Maternal cholesterol levels and autism spectrum disorder of the children: Exploring metabolic links and implications

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ABSTRACT

Introduction: While genetic predisposition plays a major role in ASD aetiology, recent research highlights the significance of prenatal environmental influences, which include maternal nutrition. Maternal cholesterol contributes to the fetal cholesterol pool, and deficiency can disrupt these critical developmental pathways. Cholesterol is crucial for many brain developmental processes and is an essential substance in the development of the fetal brain, yet its role in ASD pathogenesis remains unclear. It was suggested that cholesterol plays a critical role in synaptic plasticity and neuronal development, which are key processes in ASD pathogenesis. Alterations in lipid metabolism, particularly in the production and regulation of cholesterol, may contribute to neuroinflammation, oxidative stress, and abnormal neuronal connectivity, all of which are implicated in the development of ASD. **Materials and Methods:** A literature search was conducted using selected databases such as Scopus, PubMed and Google Scholar using the keywords 'autism spectrum disorder', 'cholesterol', 'neurodevelopment', 'prenatal or maternal nutrition' and 'lipid metabolism'. **Results:** Maternal cholesterol levels were found to have significant implications on ASD. Studies showed that both pathologically low and excessively high maternal cholesterol levels have been associated with adverse neurodevelopmental consequences, including increased ASD risk. Low maternal plasma cholesterol concentrations, particularly low LDL were associated with a 35% increased risk of ASD in their children even with a small reduction of the LDL. This association was more obvious among overweight and obese mothers, which suggested that maternal BMI may interact with lipid levels to influence the risk of ASD in newborns. Studies also found that low maternal HDL was associated with an increased risk of ASD, particularly in male offspring. It highlights the complex interplay between maternal lipid metabolism and amino acid profiles in influencing risk of ASD. Also, mothers with lipid abnormalities were found to be 16% more likely to have a child with autism than mothers without such abnormalities, therefore highlighting a potential familial link between maternal lipid profiles and ASD risk. Animal studies suggested that maternal dietary fat intake during critical developmental periods can lead to molecular changes in the brain that are relevant to ASD. Genetic disorders that impact cholesterol metabolism, such as Smith-Lemli-Opitz Syndrome (SLOS), have been associated with ASD. SLOS is defined by mutations in the DHCR7 gene, which results in the disruption of cholesterol biosynthesis, and there is a notable prevalence of ASD among those affected. This association highlights the essential role of cholesterol in neurodevelopment, and disturbances in their biochemical pathways may play a part in the pathogenesis of ASD. **Conclusion:** The findings suggest that both insufficient and excessive cholesterol levels in mothers and genetic defects in cholesterol metabolism can affect the likelihood of ASD in their children. Maintaining optimal cholesterol levels through a well-balanced diet and regular monitoring could be an effective approach to support fetal neurodevelopment and potentially lower the risk of ASD. Varying levels of dietary cholesterol intake among Malaysians due to cultural and socioeconomic factors not only influence maternal health but also the neurodevelopmental outcomes in offspring, with potential implications for disorders such as ASD.

Keywords: Maternal cholesterol, autism, children, metabolic