Research Article

Screening for Diabetes after Solid Organ Transplantation: A 10-Year Retrospective Study

Ridwan B. Ibrahim[1, 2], Sneha Kumar[1], Sahil Malik[1,2], Joseph A. Spinner[3], Daniel H. Leung[4], Sridevi Devaraj[1, 2*]

[1]*Department of Pathology and Immunology, Baylor College of Medicine, Houston, TX, USA*
[2]*Department of Pathology, Texas Children's Hospital, Houston, TX, USA*
[3]*Department of Pediatrics-Cardiology, Baylor College of Medicine, Houston, TX, USA*
[4]*Department of Pediatrics, Baylor College of Medicine and Division of Gastroenterology, Hepatology and Nutrition, Texas Children's Hospital, Houston, TX USA*

Article Info

[*]***Corresponding Author:***
Sridevi Devaraj, Ph.D., DABCC, FADLM, FRSC
Department of Pathology and Immunology
Baylor College of Medicine, Texas Children's Hospital
6621 Fannin Street, Houston, TX 77030
E-mail: sxdevara@texaschildrens.org

Keywords

Post-transplant diabetes mellitus, Immunosuppression, Solid organ transplant

Abstract

Post-transplantation diabetes mellitus (PTDM) is a common and important complication after solid organ transplantation, affecting long-term outcomes. Graft rejection, decreased patient survival, infections and increased cardiovascular risk are associated with PTDM and may arise from both transplant-related and traditional risk factors. Early screening for PTDM is crucial for early detection and management. Despite clinical guidelines recommending regular screening for PTDM, screening rates remain suboptimal. This retrospective study analyzes PTDM screening rates between January 2014-January 2024 among pediatric kidney, liver, heart and lung transplant recipients at a large quaternary academic pediatric transplant center. PTDM screening rates vary by organ type, with kidney transplant patients at 19.4%, liver transplant patients at 14.6%, heart transplant patients at 34.3% and lung transplant patients at 91.7%. These lower-than-expected rates of PTDM screening among high risk pediatric- kidney, liver and heart transplant pediatric population highlight the need for improved screening protocols and provider education post-transplantation.

Introduction

Post-transplantation diabetes mellitus (PTDM), first described in kidney transplant recipients in 1964, remains a leading complication after solid organ transplantation [1,2]. In 2014, an International Expert Panel of clinicians/researchers recommended expansion of the PTDM screening tests to include hemoglobin A1c levels since the American Diabetes Association (ADA) has incorporated hemoglobin A1c (>6.5%) as a diagnostic criterion for diabetes mellitus in the general population although the gold standard for diagnosing PTDM still remains OGTT [3,4]. However, caution must be exercised not to use A1c testing too soon after transplantation (within 45 days after transplantation) as a normal HbA1c does not rule of the presence of post-transplantation anemia and/or dynamic renal allograft function [5]. Although this transient post-transplant hyperglycemia (within 45 days after transplantation) is an important risk factor for subsequent PTDM, it should be excluded from PTDM diagnosis as this is exceptionally common in early transplant period due to high steroid and tacrolimus exposures [6,8]. PTDM should be screened for in clinically stable patients >45 days after transplantation [4]. Different factors have led to variations in the reported incidence for PTDM [1].; it has been reported in 2.5-25% of liver transplant recipients, 4-25% in kidney transplant recipients, 30-35% in lung transplant and 4-40% in heart transplant recipients [9-13]. Early detection of PTDM is critical to reduce the risks and complications of diabetes mellitus, with post-transplant follow-up of patients with transient HbA1c levels >5.7-6.4% or higher at 3, 6, 9 and 12 months, followed by annual screening thereafter [1, 14-16].

In this study, we performed a 10-year retrospective cohort study to assess the frequency of PTDM screening in our large quaternary academic pediatric transplant medical center following publication of the 2014 guideline [4].

Methods

Patient Population

This single center, retrospective cohort study included patients who received a solid organ transplant (liver, kidney, heart and lung) at the Texas Children's Hospital between January 2014 and January 2024. Patient characteristics are summarized in Table 1 which shows similar representation of male and females.

Table 1: Sociodemographic characteristics of solid organ recipients at Texas Children's Hospital (TCH) between 2014-2024.

Variable	Total
	N (%)
Liver Transplant recipient	336 (100)
Mean age at transplant (years)	6.51
Male	167 (49.7)
Female	169 (50.3)
Heart Transplant recipient	268 (100)
Mean age at transplant (years)	8
Male	152 (56.7)
Female	116 (43.3)
Lung transplant recipient	96 (100)
Mean age at transplant (years)	10.43
Male	43 (44.8)
Female	53 (55.2)
Kidney transplant recipient	284 (100)
Mean age at transplant (years)	13.11
Male	167 (58.8)
Female	117 (41.2)

The primary outcome was screening rates of PTDM within the first-year post-transplantation, as recommended by international guidelines [4]. Screening adherence was defined as having ≥ 1 fasting glucose test or HbA1c test within the first year following transplantation. Test orders from 46 days post-transplantation were assessed to diagnose PTDM in this study. Adherence rate was calculated and described for each organ group.

Results

Over the 10-year period, 984 solid organ transplantations were performed: 336 liver transplants, 268 heart transplants, 96 lung transplants and 284 kidney transplants (Table 2).

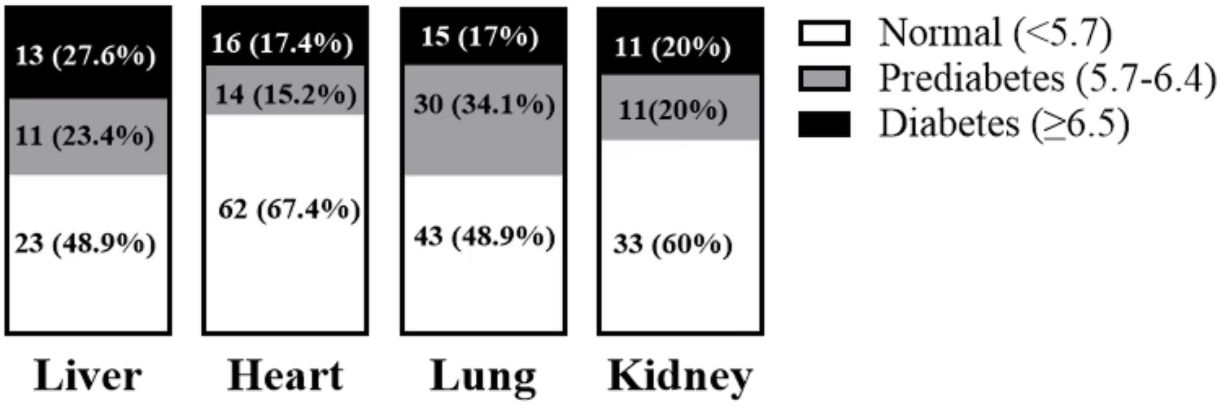
Table 2: Ten-years PTDM screening compliance data in solid organ recipient patients.

Organ Transplant	Liver	Heart	Lung	Kidney
Number of Recipients	336	268	96	284
Post-transplant OGTT test (≥45-365 days)				
Total number of tests ordered	0	0	0	0
Post-transplant HbA1c test (≥45-365 days)				
Total number of tests ordered	49	92	88	55
Percentage test ordering compliance	14.6	34.3	91.7	19.4
Total number of tests completed	47	92	88	55

Of these recipients, none had OGTT test orders ≥45 days but 14.6% (n=49), 34.3% (n=92), 91.7% (n=88) and 19.4% (n=55) of recipients have HbA1c orders for PTDM screening in liver, heart, lung, and kidney transplant recipients respectively (Table 2).

For liver, heart, lung and kidney recipients who had PTDM screening performed, the incidence for PTDM was 27.6%, 17.4%, 17.0% and 20.0% (Figure 1) while 23.4%, 15.2%, 34.1% and 20.0% were in the prediabetes class (Figure 1).

Figure 1: Solid organ recipient's classification based on HbA1c levels post-transplantation.



Of the recipients who developed PTDM, 100% of liver and lung transplant recipients were placed on injectable insulin therapy across the various race/ethnic groups (Table 3). Only one kidney transplant recipient was not placed on either insulin or metformin (Table 3). In the heart transplant group, 100% of Hispanic white and 80% of Non-Hispanic black recipients were placed on insulin therapy while 100% of Non-Hispanic whites and 20% of Non-Hispanic blacks were placed on metformin (Table 3).

Table 3: Ten-years PTDM screening compliance data in solid organ recipient patients.

Liver Transplant recipient					
Ethnicity/Race	**Non-Hispanic White**	**Hispanic White**	**Non-Hispanic Black**	**Asian**	**Others**
Prediabetes	4	6	1	-	-
Diabetes	8	4	1	-	-
On Insulin	8	4	1		
On Metformin					
Heart Liver recipient					
Prediabetes	4	7	3		
Diabetes	2	9	5		
On Insulin	0	9	4		
On Metformin	2		1		
Lung Transplant recipient					
Prediabetes	20	3	3	3	1
Diabetes	7	7	-	-	1
On Insulin	7	7	-	-	1
On Metformin	-	-	-	-	-
Kidney transplant recipient					
Prediabetes	3	4	3	1	
Diabetes	1	7	3		
On Insulin	1	6	3		
On Metformin	-	-	-		

Discussion

Post-transplantation diabetes mellitus (PTDM) describes newly diagnosed mellitus in the post transplantation setting [4]. Risk factors for PTDM can be multifactorial [17,18] with obesity, immunosuppression with glucocorticoids, tacrolimus and other drugs being the most significant post-transplant risk factors [2,19-21]. The 2014 International consensus guidelines expanded the screening parameters for PTDM to include HbA1c as OGTT which is the gold standard is not widely used as they are time consuming and impractical in many settings [4].

In this study, we assessed the screening rates for post-transplant diabetes mellitus screening in patients who received solid organ transplants at Texas Children's Hospital. We found that no patient had orders for the OGTT test within the first year, which is the recommended gold standard for diagnosing PTDM. This observation is similar to previous reports highlighting the time consuming and impractical nature of OGTT in large transplant programs where fasting glucose and/or HbA1c tests are mostly used [1,5, 22-24]. Despite the ease of ordering HbA1c, PTDM screening remained very low except for lung transplant recipients (Table 2).

Our data is similar to previous reports of PTDM occurrence in solid organ transplant recipients [1] but a lower rate for lung transplant recipient likely due to increased PTDM screening in this group. Due to different risk factors such as age, alcoholic cirrhosis hepatitis C infection, liver steatosis etc. for liver [25,26]; advanced age, elevated pre-transplant HbA1c level, cystic fibrosis KCNJ11 gene polymorphism etc. for lungs [27,28]; advanced age, pre-and post-transplant HCV infections etc. for kidney [29,30]; cytomegalovirus infection and immunosuppressive medications for heart [31], solid organ transplant recipients are at risk of developing PTDM. But patients who are prediabetic after transplantation are at higher risk as it is a harbinger for PTDM [1]. Identifying patients at risk of PTDM is important as patients can easily be counseled on dietary and lifestyle changes; or placed on insulin and other oral anti-diabetic therapies [1,6]. One limitation of this study was the exclusion of bone marrow transplant patients as we focus only on solid organ transplants. Although we examined a relatively large cohort of patients, our study is a single-centre study necessitating more studies/data from other large transplant centres nationwide or internationally for comparison.

Recently, an update to the 2014 guideline was published stressing the use of OGTT in the diagnosis of PTDM citing that hemoglobin A1c lacks diagnostic sensitivity and advocating for more research in identifying the best way to identify recipients are risk [2]. However, in a pediatric population, performing OGTT does represent a challenge.

Patient/physician education on the risk of PTDM and importance of complying with PTDM screening is necessary. Continuous knowledge of latest guidelines and adherence to them might help change physician perspective and hopeful increase their compliance for PTDM screen for solid organ transplant recipient. Additionally, programmed notifications (best practice alerts) in the electronic medical records of solid organ recipient could help remind providers at regular intervals to order these tests for their patients [32].

Credit author statement

The following statements should be used "S.D.: conceptualization, methodology; R.I, S.K, SM.: data curation; R.I.: writing - original draft preparation; S.D.: supervision; RI, SK, SM, JS, DL, SD,.: writing - reviewing and editing. All authors have read and agreed to the published version of the manuscript.

Funding and Data Availability Statement

This research received no external funding. Data will be made available upon request to the Corresponding Author.

Acknowledgments

Ridwan B Ibrahim was supported by the Ching-Nan Ou Endowment in Clinical Chemistry.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

References

1. Pham PT, Sarkar M, Pham PM, Pham PC. Diabetes Mellitus After Solid Organ Transplantation. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, et al., editors. Endotext. South Dartmouth (MA)2000.
2. Sharif A, Chakkera H, de Vries APJ, Eller K, Guthoff M, Haller MC, et al. International consensus on post-transplantation diabetes mellitus. Nephrol Dial Transplant. 2024;39(3):531-49.
3. Standards of medical care in diabetes--2011. Diabetes Care. 2011;34 Suppl 1(Suppl 1):S11-61.
4. Sharif A, Hecking M, de Vries AP, Porrini E, Hornum M, Rasoul-Rockenschaub S, et al. Proceedings from an international consensus meeting on posttransplantation diabetes mellitus: recommendations and future directions. Am J Transplant. 2014;14(9):1992-2000.
5. Sharif A, Baboolal K. Diagnostic application of the A(1c) assay in renal disease. J Am Soc Nephrol. 2010;21(3):383-385.
6. Hecking M, Haidinger M, Döller D, Werzowa J, Tura A, Zhang J, et al. Early basal insulin therapy decreases new-onset diabetes after renal transplantation. J Am Soc Nephrol. 2012;23(4):739-749.
7. Chakkera HA, Weil EJ, Castro J, Heilman RL, Reddy KS, Mazur MJ, et al. Hyperglycemia during the immediate period after kidney transplantation. Clin J Am Soc Nephrol. 2009;4(4):853-9.
858. Chakkera HA, Knowler WC, Devarapalli Y, Weil EJ, Heilman RL, Dueck A, et al. Relationship between inpatient hyperglycemia and insulin treatment after kidney transplantation and future new onset diabetes mellitus. Clin J Am Soc Nephrol. 2010;5(9):1669-1675.
9. Davidson J, Wilkinson A, Dantal J, Dotta F, Haller H, Hernández D, et al. New-onset diabetes after transplantation: 2003 International consensus guidelines. Proceedings of an international expert panel meeting. Barcelona, Spain, 19 February 2003. Transplantation. 2003;75(10 Suppl):Ss3-24.
10. Baid S, Cosimi AB, Farrell ML, Schoenfeld DA, Feng S, Chung RT, et al. Posttransplant diabetes mellitus in liver transplant recipients: risk factors, temporal relationship with hepatitis C virus allograft hepatitis, and impact on mortality. Transplantation. 2001;72(6):1066-1072.
11. Knobler H, Stagnaro-Green A, Wallenstein S, Schwartz M, Roman SH. Higher incidence of diabetes in liver transplant recipients with hepatitis C. J Clin Gastroenterol. 1998;26(1):30-33.
12. Ye X, Kuo HT, Sampaio MS, Jiang Y, Bunnapradist S. Risk factors for development of new-onset diabetes mellitus after transplant in adult lung transplant recipients. Clin Transplant. 2011;25(6):885-891.
13. Lieber SR, Lee RA, Jiang Y, Reuter C, Watkins R, Szempruch K, et al. The impact of post-transplant diabetes mellitus on liver transplant outcomes. Clin Transplant. 2019;33(6):e13554.
14. Shabir S, Jham S, Harper L, Ball S, Borrows R, Sharif A. Validity of glycated haemoglobin to diagnose new onset diabetes after transplantation. Transpl Int. 2013;26(3):315-321.
15. Palepu S, Prasad GV. New-onset diabetes mellitus after kidney transplantation: Current status and future directions. World J Diabetes. 2015;6(3):445-455.
16. Solhjoo M, Kumar SC. New Onset Diabetes After Transplant. StatPearls. Treasure Island (FL)2024.
17. Sharif A, Baboolal K. Risk factors for new-onset diabetes after kidney transplantation. Nat Rev Nephrol. 2010;6(7):415-423.
18. Pham PT, Pham PM, Pham SV, Pham PA, Pham PC. New onset diabetes after transplantation (NODAT): an overview. Diabetes Metab Syndr Obes. 2011;4:175-186.
19. Boudreaux JP, McHugh L, Canafax DM, Ascher N, Sutherland DE, Payne W, et al. The impact of cyclosporine and combination immunosuppression on the incidence of posttransplant diabetes in renal allograft recipients. Transplantation. 1987;44(3):376-381.
20. Duijnhoven EMV, Boots JMM, Christiaans MHL, Wolffenbuttel BHR, Hooff JPV. Influence of tacrolimus on glucose metabolism before and after renal transplantation: a

prospective study. J Am Soc Nephrol. 2001;12(3):583-588.
21. Hjelmesaeth J, Hartmann A, Kofstad J, Stenstrom J, Leivestad T, Egeland T, et al. Glucose intolerance after renal transplantation depends upon prednisolone dose and recipient age. Transplantation. 1997;64(7):979-983.
22. Chakkera HA, Weil EJ, Pham PT, Pomeroy J, Knowler WC. Can new-onset diabetes after kidney transplant be prevented? Diabetes Care. 2013;36(5):1406-1412.
23. Pimentel AL, Hernandez MK, Freitas PAC, Chume FC, Camargo JL. The usefulness of glycated albumin for post-transplantation diabetes mellitus after kidney transplantation: A diagnostic accuracy study. Clin Chim Acta. 2020;510:330-336.
24. Pimentel AL, Cavagnolli G, Camargo JL. Diagnostic accuracy of glycated hemoglobin for post-transplantation diabetes mellitus after kidney transplantation: systematic review and meta-analysis. Nephrol Dial Transplant. 2017;32(3):565-572.
25. Gulsoy Kirnap N, Kirnap M, Alshalabi O, Tutuncu NB, Haberal M. Posttransplant Diabetes Mellitus Incidence and Risk Factors in Adult Liver Transplantation Recipients. Acta Endocrinol (Buchar). 2020;16(4):449-453.
26. Campos MB, Riguetto CM, de Fátima Santana Ferreira Boin I, Moura AN. Risk factors associated with diabetes after liver transplant. Arch Endocrinol Metab. 2022;66(2):182-190.
27. Shitrit D, Ollech J, Amital A, Kramer MR. DIABETES MELLITUS FOLLOWING LUNG TRANSPLANTATION: INCIDENCE AND RISK FACTORS. CHEST. 2007;132(4):597A.
28. Du W, Wang X, Zhang D, Zuo X. Retrospective analysis on incidence and risk factors of post-transplant diabetes mellitus after lung transplantation and its association with clinical outcomes. Transplant Immunology. 2024;83:102008.
29. Alkadi M, Thappy S, Abuhelaiqa E, Mahmoud J, Jarman M, Khan SU, et al. Incidence and Risk Factors of Post Transplant Diabetes Mellitus in Kidney Transplant Recipients in Qatar. Transplantation. 2018;102:S648.
30. Siraj ES, Abacan C, Chinnappa P, Wojtowicz J, Braun W. Risk Factors and Outcomes Associated With Posttransplant Diabetes Mellitus in Kidney Transplant Recipients. Transplantation Proceedings. 2010;42(5):1685-1689.
31. Newman JD, Schlendorf KH, Cox ZL, Zalawadiya SK, Powers AC, Niswender KD, et al. Post-transplant diabetes mellitus following heart transplantation. The Journal of Heart and Lung Transplantation. 2022;41(11):1537-1546.
32. Ibrahim RB, Olayinka L, Chokkalla AK, Devaraj S. Postpartum Glucose Monitoring in Pregnant Women with Gestational Diabetes Mellitus: A Dual Center Experience. Ann Clin Lab Sci. 2024;54(3):331-334.