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Incidence of Type 1 Diabetes Is Not Increasing in a Population-Based Cohort in Olmsted County, Minnesota, USA

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Abstract

Objectives: To investigate the recent incidence of T1D in a US Midwestern county to determine whether this increase has been sustained and compare it with the incidence of celiac disease (CD) and also investigate the prevalence of CD, an associated autoimmune disease, within the cohort.

Patients and Methods: A broad search strategy was used to identify all incident cases of T1D in Olmsted County, Minnesota, between January 1, 1994, and December 31, 2010, using the Rochester Epidemiology Project. Diagnosis and residency status were confirmed through the medical record. Incidence rates were directly standardized to the 2010 US population. Poisson regression was used to test for a change in incidence rate. Clinical charts were reviewed to confirm case status.

Results: There were 233 incident cases of T1D. Directly adjusting for age and sex with respect to the 2010 US white population, the overall annual incidence of T1D was 9.2 (95% CI, 8.0-10.4) per 100,000 people per year among all ages and 19.9 (95% CI, 16.6-23.2) per 100,000 people per year for those younger than 20 years. There was no significant increase in the incidence of T1D over time (P=.45). Despite the overall stability in annual incidence, there was an initial increasing trend followed by a plateau. Of the 109 patients with T1D (47%) tested for CD, 12% (13) had biopsy-proven CD.

Conclusion: The incidence of T1D has stopped increasing in Olmsted County, Minnesota, in the most recent decade. Further studies are needed to confirm this finding and explore reasons for this plateau.

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Recent studies describe an increasing incidence of type 1 diabetes (T1D) by an average of 3% annually worldwide,[1] along with increases in various populations with varying degrees of genetic susceptibility. The rates at which the incidence is increasing vary depending on geographic location[1]: incidence rates ranged from 20.0 to 57.2 per 100,000 in Sweden from 2006 to 2011,[2] whereas China had the lowest reported incidence rate of 3.0 per 100,000 but also saw the mean incidence rate increase by about 14% annually from 1997 to 2011.[3] Some, but not all, studies show sex differences in incident cases. One difficulty in these reports is the varying eligibility criteria for populations enrolled in studies. Varying ages and age cutoffs have been used. Numerous European studies have used an age cutoff of less than 15 years,[4-6] whereas the US studies used an age cutoff of less than 20 years.[5] Population-based studies are difficult to perform in the United States because of the lack of population databases. One large US study showed the incidence of T1D to increase from 2002 to 2009.[7]

The environmental drivers behind the rising incidence remain unclear. To date, many theories implicate infectious causes,[8] improved sanitation, widespread use of antibiotics, increased cesarean deliveries,[9] low vitamin D levels,[10] and increased gluten consumption and timing of its introduction.[11,12]

The relationship among T1D incidence, gluten exposure, and comorbid celiac autoimmunity is of interest for several reasons. Patients with T1D are at increased risk for celiac disease (CD), another common immune-mediated disease, characterized by destruction of small-bowel mucosa with gluten exposure.[13-15] The incidence of CD also has been rapidly increasing globally at all ages[16,17] and is most likely driven by some potent environmental

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factor(s) interacting with similar human genetic susceptibilities. A closer relationship between these diseases was recently suggested; detection of CD and early treatment with mass screening have decreased the subsequent incidence of T1D in children.[18]

In this study, we analyzed the annual incidence of T1D in Olmsted County, Minnesota, from January 1, 1994, to December 31, 2010, by sex and age to determine trends in incidence, determine the proportion of the cohort with CD, and compare the T1D incidence trends with previously reported Olmsted County CD incidence trends.[16]

METHODS

This study was approved by the institutional review boards of Mayo Clinic and Olmsted Medical Center, Rochester, Minnesota. The Rochester Epidemiology Project (REP) is a database that allows for population-based studies in Olmsted County, Minnesota.[19] According to the 2010 US census, there were 144,248 Olmsted County residents. Two health systems, Mayo Clinic and Olmsted Medical Center, provide almost all the medical care in the county, including outpatient, inpatient, and emergency department settings. All residents of the county who receive any care at either institution are entered into the REP database, which links medical charts and indexes demographic characteristics, diagnoses, surgical interventions, and medications. The reliability and validity of the REP have been described elsewhere.[19]

The diagnosis and classification of diabetes has changed over the past 60 years, transitioning from classification by treatment method to classification by clinical and etiologic grounds.[20] Because of these changes and subsequent potential for incorrect coding (eg, diabetes mellitus or type 2 diabetes [T2D] rather than T1D), a broad search was first performed through several databases to identify incident cases of T1D from 1994 through 2010. The REP database served as the main database to identify patients using the terms "diabetes" and "insulin use" within 1 year of diabetes diagnosis. In addition, the REP database was searched using diagnosis codes 250.01, 250.03, 250.1, 250.11, 250.13, 250.33, 250.91, and 250.93. The lists were merged, and the charts of identified patients were then reviewed. Patients who received oral hypoglycemic agents for at least 1 year were excluded.

Mayo Clinic Life Science Systems Advanced Cohort Explorer and previous studies[13,21] were also used to identify any residual incident cases of T1D that may have been overlooked in the electronic search in Olmsted County. The Advanced Cohort Explorer is a search engine that allows for rapid searching of text within laboratory results, all aspects of clinical notes including the medical history, problem lists, and diagnostic codes in the clinical notes of the electronic medical record system at Mayo Clinic. The corresponding demographic data are also available. For this database, the terms "type 1 diabetes" and "type 1" AND "diabetes" were searched within the medical history, primary diagnosis, diagnoses, and secondary diagnoses clinical notes sections from 1994 through 2010. These lists were then merged to remove redundancy.

All identified charts were then reviewed individually to exclude patients with diabetes other than T1D in accordance with the American Diabetes Association's classification and diagnosis of diabetes.[20] *Type 1 diabetes* was defined as ketosis (ketoacidosis or greater than ketonuria), catabolic symptoms at diagnosis, insulin use from diagnosis and continued use at 1 year, and no use of oral hypoglycemic medications for longer than 1 year. Some young adults may have an inaccurate diagnosis of T2D, but after subsequent failure of oral hypoglycemic therapy, they may subsequently be realized to have had T1D.[20] These patients were included on the basis of clinical diagnosis by us or results of specific testing (ie, C-peptide or glutamic acid decarboxylase autoantibodies associated with T1D).[20] Patients who did not clearly fit the classification of T1D were included on the basis of clinical review based on glucose variability (intraday hypoglycemia and hyperglycemia documented serving as a surrogate for T1D) documented in the laboratory section of the medical record.[22] Patients with development of diabetes after long-standing chronic pancreatitis or pancreatectomy were excluded.

Latent autoimmune diabetes in adults (LADA) was recognized in the 1970s[23] as a form of diabetes that combined features of both T1D and T2D. Although the Expert Committee on the Diagnosis and Classification