Precipitating Factors for the Development of Diabetic Ketoacidosis in a Tertiary Care Hospital in Bahrain

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ABSTRACT

Background: Diabetic ketoacidosis is a commonly presenting complication of diabetes occurring commonly in type 1 and occasionally in type 2 DM patients as well, the precipitating factors for which are varied and only a few studies have explored this.

Objective : To review the causative factors that lead to the occurrence of DKA among the adult age group of patients in Bahrain.

Methods: The study was conducted in a retrospective, descriptive method in Salmaniya Medical Complex, Bahrain. The age group included consisted of adult patients of age 14 years and onwards, during a period of two years 2017-2018. Patient demographic data as well as related scientific data during the hospital stay were collected.

Results: A major precipitating factor was non-compliance (62 patients) with treatment regimen followed by infectious causes (26 patients). Poor diabetic control also caused a high occurrence of DKA (16 patients), as well as disruption in insulin supply, lead to DKA in patients on an insulin pump (3 patients). A high readmission rate was noted in the admission analysis due to repetitively occurring causative factors.

Conclusion: Preventing the occurrence of precipitating factors of DKA, through patient education and support can decrease the occurrence of this preventable complication of diabetes, leading to decrease morbidity and mortality related to DKA.

Keywords: Diabetes, Diabetic ketoacidosis, Precipitating factors.

Abbreviation,DM: Diabetes Mellitus;DKA: Diabetic ketoacidosis.

INTRODUCTION

Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes mellitus (DM). It is commonly associated with type 1 diabetes, but it is not uncommon in some patients with type 2 diabetes. It resulted from absolute or relative insulin deficiency and it is characterized by hyperglycemia, ketonemia, and acidosis[1].

DKA can be classified into mild, moderate, or severe based on the metabolic acidosis severity and mental status alteration. The most common precipitant for ketoacidosis was omission/error of insulin administration followed by acute illness[2].

Although mortality rates had fallen significantly over the past 20 years from 7.96% to 0.67%, the mortality rate is still high in non-hospitalized patients and developing countries[3]. DKA is a serious but largely preventable acute complication of diabetes mellitus. Identifying precipitating factors and increase awareness will prevent admission and associated mortality and morbidity[4] .

MATERIAL AND METHODS

This was a retrospective and descriptive study conducted at a tertiary academic center, Salmaniya Medical Complex, Bahrain. The study was approved by the secondary health care research committee at the study site. Inclusion criteria for study involvement were admission to the medical center between 2017 and 2018 with the diagnosis of DKA. Patients younger than 14 years old not fulfilling the criteria of DKA were ruled out during admission.

Statistical analysis:

The data collection form included the patient's age, gender, nationality, type of diabetes, comorbidities, HbA1c, readmissions, and precipitating factors. IBM SPSS 25 and R studio 1.1.14 were used to analyze the collected data. The variable relations were investigated with the proper statistical methods (Chi-square test and A NOVA).

Ethical approval:

The study was approved by Secondary Health Care Research Sub Committee in Salmaniya Medical Complex and an informed written consent was taken from each participant in the study.

RESULTS

Patient characteristics

A total of 224 patients were enrolled in the current study, 58.5% of whom were males while 41.5% were females. The age group ranged from 14 to more than 76 years old.

The majority of the patients were Bahraini (80.8%) while the rest were from 13 other nationalities (19.1%) (Table 1). Nearly two-thirds of them have no co-morbidities while a third has associated comorbidities (37.1%).

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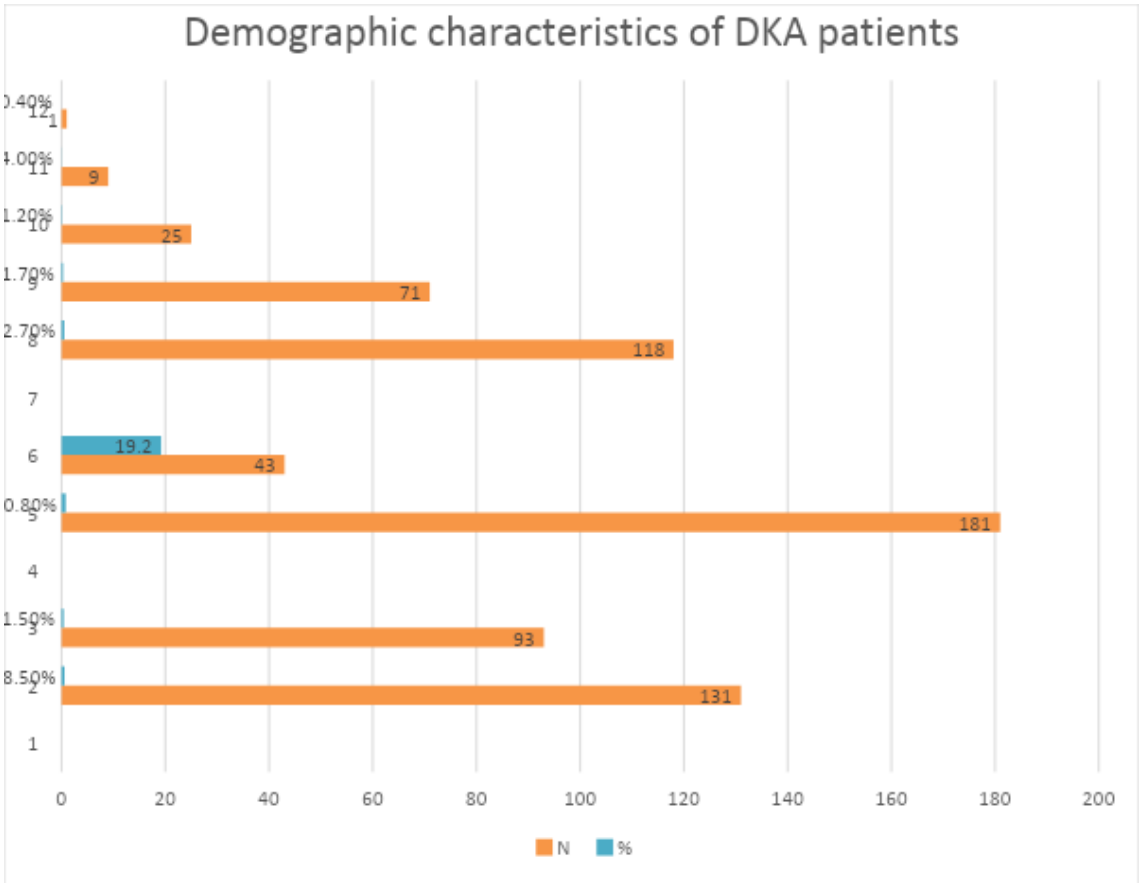
Table 1. Demographic characteristics of DKA patients

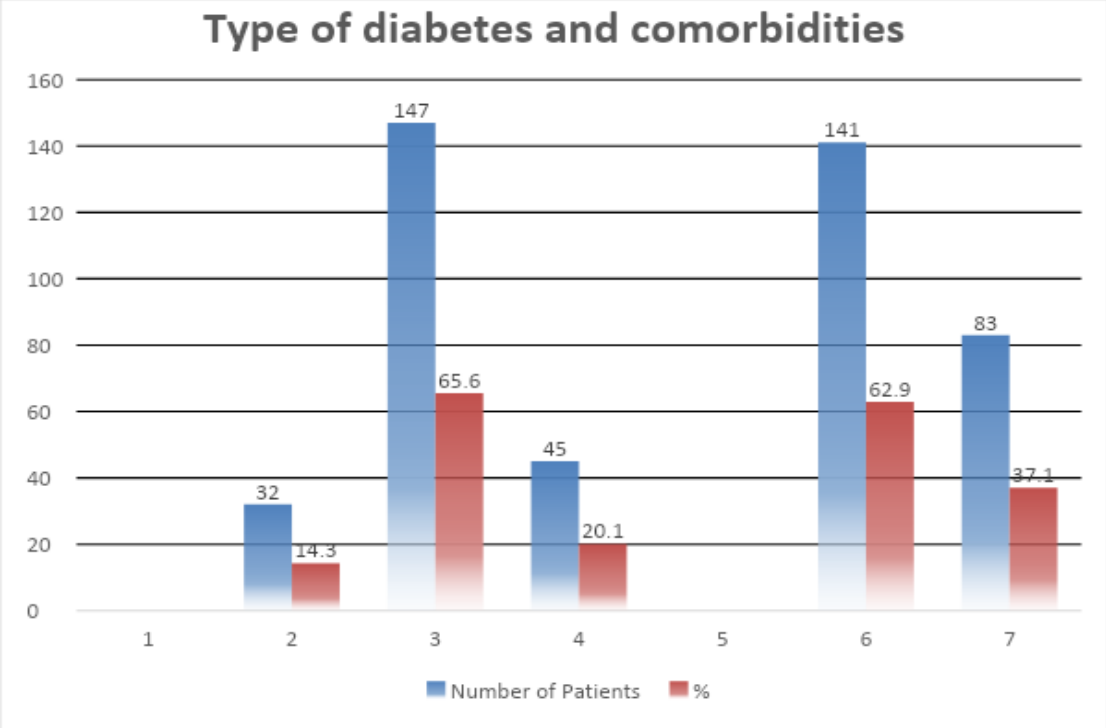
Variable	Categories	N	%
Gender			
	Male	131	58.5%
	Female	93	41.5%
Nationality			
	BAH	181	80.8%
	Non-BAH	43	19.2
Age group			
	14 - 30	118	52.7%
	31 - 45	71	31.7%
	46 - 60	25	11.2%
	61 - 75	9	4.0%
	> 76	1	0.4%



Diabetes characteristics

We categorize the patients per diabetes mellitus type. Newly diagnosed DM contributing for 14.3%, type 1 DM for 65.6% and type 2 DM for 20.1% (Table 2).

Table 2. Type of diabetes and comorbidities



At presentation gastrointestinal symptoms were most common in DKA patients. Vomiting is the main symptom followed by abdominal pain and nausea (see table 3 for details).

Table 3. Presenting symptoms of DKA patients

Type of DM	Abdominal pain	Nausea	Vomiting
New	10(31.3%)	10(31.3%)	14(43.8%)
Type 1	67(46.6%)	29(19.7%)	89(60.5%)
Type 2	17(37.8%)	11(24.4%)	19(42.2%)
p-value	***0.270***	***0.340***	***0.041****

**Statistically significant difference with Chi-square test (X2=6.4, df=2, p=0.041) at Alpha 0.05*

The mean RBS and HbA1c on admission were documented. The newly diagnosed group had the lowest HbA1c on average (91.4) and type 2 DM had the highest level (102.2) (Table 4).

Table 4. Glycemic control profile on admission

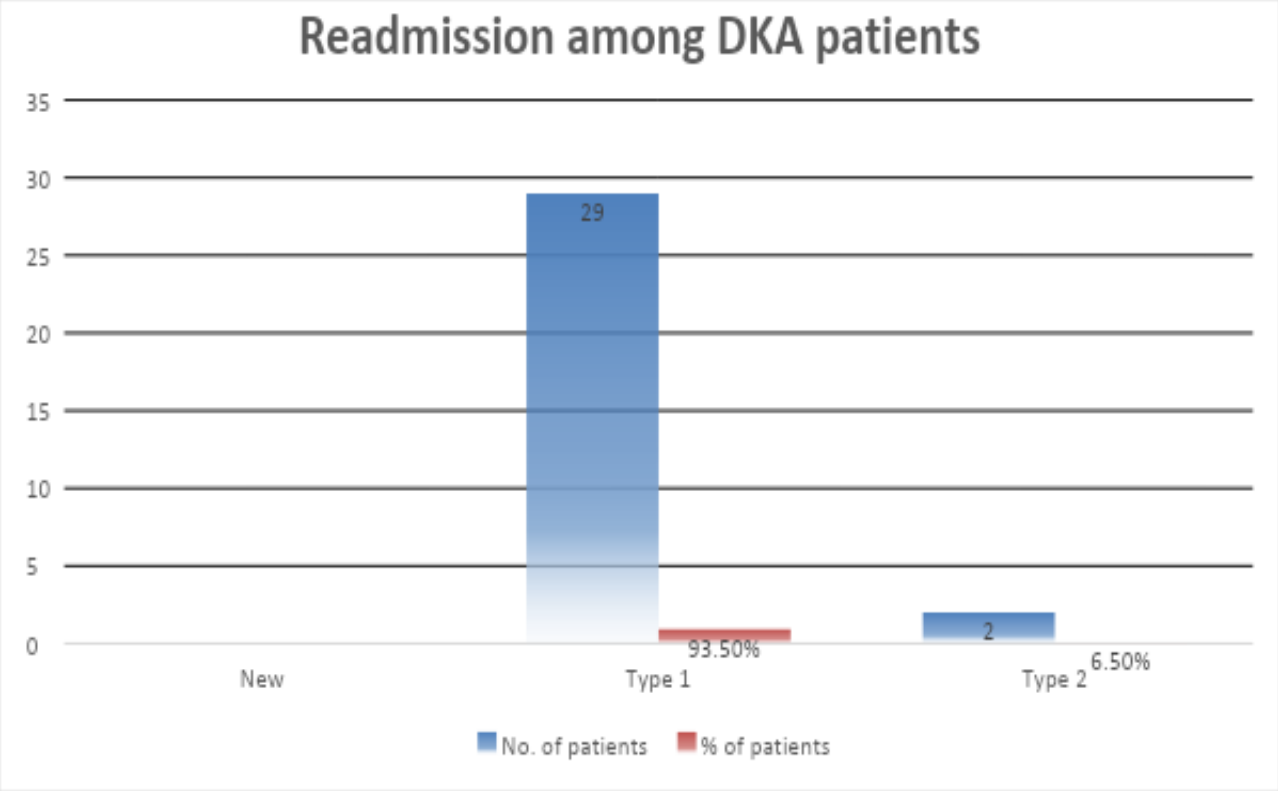
	New	Type 1	Type 2	P-value
RBS Mean(±SD)	26.7(±12.3)	27.7(±9.6)	28.7(±10.1)	0.629
HbA1c Mean(±SD)	91.4(±35.1)	92.9(±25.7)	102.2(±37.9)	0.300

Around 93.5% of the readmissions occurred for type 1 DM patients, 6.5% for type 2 DM, and 0% for the newly diagnosed DM (Table 5).

Table 5. Readmission among DKA patients

DM type	n	%
New	0	0%
Type 1	29	93.5%
Type 2	2	6.5%
p-value	***0.011****	

The statistically significant difference with the Chi-square test of independence (X^2=6.3, df=1, p=0.011)



In addition to their principle diagnosis as DKA, the predominant precipitating factor was non-compliance with medications, as it was reported in (62) patients, followed by infection (26), high HGT despite taking medication (16), and continuous subcutaneous insulin pump mechanical problem (3), Other precipitating factors are demonstrated in (Table 6).

Table 6. Precipitating factors of DKA

	New		Type 1		Type 2	
Infection	26	68.4%	12	13.7%	9	28.1%
Non-compliance	0		62	71.2%	15	46.9%
High HGT	10	26.3%	1	1.1%	4	12.5%
Missed food	0		5	5.7%	2	6.3%
Pancreatitis	2	5.2%	0		0	
Alcohol	0		0		1	3.1%
Insulin pump malfunction	0		3	3.3%	0	
Cardiac ischemia	0		0		1	3.1%
Seizure	0		3	3.4%	0	
Steroid use	0		1	1.1%	0	
Total	**38**		**87**		**32**	

DISCUSSION

Our study revealed that there was no major difference seen in the age, gender, and nationality distribution presenting with DKA with both males and females comprising a significant number, males contributing to 58.5% whilst the females being 41.55%. Bahrainis were more compared to non-Bahrainis (n=181, 30.8% vs non-Bahrainis n=43, 19.1%) but no statistically significant difference was seen (Table 1).

Younger patients in the age group of 14- 30 years made up most the subjects' mean age being 31.2 years, followed by the age group 31-45 years, with a decreasing trend in the increasing age groups.

In a study by Ahuja, the mean age of DKA presentation was similar to what we found in our study i.e. young adults mean age being 19 ±7 years (age group: 7-24 years)., however, they included the pediatric age group which was excluded in our study. The gender distribution was comparable to our study with women comprising 41.9%, and men comprising 58.1%[5] .

147 patients (65.6%) admitted were those with type 1 DM while 45 (20.1) were those having type 2 DM, and 32 (14.3%) were newly diagnosed coming with the first presentation of DKA (Table 2). Co-morbidities i.e. hypertension, dyslipidemia, coronary artery disease, chronic kidney disease among others were present in 83 (37.1) patients compared to 141 patients (62.9) without any comorbidities.

Y.XU study in China involved 643 patients with DKA. 308 patients (47.9%) with type 1 DM, 249 with (45.7%) with type 2 DM, and 41 patients with (6.4%) with atypical diabetes[6] . DM type 1 patients are at risk of developing DKA due to absolute insulinopenia which leads to increase gluconeogenesis, lipolysis, ketogenesis, and decrease glycolysis[7] .

Comparing to other articles, the presentation was variable among the patients, with gastrointestinal symptoms being the most common, vomiting being the main complaint (146.5%), followed by abdominal pain (115.7%), and then nausea (75.4%) (Table 3) [8] .

The mean RBS on admission in all the patient groups was comparable (Table 4). In type 1 DM patients was 27.2, in type 2 was 28.7, and in the newly diagnosed was 27.4 mmol. The average HbA1c on presentation was also comparable showing poor control with no statistically significant difference. Comparing to Holmes-Walker D, the effect of a transition support program in young DM patients revealed the initial mean HbA1c was 9.3 % +- 2.17%[9] .

Readmissions were seen to be very common in patients presenting with DKA (Table 5). The causative factors kept on recurring in the majority of the type 1 DM patients causing for high readmission rate. It was seen that 93.5% readmission rate overall was from type 1 DM patients. For example, younger age at DKA onset has been associated with a high risk of DKA recurrence suggests that this group of patients are more vulnerable to develop hyperglycemic crisis[10] .

Most studies demonstrated that the most common precipitating factors that came to the forefront were inadequate insulin therapy whether omitted or insufficient insulin regimen or presence of infection[8] ,[11], followed by high HGT despite taking the doses and the other causes included alcohol intake, pancreatitis, pump malfunction and others (Table 6). Mechanical problems with continuous subcutaneous insulin infusion devices (i.e. blocked pump, kinked cannula) can precipitate DKA, however, with technology improvement and patient education, the incidence of DKA has been declining in insulin pump patients[12].

Other precipitating factors include cerebrovascular and renal accidents, myocardial ischemia, pancreatitis, depression, alcohol, and illicit drug use. Also, numerous underlying medical illnesses and medications start the release of counter-regulatory hormones such as corticosteroids, sympathomimetics agents, thiazide diuretics, anti-cancer medications, and antipsychotic drugs, which may precipitate DKA[1]. Most recently, sodium-glucose co-transporter 2 (SGLT-2) inhibitors e.g. canagliflozin, dapagliflozin, and empagliflozin have emerged as triggers for DKA[13].

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The study is limited to only one of the main hospitals in Bahrain and the limited study period of two years.

CONCLUSION

In conclusion, DKA is a serious but largely preventable complication. Several precipitating factors have been identified. Medication non-compliance and infection are the most common risk factors to develop DKA.

Those at-risk individuals during the first DKA admission need target intervention such as intensified pre-discharge diabetic education. Instruction of insulin use/ medication adherence, social support, the involvement of family members in medical treatment, education about sick day management, close follow up is very important as detection of symptoms. It has been shown that three-monthly visits to the endocrine clinic will reduce the number of ER admissions for DKA . Launching of awareness and education programs in the public and through social media platforms with the aim of improving DM patient's quality of life, preventing further admission and associated morbidity and mortality.

DISCLOSURE

There is no grant support of other assistance to declare for this article, and the authors have no conflicts of interest to declare.

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