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Original Article

Post-Transplantation Diabetes Mellitus; Frequency and Related Risk Factors: a Single Center Study

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ABSTRACT. Post-transplantation Diabetes Mellitus (PTDM) is a serious complication after organ transplantation, which could lead to cardiovascular morbidity and mortality. The rate of PTDM increased in recent years, probably due to new immunosuppressive drugs such as Tacrolimus. In this study, we retrospectively evaluated the frequency of PTDM and related risk factors in 644 non diabetic patients who underwent renal transplantation. Data was analyzed by chi-square and Fisher's exact test in SPSS software ver11.5. Among 644 patients PTDM developed in 10.2% similar to literature. PTDM was significantly correlated to age (*P* value = 0.000), positive familial history (*P*= 0.003) and HBV infection (*P*= 0.046). In conclusion, PTDM is not uncommon in Iranian patients and a positive family history of diabetes, HBV infection and older age increases the likelihood to develop PTDM.

Introduction

Improvement of graft survival after transplantation in the last decade has increased the cardiovascular disease as the major cause of morbidity and mortality in the post transplant period.

Some studies demonstrated that PTDM is a strong, independent predictor of graft failure and mortality.[1]

Risk factors for post-transplant diabetes mellitus (PTDM) in kidney transplant recipients are classified into two groups: A group of risk factors similar to those in the non-transplant population, such as aging, obesity, and race. Whereas immunosuppressive medications are specific for the transplant recipients..

The incidence of PTDM has changed over the past decade with changes in definition, immunosuppressant regimens, and patient demographics.[1-8]

This study aimed to review the incidence of post-transplantation diabetes mellitus (PTDM) and risk factors for its development among renal transplant recipients in Urmia, Iran.

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Material and Method

All consecutive, non-diabetic, End-Stage Renal

Table 1. Various factors related to the development of post transplant diabetes mellitus.

Variables	*P* value
Age	< 0.001
Sex	0.172
BMI	0.405
Pre-transplant CMV-Ab (IgM)	0.143
HBsAg	0.046
HCVAb	0.55
Sessions of transplant	0.957
FH of DM	0.003
Duration of pre-transplant HD	0.143
CellCept	0.157
Sessions of pulse therapy	0.193

Disease (ESRD) patients who underwent renal transplantation (644 graft recipients) from inception of transplantation in our center (Urmia, Iran) until 2007 were enrolled in a retrospective cross-sectional descriptive study.

PTDM was defined in patients with no prior history of diabetes mellitus and having the following:

- Symptoms of diabetes (Polyuria, polydipsia and unexplained weight loss) plus random plasma glucose ≥ 200 mg/dL.
- Fasting plasma glucose ≥ 126 mg/dL (7.1 mmol/L)

The patients with these criteria defined as PTDM if there is no history of DM before renal transplantation.

The factors investigated in our study are including: age, sex, pre-transplant CMV-Ab, sessions of transplantation, family history of DM among near relatives, duration of HD before renal transplant, duration of post transplant period before PTDM, immunosuppressive regimen, function of graft, post-transplant, pulse therapy, BMI, HBsAg, HCVAb. Data extracted from patient's medical records.

Collected data were analyzed by means of descriptive statistics, Chi-square and Fisher's exact test in the statistical software of SPSS ver11.5.

Results

Among 644 renal allograft recipients, 350 patients (54.3%) were male and the mean Age was 41 ± 13.8 years (12 - 82). The frequency of post-transplant diabetes mellitus was 10.2% (66).

Various factors were associated with the development of PTDM, Table 1. Subjects were classified by age into three categories: < 40 years old, 40-69 years, and ≥ 70 years old. Frequency of PTDM in these groups was 3.8%, 15.6% and 20.3% respectively. The difference between these groups was significant and PTDM was more prevalent among elderly (P< 0.001),

Forty subjects transplanted for the second time, however no significant relationship between number of transplant and development of PTDM (P= 0.957).

Eighty five patients had a positive familial history for DM, which was significantly associated with PTDM (20% vs 8.8%; P= 0.003).

Duration of HD in the pre transplant period had no impact on the development of PTDM (P= 0.143).

Twelve cases (18.2%) of PTDM cases developed new onset diabetes mellitus in the first month after Tx, 24 (36.4%) between 2nd and 12th months, eight cases (12.1%) between 12th and 24th months and finally 22 (33.3%) cases developed PTDM after two years post-transplant.

One hundred eighty nine patients took Cellcept in their immunosuppressive regimen and the PTDM did not develop as frequently (12.2% vs to 9.6%; P= 0.175).

Graft recipients were classified by BMI into four categories: < 18.5, 18-25, 25-29 and ≥ 30, with a frequency of PTDM 5.4%, 8.8%, 11.1% and 13% respectively (P= 0.405).

Fourteen recipients were HBsAg+ having more likelihood of development of PTDM (P= 0.046).

HCVAb was present in seven cases with PTDM (P= 0.55).

There was no significant relationship between sessions of pulse therapy and development of PTDM in our study (P= 0.193).

Among patients who developed DM after transplant, 44 (66.7%) were treated by insulin, 16 (24.2%) were treated with oral agents, and finally plasma glucose was controlled by nutritional regimen and physical activity in 6 (9.1%) patients.

Discussion

The frequency of post-transplant diabetes mellitus in this study was 10.2% (66 patients), which is similar to the literature. A meta-analysis performed by Heisel et al to assess the incidence of new onset diabetes mellitus (NODM) reported incidence of 13.4% after solid organ transplantation.[2]

A comparative analysis with renal transplant waiting-list patients noted that NODM occurred among approximately six percent per year among dialysis patients.[3] While Woodward et al found the incidence of NODM of approximately 6% per year among wait-listed dialysis patients, compared to 18% over the first two years post-transplant.[3]

Varied definitions in the literature have made it difficult to assess the true incidence of post-transplant diabetes or to assess the importance of different risk factors for its development.[2] Different follow up periods in these studies can explain the difference in the prevalence of PTDM in different studies. We applied the 2003 American Diabetes Association and World Health Organization experts committee definition to identify PTDM in our study.

The literature confirms correlation between several factors and the development of PTDM. Some factors mentioned in the literature such as ethnicity[4] are permanent. Some of these factors are potentially modifiable, such as obesity.[5-8] We however did not find significant relationship between BMI and PTDM in this study.

The PTDM is more prevalent among senior recipients[1,4-7] similar to the prevalence of DM in the general population.

Despite the correlation revealed in several studies among HCV infection and PTDM,[1,8,9] there was no significant difference between the HCV Ab level among two groups with and without PTDM. This may be due to the small number of HCV patients in our study. But we found a correlation between HBsAg positivity and development of PTDM.

A significant relationship between positive family history for diabetes mellitus and development of PTDM, was noted in our study as well as by others.[10-11]

As mentioned in the literature, Tacrolimus (TRL) increases the incidence of new-onset diabetes mellitus after transplantation.[1,8,12,13] All of our patients received cyclosporine (CsA) and prednisone as their immunosuppressive therapy.

Some of our patients received Mycophenolate Mofetil (Roche), which was demonstrated in some studies to have a protective effect against PTDM.[1] We however did not find any significant relation.

New-onset diabetes after transplantation has been identified as one of the most important factors, being associated with reduced graft function and patient survival, and increased risk of graft loss.[14]

In conclusion, our study demonstrated age, family history for DM, and HBsAg positivity as significant risk factors for the development of PTDM. In patients with these risk factors one should remain vigilant in detection and management of DM to avoid long term complications.

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