

Practice evaluation of diabetes management in solid organ transplant recipients in resource-constraint country

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ABSTRACT

Objective: Post Transplant Diabetes Mellitus (PTDM) is a major concern affecting 10 to 40 percent of solid organ transplant (SOT) recipients. The objective of this audit was to check the compliance of current Diabetes management in SOT recipients at our centre with standards recommended by British Transplant Society (BTS), The Renal Association and Association of British Clinical Diabetologist (ABCD). The secondary objective of this audit was to identify areas of improvement, and make it a quality improvement project.

Methodology: The audit was conducted in a quaternary care Hospital in Lahore. The questionnaire was prepared as per BTS/ABCD recommendations. Retrospective and real time data of total 52 post Living donor Liver transplant (LDLT) and Live related Renal transplant (LRRT) recipients who were admitted or presented to Diabetes OPD was collected using direct interviews, review of confidential files, electronic notes and at times via telephonic conversation with patients.

Results: Total 52 post (SOT) recipients with 56% post liver, 40% post kidney and 4% combined Liver and Kidney Transplants were audited. The total number of patients who had diabetes pre- Transplant were 32.7% (17/52), patients with family history of Diabetes were 21.6% (11/52) and 57.7% (30/52) of patients were HCV positive. About 52% (27/52) of patients were informed about the risk of PTDM. Only 17.6% (3/17) patients who were diabetic prior to Transplant were seen in Diabetes specialist clinic pre-Transplant. A total 56% (23/52) of admitted transplant recipients achieved Target Blood sugars of 198 mg/dl (11 mmol/L) or less. Diabetes specialists reviewed 26.9% (14/52) of SOT recipients during their inpatient stay. Post discharge, 61.5% of patients checked afternoon capillary blood glucose at home and 57% (30/52) of patients had their Blood sugar levels checked in OPD. About 41.8% (18/43) of patients with high blood sugars followed up in Diabetes specialist clinic post-Transplant. Recipients who received structured Diabetic education were 43.1% (22/52). Only 5.7% (3/52) of patients started on Metformin if GFR was >30. Blood pressure control of <130/80 mm of Hg was achieved in 90% (47/52) of patients. Amongst Diabetics pre-transplant, 48% (8/17) were on statins. Compliance to Oral hypoglycemics/ Insulin was seen in 90% of SOT recipients.

Conclusion: We conclude that greater involvement of the Diabetes team and patient education is required for optimum diabetes control that can improve post-Transplant survival, prevent both immediate and long-term complications and health care costs associated with management of these complications.

KEY WORDS: Post-Transplant Diabetes Mellitus (PTDM), Solid organ Transplant (SOT), Resource constraint, British Transplant Society (BTS).

INTRODUCTION

According to the International Diabetes Federation (IDF), as of 2022, 26% of the adult population in

Pakistan suffer from Diabetes.¹ Diabetes is one of the leading causes of End stage renal disease (ESRD) and

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is also a well-recognized risk factor for Nonalcoholic steatohepatitis (NASH) related cirrhosis. Hepatitis C virus (HCV), one of the most common causes of liver disease in Pakistan, is associated with 2-3 times increased risk of both Type 2 Diabetes and Post Transplant Diabetes Mellitus (PTDM).² Nevertheless (PTDM) is another consequence occurring in 10-40% of Solid organ Transplant (SOT) recipients.³

Patients presenting to Kidney and Liver transplant centres generally have underlying Diabetes or are at risk of developing Diabetes post-Transplant, due to corticosteroids and Calcineurin inhibitor-based immunosuppression.⁴ Hyperglycemia post SOT has a significant adverse impact on outcomes post solid organ transplantation.⁵ By increasing longevity of life post SOT, we are faced with challenges of managing long term complications of Diabetes and its related health care costs. It is important to recognize these facts and steps should be taken to prevent, detect and manage Diabetes and Post Transplant Diabetes. British Transplant Society (BTS) and Association of British clinical Diabetologist (ABCD) gave recommendations about detection, management, and Prevention of Diabetes post solid organ transplant.

Limited data regarding diabetes management in PTDM is available from Pakistan therefore we conducted this audit in a quaternary care hospital, Pakistan Kidney and Liver Institute and Research Centre (PKLI & RC). The primary objective of this audit was to check the compliance of current Diabetes practice at our centre with standards recommended by BTS/ ABCD. The secondary objective of this audit was to identify areas of improvement, reasons for non-compliance and make it a quality improvement project.

METHODS

A total of 52 post Living donor Liver Transplant (LDLT) and Post Live Related Renal Transplant (LRRT) recipients over the age of 18 years, who were admitted or presented to Diabetes/ Internal Medicine OPD during the month of November 2022 were included in this audit. Questionnaire was prepared as per British

Transplant Society recommendations. Retrospective and real time data was collected using direct interviews of patients, confidential files, electronic notes and at times via telephonic conversation with patients.

RESULTS

A total of 52 patients of which 80.8% (40) were males and 19.2% (10) females were included in the study. Out of 52 patients, 55.8% (30) were LDLT, 40.4% (20) were LRRT and 3.8% (2) were combined Liver and kidney transplant recipients. The total number of patients who had diabetes pre- Transplant was 17/52 (32.7%), of which only 17.6% (3/17) patients were referred to Diabetes specialist/ Internal Medicine clinic pre-Transplant. Patients who had family history of Diabetes were 21.6% (11/52). There were 57.7% (30/52) patients who were HCV positive (Table-I).

About 52% (27/52) of patients were informed about the risk and impact of developing Post Transplant Diabetes (Table-II). A total of 56% (23/52) admitted transplant recipients achieved Target Blood sugars of 198 mg/dl (11 mmol/L) or less (Fig.1). Fifty percent 50% (26/52) of patients required Insulin administration during their hospital inpatient stay. Diabetologists/ Internal Medicine specialists reviewed 26.9% (14/52) of recipients during their inpatient stay.

After discharge from hospital, 61.5% of patients checked afternoon capillary blood glucose. During their post-Transplant OPD visits, 57% (30/52) of patients had their Blood sugar levels checked in OPD. Out of those SOT recipients who were either previously known diabetics, those with hyperglycemia during post-Transplant hospital stay and those who required Insulin during inpatient stay for glycemic control, 41.8% (18/43) followed up in Diabetes OPD. Recipients who reported to have received structured Diabetic education were 43.1% (22/52). Only 5.7% (3/52) of patients started on Metformin if GFR was >30. Blood pressure control of <130/80 mm of Hg was achieved in 90% (47/52) of patients. Statins are recommended to be prescribed to all diabetics and patients with PTDM, but we noticed that only 48% (8/17) of known diabetic

Table-I: Baseline Characteristics of study participants.

CHARACTERISTICS	COUNT	PERCENTAGE
Male	40/52	80.8%
Female	10/52	19.2%
Post-LDLT	30/52	55.8%
Post-LRRT	20/52	40.4%
Combined LDLT+LRRT	2/52	3.8%
Family History of Diabetes	11/52	21.6%
DM Pre-SOT	17/52	32.7%
Pre-transplant diabetics referred to Diabetes clinic	3/17	17.6%
HCV positive	30/52	57.7%

Table-II: Compliance related to diabetes management in study participants as per international recommendations.

FEATURES	COUNT	PERCENTAGES
Informed risk of PTDM	27/52	52%
Structured diabetic education received	22/52	43.1%
Checked afternoon capillary glucose	32/52	61.5%
BSL check in OPD appointment	30/52	57%
Insulin required during Inpatient	26/52	50%
Diabetic team inpatient review post-SOT	14/52	26.9%
DM clinic referral post Tx of Patients with DM Hx-(n=17) or with Inpatient RBS > 198 + those who were given inpatient insulin-(n=26)	18/43	41.8%
Patients started on Metformin (If GFR>30)	3/52	5.7%
BP control <130/80mm of Hg achieved	47/52	90.4%
Known Diabetics on Statins	8/17	48%
Compliance to OHG/Insulin	23/26	88.5%

patients were on statins. Eighty eight % (23/26) patients showed compliance to Oral hypoglycemics/ Insulin (Table-II). OGTT to diagnose new onset Diabetes post SOT was not routinely performed but all patients had frequent fasting plasma glucose check as follow ups.

DISCUSSION

Our audit shows that the management of diabetes in pre and post Solid organ Transplant (SOT) recipients needs improvement and is not as per international guidelines. Adequate glycemic control peri and post Solid organ transplantation is important to prevent short- and long-term complications in recipients.⁶ To avoid these complications, the Centre for Peri-operative care guidelines recommend HbA1c less than 8.5% prior to Elective surgeries.⁷ Early recognition and management of risk factors for post-transplant diabetes as well as optimization of blood sugars pre

and post SOT can result in better Transplant survival, reduce post-Transplant complications, and save the cost required to treat these complications.

We conducted this audit to standardize care of diabetes in pre and post SOT recipients. This is the first diabetes mellitus audit done in our hospital.

The risk of development of Diabetes should be assessed as a part of pre-transplant work up for all patients being considered for transplant. Once the risks have been identified Multidisciplinary team including dietician, Diabetic nurse and diabetes specialist involvement should be considered for holistic management of potential Transplant recipient. Increasing age, family history of diabetes, High BMI (>30kg/m²) and pre-existing Diabetes are the risk factors for dysregulation of blood sugars pre and post SOT. These patients should be educated about the risk of developing PTDM and how to modify the modifiable factors. They should be advised about minimizing weight gain using lifestyle measures and should see a dietitian with expertise in this area.⁸ Treatment of risk factors for PTDM such as hepatitis C should be considered in patients awaiting transplantation.⁸

While awaiting transplant, all patients should be screened yearly for Diabetes using Fasting Plasma glucose +/- HbA1c. High-risk patients should then have Oral Glucose Tolerance Test (OGTT) to confirm the diagnosis of Diabetes or screen for impaired glucose tolerance. We noticed in our audit that not all transplant recipients were aware of the risks and impact of inadequate blood sugar control post-transplant. High-risk patients and patients with pre-existing diabetes prior to transplant were not streamlined to Multidisciplinary team involvement for further work up and management.

Only 27% of admitted patients were seen by a diabetes specialist and 56% of admitted patients achieved target blood sugars indicating that greater involvement of the diabetes specialist team is required

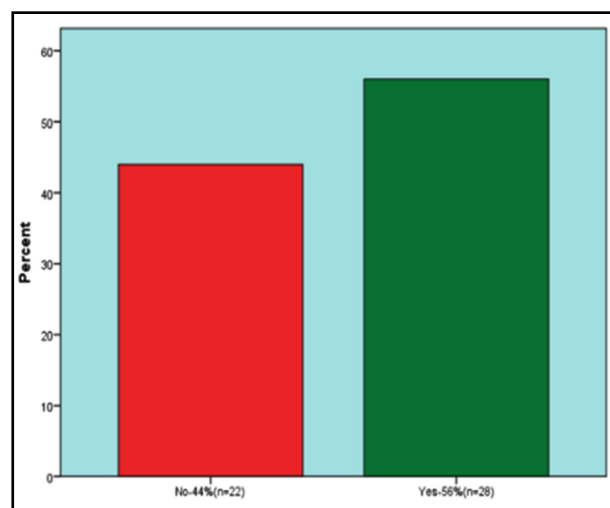


Fig.1: Percentage of patients who achieved target blood sugars immediately post SOT.

to optimize sugar control. British Transplant Society (BTS) and Association of British Clinical Diabetologist (ABCD) recommend that immediate post-transplant, early post-operative hyperglycemia (glucose >11 mmol/L (198mg/dl) on more than two occasions in 24 hours should be actively monitored and treated.⁹

Overall, 61.5% of patients checked evening BSL and 57% of patients had their capillary blood glucose checked in OPD. The optimum screening method for postoperative hyperglycemia is the use of afternoon capillary blood glucose (CBG) measurements. This is because the use of steroids and immunosuppression (especially calcineurium inhibitors such as tacrolimus) often leads to postprandial hyperglycemia, and such patients may quite frequently have normal fasting glucose levels.¹⁰

Only 41.8% of patients who were previously known diabetic and those who had high blood sugars post solid organ transplant were followed up in Diabetes clinic. Such patients need input from the multidisciplinary teams, including diabetes nurses and dietitians, to help improve lifestyle, learn insulin administration and glucose testing. Not only do these patients require glycemic control, but they also need cardiovascular risk assessment and management. Most transplant patients are seen weekly following discharge, and glucose levels should be regularly reviewed. As immunosuppression doses are reduced, hyperglycemia may improve, and clinicians may need to reduce therapy to prevent hypoglycemia. These patients also need regular screening of eyes, feet, kidneys, blood pressure, weight, smoking status, lipid check and management of cardiovascular risk factors. Glycemic targets should be individualized according to patient's preference and co-morbidities.

At six weeks post transplantation, Oral glucose tolerance test (OGTT) is the gold standard to diagnose PTDM if practically feasible. In stable patients combining the results from abnormal fasting plasma glucose (FPG) ≥ 7 mmol/L and/or HbA1c $> 6.5\%$ detects majority of PTDM cases.¹¹ In our audit, we noticed that OGTT was not routinely done on follow up, but patients had frequent fasting plasma glucose check when monitoring for tacrolimus levels. Checking HbA1c at 3 months will be an additional diagnostic tool to confirm PTDM.

Very few patients included in our audit were on oral hypoglycemics prior to solid organ transplant due to end stage renal disease and decompensated liver disease. Post transplant there was also reluctance in switching from Insulin to Oral hypoglycemics. BTS/ ABCD recommend oral hypoglycemics such as Metformin (if eGFR > 30 mL/min/1.73 m²), DPP-4 inhibitors, GLP-1 receptor agonists and insulin can all be used safely post-transplantation.^{12,13} Metformin has been recommended as the first line due to its low cost, efficacy, anti-obesity, anti-inflammatory and anti-neoplastic properties. Although SGLT2 inhibitors are cardio and reno-protective but Specialist advice should be sought when considering SGLT2 inhibitors due to the risk of genitourinary tract infections.

Dyslipidaemia is common amongst patients undergoing transplantation. KDIGO guidelines also recommend statin therapy for all renal transplant recipients aiming LDL cholesterol < 100 mg/dL.^{14,15} Hypertension is common after SOT and if uncontrolled can result in adverse graft outcomes. BTS/ ABCD recommend blood pressure control of $< 130/80$ mm of Hg in all patients with PTDM. KDIGO guidelines also recommend BP of $< 130/80$ mm of Hg for all patients with renal allografts and similar blood pressure control is recommended for patients with diabetic nephropathy. Optimum Blood pressure control and compliance with medications by patients included in our audit showed encouraging results. Less than 50% of our patients reported having structured diabetic education indicating the need for greater involvement of dietitians, diabetes specialists and diabetic nurses.^{16,17}

As per IDF, 1 in 4 adults in Pakistan suffer from Diabetes.¹ There is estimated to be one endocrinologist for every 200,000 diabetic patients in Pakistan. Health budget of Pakistan is 2.8 percent of gross domestic product (GDP) as compared to 9 to 18 percent of GDP in developed countries. Management of chronic conditions like Diabetes and its complications require multidisciplinary team involvement and frequent visits to health care providers. In a resource constraint country like Pakistan, management of such conditions becomes challenging especially when a lot of cost is being paid for a costly definitive transplant procedure. Though management of chronic conditions requires a handsome budget, adequate management prevents complications and health care cost associated with treatment of these complications. The health ministry should recognize this situation and attempts should be made to provide easy and affordable access to health care providers especially for diabetic patients planned for precious solid organ transplantation.

CONCLUSION

The results of our audit indicate that greater involvement of the Diabetes team and patient education is required for optimum management of pre-existing diabetes or PTDM in SOT recipients which will result in better post-Transplant survival, prevent both immediate and long-term complications, and save the health care costs associated with management of these complications.

Recommendations:

All diabetic patients and high-risk patients (positive family history of diabetes, high BMI and HCV positive) awaiting SOT should be referred to Diabetes clinic pre and post-Transplant to optimize blood sugar control and maintain adequate weight. These patients should get structured diabetic education including diabetes specialist review, dietician, and diabetes nurse involvement. After solid organ transplant, the Diabetes team should be involved closely to manage immediate and early postoperative hyperglycemia. At discharge,

all patients, even if not known to be diabetic must be advised to check afternoon capillary blood glucose. These patients need close monitoring and formal testing for PTDM once they are clinically stable. Arrangements should be made to check capillary blood sugars along with other vital signs during all outpatient visits. All diabetics and patients with new onset deranged blood sugars post SOT must be referred to the Diabetes clinic for complete evaluation including cardiovascular risk assessments. Efforts should be made to provide patient information leaflets written in the patient's own language about prevention and management of PTDM and Diabetes.

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Author Contribution:

Author's contribution and accountability for integrity of work: All authors were involved in audit design, collection of data, interpretation of results and drafting the report.