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Gestational Diabetes Mellitus and Maternal Microbiome Alterations

Dalia Rafat

Abstract

The maternal microbiome has been identified as a critical driver for a variety of important mother and child health outcomes. Studies have demonstrated changes in maternal microbiome during pregnancy. These changes may have an impact on the maternal metabolic profile, play a role in pregnancy problems, and contribute to the metabolic and immunological health of the offspring. Gestational diabetes mellitus is a major challenge for prenatal healthcare providers, not only because of the negative short and long-term effects on the mother's and baby's health, but also because its aetiology has been poorly understood till now. The developing link between maternal microbiome and metabolic disorders in pregnancy can be offered as a new target in their prevention and treatment, as well as in reducing their negative health outcomes; however, there has been very little research done on this. Diabetes' impact on site-specific maternal microbiome alterations during pregnancy is similarly poorly understood. Given the rising prevalence of diabetes in pregnancy and the potential importance of the maternal microbiome, more research is needed to understand and rigorously examine how metabolic disorders in pregnancy affect the pregnancy-associated microbiome, as well as whether these microbial alterations affect the health of the mother and her offspring.

Keywords: pregnancy, gut microbiota, vaginal microbiota, oral microbiota, gestational diabetes mellitus

1. Introduction

The human body harbors complex community of microorganisms over different sites in the body [1]. Numerous microorganisms live in the human body and maintain a stable symbiotic relationship with the host, which is essential for human health. These unique microbial communities residing on and in the human body comprise "Human microbiome". The Human Microbiome Project [1], launched to demonstrate the human microbial flora and its association with human health, characterized the microbial communities residing over five areas in the body: oral cavity, nasal cavity, skin, gastrointestinal tract and genitourinary system. They found that more than 10,000 microbial species harbor the human body and successfully identified around 81–99% of genera constituting the human ecosystem [1].

The significance of the human microbiome in preserving health is becoming increasingly evident, and it may potentially guard against unfavorable health outcomes by stimulating or suppressing both genetic and environmental risk factors. The gut microbiome, for example, has been linked to the body's immune system, since it protects against various invading bacteria [2]. Likewise, the healthy

vaginal microbiome has an important role in the prevention of various cervicovaginal infections [3]. Besides a variety of diseases have been linked to an imbalance in the human microbiota. The use of human microbiome as disease biomarkers has become a promising strategy [4, 5]. Studies have discovered that using microbiome composition and alterations to diagnose diseases has a lot of promise [6].

2. Pregnancy and human microbiome

Women underwent a variety of physiological changes throughout pregnancy. During pregnancy, the maternal body habitat microbiome composition changes as well [7, 8]. The maternal microbiome has been recognized as a key determinant of a range of important maternal and child health outcomes, and together with perinatal factors influences the infant microbiome [9].

The microbiome alterations and disturbances during pregnancy and neonatal life has received great interest in recent years owing to the crucial role it plays in reproductive health. These changes may have an impact on the maternal metabolic profile, play a role in pregnancy complications, and contribute to the metabolic and immunological health of the offspring [9], implying that microbial communities' interactions with pregnant women are crucial.

3. Gestational diabetes mellitus and human microbiome

Diabetes and related metabolic disorders are rapidly increasing among pregnant women throughout the world [10, 11]. Gestational Diabetes Mellitus (GDM) is a major challenge for obstetric practice not only because of the adverse short and long term fetomaternal health consequences but also because of its improperly understood etiology till now. Current prevention strategies focusing on changes to diet and physical activity have resulted in limited success leading to an urgent need for alternative strategies.

The significance of the microbiome in many physiological processes involved in health and the development of various diseases is still unknown. Due to increased inflammation, insulin resistance, and weight gain in women with GDM, it has been postulated that the physiological adaptation of the microbial pattern seen in pregnancy is disrupted in women with metabolic illnesses, such as GDM [8, 12].

Microbiome and its alterations at various body sites has been demonstrated to influence metabolic disorders by a number of researchers. As only few scant studies are done on microbiome's complexity of different body compartments in GDM [5, 13], their interactions and exact role in the pathogenesis of GDM is still not clear. Some researchers have indicated that GDM has no clear effect on the microbial composition [14] while others have found that the microbiota of GDM patients and normal pregnant women differs significantly [5, 13, 15].

Studies have demonstrated that microbiome of different body compartments like gut/oral/vaginal microbiome influences gestational development and metabolic disorders. It however is still not clear whether there is an interaction between the microbiome of the different compartments and their role in GDM pathogenesis.

3.1 GDM and gut microbiome

Human gut microbiome is becoming more well acknowledged as key contributor to host metabolism and health [16]. The maternal gut microbiota changes

dramatically during pregnancy [8] and has been linked to a variety of adverse pregnancy outcomes, including obesity, gestational hypertension and GDM [17]. Researchers are exploring the gut immune system as a new therapeutic target for systemic inflammation in insulin resistance. As a result, the gut microbiota has been the focus of several investigations on GDM and several recent investigations have found specific changes in gut microbiome between pregnant women with and without GDM [5, 18–22]. According to current theories, the proposed pathogenesis of insulin resistance due to dysbiosis of intestinal microbiota; include influencing inflammatory responses [23], boosting fat accumulation [24], controlling bile acid metabolism [25], and regulating amino acid metabolism [26].

Understanding the gut microbiota's alterations will not only help us better understand GDM pathogenesis but will also promote prospective preventive approaches for GDM based on gut microbiota modification. Although various studies have linked maternal gut microbiota dysbiosis to GDM, the exact potential role of gut microbiota in the etiology of GDM is still unclear. Future large-sampled well-designed studies are required to elucidate the role of gut bacterial dysbiosis in the pathogenesis of GDM, and in exploring gut microbiota-targeted biomarkers as potential predictors of GDM.

3.2 GDM and vaginal microbiome

The healthy vaginal microbiome has an important role in the prevention of bacterial vaginosis, vaginal candidiasis, and other cervicovaginal infections [3]. During pregnancy, there is a change in the structure of the vaginal microbiome [7, 27], which contributes in increasing the presence and stabilization of *Lactobacillus* in the vaginal microbiome [27, 28]. Besides preventing bacterial invasion, the vaginal microbiome has been postulated to play vital role in timing parturition, hormone secretion and, importantly, seedling of infant microbiome during birth.

Emerging studies have reported link between the vaginal microbiome and metabolic illnesses such GDM [20, 29]. Studies have demonstrated increased inflammatory cytokine expression in GDM, together with the presence of potentially pathogenic bacteria, indicating a dysbiotic profile of the vaginal microbiome [20].

Researchers have speculated on the role of the vaginal microbiota in pregnancy outcomes, which have been shown to have a negative impact on neonatal and infant health, as well as the association of the vaginal microbiome with both health and disease states, but there are few studies to validate these speculations. According to the limited scarce studies on this subject, pregnant women with hyperglycemia have a greater prevalence of vaginal infections, and both hyperglycemia and an aberrant vaginal dysbiosis are linked to poor fetomaternal outcomes [12, 20, 29]. Exploring the vaginal microbiome alterations of women with GDM and its relationship to adverse pregnancy outcomes could help in the early detection and treatment of dysbiotic alterations that could lead to poor maternal and neonatal outcomes.

3.3 GDM and oral microbiome

The oral microbiome has been proposed in the development of a variety of diseases, but its link to GDM is still a mystery. Recent studies have shown substantial changes in the oral microbiota between GDM and non GDM patients in pregnancy and puerperium [30] indicating potential role of the oral microbiome as noninvasive GDM biomarkers.

Numerous studies have demonstrated a link between GDM and periodontitis [31, 32]. The incidence of GDM has been reported to be higher in people with periodontitis. Periodontal infection has been linked to an increased risk of GDM via disrupting endocrine metabolism and blood glucose regulation [33], although it is unclear whether the relationships between these two diseases are caused by microbiome alterations.

Future large scale studies are required to analyze the oral microbiome of GDM patients and healthy pregnant women to see whether there are any links between GDM and two main oral diseases: dental caries and chronic periodontitis. Also studies are required to find appropriate oral microbial markers for constructing GDM classification models and establish simple and noninvasive techniques for supplementary diagnosis and daily GDM follow-up.

4. Conclusion

There is potential importance of the maternal microbiome for maternal and infant health. Pregnancy-related changes to the maternal microbiota are evolutionarily adaptive to promote the nutrition and development of the mother and fetus during pregnancy, and the child after birth. The developing link between maternal microbiota and metabolic disorders in pregnancy can be offered as a new target in their prevention and treatment, as well as in reducing their negative maternal and neonatal outcomes, however there has been very little research done on this. Lack of robust research on the impact of diabetes on the maternal microbiota during pregnancy is also a problem. Large longitudinal cohort studies of racially and ethnically diverse mother-child dyads are required to rigorously examine how hyperglycemia in pregnancy modifies the pregnancy-associated microbiota and the mother-to-newborn vertical transfer of microbiota, and to consider whether these microbial alterations affect the health of the mother and her offspring, and if these microbial alterations can ultimately be targeted for interventions that improve public health.

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