

Impact of Maternal Hyperglycemia on Fetal Neurodevelopment

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RESUMO

ABSTRACT Introduction: Maternal metabolic health during pregnancy lays the foundation for fetal neurological development. The increased incidence of Gestational Diabetes Mellitus (GDM) and pre-existing diabetes (type 1 and type 2) is a cause for concern, as a hyperglycemic environment can negatively influence fetal neurodevelopment, potentially predisposing the child to a range of long-term cognitive and behavioral disorders. Objectives: This study aims to evaluate the relationship between different types of maternal diabetes and the incidence of neurodevelopmental disorders in offspring, identifying the main molecular mediators involved in the process.

Methods: This is an integrative literature review conducted through a search in the PubMed database. The search strategy used controlled descriptors (MeSH) such as "Maternal Hyperglycemia", "Fetal Brain", "Neurodevelopmental Disorders", and "Epigenomics". Review articles, meta-analyses, and experimental studies published between 2023 and 2026, in English and Portuguese, were included. Results: The data indicate that children of mothers with diabetes are more prone to developing ASD (Autism Spectrum Disorder), especially when hyperglycemia during pregnancy is early. Delays in language performance, motor skills, and greater susceptibility to ADHD (Attention Deficit Hyperactivity Disorder) were also observed. Hyperglycemia alters the expression of enzymes with important functions in DNA methylation, such as DNMTs and TETs, in a sex-specific manner, frequently showing a greater impact on males. The hyperglycemic environment suppresses the antioxidant enzyme SOD2 (Superoxide Dismutase 2) and promotes the accumulation of advanced glycation end products (AGEs), generating a state of oxidative stress that impairs neuronal migration and synaptic formation. In addition, maternal intestinal dysbiosis caused by diabetes and fetal iron deficiency appear as other detrimental agents to brain development, reflecting in structural alterations, such as changes in the maturation of the corpus callosum. Conclusion: Maternal hyperglycemia acts as an independent and critical risk factor for neurodevelopmental impairment. Evidence reinforces that rigorous and early glycemic control is the best preventive strategy currently available. New therapies involving antioxidants, targeted nutritional supplementation, and control of gut microbiota modulation have shown promise in reducing the impact on the child's neurodevelopment. Multidisciplinary follow-up is essential for children exposed to intrauterine diabetes, enabling early detection of possible cognitive and behavioral deficits and thus more assertive treatment.

Palavras-chave: Maternal Hyperglycemia; Fetal Brain; Neurodevelopment.