Original Article

New onset diabetes after transplant in renal transplant recipients

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Abstract

Introduction: New onset diabetes after transplantation (NODAT) is a common complication of renal transplantation. Despite its prevalence and importance, the data on NODAT and its risk factors in Nepalese population are lacking and the incidence and risk factors for NODAT in Nepalese population who underwent renal transplantation at Tribhuvan University Teaching Hospital.

Methods: All the patients who underwent living donor kidney transplantation at Tribhuvan University Teaching Hospital between August, 2008 and February, 2016 were included in this study. Patients who were diagnosed with diabetes mellitus before transplantation were excluded from the study. Patients were divided into NODAT and Non-NODAT groups. Then, risk factors were compared between the two groups.

Results: A total of 350 patients who underwent living donor renal transplantation at our hospital during the study period were included. 23 patients who were diagnosed cases of Diabetes Mellitus before transplantation were excluded. In the remaining 327 cases, the incidence of NODAT was 19.57% (64 patients). Most of them (95.31%) occurred within the first 12 months' post transplantation. The mean duration of onset of NODAT was 121.46 ± 275.58 days post transplantation. Age of the recipient greater than 45 was significantly associated with NODAT than non-NODAT patients. However, there was no statistical difference in sex between NODAT and non-NODAT patients.

Conclusion: NODAT is common complication after renal transplantation. Age of recipient > 45 years is a significant risk factor for the development of NODAT. So, we have to be more vigilant in these patients.

Keywords: Renal transplantation, NODAT, Age.

Introduction

New onset diabetes after transplantation (NODAT) is a common complication of renal transplantation. It is associated with increased all-cause mortality, in particular, higher rates of cardiovascular disease, increased susceptibility to infections, acute rejection episodes, chronic graft dysfunction, and decreased quality of life.[1]Many nonmodifiable risk factors affect the development of NODAT such as patient age and ethnicbackground[2,3]. Other risk factors, such as cadaveric kidney donor and male gender, have been found only in some reports[4] but not in others[5].

Despite its prevalence and importance, the data on NODAT and its risk factors in Nepalese population are lacking. In this study, we present incidence and risk factors for NODAT in Nepalese population who underwent renal transplantation at Tribhuvan University Teaching Hospital.

Methods

Patients: We retrospectively reviewed patients, who underwent living donor kidney transplantation at Tribhuvan University Teaching Hospital between August, 2008 and February, 2016. Patients who were

diagnosed with diabetes mellitus before transplantation were excluded from the study.

Clinical data

A diagnosis of NODAT was defined according to the American Diabetes Association criteria:

1. Fasting glucose level ≥126 mg/dL or
2. Glycosylated hemoglobin [Hb A1c] ≥6.5 %, or,
3. A two-hour value in an oral glucose tolerance test ≥200 mg/dL, or
4. A random plasma glucose concentration ≥200 mg/dL in the presence of symptoms).

All the patients were divided into NODAT and Non-NODAT group. Then risk factors were compared between the two groups.

Immunosuppression

A triple regimen of calcineurin inhibitors (tacrolimus) plus mycophenolate mofetil or azathioprine plus glucocorticoids was used for maintenance immunosuppressant therapy.

Statistical Analysis

The results were compared between NODAT and non-NODAT patients. Comparisons of continuous values were made using the Student's t-test, and categorical values by Chi-squared test. All continuous data were expressed as mean ± SD and were analyzed by unpaired t test. Data were analyzed with SPSS software version 20.0 for mac. P value <0.05 was considered to indicate a statistically significant difference.

Results

During the study period, 350 patients underwent living donor renal transplantation at our hospital. From these, 23 patients who were diagnosed cases of Diabetes Mellitus before transplantation were excluded from the study.Finally, the remaining 327 cases were included in the study. The demographic profile of study population is shown in Table 1. Their age ranged between 12 and 62 (mean 34.63 ± 10.97) years. Majority of recipients were males and only 68 (20.79 %) donors were females. Chronic glomerulonephritis (CGN) was the predominant native kidney disease seen in 141 patients (43.11%). Hypertension was observed in 123 (37.61%) patients. 12 patients had focal segmental glomerulosclerosis (FSGS), 12 had obstructive nephropathy, and 4 had membranoproliferative glomerulonephritis (MPGN). One patient had ESRD due to autosomal dominant polycystic kidney disease (ADPKD), anti GBM disease and lupus nephritis each.

Among those included in the study, 64 patients (19.57%) developed NODAT. 53(82.81%) were males and 11 (17.18%) were females.Their age ranged between 18 and 62 (mean 40.37± 11.86) years.Of these, 31.25% (20 of 64 patients) were from the age group between 41 and 50 (TABLE 3). 61 of the 64 patients (95.31%) developed NODAT in the first 12 months' post transplantation. The mean duration of onset of NODAT was 121.46 ± 275.58 days post transplantation.Among the 263 patients without NODAT, 78.3% were male. 69.96% (184 of 263) were from the age group between 21 and 50 (TABLE 4). Regarding treatment of the patients with NODAT; 18 patients had their blood glucose levels controlled with diet and lifestyle modification only, 32 patients were given oral hypoglycemic agents, while insulin was prescribed to 14 patients.

Age of the recipient greater than 45 was significantly associated with NODAT than non-NODAT patients. However, there was no statistical difference in sex between NODAT and Non- NODAT patients.

Table 1: Demographic profile of study population

Total number	327
Age	34.63 ± 10.97
Age>45 years	70
Sex	
Male	**259**
Female	**68**
Cause of Esrd	
Chronic glomerulonephritis	141
Hypertension	123
Immunoglobin A nephropathy	32
Focal segmental glomerulosclerosis	12
Membranoproliferative glomerulonephritis	4
Anti glomerular basement membrane disease	1
Lupus nephritis	1
Adult polycystic kidney disease	1
Obstructive uropathy	12

Table 2: Comparison between NODAT and Non-NODAT group

	Non-NODAT	NODAT	P value
Number	263	64	
Age	**34.62 ± 11.012**	**40.37 ± 11.86**	**<0.05**
Age>45	**48**	**22**	**0.006**
Sex			
Male	206	53	0.187
Female	57	11	
Cause of Esrd			
Chronic glomerulonephritis	109	32	
Hypertension	104	19	
Immunoglobin A nephropathy	24	8	
Focal segmental glomerulosclerosis	10	2	
Membranoproliferative glomerulonephritis	4	0	
Anti glomerular basement membrane disease	1	0	
Lupus nephritis	1	0	
Adult polycystic kidney disease	0	1	
Obstructive uropathy	10	2	

Table 3: Mean blood sugar of patients with NODAT according to the age group

Nodat Age Group	Number	Mean Blood Sugar
11-20	2	142.40
21-30	17	172.10
31-40	16	177.18
41-50	20	172.92
51-60	8	179.60
>60	1	131.00

Table 4: Mean blood sugar of patients without NODAT according to the age group

Non- Nodat Age Group	Number	Mean Blood Sugar
11-20	12	90.35
21-30	89	89.35
31-40	95	89.86
41-50	40	86.99
51-60	26	90.73
>60	1	99.00

Discussion

New-onset diabetes after transplantation (NODAT), is a well-recognized complicationof organ transplantation. It has been observed after transplantation of kidney, liver, lung, heart, and other solid organs, as well as bone marrow and hematopoietic stem cells. Varying incidence rates of NODAT have been reported among recipients of different organ transplants. The estimated rates of NODAT at 12 months or longer post-transplant is approximately 20-50% for kidney transplants.[6] The wide variations in the incidence could be due to differences in study deign, study population, timing of testing and without any standard diagnostic criteria. However, since the 2003 the adoption of the International Consensus Guidelines on New-Onset Diabetes after Transplantation has standardized the diagnosis of NODAT.[2,7]Our study showed that 19.57% of our recipients developed NODAT during our study period. The incidence was 17.4% in the first 12 months' post transplantation.This is consistent with the results from previous reports done in Asian population such as Hoon Yu et al.[8]

Multiple risk factors have been associated in the development of NODAT in renal transplant patients. The pretransplant risk factors are family history, age, male

gender of donor, obesity, ethnicity, physical inactivity, hypertension, dyslipidemia and hepatitis C infection.[2,9] Other post-transplant risk factors are immunosuppressive medications including glucocorticoids and calcineurin inhibitors, CMV infection and acute rejection. Among all these risk factors, the age of the recipient at the time of transplantation is statistically the strongest predictor of the risk for NODAT. In our study as well, age of the recipients greater than 45 years of age was significantly associated with NODAT. However, sex of the recipient was not significantly associated with NODAT. Fernando G. Cosio et al also showed significant association of age of the recipient greater than 45 with development of NODAT and recipient gender is not an independent risk factor.[5]

The management of NODAT should follow the conventional approach for patients with type 2 diabetes mellitus as recommended by many clinical guidelines established by well-recognized organizations including the American Diabetes Association. The management of NODAT consists of diet control and lifestyle modification, oral hypoglycemic agents (OHA), and insulin therapy. In our study, most of our patients (78.12%) had well controlled blood sugar with OHAs and life style modifications and diet control, however 14 patients (21.8%) did require insulin therapy.

Our study had some limitations. It was a retrospective single center study. Pre-transplant OGTT was not routinely preformed at our center.

Conclusion

NODAT is common complication after renal transplantation with incidence of 19.57% in our center. Most of them (95.31%) occurred within the first 12 months' post transplantation. Age of recipient > 45 years is a significant risk factor for the development of NODAT. So, we have to be more vigilant in these patients.

Conflict of interest: None declared

References

1. Yates CJ, Fourlanos S, Hjelmesaeth J, Colman PG, Cohney SJ. New-onset diabetes after kidney transplantation-changes and challenges. *Am J Transplant.* 2012; 12(4):820-828.
2. Davidson J, Wilkinson A, Dantal J, 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.
3. Numakura K, Satoh S, Tsuchiya N, et al. Clinical and genetic risk factors for posttransplant diabetes mellitus in adult renal transplant recipients treated with tacrolimus. *Transplantation.* 2005; 80(10):1419-1424.
4. Sumrani NB, Delaney V, Ding ZK, et al. Diabetes mellitus after renal transplantation in the cyclosporine era--an analysis of risk factors. *Transplantation.* 1991; 51(2):343-347.
5. Cosio FG, Pesavento TE, Osei K, Henry ML, Ferguson RM. Post-transplant diabetes mellitus: increasing incidence in renal allograft recipients transplanted in recent years. *Kidney Int.* 2001; 59(2):732-737.
6. Kasiske BL, Snyder JJ, Gilbertson D, Matas AJ. Diabetes mellitus after kidney transplantation in the United States. *Am J Transplant.* 2003; 3(2):178-185.
7. Wilkinson A, Davidson J, Dotta F, et al. Guidelines for the treatment and management of new-onset diabetes after transplantation. *Clin Transplant.* 2005; 19(3):291-298.
8. Yu H, Kim H, Baek CH, et al. Risk factors for new-onset diabetes mellitus after living donor kidney transplantation in Korea - a retrospective single center study. *BMC Nephrol.* 2016; 17(1):106.
9. Sulanc E, Lane JT, Puumala SE, Groggel GC, Wrenshall LE, Stevens RB. New-onset diabetes after kidney transplantation: an application of 2003 International Guidelines. *Transplantation.* 2005; 80(7):945-952.