

# Vagal Withdrawal Could be Critical in the Pathogenesis of Gestational Diabetes Mellitus

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Gestational Diabetes Mellitus (GDM) is a state of Impaired Glucose Tolerance (IGT) with onset or first recognition during pregnancy. Worldwide, one in 10 pregnancies is associated with diabetes, 90% of which are GDM. Undiagnosed or inadequately treated GDM can lead to significant maternal and fetal complications. Moreover, women with GDM and their offsprings are at increased risk of developing type 2 diabetes later in life. In India, the incidence of GDM is 10-20%, which is much higher than the west. In a field study in Tamil Nadu performed under the Diabetes in Pregnancy: Awareness and Prevention project, the prevalence of GDM was 17.8% in the urban, 13.8% in the semi urban and 9.9% in the rural areas.<sup>[1]</sup> The incidence of GDM is expected to increase to > 20% i.e., at least one in every 5 pregnant women is likely to have GDM. Despite a high prevalence of GDM in Indian women, currently screening of pregnant women for GDM is not being done universally as part of the essential antenatal check-ups. GDM being a major public health problem with serious adverse effects on mother and child, there is a need of understanding the basic pathophysiology of the disease and evolving the cost-effective management strategies.

Increased glucose intake has been shown to be associated with alteration in the activity of the autonomic nervous system. Cardiovascular autonomic function and baroreflex sensitivity are inversely related to blood glucose levels in healthy individuals. During pregnancy, there are significant physiological alterations in glucose absorption and metabolism that cause an increase in insulin resistance.<sup>[2]</sup> In addition, profound hemodynamic changes occur in pregnancy, with an increase in cardiac output and a decrease in total peripheral resistance accompanied by an expanded blood volume.<sup>[3]</sup> The abrupt changes in blood glucose along with associated cardiovascular alterations may cause maternal and fetal metabolic and cardiovascular dysfunctions in pregnancy.

Heart rate variability, modulated by diverse central and peripheral inputs, provides a quantitative marker of autonomic activity. Spectral analysis of heart rate variability is an accepted method for assessing the autonomic nervous system and permits a non-invasive evaluation of the sensitivity of the sinoatrial node to sympathetic and parasympathetic activity. HRV studies in GDM have revealed

sympathovagal overactivity as the cause of autonomic imbalance leading to metabolic and cardiovascular dysfunctions.<sup>[4]</sup>

Clinically and metabolically, GDM resembles T2DM. The hallmark feature of GDM is insulin resistance. Insulin resistance in GDM is usually due to pancreatic  $\beta$  cell dysfunction, in which  $\beta$  cells of islets fail to acclimatize to the growing demands of insulin during pregnancy. Many hormones such as estrogen, cortisol, human placental lactogen which are called as diabetogenic placental hormones hinders the action of insulin on binding of insulin to its receptor in the later part of pregnancy. It could be also that the levels of prodiabetogenic placental hormones increase in GDM. As GDM is metabolically similar to T2DM, the cardiometabolic risk profile in GDM may possibly also be close to that of diabetes mellitus. However, till date, pathophysiological mechanisms of cardiometabolic risks have not been elucidated in GDM.

A recent report has demonstrated that short-term practice of yoga consisting mainly of pranayama in the later weeks of gestation could reduce the intensity of GDM and improve maternal outcomes in pregnancy.<sup>[5]</sup> Many studies have reported the beneficial effect of the practice of yoga on diabetes, confirming that the practice of yogasana can stimulate the insulin producing cells in the pancreas and by increasing insulin sensitivity that lowers blood sugar level. Although the effect of yoga on maternal and neonatal outcome variables has not been studied more in pregnancy, several studies have looked at these variables. Available evidence like Rakhshani, *et al.* reported that yoga can potentially be an effective therapy in reducing the complications of pregnancy and improving fetal outcomes.<sup>[6]</sup> Yoga also enhances the sense of well-being and decreases the level of stress. Thus, the practice of yoga leading to reduction in cardiovascular risks and complications of GDM patients indicates that improvement in fetomaternal parameters could be due to attainment of autonomic balance as yoga primarily influences the sympathovagal homeostasis. Especially, practice of slow pranayamas improves vagal tone of the individual.<sup>[7]</sup>

We have earlier reported that sympathetic activity increases in later part of pregnancy. But it appears from the recent reports that in addition to increased

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## History

- Submission Date: 28-07-2021;
- Review completed: 28-08-2021;
- Accepted Date: 06-09-2021.

DOI : 10.5530/ijcep.2021.8.3.25

## Article Available online

<http://www.ijcep.org/v8/i3>

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**Cite this article:** Pal GK, Renugasundari M. Vagal Withdrawal could be Critical in the Pathogenesis of Gestational Diabetes Mellitus. Int J Clin Exp Physiol. 2021;8(3):107-8.

sympathetic activity, there is vagal withdrawal in gestational diabetes, and decreased vagal activity decreases insulin secretion and sensitivity causing insulin resistance and diabetes in pregnancy. It is likely that the yoga consisting mainly of slow pranayama improves the vagal activity and insulin secretion in GDM and thus in turn decreases the severity of GDM. Thus, we theorize that vagal withdrawal plays a critical role in the pathophysiology of GDM. Therefore, any strategy to improve vagal strength will reduce the severity of GDM and will improve the fetomaternal outcomes in this common disorder of pregnancy. India being a developing nation, and GDM being more prevalent in India, treatment strategies should aim at increasing vagal tone in GDM women, which could be less cost effective and more socially and psychologically acceptable to the pregnant women.

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