

Beyond Refractory Anaemia: A Focused Scoping Review of Parvovirus B19 Infection in Kidney Transplant Recipients _____

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Abstract

Parvovirus B19 infection is a rare and underestimated complication encountered among kidney transplant recipients, with clinical implications extending beyond refractory anemia. This focused scoping review analyzed primary clinical evidence from 29 studies published over two decades, from 2002 to 2026, mapping current evidence across diagnostic, therapeutic and prognostic domains. Serological testing was found to be unreliable in this population, with quantitative PCR emerging as the essential diagnostic tool. Management is guided by a sequential immunosuppressive framework, though no standardised protocol exists and randomised controlled trial evidence is absent. Paediatric recipients represent a particularly vulnerable and underserved population. Prospective multicentre data and targeted paediatric research remain the most pressing unmet needs in this field.

Keywords: *Parvovirus B19; kidney transplantation; pure red cell aplasia; refractory anaemia; intravenous immunoglobulin; immunosuppression reduction; scoping review.*

Introduction

Parvovirus B19 (B19V) is a single-stranded DNA virus belonging to the Parvoviridae family that shows selective tropism for committed erythroid progenitor cells. In immunocompetent individuals, it is responsible for the development of erythema infectiosum (Fifth disease) in the pediatric population. Among adults it often presents as a self-limiting illness characterized by mild constitutional symptoms. Primary infection is resolved through a humoral response with the generation of immunoglobulin G antibodies that commonly confer lasting immunity [1].

However, in immunocompromised patients the natural history of the infection is altered. This is particularly evident among solid-organ transplant recipients, who fail to mount a robust immunological response allowing B19V to persist in the bone marrow, eliciting lytic infection of erythroid progenitor cells and profound anemia. B19V infection in this population leads to the development of pure red cell aplasia (PRCA), characterized by severe normocytic anemia, reticulocytopenia and resistance to erythropoiesis-stimulating agents (ESAs). Due to their intense maintenance immunosuppressive regimens, kidney transplant recipients are especially vulnerable to this complication [1-4].

Despite decades of accumulated clinical experience, management of B19V infection remains unstandardized. Current literature on B19V infection among kidney transplant recipients comprises primarily case-reports or small case-series,

with evidence from randomized controlled trials lacking [1]. Diagnostic methods and treatment protocols are heterogeneous and vary across institutions. Critical questions on the optimal PCR threshold for treatment initiation, IVIG dosing and duration, indications for immunosuppression modifications and treatment of refractory disease remain unanswered [1]. Moreover, recent data on B19V infection in this population, has revealed associations with antibody-mediated rejection (ABMR) and thrombotic microangiopathy (TMA) with important implications on allograft survival, pointing to clinical significance beyond refractory anemia [5-7].

This article aims to present a focused scoping review of primary clinical literature on B19V infection in kidney transplant recipients, by identifying and synthesizing key findings on the timing and clinical presentation of B19V infection following kidney transplantation, diagnosis and current treatment strategies, while highlighting priority evidence gaps for future research.

Design and Methods

This focused scoping review was conceptualized in accordance with established scoping review methodology and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) [8,9]. However, no protocol was prospectively registered, representing one of the limitations of our study. A systematic search was conducted across PubMed/MEDLINE, PubMed Central, Google Scholar, ScienceDirect, Frontiers, Wiley Online Library, MDPI, and Oxford Academic from January 2000 to March 2026. The search combined terms for Parvovirus B19 (including B19V and erythrovirus) with kidney or renal transplantation. A supplementary targeted search was subsequently performed by reference-list tracking to identify additional eligible records not captured by the database search. Only English-language publications were considered.

To be included as primary studies records were considered eligible if they: a) reported primary patient-level data, b) included adult or paediatric recipients of a kidney transplant, c) described Parvovirus B19 infection confirmed by PCR, serology, or bone marrow histology and d) were published as full-text peer-reviewed articles. Excluded study types were narrative reviews, systematic reviews, meta-analyses, editorials, and conference abstracts without full-text data.

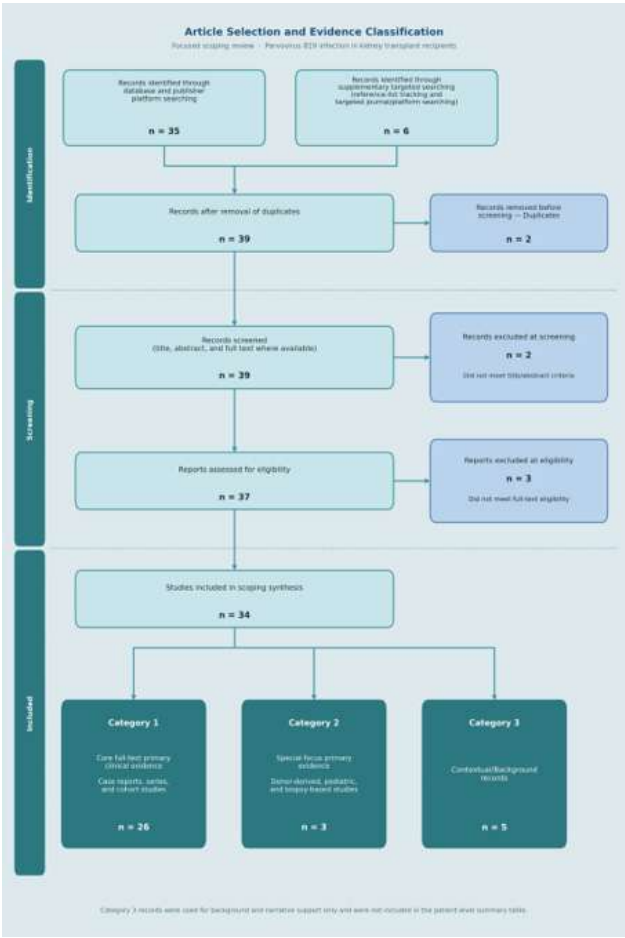
Titles, abstracts, and full texts were initially screened and categorised into three main groups, with the first two categories comprising the primary clinical evidence that was analyzed, and the third category representing records that were only utilized for narrative and background reference.

Given the heterogeneity of study designs and outcome reporting, thematic narrative synthesis was conducted across the main domains: timing and clinical presentation, diagnosis, treatment strategies and response, donor-derived transmission, graft outcomes and paediatric disease.

Results
Study Selection

Our initial database search identified 35 records, and the supplementary manual search identified a further six. After removal of two duplicate records, a total of 39 records were screened. We excluded two records at title and abstract screening, and the remaining 37 records underwent full-text review. Three were excluded at this stage as they did not meet eligibility criteria. A total of 34 records were included in the final review framework, further classified into three main categories: 29 primary studies (26 Category 1 and 3 Category 2), and five contextual records (Category 3) used for background and narrative support only. The selection process is summarized in Figure 1.

FIGURE 1. PRISMA flow diagram of study selection and evidence classification



Characteristics of included studies

The 29 primary studies were published between 2002 and 2026 across geographically diverse settings, including South Korea, the United States, India, China, Brazil, Switzerland, Italy, Japan, Vietnam, Albania, Spain, the United Kingdom, Iran, Turkey, and Greece [2-6,11-34]. Twenty-two of 29 studies were published in 2017 or later. Study designs comprised 14 single case reports, six case series (two to 21 patients), six retrospective or prospective observational cohort studies, and three special-focus primary studies. The three Category 2 studies addressed: donor-derived B19V transmission across 2,048 kidney transplants (Yu et al. [24]); intrarenal B19V infection and ABMR in 106 paediatric recipients with prospective protocol biopsy (Bertazza Partigiani et al. [5]); and a paediatric case compilation yielding 50 cases (Jia et al. [12]). Table 1 summarises all included study characteristics (Figure 2, Figure 3 and Figure 4).

TABLE 1. Characteristics of included primary studies

Study (Year) Country	Design (N)	Timing	Key findings	Treatment/Outcome
Yango, 2002 USA	CR; 1	Early	Pancytopenia; donor-derived transmission	IVIg 0.4 g/kg/d x10 + RIS; stabilized
Ki, 2005 South Korea	Cohort; 167 (52 PCR+)	Serial	PRCA in 2; PCR+ → lower Hb; graft unaffected	Variable; graft survival unaffected
Egbuna, 2006 USA	Series; 3	Mean 40 mo	EPO-resistant anemia/PRCA; 1 recurrence	RIS + IVIg 0.5 g/kg x4; resolved
Beckhoff, 2007 Switzerland	CR; 1	Early; relapse 3.5 mo	Relapsing PRCA; low-level viremia persisted	2x IVIg + RIS; resolved
Carraturo, 2012 Italy	Cohort; 64 (2 active)	≥6 mo post-Tx	B19V in 2/64; no severe anaemia in cohort	None required
Alves, 2013 Brazil	CR; 1	Late; 3–4 years post-Tx	Severe PRCA; IgM/IgG negative (PCR+)	IVIg 0.4 g/kg/d x5; Hb recovered
Krishnan, 2015 USA	Retrospective series; 3	Mean 8.6 wk	PCR-positive in 3/3; BM confirmed PRCA in 2/3; Cr↑ in 2/3;	IVIg + RIS + transfusion; 1 relapse
Baek, 2017 South Korea	Cohort; 39 PCR+	89.7% in year 1	PCR+ → lower Hb; graft survival = controls	IVIg/RIS per severity; graft survival preserved
Hai An, 2019 Vietnam	Cohort; 9/663	8/9 within 3 mo	Severe anemia + reticulocytopenia; graft dysfunction 4/9; 1 relapse	RIS + IVIg; 1 relapse
Inamdar, 2019 India	CR; 1	Recurrent course	Recurrent PRCA; collapsing glomerulopathy and allograft loss	IVIg + RIS; graft lost; re-transplantation
Inoue, 2020 Japan	CR; 1	Early	Relapsing PRCA; allograft-mediated donor transmission	IVIg + RIS; Relapse → IVIg + RIS; Hb recovered
Mascia, 2020 Italy	CR; 1	~15 mo	Aplastic/PRCA + hemolytic-microangiopathic features; atypical	IVIg 400 mg/kg x10 + transfusion; stable
Gang, 2020 South Korea	CR; 1	Recurrent episodes	Recurrent PRCA; high VL; TAC → CsA conversion	Repeated IVIg; TAC → CsA; controlled

Study (Year) Country	Design (N)	Timing	Key findings	Treatment/Outcome
Sharma, 2020 USA	CR; 1	<3 mo	B19V-associated anemia + concurrent BK & rhinovirus co-infection; no BM confirmation	IVIg weekly ×5 + RIS + cidofovir; resolved
Rodríguez-Espinoza, 2021 Spain [†]	CR; 1	Early; ~1 mo	Relapsing PRCA; repeated IVIG ineffective [†]	TAC → EVR; sustained favorable response [†]
Yu, 2021 China	Cohort; 2,048 KTRs	Early	Donor-derived: 0.4% (living), 1.5% (deceased)	IVIg + RIS; all resolved; low-level asymptomatic viremia observed; donor kidneys acceptable
Huang, 2022 China	Prospective; 12/118	Mostly within 2 wk	Anemia 100%; liver dysfunction 75%; platelet reduction 8.3%; kidney dysfunction 16.7%; PCR detected early	IS ± IVIG; Hb improved; favorable prognosis
Singh, 2023 India	Cohort; 7/714	Median 6 wk	Refractory anaemia; leukopenia 57%; no relapse	RIS ± IVIG; all resolved
Bertazza Partigiani, 2023 Italy	Peds biopsy; 106 KTRs	Biopsies 6–24 mo	Intrarenal B19V 24% at Tx; peak 40.4% at 12 mo; ABMR 50% vs TCMR 19% (p=0.04)	No protocol; Tissue PCR/DSA surveillance recommended
Yaghoubi, 2023 Iran [†]	CR; 1	18 mo	Relapsing anaemia; IVIG efficacy waning discussed [†]	IVIg + RIS; TAC/MPA stopped and TAC → CsA IVIG + RIS [†]
Jia, 2024 China	Peds cohort (50 TR total); 14 KTR	Median 14 wk	IgM+ 26%, IgG+ 24% only; anemia 100%; graft dysfunction/loss 36% overall; HSCT worse than SOT	IVIg/RIS; highlights severe/atypical pediatric transplant phenotype
Choudry, 2024 UK [†]	CR; 1	Within 1 mo	Very early PRCA; high transfusion requirement; ABMR episode subsequently [†]	IVIg courses + RIS; MMF stopped and TAC → CsA; improvement; later ABMR episode [†]
Ersal, 2024 Turkey [†]	Series; 2	One early; one late	Relapsing PRCA; IgM/IgG negative in both patients (PCR+); BM confirmed [†]	IVIg + RIS; Relapses → EVR added; no recurrence [†]
Sabancı, 2024 Turkey [†]	CR; 1 (peds)	4 wk	Recurrent PRCA; mild leukopenia/thrombocytopenia; 13-yr-old; no peds protocol (authors' statement) [†]	RIS + IVIG + transfusions; persistent 15 mo; MMF → EVR with Hb improvement [†]
Hegde, 2025 India	Cohort; 21/1,164	Median 39 d	Anemia 100%; leukopenia 14%; thrombocytopenia 9.5%; fever 47%; graft dysfunction 62%; 1 graft loss	RIS in all; IVIG in 8; Hb normalized median 30 d
Najar, 2025 USA	Series; 2 (donor-derived)	POD 53–73	Donor-derived; VL >10 ³ copies/mL; same deceased donor; Refractory anemia	IVIg + MMF withdrawal/RIS; improved
Shankar, 2025 India	Series; 10/117	Median 6 wk (range 2–462 wk)	Hypoproliferative anemia in all; retic <1%; leukopenia/thrombocytopenia 30%; Hb ↓ 3.72 g/dL; desidustat adjunct	RIS + IVIG (60%) + desidustat; most recovered; 2 deaths unrelated to B19V
Eleftheriadis, 2025 Greece [†]	CR; 1	22 yr post-Tx; PRCA 4 mo after EVR → TAC [†]	Late PRCA; IgM+; mTOR inhibitor withdrawal trigger [†]	IVIg; Hb normalized 3 wk; follow-up PCR negative [†]
Strakosha, 2026 Albania*	CR; 1	Early	EPO-resistant PRCA; living-donor KTR; IgM positive; PCR unavailable; BM confirmed	IVIg + RIS + transfusions; Hb recovered; graft preserved; recurrent anemia required second IVIG

[†] Identified via supplementary targeted searching.

* Co-authored by review team. Studies ordered chronologically.

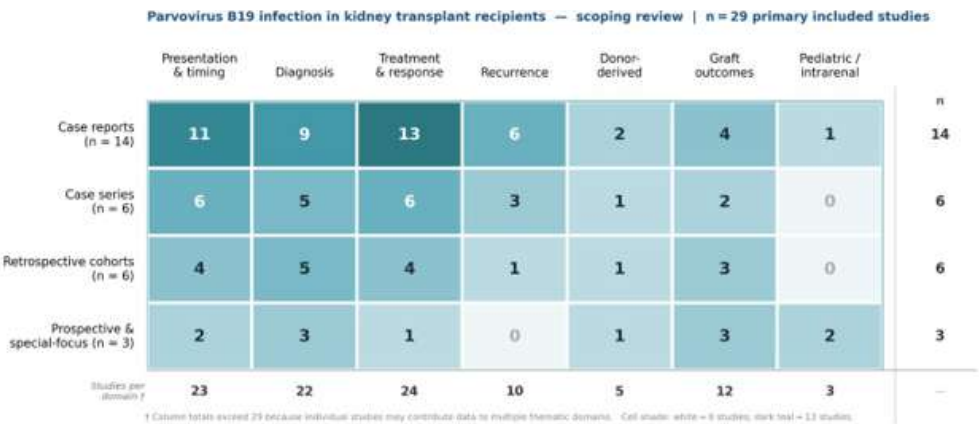
Abbreviations: ABMR, antibody-mediated rejection; B19V, Parvovirus B19; BM, bone marrow; CR, case report; CsA, cyclosporine; DCD, donation after circulatory death;

EPO/ESA, erythropoiesis-stimulating agent; EVR, everolimus; Hb, haemoglobin; HSCT, haematopoietic stem cell transplant; IVIG, intravenous immunoglobulin; KTR, kidney transplant recipient; MMF, mycophenolate mofetil; mo, months; mTOR, mammalian target of rapamycin; NR, not reported; PCR, polymerase chain reaction; POD, post-operative day; PRCA, pure red cell aplasia; peds, paediatric; RIS, reduction of immunosuppression; TAC, tacrolimus; TCMR, T-cell-mediated rejection; Tx, transplantation; VL, viral load; wk, weeks; yr, years. Diagnosis confirmed by PCR in all studies; bone marrow biopsy performed in selected cases

Timing and Clinical Presentation

B19V infection developed predominantly within the first three months post-transplantation [2,4,11,18,33]. Reported medians ranged from 39 days in Hegde et al. [11] to 14 weeks in pediatric transplant recipients in Jia et al. [12]. The earliest case occurred within the first month of the post-operative period [17] and the latest case developed 22 years post-transplant, following an immunosuppressive regimen change from everolimus to tacrolimus [13]. Therefore, timing alone cannot exclude a B19V infection. The primary clinical presentation was PRCA characterized by severe, normocytic, hypoproliferative anemia with profoundly low reticulocyte counts and ESA resistance [2-3,28,30-31,34]. Typical clinical features in immunocompetent patients such as arthropathy and rash were generally absent in this population [1]. Leukopenia and thrombocytopenia developed in 30% of recipients in the largest single-centre cohort analyzed in our study (Shankar et al. [14]), with a mean haemoglobin decline of 3.72 ± 1.22 g/dL from baseline.

FIGURE 2. Evidence map of thematic domain coverage by study design



Diagnosis

Our analysis showed serology testing to be an unreliable diagnostic tool, both in the pediatric population with the largest dataset showing IgM positivity in only 26% of cases and IgG positivity in only 24% of cases [12], as well as the adult cohort with multiple studies confirming seronegativity despite PCR-positive disease both as primary infection [15] and relapsing infection [16].

Quantitative PCR emerged as the gold standard diagnostic modality, outperforming serology testing that resulted negative even in cases of active viremia established by PCR-testing [1,4,11,14,18,33]. Furthermore PCR-testing enables evaluation of viral burden and monitoring of treatment response. However, presence of low-level viremia in the absence of a clinical and hematological constellation consistent with hypoproliferative anemia, should not prompt immediate treatment and should be interpreted with caution [24,29]. Additionally, Bertazza Partigiani et al. [5] confirmed presence of intra-renal B19V through tissue-PCR, without systemic viremia in a pediatric cohort, findings that were further solidified among adult patients by Choudry et al. [17], suggesting that tissue PCR can be incorporated as an additional diagnostic tool particularly in patients with graft dysfunction or de-novo DSA.

Bone marrow examination characterized by giant pronormoblasts with intranuclear viral inclusions, marked erythroid hypoplasia, and maturation arrest was performed selectively and reserved mainly in atypical presentations, when PCR-testing was not readily available or when a broader differential diagnosis was considered, to rule out drug-induced marrow suppression, hematological malignancy, hemophagocytic syndrome, or other viral infections [1,3,28,30,34].

FIGURE 3. Geographic distribution of included primary studies



Treatment and Recurrence

Across included studies, the management strategy was primarily composed of two pillars: reduction of immunosuppression and administration of intravenous immunoglobulin (IVIG) [1,3-4,11,14,18]. Current literature lacks formal randomized trial evidence, and reported treatment protocols reflect institutional practices and expert clinical experience [1].

Immunosuppression regimen modification typically involves reduction or temporary discontinuation of mycophenolate mofetil (MMF), the antiproliferative agent most commonly associated with erythropoietic suppression [18,20-21,23,27,31]. This may or may not be combined with calcineurin inhibitor reduction. IVIG therapy was employed in most cases with significant hematological compromise. IVIG dosing regimens and duration varied across institutions. Mascia et al. [6] used 400 mg/kg/day for ten days, while other reports described total courses of 2 g/kg administered over two days or modified shorter regimens. Decisions to initiate IVIG treatment varied based on institutional practice as well, with Hegde et al. [11] using IVIG in 38% of the cohort and Shankar et al. [14] in 60% of their cohort. Singh et al. [18] used low-dose IVIG only in patients who did not respond to immunosuppression reduction alone and Najjar et al. [19] described successful IVIG administration in two suspected donor-derived cases with exceptionally high viral loads ($>10^8$ copies/mL). Yaghoubi et al. [20] observed that the protective benefits of IVIG tended to diminish over time, in their report of relapsing B19V-associated anemia treated with both therapeutic strategies.

Hematological outcomes were generally favorable in adult recipients, with most reported cases experiencing hemoglobin recovery within several weeks [4,18,33]. Singh et al. [18] described hemoglobin improvement in some patients after immunosuppression reduction alone, and sustained hemoglobin recovery following IVIG administrations in patients who did not respond to immunosuppression modification. Transfusion dependence was a common feature across our analysis, with Shankar et al. [14] reporting need for transfusions, ranging from one to eight units of packed red blood cell transfusion, in eight out of ten patients. Of note, Shankar et al. [14] reports the first documented use of Desidustat, a novel oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), as an adjunct erythropoiesis-stimulating agent in all cases, in kidney transplant-associated B19V infection.

Emerging evidence from supplementary studies supports the consideration of mTOR inhibitor-based immunosuppression regimens in patients with recurrent or refractory disease, with multiple studies showing sustained treatment response after switching from tacrolimus to an everolimus-based regimen [16,21].

Furthermore, Eleftheriadis et al. [13] reported the development of PRCA four months following a switch from everolimus to tacrolimus, emphasizing the important antiviral properties of mTOR inhibitors.

An important distinction between haematological and virological clearance emerged across the included evidence. Patients frequently achieved haemoglobin normalisation despite incomplete or absent virological clearance, and persistent B19V DNA was associated with subsequent clinical relapse in documented cases [23,28,31]. Virological surveillance by quantitative PCR should therefore continue after apparent clinical recovery and should not be substituted by haemoglobin monitoring alone.

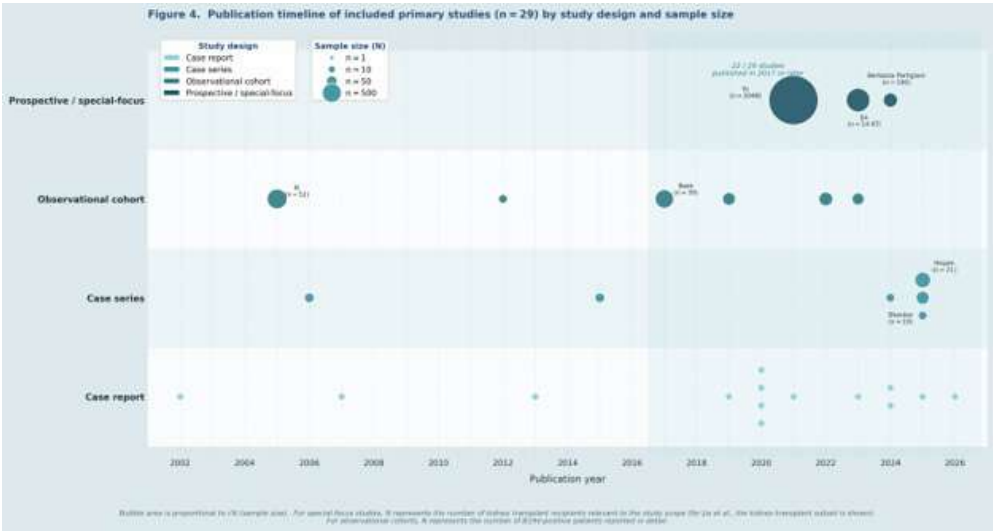
Donor-derived transmission, graft-level pathology, and paediatric disease

Donor-derived transmission is a well-established phenomenon documented by multiple case-level data from Yango et al. [22] and Inoue et al. [23]. Najjar et al. [19] confirmed simultaneous transmission in two distinct recipients that developed exceptionally high viral loads up to 10^8 copies/mL, from the same deceased donor. The most informative data emerged from Yu et al. [24], who analysed 2,048 kidney transplants retrospectively: among living donors, 15 had detectable B19V DNAemia at donation and three recipients developed donor-derived infection corresponding to a transmission rate of 0.4%, whereas in deceased donation B19V DNAemia was observed concurrently in 18 recipients and their nine corresponding donors, with a transmission rate of 1.5%. All affected recipients responded to treatment, and the authors concluded that kidneys from B19V-infected donors are clinically acceptable and that routine pre-donation screening is not currently warranted [24]. Baek et al. [25] confirmed that allograft outcomes following B19V infection did not differ significantly from controls in the adult population. Transient declines in allograft function were generally attributed to anemia-induced hemodynamic compromise. Irreversible graft loss requiring re-transplantation was documented by Inamdar et al. [26], in the context of recurrent B19V infection.

Our analysis showed that B19V impact extends beyond hematological disease, with significant implications in allograft outcomes. Mascia et al. [6] reported development of thrombotic microangiopathy and Najjar et al. [19] documented biopsy findings of borderline T-cell-mediated rejection and acute tubular damage in two donor-derived cases. Bertazza Partigiani et al. [5] showed in a pediatric cohort of 106 kidney transplant recipients, with 218 specimens analysed at 6, 12, and 24 months, persistence of intra-renal B19V independent of systemic viremia. B19V was detectable by tissue PCR in 24% of grafts at the time of transplantation,

consistent with preexisting donor-derived intrarenal infection. Overall intrarenal viral infection increased significantly between 6 and 12 months (24% vs. 44%, $p = 0.007$), while B19V prevalence peaked at 40.4% before declining to 14% at 48 months ($p = 0.02$) [5]. Notably, intra-renal B19V was more prevalent in biopsies demonstrating antibody-mediated rejection than in T-cell-mediated rejection (50% vs. 19%, $p = 0.04$), implicating intra-graft viral presence in endothelial injury and de novo donor-specific antibody development [5]. These authors recommended tissue PCR for B19V in high-risk recipients, active DSA surveillance during the first post-transplant year, and consideration of IVIG in recipients with concurrent intrarenal B19V and DSA positivity even in the absence of formal ABMR criteria [5]. These findings were corroborated in the adult population as well by Choudry et al. [17], who documented ABMR development in an adult DCD kidney recipient with early-onset B19V-associated PRCA.

FIGURE 4. Publication timeline of included primary studies



Paediatric transplant recipients, including kidney transplant recipients, demonstrated a consistently more severe disease profile across the included evidence. Jia et al. [12] compiled 50 paediatric transplant cases and documented a median time to positive B19V DNA detection of 14 weeks post-transplantation, B19V IgM positivity in only 26% and IgG in only 24% of cases, graft loss or dysfunction in 36% of recipients, and more frequent multi-lineage cytopenia than in adult series. The prognosis was reported worse among haematopoietic stem cell transplant recipients compared to solid-organ transplant recipients [12]. Bertazza Partigiani et al. [5] further demonstrated that intrarenal B19V infection, often clinically silent, was detectable in nearly one quarter of paediatric

grafts at transplantation and was independently associated with ABMR. Cases of recurrent B19V-associated anaemia have been reported after pediatric kidney transplantation [27]. The absence of a standardized management protocol for both primary and recurrent infections alongside the severity data identify the pediatric kidney transplant recipient populations as a high-risk cohort and one of the most underdeveloped management domains.

Discussion

Our focused scoping review analyzed data from 29 primary studies spanning 24 years and found that Parvovirus B19 infection among kidney transplant recipients had a heterogeneous, but consistent clinical presentation characterized predominantly by pure red cell aplasia and severe hypoproliferative anemia [2-6,11-34]. The classic presentation involving rash and generalized arthralgias commonly found in the general population, were scarcely present among transplant recipients [1]. Quantitative blood PCR emerged as the most reliable and non-invasive diagnostic test, with multiple studies both in the adult and pediatric population confirming negative serological testing can frequently be present in PCR-positive disease [12,15-16]. This lack of seroconversion potentially reflects the impaired immunological response to active infection, in these highly immunosuppressed individuals. In this context, PCR-testing for B19V when available, should represent the first-line diagnostic approach in kidney transplant recipients with unexplained, ESA-resistant anemia [1,4,10,11,14,18,33].

Bone marrow biopsy can be reserved for atypical or uncertain presentations. Complementary tissue PCR on allograft biopsy may present a potential new avenue in recipients with unexplained graft dysfunction and de-novo DSA, supported by the findings of a recent study by Bertazza Partigiani et al. [5] confirming intra-renal presence of B19V in bioptic samples in the absence of systemic viraemia and association with ABMR.

Concerning treatment strategies, a sequential therapeutic approach is preferred. First-line treatment involves reduction of immunosuppression, primarily reduction or temporary cessation of MMF depending on the severity of the presentation [1,3,4,11,18]. IVIG therapy showed significant success rates among the adult population; however, optimal dosing, duration and retreatment criteria in refractory cases remains uncertain [1,3,6,18]. The emerging evidence on the efficacy of mTOR inhibitor conversion, documented in separate case-level studies of relapsing disease and the risk of PRCA following everolimus removal, provides a rationale for considering mTOR inhibitor-based regimens in recurrent or refractory cases [13,16,21]. It is important to emphasize that while the data are not abundant enough to merit a formal recommendation, it warrants further evaluation.

Notably, a significant distinction between haematological and virological endpoints was observed. Patients experienced haematological improvement and hemoglobin normalization despite incomplete virological clearance [23,28,31]. In this context, virological surveillance should be guided by quantitative PCR-testing that should continue after apparent clinical recovery, particularly when initial infection is associated with graft loss and re-transplantation is being considered [26].

The association between B19V infection and ABMR first established in the pediatric population, and later suggested among adult recipients by Choudry et al. [17], introduces a new dimension of immunological surveillance and treatment approach [5,17]. The significantly higher prevalence of intra-renal B19V in ABMR biopsies compared with T-cell-mediated rejection biopsies, can potentially point to causality with the viral intra-renal presence contributing to endothelial activation, complement deposition, or de novo DSA development [5]. B19V-infected kidney transplant recipients, particularly those with DSA positivity may warrant a lower threshold for IVIG. Beyond ABMR the intra-renal presence of B19V has been linked to the development of allograft vascular injury and thrombotic microangiopathy (TMA) [6-7]. A proposed mechanistic basis involves a specific tropism of B19V for glomerular endothelial cells through the globoside receptor (Gb4)/P antigen, which is expressed on the erythroid progenitor cells as well [1,7]. The histological pattern of vascular injury mimics that of vascular rejection, posing a significant diagnostic challenge. Furthermore, evidence of significant glomerular injury due to development of collapsing glomerulopathy, characterized by nephrotic-range proteinuria, progressive graft dysfunction, and eventual graft loss was documented by Inamdar et al [26]. The endothelial tropism of the virus provides a unifying biologic pathway explaining the intra-renal presence of B19V and its potential link to the development of ABMR, glomerular injury and TMA.

Current literature reveals that B19V infection is more prevalent in the first year following transplantation [2,4,11,25,33]. Nevertheless, several case-level data shows that infection can develop even years after kidney transplantation, with the most extreme case being reported 22 years following transplantation [13,15,20]. In this respect, timing alone cannot reliably exclude the presence of B19V infection. The development of severe, hypoproliferative anemia or new-onset pancytopenia at any point in a kidney transplant recipient should prompt testing and evaluation for B19V. Moreover, since B19V infection may reflect an increased net state of immunosuppression, concomitant viral infections, particularly CMV, EBV, and BK virus, should be actively considered during evaluation and follow-up [32].

Finally, our analysis found the pediatric population to be particularly vulnerable to B19V infection, beyond the hematologic disease with moderate rates up to 36% of graft dysfunction or loss, compared to more benign graft outcomes in adults [5,12,25]. The humoral response impairment was more pronounced in this population, with negative serologic test results hindering timely diagnosis

[12]. The clinical phenotype among pediatric kidney transplant recipients is more heterogenous as well with patients presenting with constitutional symptoms, multilineage cytopenias and graft dysfunction, highlighting the need to adopt a lower PCR testing threshold among these patients [5,12,27]. The lack of a standardized, pediatric specific treatment or monitoring protocol emerged as an important gap in current literature [27] (Figure 5).

FIGURE 5. Clinical summary: suspicion, diagnosis, management and evidence gaps



Study Limitations and Research Priorities

Our review is subject to limitations inherent to the available evidence and our focused scoping review methodological approach. The evidence base is dominated by case reports and small case series, precluding quantitative analysis. Furthermore, the geographic distribution of the included primary studies, with limited representation from Europe and the Middle East, may affect the generalizability of our findings to these regions. The supplementary search was not systematic in scope and may not have captured all eligible records. Publication bias toward severe presentations is likely.

The most important gaps in need of addressing in additional research are conducting a prospective multicentre registry with standardized virological and haematological outcome endpoints and developing a consensus-based definition of virological clearance and retreatment thresholds. Additionally, adult protocol biopsy data incorporating B19V tissue PCR is imperative to characterize the ABMR association and designing dedicated prospective studies in paediatric kidney transplant recipients addressing treatment dosing and surveillance protocols. Finally, the development of a prospective trial to evaluate mTOR inhibitor conversion in recurrent disease, is paramount to evaluate the efficacy of this management approach.

Conclusion

Parvovirus B19 infection in kidney transplant recipients is an underrecognised and diagnostically challenging complication with clinical implications that extend well beyond refractory anaemia. This scoping review confirms that the current evidence base, while informative, remains insufficiently standardised to support definitive diagnostic or treatment protocols. Quantitative PCR testing and a sequential immunosuppression management approach represent the best-supported clinical framework to emerge from this review. Prospective multicentre studies and randomised controlled trial evidence, alongside a dedicated paediatric research agenda, are paramount to building an evidence-based clinical practice and moving beyond current expert consensus.

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Declarations

Conflicts of interest: The authors declare that they have no competing interests.

Editorial independence: E.R. is Editor-in-Chief of Medicus. To avoid any conflict of interest, this manuscript was handled entirely by an independent member of the editorial board, and E.R. was excluded from all editorial decisions regarding its peer review and acceptance.

Ethics approval and consent: Not applicable. This scoping review analysed

previously published, peer-reviewed literature and did not involve new studies on human participants or animals performed by the authors.

Author contributions: All authors contributed to the conception and design of the review, the literature search, study screening and data extraction, interpretation of the findings, and drafting and critical revision of the manuscript, and approved the final version.

Data availability: All data analysed in this review are derived from the published studies listed in the reference list; no new datasets were generated or analysed.

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