# Outcome of Kidney Transplantation in Type 1 and Type 2 Diabetic Patients and Recipients With Posttransplant Diabetes Mellitus

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**Introduction:** We aimed to assess the effects of different types of diabetes mellitus (DM) on patients receiving living donor kidney allografts.

**Materials and Methods:** A total of 111 kidney transplant patients with DM and 111 randomly selected kidney transplant recipients without DM were enrolled in the study. The characteristics of the kidney allograft recipients and the allograft and patient outcomes were assessed and compared between 4 groups of kidney recipients without DM and patients with type 1 DM, type 2 DM, and posttransplant DM.

**Results:** Of the 111 patients with DM, 36 (32.4%), 20 (18.0%), and 55 (49.6%) had been diagnosed with type 1 DM, type 2 DM, and posttransplant DM, respectively. Diabetic patients had significantly higher rates of rejection episodes ($P = .049$) and suffered more frequently from delayed graft function ($P = .03$) compared to the kidney recipients in the control group. Patient and allograft survival rates were significantly lower in the patients with DM (regardless of their DM type) compared to the nondiabetic patients ($P = .03$ and $P = .04$, respectively). Prominently, type 1 DM had significantly adverse effects on patient and allograft survival. Patients with posttransplant DM had a relatively better patient survival compared to those with type 1 DM and type 2 DM.

**Conclusion:** We found that kidney recipients with DM, especially preexisting DM, had worse patient and graft survival rates compared to the nondiabetics. These findings suggest that kidney transplant patients presenting with any type of DM should be more closely followed.

*Keywords: kidney transplantation, risk factors, diabetes mellitus, survival analysis*

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## INTRODUCTION

Over the past 2 decades, introduction of new effective immunosuppressive agents has altered the premise underlying the kidney transplantation practice. The new medications have considerably improved short-term and long-term outcomes after transplantation; however, posttransplant morbidity remains high. Overwhelming evidence suggest that in many cases, these morbidities are related to posttransplant diabetes mellitus (PTDM), and immunosuppression plays a major role in the development of PTDM. Generally, diabetes mellitus (DM) is considered as one of the most important causes of end-stage renal disease (ESRD) throughout the world.[1-3] The age-

adjusted incidence of kidney failure in diabetic patients is about 15 times more than that in their nondiabetic counterparts.[4] Impairment in insulin and glucose metabolism are responsible for the kidney damage in diabetic patients; the issue is of extreme relevance both in the healthy population and in the kidney transplant patients.[5,6]

Posttransplant DM occurs mostly in the early period after transplantation and is thought to result from insulin resistance related to the use of corticosteroids and calcineurin inhibitors. In addition, PTDM is more common in some specific racial and ethnic populations.[7,8] African Americans as well as recipients from Hispanic and Indian origins have a higher risk of developing PTDM in comparison with the Caucasians and Asians.[7,9] Other reported risk factors of PTDM include obesity, age over 45 years, family history of DM, acute rejection episodes, and the donor source.[8-15]

Although it is generally speculated that diabetes mellitus, as the cause of both ESRD and PTDM, is a risk factor of lower patient and graft survival rates, a number of surveys have reported no differences in patient and allograft outcomes between the diabetic and nondiabetic kidney allograft recipients.[16] Moreover, there is scarce data on whether there is any difference between various types of DM, especially in recipients from living donors. This study aims to evaluate differences in the outcome of living donor kidney recipients with and without diabetes mellitus and its different types, consisting of PTDM, type 1 DM, and type 2 DM.

## MATERIALS AND METHODS

A total of 222 adult kidney transplant patients (age > 20 years) who were on regular follow-up at our outpatient clinic in Baqiyatollah Hospital were selected to be included in this retrospective cohort. They consisted of 111 patients who had been diagnosed with DM and the remaining were randomly selected nondiabetic kidney recipients. All of the patients were recipients of kidney allografts from living donors at our transplantation department between 1986 and 2001. According to the World Health Organization's criteria,[17] diabetic patients were divided into 3 subgroups with respect to the type of diabetes mellitus: type 1 DM, type 2 DM, and PTDM. Type 1 DM had been diagnosed if the patient had been insulin-dependent or had no measurable level of C-peptide before transplantation. Type 2 DM had been diagnosed if the patient had not required insulin for survival, but experienced fasting hyperglycemia or abnormal glucose tolerance tests. Posttransplant DM was clinically defined by the corresponding physician of each patient; the criterion for diagnosis of PTDM was developing repeated serum glucose levels of 11.0 mmol/L or higher.

Age, sex, year of transplantation, duration of dialysis, allograft source, age and sex of the donors, delayed graft function, early and late allograft rejection episodes, graft loss, and death were recorded for all of the patients. Posttransplant information was obtained from standard transplantation follow-up protocols and all inpatient and outpatient records. Early rejection episode was defined as rejection in less than 3 posttransplant months, and any rejection episode occurred after this period was considered as a late rejection episode. Graft failure was defined by either creatinine level of 6 mg/dL for more than 3 consecutive months or a clinical diagnosis of rejection necessitating renal replacement therapy. In 30% of the cases, diagnosis of the allograft rejection was confirmed by allograft biopsy and in the remainder, it was determined clinically.

Statistical analyses were performed using the SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, Ill, USA). All numeric data were presented as mean ± standard deviation. Differences between the categorical variables were compared using the chi-square test or the Fisher exact test. The Student *t* test was used for evaluating continuous variables. The 1-way analysis of variances test was used to compare continuous variables between the three diabetic groups. The Tukey-Kramer multiple-comparison tests were used to assess differences between the individual means. Analyses of survival were performed using the Kaplan-Meier method and the log rank test. Proportional hazards analysis using the Cox regression analysis

was performed for evaluation of the independent impact of different factors on the outcome after adjustment for other contributing factors. A *P* value level of less than .05 was considered statistically significant.

## RESULTS

Of the total studied kidney allograft recipients, 111 were diabetic, of whom, 36 (32.4%), 20 (18.0%), and 55 (49.6%) were confirmed cases of type 1 DM, type 2 DM, and PTDM. Of the study population, 161 (72.5%) were men and 61 (27.5%) were women. Men also constituted 184 (82.8%) of the donors population. The mean age of the patients was 43.7 ± 10.7 years (range, 22 to 75 years) and for the donors, it was 28.5 ± 5.8 years (range, 19 to 48 years). A total of 205 (92.3%) and 17 (7.7%) allografts were harvested from living unrelated and living related donors, respectively. Mean duration of dialysis before transplantation was 22.0 ± 29.6 months (range, zero to 192 months). Panel reactive antibodies were positive in 25 patients (11.2%). Also, 14 (6.3%) patients had a history of delayed graft function. Four patients (1.8%) had a history of graft loss and 218 (98.2%) were first-allograft recipients. The diabetic patients were similar to the control group in terms of age, sex, duration of dialysis, follow-up duration, allograft source, number of transplants, and donors' age and sex (Table 1).

Diabetic patients had significantly higher rates of rejection episodes, death, and delayed graft function compared to the nondiabetic group (Table 1). On the other hand, although diabetic patients showed more than 2-fold graft loss rates, the difference was not significant. Patient and allograft survival rates were significantly lower in diabetic patients ($P = .03$ and $P = .04$, respectively). Multivariate proportional analysis confirmed this finding (Figure 1 and Table 2).

As presented in Table 1, among the subgroups of DM, type 2 diabetic patients had a significantly higher age, but patients with PTDM had a significantly longer follow-up duration and lower rate of positive panel reactive antibodies. The DM subgroups were similar in their recipients' sex distribution, donors' characteristics, number of transplants, history of delayed graft function, early and late rejection episodes, and overall

**Table 1.** Characteristics and Outcomes of Kidney Allograft Recipients With and Without Diabetes Mellitus*

| | Kidney Recipients | | | Diabetes subgroups | | | |
|---|---|---|---|---|---|---|---|
| **Parameters** | **DM** | **No DM** | ***P*** | **Type 1 DM** | **Type 2 DM** | **PTDM** | ***P*** |
| Recipient's age, y | 44.6 ± 11.2 | 42.9 ± 10.2 | .24 | 38.5 ± 8.4 | 53.6 ± 6.6 | 45.3 ± 11.7 | < .001 |
| Donor's age, y | 28.3 ± 4.9 | 28.6 ± 6.1 | .60 | 28.2 ± 4.8 | 27.7 ± 4.6 | 28.5 ± 5.3 | .84 |
| Dialysis duration, mo | 22.2 ± 30.0 | 21.8 ± 29.3 | .92 | 22.6 ± 38.5 | 12.6 ± 11.8 | 25.9 ± 26.6 | .31 |
| Follow-up duration, mo | 34.3 ± 41.5 | 42.3 ± 41.9 | .16 | 18.2 ± 24.6 | 15.0 ± 15.9 | 25.9 ± 26.6 | < .001 |
| Recipient's sex | | | | | | | |
| Male | 82 (73.9) | 79 (71.2) | | 29 (80.5) | 16 (80.0) | 37 (67.3) | |
| Female | 29 (26.1) | 32 (28.8) | .65 | 7 (19.5) | 4 (20.0) | 18 (32.7) | .29 |
| Donor's sex | | | | | | | |
| Male | 92 (84.4) | 90 (81.1) | | 31 (86.1) | 19 (95.0) | 42 (79.2) | |
| Female | 17 (15.6) | 21(18.9) | .59 | 5 (13.9) | 1 (5.0) | 11 (20.8) | .24 |
| Donor source | | | | | | | |
| Living related | 8 (7.2) | 9 (8.1) | | 4 (11.1) | 0 | 4 (7.3) | |
| Living unrelated | 103 (92.8) | 102 (91.9) | .80 | 32 (88.9) | 20 (100) | 51 (92.7) | .30 |
| Positive panel reactive antibodies | 13 (11.7) | 12 (10.8) | .83 | 7 (19.4) | 4 (20.0) | 2 (3.6) | .03 |
| Second transplants | 3 (2.7) | 1 (0.9) | .31 | 0 | 0 | 1 (1.9) | .60 |
| Delayed graft function | 11 (9.9) | 3 (2.7) | .03 | 4 (11.1) | 1 (5.0) | 6 (10.9) | .72 |
| Rejection episodes | | | | | | | |
| No | 60 (54.1) | 60 (54.1) | | 17 (47.2) | 12 (60.0) | 31 (56.3) | |
| Early | 41 (36.9) | 49 (44.1) | | 19 (52.8) | 8 (40.0) | 22 (40.0) | |
| Late | 10 (9) | 2 (1.8) | .049 | 0 | 0 | 2 (3.6) | .49 |
| Allograft loss | 17 (15.3) | 8 (7.2) | .06 | 5 (13.9) | 3 (15.0) | 9 (16.3) | .95 |
| Death | 10 (9.3) | 3 (2.8) | .049 | 5 (15.9) | 2 (10.0) | 3 (5.5) | .38 |

*Values in parentheses are percents. DM indicates diabetes mellitus and PTDM, posttransplant diabetes mellitus.

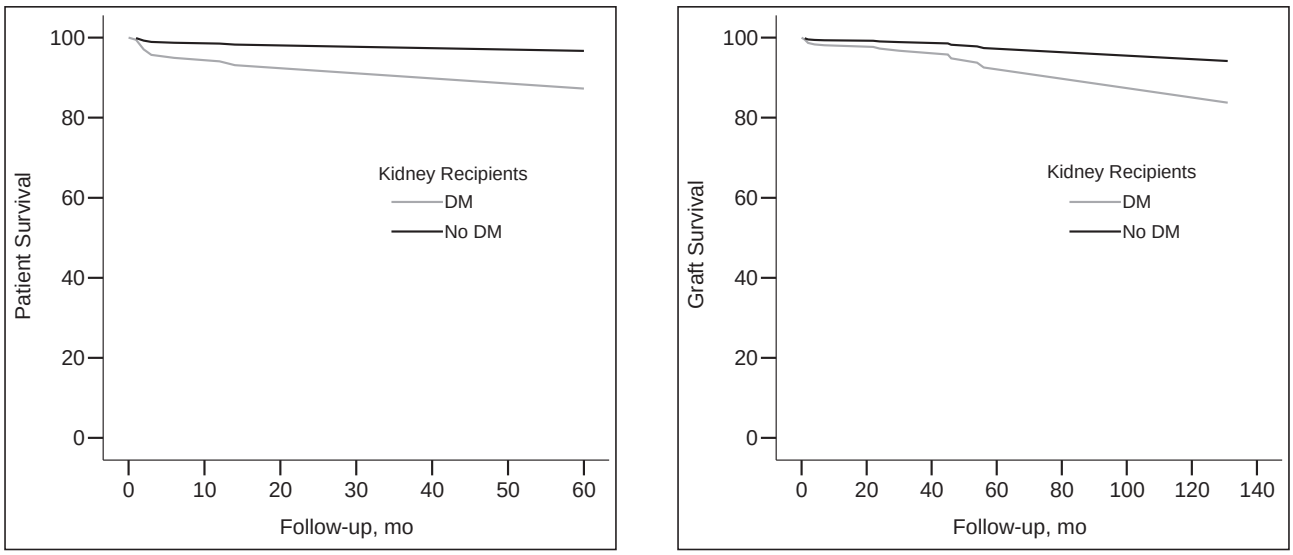


**Figure1.** Patient and graft survival rates for the patients with and without diabetes mellitus (DM).

**Table 2.** Proportional Hazard Analysis for Evaluating Independent Impact of Diabetes Mellitus on Patient and Graft Outcomes

| Variables | *P* | Exp(B) | 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower | Upper |
| **Patient** | | | | |
| Diabetes mellitus | .05 | 3.71 | 0.99 | 13.89 |
| Recipients' sex | .12 | 5.13 | 0.65 | 40.25 |
| Recipients' age | .41 | 1.02 | 0.97 | 1.07 |
| Donors' sex | .84 | 0.86 | 0.18 | 4.01 |
| Donors' age | .49 | 1.04 | 0.94 | 1.14 |
| Panel reactive antibodies | .78 | 0.74 | 0.09 | 5.96 |
| Delayed graft function | .95 | 0.93 | 0.12 | 7.59 |
| **Graft** | | | | |
| Diabetes mellitus | .03 | 2.94 | 1.09 | 7.94 |
| Recipients' sex | .45 | 0.69 | 0.26 | 1.82 |
| Recipients' age | .04 | 1.04 | 1.00 | 1.09 |
| Donors' sex | .17 | 0.48 | 0.17 | 1.36 |
| Panel reactive antibodies | .97 | 0 | 0 | … |
| Dialysis duration | .42 | 0.99 | 0.97 | 1.01 |
| Delayed graft function | .05 | 3.42 | 0.99 | 11.75 |

**Table 3.** Proportional Hazard Analysis for Evaluating Independent Impact of Different Types of Diabetes Mellitus on Patient and Graft Outcomes

| Variables | *P* | Exp(B) | 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower | Upper |
| **Patient** | | | | |
| Recipients' sex | .53 | 1.99 | 0.23 | 17.07 |
| Recipients' age | .06 | 1.07 | 0.99 | 1.16 |
| Donors' sex | .53 | 0.58 | 0.11 | 3.13 |
| Donors' age | .43 | 1.05 | 0.92 | 1.20 |
| Panel reactive antibodies | .73 | 0.68 | 0.07 | 6.20 |
| Delayed graft function | .79 | 1.35 | 0.15 | 12.33 |
| Diabetes mellitus | | | | |
| Posttransplant | .07 | 1 | … | … |
| Type 1 | .02 | 10.99 | 1.45 | 83.30 |
| Type 2 | .23 | 3.63 | 0.43 | 30.42 |
| **Graft** | | | | |
| Recipients' sex | .07 | 0.35 | 0.11 | 1.08 |
| Recipients' age | .03 | 1.07 | 1.01 | 1.13 |
| Donors' sex | .02 | 0.25 | 0.08 | 0.79 |
| Donors' age | .73 | 1.02 | 0.92 | 1.12 |
| Panel reactive antibodies | .98 | 0 | 0 | … |
| Delayed graft function | .11 | 3.21 | 0.75 | 13.72 |
| Diabetes mellitus | | | | |
| Posttransplant | .05 | 1.00 | … | … |
| Type 1 | .02 | 5.36 | 1.24 | 23.18 |
| Type 2 | .08 | 4.27 | 0.84 | 21.58 |

allograft and patients' outcomes. Multivariate proportional hazard analysis also showed similar results; however, type 1 DM was associated with the risks of patient and graft loss (Figure 2 and Table 3). We also evaluated patient and allograft survival differences between the two groups of patients with type 1 DM and the controls. We found that patients with type 1 DM were significantly more likely to lose lives and allografts than the recipients without DM ($P = .004$ and $P = .03$, respectively), which was confirmed by multivariate hazard analysis (Figure 3 and Table 4). Although type 2 DM group had relatively worse patient and graft outcome compared to the controls, the difference was not significant ($P = .07$ and $P = .07$, respectively). On the other hand, PTDM had comparable patient

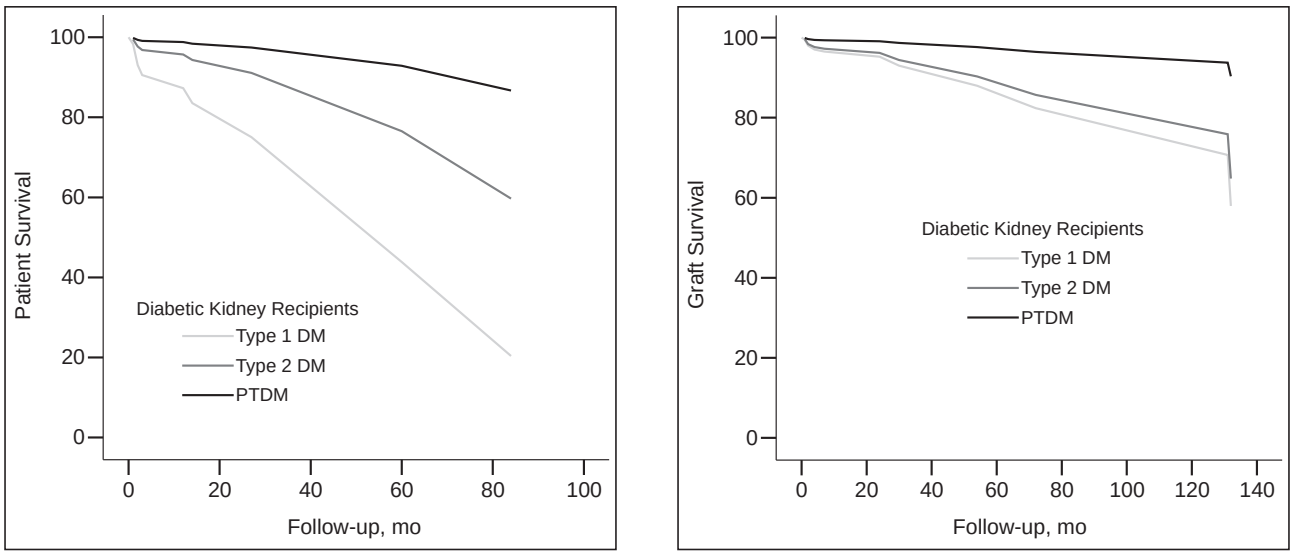


**Figure 2.** Patient and graft survival rates for the patients with different types of diabetes mellitus (DM).

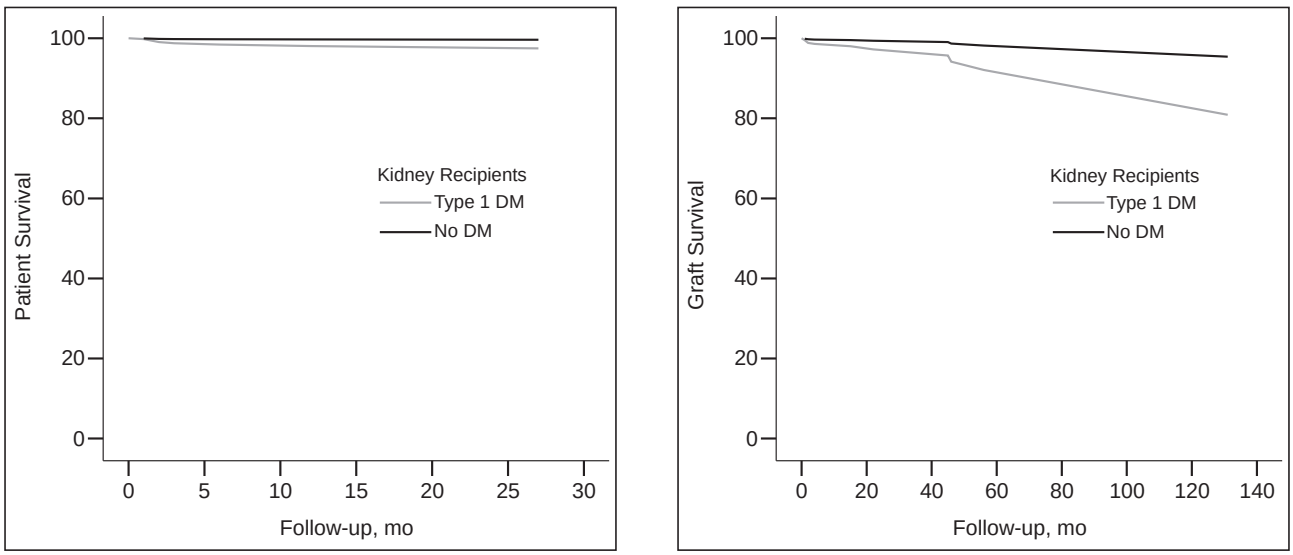


**Figure 3.** Patient and graft survival rates for the patients with type 1 diabetes mellitus (DM) versus kidney allograft recipients without DM.

and allograft outcomes with the controls.

## DISCUSSION

The proportion of patients with diabetes mellitus requiring renal replacement therapy as well as the number of kidney transplant recipients developing PTDM has drastically increased over the recent decade.[9,18-21] The lower graft and patient survival rates of the diabetic patients has made the issue of kidney transplantation a matter of dispute. The proponents of the practice account the excellent patient and graft survival rates in diabetic patients with ESRD compared to the patients undergoing dialysis.[22-24] On the other hand, opponents of performing kidney transplantation in diabetic patients argue that in the presence of allograft shortage, we should reserve kidney transplantation to those who have the best outcome. In this study, we found that diabetic recipients of living kidney transplants have worse graft and patient survival rates than their nondiabetic counterparts. Moreover, among patients with different types of DM, only type 1 DM had significant adverse effects on patient and allograft survival compared to nondiabetic patients. We also found that PTDM patients had relatively better patient survival compared to the

**Table 4.** Proportional Hazard Analysis for Evaluating Independent Impact of Type 1 Diabetes Mellitus Versus No Diabetes Mellitus on Patient and Graft Outcomes

| Variables | *P* | Exp(B) | 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower | Upper |
| **Patient** | | | | |
| Recipients' sex | .30 | 3.11 | 0.36 | 26.69 |
| Recipients' age | .47 | 1.03 | 0.95 | 1.12 |
| Donors' sex | .64 | 1.66 | 0.19 | 13.95 |
| Donors' age | .23 | 1.08 | 0.95 | 1.23 |
| Panel reactive antibodies | .98 | 0 | 0 | … |
| Delayed graft function | .99 | 0 | 0 | … |
| Type 1 Diabetes mellitus | .01 | 8.44 | 1.73 | 41.09 |
| **Graft** | | | | |
| Recipients' sex | .96 | 1.04 | 0.19 | 5.64 |
| Recipients' age | .04 | 1.07 | 1.00 | 1.15 |
| Donors' sex | .64 | 1.02 | 0.93 | 1.12 |
| Donors' age | .82 | 1.18 | 0.27 | 5.09 |
| Panel reactive antibodies | .98 | 0 | 0 | … |
| Delayed graft function | .002 | 11.26 | 2.46 | 51.59 |
| Type 1 Diabetes mellitus | .049 | 4.52 | 1.01 | 20.29 |

patients with the other types of DM.

Our findings are in accordance with some previous studies assessing the outcome differences in diabetic and nondiabetic kidney transplant recipients.[25,26] Some of the associations between DM and graft failure can be explained by the higher risk of death. Since DM is associated with an increased risk of infection, cardiovascular events, and other complications, it is plausible that DM can increase mortality. Revanur and colleagues reported a lower patient survival, but not graft survival in both patients with preexisting DM and PTDM.[27] Kronson and associates compared the outcomes of kidney transplant recipients with type 1 DM and type 2 DM and nondiabetic patients. They found that patients with type 2 DM represented lower patient and graft outcome compared to those with type 1 DM, but when death with the functioning graft was censored, they found that graft survival for these two diabetic groups and nondiabetic patients were the same.[22] Results of this study showed a significant better patient survival but not graft survival rate for PTDM in comparison with that in other diabetic patients. The better patient survival in PTDM compared to types 1 and 2 DM can be well explained by this fact that patients with PTDM usually experience hyperglycemia in a shorter time duration than patients with the other two types of DM. However, in contrast to the abovementioned studies, we did not find any differences between types 1 DM and 2 DM in terms of patient and graft survival rates.

To the best of our knowledge, this is the first study assessing and comparing survival outcomes of diabetic kidney recipients which simultaneously evaluates allograft and patient survival in 4 different subgroups (nondiabetic, type 1 DM, type 2 DM, and PTDM groups) receiving living kidney allograft. As a limitation, we did not mention how well our studied recipients had controlled their blood glucose levels; hence, we cannot have a conclusion whether hyperglycemia or some other factors are responsible for the poor outcome (eg, insulin metabolism).

## CONCLUSION

We found that diabetic kidney recipients had worse patient and graft survival compared to nondiabetics. Among diabetic patients, PTDM has relatively the best patient survival. These findings suggest that kidney transplant patients representing any types of DM should be more closely followed, and development of PTDM does not necessarily worsen the outcomes in short-term.

## CONFLICT OF INTEREST

None declared.

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