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EARLY CORRECTION OF POST-KIDNEY TRANSPLANT HYPERGLYCAEMIA IS ASSOCIATED WITH REDUCTION OF THE PREVALENCE OF POST-TRANSPLANT DIABETES MELLITUS

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Our study was focused on identification and correction of early hyperglycaemia, with the aim to reduce the risk of developing post-transplant diabetes mellitus (PTDM) and its associated complications. In a single centre, the prospective study included adult kidney transplant recipients without diabetes mellitus whose pre-transplant glucometabolic data did not show signs of diabetes mellitus. Starting from the first day after kidney transplantation, patients were closely monitored for hyperglycaemia; glucose level measurements were started to obtain pre-prandial levels. If the blood glucose level exceeded 11.1 mmol/l, hyperglycaemia was corrected with short-acting insulin. A total of 14 patients completed a three-month follow-up. During the first post-transplant week, the blood glucose level exceeded 11.1 mmol/l in nine patients (63.9%). From those patients five (55.5%) did not develop PTDM. None of the patients who did not need insulin treatment developed PTDM. Higher pre-lunch glucose levels increased the risk of developing PTDM (p = 0.006). Patients with diabetes required a two times higher insulin dosage than other patients during the first post-transplantation week. We found that hyperglycaemia is a common problem in the early post-transplant period. Early recognition and correction of inpatient hyperglycaemia was associated with reduction of the prevalence of PTDM in more than a half of the patients in the studied group at three months post transplant.

Key words: *kidney transplantation, hyperglycaemia – glucose level measurements post-transplant diabetes, early post-transplant hyperglycaemia.*

INTRODUCTION

Kidney transplantation is considered to be the therapy of choice for patients with an end-stage renal disease (ESRD) because of its ability to provide the maximum amount of replacement of renal function and a consequent improvement in patient morbidity and mortality (Palepu and Prasad, 2015). Development of post-transplant diabetes mellitus (PTDM) after kidney transplantation is a serious complication with a negative impact on graft function, patient and graft survival as well as patient quality of life and cost effectiveness of the transplantation process (Cosio *et al.,* 2002; Kasiske *et al.,* 2002; Woodward *et al.*, 2003; Cosio *et al.,* 2005; Ducloux *et al.,* 2005; Chakkera *et al.*, 2010).

Patients with PTDM develop acute rejection, infectious and cardiovascular complications, as well as the graft loss more often (Dirk *et al.,* 2008; Wojtuscizin *et al.,* 2013; Shivaswamy *et al.*, 2015). These numerous complications indicate the necessity to identify patients at high risk for developing PTDM and to modify risk factors to prevent patients from developing glucometabolic complications.

Approximately two-thirds of kidney transplant recipients with no previous history of diabetes experience inpatient

hyperglycaemia immediately after kidney transplant surgery (Chakkera *et al.,* 2010). Kidney transplant recipients are a group of patients that may benefit from targeted interventions to improve inpatient hyperglycaemia management (Chakkera *et al.,* 2009). It is not clearly known whether inpatient hyperglycaemia during the period after kidney transplantation is a transient problem that results from stresses associated with surgery, hospitalisation, and immunosuppression, and whether it poses a risk for future PTDM (Chakkera *et al.,* 2009). In our centre this problem has not been studied in depth before, therefore we have no data about the prevalence of inpatient hyperglycaemia and PTDM in our population. Our study was focused on identification and correction of early hyperglycaemia, with the aim to reduce the risk of developing PTDM and its associated complications.

MATERIALS AND METHODS

Study design and population. A single-centre prospective study was conducted. The study included all consecutive patients who underwent kidney transplantation from a living or deceased donor at the Latvian Transplantation Centre, starting from October 2018 to June 2019. None of the patients were known to be diabetic at the time of recruitment into the study. This means that all of the patients had levels of fasting blood glucose (FBG) < 7 mmol/l and glycated haemoglobin (HbA_{1c}) < 6.5% without the use of insulin or any other agents that lower the blood glucose level. Paediatric patients and patients with known diabetes mellitus before kidney transplantation were excluded from the study. Participants were informed of the aims of the study and informed consent was obtained from each participant before entry in the study. The study was approved by the local research ethics committee (No. 18/08.09.2018 /03.08.2018).

Patient data for a three-month follow-up period were analysed. The patients were divided into two groups according to their glucose metabolic status: patients who developed PTDM and those who did not.

Data collection and clinical definitions. Prior to kidney transplantation, information was collected on each patient's age, body mass index (BMI), cause of chronic kidney disease (CKD), modality of renal replacement therapy, time spent on dialysis, any previous transplantations, history of steroid use and family history of diabetes. Glucometabolic data was also collected, including FBG, pre-prandial blood glucose level, HbA_{1c}, homeostatic model assessment for insulin resistance (HOMA IR), and C peptide. After kidney transplantation, data was collected on graft function — creatinine, glomerular filtration rate (GFR) — and immunosuppressive drug level monitoring data were collected. All of the same laboratory parameters were collected at the time of discharge from the hospital and after three months. HOMA IR was calculated using glucose and insulin levels and its value > 2 was defined as insulin resistance. Graft function was calculated after the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Acute rejection was defined as sudden deterioration in graft function associated with certain immunopathological changes. All of the rejection episodes were verified with kidney biopsies.

Furthermore, beginning on the first day after kidney transplantation and continuing for the duration of the patient's hospital stay, pre-prandial blood glucose levels were assessed three times daily: in the morning (i.e. FBG), before lunch, and before dinner. Capillary blood glucose was measured with a glucose meter ACCU-CHEK® Inform (Roche Diagnostics).

Hyperglycaemia was considered when the FBG level was higher than 7 mmol/l or at least one pre-prandial blood glucose level was higher than 11.1 mmol/l during the first post-transplant week.

If the pre-prandial blood glucose level exceeded 11.1 mmol/l, the patient received short-acting insulin (NovoRapid®, Novo Nordisk) according to their blood glucose level. The blood glucose level was repeatedly measured two hours after insulin injection.

After discharge from the hospital, patients visited an outpatient clinic once per week for one month and then once per month thereafter. All laboratory parameters were recollected at the time of hospital discharge and again after three months follow-up. If patients showed levels of $HbA_{1C} \geq 6.5\%$, FBG ≥ 7 mmol/l, or pre-prandial glucose > 11.1 mmol/l, the patient was evaluated by an endocrinologist for PTDM. Patients diagnosed with PTDM received recommendations for lifestyle modification and, if necessary, medication.

Immunosuppression regimen. Induction immunosuppression was performed with anti-human T-lymphocyte immunoglobulin (ATG) from rabbits (Grafalon®; Neovii Biotech GmbH) 1.5 mg/kg for the first three to five post-transplant days in patients undergoing repeated transplantation or in patients who have experienced graft loss due to acute rejection, or 20 mg basiliximab (Simulect®; Novartis Pharma) on the transplantation day and on day four.

All patients received triple maintenance immunosuppressive therapy with a calcineurin inhibitor (CNI), mycophenolate mofetil (MMF) and corticosteroids. The initial maintenance immunosuppression consisted of methylprednisolone (SoluMedrol®; Pfizer) given intravenously for three days (500 mg, 250 mg, and 125 mg, respectively) starting from the day of the operation. Beginning from the first post-transplant day, patients received oral prednisone (Prednisolone®; Gedeon Richter) in a dose of 0.5 mg/kg per day. Dosages were gradually reduced such that the average after a month was 20 mg per day, and after three months, 15–10 mg per day. CNI and MMF were commenced on the first post-transplant day. Tacrolimus (Advagraf®; Astellas Pharma) was initiated at 0.15 mg/kg per day orally, with a whole blood concentration of 7–10 ng/ml during the first

three months. Mycophenolate mofetil (Cellcept®; Hoffmann- La Roche) was employed at an initial average dose of 2000 mg per day orally or reduced till 1000 mg per day if taken in combination with tacrolimus.

Statistical analysis. For statistical analysis, the IBM Statistical Package for the Social Sciences, version 21.0 (SPSS Inc., Chicago, Illinois, USA) was used. Descriptive statistics were used for demographical data. Patient characteristics were expressed as mean with standard deviation (SD) or by frequency and percentage. The Mann–Whitney *U*-test and Student's unpaired *t*-test or Chi-squared test were used for comparison as appropriate. A p-value of < 0.05 was used to determine significance.

RESULTS

Demographic data and baseline characteristics. A total of 23 patients underwent kidney transplantation at the Latvian Transplantation Centre between October 2018 and June 2019. Fourteen of these patients met the study inclusion criteria and had completed a three-month follow-up. After the three-month follow-up, four patients developed PTDM. All participants were Caucasians with a mean age of 44.79 ± 14.29 years. Patients who later developed PTDM were older. The two most common reasons among the participants were chronic tubulointerstitial nephritis (28.6%, n = 4) and chronic glomerulonephritis (21.4%, n = 3). Of the 14 participants, 12 (85.7%) had received their first transplantation, one (7.1%) a second, and one (7.1%) a third transplant. A total of 11 patients (78.6%) had received dialysis treatment before kidney transplantation, seven of which (63.6%) had peritoneal dialysis. Mean dialysis vintage was 16.21 ± 20.16 months. BMI was similar for both groups, with a mean BMI 22.6 ± 2.42 kg/m^2. In the group of patients who did not develop PTDM, there were two overweight and two underweight patients. For the majority of patients (78.6%) there was no positive family history for diabetes mellitus. No recipients had a history of hepatitis C virus infection. A comparison of patient characteristics between the groups is presented in Table 1.

Table 1. Baseline characteristics

Characteristics	No-PTDM (n = 10)	PTDM (n = 4)	*p*-value
Gender, male/female	6/4	1/3	0.23
Age, years	40.60 ± 13.50	55.25 ± 11.58	0.59
BMI, kg/m^2	22.72 ± 2.84	22.27 ± 0.95	0.11
Family history of diabetes	1, 10%	2, 50%	0.09
Number of transplantations:			0.05
First transplantation	10, 100%	2, 50%	
Second transplantation	0	1, 25%	
Third transplantation	0	1, 25%	
Living donor	6, 60%	0	0.04
Dialysis modality:			0.44
Pre-emptive transplantation	2,20%	1, 25%	
Prior haemodialysis	2,20%	2, 50%	
Prior peritoneal dialysis	6, 60%	1, 25%	

PTDM, post-transplant diabetes mellitus; BMI, body mass index

Table 2. Baseline glucometabolic data

Parameters	No-PTDM (n = 10)	PTDM (n = 4)	*p*-value
Pre-transplant fasting blood glucose, mmol/l	5.27 ± 0.94	4.95 ± 0.70	0.32
HbA1c, %	5.27 ± 0.51	5.55 ± 0.34	0.30
HOMA IR	2.82 ± 2.96	2.27 ± 1.25	0.50
C peptide	4.50 ± 2.47	4.58 ± 2.31	0.79

PTDM, post-transplant diabetes mellitus; HOMA IR, homeostatic model assessment for insulin resistance

Baseline glucometabolic data. Across all study participants, mean pre-transplant FBG was 5.18 ± 0.86 mmol/l. There was no significant difference in the pre-transplant FBG level between the PTDM and PTDM-free groups. All participants were diabetes-free prior to transplantation, but four participants (28.4%) had FBG > 6.0 mmol/l.

Across all study participants, the HbA_{1c} level ranged from 4.30% to 5.90%, with a mean value of 5.35 ± 0.47%. No difference in the HbA_{1c} level was observed between the study groups.

Pre-transplant HOMA-IR ranged from 0.75 to 10.99 in study participants, with a mean value of 2.66 ± 2.55. As with other glucometabolic parameters, baseline HOMA-IR did not differ between the study groups. In nine patients (63.9%), insulin resistance (i.e. HOMA-IR > 2) was observed already before transplantation. More information on baseline glucometabolic data is provided in Table 2.

Changes in glycaemia during the first post-transplant week. Average daily glucose levels were higher in patients who later developed PTDM, with a statistically significant difference in pre-lunch blood glucose levels ($p = 0.006$). For both patient groups, blood glucose levels were the highest in the evening. Five days after transplantation, there was a tendency for blood glucose levels to normalise. Patients were given the highest insulin doses after pre-lunch and pre-dinner blood glucose level measurement. Additional insulin doses were needed in patients who later developed PTDM. Daily glucose profiles and insulin doses are shown in detail in Figure 1.

During the first post-transplant week, the blood glucose level exceeded 11.1 mmol/l in nine patients (63.9%), necessitating the use of short-acting insulin. Two patients required morning insulin injections, five patients (35.5%) required pre-lunch insulin injections, and nine patients (63.9%) required pre-dinner insulin injections.

Glucometabolic data after a three-month follow-up. Of the nine patients who required insulin therapy during the first post-transplant week, five (55.5%) did not develop PTDM over the three-month follow-up and four (44.5%)

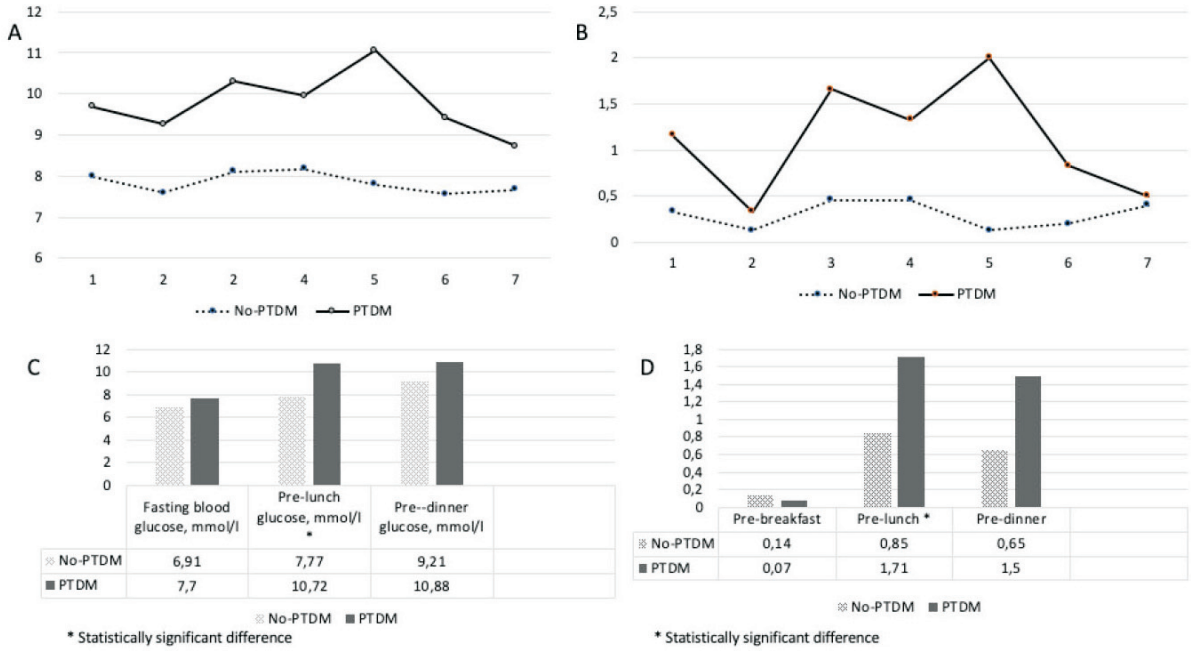

Fig. 1. **A.** Mean blood glucose level during the first postoperative week. **B.** Mean short-acting insulin doses used during the first post-operative week. **C.** Mean blood glucose level at three different time points showing pre-prandial glucose levels. Statistically significant difference was observed in blood glucose levels before lunch ($p = 0.006$). **D.** Mean short-acting insulin doses used at three different time points during the first post-transplant week. A statistically significant difference was observed in insulin doses used after pre-lunch blood glucose level measurements ($p = 0.002$).

were diagnosed with PTDM. All four PTDM patients required insulin injections during the first post-operative week, and none of the patients who were normoglycaemic during this week developed PTDM. Two of the PTDM patients were treated with an oral glucose-lowering agent (linagliptin), while the others initiated lifestyle modifications.

Schematic representation of the impact of glycaemia during the first post-transplant week of development of PTDM is presented in Figure 2. In 55.5% of patients who developed hyperglycaemia during the first post-transplant week PTDM was not observed after a three-month follow-up. None of normoglycaemic patients during the first post-transplant week developed PTDM three months later.

Across all study participants, mean FBG level after the three-month follow-up was 5.42 ± 2.13 mmol/l. The FBG level was statistically significantly higher in the PTDM group than in the PTDM-free group (7.18 ± 3.62 mmol/l vs. 4.73 ± 0.56 mmol/l, $p < 0.001$). In two participants, the FBG level exceeded 7 mmol/l. These were patients who used lifestyle modification as their only treatment for PTDM. One of those patients also had an HbA_{1C} level > 6.5%. This was the only case of HbA_{1c} level > 6.5% across all study participants; mean HbA_{1c} level was 5.55 ± 0.64%. Across all study participants, HOMA-IR rose to a mean value of 3.44 ± 2.96. Ten participants (71%) had a HOMA-IR value > 2, indicating insulin resistance. Comparison of glucometabolic parameters between PTDM and PTDM-free patients after the three-month follow up is shown in Table 3.

Development of PTDM was not correlated with factors such as age, sex, BMI, dialysis modality, pre-transplant glucose level, HbA_{1C} level, and HOMA-IR. In contrast, the following factors were associated with development of PTDM: number of transplantations ($p = 0.05$), type of donor ($p = 0.04$), and pre-lunch glucose level during the first post-transplant week ($p = 0.006$). A positive family history of diabetes trended toward an association with the development of PTDM ($p = 0.09$), as did receiving insulin therapy for early post-transplant hyperglycaemia correction ($p = 0.07$).

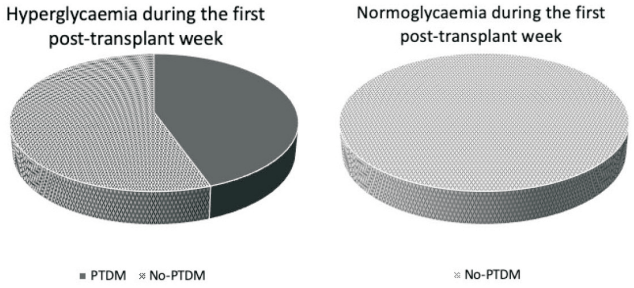

Fig. 2. Impact of glycaemia during the first post-transplant week of development of post-transplant diabetes mellitus.

Table 3. Comparison of glucometabolic data after three-month follow up

Parameters	No-PTDM (n = 10)	PTDM (n = 4)	*p*-value
Fasting blood glucose, mmol/l	4.73 ± 0.56	7.18 ± 3.62	0.001
HbA_{1c}, %	5.41 ± 0.53	5.55 ± 0.34	0.49
HOMA IR	3.72 ± 3.30	2.33 ± 1.25	0.14
C peptide	3.60 ± 3.11	2.72 ± 0.59	0.79

PTDM, post-transplant diabetes mellitus; HOMA IR, homeostatic model assessment for insulin resistance

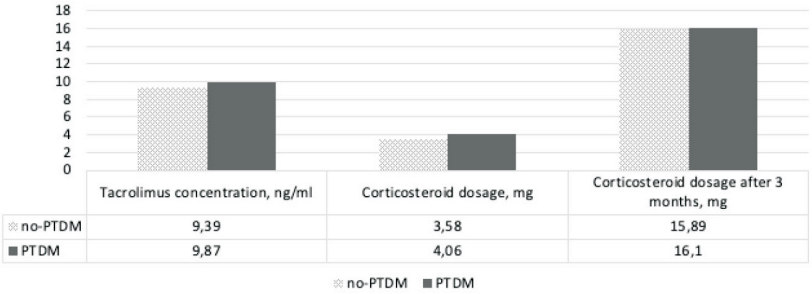

Fig. 3. Comparison of calcineurin inhibitor whole blood concentration and corticosteroid dosage.

Glycaemia and immunosuppressive regimen. Two patients (14.2%) received ATG as their induction immunosuppression, both of these patients developed hyperglycaemia and later PTDM, which was corrected with lifestyle modifications.

All patients received tacrolimus as their CNI and corticosteroids as described above. Comparison of CNI whole blood concentration and corticosteroid dosage is presented in Figure 3. Whole blood concentration of tacrolimus during the first three months was 9.52 ± 2.12 ng/ml and it did not differ significantly between patients with and without PTDM 9.87 ± 0.78 ng/ml vs. 9.39 ± 2.49 ng/ml ($p = 0.2$).

All the patients received corticosteroids as described above. Mean total steroid dose received in the hospital was 3.72 ± 0.15 mg/kg/per day. For patients who developed PTDM, the total steroid dose received in hospital was slightly higher, 4.06 ± 0.28 mg/kg/per day vs. 3.58 ± 0.61 mg/kg/per day, respectively, without a statistically significant difference. Mean dose of steroids received after three months was 16 ± 4.43 mg, without statistically significant difference between groups (15,89 mg in no-PTDM group and 16.1mg in PTDM group) ($p = 0.2$).

Glycaemia and graft function. After a three-month follow-up, all of the grafts were functioning with a mean GFR level of 56.28 ± 15.51ml/min. In the PTDM group, the GFR level was 45.75 ± 13.60 ml/min, in patients with no PTDM it was 60.50 ± 14.73 ml/min, $p = 0.14$.

One patient from the group with no PTDM developed acute humoral rejection due to discontinuation of immunosuppressive medication. No other complications were recorded.

DISCUSSION

Generally, PTDM develops in 10–20% of kidney transplant patients and in 20–40% of patients who have undergone transplantation of another solid organ (Jenssen *et al.,* 2019). Risk factors for PTDM can be divided into the two groups — modifiable and non-modifiable. Non-modifiable risk factors include age, ethnicity, male gender, family history of diabetes whereas modifiable risk factors include immunosuppression, rejection episodes, obesity, metabolic syndrome, and hepatitis C virus infection (Sharif and Cohney, 2016). It is not completely clear whether early post-operative hyperglycaemia is a transient problem or instead a risk factor for the development of PTDM (Chakkera *et al*., 2009).

The present study describes glycaemic profiles of kidney transplant recipients shortly after transplantation surgery, revealing hyperglycaemia as a common problem in the first week after transplantation. This is consistent with past studies (Cosio *et al*., 2005; Chakkera *et al.,* 2010; Rodrigo *et al*., 2011; Wojtuscizin *et al*., 2013; Shimada *et al*., 2019). Wojtusciszin *et al*. (2013) described post-transplantation glycaemic profiles in the first days following transplantation using continuous glucose monitoring. They found that 50% of transplant recipients had glucose levels > 11 mmol/l and 97% had glucose levels higher than 7 mmol/l immediately after the operation. They also reported that glycaemic status at the third month post-transplant appeared to be a good indicator for later development of PTDM (Wojtuscizin *et al*., 2013).

Other authors have also described early hyperglycaemia as an indicator for later PTDM. Cosio *et al.* (2005) found that hyperglycaemia at one-week post-transplantation was predictive of the development of diabetes at one year post-transplantation. Furthermore, Chakkera *et al.* (2010) reported that inpatient hyperglycaemia after kidney transplantation significantly increased the risk of PTDM. Rodrigo *et al.* (2011) found that a fifth day fasting blood glucose level > 126 mg/dl (7.0 mmol/l) increased the risk of PTDM by more than four times. In our study, higher pre-lunch glucose levels were associated with an increased the risk of developing PTDM.

During the follow-up, we observed that all the patients who developed PTDM experienced hyperglycaemia during the first post-operative week. Furthermore, they required larger and more frequent insulin doses than other patients. This result is consistent with Wojtuscizin *et al.* (2013) observation that early identification of hyperglycaemia in transplantation patients during the immediate post-operative period is important, not only to monitor and control hyperglycaemia, but also to predict PTDM (Cosio *et al*., 2005).

This research highlights the importance of not only recognising transplant patients at high risk for developing PTDM, but also identifies strategies that could help reduce the incidence of this complication. In our study, inpatient hyperglycaemia was managed with short-acting insulin, and promising results were observed. More than a half of patients who required correction of early hyperglycaemia did not go on to develop PTDM. This is consistent with previous studies

showing a benefit for early correction of hyperglycaemia. For example, Hecking *et al.* (2012) reported that an insulin regimen including basal insulin significantly reduced the risk of developing PTDM in post-transplant patients, presumably by insulin-mediated protection of pancreatic beta cells.

In our study, development of PTDM was not correlated with risk factors such as patient age, sex, BMI, pre-transplant glucose level, HbA_{1C} level, or HOMA-IR. Previous studies have reported BMI and steroid dosage as risk factors for PTDM. A study by Bonato *et al.* (2008) showed a relative risk of PTDM of 1.4 and 1.8 for patients with BMI between 25–30 kg/m^2 (i.e. overweight) and > 30 kg/m^2 (i.e. obese), respectively. Hjelmesaeth *et al.* (2001) reported that a rise in steroid dose by 0.01 mg/kg/day was associated with a 5% increased risk of developing PTDM. However, we did not observe an association between steroid dosage and the development of PTDM. Additionally, Gomes *et al.* (2018) demonstrated that higher pre-transplant FBG levels were predictive risk factors for PTDM.

We observed elevated HOMA-IR values in our study participants, indicating that insulin resistance could be one of the mechanisms involved in the development of PTDM. This is consistent with a previous study showing that insulin resistance and insulin secretion were significantly higher in kidney transplant recipients vs. healthy controls (Shimada *et al*., 2019). Beta cell dysfunction and insulin resistance have been identified as the main processes associated with development of PTDM (Sharif and Cohney, 2016).

Our study had some limitations that should be acknowledged. Firstly, the very low number of patients (n = 14) and PTDM events (n = 4), combined with a relatively short follow-up period, could have created biased results. This small sample size is the most likely why many of our analyses did not reach statistical significance. Secondly, our study included only white individuals and the development of PTDM could be different in other races. Furthermore, our study did not include any patients with hepatitis C infection, a known risk factor for PTDM.

This study emphasised the importance of careful glucose monitoring during the first week following kidney transplantation. We believe that further work should be done to assess the applicability of our findings to other, more diverse patient populations, and to compare our results with those from other transplant centres.

CONCLUSION

Our data indicate that hyperglycaemia is a common problem in the early post-transplant period and that a substantial number of patients require insulin therapy to manage this condition. Early recognition and correction of inpatient hyperglycaemia was associated with reduction of the prevalence of PTDM in the studied group by more than a half at three months post-transplant.

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AGRĪNA HIPERGLIKĒMIJAS KOREKCIJA PĒC NIERES TRANSPLANTĀCIJAS SAMAZINA PĒCTRANSPLANTĀCIJAS DIABĒTA ATTĪSTĪBU

Šī pētījuma mērķis bija samazināt pēctransplantācijas diabēta attīstības risku pacientiem pēc nieres transplantācijas, agrīni atklājot un koriģējot pēctransplantācijas hiperglikēmiju. Prospektīvā pētījumā iekļauti pilngadīgi Latvijas Transplantācijas centra nieres transplantācijas recipienti pacienti, kam nav zināma cukura diabēta diagnoze un kuru glikēmijas rādītāji īsi pirms nieres transplantācijas neliecina par cukura diabētu. Pirmajā dienā pēc nieres transplantācijas sākta glikēmijas kontrole trīs reizes dienā, pirms ēdienreizēm. Ja glikozes līmenis asinīs pārsniedza 11,1 mmol/l, pacientam tika veikta hiperglikēmijas korekcija ar īsas darbības insulīnu atbilstoši glikēmijas rādītājiem. Datu apkopošanas brīdī 14 pacienti bija piedalījušies pētījumā trīs mēnešus ilgi. Pirmajā pēctransplantācijas nedēļā glikozes līmenis asinīs pārsniedza 11,1 mmol/l deviņiem pacientiem jeb 63,9%. Pieciem no šiem pacientiem (55,5%) neattīstījās pēctransplantācijas diabēts. Nevienam no pacientiem, kuru glikēmijas rādītāji pirmajā nedēļā pēc transplantācijas nepārsniedza 11,1 mmol/l, neattīstījās pēctransplantācijas diabēts. Augstāks glikozes līmeņa rādītājs pirms pusdienām palielināja pēctransplantācijas diabēta attīstības risku (p = 0,006). Pacientiem, kuriem vēlāk attīstījās pēctranplantācijas diabēts, pirmajā pēctransplantācijas nedēļā bija nepieciešams divas reizes augstākas insulīna devas nekā pacientiem, kuriem diabēts neattīstījās. Hiperglikēmija ir bieži sastopama agrīnā pēctransplantācijas periodā. Agrīna hiperglikēmijas atklāšana un korekcija divas reizes samazina pēctransplantācijas diabēta prevalenci pētamajā populācijā trīs mēnešus periodā.