

Hospital Admission for Diabetic Ketoacidosis in Thai Children and Adolescents with Type 1 Diabetes: A National Study During 2015-2019

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What is already known on this topic?

Despite a globally increasing incidence of pediatric type 1 diabetes mellitus (T1D), the incidence of hospitalization for diabetic ketoacidosis (DKA), a life-threatening yet preventable complication of T1D, varies among countries. Understanding the incidence trend in DKA admission rates may strengthen the preventive measure for DKA.

What this study adds?

The incidence of T1D and DKA admissions in Thailand increased progressively during 2015-2019. School-aged children, adolescents, females, and those residing in the Northeast area were at increased risk for DKA admission. This study underscores the importance of diabetic care among Thai youth with T1D, particularly for those with higher risks.

Abstract

Objective: To study the national incidence of admission for diabetic ketoacidosis (DKA) in Thai children and adolescents with type 1 diabetes mellitus (T1D) and characterize risk factors for DKA admission.

Methods: Admission records of children and adolescents with T1D during the years 2015-2019 were retrieved from the Thai health coverage system of all schemes. Hospitalization was categorized according to patients' age groups (<1, 1-5, 6-12 and 13-17 years), sex and geographical regions (Bangkok, Central, Northeast, North and South). DKA admission incidence and rate were calculated and compared among subgroups.

Results: The annual incidences of T1D and DKA admissions per 100,000 child-years progressively increased over the study period (T1D: 12.0 to 15.0, $p < 0.001$ and DKA: 4.8 to 7.3, $p < 0.001$). About half of DKA admissions (52%) were recurrent episodes. DKA admission rate was 1.49 admissions/patient. The incidence of DKA admission was greatest in individuals aged 13-17 years (13-17 years: 10.3; 6-12 years: 6.3; 1-5 years: 1.7; and <1 year: 0.6 per 100,000 child-years, $p < 0.001$). DKA admission incidence was greater in females than males (7.6 vs. 4.3 per 100,000 child-years, $p < 0.001$). Across the geographical regions, the greatest percentage of recurrent DKA (57%), rate of increased annual incidence of DKA admission (3.8 to 7.8 per 100,000 child-years), and DKA admission rate (1.64 admissions/patient) were found in the Northeast region.

Conclusion: During the years 2015-2019, rising annual incidences of T1D and DKA admissions among Thai youth were observed. Individuals older than 6 years, being female, and resided in the Northeast region conveyed a higher risk for DKA hospitalization.

Keywords: Diabetic ketoacidosis, type 1 diabetes, hospitalization, children, adolescent

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Introduction

Diabetic ketoacidosis (DKA) is a life-threatening complication that occurs mainly in patients with type 1 diabetes mellitus (T1D). DKA is a common manifestation at the initial diagnosis of T1D in children and adolescents, with incidence varying widely from 13% to 80% (1). The worldwide incidence of T1D in children and adolescents has dramatically increased during the last 20 years, and currently, over 100,000 children develop T1D annually (2). Unlike the generally rising trend in T1D, hospitalization for DKA differs between countries. The incidence of DKA admission increased in the United States of America (USA) and Canada (3,4) but decreased in the Netherlands, Italy and Korea (5,6,7), whereas it remained stable in Germany and China (8,9). This diversity might be due to international variations in the recurrent DKA rate of individuals with established T1D, accessibility to the healthcare system, and early recognition of hyperglycemia and DKA (1,5,6).

In parallel with the global trend, the incidence of T1D in Thai children and adolescents rose from 0.14 in 1984 to 0.6 per 100,000 person-years in 2014 (10,11). A previous nationwide, population-based study demonstrated a decreasing trend of DKA incidence in Thailand during the years 2015-2020. However, the DKA incidence was calculated per the number of youth with T1D, not the total population (12). That study also excluded recurrent DKA admissions. In addition, only data from the Universal Health Coverage Scheme was analyzed (12), despite the fact that the Thai health coverage system consists of three public insurance programs, including the Universal Health Coverage Scheme, the Social Health Insurance, and the Civil Servant Medical Benefit Scheme (13). As a result, national data focusing specifically on the incidence of DKA admission and its secular trends in Thai children and adolescents with T1D remain unavailable. Recent studies revealed increased risk factors for DKA development in patients who had limited access to medical services and delayed recognition of hyperglycemia (1,14). Despite having national coverage, access to health care services is limited, particularly in rural areas where public transportation is unavailable and travel expenses are unaffordable for local low-socioeconomic status populations (15,16). Moreover, the cost of the testing strip for self-monitoring blood glucose (SMBG) is currently not covered by most insurances (17). These factors might cause a delay in detection of hyperglycemia and thus DKA.

DKA is primarily preventable, while the cost of DKA treatment is high (18). Understanding the trend in DKA

admission, identifying individuals who are vulnerable to DKA development, and the consequences of DKA are essential for implementing the national preventive strategy for DKA. Therefore, the aim of this study was to describe a robust national trend in pediatric DKA hospitalization and identify characteristics of T1D youth who had higher risks for DKA admission.

Methods

Study Population and Data Collection

The admission data of T1D and DKA were retrospectively retrieved between the years 2015 and 2019 inclusive from databases of the Universal Health Coverage Scheme, the Social Health Insurance, and the Civil Servant Medical Benefit Scheme. Inclusion criteria were hospital admissions of children and adolescents aged under 18 years who had T1D and DKA diagnosis using the International Code of Diseases (ICD)-10 of E10 and E10.1, respectively. Exclusion criteria were admissions of diabetic patients with ICD-10s other than E10. Duplicated DKA admissions of the same patients over the study period were labelled as recurrent DKA episodes. However, for the first record of DKA admission, particularly in the earlier years of the study period, we could not distinguish DKA in individuals with newly-diagnosed diabetes from those with known diabetes who had DKA before the study period began due to the lack of a specific ICD-10 code. Characteristics, including patient age and sex, hospital level and region, season, comorbidity, and discharge status were collected. Age ranges of the patients were <1, 1-5, 6-12, and 13-17 years. The hospital level included primary, secondary, tertiary, and private hospitals. The hospital region was determined based on five geographical areas of Thailand, which are Bangkok, Central, Northeast, North, and South. According to the data of the Thai meteorological department, the climate consists of three seasons, including summer, rains, and winter (19). We reported the groups of comorbidities according to ICD-10 classification, and infectious diseases were further categorized into organ systems.

The study was approved by the Ethics Committee on Human Research of the Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand (decision no: MURA2024/136, date: 16.02.2024) and conformed to the provisions of the Declaration of Helsinki. Informed consent was not obtained from the patients because the data were anonymous and were extracted from the health care schemes with permission.

Hospitalization Parameters

The parameters of hospitalization are as follows.

- Incidence of hospital admission for T1D or DKA (per 100,000 child-years) =

The number of T1D or DKA admissions x 100,000 / Total population

- The percentage of DKA admission among patients with T1D (%) =

The number of DKA admissions x 100 / The number of T1D admissions

- The admission rate of DKA (admissions/patient) =

The number of DKA admissions / The number of patients admitted for DKA

- The mortality rate of DKA (%) =

The number of deceased patients admitted for DKA x 100 / The number of DKA admissions

Statistical Analysis

IBM Statistical Package for the Social Sciences statistics for Windows, version 24.0 (IBM Corp. Armonk, NY, USA), and RStudio (R version 4.2.3; RStudio Inc, Vienna, Austria) were used for statistical analysis. Datasets were compared using the chi-squared test. A p value of less than 0.05 was considered to imply statistical significance.

Results

Overall Pediatric Hospitalization for T1D and DKA

Of 64,677,608 child-years, 8,708 admissions from individuals with T1D (13.5 per 100,000 child-years) and 3,846 admissions from individuals with DKA (5.9 per 100,000 child-years) were recorded (Tables 1, 2). DKA was the main indication (44%) for hospital admission among patients with T1D. The admission rates of T1D and DKA were 1.66 and 1.49 admissions/patient, respectively. The majority of the hospitalized patients with T1D were individuals aged 13-17 years (50%), female (60%), and those residing in the Northeast region (35%) (Table 1). Among DKA hospitalizations, 2007 (52%) were recurrent episodes, and 226 (5.9%) were identified referrals. The majority of patients with DKA were admitted to tertiary (48%) and secondary hospitals (43%), whereas the remaining patients were admitted to primary (6%) and private hospitals (3%). In addition, most DKA admissions occurred in rainy season (mid-May to mid-October, 40%) and winter (mid-October to mid-February, 34%), while 26% were observed in summer (mid-February to mid-May).

The Trend in DKA Admission During the Study Period

The annual incidence of T1D admission rose from 12.0 in 2015 to 15.0 per 100,000 child-years in 2019 ($p < 0.001$) (Figure 1). Likewise, the respective annual incidences of DKA admission increased from 4.8 to 7.3 per 100,000 child-years ($p < 0.001$). Following these findings, the respective percentages of DKA admission among T1D hospitalization increased progressively from 40% to 49% ($p < 0.001$) (Figure 2). Despite overall increases in the incidence and percentage of DKA admission, the mortality rate of DKA admission reduced from 2.4% to 1.2% ($p = 0.06$). The median (interquartile range) length of hospital stay for DKA was 5 (3, 9) days, without significant change throughout the study.

DKA Admissions According to Age Group, Sex and Region

The majority of pediatric DKA admissions in this study were patients in the age groups 13-17 years (50%) and 6-12 years (42%) (Table 2). Following from this, the highest incidence of DKA admission was identified in individuals aged 13-17

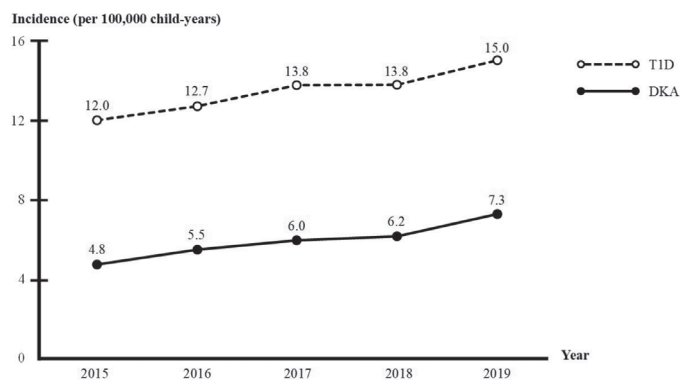


Figure 1. Incidence trend of hospital admission for type 1 diabetes mellitus and diabetic ketoacidosis

T1D: type 1 diabetes mellitus, DKA: diabetic ketoacidosis

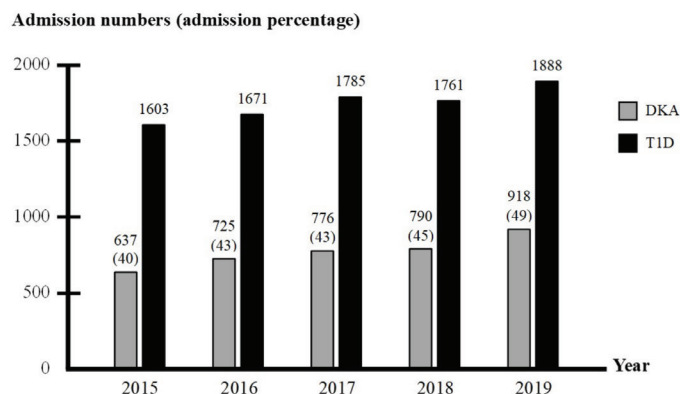


Figure 2. Hospital admission for type 1 diabetes mellitus and diabetic ketoacidosis of individuals aged under 18 years

T1D: type 1 diabetes mellitus, DKA: diabetic ketoacidosis

Table 1. Total admission, population and incidence of hospital admissions in patients with type 1 diabetes during the year 2015-2019

Year	Admission numbers					Total population					Incidence per 100,000 child-years							
	All	2015	2016	2017	2018	2019	All	2015	2016	2017	2018	2019	All	2015	2016	2017	2018	2019
Total	8,708	1,603	1,671	1,785	1,761	1,888	64,677,608	13,321,565	13,121,876	12,939,015	12,747,946	12,547,206	13.5	12.0	12.7	13.8	13.8	15.0
Age groups (years)																		
<1	50	12	19	3	9	7	3,009,424	637,546	623,309	607,525	584,548	556,496	1.7	1.9	3.0	0.5	1.5	1.3
1-5	742	150	155	172	153	112	17,194,614	3,628,116	3,566,589	3,469,756	3,328,164	3,202,009	4.3	4.1	4.3	5.0	4.6	3.5
6-12	3,545	588	705	766	715	771	25,758,480	5,189,861	5,179,687	5,140,056	5,139,904	5,108,972	13.8	11.3	13.6	14.9	13.9	15.1
13-17	4,371	853	792	844	884	998	18,715,090	3,866,042	3,752,291	3,721,698	3,695,330	3,679,729	23.4	22.1	21.1	22.7	23.9	27.1
Gender																		
Male	3,497	655	674	701	749	718	33,230,782	6,842,917	6,740,708	6,648,212	6,551,186	6,447,759	10.5	9.6	10.0	10.5	11.4	11.1
Female	5,211	948	997	1,084	1,012	1,170	31,446,826	6,478,648	6,381,168	6,290,803	6,196,760	6,099,447	16.6	14.6	15.6	17.2	16.3	19.2
Region																		
Bangkok	1,010	203	234	193	216	164	4,811,349	999,836	984,944	970,192	942,542	913,835	21.0	20.3	23.8	19.9	22.9	17.9
Central	2,286	432	438	496	438	482	16,429,931	3,341,918	3,316,553	3,286,895	3,257,522	3,227,043	13.9	12.9	13.2	15.1	13.4	14.9
Northeast	3,084	525	556	631	650	722	21,725,957	4,524,269	4,425,863	4,340,872	4,259,661	4,175,292	14.2	11.6	12.6	14.5	15.3	17.3
North	1,114	214	220	214	222	244	10,444,785	2,155,930	2,118,232	2,087,249	2,057,531	2,025,843	10.7	9.9	10.4	10.3	10.8	12.0
South	1,214	229	223	251	255	276	11,265,586	2,299,612	2,276,284	2,253,807	2,230,690	2,205,193	10.8	10.0	9.8	11.1	10.5	12.5

years (10.3 per 100,000 child-years), and it was followed by that of children aged 6-12 years (6.3 per 100,000 child-years). Recurrent DKA episodes frequently occurred in patients aged 13-17 years (57%) and those aged 6-12 years (51%). The annual incidences of DKA admission in these two groups increased from the year 2015 to 2019 [13-17 years: 9.0 to 12.7 (↑41%); 6-12 years: 4.6 to 7.8 (↑68%) per 100,000 child-years]. The percentages of DKA admission were 46% in individuals aged 6-12 years and 44% in those aged 13-17 years. Individuals aged 6-12 years also had the highest mean DKA admission rate (1.55 admissions/patient).

Regarding sex predominance, the majority of individuals admitted for DKA were female (63%). Compared to males, females had higher incidence of DKA admission (7.6 vs. 4.3 per 100,000 child-years), percentage of DKA admission (46% vs. 41%), percentage of recurrent DKA events (55% vs. 47%), and DKA admission rate (1.56 vs. 1.39 admissions/patient) (Table 2). Furthermore, the annual incidences of DKA admission from 2015 to 2019 increased more pronouncedly in females than males [5.9 to 9.5 (↑63%) vs. 3.8 to 5.2 (↑39%) per 100,000 child-years].

Across the five geographical regions, Bangkok had the highest incidence of DKA admission (9.1 per 100,000 child-years) but the lowest DKA admission rate (1.31 admissions/patient) (Table 2). The peak percentage of DKA admission was in the Central region (52%). Recurrent DKA events most frequently occurred in the Northeast region (57%). Compared with other regions, the Northeast area also had the maximum increase in annual incidence of DKA admission from 2015 to 2019 [Northeast: 3.8 to 7.8 (↑108%), North: 3.1 to 5.0 (↑62%), South: 4.3 to 6.2 (↑44%), Central: 6.5 to 8.2 (↑25%), Bangkok: 8.3 to 9.6 (↑16%) per 100,000 child-years]. In addition, the highest DKA admission rate was observed in the Northeast region (1.64 admissions/patient), which remained far above other areas for most of the study period (Figure 3).

Comorbidities of T1D and DKA Admissions

T1D patients hospitalized for DKA shared similar comorbidities to those admitted for non-DKA conditions (Table 3). Respiratory tract infections were the most common comorbidities in hospitalized T1D patients, irrespective of the presence of DKA. Mental and behavioral disorders were among the most frequent comorbidities in both groups, while adjustment disorder and major depressive disorder were common diagnoses.

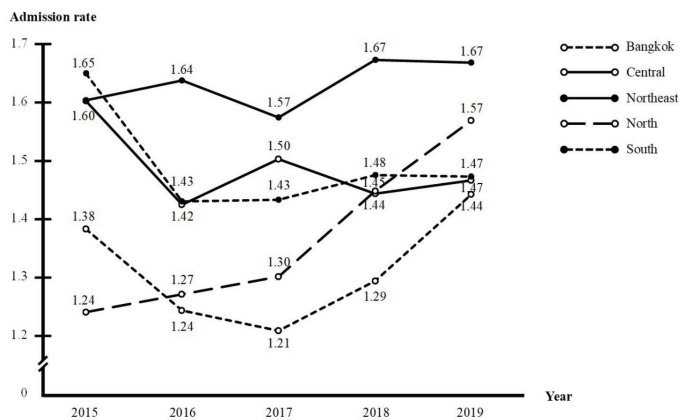


Figure 3. Trend in hospital admission rate for diabetic ketoacidosis (the number of admissions/the number of patients) according to regions

Discussion

From 2015 to 2019, the annual incidence of DKA admission increased progressively, highlighting the importance of DKA prevention. Recurrent DKA events accounted for more than half of DKA admissions. Indeed, such a proportion could be underestimated because first-recorded hospitalizations might be repeated DKA episodes in individuals with known T1D. The findings were consistent with data observed in both the USA and Canada, where incidences of DKA admission increased with the increase in recurrent DKA events (3,4). Accordingly, the increased percentage of recurrent DKA episodes might explain the increased annual incidence of DKA admission in our study. Risk factors for DKA admission could be multifactorial, and some of them affect most T1D individuals while others impact a specific group of individuals (1,3,4). Data from the

Table 2. Diabetic ketoacidosis hospitalization parameters of patients with type 1 diabetes during the year 2015-2019

Year	Total admissions (incidence per 100,000 child-years)						Percentage of DKA admission	Recurrent DKA events (%)	DKA admission rate
	2015-2019	2015	2016	2017	2018	2019			
Total	3,846 (5.9)	637 (4.8)	725 (5.5)	776 (6.0)	790 (6.2)	918 (7.3)	44	2,007 (52)	1.49
Age groups (years)									
< 1	18 (0.6)	6 (0.9)	7 (1.1)	0 (0)	4 (0.7)	1 (0.2)	36	5 (28)	1.38
1-5	288 (1.7)	42 (1.2)	67 (1.9)	70 (2.0)	56 (1.7)	53 (1.7)	39	71 (25)	1.20
6-12	1,616 (6.3)	241 (4.6)	314 (6.1)	326 (6.3)	337 (6.6)	398 (7.8)	46	831 (51)	1.55
13-17	1,924 (10.3)	348 (9.0)	337 (9.0)	380 (10.2)	393 (10.6)	466 (12.7)	44	1,100 (57)	1.50
Gender									
Male	1,442 (4.3)	257 (3.8)	266 (3.9)	255 (3.8)	328 (5.0)	336 (5.2)	41	673 (47)	1.39
Female	2,404 (7.6)	380 (5.9)	459 (7.2)	521 (8.3)	462 (7.5)	582 (9.5)	46	1,334 (55)	1.56
Region									
Bangkok	437 (9.1)	85 (8.3)	97 (9.8)	81 (8.3)	88 (9.3)	88 (9.6)	43	208 (48)	1.31
Central	1,192 (7.3)	218 (6.5)	228 (6.9)	251 (7.6)	231 (7.1)	264 (8.2)	52	612 (51)	1.48
Northeast	1,204 (5.5)	170 (3.8)	208 (4.7)	233 (5.4)	266 (6.2)	327 (7.8)	39	685 (57)	1.64
North	424 (4.1)	67 (3.1)	89 (4.2)	82 (3.9)	84 (4.1)	102 (5.0)	38	189 (45)	1.37
South	589 (5.2)	99 (4.3)	103 (4.5)	129 (5.7)	121 (5.4)	137 (6.2)	49	313 (53)	1.48

DKA: diabetic ketoacidosis

Table 3. Five most common comorbidities of hospital admission for type 1 diabetes mellitus and diabetic ketoacidosis in children and adolescents

Rank	T1D			DKA		
	ICD-10	Diagnosis	N (%)	ICD-10	Diagnosis	N (%)
1	J00-J22	Respiratory tract infections	832 (9.6)	J00-J22	Respiratory tract infections	376 (9.8)
2	A00-A09	Intestinal infections	406 (4.7)	A30-A49	Other bacterial diseases	205 (5.3)
3	N30-N39	Other diseases of urinary system	375 (4.3)	N30-N39	Other diseases of urinary system	201 (5.2)
4	F00-F99	Mental and behavioral disorders	345 (4.0)	A00-A09	Intestinal infections	142 (3.7)
5	K20-K31	Diseases of esophagus, stomach and duodenum	309 (3.5)	F00-F99	Mental and behavioral disorders	141 (3.7)

ICD-10: International Code of Diseases-10, T1D: type 1 diabetes mellitus, DKA: diabetic ketoacidosis

Thai T1D registry showed that only 28 % of youth performed SMBG at least four times/day, which is below the standard of care (17,20). On top of that, low frequency of SMBG was significantly associated with poor diabetes control, a known risk factor for developing recurrent DKA (14,17). Lack of coverage for glucose strip tests is likely a major problem for a number of Thai children and adolescents with T1D. Together with the increased incidence of DKA admission found in our study, the health insurance coverage for blood glucose strip tests in Thai T1D youth should be endorsed.

Compared to their younger counterparts, T1D patients over 6 years of age had a significantly higher incidence of DKA admission. Previous reports also showed the maximum rates of DKA admission in adolescents followed by school-aged children (18,21). Non-adherence to treatment is a common risk factor for developing DKA in adolescents (22). According to the data of T1D patients in the Thai registry, school-aged children had the lowest proportion of those achieving hemoglobin A1c targets (17). High admission rates in school-aged children might reflect a lack of comprehensive diabetic education for school personnel, which is indispensable for these vulnerable individuals (23). We believe that diabetic education for school nurses in Thailand is still lacking.

Consistent with other studies, we found that females had a higher incidence of DKA admission than males (3,4,6,7,9,24). Possible explanations might include insulin omission and intentional insulin restriction, which were more common in females and were risk factors for DKA in patients with known diabetes (14,25). Females were also more likely to receive the diagnoses of impaired psychosocial adjustment and psychiatric disorders, which were associated with poor glycemic control and diabetes-related complications (26). Interestingly, we found that mental and behavioral disorders were not uncommon in hospitalized T1D patients (Table 3). These findings reflect that female youth with T1D require more intensive and holistic care in which diabetes self-education and routine psychosocial support is essential.

Bangkok had the highest incidence of DKA admission but the second lowest DKA admission number and the lowest DKA admission rate. The total number of individuals in Bangkok was undeniably the smallest of all regions (Table 1). In addition, Bangkok has the most referral tertiary medical centers. These factors might lead to a falsely high incidence of DKA admission. In contrast, the Northeast region had the highest hospitalization parameters, including recurrent DKA admission, increased incidence of DKA admission, and DKA admission rate. Residents of the Northeast area have the lowest socioeconomic status according to poverty

indices, such as the lowest average monthly profits and the highest numbers of poor people (27). Traveling in the area is problematic while the transportation costs are high and the health care availability is the least of all regions in Thailand (16). As a result, the Northeast region had the maximum rate of unmet healthcare needs for both in-patient and out-patient departments (16). Limited access to medical services, a potential risk factor for developing DKA, would plausibly contribute to the highest DKA admission in the Northeast area (1,14).

Infections were among the common precipitating causes of DKA, with varied frequency from 14% to 58% in different countries (28). Korbel et al. (29) demonstrated that respiratory infections were the most common infectious disease in hospitalized children with T1D in the USA. Similarly, we found that respiratory tract infections were prevalent in patients with T1D hospitalized for DKA and non-DKA. Our findings thus emphasized the importance of preventive measures for respiratory infections and sick day management among youth with T1D.

Over four decades, several studies among Thai children and adolescents have focused on the regional or national incidence of T1D using either questionnaires or medical records, but none specifically reported the incidence of DKA admission (10,11,30,31,32,33,34,35). To the best of our knowledge, this is the first study using the databases of all Thai health coverage systems that show national hospitalization data of patients with T1D and DKA.

Study Limitations

Limitations of this study included a relatively short study period (5 years) and the diagnosis of T1D and DKA, which were based solely on ICD-10 codes. Hence, newly diagnosed and known T1D were indistinguishable.

Conclusion

Increased incidences of T1D and DKA admissions among Thai youth during 2015-2019 were observed. Individuals who had a higher risk of being admitted for DKA were those over 6 years of age, being female, and residing in the Northeast region.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee on Human Research of the Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand (decision no: MURA2024/136, date: 16.02.2024) and conformed to the provisions of the Declaration of Helsinki.

Informed Consent: Informed consent was not obtained from the patients because the data were anonymous and were extracted from the health care schemes with permission.

Footnotes

Authorship Contributions

Concept: Taninee Sahakitrungruang, Pat Mahachoklertwattana, Design: Taninee Sahakitrungruang, Pat Mahachoklertwattana, Data Collection or Processing: Somboon Wankanit, Kaewjai Thepsuthammarat, Pat Mahachoklertwattana, Analysis or Interpretation: Somboon Wankanit, Kaewjai Thepsuthammarat, Preamrudee Poomthavorn, Pat Mahachoklertwattana, Literature Search: Somboon Wankanit, Preamrudee Poomthavorn, Pat Mahachoklertwattana, Writing: Somboon Wankanit, Kaewjai Thepsuthammarat, Preamrudee Poomthavorn, Taninee Sahakitrungruang, Pat Mahachoklertwattana.

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