



## ASSOCIATION OF GUT MICROBIOTA WITH THE PATHOGENESIS OF GESTATION DIABETES, DEPRESSION LINKED TO IT AND FETAL OUTCOME: A REVIEW

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### Abstract

Gestational diabetes mellitus (GDM), which accounts for 86% of pregnancy-related hyperglycemia, is a kind of pregnancy-related glucose intolerance that results in hyperglycemia. Compared to prospective mothers who are healthy, pregnant women with GDM are more likely to develop maternal and neonatal issues. There has been a lot of focus on the problems with pregnant women's mental health, especially the high-risk population of GDMs. Studies show that melancholy and anxiety, in addition to physiological factors, are important causes of gestational diabetes.

It is important to completely comprehend the degree of gastrointestinal microflora changes that cause GDM and depression as well as their causative relationship with bacterial commensals.

Aim of the review is to discuss the association of gut microbiota dysbiosis and the possible mechanistic links between the gut microbiota in women and GDM as well as the association between maternal gut dysbiosis and pregnancy outcome.

**Key words:** gestational diabetes, gut microbiota, fetal outcome

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## Introduction

### Gestational diabetes and depression

Pregnancy-related carbohydrate intolerance that causes hyperglycemia is known as gestational diabetes mellitus (GDM), which accounts for 86% of pregnancy-related hyperglycemia [1]. Pregnant women with GDM are more likely to experience maternal and newborn problems compared to healthy expectant mothers [3].

Pregnant women's mental health issues, particularly the mental health of GDMs, a high-risk population, have received a lot of attention. Studies have shown that, in addition to physiological variables, sadness and anxiety have a significant role in the development of gestational diabetes [4]. On the relationship between anxiety, depression, and GDM, there is no consensus, nevertheless. On the one hand, the study discovered that anxiety and depression can cause persistent hyperactivity of the hypothalamus, pituitary, and adrenal glands, which increases cortisol secretion and insulin resistance [5] and raises the chance of developing gestational diabetes in pregnant women. The diagnosis of GDM may also, via a reverse process, increase the likelihood of prenatal or postnatal depression [6]. This shows that there might be a reciprocal association between anxiety and depression and gestational diabetes. Contrarily, some research suggests that anxiety and depression do not raise the likelihood of prenatal or postnatal depression [8–10] and that the diagnosis of GDM does not increase the incidence of GDM in pregnant women [7]. There is currently no agreement on how anxiety, depression, and GDM are related. This review is an attempt to explore the bidirectional relationship between anxiety, depression and GDM.

### Gut Microbiome and Depression

Depression is a serious mental illness caused by multiple factors [11]. It is described as low emotional disposition, loss of confidence, and apathy [12]. Depression is suggested to result from complex interactions of an individual's genetics and their environment. Dysbiosis of gut microbiota may be one of the causative factor for depression.

The synthesis of microbial lipopolysaccharides (LPS) is triggered by any variations in the gut microbiome's makeup. In turn, it sets off inflammatory reactions. The vagus nerve, which connects the process to the hypothalamic-pituitary-adrenal axis and subsequently generates behavioural effects, receives signals from cytokines. Another school of thinking contends that

neuro-inflammation comes from GI tract inflammation. After that, it stimulates microglial activity and opens the kynurenine pathway. Depression is caused by each of these processes [13]. Evidence of altered microbiota composition has been linked to depression in human studies [14]. Research has amply shown the two-way relationship between gut flora and depression. However, as was already established, it is still necessary to establish which entity causes the other [15]. Many research studies have directed their attention to understanding the interaction between the gut microbiome and the brain.

### GDM and Microbiota

As with the T2DM profile, mounting data strongly links gut microbiota dysbiosis in women with GDM. Numerous metagenomics investigations have revealed that women with GDM had enriched gut microbiota, including Ruminococcaceae, Parabacteroides distasonis, and Prevotella. These bacterial communities are linked to insulin signalling, glucose metabolism, and metabolic pathways, raising the possibility of a "gut microbiota signature" in women with GDM. Additionally, early pregnancy in GDM-afflicted women showed higher expression of serum zonulin, a marker of gut epithelial permeability, suggesting a potential relationship between gut microbiota and GDM. The interaction between gut microbiota dysbiosis and host metabolism in women with GDM is still unclear, as only a few research have produced inconsistent findings. A growing source of GDM indicators is the dysbiosis of the gut microbiota, which has been associated to gestational diabetes mellitus (GDM). However, our knowledge of how the gut microbiota affects GDM is still limited.

Recent research has linked GDM and gut microbiota [16,17]. Dysbiosis in the gut microbiota is a characteristic of GDM. Hyperglycemia and the ratio of control-enriched to GDM-enriched bacteria are inversely associated [16]. Potential biomarkers for GDM are being found in the metabolome and microbiota [18].

Although the links between GDM and gut microbiota have been shown, it is still unclear how the gut microbiota interacts with the host [19].

### Maternal mental health and fetal outcome

Since the perinatal period is crucial for neurodevelopment, it is also a vulnerable phase when a variety of exposures have been discovered to have long-lasting effects on brain growth and behaviour. Studying the molecular mechanisms underlying the influence of antenatal psychological

discomfort on foetal behaviour and infant development is fascinating.

It has been demonstrated that maternal prenatal anxiety and/or depression increases the likelihood of both future mental illness and neuro developmental problems in children. According to reports, young children with impaired emotional adjustment have greater levels of prenatal depression and anxiety [20]. Women's anxiety (and/or depression) during pregnancy has been demonstrated to affect the hypothalamic-pituitary-adrenal (HPA) axis, predicting symptoms of attention deficit hyperactivity disorder (ADHD) in children as well as childhood and adolescence [21].

Therefore, it is reasonable to attribute the pathophysiology of GDM and depression linked to GDM to the gut microbiota.

#### Future research perspectives

A study may be planned with the goal of comparing the gut microbiota of GDM patients with that of normoglycemic pregnant women as controls, assessing and comparing the depression scores of cases and controls, and discovering the relationship between depression, GDM, and gut microbiota dysbiosis as well as the relationship between depression, GDM, and gut microbiota dysbiosis and pregnancy outcome as measured by the baby's birth weight and APGAR score.

#### Expected outcome/Significance of the study

The research of the gut microbiota is encouraging and offers a number of benefits, such as risk-free and non-invasive sample collecting. Self-sampling without location restrictions is possible with a streamlined technique of sample storage and transfer, making it easier to conduct frequent tests and increasing the likelihood of identifying both GDM and depression. This could help GDM sufferers by proving that the gut microbiota plays a part in depression.

The connection between gut dysbiosis, GDM, and sadness in this study makes it new. The study may shed information on the therapeutic application of probiotics in post-GDM women as a means of preventing T2DM and depression.

Considering the importance of mother's mental health for a better foetal outcome, the study of gut microbiota causing mental health is a relatively recent area of inquiry. There are still several areas that require investigation and clarification. It may be possible to identify the cross-talk between

depression and GDM through a thorough analysis of the gut microbiota that contributes to both conditions.

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