Human Leukocyte Antigen Antibody Monitoring in Liver Transplant Recipients

Patterns of Persistence, Disappearance, De Novo Formation, and Locus-Specific Mismatch Effects

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Introduction

Liver transplantation represents a unique immunologic setting in which donor-specific HLA antibodies (DSA) may behave differently than in other solid organ transplants. Although HLA antibodies can contribute to antibody-mediated injury, liver allografts demonstrate relative resistance to antibody-mediated rejection, and circulating DSA may change substantially after transplantation.

The behavior of pre-existing versus newly formed DSA and whether donor-recipient HLA mismatch influences these patterns, remains clinically relevant to antibody interpretation and post-transplant monitoring.

We characterized persistence and disappearance of pre-existing DSA and development of de novo DSA (dnDSA) after liver transplantation, with emphasis on Class I versus Class II patterns and locus-specific effects.

Methods

A retrospective cohort of 210 liver transplant recipients was reviewed. Of these, 110 recipients underwent post-transplant DSA testing and formed the primary analysis cohort. Pre- and post-transplant HLA antibody specificities were compared to classify pre-existing DSA as persistent or disappeared and to identify dnDSA.

Class I and Class II patterns were assessed at the patient and individual DSA-specificity levels. For locus-based analyses, DRB1 and DRB3/4/5 were grouped as DR; DQA and DQB as DQ; and DPA and DPB as DP.

Locus-specific dnDSA rates were compared between cases with one versus two mismatches.

Cohort

210 liver transplants	**110** post-DSA tested
56/110 post-transplant DSA	**35/110** developed dnDSA

Key observation

Pre-existing Class I DSA frequently disappeared, while Class II, especially DQ, showed greater persistence and de novo formation.

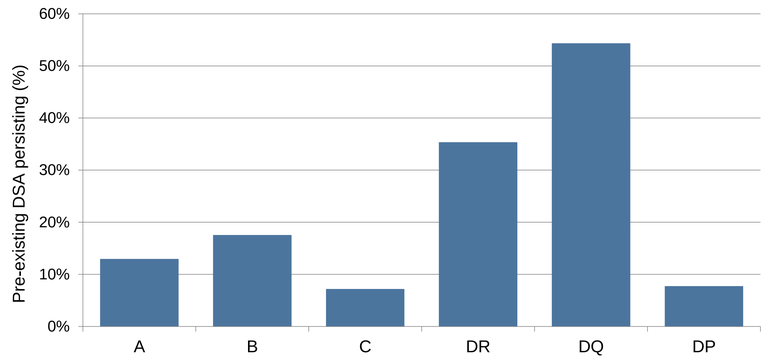
Pre-existing Class I DSA: Patient-Level Outcome

Among 41 recipients with pre-transplant Class I DSA



Class I DSA disappearance was common after liver transplantation.

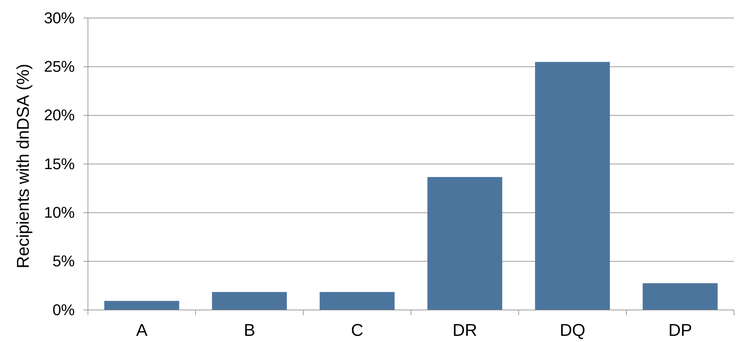
Persistence of Pre-existing DSA by Specificity



A 4/31 (13%) • B 7/40 (18%) • C 1/14 (7%) • DR 18/51 (35%) • DQ 19/35 (54%) • DP 1/13 (8%)

DSA-specificity-level analysis

De Novo DSA: Patient-Level Distribution



35/110 recipients (32%) developed *any* dnDSA

Patients may have dnDSA at more than one locus. Percentages use post-DSA-tested cohort (N=110).

Patient-level analysis

De Novo DSA Formation by Locus-Specific HLA Mismatch

HLA locus	1 mismatch	2 mismatches
A	0/50 (0%)	1/54 (2%)
B	0/29 (0%)	2/78 (3%)
C	2/52 (4%)	0/49 (0%)
DR	7/46 (15%)	7/62 (11%)
DQ	**9/61 (15%)**	**12/41 (29%)**
DP	1/30 (3%)	2/69 (3%)

Two DQ mismatches showed the highest dnDSA formation rate (29%), approximately twice the rate observed with one DQ mismatch (15%).

Patient level, locus-specific analysis

Conclusions

Pre-existing Class I DSA frequently disappeared after liver transplantation, whereas Class II DSA demonstrated greater persistence. At the individual specificity level, DQ showed the highest persistence among the Class II loci evaluated. De novo DSA developed in 35 of 110 recipients (32%) and was concentrated predominantly at Class II loci.

HLA mismatch burden showed its clearest relationship with dnDSA at DQ: dnDSA occurred in 15% of recipients with one DQ mismatch and 29% of those with two DQ mismatches. Together, these findings demonstrate distinct post-transplant behavior of Class I and Class II DSA and identify DQ as the most prominent locus for persistence and de novo antibody formation in this cohort.