

Original Article

Associations between ABO incompatibility and the risk of cytomegalovirus, BK polyomavirus, and varicella-zoster virus infections after kidney transplantation: A systematic review and meta-analysis

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Abstract

Viral infections, particularly cytomegalovirus (CMV), BK polyomavirus (BKV), and varicella-zoster virus (VZV) reactivation presenting as herpes zoster (HZ), represent major challenges following kidney transplantation. These infections pose considerable challenges for patients with ABO incompatibility, which may be associated with an increased risk of graft loss, increased morbidity, and possible mortality. The aim of this study was to determine whether ABO incompatibility increases the risk of CMV, BKV, and VZV infections among kidney transplant patients. A systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. PubMed, Scopus, and Embase were searched for relevant studies published up to March 25, 2026. Study quality was assessed using the Newcastle–Ottawa Scale (NOS). Pooled odds ratios (ORs) and 95% confidence intervals (95%CI) were calculated using R software. The certainty of evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. Of 7,433 articles identified, 26 studies involving 6,188 kidney transplant recipients were included in the final analysis. ABO incompatibility was associated with higher odds of CMV infection (OR: 1.34; 95%CI: 1.01–1.77; $p=0.020$) and BKV infection (OR: 1.84; 95%CI: 1.07–3.16; $p=0.010$). No statistically significant association was observed between ABO incompatibility and HZ (OR: 1.61; 95%CI: 0.95–2.72; $p=0.070$). No evidence of small-study effects was observed for BKV or VZV, whereas evidence of small-study effects was detected for CMV. The certainty of evidence was rated as very low for all outcomes according to GRADE. These findings suggest an association between ABO-incompatible kidney transplantation and increased odds of CMV and BKV infections. Given the observational design of the included studies and the use of unadjusted effect estimates, these findings should be interpreted as associations rather than evidence of a causal relationship.

Keywords: Kidney transplantation, ABO incompatibility, cytomegalovirus infections, BK virus, herpes zoster



Introduction

Kidney transplantation is the preferred kidney replacement therapy for eligible patients with end-stage kidney disease; however, post-transplant infections remain a major clinical challenge [1-3]. Approximately 20–60% of end-stage renal disease (ESRD) patients receiving kidney transplantation are estimated to be susceptible to opportunistic viral infections such as cytomegalovirus (CMV), BK polyomavirus (BKV), varicella-zoster virus (VZV), and other viruses after kidney transplantation, and these infections may lead to increased risks of allograft failure and mortality [4]. The incidence of opportunistic infections depends on many factors, including the intensity of immunosuppression, immune status of the patients, and the immunologic equivalency of the donor/recipient match and patient immunology, such as ABO incompatibility [5]. ABO-incompatible transplantation necessitates intensive desensitization and augmented immunosuppressive regimens—including anti-CD20 therapy, plasmapheresis or immunoadsorption, and enhanced maintenance immunosuppression—to overcome humoral barriers and prevent graft rejection [6,7]. These intensified immunomodulatory interventions, together with ABO incompatibility, are hypothesized to be the principal factors contributing to increased susceptibility to infectious complications by inducing profound lymphocyte depletion and functional impairment. Consequently, ABO incompatibility operates largely as a surrogate marker for more intensive immunosuppression, and understanding its association with post-transplant infectious outcomes is critically important for improving kidney transplant management [8].

ABO incompatibility occurs when donor ABO blood group antigens are incompatible with the recipient's preformed natural antibodies, resulting in the potential activation of immune responses directed against the graft tissue [9]. The increased risk of post-transplant infections observed in ABO-incompatible recipients is thought to arise primarily from the robust immunosuppressive and desensitization protocols required to enable successful transplantation across ABO barriers. While ABO mismatch itself triggers humoral immune activation directed against donor blood group antigens, the resultant infectious risk appears to be mediated indirectly through treatment-related immunomodulation—specifically, the use of rituximab, intravenous immunoglobulin (IVIG), high-dose calcineurin inhibitors, corticosteroids, and other desensitization agents that profoundly deplete and impair B- and T-cell function. This distinction is clinically relevant because it frames ABO incompatibility not as an independent biological determinant of infection, but as a clinical context that mandates more intensive immunosuppression, thereby increasing the risk of opportunistic viral reactivation [10].

Several studies have assessed the impact of ABO incompatibility on viral post-kidney transplant infections such as CMV, BKV, and VZV reactivation presenting as herpes zoster (HZ), among kidney transplant recipients [11-38]. However, their findings have been inconsistent, and the available evidence remains inconclusive. Some studies demonstrated a higher risk of infection among ABO-incompatible transplant recipients [13,24,25,28,31,33], whereas other studies have found no significant association or reported conflicting findings [14-23,26,27,29,30,32,34-40]. Moreover, methodological limitations—including predominantly retrospective study designs, small sample sizes, heterogeneous immunosuppressive regimens, and inconsistent definitions and reporting of viral infections—limit the generalizability of the available findings to other populations [13-38,41]. Furthermore, the association between ABO incompatibility and the risk of viral infections among kidney transplant recipients remains uncertain because evidence from individual studies has not been comprehensively synthesized [13-38,42]. A systematic review and meta-analysis is therefore needed to consolidate the available evidence, quantify the associations between ABO incompatibility and post-transplant viral infections, and inform clinical risk assessment and monitoring. Therefore, the aim of this study was to objectively and systematically assess the association between ABO incompatibility and CMV, BKV, and HZ infections in kidney transplant recipients. The findings may strengthen the evidence base for risk-stratified infection prevention and surveillance among ABO-incompatible kidney transplant recipients.

Methods

Study design and registration

A systematic review and meta-analysis was conducted to evaluate the association between ABO-incompatible kidney transplantation and the occurrence of CMV, BKV, and HZ infections. The study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [43]. Detailed filled PRISMA checklists for this study are provided in **Supplementary File 1**. The protocol was prospectively registered in PROSPERO (registration number: CRD42024577769). The literature search included studies published up to March 25, 2026.

Eligibility criteria

Eligible studies were prospective or retrospective observational cohort studies that included adult or pediatric kidney transplant recipients. The exposure was ABO-incompatible kidney transplantation, defined as transplantation across an ABO blood-group barrier, with or without desensitization, and the comparator was ABO-compatible kidney transplantation. Studies were required to have a minimum post-transplant follow-up of six months and to report at least one outcome of interest: CMV infection, BKV infection, or HZ.

CMV infection was identified using quantitative nucleic acid amplification testing (PCR) of whole blood or plasma, pp65 antigenemia testing, or histopathological examination with immunohistochemical confirmation. BKV infection was identified using quantitative plasma PCR, urine cytology for decoy cells, or histopathological confirmation of BK polyomavirus-associated nephropathy (BKVAN). HZ was defined based on a clinical diagnosis of shingles, with or without laboratory confirmation using PCR, direct fluorescent antibody testing, or serological testing. Studies were also required to provide sufficient data, including raw event counts or effect estimates with 95% confidence intervals (CIs), to permit quantitative synthesis.

Reviews, commentaries, editorials, case reports, case series involving fewer than 10 participants, animal studies, and studies without an ABO-compatible comparator group were excluded.

Quality assessment

The methodological quality of the included studies was assessed using the Newcastle–Ottawa Scale (NOS), which evaluates three domains: selection of study groups, comparability of exposed and non-exposed groups, and ascertainment of outcomes. Each study was assigned a maximum of nine points. Scores of 0–3, 4–6, and 7–9 were classified as low, moderate, and high methodological quality, respectively. Studies were not excluded based on their NOS scores.

Quality assessment was independently performed by at least two reviewers within each outcome-specific team: IEK, VP, and SWK for CMV; AA, LP, AWH, and RSN for BKV; and RM, ONA, and FT for HZ. Disagreements were resolved through discussion and, when consensus could not be reached, adjudicated by JKF.

Databases and search strategy

A systematic literature search was conducted in PubMed, Embase, and Scopus from database inception through March 25, 2026. The search was restricted to English-language publications. The search strategy combined terms related to kidney transplantation (“kidney transplantation,” “kidney transplant,” “renal transplant,” “kidney allograft,” and “renal allograft”), ABO incompatibility (“ABO blood-group system,” “blood-group incompatibility,” “ABO incompatible,” “ABO-incompatible,” and “ABOi”), and the viral outcomes of interest (“cytomegalovirus,” “CMV,” “BK virus,” “BK polyomavirus,” “BKV,” “herpes zoster,” “varicella-zoster virus,” and “VZV”). Boolean operators, phrase searching, and truncation were applied as appropriate.

The search strategy was initially developed for PubMed using Medical Subject Headings (MeSH) and free-text terms in the title and abstract fields. The strategy was subsequently adapted for Embase using Emtree terms and free-text terms in the title, abstract, and keyword fields, and for Scopus using terms in the title, abstract, and keyword fields.

Clinical trial registries, conference proceedings, and other grey-literature sources were not searched. The reference lists of eligible articles and relevant systematic reviews identified during

screening were manually examined to identify additional studies. Records identified through this supplementary search were evaluated using the same predefined eligibility criteria as those retrieved from the electronic databases.

Data extraction

Data were extracted independently by three reviewer teams using a prespecified standardized form, with each eligible study assessed by at least two reviewers. IEK, VP, and SWK extracted data for CMV outcomes; AA, LP, AWH, and RSN extracted data for BKV outcomes; and RM, ONA, and FT extracted data for HZ outcomes. The extracted information comprised the first author, publication year, country, study design, study setting, recruitment period, participant age, duration of follow-up, numbers of ABO-incompatible and ABO-compatible recipients, diagnostic criteria for viral infection, and event counts for each outcome. Any discrepancies were resolved through discussion within the respective reviewer team; when consensus could not be reached, JKF acted as the senior adjudicator.

Exposure and outcome definitions

The exposure of interest was ABO-incompatible kidney transplantation, with ABO-compatible kidney transplantation serving as the comparator. The outcomes were post-transplant CMV infection, BKV infection, and HZ among kidney transplant recipients.

CMV infection encompassed asymptomatic CMV replication, CMV syndrome, and tissue-invasive CMV disease, as defined in each included study. Asymptomatic infection was generally identified through CMV DNAemia detected by quantitative PCR or positive pp65 antigenemia in the absence of attributable symptoms. CMV syndrome was defined by evidence of viral replication accompanied by compatible clinical or laboratory manifestations. Tissue-invasive CMV disease was diagnosed based on clinical evidence of organ involvement supported by histopathological or immunohistochemical confirmation, including CMV gastritis or colitis [31].

BKV infection encompassed BK polyomavirus viruria, DNAemia, and BKVAN, according to the definitions applied in the included studies. Viruria was identified through the detection of BKV in urine by molecular testing or indirectly through decoy-cell cytology. BKV DNAemia was defined as detectable viral DNA in plasma or whole blood using quantitative PCR, with thresholds varying across studies. BKVAN was defined by histopathological evidence of BK polyomavirus infection in renal-allograft tissue.

HZ was defined as clinically diagnosed reactivation of VZV presenting as localized or disseminated HZ, with or without laboratory confirmation [44]. Primary varicella infection was not considered equivalent to HZ and should only be included if the original study reported a combined varicella-zoster outcome that could not be separated [4].

Because the included studies applied heterogeneous diagnostic definitions and severity thresholds, the primary outcome for each virus was defined as any post-transplant infection reported by the study. For CMV and BKV, this composite outcome encompassed asymptomatic viral replication, symptomatic infection, and tissue-invasive disease. For HZ, it included localized and disseminated disease. When multiple severity categories were reported within a study, the broadest mutually exclusive category was used to avoid duplicate counting and improve comparability across studies.

Statistical analysis

Data from the included studies were analyzed using crude odds ratios (ORs) with 95% CIs, based on unadjusted event counts. Between-study variance was estimated using the restricted maximum-likelihood (REML) method. Crude estimates were used because most included studies did not report adjusted effect estimates. Consequently, the pooled estimates represent unadjusted associations and should be interpreted cautiously.

Given the anticipated clinical heterogeneity arising from variations in desensitization protocols, immunosuppressive regimens, diagnostic criteria, and transplantation eras, a random-effects model was specified a priori for all primary analyses, irrespective of the observed statistical heterogeneity. The I^2 statistic and heterogeneity p -value (p -Het) were reported to quantify between-study heterogeneity but were not used to determine the choice between fixed- and random-effects models.

Funnel plots and Egger's linear regression test were used to assess funnel-plot asymmetry and potential small-study effects. Egger's test has limited statistical power and reliability when fewer than 10 studies are included; therefore, the findings from the HZ analysis, which included nine studies, were considered exploratory and interpreted with substantial caution. For all outcomes, funnel-plot asymmetry may reflect reporting bias, genuine clinical heterogeneity, small-study effects, or chance. Consequently, Egger's test *p*-values were not used alone to determine the presence or absence of publication bias.

The certainty of evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. A Z test was used to evaluate the statistical significance of the pooled estimates, with a two-sided $p < 0.05$ considered statistically significant. All analyses were performed using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) with the meta package, primarily using the metabin function. For studies containing zero-event cells, a continuity correction was applied when required to enable the calculation of effect estimates.

Results

Study selection

The study selection process is presented in the PRISMA flow diagram (**Figure 1**). A total of 7,433 records were identified through searches of PubMed ($n=2,003$), Scopus ($n=620$), and Embase ($n=4,810$). After removal of 56 duplicates, 7,377 records remained for title and abstract screening. Of these, 7,314 were excluded because they were not relevant to the research question. The full texts of the remaining 63 reports were sought and successfully retrieved for eligibility assessment. Subsequently, 37 reports were excluded: 14 because of insufficient data and 23 because they were reviews or commentaries. Ultimately, 26 studies met the eligibility criteria and were included in the meta-analysis [13-38].

Characteristics of included studies

A total of 26 studies were included, and their characteristics are presented in **Table 1**. The majority of studies were retrospective [14-16,18-27,29,32,33,35-37], alongside a few prospective [30,31,34,38] and cohort studies [13,17,28]. Sample sizes ranged from 21 to 1,032 participants, with reported ages ranging from 11 to 75 years. The studies were conducted in diverse locations, such as Japan [13,15,18,20,23,28,33,35,37], Korea [19,21,22,24,25,29,32], Germany [14,17,31,38], Sweden [16], Spain [30], France [27], the United States [34], and the Netherlands [36]. The primary outcomes included infection rates [13-38], graft rejection [22,24-28,34-36,38], renal function [15,16,19,21,26,27,29,31,32,34,37,38], and patient survival rates [13-15,18,19,22-30,32-36]. Detailed information on study design, setting, sample size, follow-up duration, and outcomes is presented in **Table 1**.

Study quality and certainty of evidence

All included studies were classified as having high methodological quality according to the NOS (**Table 1**). Detailed NOS assessments are provided in the **Supplementary File 2**.

The certainty of evidence was assessed using the GRADE framework. For CMV, concerns regarding serious risk of bias, predominantly retrospective designs, reliance on unadjusted effect estimates, and suspected publication bias resulted in a very low certainty rating. For BKV, serious risk of bias and imprecision arising from the wide confidence interval and relatively small number of events resulted in very low certainty. For HZ, serious risk of bias and imprecision due to the small number of events and a confidence interval that included the null value also resulted in very low certainty. The complete GRADE assessment is provided in **Supplementary File 3**.

Association between ABO incompatibility and CMV infection

The association between ABO incompatibility and CMV infection is presented in **Figure 2**. The meta-analysis of 25 studies [13-21,23-38] indicated that ABO-incompatible kidney transplantation was significantly associated with higher odds of CMV infection. The pooled OR

was 1.34 (95%CI: 1.01–1.77; $p=0.020$), indicating 34% higher odds of CMV infection among ABO-incompatible recipients than among ABO-compatible recipients.

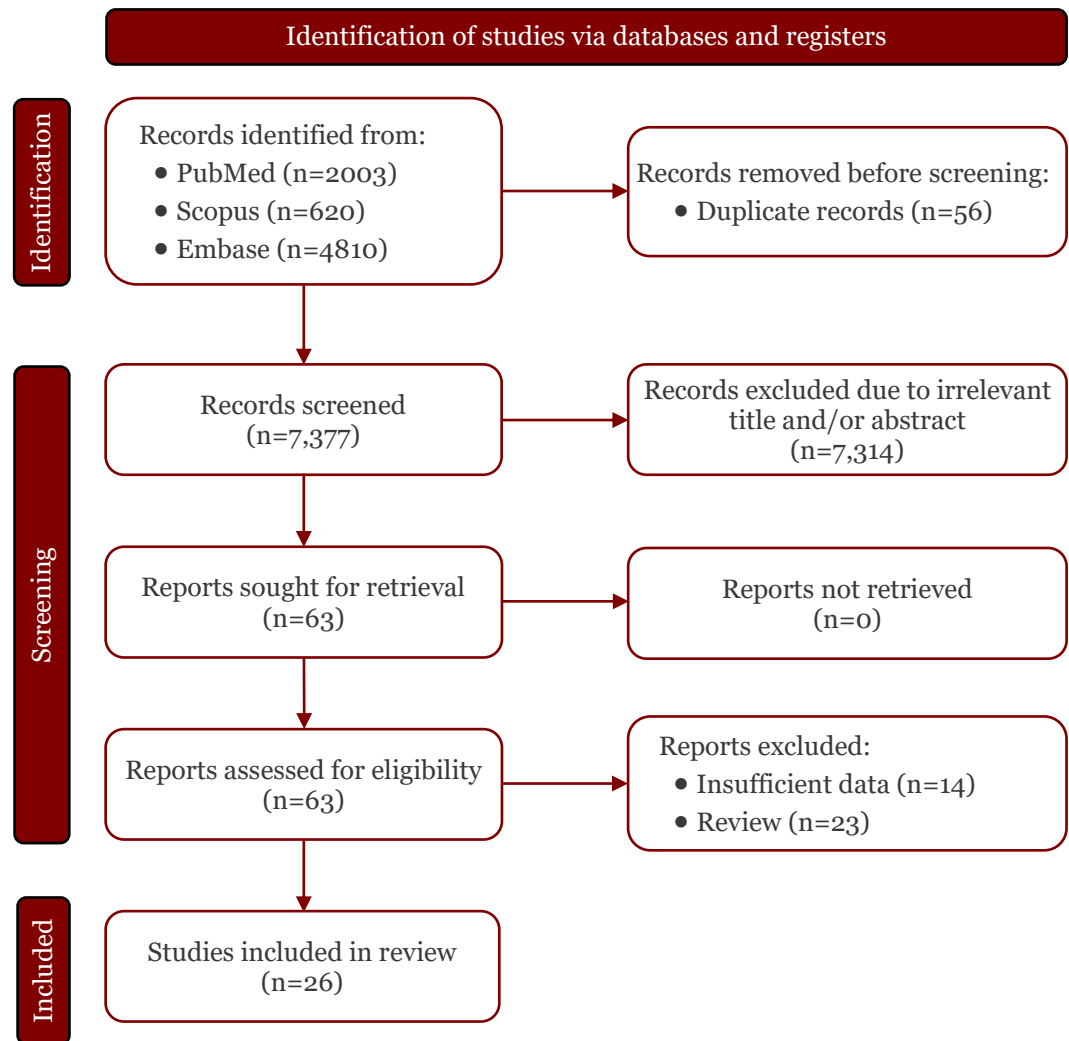


Figure 1. PRISMA flow diagram illustrating the study selection process for inclusion in the meta-analysis.

Moderate between-study heterogeneity was observed ($I^2=33.8\%$; $p\text{-Het}=0.052$). Egger's test indicated potential funnel-plot asymmetry ($p\text{-Egger}=0.013$). However, this asymmetry may reflect reporting bias, genuine clinical heterogeneity, differences in desensitization intensity across smaller studies, or chance. The trim-and-fill analysis did not impute any potentially missing studies; nevertheless, this finding does not exclude residual small-study effects or reporting bias. Therefore, the pooled estimate should be interpreted cautiously.

Association between ABO incompatibility and BKV infection

The association between ABO incompatibility and BKV infection is presented in **Figure 3**. The meta-analysis of 14 studies [14,16-19,22,24-27,31,32,34,36] indicated that ABO-incompatible kidney transplantation was significantly associated with higher odds of BKV infection. The pooled OR was 1.84 (95%CI: 1.07–3.16; $p=0.010$), indicating 84% higher odds of BKV infection among ABO-incompatible recipients than among ABO-compatible recipients. Moderate between-study heterogeneity was observed ($I^2=41.2\%$; $p\text{-Het}=0.054$). Egger's test provided no statistical evidence of funnel-plot asymmetry ($p\text{-Egger}=0.368$); however, a nonsignificant result does not definitively exclude small-study effects or publication bias.

Table 1. Baseline characteristics of studies included

Study	Country	Design	Age (years)	Recruitment years	ABO-incompatible sample size	ABO-compatible sample size	Follow-up duration (month)	Outcomes	Quality assessment
Ashimine 2014 [13]	Japan	Retrospective cohort	40.1±15.1	2005–2009	92	228	34.3	Infection, rejection, survival	High
Becker 2015 [14]	Germany	Retrospective	46 (18–65)	2001–2005	20	48	40.8	Infection, cost, survival, surgical complication	High
Fuchinoue 2011 [15]	Japan	Retrospective	43.5±13.7	2007–2010	22	61	12	Renal function, survival, infection	High
Genberg 2008 [16]	Sweden	Retrospective	35.1±14.3	2001–2009	102	83	24	Renal function, infection, B-cell	High
Habicht 2011 [17]	Germany	Retrospective cohort	45.6±2.6	2009–2010	234	600	36	Rejection, infection, surgical complication	High
Hatakeyama 2014 [18]	Japan	Retrospective	45.0±12.0	2005–2013	30	30	72	Rejection, infection, survival	High
Hwang 2013 [19]	Korea	Retrospective	44.1±9.2	2011–2015	44	44	6	Renal function, survival, infection	High
Iwai 2015 [20]	Japan	Retrospective	64.7±3.9	1989–2013	247	785	108	Rejection, infection, surgical complication	High
Jeon 2010 [21]	Korea	Retrospective	19–58	2011–2013	11	21	24.3	Renal function, infection, rejection	High
Kim 2017 [22]	Korea	Retrospective	50 (19–69)	2009–2013	30	146	21	Survival, graft function, rejection, infection	High
Kohei 2012 [23]	Japan	Retrospective	40.4±12.3	2005–2012	35	62	42	Survival, rejection, infection	High
Kwon 2016 [24]	Korea	Retrospective	41.3±12.1	2006–2012	50	100	38	Survival, infection, surgical complication, graft function	High
Lee 2016 [25]	Korea	Retrospective	43.3±13.8	2004–2014	97	106	58	Rejection, graft survival, infection	High
Melexopoulou 2015 [26]	Greece	Retrospective	39.0±11.0	2005–2013	34	68	22	Survival, graft function, renal function, infection	High
Naciri-Bennani 2016 [27]	France	Retrospective	45.0±13.5	2002–2008	113	280	36.4	Survival, graft function, infection, renal function	High
Okumi 2016 [28]	Japan	Retrospective cohort	38.1±11.7	2007–2009	21	47	16.9	Graft function, survival, infection	High
Park 2016 [29]	Korea	Retrospective	49.0±6.5	2006–2013	13	29	23	Survival, infection, renal function, surgical complication	High
Sánchez-Escuredo 2016 [30]	Spain	Prospective	44.0±13.0	2009–2011	35	138	24	Survival, rejection, infection	High
Schachtner 2015 [31]	Germany	Prospective	52 (18–65)	2001–2014	5	16	125	Infection, mortality, renal function	High
Shin 2015 [32]	Korea	Retrospective	42.8±11.8	2010–2016	71	726	41.5	Survival, renal function, infection, surgical complication	High
Shishido 2012 [33]	Japan	Retrospective	11.9±4.5	2010–2014	95	118	12	Rejection, infection, survival	High
Subramanian 2016 [34]	US	Prospective	52.2±3.6	2009–2012	73	396	45	Graft function, renal function, infection, survival	High
Tanabe 2009 [35]	Japan	Retrospective	43.0±13.5	1989–2011	52	271	110	Graft survival, mortality, infection	High
van Agteren 2014 [36]	Netherlands	Retrospective	54 (22–75)	2007–2012	18	45	60	Graft survival, infection	High
Yokoyama 2016 [37]	Japan	Retrospective	46.4±14.6	2001–2006	70	55	36	Rejection, renal function, infection	High
Zschiedrich 2015 [38]	Germany	Prospective	47.0±11.0	2008–2013	21	50	36	Mortality, graft loss, infection, renal function	High

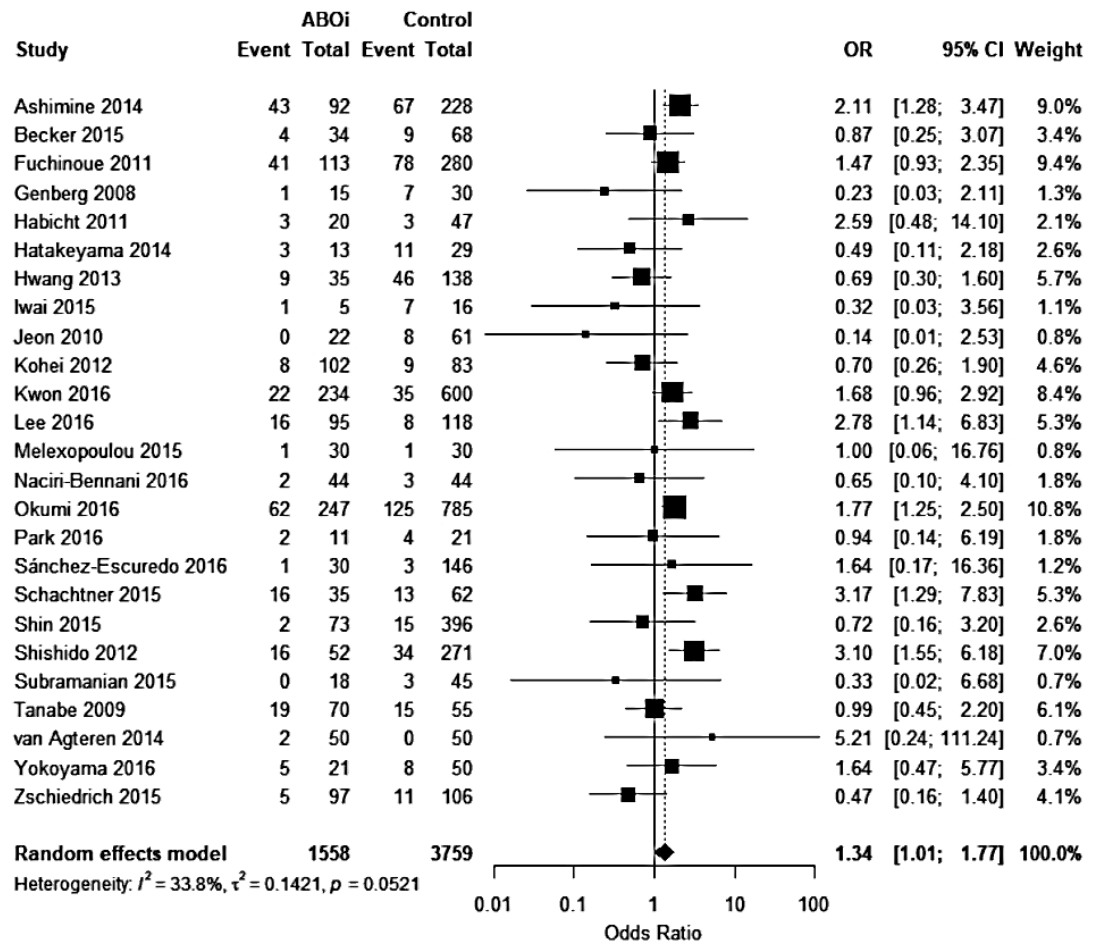


Figure 2. Association between ABO incompatibility and cytomegalovirus (CMV) infection among kidney transplant recipients. The forest plot presents the pooled odds ratio (OR) and 95% confidence interval (CI) derived using a random-effects model (OR: 1.34; 95%CI: 1.01–1.77; $p=0.020$; $I^2=33.8\%$; $p\text{-Het}=0.052$; $p\text{-Egger}=0.013$).

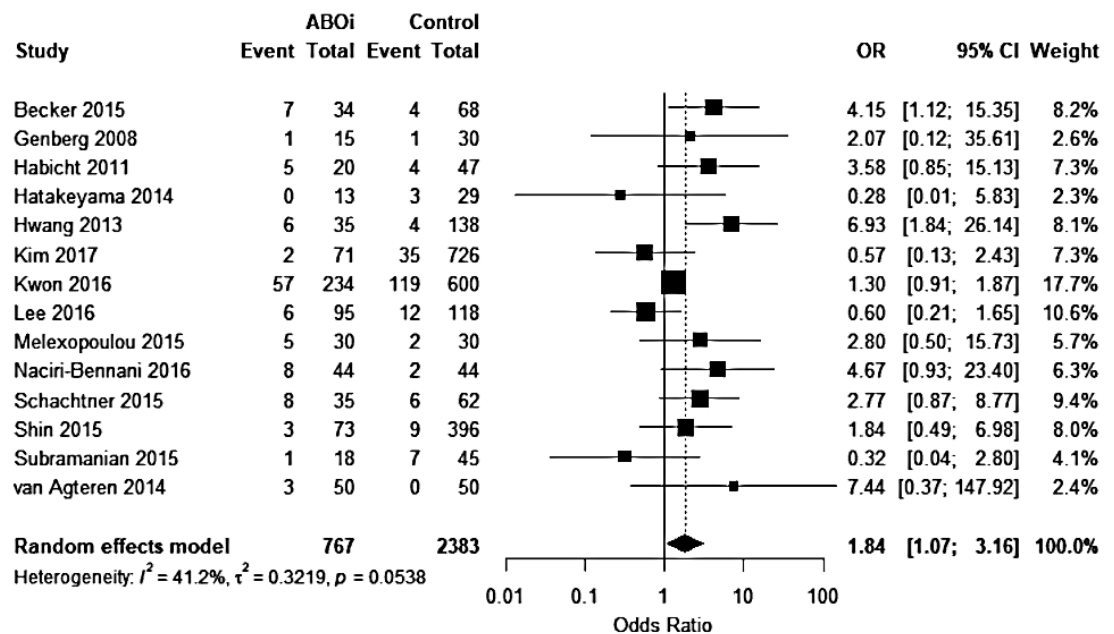


Figure 3. Association between ABO incompatibility and BK polyomavirus (BKV) infection among kidney transplant recipients. The forest plot presents the pooled odds ratio (OR) and 95% confidence interval (CI) derived using a random-effects model (OR: 1.84; 95%CI: 1.07–3.16; $p=0.010$; $I^2=41.2\%$; $p\text{-Het}=0.054$; $p\text{-Egger}=0.368$). Egger's test provided no statistical evidence of funnel-plot asymmetry.

Association between ABO incompatibility and HZ infection

The association between ABO incompatibility and HZ infection was evaluated using data from nine studies [17,19,23-25,32,33,36,38]. No statistically significant association was observed between ABO-incompatible kidney transplantation and the odds of HZ infection (**Figure 4**). The pooled OR was 1.61 (95%CI: 0.95–2.72; $p=0.070$). Between-study heterogeneity was low ($I^2=4.8\%$; $p\text{-Het}=0.395$). Egger's test provided no statistical evidence of funnel-plot asymmetry ($p\text{-Egger}=0.875$). However, because the analysis included fewer than 10 studies, Egger's test was underpowered, and its result should be considered exploratory. Visual inspection of the funnel plot did not indicate marked asymmetry, although this assessment was descriptive.

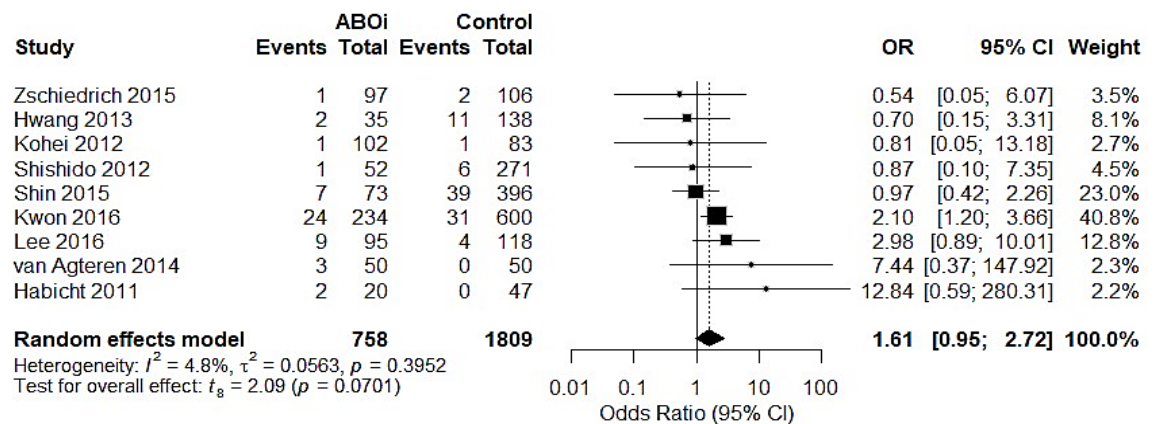


Figure 4. Association between ABO incompatibility and herpes zoster (HZ) among kidney transplant recipients. The forest plot presents the pooled odds ratio (OR) and 95% confidence interval (CI) derived using a random-effects model (OR: 1.61; 95%CI: 0.95–2.72; $p=0.070$; $I^2=4.8\%$; $p\text{-Het}=0.395$; $p\text{-Egger}=0.875$). Egger's test provided no statistical evidence of funnel-plot asymmetry; however, this finding should be interpreted cautiously because fewer than 10 studies were included.

Heterogeneity among studies and potential publication bias

The analyses demonstrated varying degrees of between-study heterogeneity (**Table 2**). Moderate heterogeneity was observed for CMV ($I^2=33.8\%$; $p\text{-Het}=0.052$) and BKV ($I^2=41.2\%$; $p\text{-Het}=0.054$), whereas heterogeneity was low for HZ ($I^2=4.8\%$; $p\text{-Het}=0.395$). For CMV, Egger's test indicated potential funnel-plot asymmetry ($p\text{-Egger}=0.013$). However, such asymmetry may arise from reporting bias, genuine clinical heterogeneity, differences in desensitization intensity across smaller studies, or chance. The trim-and-fill procedure did not impute any potentially missing studies, although this finding does not exclude residual small-study effects or reporting bias. Accordingly, the CMV findings should be interpreted cautiously. For BKV, Egger's test provided no statistical evidence of funnel-plot asymmetry ($p\text{-Egger}=0.368$). Nevertheless, given that only 14 studies were included, the test may have had limited power to detect small-study effects, and its nonsignificant result does not definitively exclude funnel-plot asymmetry. For HZ, Egger's test was considered exploratory because only nine studies were available. Neither the test ($p\text{-Egger}=0.875$) nor visual inspection of the funnel plot indicated marked asymmetry; however, these findings should not be regarded as conclusive evidence against small-study effects. The funnel plots for all outcomes are provided in the **Supplementary File 4**.

Table 2. Summary of the meta-analysis evaluating the association between ABO incompatibility and infectious complications, including CMV, BKV, and HZ infections, in renal transplant recipients

Infection	Model	NS	OR	95%CI	p-value	p-Egger	p-Het
CMV infection	Random - TF	25	1.34	1.01–1.77	0.020	0.0132	0.0521
BKV infection	Random	14	1.84	1.07–3.16	0.010	0.3684	0.0540
HZ infection	Random	9	1.61	0.95–2.72	0.070	0.8752	0.3950

BKV: BK polyomavirus; CI: confidence interval; CMV: cytomegalovirus; HZ: herpes zoster (a clinical syndrome caused by varicella-zoster virus); NS: number of studies; OR: odds ratio; $p\text{-Het}$: p -value for heterogeneity.

Discussion

This meta-analysis found that ABO-incompatible kidney transplantation was associated with higher odds of CMV and BKV infections than ABO-compatible transplantation. The magnitude of the association was greater for BKV (OR: 1.84) than for CMV (OR: 1.34). By contrast, the pooled association with HZ did not reach statistical significance (OR: 1.61; 95%CI: 0.95–2.72). These findings are broadly consistent with previous evidence suggesting that ABO-incompatible kidney transplant recipients may be more susceptible to opportunistic infections [40,45,46]. However, because the pooled estimates were based predominantly on unadjusted data from retrospective observational studies, they should be interpreted as associations rather than evidence of a direct causal effect of ABO incompatibility.

The observed associations are biologically plausible but likely reflect the clinical and therapeutic context of ABO-incompatible transplantation rather than ABO incompatibility alone. ABO mismatch exposes the graft to preformed recipient antibodies directed against donor blood-group antigens, potentially activating complement and antibody-mediated immune responses [47,48]. Successful transplantation across this immunological barrier therefore commonly requires desensitization using interventions such as rituximab, plasmapheresis, immunoadsorption, intravenous immunoglobulin, and intensified induction or maintenance immunosuppression [40,46]. These interventions may impair humoral and cellular immune function, thereby reducing control of latent or persistent viral infections [49]. ABO incompatibility should consequently be regarded as a marker of a more complex immunological and therapeutic environment rather than an isolated biological determinant of infection.

The higher pooled odds observed for BKV may be related to the particular dependence of BKV control on effective cellular immunity. Intensified immunosuppression can facilitate viral replication, progression from viruria to DNAemia, and, in some recipients, the development of BKVAN. Nevertheless, the included studies varied in their definitions of BKV infection, with outcomes ranging from viruria and DNAemia to biopsy-confirmed nephropathy. The pooled estimate therefore represents a broad spectrum of BKV-related outcomes and should not be interpreted as the effect of ABO incompatibility on clinically significant nephropathy alone.

A more modest association was observed for CMV infection. Differences in donor and recipient CMV serostatus, antiviral prophylaxis, pre-emptive treatment, surveillance schedules, and diagnostic thresholds may have influenced the effect estimates across studies. The routine use of valganciclovir prophylaxis or PCR-guided pre-emptive therapy in more recent transplantation cohorts may also have attenuated the observed association [47]. Furthermore, the CMV outcome encompassed heterogeneous clinical states, ranging from asymptomatic DNAemia to CMV syndrome and tissue-invasive disease. Consequently, the pooled estimate cannot establish whether ABO incompatibility is associated with a particular degree of CMV severity.

Although the pooled OR for HZ was greater than 1, the confidence interval included the null value, and the association was not statistically significant. This finding should not be interpreted as evidence that ABO incompatibility has no relationship with HZ. The analysis included only nine studies and relatively few events, resulting in limited statistical power and imprecision. HZ risk may also be more strongly influenced by age, baseline VZV immunity, cumulative immunosuppressive exposure, and the duration of follow-up than by the intensity of peri-transplant desensitization alone [11]. Additional studies with standardized outcome definitions and adequate follow-up are required to clarify this association.

These findings may have implications for clinical risk stratification. ABO status is known before transplantation and should not be considered a novel post-transplant predictor. Instead, it may help identify recipients exposed to more intensive desensitization and immunosuppressive regimens who could benefit from careful assessment of their overall infection risk. Clinical evaluation should incorporate donor–recipient CMV serostatus, the type and intensity of desensitization, induction and maintenance immunosuppression, antiviral prophylaxis, and other established risk factors. Monitoring and prophylactic strategies should remain aligned with current transplant-infection guidelines rather than being determined by ABO incompatibility alone. For example, regular PCR-based surveillance for CMV and BKV may facilitate early identification of viral replication, while valganciclovir prophylaxis may be appropriate for

recipients at high risk of CMV infection. Current consensus guidance also recommends monthly plasma BKV DNAemia screening during the first nine months after kidney transplantation [50]. However, the present findings do not establish that ABO-incompatible recipients require a different surveillance schedule or prophylactic regimen from those recommended on the basis of established clinical risk factors.

The between-study heterogeneity observed for CMV ($I^2=33.8\%$) and BKV ($I^2=41.2\%$) was moderate. This variability may reflect differences in desensitization protocols, immunosuppressive regimens, donor–recipient characteristics, antiviral prophylaxis, diagnostic thresholds, outcome definitions, follow-up durations, and transplantation eras. Heterogeneity was low for HZ ($I^2=4.8\%$), although this should not be interpreted as evidence of clinical homogeneity because the analysis contained relatively few studies and events. Potential funnel-plot asymmetry was identified for CMV, whereas Egger's test provided no statistical evidence of asymmetry for BKV. The HZ assessment was underpowered because fewer than 10 studies were available. Moreover, funnel-plot asymmetry may result from genuine heterogeneity or chance in addition to publication bias. Although the trim-and-fill analysis did not impute missing CMV studies, residual small-study effects or selective reporting cannot be excluded.

The certainty of evidence was rated as very low for all outcomes using the GRADE framework. This rating reflected the observational and predominantly retrospective nature of the evidence, reliance on unadjusted effect estimates, and concerns regarding risk of bias, imprecision, and potential publication bias. Accordingly, the pooled estimates do not support strong causal or practice-changing conclusions. Their principal value lies in identifying a potential association that warrants further investigation and heightened consideration within comprehensive infection-risk assessment.

Several limitations should be acknowledged. Important confounding factors could not be consistently accounted for, including the type and intensity of desensitization, rituximab exposure, induction and maintenance immunosuppression, donor and recipient viral serostatus, antiviral prophylaxis, recipient age, and comorbidities. The use of crude event counts prevented estimation of the independent contribution of ABO incompatibility. Most included studies were retrospective and therefore susceptible to selection bias, information bias, and incomplete outcome ascertainment. Considerable variation in sample size and outcome definitions may have affected the precision and comparability of the estimates. In particular, the composite outcomes combined asymptomatic viral replication with clinically significant disease. The restriction to English-language publications and the omission of clinical trial registries, conference proceedings, and other grey-literature sources may have introduced language and publication biases. Although all studies were classified as having high methodological quality according to the NOS, this classification does not eliminate the limitations inherent in observational designs or the possibility of residual confounding.

Future prospective, multicenter studies should compare ABO-incompatible and ABO-compatible recipients managed using standardized desensitization, immunosuppression, prophylaxis, and viral-surveillance protocols. Analyses should report adjusted estimates and distinguish asymptomatic viral replication from symptomatic and tissue-invasive disease. Detailed documentation of rituximab exposure, cumulative immunosuppressive burden, donor–recipient serostatus, viral load thresholds, and vaccination status would help separate the effect of ABO incompatibility from the treatment-mediated consequences of desensitization. Such evidence is required to determine whether ABO incompatibility independently contributes to post-transplant viral infections and whether tailored preventive or surveillance strategies are clinically justified.

Conclusion

This meta-analysis identified significant associations between ABO-incompatible kidney transplantation and higher odds of CMV and BKV infections, with the largest pooled OR observed for BKV infection. No statistically significant association was found for HZ. However, because the pooled estimates were derived from unadjusted data from observational studies and the certainty of evidence was very low, these findings should not be interpreted as causal. The observed associations may reflect the more intensive desensitization and immunosuppressive regimens

used in ABO-incompatible transplantation rather than ABO incompatibility itself. These findings highlight the potential importance of risk-stratified infection prevention and surveillance while underscoring the need for prospective studies that distinguish the immunobiological effects of ABO incompatibility from the treatment-mediated effects of desensitization.

Ethics approval

Not required.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

The supplementary files for this study have been deposited in Figshare (<https://doi.org/10.6084/m9.figshare.32599128>).

Declaration of artificial intelligence use

Artificial intelligence tool, Kimi AI, was used for language refinement. All AI-assisted output was critically reviewed and edited by the authors, and full responsibility for the accuracy, interpretation, and final content of the manuscript was retained by the authors.

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References

1. Garcia GG, Harden P, Chapman J, *et al.* The global role of kidney transplantation. J Nephropathol 2012;1(2):69-76.
2. Sabisi MA, Al-Shammari ZA. Major non-communicable diseases in Asia: Burden, epidemiological trends and projections, and future challenges. Narra Intern Med 2026;1(1):e7.
3. Tamara F, Fajar JK, Susanto A, *et al.* Global prevalence and potential factors influencing willingness for renal transplantation in end-stage renal disease patients: A systematic review and meta-analysis. Narra J 2024;4(3):e964.
4. Vanichanan J, Udomkarnjananun S, Avihingsanon Y, *et al.* Common viral infections in kidney transplant recipients. Kidney Res Clin Pract 2018;37(4):323-337.
5. Jordan CL, Taber DJ, Kyle MO, *et al.* Incidence, risk factors, and outcomes of opportunistic infections in pediatric renal transplant recipients. Pediatr Transplant 2016;20(1):44-48.
6. Ko Y, Kim JY, Kim SH, *et al.* Acute rejection and infectious complications in ABO- and HLA-incompatible kidney transplantations. Ann Transplant 2020;25(1):e927420.
7. Tamara F, Fajar JK, Gersom C, *et al.* Global prevalence and contributing factors of transplant renal artery stenosis in renal transplant recipients: A systematic review and meta-analysis. Narra J 2024;4(3):e1782.
8. de Weerd AE, van den Brand J, Bouwsma H, *et al.* ABO-incompatible kidney transplantation in perspective of deceased donor transplantation and induction strategies: A propensity-matched analysis. Transpl Int 2021;34(12):2706-2719.

9. Chen Y, Wan X, Cao Y, *et al.* ABO incompatibility does not affect transfusion requirements or clinical outcomes of unrelated cord blood transplantation after myeloablative conditioning for haematological malignancies. *Blood Transfus* 2022;20(2):156-167.
10. Chong AS, Alegre ML. Transplantation tolerance and its outcome during infections and inflammation. *Immunol Rev* 2014;258(1):80-101.
11. Choi BH, Han DJ. Ongoing higher infection rate in ABO-incompatible kidney transplant recipient: Is it a serious problem? A single-center experience. *Ann Surg Treat Res* 2016;91(1):37-44.
12. Dai LR, Wang XH, Hou YB, *et al.* ABO-incompatible living donor kidney transplantation failure due to acute blood group antibody-dependent rejection triggered by human parvovirus B19 infection: A case report and literature review. *Front Med* 2023;10(1):1195419.
13. Ashimine S, Watarai Y, Yamamoto T, *et al.* Neither pre-transplant rituximab nor splenectomy affects de novo HLA antibody production after renal transplantation. *Kidney Int* 2014;85(2):425-430.
14. Becker LE, Siebert D, Susal C, *et al.* Outcomes following abo-incompatible kidney transplantation performed after desensitization by nonantigen-specific immunoadsorption. *Transplantation* 2015;99(11):2364-2371.
15. Fuchinoue S, Ishii Y, Sawada T, *et al.* The 5-year outcome of ABO-incompatible kidney transplantation with rituximab induction. *Transplantation* 2011;91(8):853-857.
16. Genberg H, Kumlien G, Wennberg L, *et al.* ABO-incompatible kidney transplantation using antigen-specific immunoadsorption and rituximab: A 3-year follow-up. *Transplantation* 2008;85(12):1745-1754.
17. Habicht A, Broker V, Blume C, *et al.* Increase of infectious complications in ABO-incompatible kidney transplant recipients-a single centre experience. *Nephrol Dial Transplant* 2011;26(12):4124-4131.
18. Hatakeyama S, Fujita T, Murakami R, *et al.* Outcome comparison of ABO-incompatible kidney transplantation with low-dose rituximab and ABO-compatible kidney transplantation: A single-center experience. *Transplant Proc* 2014;46(2):445-448.
19. Hwang JK, Kim YK, Kim JM, *et al.* Comparative analysis of ABO-incompatible living donor kidney transplantation with ABO-compatible grafts: A single-center experience in Korea. *Transplant Proc* 2013;45(8):2931-2936.
20. Iwai T, Uchida J, Kuwabara N, *et al.* Clinical outcome of elderly kidney transplant recipients from spousal donors. *Urol Int* 2015;95(1):99-105.
21. Jeon BJ, Kim IG, Seong YK, *et al.* Analysis of the results of abo-incompatible kidney transplantation: In comparison with abo-compatible kidney transplantation. *Korean J Urol* 2010;51(12):863-869.
22. Kim YC, Yu MY, Lee JP, *et al.* The effect of desensitization therapy in kidney transplantation. *Clin Exp Nephrol* 2017;22(1):179-187.
23. Kohei N, Hirai T, Omoto K, *et al.* Chronic antibody-mediated rejection is reduced by targeting B-cell immunity during an introductory period. *Am J Transplant* 2012;12(2):469-476.
24. Kwon H, Kim YH, Choi JY, *et al.* Analysis of 4000 kidney transplantations in a single center: Across immunological barriers. *Medicine* 2016;95(32):e4249.
25. Lee J, Lee JG, Kim S, *et al.* The effect of rituximab dose on infectious complications in ABO-incompatible kidney transplantation. *Nephrol Dial Transplant* 2016;31(6):1013-1021.
26. Melexopoulou C, Marinaki S, Liapis G, *et al.* Excellent long term patient and renal allograft survival after ABO-incompatible kidney transplantation: Experience of one center. *World J Transplant* 2015;5(4):329-337.
27. Naciri Bennani H, Abdulrahman Z, Allal A, *et al.* Early post-transplant complications following ABO-incompatible kidney transplantation. *J Nephrothol* 2016;5(1):19-27.
28. Okumi M, Toki D, Nozaki T, *et al.* Abo-incompatible living kidney transplants: Evolution of outcomes and immunosuppressive management. *Am J Transplant* 2016;16(3):886-896.
29. Park WY, Kang SS, Park SB, *et al.* Comparison of clinical outcomes between ABO-compatible and ABO-incompatible spousal donor kidney transplantation. *Kidney Res Clin Pract* 2016;35(1):50-54.
30. Sanchez-Escuredo A, Oppenheimer F, Sole M, *et al.* Borderline rejection in ABO-incompatible kidney transplantation. *Clin Transplant* 2016;30(8):872-879.
31. Schachtner T, Stein M, Reinke P. ABO desensitization affects cellular immunity and infection control after renal transplantation. *Transpl Int* 2015;28(10):1179-1194.
32. Shin E, Kwon SW, Yang WS, *et al.* Long-term outcomes of ABO-incompatible living donor kidney transplantation: A comparative analysis. *Transplant Proc* 2015;47(6):1720-1726.
33. Shishido S, Hyodo YY, Aoki Y, *et al.* Outcomes of pediatric ABO-incompatible kidney transplantations are equivalent to ABO-compatible controls. *Transplant Proc* 2012;44(1):214-216.

34. Subramanian V, Gunasekaran M, Gaut JP, *et al.* ABO incompatible renal transplants and decreased likelihood for developing immune responses to HLA and kidney self-antigens. *Hum Immunol* 2016;77(1):76-83.
35. Tanabe K, Ishida H, Shimizu T, *et al.* Evaluation of two different preconditioning regimens for ABO-incompatible living kidney donor transplantation. A comparison of splenectomy vs. rituximab-treated non-splenectomy preconditioning regimens. *Contrib Nephrol* 2009;162:61-74.
36. van Agteren M, Weimar W, de Weerd AE, *et al.* The first fifty abo blood group incompatible kidney transplantations: The Rotterdam experience. *J Transplant* 2014;2014:913902.
37. Yokoyama T, Konno O, Kihara Y, *et al.* Clinical outcomes and results of pathological findings of 1-year protocol biopsy in recipients of abo-incompatible living donor kidney transplantants. *Transplant Proc* 2016;48(3):831-835.
38. Zschiedrich S, Janigen B, Dimova D, *et al.* One hundred ABO-incompatible kidney transplantations between 2004 and 2014: A single-centre experience. *Nephrol Dial Transplant* 2015;31(4):663-671.
39. Bocchi F, Binet I, Golshayan D, *et al.* Impact of repeated non-fatal infections on quality of life and graft function in ABO-incompatible kidney transplants. *Transpl Infect Dis* 2025;27(5):e70084.
40. Mohamed M, Sweeney T, Alkhader D, *et al.* ABO incompatibility in renal transplantation. *World J Transplant* 2021;11(9):388-399.
41. Mohseni M, Ameri H, Arab-Zozani M. Potential limitations in systematic review studies assessing the effect of the main intervention for treatment/therapy of COVID-19 patients: An overview. *Front Med* 2022;9(1):966632.
42. Koo TY, Yang J. Current progress in ABO-incompatible kidney transplantation. *Kidney Res Clin Pract* 2015;34(3):170-179.
43. Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Syst Rev* 2021;10(1):89.
44. Malahe SRK, van Kampen JJA, Manintveld OC, *et al.* Current Perspectives on the management of herpesvirus infections in solid organ transplant recipients. *Viruses* 2023;15(7):1595.
45. Huseynov A, Cicek SNK. Comparison of domino transplantation with Two-Way paired exchange and normal transplantation: Acute rejection, surgical complications, and 5-year survival outcomes. *Langenbecks Arch Surg* 2025;410(1):203.
46. Lee HR, Kim K, Lee SW, *et al.* Effect of rituximab dose on induction therapy in ABO-incompatible living kidney transplantation: A network meta-analysis. *Medicine* 2021;100(10):e24853.
47. Matteocci A, Pierelli L. Immuno-hematologic complexity of ABO-incompatible allogeneic HSC transplantation. *Cells* 2024;13(10):814.
48. van Sandwijk MS, Klooster A, Ten Berge IJ, *et al.* Complement activation and long-term graft function in ABO-incompatible kidney transplantation. *World J Nephrol* 2019;8(6):95-108.
49. Maglennon GA, McIntosh PB, Doorbar J. Immunosuppression facilitates the reactivation of latent papillomavirus infections. *J Virol* 2014;88(1):710-716.
50. Kotton CN, Kamar N, Wojciechowski D, *et al.* The second international consensus guidelines on the management of BK polyomavirus in kidney transplantation. *Transplantation* 2024;108(9):1834-1866.