Risk of Psychiatric Disorders and Suicide Attempts in Emerging Adults with Diabetes

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Running Title: Psychiatric Disorders in Young Adults with Diabetes

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ABSTRACT

Objectives: To determine the longitudinal risks of psychiatric disorders in adolescents and emerging adults with versus without diabetes.

Research Design and Method: We conducted a retrospective cohort study in Québec, Canada, using linked health administrative databases of adolescents (ages 15 years) with and without diabetes, and without prior psychiatric disorders, between 1997-2015, followed to age 25 years.

Results: Our cohort included 3,544 individuals with diabetes and 1,388,397 without diabetes. Individuals with diabetes were more likely to suffer from a mood disorder (diagnosed in the emergency department or hospital (adjusted hazard ratio 1.33, 95% confidence interval 1.19-1.50), attempt suicide (3.25, 1.79-5.88), visit a psychiatrist (1.82, 1.67-1.98) and experience any type of psychiatric disorder (1.29, 1.21-1.37)), compared to their peers without diabetes.

Conclusions: Between the ages of 15 and 25 years, the risks of psychiatric disorders and suicide attempts were substantially higher in adolescents and emerging adults with versus without diabetes.

Key words: type 1 diabetes, psychiatric disorders, adolescents, transition to adult care, emerging adult

INTRODUCTION

Adolescence and emerging adulthood (ages 18-30 years) is a challenging developmental period wherein individuals are establishing their autonomy, personal identity and making vocational and educational choices. For the adolescent with type 1 diabetes (T1D), this stage is further complicated by the daily demands of the disease as well as the transfer to adult diabetes care.

Higher risks of psychiatric disorders in individuals with versus without T1D have been previously reported, but the risk of psychiatric disorders from adolescence to emerging adulthood has not been assessed (1-3). Children and adolescents (ages ≤ 18 years) with T1D are twice as likely to have a mood disorder and almost twice as likely to attempt suicide, compared to controls without T1D (3). Psychiatric disorders are associated with both suboptimal glycemic control and increased risks of diabetic ketoacidosis (DKA) and hypoglycaemia (1). As such, we aimed to determine the longitudinal risks of new onset psychiatric disorders and suicide attempts in adolescents and emerging adults (ages 15 to 25 years) with diabetes compared to their same-aged peers without diabetes.

RESEARCH DESIGN AND METHODS

Methodology

Study design and data sources

We conducted a retrospective cohort study of adolescents and emerging adults living in Québec, Canada using the Québec Integrated Chronic Disease Surveillance System (QICDSS) database maintained at the Institut National de Santé Publique du Québec (INSPQ) (4). Our study was approved by the McGill University Health Center Research Ethic Board.

Study cohort

Using the QICDSS database, we identified all individuals born between April 1, 1982, and December 31, 1998. Exposed individuals were those diagnosed with diabetes between ages 1 to 15 years from April 1997 to December 2013. Diabetes status was identified according to the Canadian Chronic Disease Surveillance System's (CCDSS) validated definition (one hospitalization or two physician claims for diabetes within a two-year period) (4, 5).

All individuals 1 to 15 years old, identified from the QICDSS database, who did not have diabetes from April 1997 to December 2013, formed the unexposed group. Exposed and unexposed individuals were included into the cohort at age 15 years (cohort entry date) and were followed until March 31st 2015, age 25 years, death, or migration out of the province. Our follow-up period included the period of transfer from pediatric to adult care that generally occurs in Québec at age 18 years (6).

Exposed individuals were required to have at least one additional medical encounter for diabetes (outpatient or inpatient) following their diagnosis date. To decrease the possibility of capturing ongoing psychiatric events that started before and were unrelated to the unique developmental stage of adolescence and emerging adulthood, we excluded those with a diagnosis (international classification of disease code, ICD-9th and 10th revisions) of psychiatric disorders except attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) in the two years preceding the cohort entry date. Included individuals were required to have at least six months of data after their cohort entry date.

Outcomes (ICD-9 and ICD-10 codes in Appendix 1)

Our primary outcomes were 1) mood disorders diagnosed in the emergency department (ED) or hospital; 2) hospitalization for a suicide attempt; and 3) deaths by suicide; and our secondary outcomes were 1) mood disorders diagnosed exclusively in the outpatient clinic; and 2) any visit to a psychiatrist. We also examined the combined outcome of any psychiatric disorders (Appendix 2) excluding ADHD and ASD, identified according to methods adopted by the QICDSS (7).

Baseline individual characteristics

We assessed the following individual characteristics at the cohort entry date: social deprivation, material deprivation, sex, rural residency and year of birth. Material and social deprivation indices were developed by the INSPQ based on employment status, income, educational level, proportion of individuals living alone and proportions of single families (8). Rural residency was determined based on the Census Metropolitan Area and Census Agglomeration Influenced Zones developed by Statistics Canada (4, 9, 10).

Data analysis

Incidence rates were calculated per 100 person-year for all outcomes. Multivariate Cox proportional hazard models were used to compare time to mood disorders diagnosed in the ED or in-hospital in individuals with versus without diabetes. The model was adjusted for all baseline individual characteristics. We used similar models to compare all other outcomes between those with versus without diabetes.

Results were reported as adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI). Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). Statistical tests

were two-sided with significance assigned at p-value < 0.05. Supplemental analyses were

performed (appendix 3).

RESULTS

We identified 3,544 individuals with and 1,388,397 individuals without diabetes. Baseline

individual characteristics are shown in Appendix 4. The crude incidence rate of each outcome is

shown in Table 1. Individuals with (versus without) diabetes were more likely to have a mood

disorder (diagnosed in the ED or in-hospital) (1.33, 1.19-1.50), be admitted to hospital for a

suicide attempt (3.24, 1.79-5.88), visit a psychiatrist (1.82, 1.67-1.98), or have any psychiatric

disorders (1.29, 1.21-1.37) (Table 1). The risk of mood disorders diagnosed in the outpatient

clinic and the risk of schizophrenia did not vary based on diabetes status.

CONCLUSIONS

Psychiatric risk in individuals with diabetes from adolescence to emerging adulthood had not been

previously described. We found that adolescents and emerging adults with diabetes were at

increased risk for psychiatric disorders compared to those without diabetes. To our knowledge,

our study fills an important gap in the literature, as it is the only one to date that longitudinally

assessed psychiatric disorders among adolescents and emerging adults with diabetes. Previous

studies have reported increased prevalence of depressive symptoms with age (11-25 years) (1),

more common mental health referrals during emerging adulthood and a higher prevalence of self-

reported psychiatric disorders towards late emerging adulthood (11).

Our findings may be explained by several factors. First, adolescents and emerging adults with

diabetes face numerous challenges related to their diabetes management, when other social,

educational and financial competing priorities inherent to emerging adulthood occur. During this critical period, the transition to adult diabetes care may further exacerbate the risk of psychiatric disorder where underlying factors such as change in diabetes care providers, new treatment facilities, increased level of responsibility and differences in disease management might contribute to this risk. Second, limited access to psychosocial services may contribute to the increased risk of psychiatric disorders, as adult endocrinologists rarely receive a patient's psychosocial summary as part of their referral documents from their pediatric colleagues (12) and only a minority (42%) have access to mental health services for their emerging adult patients with diabetes (13).

Our observations have substantial implications for adolescents and emerging adults with diabetes. Psychiatric disorders are associated with serious adverse diabetes-related outcomes among emerging adults with diabetes, such as more frequent and longer admissions to hospital, higher frequency of DKA, more frequent and more severe hypoglycemic episodes and worsening glycemic control (1). A history of a psychiatric referral has been associated with death from acute events in individuals (ages < 40 years) with T1D (14).

In summary, the risk of developing psychiatric disorders is increased between the ages of 15 and 25 years in individuals with diabetes versus those without. Our observations highlight the importance of identifying psychiatric disorders and increasing access to mental health services during this vulnerable transition period.

AUTHORSHIP CONTRIBUTIONS

All authors contributed to the study design, interpretation of the data and revisions of the manuscript. In addition, Marie-Eve Robinson performed the statistical and data analyses and drafted the manuscript. Meranda Nakhla provided clinical expertise with respect to diabetes disease management in Quebec. Marc Simard assisted with the statistical analyses. Isabelle Larocque provided expertise on the data sources used in the study. Jai Shah provided clinical expertise with respect to psychiatric disorders management in Quebec. Elham Rahme provided methodological expertise and oversaw the statistical analyses. Marie-Eve Robinson and Elham Rahme take responsibility for the integrity of the data.

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TABLES

Table 1. Adjusted Cox proportional hazard ratios and incidence rate for all mental health

outcomes in adolescents and emerging adults with diabetes compared to those without diabetes

	Secondary outcomes		Combined outcomes			
	Mood disorders ED or hospital	Suicide attempts	Mood disorders outpatient clinic	Visit to a psychiatrist	Schizo-phrenia	Any psychiatric disorders
DM (vs. no DM) aHR	1.33	3.25	0.99	1.82	0.81	1.29
(95% CI)	(1.19-1.50)	(1.79-5.88)	(0.91-1.08)	(1.67-1.98)	(0.49-1.32)	(1.21-1.37)
DM duration* (vs. no DM)						
0 - 2 yrs aHR	1.46	4.25	1.08	2.03	1.03	1.37
(95% CI)	(1.23-1.74)	(1.77-10.23)	(0.94-1.24)	(1.79-2.30)	(0.53-1.98)	(1.24-1.51)
2 - 5 yrs aHR	1.30	1.83	0.87	1.69	1.07	1.24
(95% CI)	(1.06-1.58	(0.46-7.32)	(0.73-1.02)	(1.45-1.97)	(0.51-2.25)	(1.11-1.39)
≥5 yrs aHR	1.18	3.58	1.01	1.66	N/A****	1.23
(95% CI)	(0.93-1.49)	(1.34-9.56)	(0.85-1.20)	(1.40-1.97)	N/A****	(1.09-1.39)
Social depr** (most vs. least deprived) aHR	1.31	1.50	1.05	1.27	1.53	1.17
(95% CI)	(1.29-1.34)	(1.25-1.80)	(1.04-1.07)	(1.25-1.29)	(1.43-1.63)	(1.16-1.18)
Material depr** (most vs. least deprived) aHR	1.40	1.88	0.89	1.05	1.34	1.04
(95% CI)	(1.37-1.43)	(1.55-2.29)	(0.87-0.90)	(1.03-1.07)	(1.25-1.44)	(1.03-1.05)

Females (vs. males) aHR	1.26	1.59	1.78	1.15	0.41	1.59
(95% CI)	(1.25-1.28)	(1.42-1.77)	(1.76-1.79)	(1.13-1.16)	(0.39-0.43)	(1.58-1.60)
Rural residency*** (vs. urban) aHR	1.13	1.31	0.85	0.93	0.87	0.95
(95% CI)	(1.11-1.15)	(1.14-1.51)	(0.84-0.86)	(0.92-0.94)	(0.82-0.92)	(0.95-0.96)
Birth year aHR	1.06	1.18	1.06	1.08	0.98	1.01
(95% CI)	(1.06-1.07)	(1.16-1.20)	(1.06-1.06)	(1.08-1.08)	(0.98-0.99)	(1.01-1.01)
Individuals with DM, N (IR)	296 (1.25)	17 (0.07)	474 (2.01)	536 (2.27)	16 (0.07)	947 (4.01)
Individuals without DM, N (IR)	101,940 (0.96)	2,981 (0.03)	231,721 (2.19)	129,808 (1.23)	9,200 (0.09)	342,597 (3.23)

Table 1 Legend:

Abbreviations: aHR: adjusted hazard ratio; CI: confidence interval; Depr: deprivation; DM: diabetes mellitus; ED: emergency department; IR: incidence rate per 100 person-year; N/A: non-applicable

The model was adjusted for social deprivation, material deprivation, sex, rural residency and birth year using Cox Proportional Hazard Regression Analysis.

Cox proportional hazard regression analyses to examine deaths by suicide were not completed because fewer than five suicides were observed in the group with diabetes.

*These estimates were derived from a separate multivariate Cox Proportional Hazard Regression Analysis adjusted for diabetes duration (instead of diabetes status), social deprivation, material deprivation, sex, rural residency and birth year.

** The material deprivation index is based on employment, income and education level. The

social deprivation index is based on the proportions of individuals living alone (single, separated,

divorced or widowed) and the proportion of single-parent families. Material and social

deprivation indices were categorized into quintiles (1= least deprived, 5= most deprived).

*** Rural residency: rural population refers to population < 10,000. Urban population refers to

population > 10,000.

Rural residency and material and social deprivation indices were determined at study entry using

the individual's postal code.

**** Fewer than 5 individuals had schizophrenia and a diabetes duration of more than five years.

Appendix 1. ICD-9 and ICD-10 codes for each outcome.

Mood disorders

The primary and secondary ICD-9 codes for mood disorders are: 296, 300, 311. The ICD-10 codes for mood disorders are: F30-F48, F68.

Suicide attempts

The primary and secondary ICD-9 codes for hospitalization for a suicide attempt are: E950.0-E959.9. The ICD-10 codes for hospitalization for a suicide attempts are: ICD-10 codes: X60 to X84.

Deaths by suicide

The ICD-10 codes for death by suicide are: X60 to X84 and Y87).

Schizophrenia

The ICD-9 codes for schizophrenia are: 295. The ICD-10 codes for schizophrenia are: F20, F21, F23.2, F25).

Combined outcomes

The ICD-9 codes for the combined outcome of any psychiatric disorders are: 290-319. The ICD-10 codes for any psychiatric disorders are: F00-F99. The ICD-9 and ICD-10 codes attention deficit hyperactivity disorder (314 and F91) and autism spectrum disorders (299 and F84) were excluded.

Appendix 2. All psychiatric disorders included in the combined outcome of any psychiatric disorders

Any psychiatric disorders included:

Mood disorders, schizophrenia, schizotypal and delusional disorders, organic psychotic conditions and other psychoses, neurotic disorders, personality disorders and other nonpsychotic mental disorders, intellectual disabilities, organic mental disorders, mental behavioral disorders due to psychoactive substance, neurotic, stress-related and somatoform disorders, behavioral syndromes associated with physiological disturbances and physical factors, disorders of adult personality and behavior, mental retardation, pervasive and specific developmental disorders, behavioral and emotional disorders with onset usually occurring in childhood and adolescence and mental disorder not otherwise specified

Appendix 3. Supplemental analysis

Because the association of diabetes status and psychiatric outcomes could theoretically be modified by certain risk factors such as being female or having a low material or social deprivation indices, interaction between sex and diabetes status as well as between material and social deprivation and diabetes status was explored by adding interaction terms to the multivariate Cox proportional hazard models. The association between diabetes status and the different psychiatric outcomes did not vary by sex nor by social or material deprivation levels and were therefore not included in the main models.

In addition, because our main models evaluated the effect of diabetes itself (regardless of duration) on the various psychiatric outcomes, we conducted additional analyses whereby we included diabetes duration as our main exposure instead of diabetes status and adjusted for all covariates included in the main models. We found that individuals with shorter duration of diabetes were more likely to have a mood disorder (diagnosed in the ED or in-hospital), visit a psychiatrist or have any psychiatric disorders compared to those with longer diabetes duration (Table 1).

Appendix 4. Characteristics of the study population at the cohort entry date

	With Diabetes	Without Diabetes	P-value
	N = 3,544	N = 1,388,397	
	N (%)	N (%)	
Age at diabetes diagnosis in years			
Mean ± SD	10.68 ± 3.52	N/A	
1-4 years	247 (7.0)	N/A	
5-9 years	894 (25.2)	N/A	
10-15 years	2,403 (67.8)	N/A	
Gender (Males)	1,867 (52.7)	706,273 (50.9)	0.03
Duration of follow-up in years			
Mean ± SD	6.67 ± 2.97	7.63 ± 2.93	<0.0001
Range	1-10	0-10	
Social Deprivation†			
1 (Least deprived)	827 (23.3)	325,737 (23.5)	0.63
2	731 (20.6)	301,048 (21.7)	
3	719 (20.3)	281,238 (20.3)	
4	631 (17.8)	242,171 (17.4)	

5 (Most deprived)	504 (14.2)	187,627 (13.5)	
Material deprivation ††			
1 (Least deprived)	705 (19.9)	272,235 (19.6)	0.58
2	725 (20.5)	271,829 (19.6)	
3	640 (18.1)	265,264 (19.1)	
4	671 (18.9)	261,618 (18.8)	
5 (Most deprived)	671 (18.9)	266,875 (19.2)	
Rural Residency †††	719 (20.3)	307,905 (22.2)	0.002
Birth year			
1982	38 (1.1)	66,536 (4.8)	<0.0001
1983	66 (1.9)	85,094 (6.1)	
1984	106 (3.0)	85,093 (6.1)	
1985	124 (3.5)	83,669 (6.0)	
1986	134 (3.8)	81,074 (5.8)	
1987	156 (4.4)	79,618 (5.7)	
1988	185 (5.2)	81,773 (5.9)	
1989	226 (6.4)	86,234 (6.2)	
1990	223 (6.3)	91,002 (6.6)	

1991	253 (7.1)	89,971 (6.5)	
1992	260 (7.3)	88,616 (6.4)	
1993	278 (7.8)	84,950 (6.1)	
1994	290 (8.2)	83,090 (6.0)	
1995	305 (8.6)	80,121 (5.8)	
1996	316 (8.9)	77,993 (5.6)	
1997	308 (8.7)	73,231 (5.3)	
1998	276 (7.8)	70,332 (5.1)	
Number of ED visits in prior year			
Mean ± SD	0.73 ± 1.21	0.26 ± 0.70	<0.0001
Range	0-15.00	0-31.00	
Number of diabetes-related ED visits in the prior year			
Mean ± SD	0.30 ± 0.72	0.00 ± 0.00	<0.0001
Range	0-14	0-2	
Number of hospitalizations in prior year			
Mean ± SD	0.27 ± 0.71	0.02 ± 0.17	<0.0001

Range	0-14	0-20	
Number of outpatient clinic visits in prior year			
Mean ± SD	6.27 ± 6.42	1.73 ± 2.58	<0.0001
Range	0-92.0	0-170.0	

Table 1 Legend:

The p-value was obtained using chi-square for categorical variables or t-test for continuous variables

Abbreviations: ED: Emergency Department; IQR: Interquartile range; N/A: not applicable; SD: Standard Deviation

†Missing 50,708 of the study population: 132 with diabetes and 50,576 without diabetes

††Missing 50,708 of the study population: 132 with diabetes and 50,576 without diabetes

†††Missing 23,043 of the study population: 43 with diabetes and 23,000 without diabetes.

Rural population refers to population < 10,000. Urban population refers to population > 10,000.