Trajectory of type 1 diabetes risk shifts after age 10 years between at-risk males and females, research shows

July 23 2024

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New research to be presented at the Annual Meeting of the European Association for Study of Diabetes (Madrid, Spain, 9–13 September)

shows that the risk of developing type 1 diabetes (T1D) decreases markedly in girls after the age of 10 years, while the risk in boys stays the same.

Furthermore, the risk of T1D is significantly higher in boys with a single autoantibody than their female counterparts, suggesting sex could be linked with autoantibody development, indicating the importance of incorporating sex in the assessment of risk. The study is by Erin L. Templeman and Dr. Richard Oram, University of Exeter Medical School, Exeter, UK, and colleagues.

Autoantibodies (ABs) are proteins produced by the body's immune system, which attack other proteins in autoimmune diseases including T1D.

In contrast to most autoimmune diseases, male sex is a risk factor for type 1 diabetes (T1D). This raises the hypothesis that either immune, metabolic, or other differences between sexes may impact risk or progression through stages of T1D.

In this study, the authors aimed to assess the risk and rate of progression for individuals in the TrialNet Pathway to Prevention study that screens relatives of people with T1D for the presence of autoantibodies.

The authors studied 235,765 relatives of people with T1D. They used computer and statistical modeling to calculate risk of T1D, stated as estimated five-year risk for females and males respectively, after adjusting for confounders.

The proportion of individuals who screened positive for ABs was higher in males (females: 5.0%, males: 5.4%). Of these individuals, males were more likely to screen positive for multiple ABs (females: 1.8%, males: 2.6%). Absolute five-year risk of progression to T1D in single AB

positive individuals was significantly higher (in males (females: 14%, males: 21%).

However, similar risk was displayed across sexes when presenting with stage 1 (at least two ABs) (females: 38%, males: 38%) or stage 2 (AB and abnormal blood sugar stability) (females: 57%, males: 59%). Risk remains significantly higher in single AB positive males when adjusting for the presence of a first-degree relative with T1D and age (27% higher risk in single AB positive males compared to single AB positive females).

A large decrease in five-year T1D risk is displayed in females when screened, and autoantibody positive, after 10 years old as compared to before, aged 10 years old. In contrast, a steady decline in five-year T1D risk is displayed in males as age at screening increases.

The authors conclude, "The risk of T1D is significantly higher in males than females when presenting with a single autoantibody. Risk is similar between males and females in childhood, with the risk diverging at age 10. Risk in females then dramatically decreases, whereas risk is sustained in males. This suggests sex appears to be linked with autoantibody development, indicating the importance of incorporating sex in the assessment of risk."

On the difference in risk between boys and girls, the authors add, "We don't know and this is an interesting area where more research is needed. The change in risk at around the age of 10 raises the hypothesis that puberty related hormones may play a role."

They add, "We found the biggest differences in risk of T1D in individuals who had not progressed to stage 1 T1D, with a similar rate and risk of progression in those who were stage 1 and stage 2 T1D. Therefore, it seems most likely that explaining the mechanism of sex

differences may help us understand underlying pathogenesis of T1D and potential intervention targets, more than affecting how we screen, diagnose and intervene."

Provided by European Association for the Study of Obesity