Classifying diabetes by type 1 genetic risk shows autoimmune diabetes cases are evenly distributed above and below 30 years of age

Institute of Biomedical and Clinical Science, University of Exeter Medical School, UK.

Background and aims: There is considerable controversy about the extent to which autoimmune mediated Type 1 diabetes (T1D) presents in patients diagnosed older than 30 years. This is difficult to assess as autoantibodies are rarely measured in these individuals and clinical classification is imprecise. We recently developed T1D-GRS and have shown T1D is restricted to patients with a high T1D-GRS (>50th population TID-GRS centile). We used T1D-GRS measurement to evaluate the contribution of autoimmunity in diabetes diagnosed under 60 years in a cross-sectional study of UK adults.

Materials and methods: We analysed the development of diabetes using Kaplan-Meier estimates in 152,118 UK individuals from the UK Biobank (age 30-60 years) in different deciles of T1D-GRS.

Results: There is an excess of diabetes in the top five deciles (3436) compared to the bottom five deciles (2853) p<0.0001 consistent with 9.3% of the cohort having T1D. 48%(279/583) of T1D cases occur under 30 years where they contribute 75%(279/373) of all diabetes cases and 52%(304/583) T1D occurs aged 30-60 years contributing 5.1%(304/5916) of all cases. These T1D cases were predominantly in the top T1D-GRS decile (6.0% had diabetes vs 3.5% bottom T1D-GRS decile p<0.0001). Patients diagnosed 30-60yrs with a GRS suggesting T1D are diagnosed younger (41 vs 52 years p<0.0001), slimmer (body mass index (BMI) 27 vs 32 kg/m² p<0.0001) and progress more rapidly to insulin (72% vs 7% within one year p<0.0001).

Conclusion: T1D-GRS is a novel tool to investigate diabetes aetiology in large cohorts without antibody measurement. T1D diabetes is evenly distributed within the first six decades of life but after 30 years the increase in Type 2 diabetes makes them harder to recognise and treat correctly.