CHANGES IN NON-HLA AUTOANTIBODIES DURING BIOPSY-PROVEN KIDNEY ALLOGRAFT REJECTION

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ABSTRACT

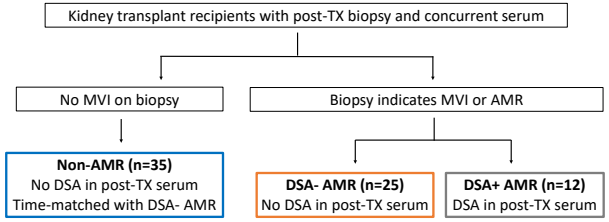
Aim: Emerging evidence implicates a role for autoantibodies against non-HLA proteins in antibody-mediated rejection (AMR) in the presence or absence of donor-specific HLA antibodies (DSA). We sought to identify non-HLA specificities associated with kidney transplant rejection and to characterize differences in antibody profiles between patients with no AMR, DSA- AMR and DSA+ AMR.

Methods: Vendor-established cutoffs for the LABScreen Autoantibody Assay from One Lambda based on the 85th percentile of healthy controls were validated against a local population of non-sensitized males and adjusted where needed. Group 3 beads were omitted from analysis due to an identified issue with lot variability. Pre- and post-transplant sera from kidney transplant recipients were assayed, with the post-transplant serum sample corresponding to biopsies scored by pathologists.

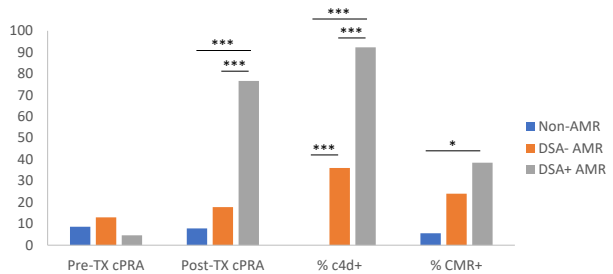
Results: In all groups, the majority of recipients exhibited a decrease in non-HLA autoantibody load post-transplant. The number of non-HLA autoantibodies was significantly higher in DSA+ AMR compared to DSA- AMR samples, with pre-transplant antibody against CXCL10 and post-transplant antibody against CXCL9 identified as significantly more prevalent in DSA+ AMR. Unexpectedly, the number of non-HLA autoantibodies was lower in DSA- AMR compared to Non-AMR samples. In particular, pre-transplant antibodies against CXCL11, GAPDH, and REG3A were significantly less prevalent among DSA- AMR patients.

Conclusions: The increase and decrease in non-HLA autoantibodies in DSA+ and DSA- patients, respectively, compared to Non-AMR patients may represent overflow versus absorption at the site of inflammation. Observation of these differences in pre- and post-transplant samples suggests this could occur in the damaged native or donor kidney.

GROUP CHARACTERISTICS



- No significant differences between groups for time of sample, recipient age, recipient sex, % deceased donor, % haploidentical related donor.



RESULTS

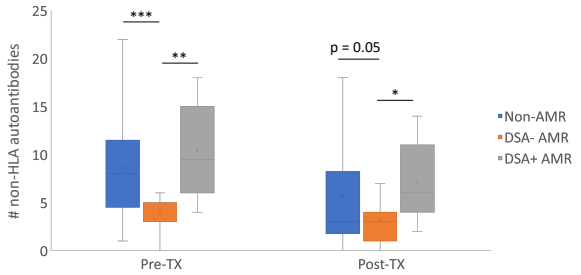


Figure 1. Non-HLA antibody load in each group. Single factor ANOVA with post-hoc pairwise testing. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

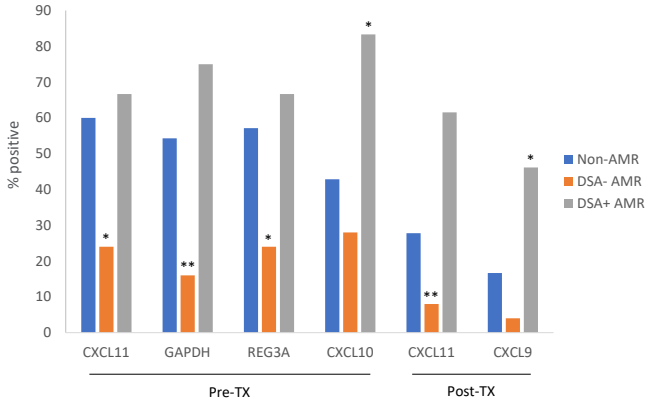


Figure 2. Prevalence of positive specificities identified as significant by Chi square test with Yates' correction. Asterisks indicate which group is significantly different from the others by post-hoc pairwise testing. * $p < 0.05$, ** $p < 0.01$.

CONCLUDING THOUGHTS

- High burden of pre-transplant non-HLA antibodies may predispose later development of HLA-DSA in DSA+ AMR
- DSA- AMR group had the lowest non-HLA antibody burden
  - Does it reflect absorption and/or pathological mechanism of MVI independent of antibodies?
- Relevant non-HLA antibody specificities in individual cases can differ from those identified in group analysis