

NON-MODIFIABLE AND POTENTIALLY MODIFIABLE FACTORS FOR THE DEVELOPMENT OF NEW ONSET DIABETES AFTER TRANSPLANTATION (NODAT): A SINGLE CENTER EXPERIENCE OF 159 RENAL TRANSPLANTATIONS.

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INTRODUCTION

It's known that renal transplantation ameliorates cardiovascular risk factors by restoring renal function, but it seems to introduce new cardiovascular and metabolic risks including impaired glucose tolerance or diabetes mellitus, hypertension, and dyslipidemia. Diabetes After Transplantation (DAT) is a serious and common complication that has been reported to occur in 4% to 25% of renal transplant recipients.

Classic risk factors for the development of NODAT are non-modifiable such as age, gender, family history of DM, HLA mismatches, Acute rejection history, Deceased donor, Male donor and modifiable or potentially modifiable like immunosuppressive therapy choices and mainly obesity. Furthermore, Associations have been reported between vitamin D receptor (VDR) gene polymorphisms, type 1 diabetes, insulin secretion, and the insulin resistance syndrome.

In this study we intend to describe association between those factors including vitamin D blood rate and occurring of NODAT in our recipients.

PATIENTS AND METHODS

A retrospective study of 159 recipients 107 men (67,3%) and 52 women (32,7%). The mean age is 32,4 years (7-70 years).

Seven patients had diabetes before receiving the graft.

NODAT occurred in 32 cases: 20,1 % of recipients with mean duration after transplantation of 24 months.

Recipients with NODAT were treated with Oral anti diabetes treatment in 24 cases and Insulin in 20 cases.

We performed univariate and multivariate association study of gender, age, BMI, mismatch number, former extra renal euration method, Kidney disease type of the recipient in one hand, in the other hand gender, age, BMI and type of donors, in addition to mean Vitamin D blood rates, induction and maintain immunosuppressive drugs, history of delayed graft function or acute rejection.

RESULTS

In our recipients, there is no association between occurring of NODAT and recipient's gender, former ERE method, kidney disease type, history of graft rejection, Vitamin D blood rates nor donors characteristics. But we noted an association of recipients with NODAT and a higher BMI ($p < 0,001$), an age more than 40 years ($p < 0,01$), greater mismatch ($p < 0,06$), using anti-thymocyte globulin for induction ($p < 0,001$). Study of the association of NODAT and vitamin D deficiency (< 20 ng/ml) showed no significant association. Study of the association of NODAT and vitamin D deficiency (< 20 ng/ml) showed no significant association.

Etude Uni variée:

	Greffés		Difference sign.
	DAT	Pas de DAT	
Vit.D M3	15.47	16.62	0,049
Vit.D M6	21.91	20,26	0,076
Vit.D M12	22.1	18,52	0,136
Vit.D M24	20,63	20,5	0,054
Vit.D M36	22,44	14,75	,213
Vit.D M48	22,53	17,5	,118
M60	20,71	22,93	0,056

	Deficit en vit D (< 20 ng/ml))	DAT		p
		Non: 117	Oui: 32	
3Mois post TR	Oui	31,5%	33,3%	0,037
	Non	68,5%	66,7%	
6Mois post TR	Oui	14,5%	25%	0,38
	Non			
12Mois post TR	Oui	38,3%	57,1%	1,65
24Mois post TR	Oui	40	50%	0,274
	Non	60	50%	

Etude Multi variée:

	RR	IC 95%	Valeur de p
Age R (\geq à 40 ans)	4,414	1,672 - 11,652	0,003
IMC R (\geq à 25 kg/m ²)	2,546	0,969 - 6,693	0,058
HLA mismatches (>3)	1,299	0,497 - 3,395	0,593
Induction par ATG	0,384	0,097 - 1,524	0,174

	RR	IC 95%	Valeur de p
Vit.DM3 < 20	1,005	[0,930; 1,086]	0,89
Vit.D M24 < 20	1,022	[0,945; 1,105]	0,59

Discussion

The DAT is associated with a family history of diabetes. It has been documented across all types of solid organ transplantation. In our study we did not study this factor. Other non-modifiable risk factors include recipient male gender; the presence of certain human leukocyte antigens (HLA) such as HLA A30, B27, and B42; increasing HLA mismatches; donor-recipient (DR) mismatch; deceased donor kidneys; male donor; and acute rejection history. Polycystic kidney disease has been suggested to confer an increased risk of developing diabetes after renal transplantation in some studies but not in others. Similar to the general population, obesity has been shown to be associated with the development of NODAT in most studies. In our study, we only confirmed the association between The older age and Obesity and overweight with DAT. The DIRECT Study (Diabetes Incidence after Renal Transplantation: Neoral versus Tacrolimus) was the first multi-center open label, randomized trial to assess glucose abnormalities in de novo kidney transplant patients who were randomized to cyclosporine or tacrolimus-based immunosuppression. The incidence of NODAT at 6-month post-transplant was significantly lower in CSA versus tacrolimus- treated patients, (26% versus 33.6%, $P < 0.046$). In our study, no significant association with Tacrolimus nor Thymoglobulin use is explained with selection error. The majority of our recipients receive those immunosuppressive drugs. In the most studies, potentially modifiable risk factors like Impaired glucose tolerance before transplantation, HCV-associated NODAT, Cytomegalovirus-associated NODAT and Vitamin D deficiency. But in our study we did not find association in multivariable analysis with Vit D insufficiency.

CONCLUSION

Risk stratification and intervention to minimize risk should be an integral part of the management of transplant recipients. Clinicians must be familiar with the patients history and risk factors of NODAT in an attempt to prevent modifiable ones.