EFFECT OF SCREENING FOR ISLET AUTOANTIBODIES ON DIABETIC KETOACIDOSIS AT
DIAGNOSIS OF TYPE 1 DIABETES IN CHILDREN

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BACKGROUND

Type 1 diabetes (T1D) ranks high among common severe chronic diseases of childhood with survival dependent on daily injections of insulin. There is significant risk of acute and long-term complications. In developing countries, diabetic ketoacidosis (DKA) affects up to 80% of children at diagnosis. With improving access to health care and community awareness in countries with model health care systems, children are being diagnosed earlier and fewer than 20% develop DKA. A DKA rate of 34% was reported for a sample of the U.S. children diagnosed with T1D in 2002-2004. DKA is life-threatening but it also has long-term detrimental effects on glycemic control and memory. The frequency of DKA at diagnosis of childhood diabetes serves as a metric of income inequality and quality of health care systems. The health insurance and health care delivery have changed remarkably in the U.S. during the past decade. While coverage has improved, the use of primary care services for prevention and early treatment appear to be lagging behind. The main objective of this study was to examine the impact of a research screening for presence of islet autoantibodies can prevent DKA at diagnosis.

METHODS

Study population

age 0-17 years
diabetes diagnosed 1/1/1998 and 12/31/2012
continuous insulin treatment
received treatment at the Barbara Davis Center at least twice between 1998-2016
Colorado resident at the time of diagnosis

Data Source

- EMR database of the Barbara Davis Center and Children’s Hospital Colorado

Variables:

Age, sex, race/ethnicity, family history of diabetes (T1, T2; in 1st or 2nd degree relatives), insurance (private, government, none),participation in research and islet autoantibody screening, residence (city, town, rural)
pH, bicarbonate, HbA1c, blood glucose

DKA definition

Blood glucose > 250 mg/dl, urine or blood ketones, and blood bicarbonate level <15 mmol/L or pH <7.30 (venous) or <7.35 (arterial or capillary)

Statistical analyses

Prevalence (%) of DKA at the time of diagnosis was calculated. Univariate analyses utilized the chi-square test for ordinal measures; medians were compared using the Mann–Whitney U test. Logistic regression analysis was used to identify factors associated with DKA.

RESULTS

- DKA status was ascertained in 3439 out of 3544 Colorado children diagnosed with T1D before 18 years of age, during 1998-2012
- DKA at diagnosis was present in 38.9 % (95% CI 37.3%-40.6%) of these children
- Baseline characteristics of the study population are summarized in Table 1

•133 children or 4% had participated in a study that screened for islet autoantibodies: Diabetes Autoimmunity Study in the Young, Type 1 Diabetes TrialNet, or The Environmental Determinants of Diabetes in the Young. DKA was present in 1339 of the youth at T1D diagnosis (38.9%; 95% CI 37.3-40.6%).

•Among those previously screened for islet autoantibodies, only 9 (6.8%) had DKA while 52 would be expected.

•In multiple logistic regression controlling for age, sex, ethnicity and health insurance, prior participation in a research screening for islet autoantibodies had a powerful protective effect on DKA at diagnosis -OR=0.2 (95%CI 0.2-0.4), independent of T1D in a 1st-degree (0.4; 0.3-0.5) or 2nd-degree relative (0.6; 0.5-0.8) Table 2

Table 1. Characteristics of Study Participants at Diagnosis of Type 1 Diabetes (N=3544)		
Characteristic		
DKA at diagnosis, % (95% CI)*	38.9	(37.3-40.6)
Sex, % male	53.8	
Age at diagnosis, y, median (IQR)	9.4	(5.6-12.6)
Race/ethnicity, %		
Non-Hispanic white	75.7	
African American	3.8	
Hispanic	16.5	
Other	4.0	
Health insurance, %		
Private	66.9	
Government	23.7	
None	8.3	
Unknown	1.1	
Family history of diabetes, %		
First-degree relative with T1D	10.2	
Second-degree relative with T1D	11.3	
First-degree relative with T2D	6.2	
Other/none	70.7	
Unknown	1.6	
Residence in Denver Metro area, %	57.5	
Participation in a research study, %	3.8	
Delay to first visit at the BDC, weeks, median (IQR)	0	(0-1)
A1c, median (IQR)	11.1%	(9.6-13.1)

Table 2. Multiple logistic regression analysis of predictors of DKA (all variables simultaneously in the model).	
Predictor	OR (95% CI)
Calendar year	1.06 (1.04-1.08)
Age, yr	
14-17	1 (Reference)
10-13	1.31 (1.04-1.65)
5-9	1.12 (0.89-1.40)
0-4	1.80 (1.41-2.31)
Race/ethnicity	
Non-Hispanic white	1 (Reference)
African American	1.80 (1.24-2.62)
Hispanic	1.21 (0.99-1.48)
Other	1.28 (0.89-1.83)
Health insurance	
None	1 (Reference)
Government plan	0.63 (0.47-0.84)
Private	0.37 (0.29-0.49)
Family history of diabetes	
None	1 (Reference)
Type 2 diabetes in a first-degree relative	0.76 (0.56-1.02)
Type 1 diabetes in a second-degree relative	0.64 (0.51-0.81)
Type 1 diabetes in a first-degree relative	0.35 (0.26-0.48)
Participation in diabetes research prior to diagnosis	
No	1 (Reference)
Yes	0.19 (0.09-0.38)

CONCLUSIONS

- Participation in research studies that screen children for islet autoantibodies and educate regarding symptoms of diabetes and home glucose monitoring during child’s illness can prevent ~80% of DKA. The existing technology is sufficient to consider a widespread screening of all children for islet autoantibodies and intensive follow-up of those positive, as one of the approaches to prevention of DKA.