

Factors Precipitating Initial Admission and Readmission Among Patients with Diabetic Ketoacidosis in Makkah, Saudi Arabia 2021

Lilah Ali Alnashri¹, Norah Ahmad Hzazi², Qasem Mohammed Alamri³, Marwan Souliman Mouawad⁴, Salman Maatoq Alsamairi³, Merae Abdullah Allihyani³, Lila Abdo Barnawi³, Hayat Abdullah Alzahrani³, Eman Hamed Allugmani³, Salwa Ali Hassan³, salman lafaa maniaullh alsulami⁵

¹Family Medicine Consultant, MAKKAH Health Cluster, Saudi Arabia.

²Pharmacist, MAKKAH Health Cluster, Saudi Arabia.

³Nursing technician, MAKKAH Health Cluster, Saudi Arabia.

⁴Infection Control, MAKKAH Health Cluster, Saudi Arabia.

⁵Health administration, Makkah Healthcare cluster, Saudi Arabia.

Abstract

Background Diabetic Ketoacidosis (DKA) is a life-threatening problem that affects people with diabetes. DKA is a metabolic emergency characterized by hyperglycemia, high-anion gap metabolic acidosis and ketonemia. DKA is sometimes the first sign of type 1 diabetes in people who have not yet been diagnosed. DKA is known to be a preventable acute complication of diabetes mellitus specifically through patient education. DKA is the most common hyperglycemic emergency and causes the greatest risk for death in patients with diabetes mellitus, almost a third of the cases occur among those with type 2 diabetes. Although mortality rates from DKA have declined to low levels in general, it continues to be high in many developing countries. DKA is characterized by hyperglycemia, metabolic acidosis and ketosis. Proper management of DKA requires hospitalization for aggressive intravenous fluids, insulin therapy, electrolyte replacement as well as identification and treatment of the underlying precipitating event along with frequent monitoring of patient's clinical and laboratory states. **Aim of the study:** To identify factors precipitating initial admission and readmission among patients with Diabetic ketoacidosis in Makkah, Saudi Arabia 2021.

Method: Retrospective by medical record review, at Diabetic center in Makkah.

Result & conclusion: none adherence to medication is the most common cause of admission and readmission (55.0% and 43.4 %) respectively. More than half (55.5%) were had abdominal pain and more than three fifths (62.8%) had pH more than 7 on admission. There was no statistical association between sociodemographic characteristics and readmission of DKA patients.

Keywords: diabetic ketoacidosis (DKA), factors precipitating, initial admission, readmission

Introduction

Diabetes mellitus (DM) is an important cause of multiple health problems that burden the healthcare system. According to the International Diabetes Federation (IDF), Globally, Saudi Arabia is the seventh country in the incidence of DM. DKA is an important complication of DM and one of the most common endocrine emergencies. It involves insufficient insulin

levels and an increase in insulin counter-regulatory hormones and peripheral insulin resistance that eventually leads to hyperglycemia, high ketone levels, acidemia, electrolyte imbalance, and dehydration. Patients frequently present with abdominal pain, nausea, vomiting, and fruity-scented breath. In addition, some patients can also present with the classic symptoms of DM, such as excessive urination and thirst (**Seth, Kaur, and Kaur, 2015**).

The most common precipitating factors for DKA are **infection (30 to 40%) and new-onset diabetes (20 to 25%)**, and inadequate insulin treatment or noncompliance include nonadherence to medications, physical or emotional trauma, and the use of medication known to increase blood glucose levels, such as corticosteroids (**Misra and Oliver; 2015**). The mortality rate following a single episode of DKA is reported to be 5.2%, and it rises by 6-fold with five or more admissions of DKA. Readmission rates for DKA have increased dramatically over the past two decades (**Gibb, Teoh, Graham, Lockman, 2016 and Benoit, Zhang, Geiss, Gregg, Albright,; 2018**) This study aims to Assess factors precipitating initial admission and readmission among patients with Diabetic ketoacidosis in Makkah, Saudi Arabia. There are only a few Saudi studies exploring DKA readmission rates.

Materials and Methods

Subjects

We reviewed the medical records for two consecutive years of all patients who were admitted through the emergency department with DKA from 1 January 2019 to 31 December 2021.

Inclusion criteria: patients older than 20 years of age. Diagnosed with DKA. Criteria for DKA: blood glucose level of more than 250 mg/dL, serum bicarbonate (HCO_3) level less than or equal 18 mEq/L, pH less than 7.30, and presence of ketonemia or ketonuria (**Kitabchi, Umpierrez, Miles, and Fisher; 2009**). Severe DKA pH less than 7.0. ICU admissions to manage the precipitating cause of the DKA, such as septic shock were not considered as severe DKA. Ethical approval was taken to accomplish the study.

Data collection

Data collection tool included patient demographic characteristics for age, gender, and nationality and clinical data for duration of admission, the precipitating cause, symptoms of the disease, history of ICU admission for DKA, history of DM; present before or not, the type and duration of DM, and the treatment used for DM management. Laboratory tests including blood pH levels, latest HbA1C, and lactic acid, complications of DM including renal disease or/and cerebral edema. History readmission also reviewed and the duration between the first and second admission, along with the precipitating factors and/or causes for the readmission; if death occurred cause of death.

DKA duration of admission was assessed based on the recovery of DKA and not on the end of the admission period, as management of DKA precipitating factor may be continue to as infection rather than the DKA itself. Resolution of DKA was defined as pH > 7.30, $\text{HCO}_3 > 18$, anion gap 10 ± 2 , and ability to tolerate oral intake as determined by the attended medical team as change to subcutaneous insulin considered DKA recovery.

The sample size was calculated using Epi Info program formula. Hence, the sample size to achieve a precision of ± 4 with a 95% confidence interval (CI) was 172, with this sample size

there was a 90% likelihood that the study will yield a statistically significant result. During the fieldwork, the sample was increased to reach 180 patients. A standardized, confidential, anonymous, self-administered questionnaire was used in this study.

Data were analyzed using IBM SPSS version 24.0. Descriptive statistics including frequencies and percentages, mean, standard deviation, median, interquartile percentiles; were used to describe the quantitative and categorical variables. Pearson's chi-square test and odds ratios were used to test and measure the association between the categorical study variables and outcome variable including history of readmission. Multivariate stepwise binary logistic regression was used to identify the independent variables associated with history of readmission. *P* value of $\leq .05$ and 95% confidence intervals were used to report the statistical significance of results.

Results

Table 1: regarding age 38.3% were between 20-30 years old. As for gender 55.0% were male. 32.2 were Saudi nationality.

Table (1): Frequency Distribution of the Studied patients Regarding Their Sociodemographic Characteristics (N = 180).

Socio-demographic data	No.	%
Age in years		
20-	69	38.3
30-	55	30.6
40-	25	13.9
50-	19	10.6
>60-	12	6.7
Sex		
Male	99	55.0
Female	81	45.0
Nationality		
Saudi	58	32.2
Syria	22	12.2
Egyptian	27	15.0
Pakistan	18	10.0
Philippines	18	10.0
Bangladesh	21	11.7
Others	16	8.9

Table2: illustrate that 38.3% of the studied patients had two days admission. As for precipitating cause for first admission, more than half 55.0% were nonadherence to medications. As regard Symptoms of the DKA disease, 55.5% had abdominal pain. 54.4% of the studied patients had history of readmission for DKA complication. Regarding, duration between first admission and readmission 62.2% readmitted before one year from first

admission. In 43.4% of the studied patients non adherence to treatment act as precipitating factor for readmission. More than half (56.7%) had type 1 DM. 62.8% had pH > 7 on admission.

Table (2): Frequency Distribution of the Studied patients Regarding Their diabetic history and clinical data Characteristics of ketoacidosis patients (N = 180).

Socio-demographic data	No.	%
Duration of admission in days		
2	20	38.3
4	55	30.6
6	30	13.9
>6	19	10.6
precipitating cause for first admission		
Nonadherence to medications	99	55.0
Infections or wounds	60	33.3
Nonadherence to diet	4	2.2
First presentation of DM	10	5.6
Others causes	7	3.9
Symptoms of the DKA disease		
Abdominal pain	100	55.5
Nausea and vomiting	122	67.7
Polyuria	70	38.8
Loss of consciousness	11	6.0
Others	100	
History of readmission for DKA		
Yes	98	54.4
No	82	45.6
Duration between first admission and readmission		
< one year	112	62.2
> One year	68	37.8
Precipitating factors for readmission		
Non adherence to treatment	78	43.4
Infection	60	33.3
Others	42	23.3
Type of diabetes		
Type 1	102	56.7
Type 2	78	43.3
Duration of DM in years		
<5	91	50.6
5-10	44	24.4
>10	45	25.0
DM treatment		
Insulin	103	57.2

Oral hypoglycemic	46	25.6
None	31	17.2
pH blood levels at the first admission		
<7	67	37.2
>7	113	62.8
HbA1C (n=100)		
>10 %	109	60.6
< 10 %	71	39.4

Table 3: shows that there was no correlation between sociodemographic characteristics including age, gender and nationality and readmission of patients with DKA

Table (3): Correlation between sociodemographic characteristics and readmission of patients with DKA. (N=180)

Socio-demographic characteristics	History of readmission for DKA		χ^2	P
	Yes	No		
Age				
20-	40 (40.8)	29 (35.4)	2.336	0.674
30-	32 (32.7)	23 (28.0)		
40-	12 (12.2)	13 (15.9)		
50-	8 (8.2)	11 (13.4)		
>60	6 (6.1)	6 (7.3)		
Gender	53 (54.1)	46	0.073	0.787
Male	45	(56.1)		
Female	(45.9)	36 (43.9)		
Nationality			2.822	0.831
Saudi	35 (35.7)	23 (28.0)		
Syria	9 (9.2)	13 (15.9)		
Egyptian	15 (15.3)	12 (14.6)		
Pakistan	9 (9.2)	9 (11.0)		
Philippines	9 (9.2)	9 (11.0)		
Bangladesh	12 (12.2)	9 (11.0)		
Others	9 (9.2)	7 (8.5)		

Discussion

Recently attention has been drawn to the extremely high prevalence of DKA in adolescence. In the UK young people aged between 16 and 18 may be admitted to a paediatric or adult unit. The paediatric and adult guidelines differ particularly around fluid replacement. This has led to confusion amongst admitting staff as to which guidance should be followed (**Dhatariya.&**

Umpierrez; 2017) In this updated guidance there is a useful discussion as to which guideline should be followed, with a sensible recommendation that the guidance used should be determined by the ward to which the person with diabetes is admitted. This will ensure that that the staff only use guidance they are familiar with, so reducing the potential for mistakes (**Sampson & Jones;2018**)

In this study, we found nonadherence to medication was the primary precipitating factor for DKA, followed by infections. There were readmission with DKA during the study period was documented. The majority of patients in the present study were type 1 DM patients. These are similar to multiple studies worldwide. Similarly, Riaz, et al.; 2014. They stated that mean age of 17.9 ± 6.4 years, mean duration of diabetes 5.37 ± 4.96 years. One hundred and fourteen (58.5%) patients were non adherent to dietary advice, 82(42.3%) non adherent to physical activity while 88.1% respondents were non adherent to their prescribed insulin regimen. Non-adherence increase the complication of diabetes which will lead to elevate cost of health care due to increase morbidity. Which cause a negative impact on patients understanding to their prescribed drug regimen by their physicians. This is in line with the result of a study done in Uganda which showed that non-adherence to drugs was significantly related with understanding of the patients about their treatment ($p=0.0.01$) (**Kalyango, Owino, and Nambuya., 2008**).

Similarly, **Roussel et al; 2021** who concluded that type 1 DM represented most of their sample; type 2 DM frequency was more than that of our study (31%). To the contrary, in countries with different genetic and socioeconomic backgrounds, such as studies by **Seth et al, 2015** in India, revealed that type 2 DM was the most prevalent type in patients admitted with DKA, and the mean age of patients was 51.46. Also, Shahid et al in **Pakistan, 2020**. DM II was the most prevalent type in patients admitted with DKA, with mean age of patients was 53.2. The higher mean age in the two studies may be explained by the fact that type 2 DM was more prevalent in their studies, and as known type 2 DM most frequently occurs in older age. Patients aged between 21 to 40 years represented most of our sample, which favors type 1 DM as triggering DKA development in our study rather than type 2 DM. Another study to **Dzherieva, Volkova, Anchutin, and Nechayeva, 2017**. They studied the frequency of different risk factors for diabetic ketoacidosis in real clinical practice in Russia. Their results illustrate that patients had a mean age of 36 (0.93) years.

Medication nonadherence was the leading factor leading to DKA in our study. Conversely, studies accomplished by **Alourfi & Homsy 2015**, in India showed that infections most often precipitated DKA. Another study with similar finding done by Mahesh, ShIvaSwaMy, R, ChandRa B, and Syed S. ,2017. in Damascus stated that infections most often precipitated DKA. Followed by insulin non adherence.

Indeed, the occurrence and recurrence of DKA is influenced by multiple factors, including patient awareness about the disease, socioeconomic factors, and the health care provided for the patient (Jimmy, and Jose, 2011). In the present study results showed that there was no relation between readmission of DKA patients and sociodemographic characteristics. Previous study to **Randall et al., 2011** have indicated that the odds of DKA readmission are increased in patients aged younger than 35 years, particularly females, or any patient with a history of depression or substance abuse, especially when insurance is self-paid or pays little of the

expense. Patients with a longer duration of diabetes also had a higher odds of recurrent DKA in another study.

Moreover, this finding is contradicted by studies from the United States and the Middle East, done by Bradford et al., who found that there is appositive correlation between sociodemographic characteristics of the studied patients and duration of DM and DKA readmission. In our study, more than half of patients had a history of a subsequent admission with DKA within a 3-year-follow up period. Another study Alourfi and Homsy 2015; had a 31% of their studied subjects had readmission due to reoccurrence of DKA. They also found that young age, an established history of DM and poorly controlled DM increased the odds of readmission with DKA.

Conclusion: none adherence to medication is the most common cause of admission and readmission. There was no statistical association between sociodemographic characteristics and readmission of DKA patients.

References:

1. Alourfi Z, Homsy H.2015. Precipitating factors, outcomes, and recurrence of diabetic ketoacidosis at a university hospital in Damascus. *Avicenna J Med.*; 5(1):11–15. doi: 10.4103/2231-0770.148503
2. Benoit SR, Zhang Y, Geiss LS, Gregg EW, Albright A. Trends in diabetic ketoacidosis hospitalizations and in-hospital mortality—United States, 2000–2014. *Morbidity and Mortality Weekly Report*. 2018;67(12):362.
3. Bradford A, Crider C, Xu X, Naqvi S. 2017. Predictors of recurrent hospital admission for patients presenting with diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Journal of clinical medicine research.*;9(1):35.
4. Brand staetter E, Bartal C, Sagy I, Jotkowitz A, Barski L. 2019. Recurrent diabetic ketoacidosis. *Archives of endocrinology and metabolism.*;63(5):531–5.
5. Dhatariya KK, Umpierrez GE. Guidelines for management of diabetic ketoacidosis: time to revise? *Lancet Diabetes and Endocrinology* 2017;5:321–323
6. Dzherieva I, Volkova N, Anchutin P, Nechayeva V. 2017. The frequency of different risk factors for diabetic ketoacidosis in real clinical practice in Russia. In: *Endocrine Abstracts [Internet]*. Bioscientifica; 2017. Available from: <https://www.endocrine-abstracts.org/ea/0049/ea0049ep539>
7. Gibb F, Teoh W, Graham J, Lockman K. 2016. Risk of death following admission to a UK hospital with diabetic ketoacidosis. *Diabetologia.* ;59(10):2082–7.
8. Kalyango J, Owino E, Nambuya A. 2008. Non-adherence to diabetes treatment at Mulago Hospital in Uganda: prevalence and associated factors.;8(2):67–73.
9. Kitabchi, A., Umpierrez, G., Miles, J., and Fisher, J.(2015). Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009 Jul;32(7):1335-43.
10. Mahesh M, ShIvaSwaMy R, ChandRa B, Syed S. 2017. The study of different clinical pattern of diabetic ketoacidosis and common precipitating events and independent mortality factors. *Journal of clinical and diagnostic research: JCDR.*;11(4):OC42.
11. Misra S, Oliver NS.2011. Diabetic ketoacidosis in adults. *BMJ*. 28(351).

12. Randall L, Begovic J, Hudson M, Smiley D, Peng L, Pitre N, Umpierrez D, Umpierrez G. 2011. Recurrent diabetic ketoacidosis in inner-city minority patients: behavioral, socioeconomic, and psychosocial factors. *Diabetes care*.;34(9):1891–6
13. Riaz M, Basit A, Fawwad A, Yakoob Ahmedani M, Ali Rizvi Z. Factors associated with non-adherence to insulin in patients with type 1 diabetes. *Pak J Med Sci*. 2014 Mar;30(2):233-9. PMID: 24772118; PMCID: PMC3998985.
14. Roussel R, Riveline J, Vicaud E, de Pouvourville G, Detournay B, Emery C, et al. . 2021. Important Drop in Rate of Acute Diabetes Complications in People With Type 1 or Type 2 Diabetes After Initiation of Flash Glucose Monitoring in France: The RELIEF Study. *Diabetes Care*;44(6):1368–76.
15. Sampson M, and Jones C. (2018).Joint British Diabetes Societies for Inpatient Care: clinical guidelines and improving inpatient diabetes care. *Diabetic Medicine* ;35:988-991
16. Seth P, Kaur H, Kaur M. 2015. Clinical Profile of Diabetic Ketoacidosis: A Prospective Study in a Tertiary Care Hospital. *Journal of Clinical and Diagnostic Research : JCDR [Internet]*. 2015.;9(6):OC01. Available from: <https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC4525534/>
17. Shahid W, Khan F, Makda A, Kumar V, Memon S, Rizwan A.2020. Diabetic Ketoacidosis: Clinical Characteristics and Precipitating Factors. *Cureus*;12(10).