

**Review Article**

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## **Maternal Obesity and Gestational Diabetes Mellitus: The Pathological Programming.**

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### **Abstract**

**Background:** Onset or development of glucose intolerance during the period of gestation is termed as gestational diabetes mellitus. Maternal obesity along with GDM is found associated with development of adverse maternal and fetal health outcomes.

**Method:** Researches with a focus on maternal obesity and gestational diabetes mellitus were included in this study.

**Results:** Elevated state of maternal body mass index is found to raise the inflammatory condition in GDM, which may play role in impacting downstream metabolic processes giving rise to manifestation of glucose dysregulation and condition of insulin resistance. Obesity in gestation, is related to the alterations in metabolic status comprising dyslipidemia, hyperinsulinemia, impaired endothelial functioning, and increased blood pressure.

**Conclusion:** Previous studies have provided findings associating the risk of GDM development with the state of BMI, which emphasizes the need to explore mechanisms governing obesity mediated GDM development and related maternal and fetal health complications during gestation. In view of existing literature, weight management and engagement in physical activities should be encouraged among women during and after the period of gestation.

### **Keywords**

Maternal Obesity, Body Mass Index, Gestational Diabetes Mellitus, Physical Activity.

Glucose intolerance with an onset or first recognition during gestation is termed as gestational diabetes mellitus (GDM) <sup>1</sup>. The insulin resistance in GDM is found associated with impaired insulin receptor auto-phosphorylation resulting from its reduced protein expression<sup>2</sup>. GDM is considered as a risk factor for various adverse health outcomes<sup>3</sup>, including the future development of type 2 diabetes<sup>2, 4-6</sup> and metabolic syndrome<sup>4</sup>. Maternal obesity coupled with GDM is found to influence perinatal outcomes<sup>7</sup>. Moreover, previous findings have indicated obesity and diabetes as two independent risk factors for multiple poor outcomes of pregnancy<sup>8</sup>.

The related consequences of maternal glucose intolerance is found to impact fetal health outcomes <sup>9,10</sup> including increased risk of early obesity, development of type 2 diabetes and metabolic syndrome<sup>4</sup>. Obesity coupled with GDM is found associated with pathogenesis of offspring congenital anomalies, including defects at craniofacial and musculoskeletal level<sup>11</sup> and large for gestational age risk<sup>12</sup>. Furthermore, obesity and GDM are found to elevate placental leptin methylation which may represent one of the possible ways through which placental epigenetic changes influence fetal health conditions<sup>13</sup>. Obesity and GDM may contribute in intrauterine reprogramming of

offspring obesity<sup>14</sup>, vascular disease<sup>15</sup>, macrosomic neonates<sup>16</sup>, cesarean delivery<sup>16</sup>, and other fetal health complications<sup>13</sup>.

Increased maternal weight is reported to be related with a higher risk of GDM<sup>17</sup>. Elevated maternal BMI status is found to mediate inflammatory responses during GDM<sup>18, 19</sup>, which may play its part in altering the maternal normal regulation of insulin signaling and the glucose transport processes<sup>19</sup>. Maternal obesity and GDM may play role in indirect programming of fetus for diseases by impacting placental functioning during period of maternal inflammatory milieu; the placenta is found to adjust to this environment of inflammation and participate as the target part and producer region of inflammatory mediators<sup>20</sup>. Obesity in gestation is found to alter metabolic status comprising dyslipidemia which is reported to be manifested approximately 10 weeks before GDM diagnosis during period of late second trimester<sup>21</sup>. Furthermore, obesity in pregnancy as in obese women (non-pregnant), is found related to altered condition of hyperinsulinemia, dyslipidemia, compromised endothelial functioning, and elevated blood pressure and enhanced inflammatory state<sup>15</sup>. These impaired conditions may underpin the mechanisms driving complications in obese women with GDM<sup>15</sup>.

The risk of GDM development is found associated positively with the state of BMI prior gestation<sup>22</sup>. In obese women, the GDM risk is found to escalate 1.3–3.8 times as compared to women having normal BMI<sup>23</sup>. Previous study presented findings indicating that reduced levels of plasma adiponectin is linked to GDM, exhibiting insight into state of insulin resistance and inflammation in GDM<sup>24</sup>. Obese women with GDM have

shown elevated insulin response but reduced sensitivity of insulin and also reduced hepatic glucose formation during period of insulin infusion with state of progressing gestation<sup>25</sup>. These abnormal conditions at metabolic level may provide insight into type 2 diabetes development in women with GDM later in life<sup>25</sup>. The diagnosis of GDM coupled with altered  $\beta$ -cell functioning and obese BMI status are found associated with future diabetes development<sup>26</sup>. Maternal serum C-reactive protein levels are found related with pre-pregnancy obese BMI status and not to GDM, depicting potential model for obesity driven inflammation at systemic level, which may further impact downstream metabolic pathways contributing toward manifestation of glucose dysregulation and insulin resistance state<sup>19</sup>.

In view of existing literature, which associate GDM risk with BMI, weight management and physical activity should be encouraged among women during the childbearing period and the time beyond<sup>22, 27-32</sup>.

#### Conflicts of interests

None.

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