Gestational Diabetes Mellitus: Risk Factors & Genetic Predispositions

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ABSTRACT

About one-fifth of entire pregnant female population develop Gestational Diabetes Mellitus (GDM) in course of their pregnancies and its incidence has been considerably augmented during the last decade. Development of the multifactorial disease GDM can be attributed to elevated insulin resistance during pregnancy triggered by a genetic predisposition to retardation of pancreatic islet β-cell functionality. Polymorphisms in multiple genes like TCF7L2, GCK, HNF4 KCNJ11, CDKAL1, IRS1 and MTNR1B are associated with increased susceptibility to GDM. Epigenetic alterations like gene silencing of pdx1 by DNA methylation and histone modification coupled with dysregulation of microRNAs like miR-155-5p, miR-21-3p, miR210-3p etc. also increases menace of GDM. GDM is a trans-generational effect that might contribute to the vast increase in the prevalence of type 2 diabetes mellitus (T2DM). An elaborate understanding of connection between specific genetic and epigenetic components associated with it may be helpful in prognosis of this disorder.

I. Introduction

Gestational Diabetes Mellitus (GDM) is a health impairment characterized by hasty glucose intolerance and insulin resistance identified for the first time during pregnancy (Veeraswamy S et al., 2012). It is identified by a retardation in insulin secretion or greater insulin resistance (Barbour LA et al, 2007). GDM is found to be closely linked with the risk of perinatal complications and also with the pertinent risk of developing T2DM in the future life of both mother and child (Ramirez-Torres MA, 2013). During the period of a typical pregnancy, numerous physiological modifications occur within the maternal body that provides a metabolic environment to favour fat deposition and optimized foetal growth. In due course of gestation, insulin secretion enhances to its optima till the third trimester, and then insulin sensitivity decreases progressively by 70% (Mithal A et al,2015). In normal pregnancy, pancreatic β-cell recompense for the heightened insulin resistance to regulate blood glucose. However, in GDM-complicated gestation, the insulin secretion capability reduces with the reduction in β-cell function and leads to deterioration of glucose tolerance (Seshiah V et al, 22004). So, it is postulated that GDM is the consequence of elevated insulin resistance during gestation triggered by a genetic predisposition to non-functionality of pancreatic islet β-cells (Ferrara A et al, 2007). Recent studies showed that about 4 million women are affected by GDM in India, at any given point of time (Permutt MA et al, 2005). The child-bearing age of present generation of women being in 30s complemented by their tendency to suffer from overweight and obesity as well as fully established metabolic syndrome, plays an important role in the increasing incidence of GDM (Carpenter MW, 2007)

Being a complex multifactor metabolic d.isorder, GDM is likely an outcome of a combination of variations in different genetic attributes. According to affirmation by several

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