

Mood Dysregulations in GDM

Subjects: **Others**

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Gestational diabetes mellitus (GDM) is a metabolic condition of increased maternal blood glucose level. GDM affects up to 36% of pregnant women. Mood dysregulations (MDs, e.g., depression, distress, and anxiety) are common among women with GDM. Symptoms of depression and anxiety usually overlap with one another as well as with distress symptoms; they develop in up to 27% and 24% of pregnancies, respectively.

Mood Dysregulations

gestational diabetes

intermittent fasting/dietary interventions

1. Overview

The co-occurrence of GDM and MDs is high, and it is closely linked to poor glycemic control, poor self-care ability, functional disability, low quality of life, and premature death. Depression in diabetics is hard to treat given the complex nature of diabetes, especially when it occurs during pregnancy^[1]. Both conditions share common risk factors, pathologies and adverse effects for mothers and their offspring^[2].

2. Adverse effects of GDM and MDs

GDM is associated with numerous morbid maternal and fetal outcomes: miscarriage, dystocia, cesarean section, neonatal death, premature birth, congenital anomalies, macrosomia (large for gestational age), respiratory distress, neonatal jaundice, hypoglycemia, hypocalcemia, and polycythemia^{[3][4][5]}. Meanwhile, MDs increase the likelihood of prematurity, birth weight abnormalities, stunted growth, cognitive and neurodevelopmental deficits, infants' temperament, anxiety, and depression, delays in fine motor and language development^{[6][7]}, not initiating breastfeeding, early termination of breastfeeding, increased formula usage^{[8][9]} [15,16], poor maternal antenatal attachment, and higher postpartum parenting stress^[8].

3. Risk factors and pathophysiological mechanisms common in GDM and MDs

The accelerated prevalence of GDM and MDs is associated with common risk factors such as poverty, unhealthy diet and sedentary lifestyle, which contribute to chronic inflammatory conditions such as obesity and type 2 diabetes mellitus (T2DM)^{[10][11][12][13]}. Sleep disturbances, some of them develop in mood disorders (e.g., apnea, poor sleep quality, and short sleep), trigger the development of GDM^{[10][11]}. Both GDM and MDs share common mechanisms^[2] illustrated in Figure 1 and described in detail in this section.

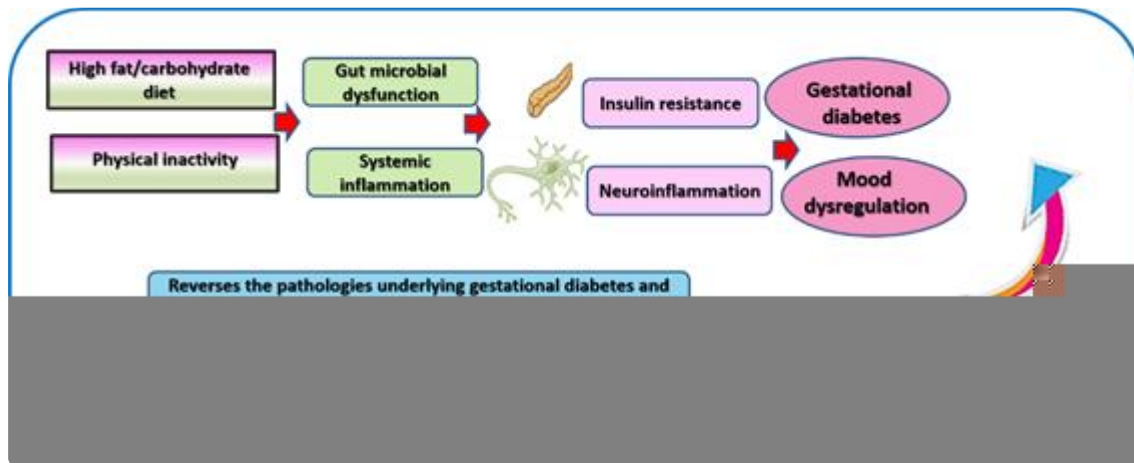


Figure 1. Schematic summary of key risk factors and pathologies contributing to gestational diabetes and maternal mood dysregulation along with the therapeutic role of dietary interventions and physical activity in reverting these conditions.

Unhealthy food (rich in fat and refined carbohydrates and deficient in dietary fibers that exist in fruits and vegetables) and physical inactivity promote the propagation of toxic endobacteria and inhibit the growth of beneficial gut microflora^{[14][15][16]}. Such imbalance result in a deficiency of nutritive metabolites produced by beneficial bacteria, which are necessary for proper immune function and overall health^{[2][17][18][19]}. In addition, toxic bacterial metabolites cause injury to the intestinal wall to cause disseminated tissue damage e.g., in the brain leading to MDs and in the pancreas leading to GDM^[2].

The inflammatory reaction and associated oxidative stress conducive to GDM and MDs is accelerated by fetal tissue and placental-related molecules [4,27-29]. Secretions of these tissues bind the receptor of advanced glycation end products (RAGE) and toll-like receptors (TLR2 and TLR4), which indirectly activate C-X-C chemokine receptor type 4 (CXCR4)^{[20][21][22][23]}.

Estrogen is a key modulators of signal transduction that regulate cognition and mood^{[15][24]}. Alterations in estrogen are a key contributor to the high development of negative emotional states among women at different stages of life^{[24][25]}. Estrogen dysfunction occurs in GDM due to oxidation of estrogen by cytochrome P450 enzymes resulting in genotoxic metabolites such as 2-hydroxyestrogen and 4-hydroxyestrogen. These metabolites exist in the blood, and they induce DNA damages in various tissues. They also bind insulin, neuroglobin, human serum albumin, and immunoglobulin. Their binding to insulin, a process known as insulin estrogenization, hinders insulin affinity of binding to insulin receptor resulting in vivid insulin resistance^[26]. In the meantime, dysfunctional estrogen is incapable of modulating brain structures

MDs in pregnancy may occur in response to the psychosocial stress imposed by pregnancy, hormonal fluctuations associated with pregnancy, as well as the inflammatory milieu generated by GDM and its underlying pathologies^[2].

4. Common non-pharmacological interventions for GDM and MDs

Physical exercise is well-known to increase the sensitivity of body tissue to insulin resulting into glycemic control^{[16][19]}. It is also an effective treatment for mood disorders^{[27][28]}. Its therapeutic effects take place through the regulation of key signaling molecules involved in cellular activities as well as correction of gut dysbiosis, thus preventing gut-related systemic inflammation^{[16][19][29][30]}.

A plethora of research emphasize the role of functional foods in the control of GDM and MDs^{[28][31][32]}. Such foods correct gut microbiome dysfunction, modulate signaling involved in metabolism, immune function, antioxidant production, autophagy, etc.^{[17][18][33][34]}. A considerable attention is paid to refraining from high fat/high carbohydrate diets and adopting dietary patterns that involve the intake of fresh fruits, vegetables, sea foods, complex carbohydrates (whole grains and bran of wheat and rice), bee products, etc.^{[2][16][35][36]}. Intermittent fasting (IF) as a form of dietary restriction has been effectively used to correct pathologies that underlie T2DM and MDs. We have recently demonstrated a case of GDM properly managed by IF indicating that this modality may prove to be effective if investigated on a large scale^[2].

5. Conclusion

Both GDM and mood disorders are common in pregnancy, and their co-occurrence leads to grave effects on mothers and their fetus. Both conditions can be exacerbated by unhealthy diet and sedentary behaviors while dietary patterns such as IF, the intake of functional foods, and physical exercise can reverse the pathologies that underlie these conditions leading to better outcomes.

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