

# Prevalence and Risk Factors of Post-Transplantation Diabetes Mellitus in Patients after Kidney Allotransplantation in Moscow



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## Abstract

**Purpose:** To find out the prevalence, and the risk factors conducive to the development of post-transplantation diabetes mellitus (PTDM) after kidney allotransplantation (KAT).

**Methods:** The medical histories of 146 recipients of kidney allotransplants received between 1989 and 2014 were reviewed in retrospect. Diabetes mellitus diagnosed before KAT was a criterion for exclusion from the study. Analysed as risk factors were: sex, age, KAT time, and the use of glucocorticoids (GCs), tacrolimus (Tc), and/or cyclosporine A (CcA). The veritability of their influence was assessed using the step-wise linear regression analysis method.

**Results:** The recipients' average age was 42.9 +/- 20.2 ( $x \pm \sigma$ ) years at the time of the study. PTDM prevalence in the general group was 21.9% (n=32). Age and the use of calcineurin inhibitors (CNIs) and GCs had the greatest impact on PTDM development ( $p=0,01$ ).

**Keywords:** Post-Transplantation Diabetes Mellitus; Kidney Allotransplantation; Glucocorticoids; Calcineurin Inhibitors; Tacrolimus; Cyclosporine

**Abbreviations:** KAT: Kidney Allotransplantation; PTDM: Post-Transplantation Diabetes Mellitus; GCs: Glucocorticoids; Tc: Tacrolimus; CcA: Cyclosporine A; CNIs: Calcineurin Inhibitors; NODAT: New Onset Diabetes After Transplantation; IGT: Impaired Glucose Tolerance; WHO: World Health Organisation; ADA: American Diabetes Association

## Introduction

The principles of the diagnosis and treatment of PTDM, or new onset diabetes after transplantation (NODAT), are based on the criteria of diabetes mellitus and impaired glucose tolerance (IGT) adopted by the World Health Organisation (WHO) and the American Diabetes Association (ADA) in 2003 [1]. PTDM is associated with a bad prognosis due to an increased risk of cardiovascular catastrophe, graft loss, death from graft loss and the recipient's death [2-4].

**Statistical Analysis:** We used step-wise linear regression analysis to predict our target variable (PTDM) using the AICC information criterion. The statistical data were processed using the IBM SPSS Statistics 22.0 software.

## PTDM Prevalence Among Recipients after KAT:

Retrospective analysis found PTDM in 32 (21,9%) of the 146 recipients who lived longer than one year after KAT. Diabetes mellitus diagnosed before KAT was a criterion for exclusion from the study. The male-to-female ratio was 46.6% and 53.4%. The average age of the KAT recipients who developed PTDM was 42,9 +/- 20,2 ( $x \pm \sigma$ ) years at the time of the study. PTDM development probability increased with the recipients' age ( $r=0.345$  with  $p \geq 0,01$ ) and was inversely correlated to time after KAT. PTDM probability was the highest in the first five and ten years after KAT: 34.4% (n = 11) and 40.6 % (n = 13) respectively and would decrease in the following years: 11 to 15 years after KAT, PTDM prevalence was 12.5% (n=4), and 9,4% (n=4) after 15 years.

**The Influence of Immunosuppressive Therapy Regimen on PTDM Prevalence:** The immunosuppressive therapy protocol included the following preparations: CcA+ MMF/AZA + GCs and Tc + MMF/AZA + GCs. CcA and Tc concentrations in plasma were kept within their therapeutic values throughout the observation period. After CcA to Tc conversion, an increase of PTDM prevalence from n=11 (18.6%) to n=21 (26%) was noted but made no statistically veritable difference. GCS was used in all the kidney transplant recipients.

#### PTDM Development Risk Factors (Linear Modelling):

The following predictors were analysed: sex, age, KAT time, and the use of GC, Tc, and/or CcA immunosuppressive therapy. The frequency fields of the patients' gender and KAT time were not included in the model for lack of those predictors' effect. The importance of using CcA, GCs, age and Tc for generating the PTDM development prognosis was 52.8%, 17.4%, 15%, and 14.8% respectively.

#### Conclusion

Older patients have more chances of developing PTDM than younger ones at the time of transplantation [4,5]. Besides age, CNI use in combination with GCs increases the PTDM development risks [6-16]. Differences in PTDM prevalence between CcA and Tc immunosuppressive regimens may partially be attributable to difference of PTDM definition and CNI dose and concentration [17-20]. Therapy including GCs remains disputable until now, but, according to clinical studies of the kidney graft, it is generally recognized that short-time 'pulse' therapy and low maintenance doses of GCs are not only safe but may reduce the PTDM development risk [21-25]. These data are of special interest in connection with the latest studies that demonstrate possibly varying, particularly autoimmune, PTDM genesis [26-30].

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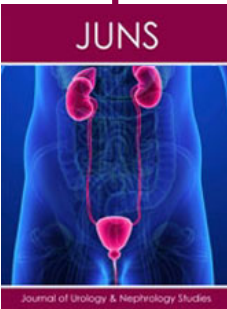
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