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ORIGINAL ARTICLE

The Incidence and Severity of Paediatric Diabetic Ketoacidosis Presenting to a Metropolitan Hospital in Western Sydney: A 10-Year Retrospective Review

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Abstract

Objectives. To report the incidence and clinical characteristics of paediatric patients presenting with diabetic ketoacidosis to the Emergency Department (ED) with new and pre-existing type 1 diabetes mellitus (T1DM).

Methodology. A ten-year retrospective data analysis was performed on children under 16 years presenting to the ED with T1DM from January 2010. Demographic and laboratory data were extracted to determine the rates of DKA. Comparative statistics were performed between age groups and pre-existing and newly diagnosed T1DM patients.

Results. A total of 196 children with T1DM were included. The mean age of the cohort was 9.3 ± 4.0 years, with female predominance (54%, $p = 0.38$). Most (60%) were newly diagnosed with T1DM, of which 38% presented in DKA. Amongst the total cohort, 43% presented in DKA.

The older children accounted for 50% of the DKA presentations in the newly diagnosed cohort. Amongst the younger age group, 42% presented with severe DKA. There were higher rates of T1DM in areas of relative socioeconomic advantage.

Conclusion. Children with T1DM presented with unacceptably high rates of DKA and posed a significant medical, psychosocial and financial burden on families and medical services. These findings suggest that a prospective public health campaign to reduce rates of DKA is warranted.

Key words: type 1 diabetes mellitus, diabetic ketoacidosis, child health, pediatrics

INTRODUCTION

One of the most prevalent endocrine diseases in the world is Type 1 Diabetes Mellitus (T1DM).[1] According to the National Diabetes Register, there were 194 new cases per 100,000 population (incidence) of T1DM in Australia in 2021.[2] Despite advances in diabetes management, there remain challenges in all age groups, such as suboptimal glycaemic control and increased frequency of diabetes complications.

The most common complication of T1DM is Diabetic ketoacidosis (DKA). Younger age, delayed diagnosis, lower socioeconomic level (SES), and living in a nation with a low prevalence of type 1 diabetes are risk factors for DKA in newly diagnosed patients.[3] Acute complications of DKA include hypokalaemia, deep vein thrombosis, cerebral oedema and death.[3]

Many community educational campaigns have been launched for T1DM awareness to prevent DKA and related complications, with mixed results.[4,5] A recent retrospective study at a large regional hospital in Queensland, Australia[6] explored the incidence of DKA over 11 years in children and youth under 18 years old at first presentation of T1DM, before and after an educational intervention. Overall, post-intervention DKA incidence had halved (from 55 to 25%). The intervention also managed to lower the incidence of severe and moderate DKA (from 49 to 33% and 27 to 17%, respectively), while mild DKA doubled from 24 to 50%.

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Our study aims to report the frequency and severity of presentations of children with T1DM presenting to a metropolitan teaching hospital in Western Sydney. We also aimed to describe the illness severity at presentation of the more vulnerable population of children under five years of age.

METHODOLOGY

A retrospective medical record review was performed at a metropolitan teaching hospital in Western Sydney over a ten-year period from January 2010 to December 2019. The data was extracted from the electronic medical record systems of the hospital for all children under 16 years of age who presented to the Emergency Department (ED) with the diagnosis of T1DM.

The extracted data included age, sex, residential postcode, age of diagnosis, family history, co-morbid conditions (i.e., asthma, coeliac disease, renal disease, psychiatric disorders etc.), presenting symptoms, laboratory investigations and diagnosis (new and pre-existing T1DM), and their subsequent admissions. The study population was divided into two age groups: younger children (less than five years old) and older children (between 5 to 16 years old). Recurrent presentation and recurrent DKA were each defined as more than one presentation without DKA, or more than one DKA presentation within the same year or more than two presentations within three years of the last admission, respectively. All data were complete with no missing values.

The International Society of Paediatric Adolescent Diabetes (ISPAD) Clinical Practice Consensus Guidelines 2022[7] defined DKA as: hyperglycaemia above 11 mmol/L and pH <7.3, or serum bicarbonate <15 mmol/L in the presence of ketonaemia (blood ß-hydroxybutyrate ≥3 mmol/L) or ketonuria (moderate or large). A venous pH of <7.3 or a serum bicarbonate of <15 mmol/L was considered mild; a pH of <7.2 and a serum bicarbonate of <10 mmol/L was considered moderate; and a pH of <7.1 and a serum bicarbonate of <5 mmol/L was considered severe.

Socioeconomic status (SES) was determined using the Socioeconomic Indexes for Areas (SEIFA).[8] This ranks Australian areas according to relative socioeconomic advantage and disadvantage based on residential postcodes. The SEIFA score is reported in deciles from one to ten, the highest decile representing an area of higher SES.

Ethics

The study was conducted in compliance with The National Health and Medical Research Council's (NHMRC) national statement on ethical conduct in human research. Human ethics approval for the study was obtained from the Nepean Blue Mountains HREC (Approval number: 2020/ETH00898).

Statistical analysis

Statistical analysis was performed using STATA version 15.0 software. Mean, standard deviation, minimum and maximum were used to describe continuous data, while frequency and percentages were used for categorical data. Data comparison by age group was done using the chi-square test or Fisher's exact test for categorical data and t-test for continuous data. Statistical significance was set at p <0.05.

RESULTS

A total of 196 children presented to the ED with T1DM, with 54% being female (n = 105). The characteristics and comorbidities of the study population are presented in Table 1.

Table 1. Patient characteristics and comorbidities of newly diagnosed T1DM

Parameter	Total (n=196)	New Diagnosis of T1DM		*P* value
		Yes (n=118)	No (n=78)	
Age at diagnosis (years)				
Mean	9.3 ± 4.0	8.8 ± 3.8	10.0 ± 4.2	0.38*
Range (Min, Max)	(1.0, 15.0)	(1.0, 15.0)	(1.0, 15.0)	
Age 5 - <16 years (%)		94 (80)		
Under 5 years (%)		24 (20)		
DKA at diagnosis (%)		45 (38)		
Sex, n (%)				
Male	91 (46)	52 (44)	39 (50)	0.42
Female	105 (54)	66 (56)	39 (50)	
Family History DM, n (%)				
Yes	62 (32)	48 (41)	14 (18)	<0.001
No	134 (68)	70 (59)	64 (82)	
Comorbidity Conditions, n (%)				
Atopy (Asthma, Hay Fever)	22 (11)	14 (12)	8 (10)	0.73
Thyroid Disease	8 (4)	3 (3)	5 (6)	0.18
Behavioural / Development Disorder	14 (7)	6 (5)	8 (10)	0.17
Coeliac Disease	8 (4)	5 (4)	3 (4)	0.89

*Chi-square test or Fisher exact test for categorical data and t-test for continuous data
DM: diabetes mellitus

Table 2. Comparisons between DKA, recurrent DKA and recurrent presenters

Parameter	DKA			Recurrent DKA[a]			Recurrent presenter[b]		
	Yes (n=84)	No (n=112)	*p* value	Yes (n=8)	No (n=76)	*p* value	Yes (n=54)	No (n=142)	*p* value
Age, n (%)									
5 - <16 years	68 (81)	92 (82)	0.83	7 (88)	61 (80)	1.00	41 (76)	119 (84)	0.20*
Under 5 years	16 (19)	20 (18)		1 (12)	15 (20)		13 (24)	23 (16)	
Sex, n (%)									
Male	39 (46)	52 (46)	1.00	2 (25)	37 (49)	0.27	23 (43)	68 (48)	0.50
Female	45 (54)	60 (54)		6 (75)	39 (51)		31 (57)	74 (52)	
Family history, n (%)									
Yes	23 (27)	39 (35)	0.26	4 (50)	19 (25)	0.13	20 (37)	42 (30)	0.31
No	61 (73)	73 (65)		4 (50)	57 (75)		34 (63)	100 (70)	

[a] Recurrent DKA: more than one presentation with DKA within the same year or more than two presentations within three years of the last admission
[b] Recurrent presenter: more than one presentation with hyperglycaemia within the same year or more than two presentations within three years of the last admission
* Chi-square test or Fisher exact test for categorical data and t-test for continuous data

Sixty percent of the children (n = 118) were newly diagnosed with T1DM during the study period, of which 38% presented with DKA (n = 45). Children under five years old represented 20% of this cohort (n = 24). The mean age at diagnosis was 8.8 years ± 3.8 years, again with a female predominance (56%) (Table 1). Amongst the total cohort of 196 children, 84 children (43%) presented with DKA. There were 73% of children with DKA who had no family history of diabetes (Table 2).

Overall, the DKA recurrence rate was 10% (n = 8), with two-thirds coming from the newly diagnosed group, with female predominance in all the groups. The older children comprised 50% or more of the overall and new T1DM cohort, while the 5-to-less than10 year old group comprised more than half of the existing T1DM group.

Table 3. Comparison of DKA severity according to age groups

DKA	Age			*p* value
	Total (n = 114)	Under 5 years (n = 12)	5 - <16 years (n = 102)	
Mild, n (%)	59 (52.0)	5 (42)	54 (53)	0.29*
Moderate, n (%)	28 (24.5)	2 (16)	26 (25)	
Severe, n (%)	27 (23.5)	5 (42)	22 (22)	

*Chi-square test or Fisher exact test

A total of 114 episodes of DKA were recorded: 52% (n = 59) were mild, 24.5% (n = 28) were moderate and 23.5% (n = 27) were severe. The severity comparison between the two age groups is shown in Table 3. Fourteen children (7%) with severe DKA were transferred to a paediatric tertiary care centre, with 78% as newly diagnosed T1DM. No mortality was recorded in our patient cohort.

There were 18 episodes of hypoglycaemia during the study period. Sixteen out of 18 children had mild hypoglycaemia (glucose 3.0-3.9 mmol/l), while two children had severe hypoglycaemia (glucose under 2 mmol/l). The mean age at presentation was 9.3 years ± 4.4 years, mainly on MDI treatment (67%). One-third of the hypoglycaemic events had seizures as their initial presentation, occurring in a younger mean age of 7.5 years ± 4.7 years.

Figure 1 represents the number of presentations during the study period, the majority of which were from the newly diagnosed group.

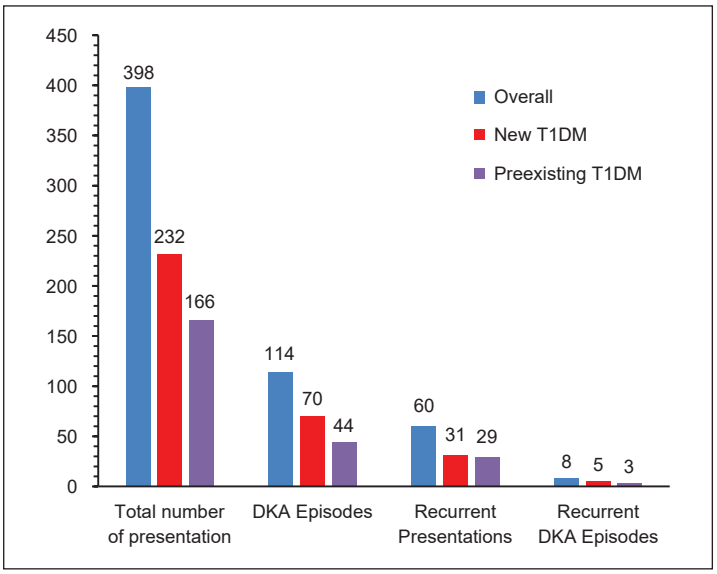

Figure 1. Hospital presentations.

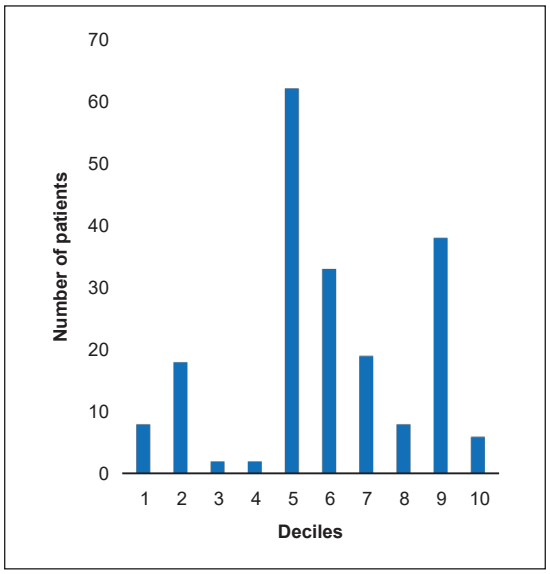

Figure 2. Socioeconomic distribution of patients.

An analysis of the SES of the 196 children in the entire cohort revealed that 32% were in the 5th decile, followed by the 9th decile (19%), while only 4% were in the 1st decile area. Similarly, most recurrent presenters were from the 5th and 9th decile with 37% and 17%, respectively, while 9% were from the 2nd decile and 5% were from the 1st decile.

DISCUSSION

During the ten-year study period, the majority (55%) of the 196 children with T1DM belonged to the older age group, consistent with the national[2] and international data[9,10] indicating that the prevalence and cumulative peak incidence of T1DM is in the 10-to-14 age group. In line with previous reports,[9,10] we noted an overall female predominance (54%) in the cohort and the newly diagnosed group. This has previously been linked to the increased prevalence of autoimmune diseases in females.[11] However, after adjusting for differences in the age structure of the populations, Australian national data reported a 1.4 times increase in T1DM among males than females.[2] Conversely, some studies found no gender difference in the overall incidence of T1DM.[12,13] Contrary to the previously reported increased prevalence of autoimmune diseases like coeliac disease and autoimmune thyroiditis,[11] asthma was the most prevalent comorbid condition, present in 11% of our cohort. This is possibly due to the increased prevalence of allergic conditions in Australia, as previously reported by large multinational studies in children.[14] Despite this increased prevalence of asthma, there was no evidence that it influenced DKA rates in our cohort. In addition, while there appears to be a possible association between atopy/asthma and T1DM, there is no clinical data to suggest that the presence of atopy or asthma alters the risk of DKA in children.

Sixty percent of the children were newly diagnosed with T1DM during the study period. There was an increasing incidence with age, which is in line with findings from a recent similar study from Sydney by Ampt A et al., who gathered data from 2001 to 2013 on the epidemiology and risk factors for DKA in Australian children aged 0 to <15 years.[15]

Over ten years, 75% of the total cohort and 37% of the pre-existing T1DM cohort had one or more episodes of DKA. Previous literature reports the risk of DKA as 1 to 10% per patient per year in children with established diabetes. The likely risk factors include higher HbA1c levels, acute gastroenteritis, peripubertal and pubertal adolescent girls, psychiatric disorders, insulin omission (accidental or intentional), unstable family circumstances and limited access to medical care.[7]

The overall international frequency of DKA at first presentation of T1DM varies from 13 to 80%,[16] depending on the T1DM prevalence, local awareness, young age (<5 years), diagnostic errors, ethnic minority, low SES and lack of access to local health care. A study from New Zealand looking at the 15-year incidence of DKA reported a lower percentage (27%) at the first presentation of T1DM[17] compared to the 48.1% reported by a study from Townsville, Queensland.[6] In contrast, we found that over one-third of the children (38%) had DKA at their first presentation, which is consistent with the previously reported paediatric data from Sydney in 2012 and 2019 and Brisbane in 2013 (i.e., 37.7 per 100 person-years, 33% and 32%, respectively). The national data also indicated relatively stable cumulative incidence rates of T1DM in Australia over the last two decades.[7] Ampt A et al. further quantified the incidence of DKA according to the age groups: 40% in 0 to 4 years, 25% in 5 to 9years, and 33% among 10 to 12-years.[15] These figures align with our findings for 5 to <10-year-old children (24%), but in contrast, we found a lower incidence (24%) of DKA at first presentation in under five-year-old children and highest in the older age group (51%). A possible explanation for this difference may be relatively fewer young families residing in our area during the study period.

National and international studies[18,19] have reported higher DKA rates in young children under five years at T1DM diagnosis. Amongst our total 114 DKA episodes, 52% were mild, while the moderate and severe episodes were 24% each. Alarmingly, among the younger age group with DKA, 42% presented with severe DKA. Like previously mentioned studies, Usher et al.,[18] conducted a systematic review that included 46 studies with more than 24,000 children in 31 countries. They identified risk factors posing the highest risk of DKA at diagnosis, which included younger age, ethnic minority, lack of health insurance, and lower body mass index. This may be due to parents and healthcare personnel having low suspicion of T1DM, atypical presentations and increased difficulty in recognising symptoms as they are young and may have difficulty communicating the symptoms of thirst, with some showing non-verbal cues, which delays diagnosis. Additionally, it has been reported that due to their less developed metabolic compensatory mechanisms, young children may be more prone to decompensation due to dehydration and acidosis, and delayed diagnosis may cause faster β-cell destruction in young children.[20]

DKA recurrence leads to complications that early targeted interventions could avoid through a multidisciplinary team. We report an overall DKA recurrence rate of 10% - 9% in recently diagnosed T1DM and 10% in existing T1DM. In terms of age groups, the older children comprised 50% or more of the overall and new T1DM, while the 5 to <10-year-old children formed more than half of the existing T1DM group. A possible explanation for frequent DKA admissions in older children may be their independence, changes in their daily routine and self-management of BSL, especially when not at home. The very high rates of DKA, approaching 50%, especially in the younger age group <5 years, highlights the need for a campaign towards community diabetes awareness and DKA awareness and prevention, like the 4T campaign first conducted in the UK, then in Newcastle, Australia. However, DKA rates remain

high in both these regions and even nationally, suggesting a lack of translation of this clinical evidence into practice within the existing primary and tertiary care systems.[21]

Studies have highlighted the association of the socio-economically disadvantaged areas with T1DM, DKA and recurrent DKA presentations.[15,22] Contrary to this, we note an increased number of patients from areas of relative socioeconomic advantage consistently with higher prevalence of T1DM, first episode of DKA, recurrent presenters and recurrent DKA presentations. This is consistent with a Western Australian study from 2006.[23] The reasons for this paradoxical observation are unclear, but this increased T1DM association with higher socio-economic areas could be due to unexplained lifestyle differences.[24] Further exploration of this is required.

We also reported the number of children presenting to the emergency department within our cohort with severe hypoglycaemia. Our rates were low, which is consistent with national and international trends for reduced frequency of severe hypoglycaemia. The latter is probably related to the introduction of continuous glucose monitoring systems and improved insulin pump technology preventing hypoglycaemia, as well as better education of families.[25-27]

The main strength of our study was the larger patient cohort, which included follow-up of ten years. The main limitation of the present study was the lack of data on ethnicity, BMI, duration of presenting symptoms and length of hospital stay. This additional data would be helpful in further understanding potential risk factors for T1DM and DKA presentations.

CONCLUSION

T1DM was more prevalent in older children, particularly females, and in areas of relative socioeconomic advantage. However, the incidence of paediatric T1DM was stable over the 10-year study period. The younger age group of under five years presented more frequently with severe DKA compared to older children. This signifies the importance of increasing community awareness about childhood diabetes and timely recognition of its symptoms to prevent DKA.

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Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

CRediT Author Statement
SS: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing – original draft preparation; **GL:** Conceptualization, Methodology, Writing – review and editing, Supervision, Project administration; **AL:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing – review and editing, Visualization, Supervision, Project administration; **HB:** Conceptualization, Methodology, Writing – review and editing, Supervision, Project administration.

Author Disclosure
The authors declared no conflict of interest.

Data Availability Statement
Datasets analyzed in the study are under license and not publicly available for sharing.

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