

Short Communication

Pancreatogenic Diabetes – Neglected, Underdiagnosed or Misdiagnosed?

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INTRODUCTION

Pancreatogenic or Type 3c diabetes is a rather new entry to the world of diabetes and accordingly is scarcely documented; less than 100 entries in a casual Pubmed search.¹ This may be due to insufficient research, inaccurate classification, rare occurrence or misdiagnosis in routine clinical practice. Nevertheless, recent data suggests that it might be more common than initially presumed and might be under or misdiagnosed in routine clinical practice.² Besides, T2DM (Type 2 Diabetes Mellitus) is common enough in global population to accidentally coexist with exocrine pancreatic disease.³

American Diabetes Association and World Health Organization have classified Pancreatogenic diabetes as type 3c diabetes mellitus (T3cDM) and refers to diabetes due to impairment in pancreatic endocrine function related to pancreatic exocrine damage due to acute, relapsing and chronic pancreatitis (of any etiology), cystic fibrosis, hemochromatosis, pancreatic cancer, pancreatectomy as well as rare causes such as neonatal diabetes due to pancreatic agenesis.⁴ Of these, chronic pancreatitis seems to be the most underlying cause. About 78.5% of T3cDM patients have chronic pancreatitis and 8% suffer from pancreatic cancer.¹ About 10% of the global diabetic population has been diagnosed for chronic pancreatitis hence, even though the true worldwide prevalence of T3cDM is unknown it is reasonable to assume that it probably ranges from 1% to 9% of patients with diabetes.⁵ The prevalence of chronic pancreatitis was found to be 114-200/100,000 persons in Southern India, which is markedly higher than that in western industrialized nations (10-15/100,000).⁶

Though pathogenesis of diabetes in chronic pancreatitis is well known, guidelines for its specific diagnosis and therapeutic regime has been only recently developed. T3cDM is unique from Type 1 and 2 as it arises from chronic inflammation and is associated with exocrine

pancreatic insufficiency, pathological pancreatic imaging and absence of T1DM- (Type 1 Diabetes Mellitus) associated autoimmune markers. It is also associated with increased incidence of pancreatic carcinoma and has distinct clinical and pathological parameters. Unlike Type 1 and 2, not much is documented about development of diabetes in chronic pancreatitis patients and additional comorbidities like maldigestion/malabsorption leading to malnutrition further increase complications.⁷

Identification of role of damaged pancreas in diabetes development is important for planning its management. Insulin resistance is a major criterion for identifying T2DM patients but T3cDM should be considered when there is ambiguity, family history of pancreatitis or early insulin requirement in adult patients. T3cDM has reduced insulin production due to β -cell dysfunction following pancreatic inflammation or absolute β -cell loss. Additionally, loss of pancreatic polypeptide which upregulates insulin receptor expression in liver can lead to hepatic insulin resistance- a physiological feature that distinguishes T3cDM from type 1. Decreased glucagon production from α -cells accounts for severe hypoglycemia in patients. If this altered physiology unique to T3cDM goes unnoticed, patients undergo suboptimal treatment. Approximately 40% of hospitalized patients are usually misdiagnosed with T2DM as opposed to 2.7% who are correctly classified as T3cDM patients.³

Chronic pancreatitis is an inflammatory disease hence, it is important to identify causative factors such as cytokines, chemokines, receptors, immune/inflammatory cells and gut microbiota variation that contribute to the anomalies in β -cell signaling pathways. Additionally, knowledge about genetic susceptibility, pre-diabetic status and glucose intolerance of chronic pancreatitis patients may help prevent clinical manifestation of T3cDM. Simultaneous indulgence in lifestyle modifications will also benefit the patients. Abstinence from smoking and alcohol will be beneficial since both are known to aggravate underlying pancreatic inflammation; alcohol abstinence also helping in

diabetes management.² A diet rich in soluble fiber and low in fats along with oral pancreatic enzyme replacement will help deal with malnutrition while vitamin D supplements will help curb osteoporosis and metabolic bone disease.⁷⁻¹¹

T3cDM is a clinically important disease which is often neglected, under diagnosed or misdiagnosed leading to its poor management. Its significance is growing due to increased frequency of pancreatic surgery and pancreatotomy, better survival of cystic fibrosis patients and increased chronic pancreatitis incidence world-wide. Studies should be encouraged in future to fill the current research gaps for better therapeutic management of T3cDM.

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ABBREVIATIONS

T2DM: Type 2 Diabetes Mellitus; T3cDM: Type 3c Diabetes Mellitus; T1DM: Type 1 Diabetes Mellitus.

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