

## **Kidney V –Non-immune Complication of Kidney Transplant**

### **Diabetes mellitus after kidney transplantation**

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Post-transplant diabetes mellitus (PTDM) or new-onset diabetes mellitus after transplantation (NODAT) is the development of diabetes mellitus after solid organ transplantation. It is a complication that is most frequently observed within the first 12 weeks after kidney transplantation and occurs in up to 25% of kidney transplant recipients. Patients with NODAT have increased cardiovascular morbidity and reduced survival.

The pathogenesis mainly involves beta-cell dysfunction in presence of insulin resistance. The pathophysiology of NODAT is almost akin to type 2 DM (T2DM) in which there is an increase in insulin resistance and a decrease in insulin secretion. NODAT more likely occurs in patients who have other risk factors for developing T2DM but the use of certain immunosuppressants such as high-dose corticosteroid and tacrolimus certainly contributes to its development.

The criteria for the diagnosis of NODAT are identical to those of DM: (1) Symptoms of diabetes and random blood glucose greater than or equal to 200 mg/dL (11.1 mmol/L); (2) Fasting blood glucose  $\geq$  to 126 mg/dL (7.0 mmol/L) which requires repetition on another day; and (3) Two-hour blood glucose  $\geq$  200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test. Although hemoglobin A1c can be used in some patients to diagnose diabetes mellitus, in the setting of kidney failure, RBC turnover makes this unreliable. Because of this, the diagnosis of NODAT based on HbA1c is not recommended in the first 3 months after the transplantation. Early detection of NODAT is helpful as it reduces the risk and complications of DM. The recommendation is for post-transplantation screening for NODAT. Many transplant centers perform the screening tests weekly in the first month and continue screening at months 3, 6, and 12 post-transplantation. After the first year, the risk of NODAT is lower, and the recommendation is for yearly screening. In our center, we routinely test fasting blood glucose at every clinic visit regardless of the duration of transplant.

The goal for management is adequate glycemic control to minimize hyperglycemic complications. The first steps for glycemic control should focus on non-pharmacological means, such as dose reduction of or switching of diabetogenic immunosuppressants to the less diabetogenic ones, and diet control. Tapering corticosteroids soon after transplant can control blood glucose without medical therapy but the risk of acute rejection has to be borne in mind. In general, steroid tapering can be hastened in patients with low immunologic risks of rejection. When pharmacologic agents are required, one needs to take into account whether the allograft is functioning well. If it is, metformin and sulfonylureas can be used although the latter can give rise to weight gain and

hypoglycemia as it enhances insulin secretion. Thiazolidinediones are selective agonists of the peroxisomal proliferator-activated receptor gamma and improve glucose tolerance and insulin sensitivity in NODAT. They are contraindicated in congestive heart failure and should be used with caution if there is graft malfunction. Dipeptidyl peptidase-4 inhibitors (DPP-4i) act by inhibiting the degradation of glucagon-like peptide 1, which results in pancreatic insulin secretion. Among the DPP-4is, linagliptin is a good choice as it can be used regardless of the level of allograft function. GLP-1 receptor agonists and insulin are usually reserved for patients with unsatisfactory control despite other approaches. Finally, coordination among the interprofessional teams such as with the diabetologist, diabetes nurse and dietician can enhance patient care and compliance, and increase patient survival following organ transplantation.