DOI: 10.4274/jcrpe.galenos.2024.2024-1-8

Research Article

Predictors and Trends of Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes Mellitus in Malaysian Children

Meenal Mavinkurve[1], Nurul Hanis Ramzi[2], Muhammad Yazid Bin Jalaludin[3], Nurshadia Samingan[3], Azriyanti Anuar Zaini[3]
[1]Department of Paediatrics, School of Medicine, International Medical University, Jalan Rasah, Seremban
[2]Institute for Research, Development and Innovation, International Medical University, Jalan Jalil Perkasa, Bukit Jalil, KL
[3]Department of Paediatrics, Faculty of Medicine, Universiti Malaya, Kuala Lumpur

What is already known?
- The average DKA rate in Malaysian children with T1DM ranges between 54-75% between 2000-2010.

What this study adds?
- The DKA rate has remained sustainedly high since the year 2000 and severe DKA comprises the largest burden
- Predictive factors of DKA are age ≥ 5 years and misdiagnosis
- There were no significant trends in the rates of children <5 years presenting in DKA nor the rates of severe DKA

Abstract
Objectives: Previous reports indicate that diabetic ketoacidosis (pDKA) rates in Malaysian children with type 1 diabetes range between 54-75%, which is higher than most European nations. Knowledge of trends and predictors of DKA can be helpful to inform measures to lower the rates of DKA. However, this data is lacking in Malaysian children. Hence, the aim of this study was to determine the predictors and trends of pDKA in Malaysian children at the initial diagnosis of T1DM.
Methods: This cross-sectional study examined demographic, clinical and biochemical data of all newly diagnosed Malaysian children aged 0-18 years with T1DM over 11 years from a single centre. Regression analyses determined the predictors and trends.
Results: The overall pDKA rate was 73.2%, of which 54.9% were severe DKA. Age ≥5 years (OR 12.29, 95% CI 1.58, 95.58, p=0.017) and misdiagnosis (OR 3.73, 95% CI 1.36, 10.24 p=0.01) were significant predictors of a DKA presentation. No significant trends in the annual rates of DKA, severe DKA nor children <5 years presenting with DKA were found over the 11-years study period. **Conclusion:** DKA rates at initial diagnosis of T1DM in Malaysian children are high and severe DKA accounts for a significant burden. Though misdiagnosis and age ≥5 years are predictors of DKA, misdiagnosis can be improved through awareness and education. The lack of downward trends in DKA and severe DKA highlights the urgency to develop measures to curb its rates.
Keywords: Diabetic Ketoacidosis, Childhood, Malaysia, Type 1 diabetes, Trend

Azriyanti Anuar Zaini, Associate Professor, Faculty of Medicine, Universiti Malaya
Kuala Lumpur, Malaysia
azriyanti@ummc.edu.my
+60122997565
0000-0001-5659-765X
09.01.2024
01.04.2024

Presented at *"12th National Pediatric Research Conference"* on 9/9/23 at International Medical University, Seremban, Malaysia

Published: 29.04.2024

1. Introduction

Type 1 diabetes mellitus (T1DM) is an autoimmune condition in children which peaks between 10-14 years of age (1). There is a wide variation in the incidence of T1DM worldwide, with higher incidence rates reported in Northern Europe as compared to Western Africa and South America (2,3). Within Asia, childhood T1DM rates have been rising in several countries such as Thailand, Hong Kong and Indonesia (4–7). In Malaysia, T1DM is the most common type of childhood diabetes, accounting for >69 % of all diabetes mellitus cases. The IDF World Diabetes Atlas reports that in 2021, the estimated number of new cases of T1DM in children aged 0-19 years was 100 and that the total number of cases was 1000 (5). A prior study by Hong et al, has showed that the DKA at diagnosis occurs in 65% of paediatric T1DM cases in Malaysia, however analysis of the risk factors for DKA nor its trends have been conducted (8,9).

Paediatric diabetic ketoacidosis (pDKA) is a severe and potentially fatal presentation of T1DM that is characterised by hyperglycaemia, dehydration, ketosis and acidosis (10). Early recognition and management of pDKA are essential for reducing mortality, morbidity and financial burden. The incidence of pDKA at initial diagnosis of T1DM varies between countries, with lower rates reported in Northern Europe and higher rates in other regions such as the UAE, Saudi Arabia, Kuwait, Malaysia and Indonesia (11–14). This variation may be explained by several contributing factors such as age, socioeconomic status, delayed or misdiagnosis, poor public awareness, educational background of the parents and the background frequency of paediatric T1DM in the population (15–17).

Trend analysis of pDKA at initial diagnosis of T1DM in children and determination of its associated risk factors has been conducted in several countries. Data from such studies are important because can be informative in terms of developing interventions to reduce the incidence of pDKA. A recent epidemiological study from Thailand has reported that there has been a reduction in pDKA over the 20-year study period (4). New Zealand and Indonesia, on the other hand, have reported a sustained high incidence of pDKA at initial diagnosis or a rise in the incidence over the respective study periods (6,18). In Malaysia, Hong et al, reported that the rate of pDKA at initial diagnosis of T1DM in 490 children from multiple centres between 2000-2010 varied between 54-75% of cases (9). Though they reported that pDKA rates were mostly high throughout the study period, there was no evaluation of severe DKA rates nor a determination of the predictors of pDKA. Furthermore, data on trends in pDKA in Malaysian children with T1DM is limited following the study by Hong et al. Nonetheless, their data is crucial in highlighting the high rates of pDKA which is undoubtedly associated with significant morbidity and financial costs (19,20). In view of the burden associated with DKA, it is important that collective efforts are required to reduce the incidence of pDKA.

Hence the objective of this study is to determine the predictors of pDKA at initial diagnosis of T1DM and to describe its trends in Malaysian children over an 11-year period.

2. Experimental subjects

All newly diagnosed cases of paediatric T1DM in Malaysian children who were managed at University Malaya Medical Centre between January 1st 2010 to December 31st 2020 were included in this study. A diagnosis of T1DM and/or DKA was made in accordance with the International Society for Pediatric and Adolescent Diabetes (ISPAD) guideline for the year in which the diagnosis was made. Body mass index (BMI) status was categorised using the World Health Organisation Z-score cut-offs (21). Non-Type 1 diabetes mellitus cases, non-Malaysians and subjects with incomplete data about the presence of DKA at diagnosis were excluded from the analysis.

3. Materials & Methods

A cross-sectional study was conducted using retrospective data that was extracted from the hospital electronic medical record system and letters from the referring physicians. Details on age, gender, ethnicity, DKA, misdiagnosis, anthropometry, intensive care admission and inpatient stay were obtained. University Malaya Medical Centre has an electronic medical record system with a proforma for in-patient admission clerking, into which details on the presenting history are entered on admission. All new diagnoses of paediatric T1DM at University Malaya Medical Centre are always admitted as inpatients irrespective of whether they present in DKA or not and all are reviewed by the Paediatric Endocrinology team. The Statistical Package for Social Sciences (SPSS for Windows, version 28.0, 2004, Chicago, IL, USA) was used for statistical analysis. Demographic data, clinical and biochemical data were analysed using descriptive statistics; means ± SD for continuous variables and frequencies or percentages for categorical variables. Comparison of DKA and non-DKA groups were conducted using independent student's t-test and Pearson's chi-squared test (χ^2) for continuous and categorical variables respectively. Logistic regression model was used to determine the predictors of DKA at initial diagnosis of T1DM. Gender and ethnicity were adjusted for as potential confounders. The odds ratios (OR) along with the respective 95% confidence intervals (CIs) were reported. The trend in DKA incidence rates over the 11-year period was analysed using Poisson regression. A 2-sided 5% significance level was used for all statistical inferences. This study was approved by the University Malaya Medical Centre Institutional Ethics Board MREC Ref: 2019325-7251.

4. Results:

4.1 Demographic, clinical and biochemical characteristics of the overall cohort

A total of 127 children aged 0-18 years with T1DM were identified during the 11-year study period. Males constituted 46.5% (n=59) and the mean age of the cohort was 8.06 +/-3.78 years. Children ≥5 years comprised 78.7 % (n=100) of the whole cohort. The predominant ethnic group was the Malays, 39.4 % (n=50). The overall rate of DKA at presentation was 73.2% (n=93) of which 54.9% of cases were *severe* DKA *(Table 1).*

4.2 DKA versus non-DKA groups

The DKA group was significantly younger at diagnosis (7.64 ± 4.03 vs. 9.19 +/- 2.77 years, p= 0.03) with 72.6 % (n=69) of pDKA group being represented by the ≥5 years age category (p=0.003). However, 26 from 27 children (96%) < 5 years presented in DKA. Misdiagnosis rates were significantly higher in the DKA group (43% vs. 17.6%, p= 0.004) as were PICU admission rates (57.1% vs. 12% p <0.001) and the length of hospital stay (7.72 vs. 5.90, p= 0.01) (*Table 2)*. Comparison of the 3 severity categories of DKA showed that the severe DKA group had a significantly higher rate of admission to PICU (p=0.001) *(Table 3).*

4.3 Predictors of pDKA: Logistic regression analysis

Binary logistic regression modelling, using DKA and non-DKA groups as the dependent variables, showed that age was a significant predictor of pDKA; ≥5 years age group (OR 12.29, 95% CI 1.58, 95.85, p= 0.017) was approximately 12 times more likely to have DKA. Similarly, misdiagnosis was determined to be a significant predictor of DKA (OR 3.73, 95% CI 1.36, 10.24, p=0.01).

4.4 Trends in DKA over the decade

The annual rate of DKA varied between 20% and 85% (Fig. 1) peaking at 85% in 2015. The rates of *severe* DKA (Fig.2) fluctuated between 28.6% to 100% over the 11-year study period. The lowest rate was in 2010. In terms of age group, the percentage of children <5 years of age who presented in DKA at the initial diagnosis of T1DM, varied from 0% -16%. The lowest rates were in 2011-2012 and the highest in 2017.

Poisson regression analysis demonstrated that there were no significant increasing nor decreasing trends in the annual rates of DKA (p=0.09), rates of *severe* DKA (p=0.64) nor the rates of younger age children (< 5 years) presenting in DKA (p=0.70) at initial diagnosis, over the 11 years.

5. Discussion

This single centre study over 11 years showed an overall pDKA rate at initial diagnosis of T1DM in Malaysian children of 73.2%. A disproportionately large percentage of the cases were *severe* DKA (54.9%). Children presenting in DKA had a mean age of 7.65 yr (± 4.03) which was significantly younger than non-DKA children. The DKA group was more likely to be misdiagnosed and require PICU admission with a longer length of inpatient stay. In particular, PICU admission rates were significantly higher in severe DKA cases. Logistic regression analysis demonstrated that children ≥5 years and misdiagnosis were the 2 main predictors of pDKA in this cohort. No significant increasing nor decreasing trends were demonstrated in the incidence of pDKA, rates of *severe* DKA, nor the rates of young children (<5 years) presenting in DKA at diagnosis over the 11-year study period.

5.1 Rates of DKA

This is the second study to investigate the annual incidence of pDKA in Malaysian children at initial diagnosis of T1DM. A previous multicentre study by Hong et al, reported an overall pDKA rate of 64.7%. Over their 10-year study period, the pDKA rate fluctuated between 54.5% to 75% (9). The mean age of their cohort presenting in DKA at diagnosis was 7.2 years and 70.4% of their <5-year-old cohort presented in DKA. Gender and ethnicity were not different between the DKA and non-DKA groups in the study by Hong et al. In the context of the study by Hong et al, our study highlights that DKA rates in Malaysian children have remained high since 2010 and have *failed to diminish* over the last 20 years. Though rates of DKA in the current 11-year study fluctuated as well, it never fell below 20%. Furthermore, a finding that was not previously reported is that this high burden of DKA is primarily contributed by a high rate of *severe* DKA cases. Interestingly, over the last 20 years, the average age of pDKA has remained stable, 7.2 yr in Hong et al's study and 7.65 yr in the current study. However, though the mean age of children presenting with DKA is represented by the *"school-going"* age group, it is important to note that the frequency of DKA was higher in children <5 years; 70.4% in Hong et al's study as compared with 96.3% in the current study.

Malaysian rates of pDKA are significantly higher than several Northern European countries but comparable to those reported within the ASEAN region (22–24) (25)(26). We hypothesize that the sustainedly high rates of pDKA, are related to several factors. These may include factors such as a lower background prevalence rate of T1DM in Malaysian children and potentially a reduced awareness that T1DM is a disease of childhood amongst the general public as well as differences in healthcare system structures. However, though these factors have been shown to correlate with high DKA rates in other countries, they have yet to be studied in the Malaysian context as potential risk factors for DKA and would require multicentre prospective studies (14,15).

5.2 Predictors of DKA at initial diagnosis of T1DM

Formatted: Font: 8 pt, Turkish, Do not check spelling or grammar

This study showed that the predictors of DKA at initial diagnosis of T1DM in Malaysian children were age ≥5 years and misdiagnosis. The study by Hong et al, did show that school-aged children comprised the largest proportion of children presenting in DKA. This study expands on the findings reported by Hong et al's by showing that age ≥5 years is indeed a predictor of DKA at initial diagnosis of T1DM. This finding is unexpected and contrary to other studies, which report that age <5 years is a risk factor for DKA, for the reasons that younger children present with less discernible symptoms, they lack the eloquence to explain their symptoms which may lead to diagnostic delays and errors (15,16). It is possible that our finding is influenced by the fact that a large proportion of our cohort (78.7%) were of school-going age, which is not dissimilar from the cohort in the study by Hong et al. Nonetheless, both studies do demonstrate that the incidence of DKA in the <5-year-old age group is comparably higher than older children, and so should still remain a cause for concern.

Misdiagnosis was another predictor of pDKA, increasing the risk of presenting in DKA by 3.5-fold which is in line with prior studies which have reported that misdiagnosis is a risk factor for DKA (15,16). However, unlike age, misdiagnosis is a *modifiable* factor for pDKA, suggesting that future efforts should focus on improving the diagnostic accuracy of pDKA by doctors through continuing professional development and implementing the recent ISPAD 2022 DKA guideline which recommends that all children who present with breathlessness or vomiting and abdominal pain without diarrhoea should have a finger prick glucose conducted as they may herald DKA (27).

5.3 Trends

This study did not demonstrate any significant increasing nor decreasing trends in the annual incidence of DKA at diagnosis. However, it is important to note that the annual rates of DKA *never fell below* 20%. New Zealand and Austria have also reported that the incidence of pDKA has remained stable over a period of time (18,28) and the SEARCH study in the US, showed that the rates of pDKA with T1DM between 2002-2010 were sustainedly high without any reprieve (29). Within the ASEAN region, Thailand has shown that the rates of pDKA have been reducing (25).

The trends in the annual rates of *severe* DKA in this study were also not significant, but never fell below 30%. These findings are not unlike what was reported by a paediatrics DKA study from New Zealand which showed high rates of severe DKA that fluctuated between 10-40% over the 15-year study period (18). On the other hand, a study from China reported that their rates of severe DKA had increased in the younger age groups (30).

The proportion of children <5 years presenting in DKA at their initial diagnosis of T1DM did not demonstrate any significant trends but fluctuated between 0-46% over the 11 years. There were some years where there were no DKA presentations in <5yr old children, for the reason that only children ≥5 years were diagnosed with T1DM in those years. This is contrary to epidemiological data from New Zealand, Italy and Finland which show that rates of DKA in children <5 yr are increasing over time (12,18,23,31). This result may be explained by the fact that Malaysian children with T1DM presenting in DKA are predominantly represented by the ≥5 yr age group.

The wide variation in trends of pDKA between nations may be related to a multitude of factors, such as differences in the local prevalence of T1DM and public awareness of childhood T1DM amongst others. A study conducted in New Zealand has demonstrated that in a group of 263 children the factors which contributed to an increased risk of DKA were reduced family awareness, prolonged delay in laboratory testing and a low level of HCP suspicion for T1DM (32). Thus, preventing a DKA presentation at initial diagnosis of T1DM requires several key components which include: a) early recognition of symptoms by the parents and child b) clinical suspicion for diabetes mellitus by the healthcare professional and c) easy access to a medical professional with the appropriate point of care testing to diagnose DM. These 3 elements rely on public awareness of diabetes mellitus as well as healthcare professional knowledge on the clinical presentation and diagnosis of paediatrics diabetes mellitus and the accessibility to basic tests to confirm a diagnosis of diabetes mellitus.

Malaysia is a low-middle income nation within the ASEAN region that has a well-supported public healthcare system and has undergone significant advancements in infrastructure over the past several decades. In relation to childhood T1DM, several measures are already in place to facilitate a timely diagnosis. For instance, point of care testing is readily available for hospitalist healthcare professionals to diagnose hyperglycaemia, ketonaemia and acidosis in children suspected to have T1DM or DKA. Training of hospitalist doctors within the public sector on the updated versions of the National Clinical Practice Guidelines (CPG) on childhood T1DM take place with every iteration of the CPG. Educational sessions are also conducted by the national paediatric endocrine society (MPEDG) for trainee paediatricians and family medicine doctors. Furthermore, the National Diabetes Institute of Malaysia and Diabetes Malaysia are instrumental in supporting people with diabetes and disseminating information about diabetes to the general public through their websites and magazines. The recently launched "Hello Type 1" by Action for Diabetes (A4D) for the Malaysian population is a website with aimed at raising awareness about T1DM in the local language of Bahasa Melayu (33). Despite these efforts, rates of pDKA have remained high. However, most of these measures have been in effect only over the last few years.

As such, future efforts should include research to understand the level of awareness of the general public and healthcare professionals about the clinical presentation of T1DM in children in tandem with measures to raise public awareness about childhood diabetes and DKA, which has been shown to be beneficial in reducing rates of DKA in the UK, with the 4 T's campaign, and the Parma campaign in Italy (34,35). Regular continuous medical education on paediatric diabetes mellitus and DKA for primary care and hospitalist professionals may help to improve diagnostic accuracy as well.

5.4 Limitations

A major limitation of this study is that it is retrospective, from a single centre and that it serves an urban catchment area which is home to pockets of affluence and a highly educated population. This region is also home to a large concentration of paediatric endocrinologists and tertiary paediatric centres with dedicated PICUs which often receive referrals for severe DKA. These limitations may inflate the rates of severe DKA and PICU usage in this study. Future studies should include multiple centres from different regions of Malaysia, so that regional differences, risk factors and trends may be evaluated.

6. Conclusion

In summary, this study demonstrates that the incidence of pDKA at initial diagnosis of T1DM in Malaysian children has remained high over the 11-year study period. Severe DKA rates comprise a significant burden of the cases and has not reduced over the 11 years. Age >5 years and misdiagnosis emerged as two predictors of pDKA, of which misdiagnosis is a modifiable risk factor. Measures to reduce DKA rates need to focus on raising public awareness, physician awareness about T1DM and DKA in children. Future research should gather data on relevant socioeconomic factors which could influence a DKA presentation. The data should also be from multiple centres or a national registry to determine the *true* national rate of pDKA and to compare regional differences. This data could assist in developing needs-based strategies to curb the rates of DKA throughout the nation by implementing cost-effective methods for resource allocation.

Author Contributions

MM contributed to the data collection, study design and manuscript writing and final approval
AAZ contributed to the study design and manuscript writing and final approval
MYJ contributed to the manuscript writing and final approval
NHR contributed to statistical analysis and final revisions
NS contributed to the data collection, manuscript writing and final approval

References

Formatted: Font: 8 pt, Turkish, Do not check spelling or grammar

1. Maahs DM, Hermann JM, Holman N, Foster NC, Kapellen TM, Allgrove J, et al. Rates of diabetic ketoacidosis: International comparison with 49,859 pediatric patients with type 1 diabetes from England, Wales, the U.S., Austria, and Germany. Diabetes Care. 2015;38(10):1876–82.
2. Gomber A, Ward ZJ, Ross C, Owais M, Mita C, Yeh JM, et al. Variation in the incidence of type 1 diabetes mellitus in children and adolescents by world region and country income group: A scoping review. PLOS Global Public Health. 2022 Nov 9;2(11):e0001099.
3. International Diabetes Federation. IDF Diabetes Atlas [Internet]. 9th ed. Brussels, Belgium: International Diabetes Federation; 2019 [cited 2020 Jul 15]. Available from: https://diabetesatlas.org/en/resources/
4. Jaruratanasirikul S, Thammaratchuchai S, Sriplung H. Trends of childhood diabetes in Southern Thailand: 20-year experience in a tertiary medical center. World Journal of Pediatrics. 2017 Dec 1;13(6):566–70.
5. IDF Diabetes Atlas 10th edition [Internet]. Available from: www.diabetesatlas.org
6. Pulungan AB, Fadiana G, Annisa D. Type 1 diabetes mellitus in children: Experience in Indonesia. Vol. 30, Clinical Pediatric Endocrinology. Jeff Corporation Co. Ltd; 2021. p. 11–8.
7. Tung JY ling, Kwan EY wai, But BW man, Wong WH sang, Fu AC cheung, Pang G, et al. Increasing incidence of type 1 diabetes among Hong Kong children and adolescents: The Hong Kong Childhood Diabetes Registry 2008 to 2017. Pediatr Diabetes. 2020 Aug 1;21(5):713–9.
8. MZ Fuziah, Hong JYH, Zanariah H, Harun F, Chan SP, Rokiah P, et al. A National Database on Children and Adolescent with Diabetes (e-DiCARE): Results from April 2006 to June 2007. Med J Malaysia. 2008;63(Suppl C):37–40.
9. Jyh H, Adam MB, ll W. Diabetic ketoacidosis at diagnosis of type 1 diabetes mellitus in Malaysian children and adolescents. Vol. 10, Malaysian Family Physician. 2015.
10. Varadarajan P. Risk factors for mortality in children with diabetic keto acidosis from developing countries. World J Diabetes. 2014;5(6):932.
11. Roche E. The National Paediatric Diabetes Register and its Impact on Healthcare. Ir Med J. 2014;107(7).
12. 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 Apr;30(4):861–6.
13. Schober E, Rami B, Waldhoer T. Diabetic ketoacidosis at diagnosis in Austrian children in 1989-2008: A population-based analysis. Diabetologia. 2010 Jun;53(6):1057–61.
14. Usher-Smith JA, Thompson M, Ercole A, Walter FM. Variation between countries in the frequency of diabetic ketoacidosis at first presentation of type 1 diabetes in children: A systematic review. Diabetologia. 2012;55(11):2878–94.
15. 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. 2011;343(7815):1–16.
16. Mavinkurve M, Jalaludin MY, Chan EWL, Noordin M, Samingan N, Leong A, et al. Is Misdiagnosis of Type 1 Diabetes Mellitus in Malaysian Children a Common Phenomenon? Front Endocrinol (Lausanne). 2021 Mar 8;12.
17. Vanelli M, Costi G, Chiari G, Giacalone T, Ghizzoni L, Chiarelli F. Effectiveness of a prevention program for diabetic ketoacidosis in children: An 8-year study in schools and private practices. Diabetes Care. 1999 Jan;22(1):7–9.
18. Jefferies C, Cutfield SW, Derraik JGB, Bhagvandas J, Albert BB, Hofman PL, et al. 15-year incidence of diabetic ketoacidosis at onset of type 1 diabetes in children from a regional setting (Auckland, New Zealand). Sci Rep [Internet]. 2015;5(May):1–7. Available from: http://dx.doi.org/10.1038/srep10358
19. Dhatariya KK, Parsekar K, Skedgel C, Datta V, Hill P, Fordham R. The cost of treating diabetic ketoacidosis in an adolescent population in the UK: a national survey of hospital resource use. Diabetic Medicine. 2019 Aug 1;36(8):982–7.
20. Vyas AK, Oud L. Temporal patterns of hospitalizations for diabetic ketoacidosis in children and adolescents. PLoS One. 2021 Jan 1;16(1 January).
21. De Onis M, Lobstein T. Defining obesity risk status in the general childhood population: Which cut-offs should we use? Vol. 5, International Journal of Pediatric Obesity. 2010. p. 458–60.
22. Roche EF, Mckenna A, Ryder K, Brennan A, Hoey H. The Incidence of Childhood Type 1 Diabetes in Ireland and the National Childhood Diabetes Register The Incidence of Childhood Type 1 Diabetes in Ireland and the National Childhood Diabetes Register The Incidence of Childhood Type 1 Diabetes in Ireland and. Ir Med J. 2014;107(9):278–81.
23. Hekkala A, Reunanen A, Koski M, Knip M, Veijola R. Age-related differences in the frequency of ketoacidosis at diagnosis of type 1 diabetes in children and adolescents. Diabetes Care. 2010 Jul;33(7):1500–2.
24. Zucchini S, Scaramuzza AE, Bonfanti R, Buono P, Cardella F, Cauvin V, et al. A Multicenter Retrospective Survey regarding Diabetic Ketoacidosis Management in Italian Children with Type 1 Diabetes. J Diabetes Res. 2016;2016.
25. Rittiphairoj T, Owais M, Ward ZJ, Reddy CL, Yeh JM, Atun R. Incidence and prevalence of type 1 diabetes and diabetic ketoacidosis in children and adolescents (0−19 years) in Thailand (2015−2020): A nationwide population-based study. Lancet Reg Health West Pac [Internet]. 2022;21(100392). Available from: https://doi.org/10.1016/j.
26. Pulungan AB, Rl Batubara J, Tridjaja B, Soesanti F, Fadiana G, Annisa D, et al. ACTA SCIENTIFIC PAEDIATRICS Profile of Diabetic Ketoacidosis in Children with Diabetes Mellitus in a Tertiary Care Hospital in Jakarta: A Retrospective Study.
27. Glaser N, Fritsch M, Priyambada L, Rewers A, Cherubini V, Estrada S, et al. ISPAD clinical practice consensus guidelines 2022: Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Vol. 23, Pediatric Diabetes. John Wiley and Sons Inc; 2022. p. 835–56.
28. Schober E, Rami B, Waldhoer T. Diabetic ketoacidosis at diagnosis in Austrian children in 1989-2008: A population-based analysis. Diabetologia. 2010 Jun;53(6):1057–61.
29. Dabelea D, Rewers A, Stafford JM, Standiford DA, Lawrence JM, Saydah S, et al. Trends in the prevalence of ketoacidosis at diabetes diagnosis: The search for diabetes in youth study. Pediatrics. 2014;133(4).
30. Peng W, Yuan J, Chiavaroli V, Dong G, Huang K, Wu W, et al. 10-Year Incidence of Diabetic Ketoacidosis at Type 1 Diabetes Diagnosis in Children Aged Less Than 16 Years From a Large Regional Center (Hangzhou, China). Front Endocrinol (Lausanne). 2021 Apr 27;12.
31. Cherubini V, Skrami E, Ferrito L, Zucchini S, Scaramuzza A, Bonfanti R, et al. High frequency of diabetic ketoacidosis at diagnosis of type 1 diabetes in Italian children: A nationwide longitudinal study, 2004-2013. Sci Rep. 2016;6:1–7.
32. Gunn ER, Albert BB, Hofman PL, Cutfield WS, Gunn AJ, Jefferies CA. Pathways to reduce diabetic ketoacidosis with new onset type 1 diabetes: Evidence from a regional pediatric diabetes center: Auckland, New Zealand, 2010 to 2014. Pediatr Diabetes. 2017 Nov 1;18(7):553–8.
33. https://hellotype1.com/my [Internet]. [cited 2023 Sep 26]. Available from: https://hellotype1.com/my
34. Vanelli M, Costi G, Chiari G, Giacalone T, Ghizzoni L, Chiarelli F. Effectiveness of a prevention program for diabetic ketoacidosis in children: An 8-year study in schools and private practices. Diabetes Care. 1999 Jan;22(1):7–9.
35. Holder M, Ehehalt S. Significant reduction of ketoacidosis at diabetes onset in children and adolescents with type 1 diabetes—The Stuttgart Diabetes Awareness Campaign, Germany. Pediatr Diabetes. 2020 Nov 1;21(7):1227–31.

Table 1: Demographic and clinical characteristics at diagnosis of T1DM

Age at diagnosis (years)	
Mean (± SD)	8.06 (±3.78)
Age group, n (%)	
<5 years ≥5 years	27 (21.3) 100 (78.7)
Gender, n (%)	
Male Female	59 (46.5) 68 (53.5)
Ethnicity, n (%)	
Malay Chinese Indian	50 (39.4) 42 (33.1) 35 (27.6)
BMI Status, n (%)[¥]	
Underweight Normal weight Overweight or Obese	19 (20.7) 61 (66.3) 12 (13.0)
Blood glucose level (mmol/L)[#]	
Mean (± SD)	27.13 (9.03)
Hba1c (IFCC) at diagnosis (mmol/mol)[#]	
Mean (± SD)	115 (5)
Presence of DKA, n (%)	
DKA Non-DKA	93 (73.2) 34 (26.8)
Severity of DKA, n (%)[*]	
Mild Moderate Severe	19 (23.2) 18 (22.0) 45 (54.9)

Data is presented as mean (±SD) for continuous variables (age, and biochemical parameters) and as a frequency and percentage for categorical variable. All percentages were calculated accounting for missing data.

[¥] *Data was analysed for n=92*

[#] *Data was analysed for n=107*

[*] *Data was analysed for n=82*

[$] *Data was analysed for n=50*

Table 2: A comparison of DKA vs. non-DKA cases

	DKA (n=93)	Non-DKA (n=34)	p-value
Age (year)			
Mean age (± SD)	7.65 (4.03)	9.19 (2.77)	**0.03**
<5 years	26 (27.4%)	1 (2.9%)	**0.003**
≥5 years	67 (72.6%)	33 (97.1%)	
Gender			
Male	43 (46.2%)	16 (47.1%)	0.93
Female	50 (53.8%)	18 (52.9%)	
Ethnicity			
Malay	41 (44.1%)	9 (26.5%)	0.16
Chinese	27 (29.0%)	15 (44.1%)	
Indian	25 (26.9%)	10 (29.4%)	
BMI Status[¥]			
Underweight	18 (26.5%)	1 (4.2%)	0.07
Normal weight	42 (61.8%)	19 (79.2%)	
Overweight or Obese	8 (11.8%)	4 (16.7%)	
HCP contact prior to diagnosis[*]			
Less than 2	55 (70.5%)	23 (85.2%)	0.13
2 or more	23 (29.5%)	4 (14.8%)	
Misdiagnoses, n (%)[**]			
Misdiagnosis	40 (43.0%)	6 (17.6%)	**0.004**
Biochemical parameters			
Mean pH (± SD)	7.07 (0.16)	7.33 (0.15)	**<0.001**
Mean Bicarbonate (mmol/l) (± SD)	8.48 (4.77)	18.64 (5.74)	**<0.001**
Mean Glucose (mmol/l) (± SD)	28.47 (8.56)	23.26 (9.39)	**0.01**
Mean HbA1c, IFCC (mmol/mol) (± SD)	115 (7.0)	115 (1.0)	0.89
Current HbA1c, IFCC (mmol/mol)	80 (3)	77 (5.0)	0.68
PICU admission, n (%)[#]			
Yes	40 (57.1)	3 (12.0)	**<0.001**
No	26 (37.1)	22 (88.0)	
Length of hospital stay, days (± SD)	7.72 (2.74)	5.90 (2.22)	**0.01**

Data is presented as mean (±SD) for continuous variables (age, biochemical parameters, and length of hospital stay) and as a frequency and percentage for categorical variable. Comparisons between type 1 diabetes mellitus (T1DM) participants with diabetic ketoacidosis (DKA) versus those who did not have DKA used independent t-test for continuous variables and $\chi 2$ test between categorical variables. Significant findings appear in bold.

[¥] *Data was analysed for n=92*

[*] *Data was analysed for n=105*

[**] Data was analysed for n=46

[#] *Data was analysed for n=91*

Table 3: Demographics at presentation of children with diabetic ketoacidosis (DKA) at diagnosis of type 1 diabetes mellitus according to DKA severity

	Mild DKA (n=19)	**Moderate DKA** (n=18)	**Severe DKA** (n=45)	**p-value**
Age at diagnosis (years)	9.04 (4.01)	7.42 (3.72)	7.32 (4.20)	0.29
Gender (males) %	47.4	44.4	46.7	0.99
Ethnicity %				
Malay	47.4	38.9	46.7	0.69
Chinese	26.3	44.4	26.7	
Indian	26.3	16.7	26.7	
BMI SDS[¥]	-1.37 (1.77)	-1.19 (1.62)	-0.81 (1.83)	0.61
Biochemical parameters, mean (± SD)				
pH	7.26 (0.05)	7.16 (0.03)	6.95 (0.10)	**<0.001**
Bicarbonate (mmol/l)	13.18 (4.22)	10.22 (2.97)	5.39 (1.93)	**<0.001**
Glucose (mmol/l)	26.31 (7.63)	28.21 (9.25)	29.30 (8.78)	0.47
HbA1c, IFCC (mmol/mol)	129 (9.0)	111 (0)	113 (5.0)	0.10
PICU admission, n (%)[¥]	2 (15.4)	3 (25.0)	32 (88.9)	**<0.001**
Length of hospital stay, days, mean (± SD)	6.46 (3.37)	7.47 (2.23)	8.31 (2.65)	0.11

Data is presented as mean (±SD) for continuous variables (age, biochemical parameters, and length of hospital stay) and as a frequency and percentage for categorical variable. Comparisons between diabetic ketoacidosis (DKA) severity groups used independent t-test for continuous variables and χ2 test between categorical variables. Significant findings appear in bold.

[¥] *Data was analysed for n=61*

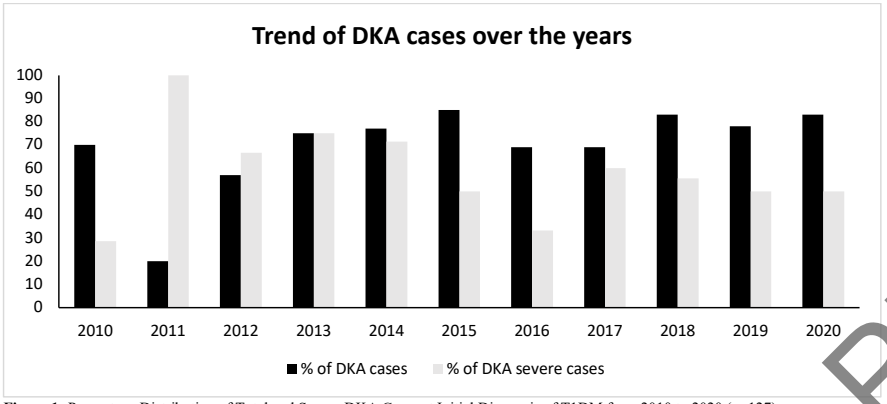

Figure 1: Percentage Distribution of Total and Severe DKA Cases at Initial Diagnosis of T1DM from 2010 to 2020 (n=127).