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ORIGINAL RESEARCH

Incidence of Childhood Type 1 Diabetes in Beijing During 2011–2020 and Predicted Incidence for 2025–2035: A Multicenter, Hospitalization-Based Study

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ABSTRACT

Introduction: China has a low incidence of type 1 diabetes mellitus (T1DM); however, based on the large population, the absolute numbers are high. Our aim was to assess the incidence of childhood T1DM in Beijing during 2011–2020, predicted incidence for 2025–2035, and to determine the incidence of diabetic ketosis or diabetic ketoacidosis (DK/DKA) in this population.

Methods: Data on patients aged less than 15 years of age with newly diagnosed T1DM between January 1, 2011 and December 31, 2020 was obtained from five tertiary hospitals in Beijing and retrospectively analyzed.

Yuchuan Li and Kun Qian contributed equally to this work.

Xiaobo Chen, Hui Chen, and Chunxiu Gong also contributed equally to this work.

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Results: In all, 636 children aged less than 15 years were diagnosed with T1DM during 2011–2020. The incidence of T1DM was 3.11–5.46 per 100,000 per year, with an average increase of 5.10% per year. The age-specific incidence for ages 0–4 years, 5–9 years, and 10–14 years was 2.97, 4.69, and 4.68 per 100,000 per year, respectively. The highest average annual increase (7.07%) in incidence was for the youngest age group. DK or DKA was present at the time of diagnosis of T1DM in 84.6% of patients. The age-specific incidence of T1DM among children aged less than 15 years was predicted to be 7.32, 11.4, and 11.52 per 100,000 in 2035 for ages 0–4 years, 5–9 years, and 10–14 years, respectively.
Conclusions: The was a gentle increase in the incidence of childhood T1DM during 2011–2020 in Beijing. This increase is expected to continue for the next 15 years.

Keywords: Type 1 diabetes; Incidence; Childhood; Hospitalization data

Key Summary Points

Why carry out this study?

China has a low incidence of type 1 diabetes mellitus (T1DM); however, based on the large population, the absolute numbers are high. The IDF Atlas (10th Edition) shows that China ranks fourth in terms of the absolute number of cases.

Long-term sustainability studies have been conducted on the incidence of T1DM among children in Beijing. The WHO survey for the period 1988–1994 revealed an incidence of 0.94 per 100,000. The average age-standardized incidence rate was determined to be 1.7 per 100,000 per year for the period 1995–2010 in Beijing.

It would be worthwhile knowing the changes in the incidence of childhood diabetes in the 10 years after 2010.

What was learned from the study?

The incidence of T1DM in patients aged less than 15 years was 3.11–5.46 per 100,000 per year during 2011–2020, with an average increase of 5.10% per year. The highest average annual increase (7.07%) in incidence was for the youngest age group (0–4 years).

This study indicates a gentle increase in the incidence of children T1DM during 2011–2020 in Beijing. This increase is expected to continue for the next 15 years. Diabetic ketosis or diabetic ketoacidosis was present at the time of diagnosis of T1DM in 84.6% of patients.

INTRODUCTION

The latest publication from the International Diabetes Federation (IDF) Atlas (10th Edition) shows that type 1 diabetes mellitus (T1DM) incidence has been increasing in recent decades in nearly all countries studied [1]. Other studies also have shown a rapid increase in the incidence of childhood T1DM in patients aged less than 15 years [2–11]. Furthermore, the EURODIAB study [12] and the DIAMOND project [5] have shown a significantly wide variation in the incidence of T1DM worldwide. In recent years, while the increase of incidence has tended to be steeper in countries with low prevalence [13–16], the increase in countries with a higher prevalence, such as Finland, Sweden, and Norway, has appeared to plateau [17, 18].

According to a World Health Organization (WHO) survey, the average incidence of childhood T1DM for the period between 1988 and 1994 was 0.94 per 100,000 in China [19]. Even though the incidence of T1DM in China is low, as a result of having largest population in the world, the absolute numbers are high. The IDF Atlas (10th Edition) shows that China is fourth when the absolute number of cases is ranked [1]. Beijing, the capital of China, alone has a population of more than 20 million. As a result, the total number of patients with T1DM is

considerable but the incidence rate appears low. Gong et al. reported that the incidence of childhood T1DM among individuals aged less than 15 years ranged from 0.935 to 3.26 per 100,000 per year from 1995 to 2010 in Beijing, with an average annual increase of 4.36% [20, 21].

It would be worthwhile knowing the changes in the incidence of childhood diabetes during the 10-year period after 2010. Currently, China does not have any national diabetes registration system. However, hospital registration data is a reliable and valuable source of information regarding epidemiological trends in T1DM, as every patient with newly diagnosed childhood T1DM requires hospitalization for treatment. In this study, we sought to evaluate the incidence of T1DM in Beijing among patients aged less than 15 years during the period 2011–2020 in order to predict the incidence of T1DM in the future and to determine the incidence of diabetic ketosis or diabetic ketoacidosis (DK/DKA) in this population.

METHODS

This study was designed as a multicenter retrospective investigation of data collected from hospital registration systems in Beijing. In this study, we collected data from hospital case records to analyze the incidence of childhood T1DM and DK/DKA in T1DM. Data for this study were collected from five tertiary hospitals located in Beijing, namely the Beijing Children's Hospital, Capital Institute of Pediatrics, Peking University Third Hospital, Peking University First Hospital, and Beijing Friendship Hospital. Of these five hospitals, two were children's hospitals that house the only endocrine wards for pediatric inpatients and have pediatrics endocrinology and diabetes clinics in Beijing. Before the global COVID-19 pandemic, Beijing Children's Hospital had an annual outpatient population of 3 million, and the children's Hospital affiliated to the Capital Institute of Pediatrics had an annual outpatient population of 2.2 million, accounting for 80–90% of the entire pediatric outpatient population in Beijing. Although there are 40 class A tertiary hospitals, i.e., high-rank hospitals, with pediatric outpatients in Beijing, most offer only general pediatric clinics. As T1DM is a specialized disease, the majority of children with newly diagnosed T1DM are sent to the aforementioned two children's hospitals.

Patients were included in the study if they met the following criteria: (1) newly diagnosed T1DM on the basis of the 2018 International Society for Pediatric and Adolescent Diabetes guidelines criteria [22] and the 1985 WHO diagnostic criteria for diabetes [23]; (2) age less than 15 years; (3) admission to any of the five participating hospitals between January 2011 and December 2020 (only one admission was taken into consideration for subjects admitted to more than one of the five hospitals); (4) permanent residents were defined as those who had registered permanent residence in Beijing and lived in Beijing since birth; and (5) availability of data on gender, date of birth, date of T1DM diagnosis, and the presence or absence of ketosis or ketoacidosis at the time of diagnosis of T1DM.

The diagnosis of DK/DKA was based on the following criteria: (1) diagnosed T1DM; (2) symptoms include vomiting, abdominal pain, stupor, coma, dehydration, flushing of the cheeks, cherry red lips, deep breathing, etc.; (3) urine ketone positive, blood D-3-hydroxybutyrate above the reference range; (4) when blood gas analysis shows $pH < 7.30$, $HCO_3^- < 15$ mmol/L, DKA was diagnosed.

Additionally, we excluded patients with any of the following conditions: type 2 diabetes; maturity-onset diabetes of the young; impaired glucose tolerance; latent diabetes; and secondary diabetes due to steroid use, Down syndrome, congenital malformations of the pancreas, patients who are not permanent residents in Beijing, etc.

The study was approved by the ethics committee at Beijing Children's Hospital (No. 2015-126). As this was a retrospective epidemiological study, informed consent was not requested.

Statistical Methods

The incidence was determined for each calendar year and for a population of 100,000 at risk without adjustment. For the determination of incidence, the numerator was the calculated annual number of newly diagnosed patients; the denominator was obtained using permanent resident population data from the Beijing Bureau of Statistics. Adjustments of the incidence were made for age and sex with the direct method, with the data for the standard population by age and sex groups derived from the Beijing Bureau of Statistics. Assuming a Poisson distribution, the 95% confidence intervals (95% CIs) and the incidence according to sex, age, and calendar year and their interactions were assessed using Poisson regression models. A base model was formulated for age (0–4 years, 5–9 years, and 10–14 years), sex, and age by sex interaction. Subsequently, for the prediction of the incidence up to 2035, the base-year incidence was extrapolated on the basis of the annual percentage increase in incidence by age and sex, which was estimated by Poisson regression analysis. The values of prevalence were derived on the basis of cumulated incidence.

RESULTS

Incidence of Type 1 Diabetes Mellitus and Temporal Trends

From the available data, we found that 636 patients, including 285 boys and 351 girls, under the age of 15 years were newly diagnosed with T1DM at one of the five participating hospitals between 2011 and 2020. The percentage of patients diagnosed with T1DM by age group was as follows: 31.8% (n = 202) aged 0–4 years, 39.3% (n = 250) aged 5–9 years, and 28.9% (n = 184) aged 10–14 years. The incidence of T1DM among individuals aged less than 15 years for the years between 2011 and 2020 was 3.11–5.46 per 100,000 per year, with the average being 3.96 per 100,000 per year (95% CI 3.66–4.28) (Fig. 1; Table 1).

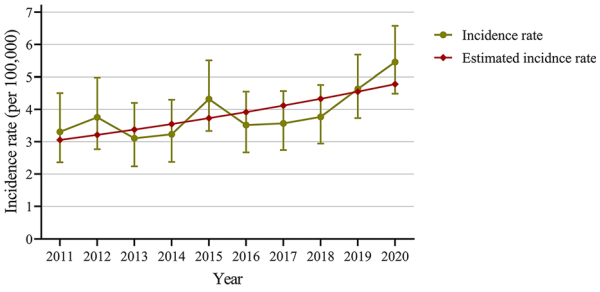

Fig. 1 Incidence rate of childhood type 1 diabetes in Beijing; error bars represent 95% confidence intervals

Additionally, the average incidence standardized by age was 3.94 per 100,000 per year, while the average annual increase in T1DM incidence was 5.10% (95% CI 2.20–8.08) (Fig. 2; Table 1).

The age-specific incidences for ages 0–-4 years, 5–9 years, and 10–14 years were 2.97 (95% CI 2.58–3.41), 4.69 (95% CI 4.13–5.31), and 4.68 (95% CI 4.03–5.40) per 100,000 per year, respectively. The trends were similar for the different age groups. The maximum average annual increase was noted for the youngest age group 0–4 years, at 7.07% (95% CI 1.76–12.66%); the increase for ages 5–9 years and 10–14 years were 3.76% and 4.17%, respectively (Fig. 3; Table 1).

The overall incidence of T1DM in boys and girls was 3.44 and 4.52 per 100,000 per year, respectively, with an overall male-to-female ratio of 1:1.31. The trends were similar for the two sex groups (Fig. 4; Table 1).

The model including the calendar year, age, as well as sex was deemed to be the best fitting model (Table 2). The Poisson models did not show any evidence of overdispersion, which is consistent with our results.

Incidence Prediction

The age-specific incidence of T1DM among children aged less than 15 years was expected to continually increase and for ages 0–4 years, 5–-9 years, and 10–14 years was predicted to be 4.54, 7.08, and 7.15 per 100,000 persons in 2025, respectively. The corresponding values were 5.76, 8.98, and 9.08 per 100,000 persons in

Table 1 Age- and sex-specific increase incidence rates of type 1 diabetes in Beijing per 100,000 per year during 2011–2020 by two 5-year periods

	Age (years)	2011–2015						2016–2020						2011–2020					
		Incidence rate	CIL	CIU	Annual increase (%)	CIL	CIU	Incidence rate	CIL	CIU	Annual increase (%)	CIL	CIU	Incidence rate	CIL	CIU	Annual increase (%)	CIL	CIU
Total	0–4	2.49	1.95	3.13	0.64	− 14.52	18.48	3.34	2.79	3.97	16.36	2.66	31.89	2.97	2.58	3.41	7.07	1.76	12.66
	5–9	4.48	3.62	5.47	− 5.86	− 18.44	8.66	4.83	4.10	5.65	26.65	12.41	42.69	4.69	4.13	5.31	3.76	− 0.80	8.53
	10–14	4.26	3.34	5.35	25.80	6.67	48.36	5.01	4.12	6.04	− 7.85	− 19.11	4.98	4.68	4.03	5.40	4.17	− 0.89	9.48
	All	3.56	3.13	4.04	4.64	− 4.35	14.47	4.25	3.84	4.69	12.95	5.15	21.33	3.96	3.66	4.28	5.10	2.20	8.08
Boys	0–4	2.31	1.61	3.22	− 3.27	− 23.53	22.34	3.11	2.38	3.98	5.33	− 11.99	26.06	2.76	2.24	3.37	5.55	− 1.92	13.59
	5–9	3.29	2.30	4.55	9.86	− 13.42	39.40	4.10	3.19	5.20	20.16	0.78	43.25	3.78	3.09	4.58	7.27	− 0.09	15.16
	10–14	3.91	2.73	5.44	17.36	− 7.31	48.62	4.32	3.20	5.71	− 3.09	− 20.65	18.36	4.14	3.30	5.13	2.64	− 4.60	10.43
	All	3.03	2.48	3.66	6.93	− 6.68	22.53	3.74	3.21	4.33	8.86	− 2.04	20.99	3.44	3.05	3.86	5.37	1.04	9.88
Girls	0–4	2.67	1.89	3.67	4.41	− 16.82	31.07	3.58	2.78	4.55	27.60	6.90	52.30	3.19	2.61	3.86	9.34	1.80	17.44
	5–9	5.75	4.37	7.41	− 14.19	− 28.49	2.96	3.11	2.38	3.98	35.15	14.68	59.27	5.66	4.78	6.66	3.41	− 2.59	9.78
	10–14	4.63	3.29	6.32	34.20	6.44	69.21	5.61	4.49	6.92	− 11.87	− 25.77	4.63	5.25	4.27	6.38	2.16	− 4.31	9.06
	All	4.13	3.47	4.89	2.90	− 8.70	15.97	4.80	4.18	5.48	16.36	5.56	28.26	4.52	4.06	5.01	4.84	0.97	8.85

CIL lower bound of 95% CI, *CIU* upper bound of 95% CI

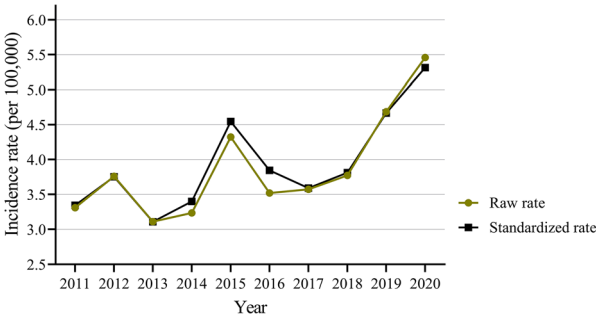

Fig. 2 Age-standardized incidence rate of childhood type 1 diabetes in Beijing

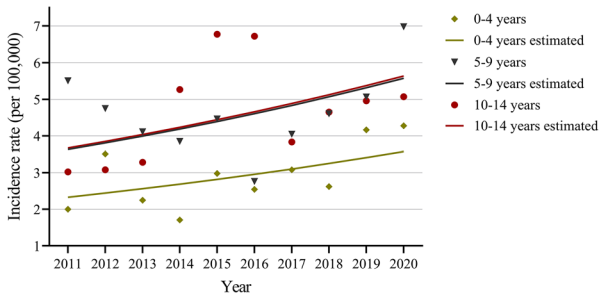

Fig. 3 Time trends in age-specific incidence rates of type 1 diabetes

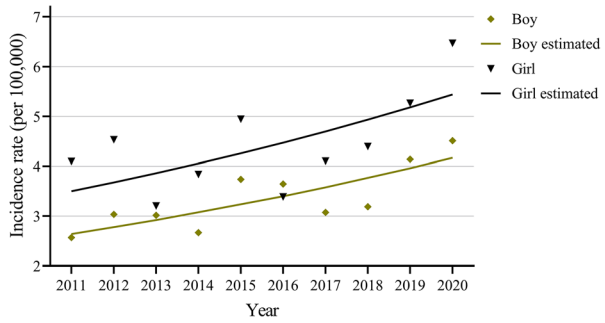

Fig. 4 Time trends in type 1 diabetes incidence in boys and girls

2030, and 7.32, 11.4, and 11.52 per 100,000 persons in 2035, respectively (Fig. 5).

In addition, the predicted sex-specific incidence by 2025 for boys and girls would be 5.33 and 7.00 per 100,000 persons, by 2030 it would be 6.83 and 8.97 per 100,000 persons, and by 2035 it would be 8.76 and 11.51 per 100,000 persons, respectively (Fig. 6).

Table 2 Summary of Poisson regression analyses fitted to data for type 1 diabetes incidence rates

Model	Residual deviance	Residual df	Change in deviance	Change in df	*P* value
Null	108.81	59			
Year	96.50	58	12.31	1	< 0.001
Year + age	69.02	56	27.48	2	< 0.001
Year + age + sex	57.62	55	11.40	1	< 0.001
Year + age + sex + age × sex	53.74	53	3.88	2	0.1438

df degree of freedom

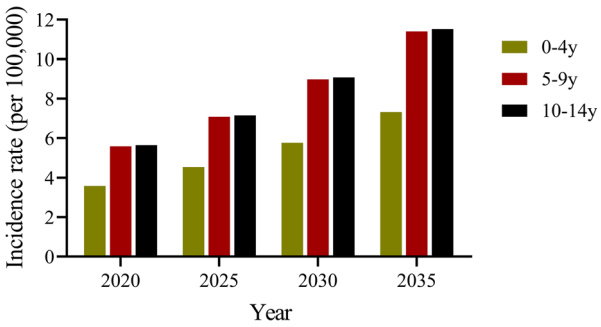

Fig. 5 Predicted future incidence rates of children type 1 diabetes in Beijing per 100,000 per year by age group (numbers for year 2020 are the actual ones)

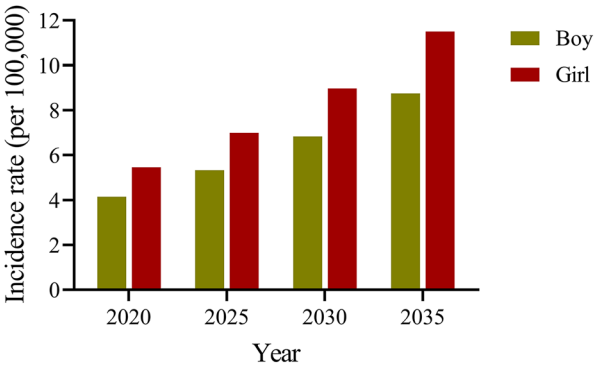

Fig. 6 Predicted future incidence rates of children type 1 diabetes in Beijing per 100,000 per year by sex (numbers for year 2020 are the actual ones)

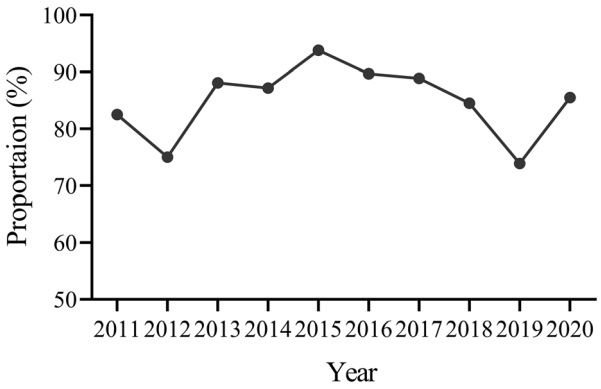

Fig. 7 Proportion of diabetic ketosis/diabetic ketoacidosis in type 1 diabetes during 2011–2020

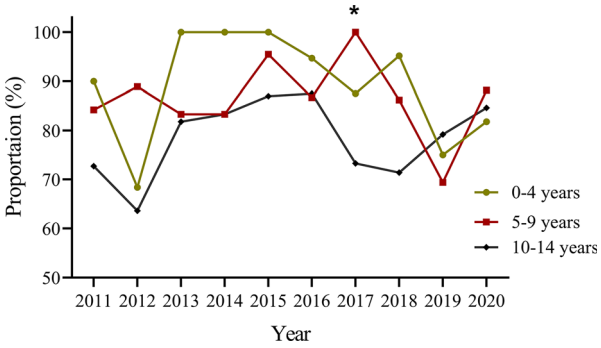

Fig. 8 Proportion of diabetic ketosis/diabetic ketoacidosis type 1 diabetes by age group. *$P < 0.05$

Proportion of Diabetic Ketosis or Diabetic Ketoacidosis Among Patients with Type 1 Diabetes Mellitus

In all, 538 patients (84.6%, 95% CI 81.6%–87.3%) had DK/DKA at the time of diagnosis of T1DM, between 2011 and 2020. The lowest proportion was 73.9% in 2019 and the highest was 93.8% in 2015 (Supplementary Table 1; Fig. 7).

There was no difference in the proportion of DK/DKA between boys and girls for the 0–-4 years group and 10–14 years group, but there was a difference between 5 and 9 years ($P = 0.044$) (Supplementary Table 2).

The proportion of DK/DKA in the 10–14 year group was lower than that in the other two groups in 2017 ($P < 0.05$); there was no statistical difference in DK/DKA proportion among the three groups in other years (Supplementary Table 3; Fig. 8).

The proportion of DK/DKA in boys was lower than that in girls in 2020 ($P < 0.05$), and there was no statistical difference in other years (Supplementary Table 3; Fig. 9).

DISCUSSION

The present study was designed as a multicenter investigation of the temporal trends in the incidence of T1DM among children in Beijing. The results of this retrospective study revealed a gentle increase in the incidence of childhood T1DM in patients aged less than 15 years during

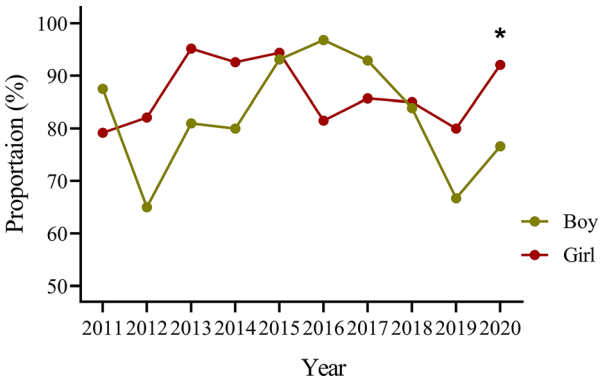

Fig. 9 Proportion of diabetic ketosis/diabetic ketoacidosis in type 1 diabetes by sex. $^{*}P < 0.05$

2011–2020. The average incidence (standardized for age) was determined to be 3.94 per 100,000 per year. Additionally, the relative annual increase in the incidence of T1DM was 5.10% after adjustment for age and sex.

A steady increase in the incidence of type 1 diabetes has been reported worldwide [1]. Finland has the highest incidence of T1DM among countries with historically high values, reaching 40 per 100,000 people per year in the 1990s. The average age-standardized incidence was 42.9 per 100,000 per year during 1980–2005. During this period, incidence increased from 31.4 per 100,000 per year in 1980 to 64.2 per 100,000 per year in 2005 [24]. The SEARCH for Diabetes in Youth Study in the USA showed that the age- and sex-adjusted incidence of T1DM increased from 24.4/100,000 in 2002 to 27.4/100,000 in 2009. The relative annual increase in T1DM incidence was 2.72% [10]. Asian countries show lower incidences of T1DM than did Europe and the USA. These geographic differences in T1DM incidence may reflect population variations in the frequency of T1DM susceptibility or protective genes and/or environmental factors. Although the incidence of T1DM is relatively lower in Asian countries, increasing trends in the incidence of T1DM have also been observed. An epidemiologic study based on a Korean national database showed that the incidence of T1DM children was 4.45 per 100,000 persons between 2007 and 2017 [25]. A study from Japan showed that the incidence of children T1DM was 1.5 per 100,000 persons from 1986 to 1990 [26]. A recent study reported that the incidence of T1DM from 2005 to 2010 was 2.25 per 100,000 persons in Japan [27], suggesting that the incidence is increasing in Japan. Long-term sustainability studies have been conducted on the incidence of T1DM among children in Beijing. The WHO survey for the period 1988–1996 revealed an incidence of 0.94 per 100,000 [19]. Gong reported that the average age-standardized incidence rate was 1.7 per 100,000 per year for the period 1995–2010, with an average annual increase of 4.36% in the incidence of T1DM in these five hospitals [21]. As 10 years have passed since that study, it is necessary to update this data. This study shows a gentle increase in incidence in 2011–2020 compared to 1995–2010. Liu and colleagues reported a population-based registry study of T1DM in the greater Beijing area, including153 hospitals. There were 961 patients with T1DM aged 0–14 years from 2007 to 2017. The incidence of T1DM in patients aged 0–14 years was 3.41–4.27 per 100,000 persons, except for 6.11 per 100,000 persons in 2015 [28]. The incidence is consistent with our study.

The reasons why the absolute number of cases in Liu's article is higher than ours are as follows: Firstly, as mentioned earlier, most but not all pediatric patients are admitted to the two specialized pediatric hospitals. Secondly, the 153 hospitals in Liu's study refer to the greater Beijing area, which includes some provinces around the capital.

Our study revealed that the incidence of T1DM is steadily increasing. Furthermore, a smooth increase was also noted in both age-specific and sex-specific incidence. The lowest incidence was noted for the age group of 0–-4 years. However, the rate of increase in the incidence was highest for the youngest age group (0–4 years). This finding is consistent with those of other studies [11, 24, 29–32]. A 1989–2003 European study also showed that the most rapid increases in T1DM incidence were observed in children less than 5 years of age [29].

While some previous studies have shown that the incidence of T1DM in boys exceeds that in girls [33, 34], others have shown no sex-related difference in this regard [24]. In a

Taiwanese nationwide epidemiologic study, the incidence of childhood-onset T1DM (per 100,000 persons) was 3.56 among boys and 5.88 among girls in 1999 to 2000 and increased significantly with an incidence of 4.42 among boys and 6.92 among girls in 2009 to 2010 [35]. Nishioka and colleagues reported that in Japan, the incidence of T1DM in patients aged 0–19 for men was 3.94/100,000 person-years, while that for women was 5.22/100,000 person-years [36]. A study from China's Henan province showed that the female-to-male incidence rate ratio was 1.32 (95% CI 1.20, 1.45) in the 0–14 years age group [37]. In this study, the male-to-female ratio of the incidence of T1DM was 1:1.31, which was consistent with previous studies. At present, there is no definitive consensus on the sex-related differences of diabetes incidence.

In this study, we also sought to determine the changes in the incidence of DK/DKA in T1DM among children in Beijing in order to identify the temporal trends. We found that while there was an increase in the incidence of T1DM, the percentage of patients having DK/DKA at the time of T1DM diagnosis remained relatively stable, at around 84.6%. Liu and colleagues reported that the proportion of DKA at diagnosis was 52.52% in patients aged 0–-4 years, which is lower than that in this study [28]. We analyzed the reasons as follows: First, we counted DK/DKA, while Liu's article counted only DKA. Second, our study included five tertiary hospitals, two of which were children's hospitals with the only pediatric inpatient endocrine wards in Beijing. Most cases of DK/DKA were diagnosed at these two hospitals. DK/DKA may often be detected at the time of diagnosis of T1DM because DK/DKA has an acute presentation, while the typical early signs and symptoms of diabetes may easily be ignored by parents. However, clinical manifestations of DK/DKA in young children are not characteristic and therefore misdiagnosis or delayed diagnosis is common, especially by physicians not specializing in pediatric endocrinology or diabetes.

This study has some limitations. For convenience, ketosis and ketoacidosis were considered as a single entity since the number of cases was small. Additionally, this study was based on retrospective data only from five hospitals in Beijing.

CONCLUSIONS

A gentle increase in the incidence of pediatric T1DM was noted in Beijing during 2011–2020. It is expected that during the next 15 years, there will be a greater increase in incidence of pediatric T1DM, with a high number of patients presenting with ketoacidosis and requiring hospitalization. This descriptive epidemiological study may facilitate the planning of appropriate health services and promote the establishment of a national diabetes registration system to better assess the incidence of diabetes in China.

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Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Authors' Contributions. Yuchuan Li and Kun Qian analyzed the data and wrote the manuscript. Di Wu performed the primary extraction, collation of the data and revised the submission. Xinli Wang, Hong Cui, Geheng Yuan, Jinfang Yuan, Lijun Yang, Liya Wei, Bingyan Cao, Chang Su, Xuejun Liang, Min Liu, Wenjing Li, Miao Qin, Jiajia Chen, Xi Meng, Rui Wang, Shan Su collected data. Hui Chen directed statistical analyses of the data and created the tables and figures. Xiaobo Chen and Chunxiu Gong designed the study.

Disclosures. All the authors declare that they have no conflict of interest.

Compliance with Ethics Guidelines. The study was approved by the ethics committee at Beijing Children's Hospital (No. 2015-126). As this was a retrospective epidemiological study, informed consent was not requested.

Data Availability. The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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