Understanding Zinc Transporter 8 (ZnT8) Autoantibodies: What We Learned from ENDIA

What We Studied

We followed 1,473 children in the ENDIA study who have a family member with type 1 diabetes. We tested their blood regularly (every 3-6 months) for about 7 years (at the time of publication) to see when and how autoantibodies developed. Islet autoantibodies are proteins made by the immune system that can signal type 1 diabetes may develop in the future.

What We Found

1. ENDIA results match international patterns

- For three autoantibodies (insulin, GAD, and IA-2), Australian children showed the same patterns as children in the USA and Europe
- ENDIA is one of the first studies worldwide to follow ZnT8 autoantibodies from pregnancy through early childhood

2. Not all ZnT8 autoantibodies mean the same thing

We found two different patterns:

- Children who develop multiple autoantibodies: When ZnT8 autoantibodies appeared alongside other autoantibodies, they were confirmed by a German laboratory using completely different testing methods. These children have increased diabetes risk.
- Children with only ZnT8 autoantibodies: When ZnT8 remained the only autoantibody present, the German laboratory using different testing methods could NOT detect them. This suggests these autoantibodies are <u>not</u> important for type 1 diabetes risk.

3. Why does this happen?

- The ZnT8 test used in Australia (and commonly worldwide) is an ELISA test
- This test sometimes detects ZnT8 autoantibodies that don't appear to increase diabetes risk
- Only when other autoantibodies also develop are the ZnT8 autoantibodies confirmed as "real" risk markers by other testing methods

4. Maternal antibodies don't affect your child's risk

- If you have type 1 diabetes and are pregnant, your autoantibodies can pass to your baby
- These maternal antibodies take about 9-15 months to disappear from your child's blood

• The good news: These maternal antibodies have **no effect** on your child's risk of developing their own autoantibodies or diabetes

What This Means for ENDIA Participants

- If your child tests positive for ZnT8 autoantibodies alone, this likely means minimal or no increased diabetes risk, but we will continue monitoring to see if other autoantibodies develop
- Testing in the first 9-15 months may detect maternal antibodies rather than the child's own antibodies (if the mother has type 1 diabetes)
- Multiple autoantibodies remain the strongest predictor of type 1 diabetes risk
- **ENDIA is contributing unique knowledge** about ZnT8 autoantibodies in early childhood that will help improve screening programs worldwide

The bottom line: Single ZnT8 autoantibodies that remain alone appear to have minimal importance for type 1 diabetes risk. The real concern is when multiple different autoantibodies develop together - this is when risk increases and when ZnT8 autoantibodies are confirmed as meaningful by multiple testing methods.

Access the full paper via Diabetologia at the link below.