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Clinical profile of Libyan patients admitted with diabetic ketoacidosis

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Abstract: Diabetic ketoacidosis is a serious, medical emergency that can be fatal but treatable, we aimed to evaluate the clinical profile of patients admitted with diabetic ketoacidosis. This case series study enrolled 213 non-pregnant adult and adolescent patients admitted with diabetic ketoacidosis at Tripoli Diabetes Hospital from January to September 2023. Demographic data, clinical characteristics, laboratory findings, precipitating factors, and patient outcomes were extracted from medical records and analyzed. Type 1 diabetes mellitus was present in 187 (87.8%) of patients, the age range 11-84 years, (30.26±13.28), with 130 patients ≤30 years old (61.0%), females accounting for 110 of the patients (51.6%), 109 had a diabetes duration of less than 10 years (51.2%). The most common precipitating factor was insulin omission 92 (43.2%) in patients with known diabetes mellitus, whereas, diabetic ketoacidosis as the first presentation of diabetes mellitus in 24 patients (11.7%), systolic blood pressure ranged 50-160 mmHg (112.82±16.19), diastolic blood pressure varied 30-100 mmHg (70.24±11.32). Plasma glucose at presentation ranged 183-1494 mg/dl (462.92±169.85), with Eu-glycemic diabetic ketoacidosis 100-249 mg/dl were in nine patients (4.2%), whereas most of cases (135 patients, 63.4%) present with plasma glucose 250-500 mg/dl, while hyperosmolar status (≥701 mg/dl) were present in 13 patients (6.1%). Venous pH varied from 6.7-7.42 (7.13±0.14), 132 (62.0%) patients presented with pH <7.24, while severe acidosis was pH < 7 in 32 of patients (14.6%), serum bicarbonate with 10.93±4.95, severe (<5 mmol) in 91 patients (42.7%) and moderate (5-10 mmol) were in 79 patients (37.08%). The mean length of hospital stay was 3.33 days, with an average of 2.11 days spent in the high-dependent unit. Serum potassium varied from 2.4-6.7 meq/L with 3.66± 0.63, most common complications of diabetic ketoacidosis treatment were hypokalemia observed in 82 (35.7%) of cases, and hypoglycemia was detected in 41 patients (19.2%). 170 patients were discharged in good condition (79.8%), and 17.8% of patients were transferred to another hospital to receive further management for co-morbid diseases with diabetes after controlling their hyperglycemic crises. The majority of patients presented with the critical status of diabetic ketoacidosis. The findings emphasize the importance of patient education about prevention measures prompt presentation to the hospital, and clinicians' awareness for early and aggressive treatment of hyperglycemic crises.

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Introduction

Diabetic ketoacidosis (DKA) is a frequent and potentially life-threatening complication of type 1 diabetes mellitus (T1DM), also it could happen in type 2 diabetes mellitus (T2DM) during severe stress [1]. Though preventable and despite advances in monitoring technologies, insulin therapeutics and insulin delivery systems, the rates of community and hospital-acquired DKA remain largely unchanged. Although mortality today is relatively low it is generally accepted that mismanagement after hospital admission is an important contributory factor to hospital mortality, morbidity, increased length of stay and high readmission rates. The annual incidence of DKA in Libyan diabetics is unidentified. The overall mortality rate from DKA in Libya ranges from 2.0% to 10.0% of all DKA admissions [2-5]. DKA by definition consists of the triad: hyperglycemia (> 200 mg/dL) ketonemia (>3.0 mmol/L or significant ketonuria ≥2+) and high anion gap metabolic acidosis (a bicarbonate concentration of <15.0 mmol/L and/or venous pH <7.3). The American Diabetes Association (ADA) definition is slightly different, and it also uses the anion gap as part of the diagnostic criteria to judge severity [6]. The most common equation to calculate anion gap is $([Na^+] + [K^+]) - ([Cl^-] + [HCO3^-])$. Eu-glycaemic DKA is serious and usually misdiagnosed where the glucose is normal, or not particularly elevated. Occurs in partially treated DKA cases as well as with the widespread use of the sodium-glucose cotransporter (SGLT) inhibitor class of drugs in patients with T2DM, which has emphasized the significance of using pH and ketones (instead of the older 'sugar-centric' care) to guide the diagnosis and management, it is worthy to rule out another source of ketoacidosis, like alcoholic ketoacidosis and starvation ketosis [1, 7].

Patients who present with repeated events of DKA include a significant percentage of all DKA admissions - in the UK accounting for 66.0% of those with T1DM and 35.0% of those with T2DM [8]. A lot of these patients have disintegrated care and social, behavioral, or psychological concerns that demand to be accounted for [9]. Other risk factors for repeated events consist of female sex, adolescence, low socioeconomic status, and prior DKA admissions. Recurrent episodes of DKA are associated with an increased risk of long-term cognitive decline and premature mortality [10]. According to the Joint British Diabetes Societies (JBDS), the severity of DKA was defined by the presence of at least one of the following: blood ketones over 6.0 mmol/L, bicarbonate level below 5.0 mmol/L, venous/arterial pH below 7.0, hypokalemia on admission (under 3.5 mmol/L), Glasgow Coma Scale (GCS) less than 12 or abnormal AVPU scale (Alert, Verbally responsive, Pain responsive, Unresponsive), oxygen saturation below 92.0% on air (assuming normal baseline respiratory function), systolic blood pressure (BP) below 90 mmHg, pulse over 100 or below 60 bpm, and anion gap above 16 [1]. If the patients with any of these signs, resuscitation and treatment should be started without delay, and an intensive monitoring regimen put in place. Hypokalemia and hyperkaliemia are potentially life-threatening disorders in the course of the treatment of DKA. Due to the risk of acute pre-renal kidney damage related to severe dehydration. The blood sugar may drop very quickly as ketoacidosis is treated and a common fault is to permit the blood sugar to fall to hypoglycemic levels. Cerebral oedema affecting symptoms is quite rare in adults, though may occur in those who are physically slight or in younger adults. Numerous other complications include venous thromboembolic disease, transient acute kidney injury that may occur in up to 50.0% of adults, pulmonary oedema; a rise in pancreatic enzymes, with or without acute pancreatitis; cardiomyopathy; rhabdomyolysis; and gastrointestinal bleeding [9]. The two most common triggering reasons for DKA are insufficient or unsuitable insulin therapy and infections [11]. The common causes for missing insulin amongst patients with DM comprise insulin unavailability, and the care for injected sites, in fact, many patients prefer a self-directed decrease of insulin dosage and frequency to delay the need for a further vial. Insulin is omitted due to ill health and the incorrect idea that drugs should not be taken when ill. Quite often, DKA can be the first presentation of DM [1]. By understanding the clinical profile of DKA

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patients, healthcare providers can tailor interventions to address the specific needs of the Libyan population. Targeted educational programs can focus on promoting insulin adherence, recognizing and managing infections, and improving overall diabetes management. Additionally, efforts should be made to enhance access to healthcare services, ensure a continuous supply of insulin and other diabetes medications, and improve diabetes education and support systems. This study aims to evaluate the profile of admitted patients (non-pregnant adults and adolescents) at Tripoli Diabetes Hospital presented with DKA.

Materials and methods

Study setting: The study was conducted at the Tripoli Diabetes Hospital (teaching hospital, Tripoli) which provides diabetes care in most western parts of Libya for adult and adolescent diabetes patients, involving in-patient care with high-dependent unit and medical words, and specialized diabetes out-patients clinic including diabetes foot care, ophthalmology clinic, dental clinic, antenatal diabetes care for pregnant female, cardiology out-patients clinic as well as specialized diabetes out-patients clinics.

Data collection: Data were collected from medical records of Libyan patients admitted with DKA during the study period from January to September 2023. A standardized data collection form was used to collect information on the following variables: demographic information: this included age, gender, diabetes duration and type of diabetes based on clinical diagnosis and treatment history. Clinical characteristics: information on the clinical presentation of DKA, including initial blood pressure, and possible precipitating factors such as (insulin omission, infection, inadequate diabetes management, medication non-compliance, or any other identifiable triggers). Laboratory results: data on initial blood glucose levels, pH, bicarbonate levels, and electrolyte levels. Patient outcomes: this included the length of hospital stay, complications during hospitalization, and discharge status (discharged in good condition, transferred to another facility, or mortality).

Ethical consideration: The study was conducted by ethical principles and guidelines. Patient confidentiality was maintained throughout the study, and all data were de-identified to ensure anonymity. The Bioethics Committee approved the study at the Biotechnology Center, Tripoli, Libya (Ref No; NBC:001.H.23.22). Verbal consent was obtained from all the participants.

Statistical analysis: Analyzed using SPSS software, descriptive statistics was used to summarize the data. Continuous variables were reported as means with standard deviations or medians with interquartile ranges (IQR), depending on their distribution. Categorical variables were presented as frequencies and percentages.

Results

As shown in **Table 1**, T1DM was present in 187 patients (87.8%), the age range 11-84 years (30.26±13.3) with 130 patients ≤30 years old (61.0%), females accounting for 110 of the patients (51.6%), 109 had a duration of diabetes <10 years (51.2%). The most common precipitating factor was insulin omission in 92 patients (43.2%) with known DM, whereas DKA was the first presentation of DM in 24 patients (11.7%), systolic BP ranged from 50-160 mmHg (112.82±16.2), and diastolic BP varied 30-100 mmHg (70.24±11.3). PG at presentation ranged 183-1494 mg/dl (462.92±169.9) with Eu-glycemic DKA (100-249 mg/dl) were in nine patients (4.2%), whereas most of cases (135 patients, 63.4%) present with PG (250-500 mg/dl), while hyperosmolar state (≥701 mg/dl) were present in 13 patients (6.1%). In **Table 2**, venous pH varied from 6.7-7.42 (7.13±0.14), 132 patients presented with pH <7.24 (62.0%), while severe acidosis was pH <7 in 32 patients (14.6%), about serum

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bicarbonate with 10.93±4.95, severe (< 5 mmol) in 91 patients (42.7%) and moderate (5-10 mmol) were in 79 patients (37.1%). The mean length of hospital stay was 3.33 days, with an average of 2.11 days spent in the high-dependent unit (HDU). Serum potassium varied 2.4-6.7 meq/L with 3.66±0.6, most common complications of DKA treatment were hypokalemia observed in 82 of cases (35.7%) and hypoglycemia was detected in 41 patients (19.2%). 170 patients (79.8%) were discharged in good condition, and 17.8% of patients were transferred to another hospital to receive further management for co-morbid diseases with DM after controlling their hyperglycemic crises.

Table 1: General distribution of Libyan patients admitted with diabetic ketoacidosis

Age		
	Age ≤ 30	(130) 61.0%
	Age > 30	(83) 39.0%
Gender		
	Female	(110) 51.6%
	Male	(103) 48.6%
Type of diabetes mellitus		
	Type 1	(187) 87.8%
	Type 2	(26) 12.2%
Duration of diabetes mellitus		
	≤ 10 years	(109) 51.2%
	11-20 years	(76) 35.7%
	≥ 21 years	(28) 13.1%

Table 2: Clinical distribution of the patients admitted with diabetic ketoacidosis

ECG		
	Normal sinus	(188) 88.6%
	Acute arrhythmia	(21) 10.0%
	Left Bundle Branch Block	(02) 0.90%
	Acute coronary syndrome Ischemia	(20) 0.50%
Plasma glucose at presentation		
	100-249 mg/dl (Eu-glycemic DKA)	(09) 4.2%
	250-500 mg/dl	(135) 63.4%
	500-700 mg/dl	(56) 26.3%
	701-1500 mg/dl (hyperosmolar state)	(13) 6.1%
ABG		
	pH (7.25-7.3)	(49) 23.5%
	pH (< 7.24-7.0)	(132) 62.0%
	pH (< 7.0)	(32) 14.6%
	HCO_3 (15-18)	(43) 20.22%
	HCO_3 (10-15)	(79) 37.08%
	HCO_3 (< 10)	(91) 42.70%

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In **Table 3**, the distribution of the patients admitted with diabetic ketoacidosis by factors at Tripoli Diabetes Hospital is shown. Regarding omission insulin, about 10.0% of the patients were newly diagnosed, 25.0% of the patients were unknown and about 20.0% of the patients had infection.

Table 3: Distribution of the patients admitted with diabetic ketoacidosis by factors at National Diabetes Hospital

Precipitating factors	**Omission insulin**	**(92) 43.2%**
	Newly diagnosed	(24) 11.5%
	Infection	(42) 19.5%
	Unknown	(55) 25.8%
Infection		(42) 19.5%
	Respiratory	(10) 11.8%
	Covid-19 proven	(04) 02.3%
	GUT	(20) 23.9%
	GIT	(06) 03.3%
	Foot infection	(02) 01.4%

Discussion

We conducted a single-center, retrospective study of patients presenting to the emergency with a diagnosis of DKA, out of which about 90.0% of patients were T1DM, the age 11-84 years, with 60.0% below 30 years old, females accounted for about the half of the patients, about 50.0% had a duration of diabetes < 10 years. The most common precipitating factor was insulin omission in patients with known DM, whereas DKA was the first presentation of DM, systolic BP ranged from 50-160 mmHg, and diastolic BP varied from 30-100 mmHg. PG at presentation ranged from 183-1494 mg/dl, with Eu-glycemic DKA were 4.2% of patients, whereas most of the patients presented with PG (250-500 mg/dl) while hyperosmolar status was present in 6.1%. Venous pH varied from 6.7-7.42, 62.0% of the patients presented with pH <7.24, while severe acidosis was pH <7 in 14.6% of patients, about serum bicarbonate with 10.93±4.9 milli-mole, severe (<5 mmol) in 42.7% patients and moderate (5-10 mmol) were in 37.08% patients. The mean length of hospital stay was 3.33 days, with an average of 2.11 days spent in the high-dependent unit. Serum potassium varied from 2.4-6.7 meq/L, the most common complications of DKA treatment were hypokalemia observed in 35.7% of cases and hypoglycemia was detected in 20.0%. 80.0% were discharged in good condition, and 20.0% of patients were transferred to another hospital to receive further management for co-morbid diseases with diabetes after controlling their hyperglycemic crises. There 90.0% of patients were T1DM, similar to a previous study [12]. DKA occurs commonly in T1DM in 80.0% of patients, as compared with the study conducted in Brazil [13]. T1DM was in 65.0% of total cases presented with DKA, Mishra has reviewed the pathophysiology of ketosis-prone T2DM in his recent article and shown that DKA is not just a feature restricted to T1DM but can be a complication of T2DM usually with a precipitating factor and in some races even without precipitating cause [14]. Moreover, in India, due to poor socio-economic status, many patients with T2DM tend to have poor compliance and poor control of blood sugar levels so any precipitating factor tends to land them in a state of DKA [15, 16]. A study evaluating 138 consecutive admissions for DKA at a large academic center observed that 21.7% had T2DM [17]. In a study conducted in Taiwan, the patients attacked with DKA were predominantly T2DM (98 vs. 39 patients [18].

The majority of patients with DKA were young adults, the mean age of patients in the present study group was 30.26±13.3 years (60.0% of patients are ≤30 years old). This also points in favor of T1DM to be causing DKA more than T2DM. This is consistent with a previous study that reported a higher incidence of DKA in the younger

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population, with a mean age was 33.6±14.0 years, about 45.0% were below 30 years mainly 82.0% with T1DM [12]. Several studies oppose this finding. Thus, in a study by Adhikari and others [15], the mean age was 44.78 years, other studies reported that the mean age of patients admitted for DKA was between 40-50 years [19, 20], and Beigelman et al. [21] reported 47 years as the mean age of presentation for DKA.

Currently, female patients were half of the cases, whereas in the former study, 55.0% were female patients [12], and the duration of DM in more than half of the patients was 10 years or less, this is going with the preceding study [12] that the duration of DM less than 10 years in 60.0% of all cases. The ratio of newly diagnosed with DM presented with DKA has variably been reported. In the current study, it was 11.7% of the patients, the result matches with a study [11] that 14.0%. Kretz and others [22] reported that 10.0% of patients are freshly diagnosed. 15.4% of cases in a study conducted by Rachel et al. [14] first presented with DKA, as well as Casteels and Mathieu found DKA was the presenting illness in 20.0-25.0% of newly diagnosed patients with T1DM [23], Westphal found ketosis onset diabetes in 27.0% of the patients [24]. Numerous patients had more than one precipitating factor patients who were non-compliant to treatment had infection or associated stressful situations like acute coronary syndrome ischemia (diagnosed in 0.50% of patients), and sinus tachycardia in 88.60%, acute arrhythmia in 10.0% and left Bundle Branch Block in 0.90%. Approximately, 45.0% of the admissions involved discontinuation of insulin, and almost 25.0% had unidentified cause and 20.0% had an identifiable infection when an intensive search was undertaken. This is consistent with a previous study [12] that the most frequent precipitant factor was insulin omission in patients with known DM. 74.0% of all cases. In our study, urinary tract infection was most common, followed by pneumonia, COVID-19 infection, gastrointestinal infection and foot infection of patients presented with DKA. Previously, it was shown that the most frequent precipitating factors for DKA were poor compliance with treatment (51.9%) and infection (44.2%), urinary tract infection was most common, followed by pneumonia and skin or soft tissue infection [13]. Several factors such as hyperglycemia, leucocyte dysfunction, macro-vascular disease and acidosis predispose DM with ketoacidosis to common and rare infections. This is in line with a previous study which showed that infection of any site is an important precipitating factor in triggering DKA [25]. Adhikari et al. [16] showed diabetic foot as the infection precipitating DKA in 30.2% of patients. The systolic BP ranged from 50-160 mmHg, and the diastolic blood pressure varied from 30-100 mmHg in contrast with the prior study [11]. 20.5% presented with BP < 90/60, regarding PG level at presentation ranged from 183-1494 mg/dl. Among the patients, 4.2% had Eu-glycemic DKA (PG between 100-249 mg/dl, while most cases presented with PG levels between 250-500 mg/dl. The hyperosmolar state was observed in 6.1% of patients. This is going with a previous study where the highest PG was 1400 mg/dl recorded in one case, and most of the values were between 300-599 mg/dl, about 65.0% of all initial blood sugar values. The majority of patients admitted with DKA in this study presented with a critical state of DKA, considering venous pH varied from 6.7-7.42, with 62.0% of patients presenting with a pH less than 7.24. Severe acidosis (pH < 7) was observed in 14.6% of patients. The mean serum bicarbonate level was 10.93±4.9, with 42.7% of patients experiencing severe bicarbonate depletion and 37.1% of patients showing moderate bicarbonate depletion (5-10 mmol), dissimilarity with the prior study [12] were only 2.0% were required $NaHCO_3$ presented with PH ≤ 6.9, and 43.0% of cases with mild DKA. In contrast, Rachel et al. [13] showed that the median PG was 466 mg/dl, arterial pH, 7.18±0.2, serum bicarbonate, 7.5±4.8, as the ADA criteria for DKA severity, 71.0% of patients met the criteria for severe DKA, 21.0% had moderate DKA and 8.0% had mild DKA.

In the current study, regarding patients admitted, 80.0% were discharged in good condition and 20.0% of patients were transferred to another hospital to receive further management for co-morbid disease with diabetes after controlling their hyperglycemic crises. However, the outcomes in the preceding study were discharged in good

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condition at 95.0%. Delayed presentation and poor compliance related to psychological problems and lack of education to patients and their families about the appropriate insulin dose and the care for injected sites, as other factors that affected the selection of better antibiotics were contributory [26], postponed in hospitalization from the patients, the severity of acidosis they presented with and presence of comorbid diseases appeared to be a major risk factor for the critical state of DKA in most of the studied patients. However, it should be mentioned that this study is retrospective, it is subject to the inherent limitations of such designs, including potential missing data or incomplete medical records, conducted at a single center, the study period was limited, which may not capture the full spectrum of DKA cases in the population.

Conclusion: Diabetic ketoacidosis is a common acute complication of diabetes mellitus, affecting female patients of diabetes mellitus type 1, with the majority of patients presenting with a critical status of diabetic ketoacidosis. This study emphasizes the importance of educating patients about prevention, focusing on promoting insulin adherence, recognizing and managing infections, and prompt presentation. Efforts should be made to enhance access to healthcare services, ensure a continuous supply of insulin and other diabetes medications, and improve diabetes education and support systems programs.

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