DOI: https://doi.org/10.53350/pjmhs2023173388

ORIGINAL ARTICLE

Prevalence of Early Hyperglycemia in Kidney Transplant Recipient in a Tertiary Care Hospitals in Pakistan

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ABSTRACT

Background: The prevalence of diabetes after renal transplant is higher than before renal transplantation. A significant proportion of transplant patients develop new-onset diabetes (NODAT), which accounts for 30-50% of all deaths in kidney transplant patients and is related with amplified mortality, mainly due to macroangiopathy. This study was conducted to determine the prevalence of early hyperglycemia in kidney transplant recipients for the enhanced pharmacologic management.

Study Setting: The current descriptive, cross-sectional study was carried out in the Department of Urology/ Nephrology, Pakistan Institute of Medical Sciences (PIMS), Islamabad and Islam Medical College/ Teaching Hospital, Sialkot. The duration of study was one year from October 2021 to September 2022.

Methods: A total of 67 patients who underwent renal transplant during the period in PIMS and at other center within the same vicinity and same protocol of management were enrolled in the study. All patients were followed and fasting blood sugar measurement was performed at bed side on day 5 post-transplantation by FDA and international organization for standardization (ISO) 15197-2003 certified Accu-chek device.

Results: A total of 67 patients were enrolled. The mean (± SD) age of patients was 34.5 (± 10.2) years. Out of 67 patients, 48 (72%) patients were males. Out of 67 patients, 19 (28%) patients had positive family history for DM. The mean (± SD) value of fasting blood sugar levels of all the enrolled patients was 129.3 (± 22.4) mg/dL. Out of 67 patients, 41 (61%) were diagnosed to have early hyperglycemia on 5th day after renal transplant. The comparison between the Early hyperglycemic and normoglycemic patients regarding their age, gender, BMI, pre-transplant lipid profile and family history of diabetes showed no statistically significant differences ($p>0.05$).

Conclusion: Study shows that out of 67 patients with post renal transplant, 41 (61%) had early hyperglycemia (fasting blood glucose levels ≥126 mg/dL) during their hospital stay. No statistically significant differences were seen in terms of traditional risk factor for diabetes like age, gender, BMI, lipid profile and family history for diabetes between patients who developed early hyperglycemia and those who did not.

Keywords: Renal transplant, hyperglycemia, Adult, end-stage renal disease.

INTRODUCTION

Diabetes is the important contributor of end-stage renal disease. Hyperglycemia may also occur as a complication after solid organ transplantation. Early hyperglycemia during the post-transplant hospital stay has been related with the progression of new onset post-transplant diabetes. In addition, a significantly increased risk of cardiovascular events was seen in subjects who established diabetes after transplantation. In kidney transplant recipients, it can develop as a result of surgery and the use of immunosuppressive drugs. The surgery stress and exposure to immunosuppressant can cause metabolic changes that may cause or exacerbate hyperglycemia. Insulin resistance, along with hypertension and hyperlipidemia, are already established factors in most patients undergoing kidney transplant surgery.

Hyperglycemia observed during hospitalization after kidney transplantation in non-diabetic patients is called early hyperglycemia. Persistence of hyperglycemia after hospitalization after kidney transplant surgery is called post-transplant diabetes. Early hyperglycemia has been related with the progression of newly diagnosed diabetes after transplantation. In addition, a substantial rise in the cardiovascular events risk was observed in patients who developed new diabetes after transplantation.

In the past, it was common practice among kidney transplant recipients to focus on diabetes management after discharge, rather than hospitalization. but the accent is currently being modified to effectively control early hyperglycemia during the patient's hospital stay. Early detection and effective treatment of hyperglycemia immediately after kidney transplantation may have clinically important implications for graft survival and long-term patient acceptability.

Newly diagnosed post-transplant diabetes may also rise the danger of graft loss and non-fatal macrovascular events. The spectrum of diabetic complications related with new-onset post-transplant diabetes (NODAT) is similar to that seen in type-2 diabetes, but complications appear to be much common. As in the overall people, even non-diabetic levels of hyperglycemia were related with augmented morbidity and mortality in renal transplant patients. Using the relevant renal transplant population, this study was conducted for the general purpose of describing the incidence of early hyperglycemia in renal transplant patients in order to determine the pharmacological management strategies for optimal glucose control.

MATERIAL AND METHODS

This descriptive, cross-sectional study was carried out in the Department of Urology/ Nephrology, Pakistan Institute of Medical Sciences (PIMS), Islamabad and Islam Medical College/ Teaching Hospital, Sialkot. The duration of study was one year from October 2021 to September 2022. A total of 67 patients who endured renal transplant and fulfilled the criteria of inclusion were included in the study. The sample size was estimated before the commencement of study using the WHO formula for calculation of sample size. The margin of error was assumed as 5%, confidence interval was selected as 90%, anticipated population proportion was chosen as 6.7(4) and the relative precision was assumed as 10%, the required sample size was 67 patients**.** A non-probability consecutive sampling technique was applied to select cases. Data was collected on the well-structured Proforma, especially designed for the current study. Informed written consent was taken pre-transplant.

The demographic characteristics of patients were asked and recorded pre-transplant. Patient fasting blood sugar level, anti-hyperglycemic if any and immunosuppressant record was taken on day 5 of post-renal transplant. Fasting blood sugar measurement

was performed at the bed side on day 5 post-transplant surgery by standardized glucose monitoring electronic device. The FDA and international organization for standardization (ISO) 15197-2003 certified Accu-chek device was used. Procedure involved a small drop of blood obtained by pricking the skin of fingertip with a small disposable lancet after the area is sterilized with cotton swab. The obtained blood was placed on a test-strip that the glucometer read and uses to calculate blood glucose level. All the data collection and study procedures were performed by the researcher himself to limit the selection bias and maintain the quality of data. All the information was recorded in a self-designed attached Proforma (annexure). The study outcome was judged in terms of incidence of hyperglycemia in the early period after kidney transplantation.

Data was entered and analyzed by using SPSS version 20 software. Data was analyzed and presented according to the type of the variable. In this regard, for contiguous variables, like age and laboratory findings, mean with S.D, range and median (maximum and minimum) were documented and calculated. On the other hand, for categorical variables, like gender, family history of diabetes and status of hyperglycemia, frequencies and percentages were calculated and reported. To compare the differences in terms of demographic characteristics between the patients who had post transplant hyperglycemia and those who did not, Student t-test for continuous variable like age and pre-transplant laboratory parameters, and Chi-square test for categorical variables like gender, family history of diabetes, age used. The level of significance was selected at 5% categories were ($p \leq 0.05$).

RESULTS

A total of 67 patients were enrolled. The mean (± SD) age of patients was 34.5 (± 10.2) years. Out of 67, majority of patients, 36 (54%), were age up to 35 years at the time of enrolment. Out of 67 patients, 48 (72%) patients were males.

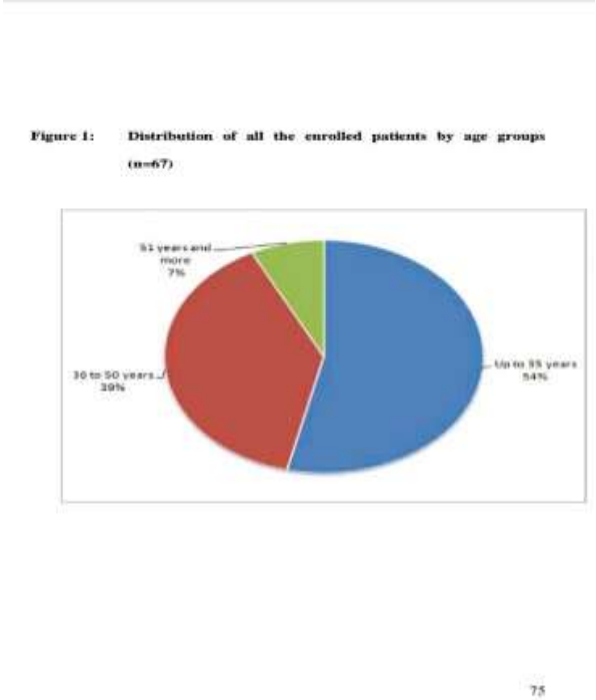

Figure 1: The mean (± SD) value of BMI of patients was 19.9 (± 3.9). Majority of patients, 32 (48%), had BMI between 18.5 and 25.

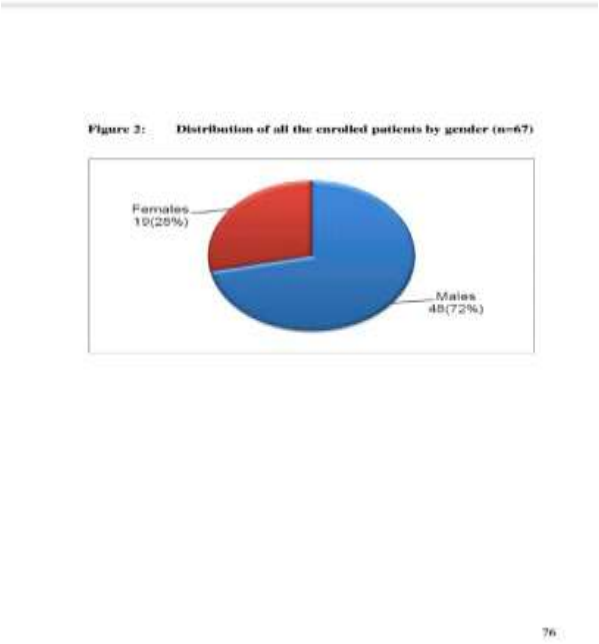

Figure 2: Out of 67 patients, 19 (28%) patients had positive family history for DM. The mean (± SD) serum total cholesterol levels was 141.3 (± 25.2) mg/dL, serum triglycerides levels was 140.3 (± 28.1) mg/dL, serum HDL levels was 33.2 (± 8.6) mg/dL, and serum LDL levels was 82.9 (± 15.0) mg/dL.

Table-1: shows the Lipid profile of patients

Values	Lipid profile			
	Total cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
Mean (±SD)	141.3 (±25.2)	140.3 (±28.1)	33.2 (±8.6)	82.9 (±15.0)
Median	143.0	141.0	33.5	83.5
Mode	145.0	136.0	39.0	82.0

The mean (± SD) value of fasting blood sugar levels of all the enrolled patients was 129.3 (± 22.4) mg/dL. Out of 67 patients, 41 (61%) were diagnosed to have early hyperglycemia on 5th day after renal transplant.

Table-2: shows the distribution of BMI, gender and association with hyperglycemic and normoglycemics

Variables	Hyperglycemic patients	Normoglycemic patients	p-value
	n=41 (%)	n=26 (%)	
Gender			
Males	28 (68%)	20 (77%)	0.443
Females	13 (32%)	6 (23%)	
BMI			
Mean (±SD)	20.3 (± 3.3)	19.9 (± 3.1)	0.622
Median	19.5	19.0	
BMI categories			
Less than 18.5	16 (39%)	10 (38%)	1.00
18.5-25	20 (49%)	12 (46%)	0.940
More than 25	5 (12%)	4 (15%)	0.752

The comparison between the Early hyperglycemic and normoglycemic patients regarding their age, gender, BMI, pre-transplant lipid profile and family history of diabetes showed no statistically significant differences (p>0.05).

Table-3: shows the patients BMI

Body mass index (BMI)	Number
Mean	19.9
Standard deviation	3.9
Median	20.0
Range (min - max)	(17- 32)

Table-4: shows the distribution of patients with reference to Lipid profile hyperglycemic and normoglycemics

Lipid profile	Hyperglycemic patients n=41	Normoglycemic patients n=26	p-value
Total cholesterol			
Mean (±SD)	142.5 (±29.2)	140.5 (±24.8)	0.773
Median	145.0	142.0	
Triglycerides			
Mean (±SD)	141.5 (±27.3)	139.8 (±21.5)	0.778
Median	143.0	140.0	
HDL			
Mean (±SD)	32.8 (±8.9)	34.7 (±6.3)	0.310
Median	31.8	35.0	
LDL			
Mean (±SD)	84.5 (±25.4)	80.8 (±22.4)	0.791
Median	85.8	81.0	

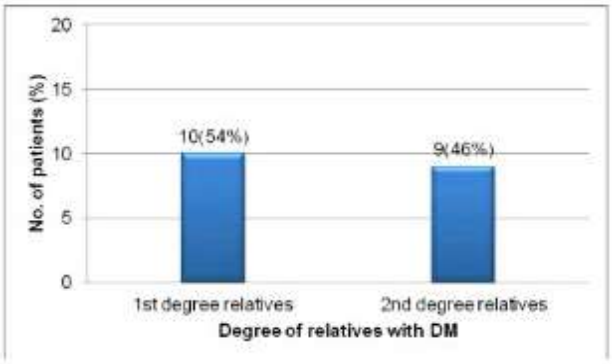

Figure-3: shows the positive family history of patients with DM

DISCUSSION

Advances in the immunotherapeutic regimen over the past two decades, coupled with improved recipient outcomes, have resulted in a shift from chronic allograft failure to patient death as the important cause of long-term graft rejection. Death after a functional renal transplant is often caused by cardiovascular disease, which is considered a common and dangerous disease. However, other metabolic disorders, such as obesity, dyslipidemia, and incipient diabetes, are increasingly recognized as a major post-transplant complication and contribute significantly to unsatisfactory recipient outcomes. Early hyperglycemia is usually seen postoperatively, immediately after the patient discharged. Insulin resistance, along with hypertension and hyperlipidemia, is already an established factor in most patients undergoing kidney transplant surgery. Recipients already predisposed to glucose dysregulation present as transplant-related hyperglycemia when exposed to transplant-specific factors such as stress and medication, often a modifiable diabetes exposure.

Given the importance of better management of early hyperglycemia, a wide range of prevalence rates, ranging from 6.7% to 87%, have been documented in various research sources. In the United States, Chakkera and colleagues held a retrospective study to determine the early hyperglycemia prevalence among renal transplant patients. The mean hospital stay duration was 4.6 ± 2.2 days. Of the 424 patients, 105 (25%) had pre-transplant diabetes and 319 had normal glucose levels. The mean (±SD) age of the participants at the transplantation time was 51 years (±9). During the hospital stay, 125 pre-transplant diabetic patients developed early hyperglycemia, while 278 (87%) of the 319-pre-transplant normal-glucose patients developed post-transplant early hyperglycemia. Hyperglycemia persisted throughout the hospital stay, and 66% required insulin at discharge. In contrast to traditional risk factors for diabetes, factors such as transplant age, gender, pre-transplant BMI, and ethnicity were not significantly related with the incidence of early hyperglycemia, which is comparable to the results of our study.

F. Maldonado et al. performed a retrospective review of all initial kidney transplants without a personal history of diabetes (DM) and 6-month follow-up to gather data on the epidemiology and risk factors of post-transplant diabetes mellitus (PTDM). There were 163 patients in all, 57.6% of whom were men, 66% of whom received organs from cadavers, and 12% of whom had first-stage diabetes mellitus in their families. The transplant recipients were 39 years old on average. 55/92 (59%) individuals had early hyperglycemia, and 15 (27%) of these patients went on to develop PTDM. In patients with PTDM, early hyperglycemia occurred 87% of the time, as opposed to 54% of patients without this condition. They established risk factors for the emergence of PTDM, such as early hyperglycemia, and validated the significant prevalence of PTDM.

In 2003, Woodword et al. and Kasiske et al. conducted two larger US epidemiological studies to determine the prevalence of hyperglycemia among kidney transplant patients in the USA. Woodword et al. and Kasiske et al. used US Renal Data System data on Medicare beneficiaries for 1994-1998 and 1996-2000, respectively. Woodword et al. found the incidence of hyperglycemia to be 18% in kidney transplant patients in the first two years after renal transplant. Kasiske et al. were found to be 9.1%, 16% and 24% correspondingly at 3, 12 and 36 months after kidney transplantation.

Concerning our study findings of significantly lower BMI and lipid profile, Altaf A and colleagues conducted a study in 2007 to assess lipid dysfunction in maintenance hemodialysis patients in a nephrology department in Pakistan. There were 140 total participants, including 70 maintenance hemodialysis (MHD) patients and 70 healthy controls. BMI was calculated in accordance with WHO recommendations. The following measurements were examined and calculated: TC, TG, HDL-C and LDL cholesterol. Patients with HDL had a mean BMI (SD) of 20.07 (3.66), which was considerably lower than the 22.88 (3.97) kg/m2 in the control group (p 0.001). Comparable outcomes were seen for lipid profiles, which were lesser than in the control group. Among MHD patients, the average lipid profile was as follows: (a) total cholesterol 3.84 mmol/L, LDL-C 2.21 mmol/L, HDL-C 0.95 mmol/L, no HDL-C 2.88 mmol/L, and triglycerides 1.68 mmol/l. Patients on hemodialysis in Pakistan had significantly lower BMIs, total cholesterol, LDL cholesterol, and non-HDL cholesterol than the general population, which is an indication of malnutrition, which can cause inflammation, speed up the atherosclerotic process, and cause cardiovascular issues. The outcomes match those of our investigation.

The best course of action for end-stage renal illness is a kidney transplant. However, the presence of hyperglycemia following kidney transplantation lessens the benefits of the transplant by lowering the patient's and allograft's survival and quality of life. Early hyperglycemia was substantially linked to the

onset of new diabetes following transplantation, according to research sources. However, the aetiology of acute hyperglycemia in this population has not been explored and most definitely warrants inquiry. The frequency of early hyperglycemia and high insulin needs are probably caused by a combination of stress and medications. One of the most serious side effects of allogeneic vascular transplantation is diabetes. Patients with this condition are at risk of developing numerous secondary complications. Chronic hyperglycemia leads to vascular changes that significantly reduce graft and patient survival: 3-year graft survival 71% versus 86% in patients without DM, 2-year patient survival 67% versus 83% in both groups, respectively. reaches. This is due to the 5-fold difference in the incidence of cardiovascular complications in diabetic patients compared to the non-diabetic group. Data from some studies have also shown that severe infections may shorten the survival of patients.

Given the high incidence of early hyperglycemia after kidney transplantation, its early detection may allow for a useful intervention that could minimize the further development of newly diagnosed diabetes in adult populations. In this context, as others have suggested, appropriate monitoring and treatment of hyperglycemia immediately after transplantation can significantly improve patient and graft survival. On the other hand, the fasting glucose level on the fifth day after transplantation may be a useful, early and simple test to detect patients at risk of developing diabetes within one year after transplantation.

CONCLUSION

In summary, our study shows that 41 (61%) of 67 kidney transplant patients had early hyperglycemia (hypoglycemic medication or fasting blood glucose ≥126 mg/dL) on day 5 of hospitalization. The mean fasting blood glucose on day 5 in transplant patients was 129 mg/dl. The diabetes risk factors as age, gender, BMI, pre-transplant lipid profile, and family history of diabetes did not statistically differ between patients with and without early hyperglycemia. It has been found that a significant proportion of our patients are malnourished prior to transplantation, and if prevented by low BMI, cholesterol and HDL values, cardiovascular complications will be positively affected. Early detection and intensive treatment of early hyperglycemia in kidney transplant patients can significantly limit the development of NODAT in our population and contribute to long-term patient and transplant survival. However, a nationwide large-sample multicenter observational study is needed to determine the true incidence of post-transplant hyperglycemia in kidney transplant patients in Pakistan.

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