Frequency and Risk Factors of Diabetic Ketoacidosis in a Specialized Children's Hospital, Riyadh: A Cross-Sectional Study

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ABSTRACT

Objectives: Diabetic-ketoacidosis (DKA) is a life-threatening complication and a leading cause of hospitalization in Type-1-diabetes (T1DM) patients. We aimed to assess the risk factors of admissions of children with DKA in a specialized children hospital in order to reduce morbidity and to inform appropriate prevention and intervention strategies.

Methods: A retrospective review of all DKA admissions at King Abdullah Specialized Children's Hospital, Riyadh (March 2015–December 2017). Data were gathered from newly diagnosed of T1DM and known patients ≤14-year-old with DKA criteria. The main variables were frequency, precipitating factors, and other characteristics of DKA admissions in both groups.

Results: A total of 116/562 patients with T1DM (mean age 8.97±3.08 years) had 146 DKA episodes, of which 26/116 (34%) were newly diagnosed. The frequency of DKA admissions

were 146/562, 26%, of which (n=42/146, 28.7%) were newly diagnosed vs. (n=104/146, 71.2%) known patient of T1DM. The majority were 10-14 years (p≤0.001) and 55.5% were females. Missing insulin was the main precipitating cause of DKA (p=0.001) among known patients with T1DM. Recurrent episodes (n=30/164, 20.5%) occurred in 15/116 patients and were more common in children ≥10 years of age (P=0.024). The mean length-of-stay was 2.67±2.04 days and increased with DKA severity (P=0.008).

Conclusions: In our study, the majority of DKA episodes were in patients with known T1DM; and missing insulin was the leading cause of DKA. In addition to awareness campaigns to prevent DKA as an initial presentation, intervention strategies should also target high risk groups of known patients of T1DM such as adolescents and patients with recurrent episodes.

Keywords: Diabetic ketoacidosis; Missing insulin; Risk-factors; Admissions; Saudi Arabia.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) usually occurs due to insulinopenia, either secondary to autoimmune process as in the majority of cases or idiopathic.(1–3) Diabetic Ketoacidosis (DKA) is a leading cause of hospitalization and mortality in children with T1DM, which increases the importance of studying DKA, its frequency, and the characteristics of hospital admissions.(4,5) In Saudi Arabia, the prevalence of T1DM was previously reported as 109.5 per 100,000 children and adolescents.(6) The frequency of DKA among T1DM children in Saudi Arabia is double the world's average.(7) In many cases, DKA can be the first presentation of T1DM in newly diagnosed patients. However, it is usually associated with a precipitating factor in patients previously known to have T1DM and on insulin treatment. This could be due to infections or other illnesses, problems with insulinization in relation to technical, psychosocial issues, or due to other intercurrent events, such as surgery.

Many factors might influence morbidity and mortality in DKA. The severity of the DKA episode at presentation can potentially affect the outcome. Other parameters, such as effective mental status, anion gap, and serum osmolality, should be taken into consideration during severity assessment.(8) Also, the length of hospital stay (LOS) is another important parameter that reflects on the morbidity of DKA. In general, LOS for patients with diabetes depends on the severity, underlying cause, and the clinical course during hospital admission.(9)

Studying the frequency and risk factors of DKA hospital admissions can reshape preventive strategies including educational programs for high-risk patients and would potentially improve the quality of care provided to these patients by conducting further follow up studies. A previous study in our old hospital had looked at the clinical and biochemical characteristics of DKA admissions in the pediatric department (1995–2008).(10) Our study was conducted at the more recently established Specialized Children's Hospital (KACSH) assessing the progress in patients' care and clinical outcome of DKA. The advanced settings in KASCH included: receiving care in specialized wards with trained nurses as well as easy access to high dependency and pediatric intensive care services, doubling the numbers of serving staff including physicians and diabetes educators with regular attendance of dieticians in diabetes clinics, conducting group educational activities and sessions in special events (such as prior to Ramadan) on regular basis and the nearby presence of all collaborating specialties, such as ophthalmology and psychology/psychiatry services, in the new tertiary settings allowing easy review and referrals of these patients. Moreover, adult diabetes clinics more recently run within the premises of KASCH to facilitate starting proper transitional care service and to promote establishing a diabetes centre in the near future.

In this study, we aimed to assess the characteristics of hospital admissions with DKA in newly diagnosed and known patients with T1DM who received care in these advanced settings to facilitate further improvement and adjustment of the service.

MATERIALS & METHODS

Study Design

This is a retrospective chart review of all children admitted with DKA (March 2015–December 2017). Data were extracted from electronic records of children ≤ 14 years old who had the biochemical criteria of DKA on admission; it is determined based on the first serum bicarbonate and pH level and categorized as mild < 7.3, moderate < 7.2, and severe < 7.1 respectively.(11) Characteristics of hospital admissions were assessed in newly diagnosed and known patients with T1DM. These included DKA frequency, precipitating causes of DKA such as infections or missing insulin, severity, HbA1C prior to DKA episode, duration of DKA episodes in hours, and length of hospital stay.

Study Area/Setting

The study was conducted at King Abdullah Specialist Children's Hospital (KASCH). KASCH is the only specialized children's hospital in Saudi Arabia and opened in early 2015 to provide tertiary care of children 0–14 years old. The endocrinology department provides inpatient and outpatient consultations, diagnostic evaluation, and management of children and adolescents with diabetes, mainly T1DM. The department also provides inpatient and outpatient care for diabetic children, including intensive education utilizing the latest technology for children with diabetes.

Study Subjects

We targeted all DKA patients admitted between March 2015 and December 2017 to pediatric wards of KASCH. We included those who fulfilled the biochemical criteria of DKA [pH < 7.30, HCO3 < 15 mmol/l, Glucose > 11.2 mmol/l (200 mg/dl) and detection of ketone bodies in urine or blood].(11) Newly diagnosed patients with T1DM were identified based on the criteria of American Diabetes Association (ADA) which, consist of a random plasma glucose 11.2 mmol/l (200 mg/dl) or more with the presence of hyperglycemic symptoms or crisis.(12) However, in known patients of T1DM with already established diagnoses, we just reviewed their follow-up records for further information.

Patients labelled with infection as a precipitating cause of DKA in our study had to fulfil the laboratory criteria and symptomatology of infections and not just the presence of leukocytosis that could be a feature of DKA. Social crisis was identified in the patient's file by the support of the social services department. Occasionally, these were also reported and documented by diabetes educators or other members of the team especially during annual reviews when overall enquiries were conducted about patients' surroundings. Exclusion criteria consisted of patients with non-T1DM, patients with another diagnosis that affects ketone production, such as concomitant metabolic diseases and patients with incomplete biochemical criteria of DKA (possibly DK but not DKA, i.e., without acidosis).

Statistical analysis

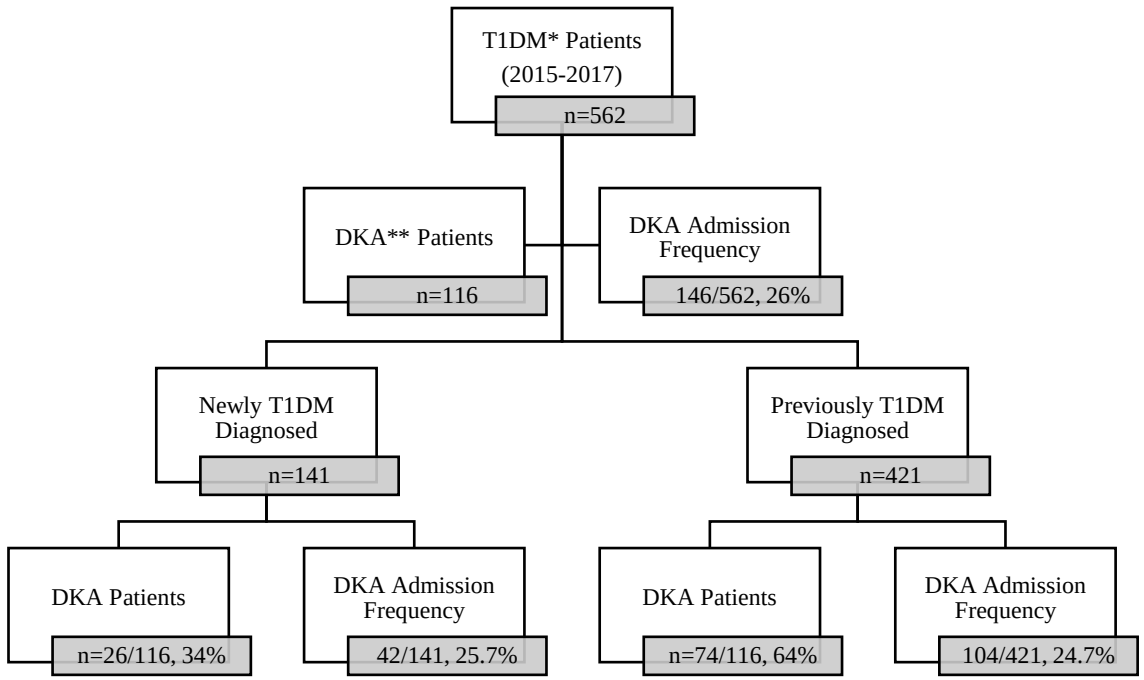
The sample size of this study was calculated using the formula N= [z [of 1- α]2 p (1-p)] / d2, where p is the previously reported prevalence of DKA (55.3%) among type 1 diabetes patients in Saudi Arabia.(13) Therefore, with a margin of error of 5% and a confidence level of 95%, a recommended collective sample size of 96, which was rounded to 100, was deemed necessary

to detect significance difference. Data cleaning, management, and analyses were performed using the Statistical Package for Social Sciences (SPSS) version 20. For descriptive statistics, frequencies, and percentages were presented for categorical variables such as gender, place of admission, and DKA severity. Means and standard deviations were calculated for numerical variables, such as HbA1C during DKA episode, duration of DKA recovery, and length of hospital stay. For inferential statistics, the Chi-square test was used to test the association between categorical variables, while the t-test and ANOVA were used to test the association between categorical and numerical variables. A test was considered significant if P-value was less than 0.05.

RESULTS

On average, we treated 562 children with T1DM patients annually in our institute during the study period, of which 141/562, 25% were newly diagnosed vs. 421/562, 75% known patients of T1DM (Figure 1). The frequency of DKA admissions among all patients with T1DM was 26% (n = 146/562), of which 25.7% (n = 42/141) among newly diagnosed patients and 24.7% (n = 104/421) episodes were in the known patients (Figure 1). DKA admissions constituted 146/311 (47%) of all inpatient admissions of children with T1DM during the study period. The total number of patients with DKA was 116, mean age 8.97 ± 3.08 years, and they had 146 DKA episodes [81/146 (55.5%) in females vs. 64/146 (44.5%) in males] (Table I). The majority of DKA patients were in the age group 10–14 years ($p \leq 0.001$), of which 74/116 (64%) of DKA patients were previously known to have T1DM (Table I). Missing insulin was the main identifiable precipitating cause ($p = 0.001$) of DKA in known patients with T1DM (Figure 2). DKA recurrent episodes (n = 30/146, 20.5%) occurred in 15/116 patients. Recurrence was more common in children ≥ 10 years old ($P = 0.024$). In 3/15 patients who had recurrence, each of them had DKA recurred 5 times during the study period, i.e., they represent 50% of the DKA recurrent episodes in our cohort. The first of these patients was 11 years old boy with social

crisis who was missing insulin and had these repeated episodes over 8 months period with almost 1-2 months a gap between the episodes. The other two patients were girls, 12 and 16 years old, who were uncontrolled in their diabetes management and they had DKA because of either infection or missing insulin doses for different reasons including adolescents' behaviour and a fear of weight gaining with regular treatment of insulin. When comparing children who had single and recurrent episodes of DKA, the latter group tends to have a shorter length of stay (LOS) (P = 0.001) but there was no difference in DKA severity or HbA1C level on admission between the two groups (Table II). The overall mean of LOS was 2.67 ± 2.04 days. Newly diagnosed patients had increased LOS duration and prolonged recovery from the DKA (Table II). The severity of DKA was also associated with increased LOS but not with the HbA1C level on admission (Table III).



* T1DM-Type 1 diabetes mellitus; ** DKA-Diabetic ketoacidosis

Figure 1: Frequency of diabetic ketoacidosis in newly diagnosed and known patients with type 1 diabetes.

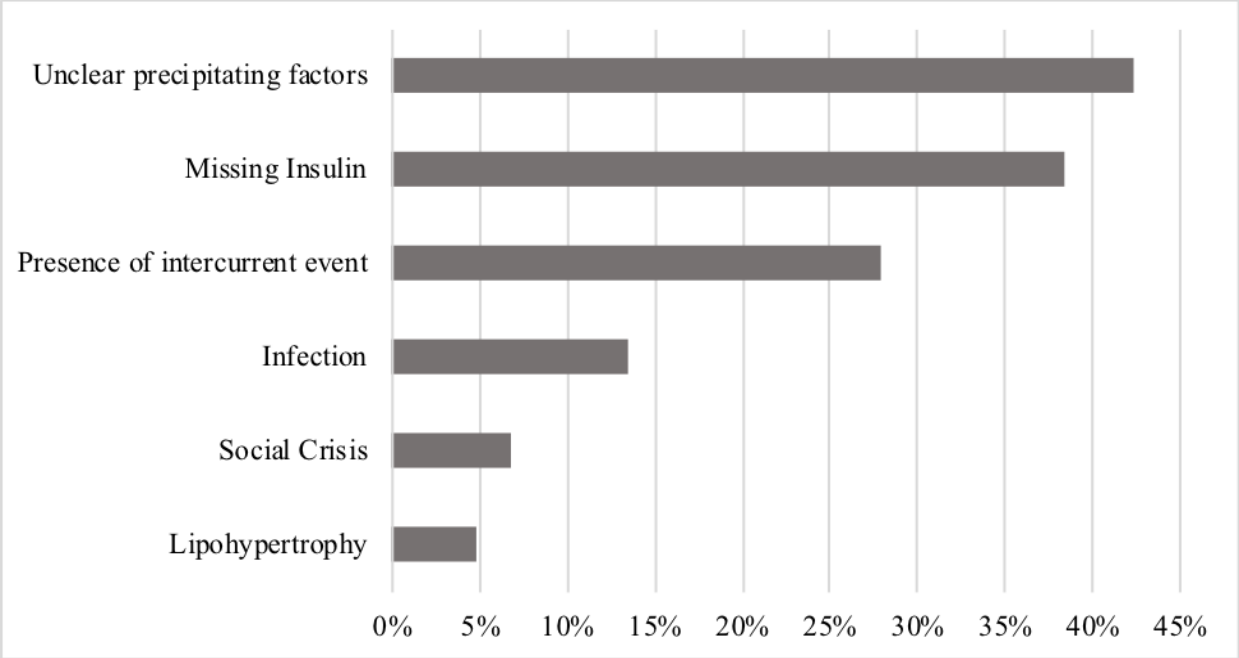


Figure 2: Precipitating factors of diabetic ketoacidosis in known patients with type 1 diabetes.

Table I: Characteristics of admissions with diabetic ketoacidosis in newly diagnosed and known patients with type 1 diabetes:

Variable	**Number (%)**	**Newly Diagnosed T1DM*** **Number (%)**	**Known patients with T1DM** **Number (%)**	***p***
Age (years) *Less than 5* *5 - 10* *More than 10*	 18 (12.3%) 66 (45.2%) 62 (42.5%)	 12(66.70%) 20(30.30%) 10(16.10%)	 6(33.30%) 46(69.70%) 52(83.90%)	**<0.001**
Gender *Male* *Female*	 65 (44.5%) 81 (55.5%)	 24(36.90%) 18(22.20%)	 41(63.10%) 63(77.80%)	0.066
Place of Admission *PICU*** *HDU**** *Ward*	 52 (35.6%) 20 (13.7%) 74 (50.7%)	 18(34.60%) 9(45.00%) 15(20.30%)	 34(65.40%) 11(55.00%) 59(79.70%)	0.046
Severity *Mild* *Moderate* *Severe*	 42 (28.8%) 98 (67.1%) 6 (4.1%)	 12(28.60%) 28(28.60%) 2(33.30%)	 30(71.40%) 70(71.40%) 4(66.70%)	1

*T1DM - Type 1 diabetes mellitus; **PICU - Pediatric intensive care unit; ***HDU - High dependency unit

Table II: Glycated hemoglobin, duration of ketoacidosis episode and length of hospital stay in newly diagnosed and known patients with type 1 diabetes.

Variable	Newly Diagnosed T1DM* Median (IQR)**	Previously Diagnosed T1DM Median (IQR)	*p*
HbA1C Prior to DKA Episode (%)	11.8 (10.7-13.2)	11.1 (10.4-12.3)	0.161
Duration of DKA Episode (Hours)	11 (10-20)	9 (6-13)	**0.006**
LOS* (days)**	4 (2-5)	2 (1-2)	**<0.001**

*T1DM- Type 1 diabetes mellitus; **IQR- Interquartile range; *** LOS-Length of Stay

Table III: Association of severity of diabetic ketoacidosis with length of stay and glycated haemoglobin.

Variable	Severity	Median	IQR* 1	IQR 3	*p*
LOS (days)**	Mild	2	1	4	**0.008**
	Moderate	2	1	3	
	Severe	4.5	4	10	
HbA1C prior to DKA episode* (%)**	Mild	11.04	10.43	13.08	0.434
	Moderate	11.52	10.47	12.6	
	Severe	12.08	12	13.4	

*IQR- Interquartile range; **LOS-Length of Stay; ***HbA1C-Hemoglobin A1C

DISCUSSION

Diabetic ketoacidosis constitutes almost half of the admissions of patients with T1DM in our study. Approximately two-thirds of the admitted patients are known patients of T1DM. This emphasizes the importance of investigating DKA admissions. Our institution has evolved into a specialized children's centre and new protocols have been implemented which differ from the previous studies that have been published in the same centre.(10) Missing the injections, presence of an intercurrent event, and infections, were the common identifiable causes of DKA in our patients. Younger age was associated with recurrent DKA. In general, severity was associated with increased LOS, and younger patients have more recurrent episodes. Advanced services in a tertiary setting could potentially improve patient identification and reduce the LOS in DKA management. The overall LOS was comparable to other international centres of similar settings.

The frequency of DKA among T1DM patients highly varies between different studies, populations, and different countries.(14) As reported in the EURODIAB project, the frequency ranged from 26% to 67% (15). In Arab countries, the frequency ranged from 17% in Egypt to 100% in Algeria, Morocco, and Tunisia, as reported in a systematic review that reviewed 29 studies.(16) In Saudi Arabia, the estimated frequency of DKA among children with T1DM ranges from 38% to 55.3%, but all of these studies were conducted outside Riyadh, the capital city of Saudi Arabia.(17–20) Here we detected a DKA frequency of 25% in newly and previously diagnosed T1DM patients in agreement with previous findings. The leading cause of this considerable variation is not well known. However, many variables were found to be inversely related to DKA frequency, such as expenditure on healthcare, gross domestic product (GDP), background incidence of T1DM, and latitude.(14) A unique feature in Arab countries is that the higher the incidence and prevalence of T1DM, the higher the DKA frequency emphasising the importance of more intensification of awareness programs that increase the

public awareness.(16) This could also be explained by deficiency of resources is some clinical institutes where extra support is required. In this study, the transformation of the diabetes services into tertiary settings has led to improvement in the characteristics of DKA admission in our institute.(10)

Previous studies have shown that poor compliance with insulin treatment and infections are the main identifiable precipitating factors of DKA.(21,22) Our study confirms the finding of missing insulin and infection as the leading causes of DKA in known patients of T1DM, emphasising the importance of rehearsing the sick-day rules periodically in outpatient clinics, especially in high-risk groups. During poor compliance to insulin the presence of intercurrent events, such as surgery and acute social crisis, are additional contributing factors, though in a fewer number of cases. Missing insulin is probably more prevalent than being reported in many studies including ours, and it is very likely to be the cause of DKA in patients with unidentified precipitating factors despite thorough investigations during hospital admission. The majority of patients belonging to the "unidentified precipitating cause" group were probably missing their insulin doses although other factors might have a role that was not explored in our study. DKA could also be related to starting puberty that is commonly associated with non-compliance with regular clinic visits and without adequate adjusting their insulin doses. Inadequate insulin during a time of increased body requirement of insulin puts these children at a higher risk of developing DKA.

As mentioned previously, infection is one of the leading causes of DKA in our study. Hamed et al. found that infection is the main precipitating cause of DKA, accounting for 46.5%. Further they reported the most common sources of infection; urinary tract infection (31.2%) and respiratory tract infection (26.8%).(23) Another study, reported that infection was the

leading cause of DKA in Intensive Care Unit and associated with female gender, neurological symptoms at presentation, and lack of clearance of ketonuria.(24)

We compared our findings regarding age-gender distribution and risk factors to that in Naeem et al, done in sub-tertiary settings in the same institute, and also compared to other relevant studies. The mean age of patients with DKA has dropped to 8.9 (6-11) years from 11 (8-13) years of age in the study by Naeem et al. However, there are still higher rates of DKA admissions for children more than ten years of age. As reported by Randal et al., where younger age was significantly associated with recurrent DKA, our data showed that DKA recurrence was more common in children > 10-year of age.(25,26) There is also a drop in the percentage of newly diagnosed patients of DKA from 46% to 36% in our study, although Naeem's data was of a longer duration. Missing insulin was the most common precipitating factor in both studies but was much lower in our study (39%) than in the work by Naeem et al. (79%). DKA duration had also dropped significantly in our tertiary centre, to a median of 10 h (6–16 h) compared to 20 h (12–28 h) in Naeem's study, reflecting the value of advanced tertiary care settings. Of note, unlike as in Naeem et al., we reported on the frequency of DKA in previously as well as newly diagnosed patients with T1DM and on the recurrent episodes of DKA in order to inform further interventional strategies.(27)

In previous reports, females had more recurrent DKA episodes than males, which were observed in our study.(21,25). This could be related to the effect of insulin on weight gaining, which is usually a major concern for female teenagers, making them skip insulin doses.(21) Also, Rodin et al. state that female patients with diabetes seem to have a higher risk of eating disorders, such as anorexia nervosa and bulimia.(28) These psychological problems are associated with poor glycemic control and recurrence and can predispose patients to the rapid

development of complications of diabetes, such as retinopathy.(29) Our study showed a significant association of DKA in previously known patients with lipohypertrophy but not with psychosocial issues. Similarly, other studies have found a high prevalence of DKA in girls, in children less than five years old, and in those who had lipodystrophy.(30) Apart from the age factor, there were no other predictors of recurrence in our study.

One of the critical DKA clinical characteristics is the severity of the episode, as it guides different aspects of management. Education and awareness tend to reduce the severity of DKA as expected and been reported in a study conducted in the Northwest of Saudi Arabia, where the DKA rates were decreased from 48% to 39% in a 4-year period.(18) Patient's education improves patient's motivation and does not only reduce the severity and risk of recurrence of DKA episodes but it also represents the corner stone of preventing DKA in patients with T1DM.(31) Proper education should focus on all elements of intensification of therapy including: multiple-component insulin regimen, careful balance of food intake, activity, and insulin dosage, daily self-monitoring of blood glucose, defined individualized target blood glucose levels and patient adjustments of food intake and insulin dosage and use of insulin supplements according to predetermined plan. The severity of DKA episodes has slightly improved in our study, with a mean biochemical pH level of 7.18 ± 0.09 compared to 7.15 ± 0.11 in Naeem et al.(27) Overall, using more intensive insulin therapy in outpatient management in KASCH had positive effects on DKA events and patients glycemic control including milder episodes, shorter LOS, and lower hemoglobin A1C (HbA1c) level.

Usually, DKA patients are discharged within two days. However, some are reported to have high readmission rates within a month of discharge for variable reasons.(32) The LOS in our study was 2.67 ± 2.04 days, which is similar to other studies of DKA in equivalent settings.(32)

The variability in LOS could depend on many factors. Hospitalization or LOS for patients with T1DM depends on the severity, underlying cause, and the clinical course during hospital admission.(9) Patients with mild or moderate DKA tend to stay longer in the ER waiting area than patients with severe DKA.(33) According to a study conducted in Ontario, Canada, LOS for children with DKA has decreased from 4.5 to 3.2 days due to effective measures been taken.(32) Of which was optimizing the medical care and effective use of ambulatory care in the form of a pediatric assessment unit that helped to decrease the rate of admission of patients with T1DM to the pediatric ward.(32)

This study helped to assess some characteristics of DKA admissions and the risk factors for a Saudi population in Riyadh. Since T1DM has multiple confounding factors that could affect clinical outcome including psychosocial wellbeing and family dynamics, a limitation in our study is that we did not explore the effects of these factors. In addition, this is a retrospective cohort study that should usually trigger further trial studies to implement changes in clinical interventions.

CONCLUSION

Missing insulin is still a major cause of DKA in known patients with T1DM even in advanced settings of patient care. Adopting a system of intensive insulin therapy with adequate resources is essential to prevent or reduce the severity of DKA in high-risk groups of adolescents, poorly controlled patients and those with recurrent episodes. Patient's education requires frequent contact between patient/parents and diabetes team when patients are empowered to have a positive contribution in their management.

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ETHICAL APPROVAL

This study has been approved by King Abdullah International Medical Research Center in Riyadh, Saudi Arabia, with a reference number (RSS18/017/R).

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CONFLICT OF INTEREST

Authors declare that this manuscript was uploaded in a preprint platform called Authorea. It is an interactive website for scholars to upload their papers before peer-review. The DOI is added in the references (34).

AUTHORS' CONTRIBUTION

AB conceived the idea, study design, data analysis, drafting and editing of the manuscript. GLJ contributed to the study design, data collection, data analysis, drafting and editing the manuscript. MKA contributed to the study design, data collection, drafting and editing the manuscript. AFA contributed to the study design, data collection, drafting and editing the manuscript. MSM performed data analysis, drafting and editing the manuscript. ANA, FA, and IA contributed to drafting, editing, and approving the final manuscript. This manuscript has

been reviewed and approved by all authors, and they are accountable for the content and similarity index of the manuscript.

REFERENCES

1. Roglic G. WHO Global report on diabetes: A summary. Int J Noncommunicable Dis [Internet]. 2016 Apr 1;1(1):3–8. Available from: https://www.ijncd.org/article.asp?issn=2468-8827
2. Moini J. Type 1 Diabetes. In: Epidemiology of Diabetes [Internet]. Elsevier; 2019. p. 75–90. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780128168646000067
3. Association AD. Diagnosis and classification of diabetes mellitus. Diabetes Care [Internet]. 2010 Jan;33 Suppl 1(Suppl 1):S62–9. Available from: https://pubmed.ncbi.nlm.nih.gov/20042775
4. Umpierrez GE, Murphy MB, Kitabchi AE. In Brief Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar Syndrome. Vol. 15, Diabetes Spectrum. 2002.
5. Vellanki P, Umpierrez GE. Increasing hospitalizations for DKA: A need for prevention programs. Vol. 41, Diabetes Care. American Diabetes Association Inc.; 2018. p. 1839–41.
6. Al-Herbish AS, El-Mouzan MI, Al-Salloum AA, Al-Qurachi MM, Al-Omar AA. Prevalence of type 1 diabetes mellitus in Saudi Arabian children and adolescents [Internet]. Vol. 29, Saudi Med J. 2008. Available from: www.smj.org.sa
7. Robert AA, Al-Dawish A, Mujammami M, Dawish MA Al. Type 1 Diabetes Mellitus in Saudi Arabia: A Soaring Epidemic. Menahem S, editor. Int J Pediatr [Internet]. 2018;2018:9408370. Available from: https://doi.org/10.1155/2018/9408370
8. Trachtenbarg DE. Diabetic ketoacidosis. Am Fam Physician. 2005 May;71(9):1705–14.

9. Guisado-Vasco P, Cano-Megías M, Carrasco-de la Fuente M, Corres-González J, Matei AM, González-Albarrán O. Clinical features, mortality, hospital admission, and length of stay of a cohort of adult patients with diabetic ketoacidosis attending the emergency room of a tertiary hospital in Spain. Endocrinol y Nutr. 2015 Jun 1;62(6):277–84.
10. Naeem MA, Al-Alem HA, Al-Dubayee MS, Al-Juraibah FN, Omair A, Al-Ruwaili AS, et al. Characteristics of pediatric diabetic ketoacidosis patients in Saudi Arabia. Saudi Med J. 2015/01/30. 2015;36(1):20–5.
11. Diabetic Ketoacidosis: Evaluation and Treatment. Am Acad Fam PHYSICIANS [Internet]. 2013;1;87(5):33. Available from: http://www.aafp.org/afp.xml
12. T1DM Diagnosis [Internet]. American Diabetes Association. 2021. Available from: https://www.diabetes.org/a1c/diagnosis
13. Al Shaikh A, Farahat F, Saeedi M, Bakar A, Al Gahtani A, Al-Zahrani N, et al. Incidence of diabetic ketoacidosis in newly diagnosed type 1 diabetes children in western Saudi Arabia: 11-year experience. J Pediatr Endocrinol Metab [Internet]. 2019;32(8):857–62. Available from: https://doi.org/10.1515/jpem-2018-0548
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. Vol. 55, Diabetologia. 2012. p. 2878–94.
15. Lévy-Marchal C, Patterson CC, Green A. Geographical variation of presentation at diagnosis of type I diabetes in children: the EURODIAB study. European and Dibetes. Diabetologia. 2001 Oct;44 Suppl 3:B75-80.
16. Zayed H. Epidemiology of diabetic ketoacidosis in Arab patients with type 1 diabetes: A systematic review. Vol. 70, International Journal of Clinical Practice. Blackwell Publishing Ltd; 2016. p. 186–95.

17. Habib H. Frequency and clinical characteristics of ketoacidosis at onset of childhood diabetes mellitus in Northwest Saudi Arabia. Saudi Med J. 2005 Dec 1;26:1936–9.

18. Ahmed AM, Al-Maghamsi M, Al-Harbi AM, Eid IM, Baghdadi HH, Habeb AM. Reduced frequency and severity of ketoacidosis at diagnosis of childhood type 1 diabetes in Northwest Saudi Arabia. J Pediatr Endocrinol Metab. 2016 Mar 1;29(3):259–64.

19. Abduljabbar M, Aljubeh J, Amalraj A, Cherian M. Incidence trends of Childhood type 1 diabetes in eastern Saudi Arabia. Saudi Med J. 2010 Apr 1;31:413–8.

20. Albishi L, Altoonisi M, Alblewi S, Osman R, Ahmed N, Fararjeh M. Clinical Demographic Patterns of Type 1 Diabetes in Saudi Children in Tabuk City, 2000-2010. J Diabetes Mellit. 2017 May 1;7:41–54.

21. Al-Hayek AA, Robert AA, Braham RB, Turki AS, Al-Sabaan FS. Frequency and associated risk factors of recurrent diabetic ketoacidosis among Saudi adolescents with type 1 diabetes mellitus. Saudi Med J. 2015;36(2):216–20.

22. Maldonado MR, Chong ER, Oehl MA, Balasubramanyam A. Economic impact of diabetic ketoacidosis in a multiethnic indigent population: analysis of costs based on the precipitating cause. Diabetes Care. 2003 Apr;26(4):1265–9.

23. Hamed ZS, Gawaly A, Abbas K, El Ahwal L. Epidemiology of infection as a precipitating factor for diabetic ketoacidosis at Tanta University Hospital. Tanta Med J [Internet]. 2017 Apr 1;45(2):68–72. Available from: http://www.tdj.eg.net/article.asp?issn=1110-1415

24. Azoulay E, Chevret S, Didier J, Neuville S, Barboteu M, Bornstain C, et al. Infection as a Trigger of Diabetic Ketoacidosis in Intensive Care—Unit Patients. Clin Infect Dis [Internet]. 2001 Jan 1;32(1):30–5. Available from: https://doi.org/10.1086/317554

25. Wright J, Ruck K, Rabbitts R, Charlton M, De P, Barrett T, et al. Diabetic ketoacidosis

(DKA) in Birmingham, UK, 2000-2009: An evaluation of risk factors for recurrence and mortality. Br J Diabetes Vasc Dis. 2009;9(6):278–82.

26. Randall L, Begovic J, Hudson M, Smiley D, Peng L, Pitre N, et al. Recurrent diabetic ketoacidosis in inner-city minority patients: Behavioral, socioeconomic, and psychosocial factors. Diabetes Care. 2011 Sep;34(9):1891–6.

27. Naeem MA, Al-Alem HA, Al-Dubayee MS, Al-Juraibah FN, Omair A, Al-Ruwaili AS, et al. Characteristics of pediatric diabetic ketoacidosis patients in Saudi Arabia. Saudi Med J. 2015;36(1):20–5.

28. Rodin GM, Daneman D. Eating Disorders and IPPM A problematic association.

29. Pinhas-Hamiel O, Hamiel U, Levy-Shraga Y. Eating disorders in adolescents with type 1 diabetes: Challenges in diagnosis and treatment. World J Diabetes [Internet]. 2015 Apr 15;6(3):517–26. Available from: https://pubmed.ncbi.nlm.nih.gov/25897361

30. Karges B, Neu A, Hofer SE, Rosenbauer J, Kiess W, Rütschle H, et al. Frequency and influencing factors of ketoacidosis at diabetes onset in children and adolescents - A long-term study between 1995 and 2009. Klin Padiatr. 2011;223(2):70–3.

31. Chafe R, Albrechtsons D, Hagerty D, Newhook LA. Reducing episodes of diabetic ketoacidosis within a youth population: A focus group study with patients and families. BMC Res Notes. 2015;8(1):1–8.

32. Curtis JR, To T, Muirhead S, Cummings E, Daneman D. Recent trends in hospitalization for diabetic ketoacidosis in Ontario children. Diabetes Care. 2002/08/28. 2002;25(9):1591–6.

33. Brzezicki A, Mcgibbon AM. DKA Management in the Emergency Room and Length of Stay. Can J Diabetes. 2016 Oct;40(5):S44.

34. Babiker A, Aljahdali G, Alsaeed M, Almunif A, Mohamud M, Abid O, et al. Characteristics of admissions with diabetic ketoacidosis in a specialized children

hospital : Missing insulin is still a challenge ! [Internet]. 2020. p. 2–3. Available from: https://authorea.com/users/331920/articles/458409-characteristics-of-admissions-with-diabetic-ketoacidosis-in-a-specialized-children-hospital-missing-insulin-is-still-a-challenge?commit=36a67fee873e63287d3457daa4f1461a768e2178