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Letter to The Editor

Adiponectin and Fetuin-A; Newer Biomarkers as Predictors of Type 2 Diabetes Mellitus in offsprings of Diabetic parents

Parinita Kataraki[1], and Usha Adiga[2]*.

[1]Professor & Head, Dept of Biochemistry, Srinivas Institute of Medical Sciences, Mangalore, Karnataka, India.
[2]Professor, Dept of Biochemistry, K S Hegde Medical Academy, Mangalore, Karnataka, India.

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Corresponding author

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INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both and is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. In India, more than 62 million people are diagnosed as diabetic which will rise to 87.0 million by 2030. It has been reported that diabetes is disproportionately high in young to middle aged adults which could have long lasting adverse effects on a nation's health and economy. First degree relatives of patients with type 2 diabetes frequently show abnormal glucose tolerance and have a 30% - 40% risk of developing type 2 diabetes themselves.

Prior studies in adults have suggested a strong hereditary component in risk for type 2 diabetes. A family history of type 2 diabetes increases the risk of developing the disease. Moreover, the high concordance of type 2 diabetes in identical twins and the aggregation of type 2 diabetes in families support the existence of genetic determinants for type 2 diabetes in families. The risk for developing type 2 diabetes increases when one or both parents are affected. Some studies have suggested that adult offspring whose mothers have diabetes are more likely to develop the disease themselves than are offspring whose fathers have diabetes (1).

Adiponectin and insulin resistance

Adiponectin, is a novel peptide expressed specifically and abundantly in adipose tissue. Adiponectin is a 244 a.a. protein that regulates the metabolism of lipids and glucose. Adiponectin decreases insulin resistance and body weight by increasing lipid oxidation in muscle and other organs such as the pancreas and liver . Plasma Adiponectin concentrations are also reduced in individuals with obesity, diabetes mellitus, or coronary heart disease(2). In contrast to other adipokines (such as leptin, interleukin-6 and others) that are often elevated in obese subjects, adiponectin is reduced. In animal studies, adiponectin has been shown to have insulin-sensitizing properties. Administration of adiponectin reversed insulin resistance in various mouse models of obesity and diabetes(2). Obesity and hyperinsulinemia are suggested as the potential mechanisms for the suppression of adiponectin levels in the body, and ethnicity may play a role in adiponectin regulation among different groups(3). Adiponectin, a 30-kDa complement C1-related protein, is the most abundant secreted protein expressed in adipose tissue, and plays a crucial role in the regulation of insulin sensitivity and glucose metabolism. Lower circulating adiponectin levels is associated with obesity and negatively correlated with insulin resistance6. In addition, it has been proposed that adiponectin exerts antidiabetic, anti-atherogenic and antiinflammatory activities in metabolic diseases. Therefore, circulating adiponectin levels might represent a significant clinical diagnostic biomarker for the future development of prediabetes. However, its role in the development of diabetes remains unclear.(4)

Feutin A and insulin resistance

In contrast to adipocytokines, fetuin-A is produced in hepatocytes and secreted into serum, where it is found in high concentrations. In vitro, fetuin-A reversibly binds the insulin receptor tyrosine kinase in muscle and fat and decreases downstream signal cascades, which results in insulin resistance in these target tissues (5). Fetuin-A is an important player in the enhancement of insulin resistance. Diagnosing pre diabetes has been a challenging task and till date it is done based on the levels of plasma glucose and glycosylated hemoglobin (HbA1c) which are essentially affected by a number of factors which includes diet also. Experimentally it has been proven that knocking out the gene for fetuin A made the mouse completely fetuin A deficient, thus enhancing their glucose clearance and insulin sensitivity , these mice were resistant to weight gain and had decreased body fat thus suggesting that fetuin A may play a significant role in regulating post prandial glucose disposal, insulin sensitivity, weight gain and fat accumulation. Combination of environmental and genetic factors result in molecular defect in insulin resistance and secretion.

Fetuin A has been suggested to be a link between obesity and insulin resistance. It has been suggested to be a risk factor for type 2 diabetes in people with normoglycemia (6-8)

Shahid et al showed that T2DM associated risk factors are more vigorously expressed in male offspring with a history of diabetes in both parents, thus underscoring the importance of genetic determinants in the onset of T2DM. The results of this study provided useful indicators of potential susceptibility to T2DM at an early stage of life(9).

Urbanavičius et al showed that adiponectin level was similar in IGT and type 2 diabetes groups and was significantly lower than in control subjects(10).Şiraz et al concluded that fetuin-A is a reliable parameter in the prediction of complications and poor glycemic control in patients with T1DM(11).Young Suk Shim et al suggested that fetuin A can be an alternate marker for insulin resistance and cardiovascular risk in prepubertal children(12).

There are few studies which have shown hypoadiponectinemia is associated with family history of diabetes but not all. Purpose of this article was to highlight on any significant difference in the level of total serum adiponectin and their association with fasting insulin, glucose and insulin resistance in offspring of diabetics.

Future Research Perspective

Keeping in view, the role of fetuin A in regulating glucose homeostasis and a possible role in development of insulin resistance, a study can be conducted to evaluate the role of fetuin A in predicting pre diabetes and its progression to diabetes. However to the best of our knowledge, there are not many Indian studies which assess the risk of development of type 2 diabetes in offsprings of diabetic parents.

Significance of such research endeavor

The association of fetuin A and adiponectin levels with insulin resistance, if established may help in understanding the pathogenesis and the risk of type 2 diabetes in the offsprings of diabetic parents. The above mentioned parameters may emerge as newer biomarkers for the detection of risk of developing type 2 diabetes in the offsprings at an early stage.

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