GESTATIONAL DIABETES MELLITUS: HORMONAL CHANGES AND MECHANISMS OF INSULIN RESISTANCE

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Relevance of the Study

Gestational diabetes mellitus (GDM) is a pregnancy-specific metabolic disorder characterized by glucose intolerance first detected during pregnancy. It has become a major global health concern due to its rising prevalence, closely linked to increasing maternal age, sedentary lifestyles, obesity, and urbanization. According to recent epidemiological data, GDM affects approximately 7–10% of pregnancies worldwide, with significantly higher rates in some Asian and Middle Eastern countries.

Physiologically, pregnancy induces a state of progressive insulin resistance to ensure adequate glucose supply for the growing fetus. While this adaptation is beneficial in normal pregnancies, in predisposed women it leads to hyperglycemia, β-cell dysfunction, and the clinical manifestation of GDM. Elevated levels of placental hormones — including human placental lactogen (hPL), cortisol, estrogen, progesterone, and placental growth hormone — antagonize insulin action, decrease maternal insulin sensitivity, and alter lipid and carbohydrate metabolism.

The importance of this topic stems from the fact that untreated GDM increases the risk of preeclampsia, cesarean delivery, and type 2 diabetes in mothers, as well as macrosomia, birth injuries, neonatal hypoglycemia, and long-term metabolic disorders in offspring. Early detection, pathophysiological understanding, and effective interventions are therefore essential to improve maternal-fetal health outcomes globally.

Aim of the Study

The aim of this study is to analyze hormonal changes and insulin resistance mechanisms in the pathogenesis of GDM, assess maternal and fetal risks associated with hyperglycemia during pregnancy, and summarize evidence-based strategies for screening, prevention, and management.

Materials and Methods

This review analyzed 65 peer-reviewed articles published between 2010 and 2024 in journals indexed in PubMed, Scopus, and Web of Science. Clinical guidelines from the American Diabetes Association (ADA), the International Federation of Gynecology and Obstetrics (FIGO), and the World Health Organization (WHO) were also reviewed.

Search keywords included *gestational diabetes mellitus, insulin resistance, pregnancy hormones, maternal-fetal outcomes, hyperglycemia,* and *beta-cell dysfunction*. Data were extracted on:

- Prevalence and risk factors of GDM
- Hormonal changes during pregnancy
- Pathophysiological mechanisms of insulin resistance
- Diagnostic strategies and screening protocols
- Maternal and fetal complications
- Preventive and therapeutic interventions

Results

The literature analysis yielded the following findings:

1. Hormonal Changes and Insulin Resistance

- **Human Placental Lactogen (hPL):** Secreted by the placenta, hPL levels rise progressively with gestational age, inducing lipolysis and reducing maternal glucose utilization to prioritize fetal glucose supply.
- **Cortisol:** Increased maternal cortisol stimulates hepatic gluconeogenesis and inhibits insulin action, exacerbating hyperglycemia.
- **Estrogen and Progesterone:** These hormones impair insulin receptor signaling and modulate pancreatic β-cell response. Elevated progesterone levels may contribute to β-cell exhaustion in predisposed women.
- **Placental Growth Hormone and Adipokines:** Altered secretion of leptin, adiponectin, and resistin further worsens insulin resistance and promotes a pro-inflammatory metabolic environment.

2. Maternal Complications

Women with untreated GDM face higher risks of:

- Gestational hypertension and preeclampsia (15–20%)
- Polyhydramnios and preterm delivery (10–15%)
- Cesarean section due to macrosomia or obstetric complications (25–30%)
- Future type 2 diabetes mellitus, with a 40–60% risk within 10 years postpartum

3. Fetal and Neonatal Complications

Maternal hyperglycemia leads to fetal hyperinsulinemia, resulting in:

- Macrosomia (birth weight >4 kg) in 15–25% of cases
- Neonatal hypoglycemia due to sudden withdrawal of maternal glucose post-delivery
- Respiratory distress syndrome and electrolyte imbalances
- Long-term metabolic disorders including childhood obesity and early-onset type 2 diabetes

4. Screening and Early Diagnosis

- Universal screening at 24–28 weeks with oral glucose tolerance test (OGTT) identifies asymptomatic cases and reduces complications by 50–60%.
- Early screening in high-risk women (obesity, polycystic ovary syndrome, family history of diabetes) before 20 weeks allows preventive lifestyle interventions.

5. Preventive and Therapeutic Interventions

- **Lifestyle modifications:** Diet with low glycemic index foods and regular moderate exercise reduce GDM incidence by 20–30%.
- **Pharmacotherapy:** Insulin remains the gold standard when lifestyle measures fail; metformin may be used selectively.
- **Postpartum follow-up:** Glucose testing at 6–12 weeks postpartum and annually thereafter detects persistent hyperglycemia or early type 2 diabetes.

Conclusion

Gestational diabetes mellitus arises from a complex interplay between hormonal changes and insulin resistance during pregnancy. These pathophysiological mechanisms predispose mothers and fetuses to severe short- and long-term complications.

Early risk stratification, universal screening, lifestyle interventions, and strict glycemic control are essential to improving outcomes. Standardized international guidelines and multidisciplinary care models should be implemented to address the rising global burden of GDM and reduce its impact on maternal and child health.

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