

# Non-HLA and Anti-HLA Antibodies in a Long Term Follow-Up; Incidence and Importance in Renal Transplantation



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**Introduction:** The detection of antibody mediated injury is becoming increasingly important in post-transplant patient care. The role of donor specific anti-HLA antibodies in kidney transplant damage is known, while the significance of non-HLA antibodies remains an unresolved concern. Non-HLA antibodies develop to self-antigens, which are present also in the allograft tissue.

**Aim:** The aim of the study was to determine the presence of non-HLA and anti-HLA antibodies in "stable" patients 5 years after kidney transplantation and their influence on renal function.

**Methods:** We evaluated the presence of non-HLA and anti-HLA antibodies in 35 consecutive renal transplant patients with stable renal function (the increase of creatinine < 0.2 mg/dL) 5 years after transplantation. Pre-transplant screening for donor specific antibodies carried out by CDC cross-match was negative in all patients. Anti-endothelial cell antibodies (AECA), anti-angiotensin II type 1 receptor antibodies (anti-AT1R), and anti-endothelin receptor antibodies (anti-ETAR) were assayed as non-HLA antibodies. AECA were detected by an indirect immunofluorescent test and anti-AT1R and anti-ETAR by ELISA. Anti-HLA antibodies were tested by Flow-PRA.

**Results:** Non-HLA antibodies were found in 12 (34%) patients including: AECA in 5 (14%), anti-AT1R in 6 (17%), anti-ETAR in 4 (11%), both anti-AT1R and anti-ETAR were present in 3 patients.

Anti-HLA antibodies were present in 13 (37%) patients including anti-HLA class I and class II antibodies in 3 patients, class I only in 7 and class II only in 3 patients.

Seven patients had both non-HLA antibodies and anti-HLA antibodies: 1 patient had AECA, 3 anti-AT1R and 3 anti-ETAR antibodies.

The patients were divided in two groups: an antibody-negative group included patients without any antibodies (n=13) and an antibody-positive group included patients with antibodies (non-HLA and/or anti-HLA; n=22).

The number of HLA mismatches was 3.00 and 3.06 in the groups.

Renal function in the antibody-negative group was significantly better comparing to the antibody-positive group (Table). Biopsy proven acute rejection occurred in 2/13 (15%) patients from the antibody-negative group but in 8/22 (36%) patients from the antibody-positive group.

Antibody mediated rejection was diagnosed in 2 patients with anti-HLA antibodies (one patient had additionally AECA).

**Conclusions:** Our preliminary data showed high prevalence of the production of autoantibodies and alloantibodies in stable patients 5 years after kidney transplantation. Simultaneous production of these antibodies and their association with renal function may suggest active humoral immune response, which is poorly controlled by immunosuppression.

	12-month	24-month	36-month	48-month	60-month
Antibody-negative group (n=13)	1.16±0.2	1.26±0.2	1.25±0.2	1.24±0.2	1.24±0.2
Antibody-positive group (n=22)	1.3±0.4	1.46±0.3	1.51±0.43	1.60±0.4	1.71±0.6
p	NS	NS	0.01	0.02	0.002

[Transplant renal function (serum creatinine-mg/dl)]

## Assigned speakers:

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