder cells
- **Latent infection** with occasional shedding in urine



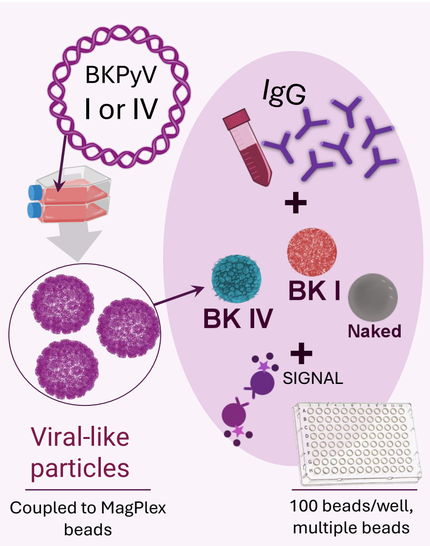
BKPyV *Human polyomavirus 1* is a small, nonenveloped virus with circular **dsDNA** genome, ~5kb in size. Structurally, it is similar to **JC polyomavirus** and **SV40**. BKPyV is ubiquitous, with 90-99% seroprevalence in adults. **Viral subtypes (I-IV)** are geographically distributed, with **I**(b2) and **IV**(c2) being most common in Europe. **Compromised immunity** can lead to reactivation in the reno-urinary tract. Pathology includes **nephropathy**, ureteral stenosis, hemorrhagic cystitis.

3 AIM

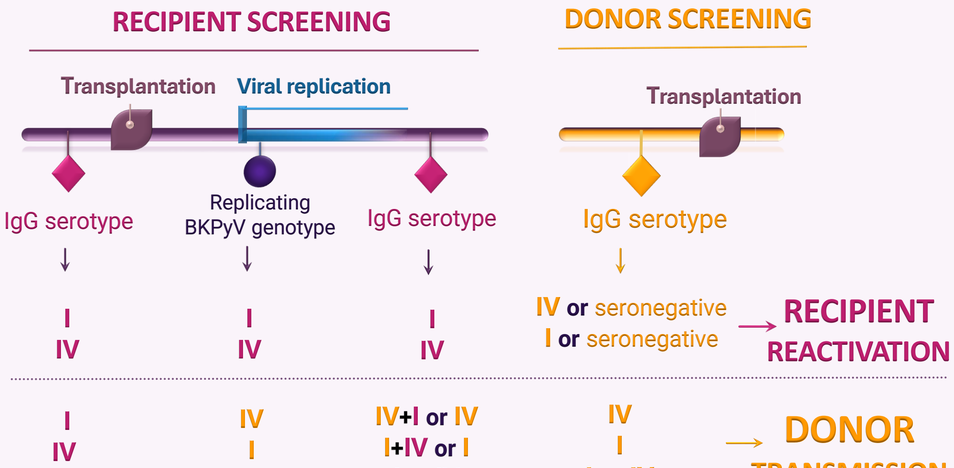
Investigate **kidney transplant donor-recipient** pair BKPyV status before transplantation and analyze the risk of disease outcome, based on:

- **Anti-BKPyV IgG** levels in donors and recipients
- Donor or recipient **origin** of replicating virus
- Donor-recipient **serotype mismatch**
- Living donor **urine** BKPyV DNA status

Our study included patients, transplanted at Uppsala University Hospital during 2016-2018. **Kidney transplant recipients** (n=195) were categorized according to BKPyV-DNA loads in **plasma** and **urine** during 18-month post-transplantation period. **High DNAemia** was >10 000 BKPyV DNA copies/ml in plasma. **Donor-recipient BKPyV serotypes and IgG levels** were tested using a novel **Luminex-based immunoassay**. Additionally, the **living donors** were screened for BKPyV presence in urine.

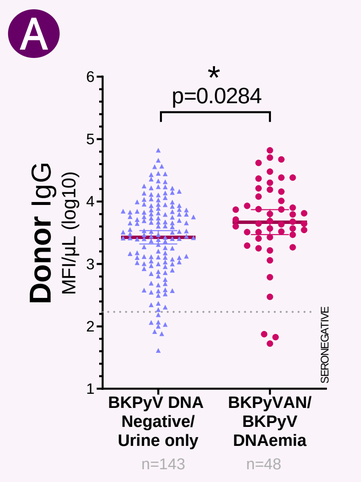


Serology using Luminex

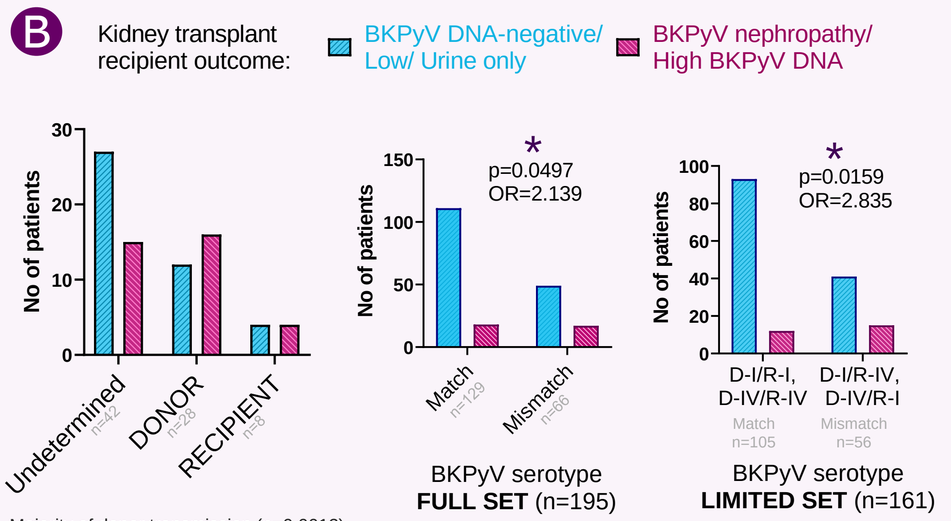


Recipient and donor screening protocol to determine the viral origin

5 RESULTS

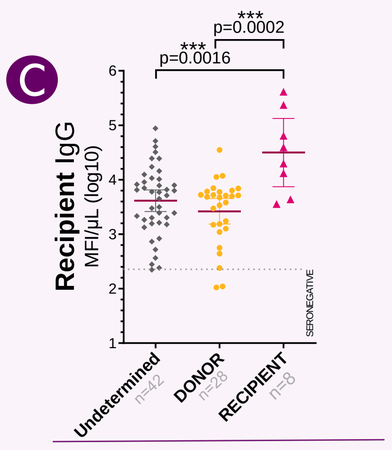


Donor IgG & recipient outcome (n=191)

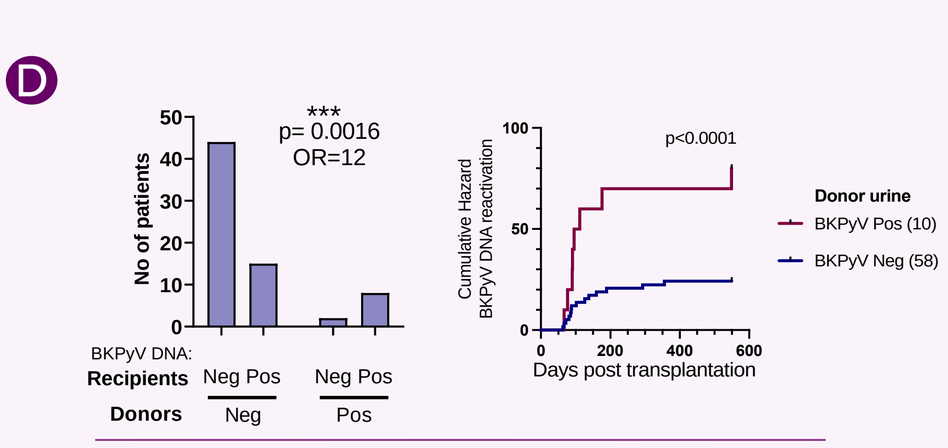


BKPyV-positive patient viral origin & outcome (n=76)

Risk of high BKPyV DNAemia & nephropathy in donor-recipient serotype mismatch



Viral origin & recipient IgG before transplantation (n=76)



Living donor urine screening for BKPyV analyzed with recipient outcome & time to BKPyV reactivation (n=68)

6 CONCLUSIONS

A. **Higher donor IgG** levels were associated with BKPyV-positive and DNAemic recipients.
B. Out of 36 patients, viral origin was determined to be **28 - donor transmission**, **8 - recipient reactivation**. Donor-recipient **serotype mismatch** was associated with disease.
C. Higher IgG levels before transplantation found in **recipients with reactivation** from their own urinary tract.
D. **Living donor viruria** was associated with BKPyV DNA-positive recipients and faster time to reactivation.

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