Monitoring high risk relatives in the TrialNet Pathway to Prevention is associated with less severe clinical presentation

C Gillum[1], C Pope[1], S Loud[1], T Hughes[1], B Thorne[1], Y Liu[1,2], PJ Bingley[1] and the Type 1 Diabetes TrialNet Study Group

[1]Diabetes and Metabolism, Level 2, Learning and Research Building, University of Bristol, Southmead Hospital, Bristol, BS10 5NB

[2] Diabetes Centre, 3rd Floor, Southwark Wing, Guy's Hospital, London, SE1 9RT

Background

TrialNet is an international network of leading academic institutions, physicians, scientists and healthcare teams dedicated to the prevention of type 1 diabetes (T1D). The UK TrialNet network comprises the Clinical Centre in Bristol and 28 affiliate sites, as well as 37 satellite screening sites. The data presented here relates to those screened in the UK.

The TrialNet Pathway to Prevention (PTP) study is an observational study in which relatives of people with T1D are screened to assess their risk of developing T1D. Participants have a blood test to look for diabetes-related autoantibodies (GADA, IA-2A, mIAA, ICA and ZnT8A). From this, it is possible to identify those individuals who are at greater risk and therefore eligible for closer monitoring, and potentially eligible to take part in TrialNet T1D prevention studies.

Objective

To evaluate the characteristics of presentation of Stage 3 (clinically overt T1D) in autoantibody-positive relatives (Stage 1 and 2) who are followed up in semi-annual monitoring.

Methods

Positive participants who enrolled into semi-annual monitoring were identified by the TrialNet website. Those diagnosed with T1D were then found through the UK database and their diabetes onset forms by TrialNet. Data were collected from these forms and the UK TrialNet teams. Data collected included age, autoantibodies, presentation at diagnosis and blood glucose values (Fig.1).

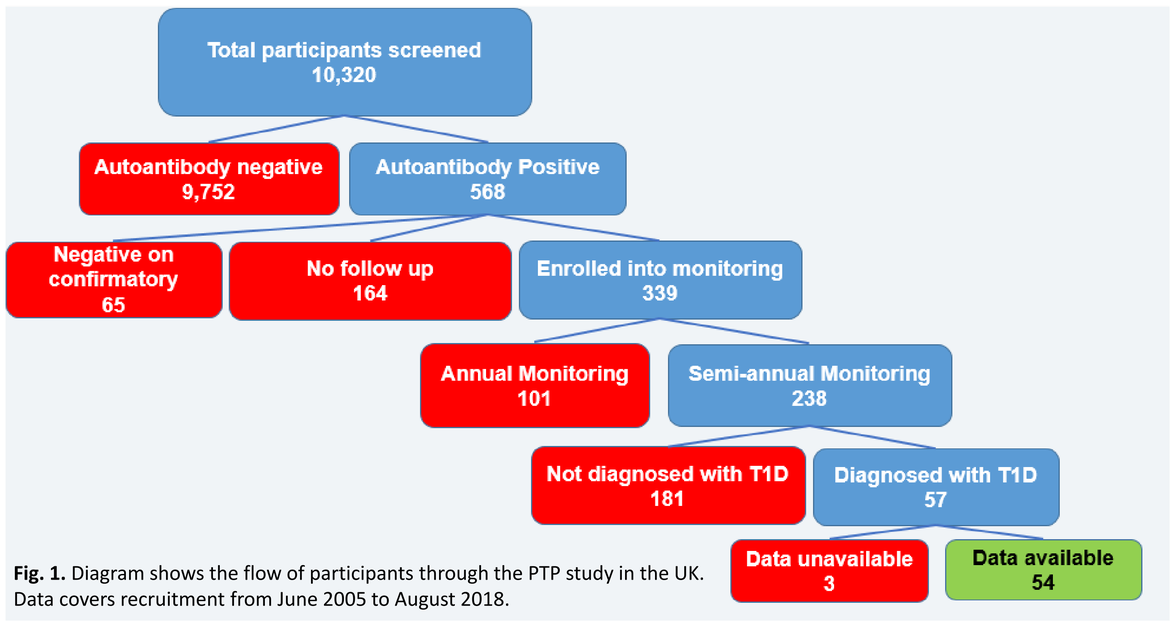

Fig. 1. Diagram shows the flow of participants through the PTP study in the UK. Data covers recruitment from June 2005 to August 2018.

Results (1)

Data relating to 5 different signs and symptoms of T1D were collected. Presence of all signs and symptoms were low with polyuria the most frequent, reported by 40% of participants.

48 participants reported no prior weight loss, and of those 5 participants who did lose weight the maximum reported loss was 2kg. 28 participants had no signs or symptoms at diagnosis.

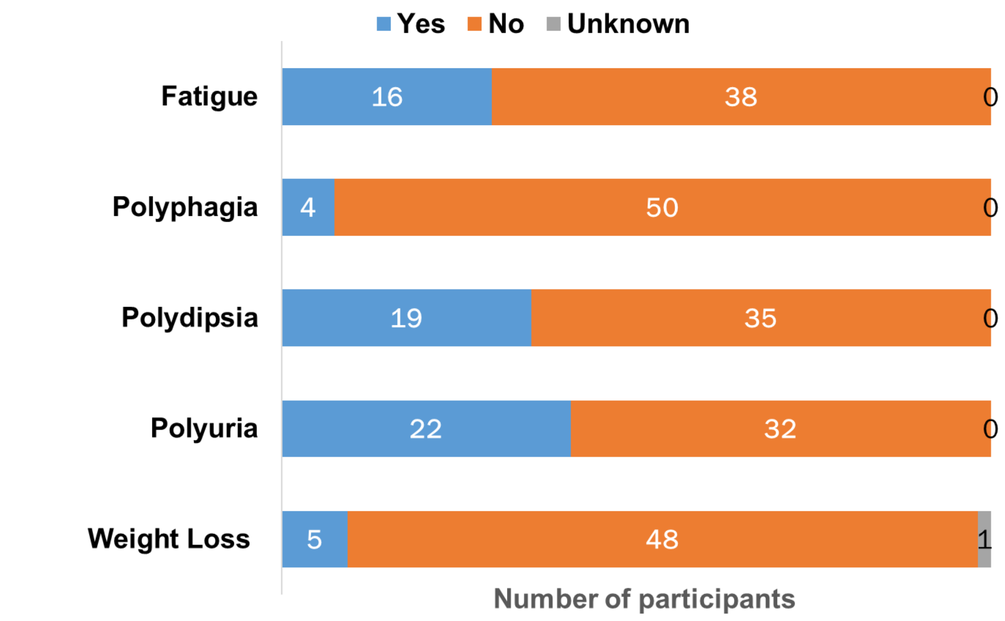

Fig. 2. Diagram shows the incidence of fatigue, polyphagia, polydipsia, polyuria and weight loss among semi-annual monitoring participants at the time of T1D diagnosis.

Results (2)

- HbA1c, blood glucose level and length of hospitalisation data were collected. 18 participants were hospitalised at diagnosis, and of these more than 50% only stayed 1–2 days. One participant was an inpatient overnight due to hospital policy and was discharged the following morning (Fig. 3).

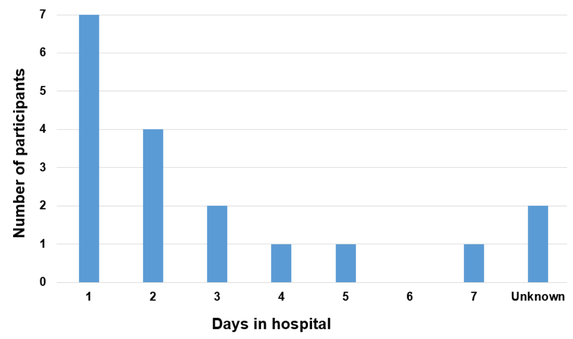

Fig. 3. Graph to show participants length of hospital admission on diagnosis of T1D.

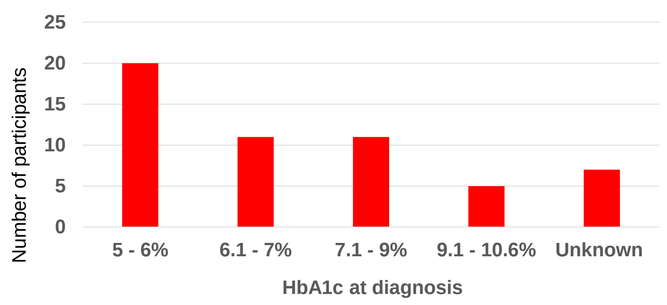

Fig. 4. Graph to show HbA1c of participants at diagnosis.

- More than 1/3 of participants had a normal HbA1c at diagnosis, indicating that their blood glucose levels had been in range for the majority of the period before diagnosis (Fig. 4).
- Random blood glucose levels ranged from 5.4-44.4mmol/L.
- 28% of participants had a random blood glucose of <11.1mmol/L at diagnosis (red line), the level at which a clinical alert of T1D is triggered (Fig. 5).

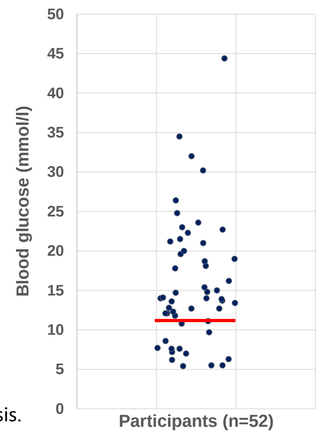

Fig. 5. Blood glucose values at T1D diagnosis.

Results (3) - DKA

- Only one participant in semi-annual monitoring presented in DKA at diagnosis (Fig. 6). This equates to less than 2% of participants, compared with previously reported UK incidence of 25% (1).

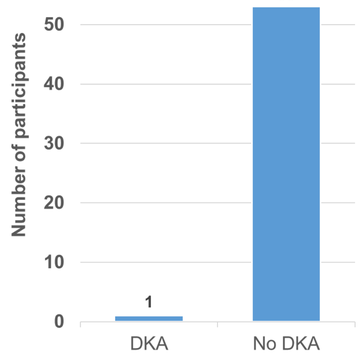

Fig. 6. Incidence of DKA at diagnosis.

Discussion - DKA

- The participant who presented in DKA was a quiet teenager living in a busy household, factors which may have had an influence on her presentation.
- This participant presented with signs of polyuria, polydipsia, weight loss and fatigue. Her blood glucose level was 44.4mmol/L, and she had ketones of 6 and subsequently spent 4 days in hospital.

Summary

- Low frequency of signs and symptoms at diagnosis
- >50% of participants spent ≤2 nights in hospital on admission
- >1/3 of participants at diagnosis had a normal HbA1c (<6%)
- 28% of participants had a blood sugar level <11.1mmol/L at diagnosis
- Only 1 participant presented in DKA (<2%) compared with the UK reported incidence of 25%.

Interpretation

- Screening and monitoring in PTP resulted in increased awareness of progression of diabetes.
- Early identification of progression allows for intervention prior to significant signs and symptoms
- Taking part in PTP also enabled participants to adjust to the possibility of developing T1D with support from their research team.

References

1. Lokulo-Sodipe K, Moon R, Edge J and Davies J (2013). Identifying targets to reduce the incidence of diabetic ketoacidosis at diagnosis of type 1 diabetes in the UK. BMJ

TrialNet UK Affiliate site Principal Investigators			
Aberdeen: Dr. Amalia Mayo	Cardiff: Prof. John Gregory	Leicester: Dr. James Greening	Sheffield Teaching: Prof. Simon Heller
Barts Health: Dr. Ashraf Gabr	East Lancashire: Dr. Chris Gardner	Liverpool: Dr. Princy Paul	Sheffield Children's: Dr. Neil Wright
Belfast: Dr. Noina Abid	Exeter: Dr. Chris Moudiotis	Manchester: Dr. Ian Doughty	Southport & Ormskirk: Dr. May Ng
Birmingham Adults: Dr. Parth Narendran	Glasgow: Dr. James Boyle	Newcastle: Dr. Nicola Leech	St. Georges, London: Dr. Mimi Chen
Birmingham Children's: Prof. Tim Barrett	Harrogate: Dr. Peter Hammond	Norwich: Dr. Vipan Datta	Taunton: Dr. Isy Douek
Brighton: Dr. Shankar Kanumakala	Hull: Dr. Thozhukat Sathyapalan	Nottingham: Dr. Louise Denvir	
Cambridge: Dr. Mark Evans	Leeds: Dr. Fiona Campbell	Plymouth: Dr. Patrick English	