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Opinion Article

Genetic Causes of Neonatal Diabetes

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DESCRIPTION

Neonatal diabetes is a rare form of diabetes that affects infants within the first six months of life. The condition is characterized by high blood sugar levels (hyperglycemia) and impaired insulin production. This condition is distinct from type 1 diabetes and type 2 diabetes which typically develop later in life.

There are two forms of neonatal diabetes: Transient Neonatal Diabetes Mellitus (TNDM) and Permanent Neonatal Diabetes Mellitus (PNDM). The two forms of neonatal diabetes differ in terms of their underlying causes, clinical presentation, and long-term outcomes.

Transient Neonatal Diabetes Mellitus (TNDM) is a temporary form of diabetes that usually resolves by the time the child reaches 18 months of age. The condition affects approximately 1 in every 120,000 to 500,000 newborns. TNDM is caused by abnormalities in chromosome 6, which leads to a decrease in the production of insulin in the pancreas.

Infants with TNDM usually present with symptoms such as hyperglycemia, poor feeding, dehydration, and lethargy within the first few weeks of life. The diagnosis is usually confirmed by measuring blood glucose levels and conducting genetic testing to identify the underlying chromosomal abnormality.

Treatment for TNDM typically involves the use of insulin therapy to manage blood glucose levels. In most cases, the condition resolves within the first 18 months of life, and insulin therapy can be discontinued. However, children with TNDM may be at an increased risk of developing type 2 diabetes later in life and regular monitoring of blood glucose levels is recommended.

Permanent Neonatal Diabetes Mellitus (PNDM) is a rare form of diabetes that persists throughout the individual's life. The condition affects approximately 1 in every 400,000 to 500,000 newborns. PNDM is caused by mutations in several genes that regulate insulin production in the pancreas.Infants with PNDM usually present with symptoms such as hyperglycemia, dehydration, and failure to thrive within the first few weeks of life. The diagnosis is usually confirmed by measuring blood glucose levels and conducting genetic testing to identify the underlying genetic mutation.Treatment for PNDM typically involves the use of insulin therapy to manage blood glucose levels. In some cases, sulfonylurea therapy may also be used to stimulate insulin production. Regular monitoring of blood glucose levels is necessary to prevent complications such as hypoglycemia and diabetic ketoacidosis.

Long-term outcomes for individuals with PNDM vary depending on the underlying genetic mutation. Some individuals may develop other medical conditions such as intellectual disability, epilepsy, or developmental delay. Regular monitoring of blood glucose levels and regular follow-up with a healthcare provider is essential to prevent complications and ensure optimal management of the condition.

Diabetes that appears within the first six months of life is more likely to be type 2 diabetes caused by a single gene mutation, hence molecular genetic testing for this population of patients should be considered mandatory. People who are diagnosed with diabetes after the age of six months should also undergo genetic testing if their diabetes symptoms are unusual for type 1 diabetes, have characteristics that are consistent with a known monogenic cause, or if there is other affected family members who have a history of NDM or a pattern that suggests Mendelian inheritance. The majority of patients are able to switch from insulin injections to sulfonylureas because to the use of pharmacogenetics in KATP channel-related NDM.It is impossible to emphasise the profound effects of this change on patients and their families. Glucokinase activators and medications that reduce ER stress may soon provide patients with diabetes caused by GCK or INS with the same revolutionary therapeutic alternative. The genetic repercussions of a monogenic NDM diagnosis for a subject's parents, siblings, offspring, and more distant relatives are equally important to these therapeutic concerns. To fully grasp the recurrence risk of NDM, which varies depending on the molecular aetiology, families with a molecular genetic diagnosis of TNDM or PNDM should get genetic counselling.

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