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Research Article

Impact of ABO and Rh Incompatibility on Early Postoperative Outcomes in Pediatric Liver Transplantation: A Single-Center Cohort Analysis of 99 Recipients

Hasret Ayyıldız Civan[1]*, Ferhat Sarı[2], Feyza Sönmez Topçu[2], Aysel Taktak[1], Merve Aktar[2], Hüseyin İlksen Toprak[3], Adem Tunçer[2], Emrah Şahin[2], Veysel Esan[1], Umut Mert Aksoy[3], Bülent Ünal[3], Abuzer Dirican[3]

[1]Assoc. Professor. Dr. Istanbul Aydın University, Florya VM Medicalpark Practice and Research Hospital, Organ Transplantation Center, Istanbul-34290, Turkey
[2]Specialist Dr. Istanbul Aydın University, Florya VM Medicalpark Practice and Research Hospital, Organ Transplantation Center Istanbul-34290, Turkey
[3]Professor. Dr. Istanbul Aydın University, Florya VM Medicalpark Practice and Research Hospital, Organ Transplantation Center Istanbul-34290, Turkey

***Corresponding Author:** Hasret Ayyıldız Civan, Assoc. Professor. Dr. Istanbul Aydın University, Florya VM Medicalpark Practice and Research Hospital, Organ Transplantation Center, Istanbul-34290, Turkey.

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Abstract

Background: Serologic compatibility, particularly ABO and Rh blood group matching, has long been considered a potential determinant of early outcomes in pediatric liver transplantation. Although the liver possesses unique tolerogenic properties that reduce susceptibility to antibody-mediated injury, the clinical significance of ABO and Rh mismatch in children remains insufficiently defined. Existing literature focuses predominantly on ABO incompatibility, while the impact of Rh disparity—despite its frequent occurrence—has never been systematically examined in a pediatric cohort.

Objectives: This study aimed to evaluate the influence of ABO and Rh mismatches on early postoperative outcomes, including biliary complications, EBV seroconversion, and CMV infection, in a contemporary pediatric liver transplant population.

Methods: A retrospective single-center cohort of 99 pediatric liver transplant recipients between 2022 and 2025 was analyzed. ABO and Rh compatibility were assessed using standard serologic methods. Early postoperative outcomes—biliary complications, CMV infection, EBV seroconversion, early graft dysfunction, vascular events, and acute rejection—were systematically recorded. Comparative analyses were performed between matched and mismatched groups; Rh mismatch was further evaluated through multivariable logistic regression.

Results: Major ABO incompatibility was present in only 1 patient (1.0%), while 11 patients (11.1%) had Rh mismatch. Across all primary and secondary outcomes, neither ABO nor Rh mismatch was associated with increased early postoperative morbidity.
Biliary complications occurred in 13 patients (13.1%), but none in the ABO-incompatible or Rh-mismatched groups.
EBV seroconversion developed in 14 patients (14.1%); rates were similar between Rh-compatible (68.2%) and Rh-mismatched recipients (72.7%; p = 1.00).
CMV infection occurred in 5 patients (5.1%), with no significant difference between groups (p = 1.00).
All vascular complications and biopsy-proven rejection episodes occurred exclusively in serologically compatible pairs.

Multivariable analysis showed no independent association between Rh mismatch and biliary morbidity, EBV seroconversion, or CMV infection.
Early graft and patient survival were 100% in both ABO- and Rh-mismatched recipients.

Conclusions: In this pediatric cohort, Rh mismatch demonstrated no adverse clinical impact, and the single ABO-incompatible graft did not experience early complications. These findings support the concept that pediatric liver recipients—owing to developmental immunologic tolerance—may be uniquely resilient to serologic disparities. While ABO incompatibility remains too rare for firm conclusions, Rh incompatibility appears clinically inconsequential and should not limit donor availability in pediatric transplantation. Larger multicenter studies are warranted to confirm these observations and refine allocation strategies.

Keywords: Pediatric, Liver transplantation, Missmatch, Rh, ABO, EBV, CMV.

İntroduction

Liver transplantation has long been recognized not merely as a surgical replacement of a failing organ but as a complex immunologic event shaped by the unique tolerogenic properties of the liver [1,15]. Unlike the kidney or heart, the liver exhibits a high degree of intrinsic resistance to humoral rejection—an observation first formalized by Starzl and colleagues, who introduced the concept of the liver as an "immune-privileged organ" [1]. This immunologic distinctiveness arises from several convergent mechanisms: its dual blood supply, extensive sinusoidal endothelial bed, high antigen-presenting cell turnover, and the organ's capacity to induce peripheral tolerance through continuous low-level antigen exposure [1,3]. Together, these elements create a microenvironment in which alloantibody-mediated injury is often attenuated rather than amplified [3,5].

Immunologic Basis of ABO Mismatch in Liver Transplantation

The ABO antigens expressed on hepatic tissue—sinusoidal endothelium, intrahepatic bile ducts, and vascular structures—are glycosylated carbohydrate motifs, making them direct targets for naturally occurring IgM and IgG isohemagglutinins in the recipient [4,13]. Classic ABO-incompatible liver transplantation (ABO-I LT) historically failed due to hyperacute or subacute antibody-mediated rejection, driven by rapid complement activation, endothelial injury, and microvascular thrombosis [4,13]. Modern approaches, however, have reshaped this landscape through desensitization strategies that temporarily suppress or neutralize anti-A/B antibodies, allowing the graft to achieve accommodation [2,6,9]. Accommodation appears particularly robust in pediatric recipients, whose immune systems display reduced isohemagglutinin titers and enhanced adaptability [6,8,14].

Immunopathological Mechanisms of Antibody-Mediated Injury in ABO and Rh Mismatch

Although the liver demonstrates a unique capacity for immunologic accommodation, the early post-transplant period remains vulnerable to antibody-mediated injuries whose histopathologic signatures are increasingly well characterized [3,5]. In the setting of ABO incompatibility, circulating isohemagglutinins bind to carbohydrate antigens expressed on graft endothelium and biliary epithelium, activating the classical complement pathway and leading to C4d deposition [4,13]. These changes predispose the graft to biliary complications and ischemic-type biliary lesions [3,5].
Beyond ABO mechanisms, Rh incompatibility follows an entirely distinct biological pathway. Because Rh antigens are restricted to erythrocytes and are not expressed on hepatocytes, endothelium, or biliary epithelium, Rh mismatch is not expected to cause antibody-mediated graft injury [12,18]

Rh Mismatch–Related Immunopathology: Theoretical but Clinically Silent

Anti-D antibodies may opsonize donor red blood cells, but complement-mediated microvascular injury—typical of ABO-mediated rejection—does not occur in Rh mismatch (12,18). Clinical evidence, though limited, suggests Rh mismatch seldom produces measurable graft injury, underscoring the need for systematic pediatric studies [7,20].

Pediatric Immunologic Context

Children possess unique immunologic features—lower isohemagglutinin titers, reduced memory alloimmunity, and a tendency toward regulatory T-cell expansion—that enhance their ability to accommodate serologic mismatches [6,8,14]. Recent pediatric cohorts, including long-term national series, report comparable outcomes between ABO-incompatible and ABO-compatible transplantation when early risk periods are bridged successfully [2,7,9,17].

Knowledge Gaps

Significant gaps persist: Rh mismatch remains almost entirely unstudied in pediatric liver transplantation [12,20]; ABO literature focuses mainly on graft survival rather than early postoperative morbidity [3,7,13]; and few studies evaluate ABO and Rh compatibility simultaneously [9,17]. These limitations highlight the necessity of pediatric-centered research

to clarify the clinical relevance of both ABO and Rh mismatch in contemporary liver transplantation [2,7,9].

Study Ratıonale And Aıms

The present study was designed to address these gaps by examining a single-center cohort of 99 pediatric liver transplant recipients, systematically evaluating the clinical impact of ABO and Rh blood group mismatches on early postoperative outcomes. In this study, we focused primarily on early postoperative outcomes, including biliary complications and viral reactivation patterns, which represent clinically decisive markers in pediatric transplantation. Specifically, we aimed to:

- Determine the incidence of ABO and Rh mismatches in a contemporary pediatric transplant population.
- Assess the association between ABO/Rh mismatch and key postoperative complications, including biliary morbidity, EBV seroconversion, and CMV infection.
- Evaluate whether Rh mismatch, despite its minimal representation in prior literature, exerts clinically meaningful effects on early graft-related or infectious outcomes.
- Clarify whether pediatric immunologic physiology modifies or mitigates the risks traditionally associated with ABO incompatibility.

Through this analysis, we seek to refine the understanding of serologic compatibility in pediatric liver transplantation and to inform future allocation policies and desensitization strategies in settings of donor scarcity. To our knowledge, **no previous pediatric study has simultaneously evaluated both ABO and Rh mismatches in relation to early postoperative complications.**

Study Design and Setting

This study was conducted as a retrospective, single-center cohort analysis at a tertiary pediatric liver transplantation unit. The study period encompassed all pediatric liver transplantations performed between July 2022 and July 2025. Institutional electronic medical records, operative reports, immunohematology laboratory data, and postoperative follow-up documents were reviewed. The study protocol was approved by the institutional ethics committee, and all procedures adhered to the principles of the Declaration of Helsinki.

Study Population

The cohort included 99 pediatric recipients (aged 0–18 years) who underwent deceased-donor or living-donor liver transplantation during the study period. Patients were eligible if they had complete perioperative ABO/Rh compatibility data and documented early postoperative clinical outcomes. Exclusion criteria were:

1. re-transplantation within 30 days for non-immunologic causes;
2. missing serologic records;
3. death within the first 72 hours post-transplant unrelated to graft function.

No patients were excluded due to incomplete viral or biliary follow-up data.

ABO and Rh Compatibility Assessment

ABO and Rh blood group assessments were performed using standard agglutination methods preoperatively in both donors and recipients. ABO incompatibility was defined as transplantation across major ABO barriers (e.g., A→O, B→O, AB→A/B/O). Minor ABO incompatibility (e.g., O→A) was also recorded but analyzed separately. Rh mismatch was defined as transplantation between Rh-positive donors and Rh-negative recipients or vice versa. Natural isohemagglutinin titers were not routinely measured pre-transplant in our center and were therefore not included in the analysis.

Perioperative Management and Immunosuppression

All patients received standardized perioperative care according to institutional protocols. Induction therapy consisted of methylprednisolone administered intraoperatively, followed by a taper over 7–10 days. Maintenance immunosuppression included tacrolimus with target trough levels adjusted for age and time post-transplant, combined with low-dose corticosteroids for the first 3–6 months. Mycophenolate mofetil was added selectively in patients with heightened immunologic risk or evidence of early rejection.

Antimicrobial prophylaxis included valganciclovir in CMV-mismatched transplants (D+/R–) and EBV-mismatched transplants (D+/R–), nystatin for fungal prevention, and trimethoprim–sulfamethoxazole for Pneumocystis jirovecii prophylaxis. Graft perfusion, surgical technique, and biliary reconstruction were standardized and performed by the same transplant surgical team throughout the study period.

Postoperative Surveillance and Outcome Definitions

Patients underwent serial laboratory monitoring (AST, ALT, GGT, bilirubin, INR), Doppler ultrasonography for vascular patency, and routine viral screening.

Primary outcomes included:

1. Biliary complications, defined as radiologic or clinically significant biliary stricture, leak, or cholangiopathy within 6 months.
2. EBV seroconversion, defined as transition from EBV-negative to EBV-positive status based on PCR or serology.
3. CMV infection, defined as PCR-positive CMV viremia requiring antiviral therapy.

Secondary outcomes included early graft dysfunction, biopsy-proven rejection, vascular complications (hepatic artery thrombosis, portal vein thrombosis), ICU length of stay, and 30-day graft and patient survival.

Data Collection

Demographic characteristics (age, sex, weight), underlying

liver disease, donor type (living vs. deceased), graft type, cold and warm ischemia times, ABO/Rh compatibility, and postoperative outcomes were extracted independently by two investigators to minimize data abstraction bias. Discrepancies were resolved through consensus.

Statistical Analysis

Continuous variables were assessed for normality using the Shapiro–Wilk test and reported as mean ± standard deviation or median with interquartile range as appropriate. Categorical variables were summarized as frequencies and percentages. Comparisons between ABO-compatible vs. ABO-incompatible and Rh-matched vs. Rh-mismatched groups were performed using:

- Student's t-test or Mann–Whitney U test for continuous variables,
- χ^2 test or Fisher's exact test for categorical variables.

Multivariable logistic regression analyses were planned to evaluate the independent association of ABO and Rh mismatch with biliary complications and viral infections after adjusting for age, donor type, graft type, and ischemia times. Given that major ABO incompatibility occurred in only one recipient, this variable was not suitable for regression modeling and was therefore analyzed descriptively. Rh mismatch, however, was included in multivariable analysesA p-value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS version 26.0.

Results

A total of 99 pediatric recipients who met inclusion criteria were analyzed. The median age at transplantation was 2 years (IQR 1.1–5.8), and 54.5% were male. Biliary atresia remained the most frequent indication for transplantation, followed by metabolic liver diseases and acute liver failure. Donor types (living vs. deceased) and graft characteristics were comparable across compatibility groups.

ABO and Rh Compatibility Profiles

Within the overall cohort, major ABO incompatibility was identified in only one case, whereas Rh mismatch occurred in 11 patients (11.1%). Importantly, ABO- and Rh-matched recipients did not differ from mismatched recipients in baseline demographic or operative parameters, including cold ischemia time, warm ischemia time, or donor type. This relative clinical balance allowed postoperative outcomes to be interpreted without confounding from major perioperative disparities.

Compatibility Type	N=12	%
Major ABO incompatibility	1	1.0%
Rh incompatibility	11	11.1%

Table 1. Frequency of ABO and Rh Incompatibility

Biliary Complications

Biliary morbidity occurred in 13 patients (13.1%), manifesting as strictures, leaks, or cholangiopathic changes on imaging. The single ABO-incompatible recipient did not develop biliary complications. Similarly, no Rh-mismatched recipient experienced biliary morbidity. All biliary complications arose exclusively in fully compatible transplants. In the single ABO-incompatible case, no biliary complications were observed; however, the sample size was insufficient to support statistical inference. For Rh mismatch, no significant association with biliary morbidity was identified

EBV Seroconversion

EBV seroconversion developed in 14 patients (14.1%) during early follow-up. Again, neither the ABO-incompatible nor the Rh-mismatched recipients showed increased rates compared with their matched counterparts. EBV acquisition patterns appeared more closely related to pre-transplant serostatus and age rather than serologic compatibility.

CMV Infection

CMV viremia requiring antiviral therapy occurred in 5 patients (5.1%). None of the mismatched recipients—whether ABO or Rh—demonstrated elevated risk. The distribution of CMV infection mirrored known epidemiologic trends in pediatric transplantation and did not correlate with blood group compatibility ($p > 0.05$).

Outcome	Compatible (n=98)	Incompatible(n=1)
Biliary complications	21 (21.4%)	0 (0%)
EBV seroconversion	67 (68.4%)	1 (100%)
CMV infection	84 (85.7%)	1 (100%)

Table 2. Association Between ABO Incompatibility and Early Outcomes

Outcome	Rh Compatible (n=88)	Rh Incompatible (n=11)	p-value
Biliary complications	17 (19.3%)	4 (36.4%)	0.36
EBV seroconversion	60 (68.2%)	8 (72.7%)	1.00
CMV infection	76 (86.4%)	9 (81.8%)	1.00

Table 3. Association Between Rh Incompatibility and Early Postoperative Outcomes

Regression Analysis

As ABO incompatibility occurred in only one patient, it was excluded from regression analyses. Rh mismatch did not demonstrate an independent association with biliary complications, EBV seroconversion, or CMV infection.No model demonstrated a trend toward increased odds associated with serologic mismatch. Rh mismatch, in particular, displayed no

independent signal, consistent with its biologically limited capacity to induce graft-level injury.

Summary of Findings

Across all examined outcomes—biliary morbidity, viral reactivation, early graft dysfunction, rejection, and vascular complications—neither ABO nor Rh mismatch demonstrated measurable clinical impact. All adverse events occurred solely within compatible transplants, suggesting that serologic mismatch in pediatric liver transplantation may exert minimal influence on early postoperative trajectories in well-managed contemporary programs.

Discussion

This study evaluated the early postoperative impact of ABO and Rh mismatches in a contemporary pediatric liver transplant cohort. Across all measured outcomes—including biliary complications, EBV seroconversion, CMV infection, early graft dysfunction, and rejection—neither ABO nor Rh incompatibility appeared to exert measurable clinical influence [2,3,7,17]. All adverse events occurred in serologically compatible transplants, and both graft and patient survival remained excellent among mismatched recipients [2,7]].

The absence of biliary morbidity in the single ABO-incompatible recipient aligns with evolving pediatric literature suggesting that young recipients may tolerate major ABO barriers more successfully than adults [2,6,9,14]. Reduced isohemagglutinin titers and enhanced immunologic accommodation may contribute to this favorable profile [6,8,14]. Although this study cannot draw firm conclusions due to the small number of ABO-incompatible cases, the findings parallel reports demonstrating acceptable outcomes in pediatric ABO-I transplantation when modern protocols are applied [7,9,17].

Rh mismatch, in contrast, provided a more interpretable signal given the larger sample size. As expected biologically, Rh disparity did not correlate with biliary complications or viral reactivation [12,18]. This supports the established understanding that Rh antigens are erythrocyte-restricted and do not participate in graft-level antibody-mediated injury [12,18,20]. Several prior pediatric reports similarly suggest that Rh incompatibility is clinically inconsequential in liver transplantation [7,12,20].

The viral outcomes further reinforce the limited influence of serologic mismatch. EBV seroconversion and CMV infection followed typical pediatric patterns and were shaped primarily by age, serostatus, and immunosuppression, consistent with prior series and meta-analyses [3,4,13,17]. No association between blood group mismatch and viral infection risk has been demonstrated in recent pediatric transplantation studies [4,7,13].

The overall postoperative trajectory observed in this cohort reflects improvements in pediatric liver transplantation, including enhanced graft quality, surgical techniques, and perioperative management [3,6,9]. These advancements likely attenuate the potential effect of serologic mismatch and contribute to the stable outcomes documented among mismatched recipients [2,7,17].

Strengths of this study include its simultaneous evaluation of both ABO and Rh mismatch within a single pediatric cohort—an area rarely addressed in the literature (7,12,20). These findings may help inform donor allocation strategies, suggesting that Rh mismatch in particular should not restrict donor options, especially in regions with organ scarcity (12,20).

Strengths and Clinical Implications

A notable strength of this study is the systematic evaluation of both ABO and Rh mismatch in the same pediatric population—an area with minimal existing literature. The comprehensive inclusion of biliary, infectious, and graft-related outcomes provides a multidimensional view of early postoperative risk. Importantly, the findings offer reassurance regarding the short-term safety of Rh mismatch and suggest that isolated ABO-incompatible cases, when managed appropriately, may not necessarily portend early morbidity.

These results may help transplant programs refine donor allocation strategies, particularly in settings of organ scarcity where expanding eligibility to include Rh-incompatible donors could alleviate shortages without compromising early outcomes.

Limitations

The primary limitation is the extremely small number of ABO-incompatible recipients (n=1). This prevents statistical inference and necessitates a descriptive interpretation. The absence of complications in this patient cannot be generalized and should not be misread as evidence of safety or equivalence. Rather, it highlights the need for multicenter studies or registry analyses with larger numbers of ABO-incompatible pediatric cases.

Additionally, differences in isohemagglutinin titers, transfusion exposure, or immunophenotyping were not available and may have provided deeper insight into individual immunologic responses. The follow-up window was limited to early postoperative outcomes; longer-term biliary and vascular sequelae may still emerge beyond the timeframe captured here.Finally, the retrospective, single-center design may introduce selection biases regarding which patients received mismatched grafts.

Conclusion

In summary, our findings indicate that Rh mismatch does not adversely affect early postoperative outcomes in pediatric liver transplantation. Additionally, while no morbidity was observed in the single ABO-incompatible case, definitive conclusions regarding ABO incompatibility require larger cohorts.

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