Impact of pregnancies on immunization and outcome in kidney transplantation

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Background: The effect of pre-transplant pregnancies on HLA alloimmunization and outcome after kidney transplantation is so far not well known. The purpose of this study was to investigate the impact of pre-transplant pregnancies in kidney transplant recipients on immunization as well as on immunologic and overall outcome.

Methods: A retrospective single center long-term observational study was conducted. 397 women with end-stage renal disease and no prior transplantation were enrolled in the study. The pre-transplant-screening was performed between 1999 and 2014. 204 of these women so far received a kidney transplant. Baseline characteristics including history of transfusion and pregnancy as well as pre-transplant and if applicable post-transplant solid phase HLA-diagnostic and immunologic outcome were assessed over a maximum of 15 years.

Results: Baseline characteristics at pre-transplant screening are shown in table 1. There was a significant difference in age between nulligravidous women and women with a history of pregnancy.

Table 1

	no pregnancies (n=70)	history of pregnancy (n=327)	p
Mean age, years (SD)	39 (14)	53 (12)	<0.001
Median no. of pregnancies		2 (1-3)	
Cause for ESRD			
glomerulonephritis, n	23 (33%)	111 (34%)	0.222
polycystic, n	8 (11%)	67 (21%)	
hypertension, n	7 (10%)	38 (12%)	
diabetes, n	3 (4%)	20 (6%)	
other, n	21 (30%)	59 (18%)	
unknown, n	8 (11%)	32 (10%)	
Type of dialysis			
hemodialysis, n	52 (74%)	252 (77%)	0.609
peritoneal dialysis, n	10 (14%)	49 (15%)	
preemptive listing, n	8 (11%)	26 (8%)	
History of blood transfusion, n	33 (47%)	147 (45%)	0.792
Median number of PRBC (IQR)	0 (0-2)	0 (0-2)	0.645

Women with a history of pregnancy had a significantly higher alloimmunization rate than nulligravidous women (rate of patients with anti-HLA class I 37% vs. 13%, p<0.001 and anti-HLA class II 32% vs. 11%, p<0.001, (fig. 1A)). The rate of immunized women increased with the number of pregnancies significantly (fig. 1B). Differentiation of the type of HLA-antibodies depending on the history of pregnancy is shown in figure 1C.
The multivariate analysis adjusted for age identified pregnancy as an independent risk factor for HLA-immunization (OR 3.94, p<0.001) (table 2).

Figure 1

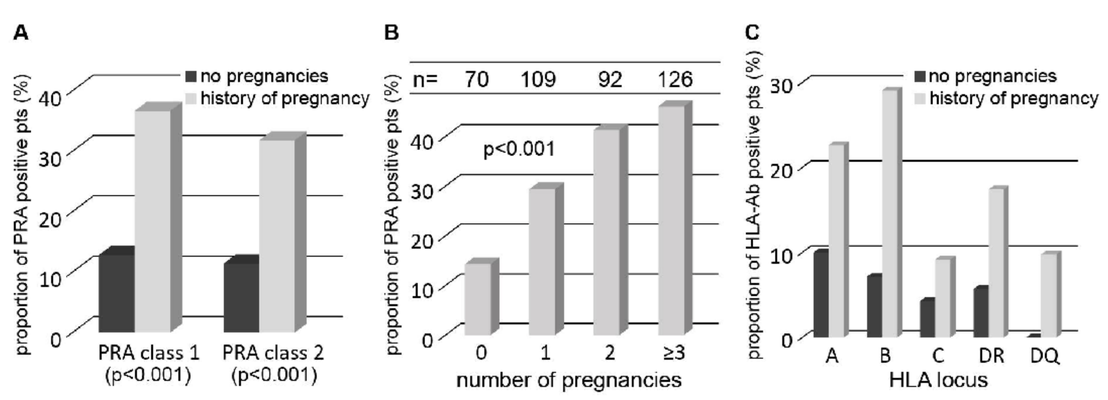


Table 2

Multivariate analysis adjusted for age			
	OR	95% CI	p
History of pregnancy	3.94	1.94-7.99	<0.001
History of blood transfusion	1.50	0.98-2.30	0.059

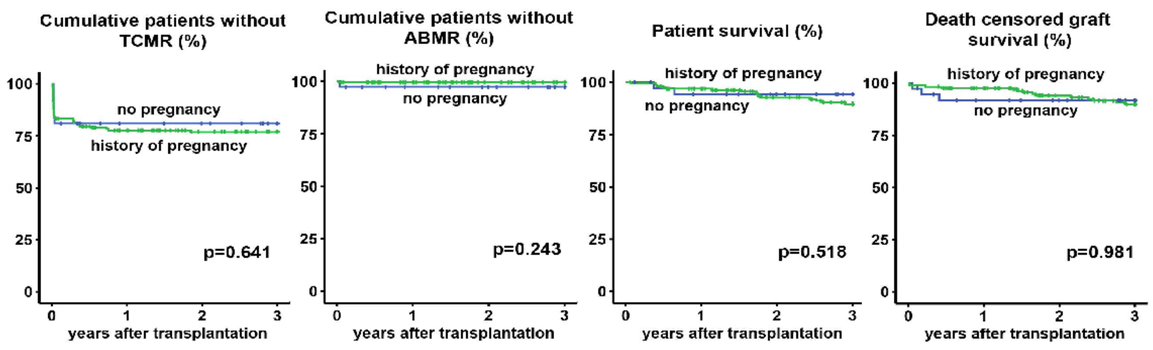
So far 204 of the women were transplanted. Tissue typing of the partner was performed wherever possible to verify possible pregnancy-associated HLA-antibodies. Paternal antigens were prohibited even in the case of low titer HLA-antibodies. At time of transplantation there was a significant difference in recipient age and donor age between the groups (table 3).

Table 3

	no pregnancies (n=37)	history of pregnancy (n=327)	p
Mean age, years (SD)	40 (15)	55 (12)	<0.001
Median follow up, years (SD)	3.7 (2.0-7.2)	4.5 (1.8-7.8)	0.590
Time on dialysis (months)	64 (51)	54 (35)	0.169
Mean donor age , years (SD)	48 (13)	56 (14)	0.004
Living donor, n	14 (38%)	42 (25%)	0.153
Median HLA-mismatches (IQR)	3 (2-3)	3 (2-3)	0.399
Median cold ischemia time, hours (IQR)	7 (3-12)	8 (4-13)	0.660

After 3 years of follow-up nulligravidous women vs. women with a history of pregnancy showed no significant difference regarding the predicted incidence of antibody-mediated rejections (3% vs. 1%, p=0.243), T-cell mediated rejections (19% vs. 23%, p=0.641) and death censored graft failure (8% vs.10%, p=0.981) (figure 2).

Figure 2



Conclusions: Pregnancies are a strong risk factor for the development of HLA antibodies in solid organ transplantation. Due to careful selection of donors with avoidance of preformed donor specific antibodies the impact on the immunologic and overall outcome can be minimized.

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