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A SYSTEMATIC REVIEW ON THE NEW ONSET DIABETES AFTER TRANSPLANT (NODAT)

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ABSTRACT

NODAT (new-onset diabetes mellitus after transplantation) is the emergence of diabetes in previously non-diabetic individuals following organ transplantation. The estimated rates of NODAT at one year post-transplant is 2% to 53% of all solid organ transplants which is greater in kidney transplants than other solid organ transplants. Aside from established risk factors for type 2 diabetes, Corticosteroids exposure affects glucose metabolism by lowering glucose consumption and increasing hepatic gluconeogenesis. Additionally, Corticosteroids drastically lower insulin secretion. However, NODAT has a detrimental effect on patient mortality, cardiovascular risk, and renal allograft survival. Long-term patient survival and graft outcome may be enhanced by the identification of high-risk patients and the execution of interventions to decrease the development of NODAT. This systematic review expands the understanding of most relevant risk variables, diagnostic criteria, and management practices.

KEYWORDS: NODAT, Post-transplantation.

INTRODUCTION

New-onset diabtes after transplantation (NODAT) is a serious and frequent metabolic complication after renal transplantation. This entity is currently well defined since the publication of the International Consensus Guidelines in 2003.

NODAT was identified in accordance with the FBG concentrations recommended by the American Diabetes Association guideline; FBG: 126 mg/dl (7.0 mmol/l) and not on oral hypoglycemic medications or insulin at any point of follow-up within one year following

renal transplant or other transplants.[4] Replacement treatment is considered to be the gold standard for patients with end-stage kidney, liver, lung, heart, and other solid organ illnesses, as well as bone marrow and hematopoietic stem cell diseases.[1] However, post-transplant problems, particularly "new-onset diabetes after transplantation" (NODAT), have been known to increase the risk of morbidity and mortality in these individuals. In fact, NODAT is currently thought to be a primary driver of renal allograft loss, infection, and increased risk of cardiovascular morbidity and mortality, and so it can have a substantial impact on the clinical outcome of transplant recipients.[5]

The anticipated rates of NODAT at 12 months or longer post-transplant are roughly 20-50% for kidney transplants, 9-30% for liver transplants, 28-30% for heart transplants, 6-45% for lung transplants, and roughly 15% for bone marrow transplants.[1] However, Transient hyperglycemia after transplant is thought to be due to the surgical stress–induced hyperglycemia-related insulin resistance from counter-regulatory stress hormone release (*e.g.*, cortisol, growth hormone).[8] In patients examined at the height of perioperative stress, acute hyperglycemia is more likely to be seen. NODAT is predictable by evaluvation of the risk factors such as pre-diabetic status and obesity.[7] Still, prospective biomarkers helping to stratify patients at high risk or low risk for NODAT are scarce, and no algorithm to predict NODAT in posttransplant recipients has been validated.

PREVALENCE, RISK FACTORS & MANAGEMENT

Prevalence

NODAT has been a serious complication after any solid organ transplant. Prevalence of NODAT may vary from 2% to 53%. A recent Indian study showed prevalence of NODAT to be 26.7%.[5] As the transplant services are advancing there has been a tremendous increase in the numbers of patients receiving solid organ transplantation.[6] Several risk factors which may lead to this increasing rate of NODAT are the following:

Risk factors

- Older age has been identified as an important risk factor for the development of NODAT. Transplant recipients older than 45 years are 2.2 times more likely to develop NODAT than those younger at the time of transplantation.
- Race / ethnicity: There has been a large literature suggesting that African Americans and Hispanics are at a greater risk of developing NODAT compared to whites.

- Family history of diabetes mellitus: Is similar to type 2 diabetes in the general population, genetic and environmental factors have been compared to play a role in the development of NODAT. There is strong evidence that people with a family history of diabetes among first-degree relatives have a greater chance of developing NODAT.
- Corticosteroid-associated NODAT: The diabetogenic effect of corticosteroids has been suggested to be dose-dependent. Some studies have shown that oral prednisolone dose reduction to 5 mg daily significantly reduces glucose tolerance during the first year after transplantation.
- Calcineurin inhibitor(CNI)-associated NODAT: tacrolimus has more consistently been shown to have a greater diabetogenic effect than cyclosporine.
- Effects of sirolimus on glucose metabolism diabetogenic effects either used alone or in combination therapy with CNI, increasing peripheral insulin resistance and impairs pancreatic beta cell response.
- Obesity, Analysis of the USRDS database revealed that obesity as BMI ≥30 kg/m2 is one of the strongest risk factors for NODAT.
- Other factors may include Physical inactivity, Hypertension, Dyslipidemia, Hepatitis C infection etc.

Management of NODAT

As the best option for treating NODAT will be steroid free regimen or tampering the daily doses of steroid drugs. Among diabetes treatment options, incretin therapies uniquely counteract immunosuppressant drugs' interference with insulin secretion.[6] Also Incretin class of agents including glucagon-like peptide-1 (GLP-1) agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors stimulate beta-cell function, slows gastric emptying and also reducing insulin resistance. GLP-1 agonists cannot be used with patients who have a low GFR and may cause nausea. DPP-4 inhibitors can be used in patients with low GFR, low hypoglycemia potential, rarely cause nausea. Within this class, linagliptin has primarily nonrenal route of elimination, with only 5% of the dose being excreted via the kidneys. Thus, linagliptin needs no dose adjustment in patients with impaired renal function.[3]

CONCLUSION

NODAT in transplant recipients is more common in those with higher pretransplant BMI, pretransplant total cholesterol, triglyceride, and FBS. Beta-cell secretory defect is more relevant as etiological factor rather than insulin resistance. Most of the steroid drugs interfere

with the insulin production and glucose metabolism. On the other hand steroid medications and other immunosuppressive drugs are vital for transplant patients even though there is a chance of developing condition called NODAT. Management with incretin therapies have been a great option along with steroid free regimen or tampering the daily doses of steroid drugs. Knowing the high risk patients will also help in managing the risks and patient survival.

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