

Admission Pattern of Diabetic ketoacidosis at the National Diabetes Hospital in Tripoli-Libya- 2015

Samia Elmiladi^{1,2@}, Lila Esabi², Ashia Elhadi¹, Aya Elfoghi¹ and Ziad Salama¹

¹National Diabetes Hospital; ²Faculty of Medicine, University of Tripoli, Tripoli, Libya

Received 12 October 2015/ Accepted 8 December 2015

ABSTRACT

Diabetic ketoacidosis (DKA) is a frequent cause of morbidity and mortality in type-1 DM; however, occasionally it may occur in type-2 DM during severe stress.

The aim of this study is to review the profile of admitted patients (non-pregnant adult and adolescents) at the national diabetes hospital presented with DKA in 2015.

A descriptive case series study for 200 in-patient with DKA admitted to Tripoli diabetes hospital, which is a teaching hospital located in Tripoli- Libya providing a tertiary level medical care, the enrolled patients admitted in a period of 9 months from August 2014 to April 2015.

Demographic data was extracted from the medical records including age, gender, duration of DM, type of DM, precipitating factors, clinical characters, laboratory results at presentation including: initial blood sugar, ketone bodies, pH, HCO₃, and admission to the word or medical intensive care unit (MICU), and the outcome of the patient. The collected data analyzed by using SPSS software.

During the study period, 200 DKA patients were admitted to the MICU 186(93%) at the national diabetes hospital in Tripoli. The mean age of all patients was 33.6±14 years, about 45% were below 30 years and 55% were females, with duration of DM less than 5 years in 34% of all patients, 82% of DKA patients under this study were with Type 1, the most frequent precipitating factor was insulin omission in patient with known DM (74%), about 14% were new cases, only one case recorded as exercise induced DKA, and 193(96.5%) were discharge in good condition.

Within the boundaries of this study, we can conclude that DKA affected mainly patients below 30 years with no sex difference, and less than 5 years duration of type 1 DM. Omission of insulin dose in known diabetic and infection are the commonest precipitating factors. Good education and awareness of sick day management are recommended.

Keywords- Diabetes; Ketoacidosis; Precipitating factors.

INTRODUCTION

Diabetic ketoacidosis (DKA) is a frequent source of morbidity and mortality in type-1 DM, however, occasionally it also happen in type-2 DM during severe stress.¹⁻⁶

The annual incidence of DKA in Libyan diabetics is unknown. The overall mortality rate from DKA in Libya ranges from 2 to 10% of all DKA admissions according to different reports.^{1-3,7}

DKA by definition consists of triad: hyperglycaemia, ketonaemia and high anion gap metabolic acidosis.⁸

The underlying mechanisms are absolute deficiency of insulin with elevated levels of counter-regulatory hormones like glucagon, catecholamine, cortisone and growth hormone.⁹

The patient with DKA usually presents with prostration, polyuria, polydipsia, and nausea, vomiting, generalized abdominal pain in more than 50% of patients¹⁰, weight loss and often with mental changes, varying from complete alertness to profound lethargy and coma.

Physical findings include loss of skin elasticity, dehydration, tachycardia and hypotension and Kussmaul (fast and deep) breathing.

A major reason for hyperglycaemic crises is infections followed by discontinuation of diabetic medications and/or inadequate dose in type 1 diabetes. Age is a critical factor: e.g., teenagers and adolescents are glaringly neglectful of their insulin regimen. Pump failure, tube leakage, insulin use beyond the expiration date, pump exposure to increased temperature, catheter blockage or dislodgement, or infection of the site of infusion, especially in cases where the catheter/ tubing apparatus are not replaced in time, all can lead to intermittent insulin delivery.¹¹

A variety of different conditions can cause DKA.¹²

- Noncompliance
- Acute illness
- Infection 30-40%
- Viral syndrome
- Urinary tract infection
- Pelvic inflammatory disease
- Pneumonia
- Mucormycosis
- Malignant otitis externa



- Periodontal abscess
- Dental infection
- Cytomegalovirus infection
 - Noninfectious acute illness
- Cerebrovascular accident
- Myocardial infarction
- Acute pancreatitis
- New-onset diabetes (20-25%)
- Drugs
 - Clozapine, Lithium, Olanzapine
 - Cocaine
 - Orlistat
 - Terbutaline
 - Indinavir,
 - Alpha-Interferon,
 - Corticosteorid
- HAART
- Malfunction of insulin pump

The two commonest precipitating factors of DKA are inadequate or inappropriate insulin therapy and infections.¹³

The common reasons for omitting insulin among patients with DM include insulin un-availability, in fact many patients preference to self-directed decrease of insulin dosage and frequency in order to delay the need to a further vial. Insulin is also omitted due to ill health and incorrect idea that drugs should not be taken when ill. Quite often, DKA can be the first presentation of DM.¹⁴

The patient with DM must be taught the value of Self-Monitoring of Blood Glucose (SMBG), analysis of blood sugar records and implications of different glucose readings. Furthermore, they must be taught how to handle sick days; for example, not to stop insulin dose, eat foods that are easy to digest and drink sugar-free fluids when appetite is suppressed or lost. They must be counseled to promptly communicate with their doctors.

The aim of this study is to review the profile of admitted patients (non-pregnant adult and adolescents) in national diabetes hospital presented with DKA in 2015.

MATERIALS AND METHODS

A case series study conducted by reviewing the medical records of 200 patients with DKA admitted to Tripoli National Diabetes Hospital which is a teaching hospital located in Tripoli- Libya, providing diabetes care of most western part of Libya for adult and adolescent diabetes patients, involving in-patient care with MICU and words, and specialized diabetes out-patients clinic including diabetes foot care, ophthalmology clinic, dental clinic and antenatal diabetes care for pregnant females.

The enrolled patients for this study admitted within the period between 8/2014 to 4/2015; Demographic data were collected from the medical records as age and gender in addition to duration of DM, type of DM, precipitating factors, clinical characters, laboratory results at presentation including; initial blood sugar, ketone bodies, pH, HCO₃, type of admission (word or MICU), patient's outcome, also the patients were classified as having type 1 or type 2 diabetes or atypical diabetes based on clinical diagnosis and treatment history.

The criteria used to diagnose DKA in the included series are: Hyperglycemia, pH<7.3, and/or serum bicarbonate ≤18 mmol/l and the presence of ketonuria (2+ or more).¹⁵

The severity of DKA was defined according to the American diabetes association (ADA) criteria^{15,16}, as follows; Mild: pH 7.25-7.30, moderate: pH 7.24-7, and severe: pH<7 (Table 1).

The collected data were statistically analyzed by using of the Statistical Package for Social Sciences (Windows version 16.0; SPSS Inc., Chicago [IL], US).

RESULTS

During the study period, 200 DKA cases were admitted to the national diabetes hospital in Tripoli (Table 2 - 6).where 14 cases (7%) admitted to medical wards and 186 cases (93%) to the MICU. The mean age of all cases was 33.6±14 years, about 45% were below 30 years; and 55% were females, with duration of DM less than 5 years in 34% of all cases. most of DKA cases were with Type 1DM (82%), the most frequent precipitating factor was insulin omission in patient with known DM (74%), about 14% were new cases, exercise induced DKA recorded in only one case and one patient was Asymptomatic, 41 cases (20.5%) presented with blood pressure <90/60. The highest blood sugar level in this series was 1400 mg/dl recorded in one

Table 1: Diagnostic criteria for DKA.¹⁴

	Mild DKA	Moderate DKA	Severe DKA
Arterial pH	7.25–7.30	7.00 to 7.24	>7.00
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10
Urine ketone Nitroprusside reaction method	Positive	Positive	Positive
Serum ketone	Positive	Positive	Positive
Effective serum osmolality 2 measured Na(mEq/l)+ glucose (mg/dl)/18	Variable	Variable	Variable
Anion gap‡ (Na)- (Cl+ HCO ₃ (mEq/l)	>10	>12	>12
Mental status	Alert	Alert/drowsy	Stupor/coma



Table 2: Distribution of personal data among patients admitted with DKA to National Diabetes Hospital Tripoli-Libya 2015

Character	Frequency	Percentage
Sex:		
Female	110	55%
Male	90	45%
Age in years		
10-29	90	45%
30-49	68	34%
50-69	26	13%
70-89	12	6%
>90	4	2%

Table 3: Distribution of clinical data among patients admitted with DKA to National Diabetes Hospital Tripoli-Libya 2015

Character	Frequency	Percentage
Type		
DMI	164	82%
DMII	36	18%
Duration of DM in years		
0-5 years	68	34%
6-10 years	53	26.5%
11-15 years	29	14.5%
16-20 years	27	13.5%
<21 years	23	11.5%
Symptoms		
Present	199	99.5%
Absent	1	0.5%
Keton bodies		
Present	195	97%
Absent	5	2.5%
pH		
≥7	196	98%
≤6.9	4	2%
Admission to		
MICU	186	93%
The ward	14	7%
Outcome		
DAMA	7	3.5%
Discharge	193	96.5%



Table 4: Distribution of DKA precipitating factors among patients admitted to National Diabetes Hospital Tripoli-Libya 2015

Precipitating factors of DKA	Frequency	Percentage
<i>Omission of the dose</i>	74	37 %
<i>Respiratory infection</i>	33	16.5%
<i>New cases</i>	29	14.5%
<i>Urinary tract infection</i>	24	12%
<i>Others</i>	21	10.5%
<i>Foot infection</i>	10	5%
<i>Wrong dose</i>	8	4%
<i>Exercise induced</i>	1	0.5%
<i>Total</i>	200	100%

Table 5: Distribution of presenting Blood Sugar level among patients with DKA admitted to National Diabetes Hospital Tripoli-Libya 2015

Blood sugar	Frequency	Percentage
<i>100-299 mg/dl</i>	31	15.5%
<i>300-599 mg/dl</i>	125	62.5%
<i>600-899 mg/dl</i>	40	20%
<i>900-1199 mg/dl</i>	3	1.5%
<i>>1200 mg/dl</i>	1	0.5%
<i>Total</i>	200	100%

Table 6: Distribution of DKA severity and HCO₃ values among patients admitted with DKA to National Diabetes Hospital Tripoli-Libya 2015

Severity of DKA (HCO ₃ value)	Frequency	Percentage
<i>Mild (18-15)</i>	86	43%
<i>Moderate (<15-10)</i>	73	36.5%
<i>Sever (<10)</i>	41	20.5%

Table 7: Comparison between this study and King Abdul Aziz university hospital study.²⁶

Character	Current study	The King Abdul Aziz University Hospital study
<i>The mean age</i>	33.6(16-81)years	22.5 (0.5-87) years
<i>Male : Female ratio</i>	1:1.2	1.4:1
<i>Precipitating factors</i>		
<i>Poor compliance</i>	37%	54.4%
<i>Infection</i>	33.5%	28%



case, most of values were between 300-599 mg/dl documented in 125 cases (62.5%) of all initial blood sugar values, ketone bodies present in 97.5% (195 cases) at presentation, only 4(2%) were presented with $\text{pH} \leq 6.9$ and require NaHCO_3 , according to the diagnostic criteria of DKA 86(43%) of cases had mild DKA, regarding the outcome of these patients; 193(96.5%) were discharged in good condition and 7(3.5%) (Table 3). Discharge Against Medical Advice (DAMA).

DISCUSSION

Worldwide the incidence of diabetes mellitus is increasing, as well as the presentation of diabetes emergencies including hypo- and hyperglycemia to hospital casualties. Recognizing these conditions will be vital to ensure correct and efficient initial management. Hyperglycaemic emergencies include Diabetic Keto Acidosis (DKA) and Hyperglycaemic Hyperosmolar State (HHS).

Type 2DM is being identified in younger adults as well as children, because of increasing obesity and sedentary lifestyles thus distinguishing between DKA and HHS can be difficult based on phenotypic appearances only. DKA comprise the most serious, and life threatening, of acute metabolic complications of DM, but reduction in mortality is possible by earlier diagnosis and better treatment.¹⁷⁻²¹

It's important to recognize the precipitating factors of DKA for prevention as well as prompt and efficient management to decrease morbidity and mortality. This study revealed many precipitating factors like Omission of insulin dose, Respiratory infection, newly diagnosis cases with DM, foot infection, Urinary tract infection and exercise induced DKA, and presentation with unclear precipitating factor (10.5%). Also that the most common precipitating factor of DKA (accounted for more than one third (37%) of cases) is insulin omission in known patients with DM, as a result of poor compliance that related to psychological problem and lack of education to patients and their family about the appropriate insulin dose and the care for injected site. That was supported by most of cases occur at younger age (10-29 year) i. e teenager and early adolescence when the responsibility of treatment transfer from parent (usual responsible adults) to the patient himself.

Also insulin dose omission may explain the association between DKA occurrence and history of recurrent DKA episodes as in other studies like, UK observation survey, 22.5% of recorded DKA cases related to recurrent episodes of DKA of known patients with DM²², whereas in Colorado accounted for 80%.²³

The main direct reason for the repeated DKA in children and teenagers is insulin omission, indicated the essential for confirming use of insulin by responsible adults is important.^{22,23}

In fact, common causes for insulin dose omission among patients with DM include insulin un-availability that leads to reduction in insulin dose and frequency with the aim of postponement the requirement to an additional ampoule. Also insulin doses are omitted during sick days and wrong impression that insulin doses should not be taken when

sick with poor food intake.¹⁴

A study was revealed the precipitating factors of diabetic ketoacidosis (DKA) at a public hospital in a middle-income country. Eighty patients with type 1 diabetes who had an emergency hospitalization for DKA between January 2005 and March 2010 at a tertiary care teaching hospital in Southern Brazil were studied. The mean age of patients was 26 ± 13 years. The most common DKA precipitating factor was treatment non-adherence: 39% of cases when all patients were evaluated and 49% when only patients with previous type 1 diabetes diagnosis were analyzed. Comparison between patients with DKA precipitated by treatment non-adherence and by other causes showed that the former group had more episodes of previous DKA and more frequently reported insulin omission previous to DKA.²⁴

A retrospective cohort study of 220 patients hospitalized with DKA during the period first January 2003 to first January 2010, concluded that the commonest precipitating factors for the development of DKA were related to compliance with insulin therapy and infections.²⁵

For the present study the second important factor is Respiratory Tract Infection (16.5%) that may be because of the study period mostly during Autumn and Winter seasons (from Aug 2014 to April 2015), followed by foot and Urinary Tract Infection. And the initial presentation with DKA in newly diagnosed DM (mostly in Type 1DM) only represent small but significant percentage (14.5%).

There was a study²⁶ conducted in King Abdul Aziz University Hospital show sixty-eight patients were admitted with DKA at, Jeddah, Kingdom of Saudi Arabia, hospital over a 2-year period, (April 1999 through to April 2001; Table 7).

These results are consistent with our study that reveals employing a patient education program to improve understanding of DM is the most important measure in the avoidance of DKA.

However, some recent studies suggested that infection may be the most important precipitating factor as in Damascus²⁷, the US,²⁸ Pakistan,²⁹ and India.³⁰

A retrospective study²⁷ was conducted in Damascus(the capital of Syria), included 115 patients admitted with DKA, there were 92 single admission and 23 recurrent admissions (eight patients). The order of precipitating factors of recurrent DKA or single admissions were the same with different percentage. The first and second factors were infection (74% and 48%) and treatment problems (17% and 24%), respectively. Infections were the predominant precipitating factors for DKA in all admissions, followed by insulin-related problems.

CONCLUSION

DKA is a common acute complication of DM, affecting female patients with DMI mainly due to insulin omission and infection as major precipitating factors, with MICU admission.



RECOMMENDATIONS

Blood sugar goals should be individually targeted, with the utilization of added corrective insulin dose and treat underlying infections promptly. Also by applying a patient education program to raise understanding of DM is the most vital measure in the avoidance of DKA, the authorities should make certain accessibility of insulin to every patients, free of charge or at lower cost.

During acute illness, instructions should be given to patient and the family members regarding documenting blood glucose, insulin administration, oral intake, weight changes, temperature and urine and blood ketone testing. Patients should be advised not to discontinue insulin and always take doctors opinion in the initial days of the illness.

REFERENCES

1. Roacid R and Kablan A (2004) Diabetic Ketoacidosis in Benghazi characteristics and outcome in 211 patients, *Garyounis Med J.* **21**(1), 11-14.
2. EL-sharief H J (2006) Diabetic Ketoacidosis TMC experience, *Jamahiriya Med J.* **5**(1), 51-54.
3. Elmehdawi RR and Elmagerhei HM (2010) Profile of diabetic ketoacidosis at a teaching hospital in Benghazi, Libyan Arab Jamahiriya, *East Mediterr Health J.* **16**(3), 292-299.
4. Seyoum B and Berhanu P (2007) Profile of diabetic ketoacidosis in a predominantly African American urban patient population, *Ethn Dis.* **17**(2), 234-237.
5. Newton CA and Raskin P (2004) Diabetic ketoacidosis in type 1 and type 2 diabetes mellitus: clinical and biochemical differences, *Arch Intern Med.* **27**(17), 1925-1931.
6. Umpierrez GE, Smiley D and Kitabchi AE (2006) Narrative review: ketosis-prone type 2 diabetes mellitus, *Ann Intern Med.* **144**(5), 350-357.
7. Lakhdar AA and Elharboush S (1999) Characteristics and outcome of ketoacidosis in Libyan diabetic patients, *Diabetes Int.* **16**(6), 171-173.
8. Kitabchi AE and Wall BM (1995) Diabetic Ketoacidosis, *Med Clin North Am.* **79**, 9-37.
9. Kitabchi AE, Umpierrez GE, Fisher JN, Murphy MB and Stentz FB (2008) Thirty years of personal experience in hyperglycemic crises: diabetic ketoacidosis and hyperglycemic hyperosmolar state, *J Clin Endocrinol Metab.* **93**(5), 1541-1552.
10. Matz R (1972) Hypothermia in diabetic acidosis, *Hormones* **3**, 36-41.
11. Chaithongdi N, Subauste JS, Koch CA and Geraci SA (2011) Diagnosis and management of hyperglycemic emergencies, *Hormones* **10**(4), 250-260.
12. Marshal SM, and Alberti KGM (1987) Diabetic ketoacidosis, *Diabetes Ann.* **3**, 498-526.
13. Ogbera AO, Awobusuyi J, Unachukwu C, and Fasanmade O (2009) Clinical features, predictive factors and outcome of hyperglycaemic emergencies in a developing country, *BMC Endocr Disord.* **10**(3), 9.
14. Kitabchi AE, Umpierrez GE, Murphy MB and Kreisberg RA (2006) Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American Diabetes Association, *Diabetes Care* **29**(12), 2739-2748.
15. Kitabchi AE, Umpierrez GE, Murphy MB, Barrett EJ, Kreisberg RA, Malone JJ, et al. (2004) American Diabetes Association Hyperglycemic crises in diabetes, *Diabetes Care* **27**(1), 94-102.
16. Roche EF, Menon A, Gill D and Hoey H (2005) Clinical presentation of type 1 diabetes, *Pediatr Diabetes* **6**, 75-78.
17. Abbas K, Guillermo U, John M and Joseph F (2009) Hyperglycemic crises in adult patients with diabetes, *Diabetes Care* **32**(7), 1335-1343.
18. Hansen TK and Moller N (2010) Acute Metabolic Complications of Diabetes: Diabetic Ketoacidosis and Hyperosmolar Hyperglycemia. In Holt RIG, Cockram CS, Flyvbjerg A, Goldstein BJ, editors. Textbook of Diabetes. 4th ed. West-Sussex: Wiley-Blackwell; pp. 546-552.
19. Nyenwe EA and Kitabchi EA (2011) Evidence-based management of hyperglycemic emergencies in diabetes mellitus, *Diabetes Research and Clinical Practice* **94**(3), 340-351.
20. Joint British Diabetes Societies (2012) Inpatient Care Group. The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes, NHS.
21. Joint British Diabetes Societies (2010) Inpatient Care Group. The Management of Diabetic Ketoacidosis in Adults, NHS. Malone JJ and Root AW (1981) Plasma free insulin concentrations: keystone to effective management of diabetes mellitus in children, *J Pediatr.* **99**, 862-867.
22. Malone JJ and Root AW (1981) Plasma free insulin concentration: keystone to effective management of diabetes mellitus in children, *J Pediatr.* **99**, 862-867.
23. Edge JA, Hawkins MM, Winter DL and Dunger DB (2001) The risk and outcome of cerebral oedema developing during diabetic ketoacidosis, *Arch Dis Child.* **85**, 16-22.
24. Weinert LS, Scheffel RS, Severo MD, Cioffi AP, Teló GH, Boschi A, et al. (2012) Precipitating factors of diabetic ketoacidosis at a public hospital in a middle-income country, *Diabetes Res Clin Pract.* **96**(1), 29-34.
25. Barski L, Nevzorov R, Rabaev E, Jotkowitz A, Harman-Boehm I, Zektser M, Zeller L, Shleyfer E and Almog Y (2012) Diabetic ketoacidosis: clinical characteristics, precipitating factors and outcomes of care, *Isr Med Assoc J.* **14**(5), 299-303.
26. Qari F (2002) Precipitating factors for diabetic ketoacidosis, *Saudi Medical Journal* **23**(2), 173-176.
27. Alourfi Z and Homsy H (2015) Precipitating factors, outcomes, and recurrence of diabetic ketoacidosis at a university hospital in Damascus, *Avicenna J Med.* **5**(1), 11-15.
28. Savage MW, Dhatariya KK, Kilvert A, Rayman G, Rees JA, Courtney CH, et al. (2011) Joint British Diabetes Societies. Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis, *Diabet Med.* **28**, 508-515.
29. Naveed D, Bilal N, Nasir B and Lodhi BU (2009) Precipitating factors for diabetic ketoacidosis, *Kust Med J.* **1**, 6-8.
30. Ganie MA, Koul S, Razvi HA, Laway BA and Zargar AH (2012) Hyperglycemic emergencies in Indian patients with diabetes mellitus on pilgrimage to Amarnathjiyatra, *Indian J Endocrinol Metab.* **16**(1), 87-90.

