Cesarean section and interferon-induced helicase gene polymorphisms combine to increase childhood type 1 diabetes risk.

Abstract:

The incidence of type 1 diabetes is increasing. Delivery by cesarean section is also more prevalent, and it is suggested that cesarean section is associated with type 1 diabetes risk. We examine associations between cesarean delivery, islet autoimmunity and type 1 diabetes, and genes involved in type 1 diabetes susceptibility. Cesarean section was examined as a risk factor in 1,650 children born to a parent with type 1 diabetes and followed from birth for the development of islet autoantibodies and type 1 diabetes. Children delivered by cesarean section (n = 495) had more than twofold higher risk for type 1 diabetes than children born by vaginal delivery (hazard ratio [HR] 2.5; 95% CI 1.4-4.3; P = 0.001). Cesarean section did not increase the risk for islet autoantibodies (P = 0.6) but was associated with a faster progression to diabetes after the appearance of autoimmunity (P = 0.015). Cesarean section-associated risk was independent of potential confounder variables (adjusted HR 2.7; 1.5-5.0; P = 0.001) and observed in children with and without high-risk HLA genotypes. Interestingly, cesarean section appeared to interact with immune response genes, including CD25 and in particular the interferon-induced helicase 1 gene, where increased risk for type 1 diabetes was only seen in children who were delivered by cesarean section and had type 1 diabetes-susceptible IFIH1 genotypes.
These findings suggest that type 1 diabetes risk modification by cesarean section may be linked to viral responses in the preclinical autoantibody-positive disease phase.