Glucose Intolerance and Insulin Resistance After Renal Transplantation in Children and Adolescents

Nur Canpolat[1], Salim Çalışkan[1], Manolya Kara Acar[2], Şükran Pehlivan[1], Mehmet Taşdemir[1], Lale Sever[1]

[1]Department of Pediatric Nephrology, [2]Department of Pediatrics, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul, Turkey

Objectives:

• In recent years, post-transplant hyperglycemia (glucose intolerance and diabetes mellitus) has become the focus of attention in renal transplant recipients because of its increasing prevalence in clinical application of tacrolimus. However, post-transplant hyperglycemia reflects both pre-transplant and transplant-induced abnormalities in glucose metabolism. Hyperparathyroidism and 25-OH vitamin D deficiency have been linked to impaired glucose tolerance in dialysis patients. These metabolic derangements and the effect of pre-transplant abnormalities in glucose and insulin metabolism have received little attention in pediatric post-transplant patients.

• The present study aimed to address the presence of post-transplant glucose and insulin abnormalities and their associations to potential risk factors in children and adolescents, with a particular focus on the presence of pre-transplant glucose intolerance.

Methods:

• This is a retrospective single center study involving 21 renal transplant children and adolescents (11 female; aged between 8 and 21 years) on a standard triple therapy regimen of steroid, tacrolimus and mycophenolate mofetil/sodium.
• Anthropometric indices, including weight, height, and body mass index (BMI) were measured.
• Laboratory measurements included a pre- and post-transplant oral glucose tolerance test (OGTT) as well as fasting insulin, and post-transplant GFR, hemoglobin, albumin, ferritin, C- reactive protein (CRP), parathyroid hormone (PTH) and 25-OH vitamin D.
• The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as an estimate of insulin resistance using fasting levels of plasma glucose and insulin. Insulin resistance was defined as a HOMA-IR ≥ 95th percentile according to sex and pubertal stages.
• The definition of glucose intolerance and the diagnosis of diabetes mellitus were based on the American Diabetes Association criteria.

Results:

Table 1: Characteristics of the patients

Number of patients	21
Gender (male/female)	10/11
Current age (years)	16.7 ± 4.6
Age at transplantation (years)	14.8 ± 4.4
Time on ESRD (months)	51.1 ± 36.0
Time on transplantation (months)	22.9 ± 15.1
Pre-transplant RRT (PD/HD)	15/6
Donor (living/cadaveric)	15/6
Pre-transplant IR, *n* (%)	1 (4.7)
Post-transplant IR, *n* (%)	2 (9.5)
Pre-transplant abnormal OGTT, *n* (%)	11 (52)
Post-transplant abnormal OGTT, *n* (%)	6 (29)
Post-transplant DM, *n* (%)	1 (4.7)

Table 2: Glucose and insulin parameters

	Pre-transplant	Post-transplant	*P* value
Fasting glucose (mg/dl)	95 ± 13	89 ± 7.8	NS
2-hour glucose (mg/dl)	126 ± 36	118 ± 38	NS
Fasting plasma insulin (µU/ml)	6.07 ± 4.54	8.71 ± 4.60	0.003
HOMA-IR	1.42 ± 1.04	1.93 ± 1.02	0.019

▪ Table 1 shows clinical characteristics of the patients. Post-transplant BMI-SDS adjusted by height was 0.46±1.12; only one patient exceeds 2SD. Post-transplant serum levels of 25-OH vitamin D, PTH and CRP were 15.2±11.3 ng/mL, 106±88 pg/mL and 0.39±0.13 mg/dL, respectively.
▪ A total of six patients (29%) showed post-transplant hyperglycemia (4 glucose intolerance, 2 diabetes mellitus). Of these, three had pre-transplant glucose intolerance. However, eight pre-transplant patients with glucose intolerance showed a normal post-transplant OGTT. There was no association between the presence of pre- and post-transplant glucose intolerance.
▪ Univariate analyses showed that higher levels of post-transplant fasting glucose were significantly associated with lower levels of 25 (OH) vitamin D (r= -0.608, p= 0.012), and higher levels of post-transplant 2-hr glucose were significantly associated with higher PTH levels (r= 0.456, p= 0.038).
▪ Insulin resistance was present in one patient (5%) in the pre-transplant period and in 2 patients (9.5%) in the post-transplant period.
▪ As shown in Table 2, post-transplant insulin and HOMA-IR levels were significantly higher than the pre-transplant levels.
▪ Higher levels of post-transplant fasting glucose were significantly associated with lower levels of 25 (OH) vitamin D (r= -0.608, p= 0.012), and higher levels of post-transplant 2-hr glucose were significantly associated with higher PTH levels (r= 0.456, p= 0.038).
▪ Higher post-transplant HOMA-IR was independently associated with higher CRP (p< 0.001), higher SD scores of BMI (p= 0.003) and lower 25(OH) vitamin D levels (p= 0.019).

Conclusions:

Post-transplant hyperglycemia seems to be associated with vitamin D deficiency and hyperparathyrodism, but not with the presence of pre-transplant glucose intolerance. Obesity (higher BMI), inflammation and vitamin D deficiency appear to be the risk factors for insulin resistance after transplantation.

References:

1- Davidson J, Wilkinson A, Dantal J et al. New-onset diabetes after transplantation: 2003 International Consensus Guidelines. Transplantation 2003; 75: SS3–SS24
2- Hur KY, Kim MS, Kim YS et al. Risk factors associated with the onset and progression of posttransplantation diabetes in renal allograft recipients. Diabetes Care 2007; 30: 609–615
3- Bergrem HA, Valderhaug TG, Hartmann A. et al. Glucose tolerance before and after renal transplantation. Nephrol Dial Transplant 2010; 25: 985-992