Major international study finds no link between viral infection and rapidly developing Type 1 diabetes in young children

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Some of the earliest results from The Environmental Determinants of Diabetes in The Young (TEDDY) study - a major Europe-USA consortium exploring the causes of type 1 diabetes in children – has found no evidence for viral infection as a cause of the rapid-onset form of the condition. The research appears in *Diabetologia*, the journal of the European Association for the Study of Diabetes (EASD) and is by Professor Anette-Gabriele Ziegler of the German Research Centre for Environmental Health (Helmholtz Zentrum München), Munich, Germany, and colleagues across the USA and Europe, including Drs Hye- Seung Lee and Jeffrey Krischer from the University of South Florida, Tampa, FL, USA, Dr. Thomas Briese from Columbia University, New York, NY, USA, and Dr Beena Akolkar, National Institute of Diabetes and Digestive and Kidney Diseases, USA.

Viral infection could be one of several potential causes of type 1 diabetes, in which the body's own immune system gradually destroys the pancreatic islet beta cells that make insulin—meaning those affected must take insulin for the rest of their lives. The onset of the disease can be rapid, or take place over many years.

In this new study, the authors assessed whether early viral infection in babies had any association with rapid-onset type 1 diabetes. They analysed initial data from the TEDDY study—a collaboration between Europe (Finland, Germany, Sweden) and the USA (Washington State,

Colorado, Georgia, and Florida). TEDDY's main focus is to identify environmental factors associated with an increased risk for developing autoimmunity and type 1 diabetes.

Between 2004 and 2010, the study screened 420,000 infants younger than 4.5 months and found 21,589 with a genetic predisposition to type 1 diabetes. Families were invited to participate in a prospective collection of detailed infectious, dietary, and developmental data with the hope of identifying environmental factors triggering beta-cell inflammation and diabetes; a total of 8,677 children were enrolled. Of those, 932 had a sibling or parent with type 1 diabetes and 7,745 had no family history. The children visited clinics and had blood taken every 3 months up to age 4 years for detection of markers of beta cell-autoimmunity (islet autoantibodies), presence of viruses, and additional measurements.

The researchers found that 355 children developed islet autoantibodies and 86 of these had progressed to type 1 diabetes by July 2011. Progression time from the appearance of islet autoantibodies to diabetes onset varied, but was rapid and within 6 months in 24 of the children. For 14 of these 24 children, aged between 6 and 24 months, TEDDY researchers had samples of their blood plasma from either side of the time point where autoantibodies first emerged and tested these samples for the presence of viruses using state-of-the-art sequencing. Blood plasma samples from 14 control children, matched for age, study centre and family history of type 1 diabetes were tested in the same manner. Only one of the 14 children who had rapidly progressed to type 1 diabetes had detectable levels of viruses in its plasma samples. This analysis, theoretically capable of detecting all possible known and novel viral agents, found little difference between the cases and the controls.

Progression to diabetes was also not found to be associated with reported infectious episodes analysed in all 24 children who rapidly progressed to diabetes and 72 matched control children. These included recognisable

gastrointestinal or respiratory illnesses.

Professor Ziegler says: "These findings cannot exclude the possibility that a causative virus is acquired before the age of 6 months and absent or only present for a brief time in plasma during the months leading to the appearance of beta-cell autoantibodies and progression to diabetes. However, the findings make us again reflect on whether a virus triggers type 1 diabetes."

She adds that one unexpected finding was the lower frequency of fever reported for patients than for controls. She says: "This is a potentially important finding that needs to be substantiated in a larger study. If confirmed, it suggests a protective effect of fever as a marker of more vigorous infection defence and effective virus elimination." Such a study is planned for the entire TEDDY cohort.

She concludes: "Our study of rapid-onset diabetes in early childhood did not provide evidence of viral infection around the time of onset of beta-cell autoimmunity in these children."

Provided by Diabetologia