

Glycemic control and kidney function in pretransplant versus post-transplant diabetes mellitus among solid-organ transplant recipients: a single-center cross-sectional study

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Abstract

Background

Diabetes contributes substantially to long-term morbidity after solid-organ transplantation. However, direct comparisons of kidney function and glycemic control between pretransplant diabetes mellitus (PDM) and post-transplant diabetes mellitus (PTDM), particularly in cohorts with prolonged follow-up and a predominance of non-kidney transplant recipients, remain limited.

Methods

This single-center, retrospective, cross-sectional study included 119 adult solid-organ transplant recipients with diabetes followed between July 2023 and October 2025. Kidney function, glycemic control, and treatment patterns were compared between PDM and PTDM, early- and late-onset PTDM, and sodium-glucose cotransporter 2 inhibitor users and non-users. Multivariable logistic regression evaluated factors independently associated with PTDM.

Results

The cohort included liver (52.1%), kidney (35.3%), and heart (12.6%) transplant recipients. Most patients had PTDM (62.2%). Mean time since transplantation was 13.97 ± 7.59 years, mean estimated glomerular filtration rate (eGFR) was 60.46 ± 28.79 mL/min/1.73 m², and mean glycated hemoglobin was $7.37 \pm 1.82\%$; 52.9% of patients had an HbA1c level > 7%. Compared with patients with PTDM, those with PDM were older (64.77 ± 10.50 vs. 59.66 ± 12.16 years; $P = 0.031$), had a shorter time since transplantation (10.51 ± 6.46 vs. 16.27 ± 7.44 years; $P < 0.001$), and had lower eGFR (52.15 ± 22.54 vs. 65.33 ± 30.83 mL/min/1.73 m²; $P = 0.017$), whereas glycemic control was similar. In multivariable analysis, age and time since transplantation remained independently associated with PTDM, whereas eGFR was not independently associated with diabetes group (adjusted odds ratio 1.018 per 1 mL/min/1.73 m² increase, 95% confidence interval 0.995–1.042; $P = 0.133$). Early - and late-onset PTDM had comparable kidney function and glycemic control. Sodium-glucose cotransporter 2 inhibitor users were older and more frequently had eGFR categories G3-G5.

Conclusions

Long-term solid-organ transplant recipients with diabetes had a substantial burden of kidney dysfunction and suboptimal glycemic control. Prospective studies are needed to clarify longitudinal cardiorenal outcomes and the role of newer glucose-lowering therapies.

BACKGROUND

Diabetes mellitus is a common and clinically consequential condition in solid-organ transplant recipients. Hyperglycemia may be present before transplantation as pretransplant diabetes mellitus (PDM) or may develop after transplantation as post-transplant diabetes mellitus (PTDM). Both conditions are associated with increased risks of cardiovascular disease, infection, hospitalization, graft dysfunction, and mortality, making long-term metabolic care an integral component of transplant follow-up [1–4].

The pathophysiology of post-transplant hyperglycemia is multifactorial. Calcineurin inhibitors, particularly tacrolimus, impair pancreatic beta-cell function and insulin secretion, whereas glucocorticoids increase hepatic glucose production, reduce peripheral glucose uptake, and promote weight gain and insulin resistance [1, 3, 5, 6]. Surgical stress, systemic inflammation, infections, changes in body composition, and pre-existing susceptibility to type 2 diabetes further contribute to dysglycemia. Consequently, PTDM may arise from a variable combination of beta-cell toxicity and insulin resistance, while recipients with PDM may experience worsening glycemic control after transplantation because of the same exposures [1–6].

Kidney dysfunction is also frequent after solid-organ transplantation and may reflect the combined effects of diabetes, aging, perioperative kidney injury, infection, hypertension, and chronic exposure to nephrotoxic immunosuppressive agents. Diabetic kidney disease is characterized by albuminuria and progressive loss of glomerular filtration, whereas calcineurin-inhibitor nephrotoxicity involves vascular, tubulointerstitial, and glomerular injury [7–9]. Importantly, chronic kidney disease is not confined to kidney transplant recipients; clinically relevant reductions in kidney function are also common after transplantation of nonrenal organs [10].

Despite the prognostic importance of hyperglycemia and kidney dysfunction, several uncertainties remain. Most studies have focused on the incidence and early course of PTDM, kidney transplant populations, or outcomes associated with PDM and PTDM separately. Direct comparisons of long-term glycemic control and kidney function between PDM and PTDM are scarce, particularly in cohorts predominantly composed of liver and heart transplant recipients. It also remains unclear whether the timing of PTDM onset retains clinical relevance after many years of follow-up and how newer cardiorenal-protective glucose-lowering therapies are used in routine transplant care. This study therefore compared kidney function and glycemic control between patients with PDM and PTDM in a long-term, single-center cohort of solid-organ transplant recipients, most of whom had received non-kidney transplants. Secondary analyses compared early- and late-onset PTDM and characterized recipients treated with SGLT2 inhibitors.

METHODS

Study design and setting

This single-center, retrospective, cross-sectional study was conducted at the transplant outpatient clinic of the Endocrinology Service, Federal University of Minas Gerais, Belo Horizonte, Brazil. The medical records of all potentially eligible adult solid-organ transplant recipients with diabetes who attended the clinic between July 2023 and October 2025 were reviewed

Study population

Patients were eligible if they were 18 years or older, had undergone solid-organ transplantation, and had been diagnosed with diabetes mellitus either before or after transplantation. Recipients of simultaneous pancreas-kidney transplantation were excluded. Patients whose medical records lacked information on specific variables were excluded from the corresponding analyses.

Data collection and study variables

Data were obtained through a standardized retrospective review of medical records. The variables assessed were sex, age, transplanted organ, date of transplantation, time since transplantation, timing of diabetes diagnosis in relation to transplantation, duration of diabetes, interval between transplantation and PTDM diagnosis, current glucose-lowering therapy, most recent HbA1c measurement, body mass index (BMI), serum creatinine, eGFR calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, and current immunosuppressive therapy, including glucocorticoids, tacrolimus, everolimus, sirolimus, cyclosporine, and mycophenolate.

Exposure to immunosuppressive therapy

Exposure to each immunosuppressive agent was defined as documented use throughout at least two consecutive outpatient follow-up intervals. Because visits were generally scheduled at 3-month intervals, this definition corresponded to an estimated minimum exposure of approximately 6 months.

Definitions and study groups

Patients were classified as having PDM or PTDM. PDM was defined as diabetes diagnosed before transplantation. PTDM was defined as newly diagnosed diabetes after transplantation in individuals without documented diabetes before transplantation.

PTDM was diagnosed at least 3 months after transplantation when either of the following criteria was met: fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L) on two separate occasions or a 2-h plasma glucose concentration ≥ 200 mg/dL (11.1 mmol/L) during a 75-g oral glucose tolerance test. After the first post-transplant year, an HbA1c level $\geq 6.5\%$ (48 mmol/mol) was also accepted as a diagnostic criterion for PTDM.

The PTDM group was further stratified according to the timing of diagnosis. Early-onset PTDM was defined as PTDM diagnosed within the first year after transplantation, whereas late-onset PTDM was defined as PTDM diagnosed more than 1 year after transplantation.

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation, and categorical variables as absolute frequencies and percentages, according to data availability. Comparisons were performed between patients with PDM and PTDM, between early- and late-onset PTDM, and between SGLT2 inhibitor users and non-users. Continuous variables were compared using the independent-samples Student t test. Categorical variables were compared using the Pearson chi-square test or Fisher exact test, as appropriate. Variables that were statistically significant in univariable analyses were subsequently entered into a multivariable logistic regression model to identify factors independently associated with PTDM, with PDM as the reference category. Missing observations were excluded from the corresponding analysis. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Analyses were performed using IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, USA).

RESULTS

Baseline characteristics of the study population

The baseline characteristics of the study population are summarized in Table 1. A total of 119 patients were included. Mean age was 61.27 ± 12.28 years, mean BMI was 27.56 ± 5.17 kg/m², and 68.1% of participants were male. Liver transplantation was the most common procedure, accounting for 52.1% of the cohort, followed by kidney transplantation (35.3%) and heart transplantation (12.6%).

Mean time since transplantation was 13.97 ± 7.59 . Mean eGFR was 60.46 ± 28.79 mL/min/1.73 m², and 47.4% of participants were in eGFR categories G3-G5. Mean HbA1c was $7.37 \pm 1.82\%$, and 52.9% of participants had an HbA1c level $> 7\%$. Insulin was used by 75.6% of participants, metformin by 53.8%, SGLT2 inhibitors by 29.4%, sulfonylureas by 7.6%, and DPP-4 inhibitors by 4.2%. Tacrolimus was used by 71.4%, corticosteroids by 47.1%, cyclosporine by 14.3%, sirolimus by 5.9%, and statins by 66.4%.

Table 1. Baseline characteristics of the study population	
Characteristic	Value
Age, years	61.27 ± 12.28
Sex, %	
Male	68.1
Female	31.9
BMI, kg/m ²	27.56 ± 5.17
Transplanted organ, %	
Heart	12.6
Kidney	35.3
Liver	52.1
Time since transplantation, years	13.97 ± 7.59
eGFR, mL/min/1.73 m ²	60.46 ± 28.79
CKD category, %	
G1	15.0
G2	32.7
G3a	15.9
G3b	18.4
G4	4.2
G5	6.7
HbA1c, %	7.37 ± 1.82
HbA1c, ≤ 7%	47.1%
HbA1c, > 7%	52.9%
Glucose-lowering therapy, %	
Insulin	75.6
Metformin	53.8
Sulfonylureas	7.6
DPP-4 inhibitors	4.2
SGLT2 inhibitors	29.4

Table 1. Baseline characteristics of the study population	
Characteristic	Value
Other pharmacological therapies, %	
Glucocorticoids	47.1
Tacrolimus	71.4
Sirolimus	5.9
Cyclosporine	14.3
Statins	66.4

BMI, body mass index; CKD, chronic kidney disease; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; PDM, pre-existing diabetes mellitus; PTDM, post-transplant diabetes mellitus; SGLT2, sodium–glucose cotransporter 2.

Comparison between patients with PDM and PTDM

The clinical and transplant-related characteristics of patients with PDM and PTDM are presented in Table 2. Regarding diabetes-group classification, data was available for 118 participants due to one missing value: 44 (37.3%) had PDM and 74 (62.7%) had PTDM.

Patients with PDM were older than those with PTDM (64.77 ± 6.46 vs. 59.66 ± 12.16 years; $P = 0.031$), had a shorter time since transplantation (10.51 ± 6.46 vs. 16.27 ± 7.44 years; $P < 0.001$), and had lower mean eGFR (52.15 ± 22.54 vs. 65.33 ± 30.83 mL/min/1.73 m²; $P = 0.017$).

No significant between-group differences were observed in sex distribution, BMI, transplanted organ, HbA1c, or the use of insulin, SGLT2 inhibitors, tacrolimus, cyclosporine, sirolimus, or corticosteroids. Metformin, sulfonylurea, DPP-4 inhibitor, and statin use are presented descriptively because P values were unavailable for these comparisons.

Table 2
Comparison of clinical characteristics between the PDM and PTDM groups

Characteristic	PDM	PTDM	P value
<i>n</i>	44	74	
Age, years	64.77 ± 10.50	59.66 ± 12.17	0.031
Sex, % Male	68.18	64.86	0.735
Female	31.82	35.14	
BMI, kg/m ²	26.8 ± 4.59	27.69 ± 4.77	0.324
Transplanted organ, %	31.81	36.48	0.872
Kidney			
Heart	13.64	12.16	
Liver	54.55	51.36	
Time since transplantation, years	10.51 ± 6.46	16.27 ± 7.44	< 0.001
eGFR, mL/min/1.73 m ²	52.15 ± 22.54	65.33 ± 30.83	0.017
HbA1c, %	7.31 ± 1.54	7.21 ± 2.11	0.782
Insulin use, %	81	72.97	0.385
SGLT2 inhibitor use, %	34.09	27.03	0.546
Tacrolimus use, %	75.55	68.91	0.620
Cyclosporine use, %	15.55	13.51	0.930
Sirolimus use, %	4.44	6.75	0.929
Corticosteroid use, %	38.64%	51.35%	0.251
Metformin use, %	44.44	59.45	0.131
Sulfonylurea use, %	4.44	9.45	0.480
DPP-4 inhibitor use, %	6.66	2.70	0.365
Statin use, %	68.18	64.86	0.693

BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; PDM, pre-existing diabetes mellitus; PTDM, post-transplant diabetes mellitus; SGLT2, sodium–glucose cotransporter 2.

Factors associated with PTDM

Multivariable logistic regression included 102 participants, with PTDM as the dependent outcome and PDM as the reference category (Table 3). Older age was independently associated with lower odds of belonging to the PTDM group (adjusted OR 0.909 per year, 95% CI 0.839–0.985; $P = 0.020$), corresponding to an approximately 9% reduction in the odds for each additional year of age. Conversely, each additional year since transplantation was associated with 29% higher odds of PTDM classification (adjusted OR 1.290, 95% CI 1.153–1.443; $P < 0.001$). Sex, BMI, HbA1c, eGFR, SGLT2 inhibitor use, corticosteroid use, and tacrolimus use were not independently associated with PTDM.

Table 3
Multivariable logistic regression for factors associated with PTDM

Variable	B	SE	OR	95% CI for OR	P value
Intercept	2.410	3.749	11.137	0.007–17.294.655	0.520
Age, years	−0.096	0.041	0.909	0.839–0.985	0.020
Male sex	0.748	0.622	2.112	0.624–7.147	0.229
BMI, kg/m ²	0.017	0.063	1.017	0.898–1.152	0.786
HbA1c, %	−0.242	0.144	0.785	0.592–1.040	0.092
eGFR, mL/min/1.73 m ²	0.018	0.012	1.018	0.995–1.042	0.133
SGLT2 inhibitor use	0.013	0.632	1.013	0.294–3.493	0.984
Corticosteroid use	0.447	0.686	1.563	0.408–5.996	0.515
Tacrolimus use	−0.377	0.720	0.686	0.167–2.815	0.601
Time since transplantation, years	0.254	0.057	1.290	1.153–1.443	< 0.001

B, regression coefficient; BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; OR, odds ratio; PDM, pretransplant diabetes mellitus; PTDM, post-transplant diabetes mellitus; SE, standard error; SGLT2, sodium-glucose cotransporter 2.

Comparison between early- and late-onset PTDM

The characteristics of patients with early- and late-onset PTDM are presented in Table 4. Among the 70 patients with precise information on the timing of PTDM diagnosis, 34 developed PTDM within the first year after transplantation and 36 developed PTDM more than 1 year after transplantation. Four patients were excluded from this analysis because the timing of PTDM diagnosis was not precisely documented.

The distribution of transplanted organs differed between groups ($P = 0.035$). Heart transplantation was more frequent in early-onset PTDM than in late-onset PTDM (23.5% vs. 2.%), whereas kidney and liver transplantation were proportionally more frequent in the late-onset group. Time since diabetes diagnosis was longer in the early-onset group (13.75 ± 7.05 vs. 10.47 ± 5.51 years; $P = 0.036$).

No significant differences were observed in age, sex distribution, BMI, eGFR, the proportion of patients in eGFR categories G3-G5, HbA1c, or the evaluated glucose-lowering, immunosuppressive, and statin therapies

Table 4
Comparison of characteristics between early- and late-onset PTDM groups*
Characteristic Early PTDM (n = 34) Late PTDM (n = 36) P value

Age, years	59.53 ± 9.17	61.00 ± 13.17	0.600
Sex, n (%)			0.131
Male	26 (76.5)	21 (58.3)	
Female	8 (23.5)	15 (41.7)	
BMI, kg/m ²	26.50 ± 3.60	28.70 ± 5.50	0.068
Transplanted organ, n (%)			0.035
Heart	8 (23.5)	1 (2.8)	
Kidney	11 (32.4)	15 (41.7)	
Liver	15 (44.1)	20 (55.6)	
Time since diabetes diagnosis, years	13.75 ± 7.05	10.47 ± 5.51	0.036
eGFR, mL/min/1.73 m ²	66,23 ± 28,76	60,60 ± 32,19	0.456
eGFR categories G3–G5, n (%)	9 (26.5)	16 (44.4)	0.330
HbA1c, %	7.60 ± 2.40	7.30 ± 1.50	0.480
Insulin use, n (%)	23 (67.6)	29 (80.6)	0.278
Metformin use, n (%)	18 (52.9)	25 (69.4)	0.220
Sulfonylurea use, n (%)	2 (5.9)	5 (13.9)	0.430
DPP-4 inhibitor use, n (%)	0 (0.0)	1 (2.8)	1.000
SGLT2 inhibitor use, n (%)	8 (23.5)	12 (33.3)	0.433
Glucocorticoid use, n (%)	18 (52.9)	17 (47.2)	0.811
Tacrolimus use, n (%)	21 (61.8%)	26 (72.2)	0.447
Sirolimus use, n (%)	4 (11.8)	1 (2,8)	0.192
Cyclosporine use, n (%)	5 (14.7)	5 (13,9)	1.000
Statin use, n (%)	22 (64.7)	25 (69.4)	0.514

BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; PDM, pre-existing diabetes mellitus; PTDM, post-transplant diabetes mellitus; SGLT2, sodium–glucose

cotransporter 2.

Comparison between SGLT2 inhibitor users and non-users

The characteristics of SGLT2 inhibitor users and non-users are presented in Table 5. SGLT2 inhibitor users were older than non-users (63.3 ± 7.8 vs. 57.7 ± 12.6 years; $P = 0.004$). The distribution of transplanted organs differed between groups ($P = 0.019$): heart and kidney transplantation were more frequent among users, whereas liver transplantation was more frequent among non-users.

The proportion of patients in eGFR categories G3-G5 was higher among SGLT2 inhibitor users than among non-users (65.71% vs. 34.52%; $P = 0.008$), although mean eGFR did not differ significantly (54.3 ± 21.2 vs. 59.8 ± 37.3 mL/min/1.73 m²; $P = 0.129$).

Metformin use (71.43% vs. 46.43%; $P = 0.022$) and statin use (94.29% vs. 55.95%; $P = 0.003$) were more frequent among SGLT2 inhibitor users. No significant differences were observed in sex distribution, BMI, time since diabetes diagnosis, diabetes group, HbA1c, or the use of insulin, sulfonylureas, DPP-4 inhibitors, corticosteroids, tacrolimus, sirolimus, or cyclosporine.

Table 5
Comparison of characteristics between SGLT2 inhibitor users and non-users

Characteristic	SGLT2 inhibitor users (n = 35)	Non-users (n = 84)	P value
Age, years	63.30 ± 7.80	57.70 ± 12.60	0.016
Sex, n (%)			0.853
Male	23 (65.7)	56 (67.5)	
Female	12 (34.3)	27 (32.5)	
BMI, kg/m ²	26.80 ± 4.50	27.90 ± 5.50	0.298
Transplanted organ, n (%)			0.019
Heart	8 (22.9)	7 (8.3)	
Kidney	15 (42.9)	27 (32.1)	
Liver	12 (34.3)	50 (59.5)	
Time since diabetes diagnosis, years	15.00 ± 9.06	15.01 ± 9.01	0.996
Diabetes group, n (%)			0.417
PDM	15 (42.9)	29 (34.9)	
PTDM	20 (57.1)	54 (65.1)	
eGFR categories G3-G5, n (%)	23 (65.7)	29 (34.5)	0.002
eGFR, mL/min/1.73 m ²	54.30 ± 21.20	59.80 ± 37.30	0.415
HbA1c, %	7.30 ± 1.20	7.40 ± 2.00	0.783
Insulin use, n (%)	29 (82.9)	61 (72.6)	0.236
Metformin use, n (%)	25 (71.4)	39 (46.4)	0.013
Sulfonylurea use, n (%)	2 (5.7)	7 (8.3)	1.000
DPP-4 inhibitor use, n (%)	1 (2.9)	4 (4.8)	1.000
Glucocorticoid use, n (%)	19 (54.3)	35 (41.7)	0.208
Tacrolimus use, n (%)	21 (60.0)	75 (89.3)	< 0.001
Sirolimus use, n (%)	2 (5.7)	5 (6.0)	1.000
Cyclosporine use, n (%)	8 (22.9)	9 (10.7)	0.094
Statin use, n (%)	33 (94.3)	45 (53.6)	< 0.001

BMI, body mass index; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; PDM, pretransplant diabetes mellitus; PTDM, post-transplant diabetes mellitus; SGLT2, sodium-glucose cotransporter 2.

DISCUSSION

This single-center, real-world study evaluated solid-organ transplant recipients with diabetes after a prolonged post-transplant period, averaging approximately 14 years. Liver transplantation accounted for more than half of the procedures, reflecting the center's extensive experience with these recipients. PTDM was more frequent than PDM among participants with available classification. The cohort had a substantial metabolic and kidney disease burden: mean eGFR was approximately 60 mL/min/1.73 m², 47.4% of participants were in eGFR categories G3-G5, mean HbA1c was 7.37%, 52.9% had an HbA1c level > 7%, and approximately three-quarters were receiving insulin. These findings characterize a clinically complex population in which diabetes, immunosuppressive exposure, aging, and transplant-related factors likely contributed to kidney dysfunction and suboptimal glycemic control [1, 2, 7, 10].

Patients with PDM were older, had a shorter time since transplantation, and had lower mean eGFR than those with PTDM in unadjusted analysis. In multivariable logistic regression, age and time since transplantation remained independently associated with PTDM, whereas eGFR was no longer independently associated with diabetes group. Thus, the observed difference in kidney function appears to be explained at least partly by differences in age and post-transplant follow-up rather than by diabetes classification itself. The direction of the follow-up difference is clinically noteworthy: despite having spent fewer years after transplantation, patients with PDM had lower unadjusted eGFR, potentially reflecting older age, longer lifetime exposure to diabetes, greater pretransplant cardiorenal burden, or kidney injury already present at transplantation. Because pretransplant kidney function and diabetes duration were not uniformly available, these mechanisms could not be tested directly. Previous studies have linked pretransplant diabetes with adverse kidney, graft, and survival outcomes after liver and kidney transplantation, although differences in study populations and outcomes limit direct comparison [7, 10–12].

HbA1c was similar between PDM and PTDM, with mean values above 7% in both groups; overall, 52.9% of participants had an HbA1c level > 7%, and insulin use was frequent. Although individualized and less stringent glycemic targets may be appropriate for older recipients, patients with chronic kidney disease, or those at high risk of hypoglycemia, the combination of long-standing diabetes, frequent insulin treatment, and more than half of the cohort having HbA1c > 7% suggests room for improvement at the population level. Progressive beta-cell dysfunction, cumulative hyperglycemic exposure, aging, calcineurin-inhibitor use, hypertension, and previous kidney injury may all contribute to the difficulty of achieving glycemic targets and preserving kidney function [1, 2, 7–10].

Early- and late-onset PTDM showed broadly similar long-term kidney, glycemic, and treatment profiles. Mean eGFR and HbA1c were comparable, while the main differences were the distribution of

transplanted organs and the longer duration of diabetes in the early-onset group. Early post-transplant hyperglycemia may initially result from surgical stress, infection, high-dose corticosteroids, and calcineurin-inhibitor toxicity, whereas late-onset PTDM may more closely resemble type 2 diabetes associated with aging, weight gain, insulin resistance, progressive beta-cell dysfunction, and prolonged immunosuppressive exposure [1, 2]. Over time, however, these mechanisms may converge into a common chronic phenotype characterized by beta-cell failure, greater treatment intensity, and cardiorenal complications. Previous studies have similarly emphasized the prognostic importance of persistent rather than transient PTDM [13, 14].

SGLT2 inhibitor users were older and more frequently had moderate-to-advanced chronic kidney disease than non-users, despite similar mean HbA1c and eGFR. This pattern probably reflects preferential selection of patients at higher cardiorenal risk rather than an adverse effect of SGLT2 inhibitor therapy. More frequent metformin and statin use among SGLT2 inhibitor users also suggests a more intensive cardiometabolic treatment strategy. Medication-access criteria within the Brazilian public health system may additionally influence prescribing patterns [15]. Although transplant-specific evidence remains limited, a randomized trial in stable kidney transplant recipients with PTDM found that empagliflozin improved glycemic control and body weight without relevant changes in eGFR, immunosuppressive drug concentrations, or adverse events [16]. Systematic reviews and observational studies have reported favorable glycemic and metabolic effects without major kidney safety signals, but most evidence is short-term and focused on kidney transplantation [17, 18]. Confounding by indication prevents the present cross-sectional analysis from establishing effectiveness or safety.

This study has several strengths. It describes a real-world cohort evaluated late after transplantation, with a mean post-transplant follow-up of approximately 14 years. Care in a specialized endocrine transplant clinic provided relative consistency in assessment and management. Most participants were non-kidney transplant recipients, particularly liver transplant recipients, an underrepresented group in studies of PTDM and newer glucose-lowering therapies. In these patients, eGFR predominantly reflects native kidney function and may capture the cumulative effects of diabetes, aging, calcineurin inhibitors, perioperative injury, and other post-transplant exposures. The comparisons between PDM and PTDM, early- and late-onset PTDM, and SGLT2 inhibitor users and non-users provided complementary perspectives on this heterogeneous population.

The study also has important limitations. Its retrospective, cross-sectional design precluded assessment of causality and longitudinal changes in glycemic control or kidney function. The single-center setting and relatively small sample limited statistical power and generalizability. Including liver, kidney, and heart transplant recipients introduced clinical heterogeneity. Although the multivariable model adjusted for age and time since transplantation, residual confounding remains possible, and the model could not account for several clinically relevant variables. Serial HbA1c and eGFR measurements, albuminuria, pretransplant kidney function, acute kidney injury, rejection, graft function, tacrolimus concentrations, cumulative corticosteroid exposure, cardiovascular events, hypoglycemia, and continuous glucose-monitoring data were not consistently available. Some variables had missing observations, and P values

were unavailable for selected treatment comparisons in Table 2. Analyses of glucose-lowering therapy were susceptible to confounding by indication and contraindication.

Prospective, multicenter, and organ-specific studies should assess longitudinal kidney, glycemic, cardiovascular, graft, and survival outcomes in transplant recipients with diabetes. SGLT2 inhibitors and glucagon-like peptide-1 receptor agonists are promising, but transplant-specific evidence remains based mainly on small or observational kidney transplant studies [16, 17, 19]. Studies in liver and heart transplant recipients are particularly needed to determine whether earlier and more systematic use of cardiorenal-protective therapies can improve kidney trajectories, cardiovascular outcomes, graft survival, and mortality in patients with PDM or PTDM.

CONCLUSIONS

Long-term solid-organ transplant recipients with diabetes had a high burden of kidney dysfunction and suboptimal glycemic control. Patients with PDM were older, had a shorter time since transplantation, and had lower eGFR than those with PTDM in unadjusted analysis; however, eGFR was not independently associated with diabetes group after adjustment for age and time since transplantation. Early- and late-onset PTDM had similar long-term kidney and glycemic profiles. SGLT2 inhibitors were used more frequently in older patients and those with more advanced chronic kidney disease, likely reflecting selection for cardiorenal protection. Integrated metabolic, kidney, and cardiovascular care and prospective evaluation of newer therapies are warranted in this high-risk population.

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Research Ethics Committee of the Federal University of Minas Gerais, Belo Horizonte, Brazil (approval number 57752922.2.0000.5149). The study was conducted in accordance with the principles of the Declaration of Helsinki. Because this was a retrospective study based exclusively on the review of existing medical records, with no direct contact with participants or study-related interventions, the requirement for individual informed consent was waived by the Research Ethics Committee. All data were handled confidentially and analyzed in an anonymized manner.

Consent for publication

The final version of the manuscript has been reviewed and approved by all authors, who consented to the publication of the information described herein.

Competing interests

The authors declare no competing interests.

Data Availability declaration

The datasets generated and/or analyzed during the current study are not publicly available because they contain information that could compromise participant privacy and confidentiality. However, de-identified data may be made available by the corresponding author upon reasonable request and subject to approval by the Research Ethics Committee of the Federal University of Minas Gerais.

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Author Contribution declaration:

Study concept and design: HBF, EF and MWL and FMA.

Data collection: LBI, EF, AGD, YPY and IRE.

Data analysis and discussion: all authors.

Statistical analysis: HBF and YPY.

Drafting of the manuscript: HBF, LBI, AGD and MWL.

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