Letter to Editor

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The Interactions between Maternal Diet during Pregnancy and Neonatal Diabetes Mellitus

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Dear editor,

Neonatal diabetes mellitus (NDM), characterized by hyperglycemia occurring in the first few months of life and impaired insulin production, can be categorized into transient NDM (TNDM) or permanent NDM (PNDM).[1] Studies have searched the contributing genetic factors to NDM and their interaction with dietary components. Nutrigenetics concentrates on understanding how genetic variations affect an individual's response to nutrients and dietary patterns. In the context of NDM, researchers have explored specific genetic mutations leading to impaired insulin production and glucose regulation in neonates. The overexpression of chromosome 6q24 is the cause of most TNDM cases, and mutations in the adenosine triphosphate-sensitive potassium (KATP) channel lead to the majority of PNDM cases. The improved understanding of the etiology of the disease evolved the diagnosis and management with oral sulfonylureas.[1]

Although NDM is not caused by maternal nutrition during pregnancy, the diet and nutritional status of a pregnant woman can have an impact on her health as well as the health of her developing baby. Additionally, it may indirectly affect the health of the pancreas and other bodily systems.[2,3] Moreover, maternal and early life exposures during pregnancy and lactation, like maternal obesity or diabetes, affect the infant microbiome and the occurrence of common diseases, such as diabetes, allergic and atopic disease, cardiovascular disease, and obesity in the infant.[4] The role of nutrition in the "metabolic

memory" is essential, although the precise mechanism by which nutrient signals during developmental stages influence metabolism and the development of lifestyle-related diseases in later life is not yet fully comprehended.[5]

NDM is a monogenic disorder with a genetic basis, and the influence of epigenetic factors significantly contributes to the susceptibility of individuals to NDM. For instance, certain epigenetic modifications, such as alterations in DNA methylation patterns in the umbilical cord blood of newborns at risk of GDM, have been found to potentially impact the expression of genes related to glucose metabolism. Seven genes related to NDM have been identified to exhibit significant changes in expression patterns in response to exposure to GDM, including four upregulated genes (*TRIB1, POU2F1, PON1*, and *TXNIP*) and three downregulated genes (*PGC1α, MEST, and NRF2*).[3,6] Despite emerging studies investigating the potential role of the gut microbiota, which can be transmitted from mother to newborn, in the context of NDM, our understanding of the precise nature of gut microbiota dysbiosis in NDM remains largely unexplored. Modulating the gut microbiota through dietary interventions is a critical factor in the pathogenesis of islet autoimmunity.[6] The association between GDM and maternal obesity with changes in the composition of the gut microbiota in newborns highlights a potential link between dietary factors, imbalances in gut microbiota, and NDM. Notably, both diet and dysbiosis in the gut microbiota have the potential to serve as prognostic biomarkers for NDM in the context of GDM.[3,7] Furthermore, Short-Chain Fatty Acids (SCFAs), which act as epigenome modifiers, can alleviate intestinal inflammation and influence NDM-relevant gene expression.[3]

Maternal dietary patterns during GDM have been linked to different changes in gene expression patterns in the field of NDM.[6] The interaction between complex carbohydrate or low-fat diets and short-chain fatty acids (SCFAs) derived from the gut microbiota, particularly the Bifid bacterium and Roseburia, involves the regulation of specific genes such as downregulation of *TRIB1* and the upregulation of *PGC1α*.[4] On the other hand, the abundance of certain gut bacteria, such as *P. copri* and *E. cloacae* is increased by a high-fat diet, which may induce genetic changes in the neonate's gut microbiota[8], with significant consequences for NDM. Specifically, in response to a high-fat diet, the *NRF2* and *PDX1* genes show downregulation, while the *TXNIP* gene is upregulated. Producing SCFAs, elevated levels of Bacteroides, *E. faecalis*, and Alistipes in response to a high-fat diet may have a protective effect against NDM, leading to the upregulation of *NRF2* and *PGC1α* genes and the downregulation of *TRIB1*. However, more extensive research is required to understand the epigenetic mechanisms through which bacteria such as Bacteroidetes *P. Copri* and *E. Cloacae* may influence gene expression, and clarify the mechanisms underlying the pro- and anti-inflammatory effects of commensal and pathogenic bacteria on the susceptibility to genes associated with neonatal diabetes in response to maternal dietary patterns during GDM.[6,9] Understanding the interplay between genetic factors and maternal diet could provide valuable insights into the mechanisms underlying neonatal diabetes. Studies could be conducted to analyze the dietary patterns of pregnant women and assess their association with neonatal diabetes incidence. Additionally, genetic studies involving large cohorts of neonatal diabetes cases and controls could help identify specific genetic variants that contribute to the risk. Integrating both dietary and genetic data could provide a more comprehensive understanding of the relationship between maternal diet, genetic factors, and neonatal diabetes. Understanding the genetic mutations associated with NDM and their interaction with nutrition can contribute to personalized approaches for diagnosis, treatment, and prevention.

Conflict of Interest

The authors declare no conflicts of interest.

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Ethical Considerations

None.

Author's Contribution

Writing- original draft preparation, M.S.A.; editing the manuscript, H.N. Both authors have read and agreed to the published version of the manuscript.

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