Temporal Trends in Diabetic Ketoacidosis Prevalence at Diagnosis of Diabetes Among Children in Canada: A Population-Based Retrospective Cohort Study

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Abstract

BACKGROUND: Diabetic ketoacidosis (DKA) at type 1 diabetes (T1D) diagnosis is a preventable life-threatening complication. The frequency of DKA at diabetes onset varies significantly worldwide (12.8-80%) and is inversely related to the reported geographic incidence of T1D. Canadian data on the temporal trends of DKA prevalence at T1D onset in children is unknown. We aimed to determine the temporal changes in DKA prevalence at diabetes diagnosis in Canada.

METHODS: We conducted a population-based cohort study of children (ages 1–17 years) living in Quebec, Canada, diagnosed with diabetes between 2001 and 2014, using multiple health administrative linked databases available at the Institut national de santé publique du Québec through the Quebec Integrated Chronic Surveillance System (QICDSS). We used multivariate Poisson regression analysis with robust error variance to determine trends in DKA prevalence.

RESULTS: We found that 26% (1471/ 5741) of children presented with DKA at diabetes diagnosis. The incidence of diabetes was stable at 30 per 100,000 per year during the study period. The age- and sex-standardized rates of DKA increased from 22% (95% confidence interval (CI), 17%-26%) in 2001 to 30% (95% CI, 24%-36%) in 2014. The relative increase of DKA prevalence at diabetes diagnosis over the study period was 2.0% per year (Rate ratio (RR) 1.02; 95% CI, 1.01, 1.03).

INTERPRETATION: Despite a stable incidence of T1D, we found that the DKA prevalence at diabetes onset increased between 2001 and 2014. Our findings are concerning and warrant a need to continue to campaign to recognize T1D before DKA supervenes.

Introduction

Type 1 diabetes (T1D) is one of the most common chronic diseases of childhood with significant morbidity and mortality.[1,2] The incidence of T1D in children and adolescents is increasing by 3–5% per year worldwide and in Canada its incidence is among the highest in the world (30/100,000 cases per year).[1-5]

The diagnosis of T1D is preceded by typical symptoms of polyuria, polydipsia, weight loss and fatigue. If left undiagnosed and untreated, diabetic ketoacidosis (DKA) develops. DKA is an acute avoidable life-threatening complication and the leading cause of preventable hospitalizations, emergency department visits and deaths in the T1D population.[1,6,7] The economic costs of one DKA hospitalization are high, ranging from $4125 to $11,196 U.S.[8] In addition to acute morbidity risk, DKA is also associated with long-term morbidity. Recent studies suggest that DKA at diagnosis predicts poor long-term glycemic control, independent of demographic and socioeconomic factors.[9,10]

Globally, DKA rates at T1D diagnosis varies between 12-80% and is inversely correlated with the population incidence of T1D, suggesting that increased awareness of T1D results in earlier diagnosis and treatment, leading to a decreased DKA risk.[11] Despite a global increase in the incidence of T1D, most jurisdictions have reported stable rates of DKA [12-17] Other countries, such as Italy and Finland, have reported decreasing DKA rates at diabetes diagnosis, coinciding with diabetes awareness programs.[18,19] In the United States, temporal trends in DKA rates at diabetes diagnosis have been conflicting.[12,20] The SEARCH for diabetes in youth study, a multi-centre registry of youth with diabetes in the U.S., reported stable temporal trends in DKA incidence at diabetes diagnosis over three time periods (2002- 2003, 2004-2005, and 2008-2010).[12] Colorado,

on the other hand, demonstrated increasing trends of DKA rates at T1D diagnosis between 1998-2012.[20] Since, DKA is an avoidable complication of T1D, knowledge of the population burden of DKA is important in identifying whether gaps in health care access and/or in knowledge of the early symptoms of T1D exist in both the lay and medical community. Thus, we aimed to examine the temporal trends in DKA prevalence at T1D diagnosis among children and adolescents in Quebec, Canada from 2001 to 2014.

Methods

Study design

We conducted a population-based retrospective cohort study of children (ages 1–17 years) living in Quebec, Canada, diagnosed with diabetes between April 1st, 2001 and March 31st, 2014. Quebec is Canada's second largest province with over 8 million residents with universal public health insurance coverage system through which all residents are insured for medically necessary health care services. As such, all encounters with the health care system are contained within the health administrative data and selection bias was minimized. The study was approved by the McGill University Health Centre Research Ethics Board.

Data Sources

We used multiple health administrative databases of all individuals with diabetes available at the Institut national de santé publique du Québec through the Quebec Integrated Chronic Surveillance System (QICDSS). The QICDSS includes the Registered Persons Database (patient demographics), Physician Claims Database (physician remunerated services across all clinical

settings) and the Hospital Discharge Database (MED-ECHO). The régie de l'assurance maladie du Québec (RAMQ) linked these databases using a unique indiviual encoded identifier.

Cohort identification

We identified our cohort using the Canadian Chronic Disease Surveillance System's (CCDSS) validated definition to identify diabetes within administrative data. This definition has been shown to have a 99.9% specificity and 94% sensitivity in identifying those < 18 years of age with diabetes within Canadian health administrative databases.[21] This case definition requires one hospitalization, or two physician visits claims for diabetes in two-years. The date of diagnosis of diabetes was the first physician visit claim, or first hospitalization coded for diabetes, whichever occurred first. The CCDSS definition does not distinguish between T1D and type 2 diabetes; however the vast majority of Canadian children and youth with diabetes have T1D (95%).[22] Further, in Canada, the incidence of T1D is 32 cases per 100,00 and of non-T1D (including type 2 diabetes) is 2.3 cases per 100,000 children and youth per year.[23,24] Patients with invalid health insurance numbers were excluded.

Outcome

Our primary outcome was DKA at the time of a diabetes diagnosis. We identified DKA episodes diagnosed within three days of the date of diagnosis of diabetes and taking place during outpatient or emergency department visits (Physicians Service Claims Database, using the International Classification of Diseases' Quebec specific diagnosis codes [ICD-9] 250.1- 250.2) or during a hospitalization (using MED-ECHO hospital data, principal or secondary diagnosis of DKA ICD-9 codes before 2006 and ICD-10 codes E10.10-E14.10 and E10.12-E14.12 after 2006). We chose

a 3-day window as this was considered a reasonably short period whereupon a patient was likely in DKA at the time of diagnosis.[25] These DKA codes have been used in previous Canadian studies in children to identify DKA within Canadian health administrative databases, ensuring that outcomes were measured consistently and using the same criteria.[25-27] Moreover, the health records in the Physicians Service Claims Database were collected prospectively and the database was not established to compare DKA prevalence at diabetes diagnosis by year. Therefore, systematic differences in the accuracy of reported information between groups of patients in the cohort is unlikely, minimizing recall bias.

Patient characteristics at diagnosis

The following patient characteristics at diagnosis (Registered Persons Database) were included: age at diabetes diagnosis, sex, calendar year, combined material and social deprivation index (proxy for socioeconomic status [SES]) and rural status. Deprivation index and rural status were assigned from the individual's residential postal code at diabetes diagnosis.

Age was categorized into the following age groups: 1-4 years, 5-11 years and 12-17 years. SES was determined using the Pampalon index, a validated area-based material and social deprivation index for Canada.[28] The study cohort was divided across quintiles of their combined material and social deprivation indices (Q1= least deprived, Q5=most deprived). The material and social quintiles were combined, and individuals were grouped into 3 categories: least deprived (Q1-Q2), moderately deprived (Q3) and most deprived (Q4-Q5). Rural status was defined as urban (population > 100,000) small cities (population 10,000-100,000) and rural (population <10,000).

Statistical analysis

To compare DKA prevalence at diabetes diagnosis by year, we used direct standardization to control for differences in age distribution and stratified by sex (standardized to 2001 Quebec age distribution). We used t-tests to compare continuous variables and Pearson's chi-square to compare categorical variables between those that presented in DKA versus those that did not present in DKA. Multivariate Poisson regression analyses with robust error variance were used to model the relationship between calendar year and DKA prevalence at diabetes onset, adjusted for sex, age-group at diagnosis, rural status and SES.[29] Individuals with missing variables were included. Statistical tests were two-sided with a significance level of $P<0.05$. Analyses were performed using SAS 9.4 (SAS Institute, Care, NC).

Results

We identified 5,741 new cases of diabetes. The mean age at diagnosis was 10.1 years (SD 4.8 years) and 52% were males. Overall, 25.6% of the study population presented with DKA at diabetes diagnosis (Table 1). The rates of DKA were 29.1, 30.1% and 20.5% in the 1-4, 5-11 and 12-17 year old age-groups, respectively (Table 2).

Over the study period, the incidence of diabetes remained stable with a rate of approximately 30 cases per 100,000 children per year. Age- and sex-standardized DKA prevalence at diabetes diagnosis increased from 22% (95% confidence interval (CI), 17%-26%) in 2001 to 30% (95% CI, 24%-36%) in 2014 (Table 1 and Figure 1). In the multivariate analysis, the relative increase in DKA over the study period was 2.0% per year (Rate Ratio (RR) 1.02; 95% CI, 1.01-1.03, P for trend <.001). Those diagnosed with diabetes in 2014 were 39% more likely to present with DKA compared to children diagnosed in 2001 (RR 1.39, 95% CI, 1.08-1.79). Across the entire study period, children ages 12-17 years were 30% less likely to present with DKA than children ages

1-4 years (RR 0.70, 95% CI, 0.62-0.79), while children living in small cities were 16% more likely to present with DKA compared to children living in urban settings (RR 1.16, 95% CI 1.02-1.32) (Table 1). There was no association between SES and DKA risk at diabetes diagnosis.

Interpretation

In this population-based study, over a quarter of children presented in DKA at diabetes onset. DKA prevalence at diabetes diagnosis increased between 2001 to 2014 from 22% to 30%, representing a relative increased risk of 2% per year, despite a stable incidence of diabetes over the same time frame. Our results suggest that an increasing number of children are experiencing delays in the diagnosis and treatment of diabetes. We found that DKA risk was higher among younger children and among those living in smaller versus urban cities.

Colorado is the only other jurisdiction that has reported increasing temporal trends in DKA prevalence at diabetes diagnosis; where, amongst 3439 children with T1D, 38.9% had DKA at T1D diagnosis and the prevalence of DKA at diagnosis increased by 55% (from 29.9% to 46.2%) between 1998 and 2012.[20] The U.S. SEARCH for Diabetes in Youth Study reported stable temporal trends in DKA prevalence at diabetes diagnosis from 2002-2010.[12] Their prevalence of DKA at diagnosis were similar to ours, wherein approximately one-third of youth presenting with new onset T1D were in DKA.[12] In Germany, among 14, 664 patients with T1D, DKA prevalence at diagnosis was 21.1%; however, despite an increasing annual T1D incidence of 4.4%, temporal trends in DKA prevalence at diabetes diagnosis remained stable (1995-2007).[15] Austria has also reported stable temporal trends in DKA prevalence at diabetes diagnosis (1998 – 2008) with a DKA prevalence somewhat higher than observed in our population at 37.2%.[16] Other jurisdictions, such as Finland have reported declines in DKA prevalence at diagnosis with rates of 18.9% in

1982-1991, compared to 15.2 % in 1992-2001 (P = 0.028).[18]

Reasons for our increasing trend is unclear. In the Colorado study, the increasing trends in DKA were partially attributed to the increasing prevalence of child poverty in Colorado. In our study, we did not find any association between SES disparities and DKA risk, which may be explained by Canada's universal coverage health care system. However, our DKA prevalence at diagnosis is high and is increasing. Limited and deteriorating access to primary health care in Canada may be one contributing factor. We have previously documented that 41% of children with newly-diagnosed T1D living in Quebec did not have a usual provider of primary care, and that having a primary care provider was associated with a reduced DKA risk at diagnosis in children >5 years.[25] Furthermore, despite having a universal coverage health care system, wait times for urgent primary care visits are higher in Canada than in other countries and continue to increase.[30]

Lack of physician and public awareness of the signs or symptoms of T1D may be another contributor to the increasing trends in DKA. In Finland, increasing physician and public awareness through two mechanisms may have arguably contributed to the observed decrease in DKA prevalence at diagnosis.[18] First, Finland has one of the highest worldwide incidence rates of T1D such that public and physician awareness of the symptoms and signs are high, and the diagnosis is often made before DKA develops. Second, a T1D prediction and prevention trial was carried out in the Finish population, whereupon newborn infants carrying HLA-conferred susceptibility to T1D were invited to participate in regular follow-up to detect possible signs of diabetes, plausibly increasing awareness.[31] In addition, studies in other jurisdictions evaluating educational campaigns have shown that by increasing public and physician awareness on the symptoms of diabetes, DKA rates at diagnosis decrease. [19]

Other factors associated with DKA risk included younger age and living in a small city. Younger age has consistently been identified as a risk factor for DKA at diabetes onset, including in a systematic review of 46 studies which identified younger age, particularly < 2 years old, as a major risk factor for DKA at diagnosis.[32] Several factors may account for this increased DKA risk, including: 1) physicians may have a lower index of suspicion for T1D in younger children, 2) younger children may have a faster metabolic decompensation, 3) younger children may not be able to verbalize their diabetes symptoms and, 4) their symptoms may be more subtle and not as apparent as in older children, leading to delayed diagnosis and treatment.

We also found that children living in small cities were at increased risk of DKA compared to children living in urban settings. This is in contrast to European data wherein no association between DKA risk and urban-rural status had been found.[32] Our observations, could be explained, in part, by differing distribution of health care resources and access across regions.[33] Nonetheless, this could not be confirmed in our study.

SES was not a significant predictor of DKA, which is contrary to what was reported in Colorado[20] and in another study from New York state demonstrating that lack of private insurance (a proxy for SES) is a risk factor for DKA at diagnosis of diabetes.[34] Because children in Quebec have universal health care coverage, SES might have had less of an impact on DKA risk as compared to children in jurisdictions without a universal health care coverage system. However, in two Canadian studies, the risk of DKA at diabetes onset was associated with lower income quintiles [35] and greater social and material deprivation.[25] It is possible that other factors such as sub-optimal health care access and T1D awareness mitigated the effect of SES on DKA risk in our study.

The strengths of our study are its large sample size, long period of observation and our ability to capture data from all children diagnosed with diabetes in Quebec across all clinical settings,

strengthening the generalizability of our study. However, our study has limitations. The diagnosis of DKA was based on administrative data and not on biochemical grounds, as such we could not distinguish between the varying severities of DKA. Using health administrative databases, we could not distinguish between T1D and type 2 diabetes, nevertheless, approximately 95% of children < 18 years of age have T1D.[22] Since DKA can occur in both forms of diabetes, our increasing trends of DKA at diagnosis is a concerning observation irrespective of the type of diabetes the child has, highlighting the importance of determining the underlying drivers.

In this large population-based study we have demonstrated increasing temporal trends in DKA risk at diabetes diagnosis despite a stable incidence of diabetes in Quebec. Our results are concerning and underscore the need to increase physician and public awareness of the signs and symptoms of childhood diabetes before DKA develops. As other jurisdictions have demonstrated stable or decreasing trends in DKA prevalence, future research, potentially through international collaborations, should investigate the reason for our increasing DKA trends, so as to develop targeted and effective interventions.

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References

1. Dahlquist G, Kallen B. Mortality in childhood-onset type 1 diabetes: a population-based study. *Diabetes care.* 2005;28:2384-7.
2. Edge JA, Ford-Adams ME, Dunger DB. Causes of death in children with insulin dependent diabetes 1990-96. *Archives of disease in childhood.* 1999;81:318-23.
3. Fox DA, Islam N, Sutherland J, Reimer K, Amed S. Type 1 diabetes incidence and prevalence trends in a cohort of Canadian children and youth. *Pediatric diabetes.* 2018;19:501-5.
4. I. NMRLREL. Trends in diabetes prevalence and incidence in children and youth in Quebec, Canada 2000-2008: a population-based study. Paper presented at: International Society of PEdiatric and Adolescent Diabetes; Oct 19-22, 2011; Miami.
5. Patterson CC, Dahlquist GG, Gyurus E, Green A, Soltesz G. Incidence trends for childhood type 1 diabetes in Europe during 1989-2003 and predicted new cases 2005-20: a multicentre prospective registration study. *Lancet (London, England).* 2009;373:2027-33.
6. Glasgow AM, Weissberg-Benchell J, Tynan WD, et al. Readmissions of children with diabetes mellitus to a children's hospital. *Pediatrics.* 1991;88:98-104.
7. Keenan HT, Foster CM, Bratton SL. Social factors associated with prolonged hospitalization among diabetic children. *Pediatrics.* 2002;109:40-4.
8. Tieder JS, McLeod L, Keren R, et al. Variation in resource use and readmission for diabetic ketoacidosis in children's hospitals. *Pediatrics.* 2013;132:229-36.

9. Duca LM, Wang B, Rewers M, Rewers A. Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes Predicts Poor Long-term Glycemic Control. *Diabetes care.* 2017;40:1249-55.

10. Shalitin S, Fisher S, Yackbovitch-Gavan M, et al. Ketoacidosis at onset of type 1 diabetes is a predictor of long-term glycemic control. *Pediatric diabetes.* 2018;19:320-8.

11. Jefferies CA, Nakhla M, Derraik JG, Gunn AJ, Daneman D, Cutfield WS. Preventing Diabetic Ketoacidosis. *Pediatric clinics of North America.* 2015;62:857-71.

12. Dabelea D, Rewers A, Stafford JM, et al. Trends in the prevalence of ketoacidosis at diabetes diagnosis: the SEARCH for diabetes in youth study. *Pediatrics.* 2014;133:e938-45.

13. de Vries L, Oren L, Lebenthal Y, Shalitin S, Lazar L, Phillip M. Decrease in frequency of ketoacidosis at diabetes onset over the past two decades - perspectives of a paediatric tertiary care centre. *Diabetic medicine : a journal of the British Diabetic Association.* 2012;29:e170-5.

14. Jefferies C, Cutfield SW, Derraik JG, et al. 15-year incidence of diabetic ketoacidosis at onset of type 1 diabetes in children from a regional setting (Auckland, New Zealand). *Scientific reports.* 2015;5:10358.

15. Neu A, Hofer SE, Karges B, Oeverink R, Rosenbauer J, Holl RW. Ketoacidosis at diabetes onset is still frequent in children and adolescents: a multicenter analysis of 14,664 patients from 106 institutions. *Diabetes care.* 2009;32:1647-8.

16. Schober E, Rami B, Waldhoer T. Diabetic ketoacidosis at diagnosis in Austrian children in 1989-2008: a population-based analysis. *Diabetologia.* 2010;53:1057-61.

17. Trellu M, Lacombe S, Morin D, Dalla-Vale F. [Epidemiology of diabetes in children in Languedoc-Roussillon (France)]. *Archives de pediatrie : organe officiel de la Societe francaise de pediatrie.* 2015;22:241-6.

18. Hekkala A, Knip M, Veijola R. Ketoacidosis at diagnosis of type 1 diabetes in children in northern Finland: temporal changes over 20 years. *Diabetes care.* 2007;30:861-6.

19. Vanelli M, Chiari G, Ghizzoni L, Costi G, Giacalone T, Chiarelli F. Effectiveness of a prevention program for diabetic ketoacidosis in children. An 8-year study in schools and private practices. *Diabetes care.* 1999;22:7-9.

20. Rewers A, Dong F, Slover RH, Klingensmith GJ, Rewers M. Incidence of diabetic ketoacidosis at diagnosis of type 1 diabetes in Colorado youth, 1998-2012. *Jama.* 2015;313:1570-2.

21. Dart AB, Martens PJ, Sellers EA, Brownell MD, Rigatto C, Dean HJ. Validation of a pediatric diabetes case definition using administrative health data in manitoba, Canada. *Diabetes care.* 2011;34:898-903.

22. Shulman R, Miller FA, Stukel TA, Daneman D, Guttmann A. Resources and population served: a description of the Ontario Paediatric Diabetes Network. *CMAJ open.* 2016;4:E141-6.

23. Amed S, Dean HJ, Panagiotopoulos C, et al. Type 2 diabetes, medication-induced diabetes, and monogenic diabetes in Canadian children: a prospective national surveillance study. *Diabetes care.* 2010;33:786-91.

24. Guttmann A, Nakhla M, Henderson M, et al. Validation of a health administrative data algorithm for assessing the epidemiology of diabetes in Canadian children. *Pediatric diabetes.* 2010;11:122-8.

25. Nakhla M, Rahme E, Simard M, Larocque I, Legault L, Li P. Risk of ketoacidosis in children at the time of diabetes mellitus diagnosis by primary caregiver status: a population-based retrospective cohort study. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne.* 2018;190:E416-e21.

26. Nakhla M, Rahme E, Simard M, Guttmann A. Outcomes associated with a pediatric clinical diabetes network in Ontario: a population-based time-trend analysis. *CMAJ open.* 2017;5:E586-e93.

27. Shulman R, Stukel TA, Miller FA, et al. Low socioeconomic status is associated with adverse events in children and teens on insulin pumps under a universal access program: a population-based cohort study. *BMJ open diabetes research & care.* 2016;4:e000239.

28. Pampalon R, Hamel D, Gamache P, Philibert MD, Raymond G, Simpson A. An area-based material and social deprivation index for public health in Quebec and Canada. *Canadian journal of public health = Revue canadienne de sante publique.* 2012;103:S17-22.

29. Blais C, Jean S, Sirois C, et al. Quebec Integrated Chronic Disease Surveillance System (QICDSS), an innovative approach. *Chronic diseases and injuries in Canada.* 2014;34:226-35.

30. Information CIfH. Health Care in Canada, 2012: A Focus on Wait Times.

31. Kupila A, Muona P, Simell T, et al. Feasibility of genetic and immunological prediction of type I diabetes in a population-based birth cohort. *Diabetologia.* 2001;44:290-7.

32. Usher-Smith JA, Thompson MJ, Sharp SJ, Walter FM. Factors associated with the presence of diabetic ketoacidosis at diagnosis of diabetes in children and young adults: a systematic review. *BMJ (Clinical research ed.).* 2011;343:d4092.

33. Guttmann A, Shipman SA, Lam K, Goodman DC, Stukel TA. Primary care physician supply and children's health care use, access, and outcomes: findings from Canada. *Pediatrics.* 2010;125:1119-26.

34. Mallare JT, Cordice CC, Ryan BA, Carey DE, Kreitzer PM, Frank GR. Identifying risk factors for the development of diabetic ketoacidosis in new onset type 1 diabetes mellitus. *Clinical pediatrics.* 2003;42:591-7.

35. Bui H, To T, Stein R, Fung K, Daneman D. Is diabetic ketoacidosis at disease onset a result of missed diagnosis? *The Journal of pediatrics.* 2010;156:472-7.

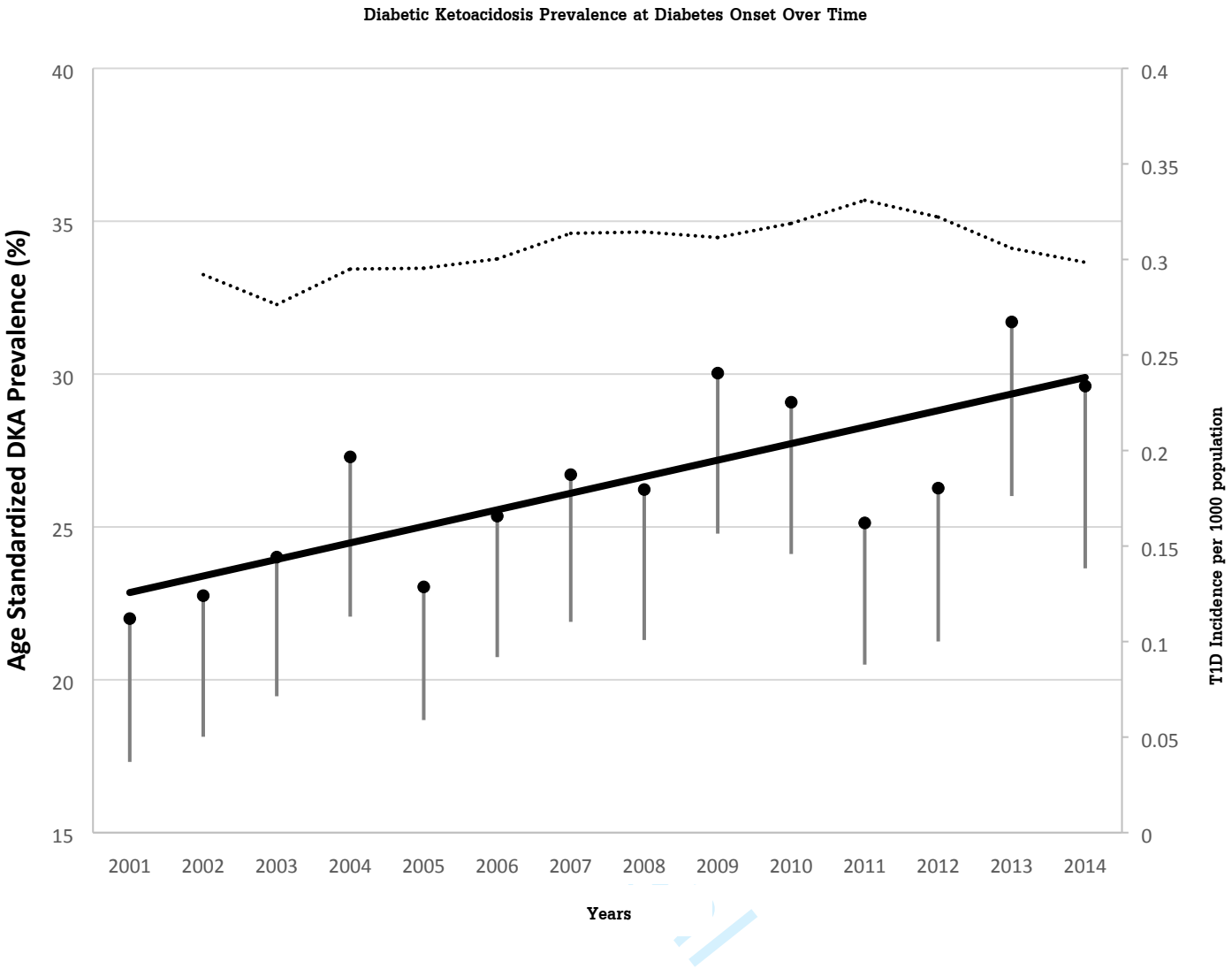

Figure 1. Age- and sex-standardized prevalence of diabetic ketoacidosis at diabetes diagnosis over time

Legend:
Black circle: point estimate of age- and sex- standardized DKA prevalence
Vertical black bars: 95 % confidence interval of age- and sex- standardized DKA prevalence
Black line: trend in age- and sex- standardized DKA prevalence over time
Dotted line: T1D incidence per 1000 population over time
Abbreviations: DKA: diabetic ketoacidosis; T1D; Type 1 Diabetes

Table 1. Crude proportions and adjusted rate ratio of diabetic ketoacidosis at diabetes diagnosis by calendar year

Covariate	Diabetic Ketoacidosis (DKA) Crude proportion		Adjusted Prevalence Rate Ratio (95% CI)*
	N	%	
Calendar Year			
Total	1471	25.6	
2001	80	21.3	1.0
2002	89	22.1	1.05 (0.80-1.36)
2003	100	23.2	1.08 (0.83-1.39)
2004	104	27.0	1.31 (1.01-1.68)
2005	102	23.0	1.10 (0.85-1.42)
2006	108	25.2	1.17 (0.91-1.51)
2007	114	26.9	1.26 (0.98-1.61)
2008	107	24.5	1.15 (0.90-1.49)
2009	126	29.1	1.40 (1.10-1.78)
2010	126	27.5	1.28 (1.01-1.63)
2011	106	24.7	1.16 (0.90-1.50)
2012	99	25.2	1.19 (0.92-1.54)
2013	113	30.4	1.43 (1.12-1.83)
2014	97	29.4	1.39 (1.08-1.79)

Note: CI= confidence interval, DKA= diabetic ketoacidosis, RR=Rate Ratio.

*Adjusted for age group, sex, socioeconomic status and rural status.

Table 2. Crude proportions and adjusted rate ratio of diabetic ketoacidosis at diabetes diagnosis Using Poisson Regression

Age group	No. and % of patients with DKA, by characteristic		Adjusted RR (95% CI)*
	N	%	
1-4 y.o.	286	29.1	1.0
5-11 y.o.	659	30.1	1.03 (0.92-1.16)
12-17 y.o.	526	20.5	0.70 (0.62-0.79)
Sex			
Male	793	26.5	1.00
Female	678	24.7	0.96 (0.92-1.01)
Socioeconomic Status**			
Least Deprived	597	24.7	1.00
Moderately Deprived	295	26.5	1.09 (0.97-1.23)
Most deprived	528	26.1	1.06 (0.96-1.18)
Rural Status***			
Urban (including population > 100,000)	956	25.2	1.00
Small Cities 10,000-100,000	205	29.2	1.16 (1.02-1.32)
Rural (<10, 000)	294	24.4	0.95 (0.85-1.06)

Note: CI= confidence interval, DKA=diabetic ketoacidosis, RR=Rate Ratio.
*Adjusted for age group, sex, socioeconomic status, rural status, and year.

**Missing SES study population n=189, n= 138 (without DKA) and n=51 (with DKA); Social and material quintiles were combined into a 5 X 5 table, the 25 combined categories were grouped into 3 categories: least deprived, moderately deprived, most deprived

*** Missing rural status n=48, n=32 (without DKA), n= 16 (with DKA)