

Clinico-laboratory characteristics of diabetic keto acidosis in adults in a tertiary hospital in Saudi Arabia

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Abstract. – Objective: The present study is undertaken to evaluate the magnitude of DKA in Saudi population with specific emphasis on clinical laboratory characteristics over 20 years.

Material and Methods: A prospective analysis of hospital records of 240 episodes of DKA requiring inpatient admission from December 1985 to December 2005 in adult patients in a tertiary hospital was performed. Besides the demographic data of the patients, the clinico-laboratory parameters relevant to the diabetes and DKA status were thoroughly reviewed.

Results: 150 males and 90 females were admitted with DKA with a mean age of 21.77 ± 7.2 years. 16.6% (n=40) were diagnosed to have DM for the first time and others had a mean duration of DM of 5.02 ± 4.88 years with an average daily insulin requirement being 45.09 ± 23.9 units. 80.4% of the DKA episodes occurred in intermediate, secondary school and University level students. The commonest precipitating factors were missed insulin doses (51.2%) and respiratory tract infections (22.5%). The mean duration of stay in the hospital was 6.56 ± 3.4 days and there were no deaths reported because of DKA. The mean blood sugar on presentation was 23.49 ± 8.3 mmol/L whereas the mean pH and bicarbonate levels on presentation were 7.21 ± 0.1 and 14.7 ± 4.3 meq/L respectively. Blood pH was found to be significantly lower in female patients. Among patients below 20 years of age, females have significantly lower bicarbonate levels (11.7 ± 6.2). Among patients above 20 years of age females had significantly longer duration of diabetes (8.86 ± 8.36 years; $p < 0.04$).

Conclusions: By providing intensive education and increasing the awareness of DKA, a major reduction in morbidity and hospitalizations due to DKA may be expected.

Key Words:

Diabetes Mellitus, Ketoacidosis, Characteristics, DKA, Tertiary Level Care.

Introduction

Diabetic ketoacidosis (DKA) is a serious acute complication of diabetes mellitus. According to American Diabetes Association the mortality rate in patients with DKA is reported to be less than 5%¹. However, it is reported that there has been a 4.2% decrease of death rate per year in United States during 1985-2002². Mortality in patients developing DKA is predominantly due to the underlying morbidities such as sepsis or myocardial infarction³.

The most common precipitating factor in the development of DKA is missed insulin doses. Other factors which may precipitate the incidence of DKA are infections, cerebrovascular accident, alcohol abuse, pancreatitis, myocardial infarction, trauma and drugs such as corticosteroids, thiazides and sympathomimetic agents. In addition, new onset type 1 diabetes, or discontinuation of or inadequate use of insulin in type 1 diabetic patients result in development of DKA.

In young patients with type 1 diabetes, psychological problems with eating disorders may be a contributing factor for 20% of recurrent ketoacidosis⁴.

The insulin deficiency in combination with increased levels of stress hormones, stimulate lipolysis resulting in the production of acetyl CoA from fatty acids. This acts as substrate for the hepatic synthesis of ketone bodies such as acetoacetate, beta-hydroxybutyrate and acetone. In addition lack of insulin results in decreased glucose utilization and increased gluconeogenesis. Decreased glucose utilization results in reduction of oxaloacetate production. Thus the amount of oxaloacetate available for condensation with acetyl CoA in tricarboxylic acid cycle (TCA) is reduced. This diverts the acetyl CoA from entering into the TCA cycle. This adds to the acetyl CoA already available from the lipolysis and leads to the formation of ketone bodies.

Increased ketone bodies in the blood lead to increase in the concentration of H⁺ resulting from the ketone acids. This is initially buffered by bicarbonate. During this stage, blood will show low bicarbonate levels and a normal pH, as the pH is maintained at the expense of bicarbonates. As the concentration of H⁺ exceeds the buffering capacity of bicarbonates, the bicarbonate reserves become depleted and acidosis results.

DKA presents with three classical features such as hyperglycaemia, ketosis and acidosis. The diagnosis of DKA is based on the clinical features such as uncontrolled diabetes, presence of ketosis and acidosis (bicarbonates <15 mmol/l and arterial blood pH <7.3)⁵. The classical clinical features include a history of polyuria, polydipsia, polyphagia, weight loss, vomiting, abdominal pain, dehydration, clouding of sensorial, and finally coma. Physical findings may include poor skin turgor, Kussmaul respiration, tachycardia, hypotension, alteration in mental status and shock. Up to 25% of patients have emesis which may be coffee-ground in appearance and guaiac positive. Even though infection may be one of the precipitating factors, the patient may be normothermic or even hypothermic due to peripheral vasodilation¹.

DKA is closely related to a similar condition called hyperosmolar hyperglycemic state (HHS) which is reported to have higher mortality rates (15%) than DKA. Thus it becomes essential to diagnose accurately to rule out HHS in patients presenting with similar features. HHS is caused by plasma insulin concentrations which are inadequate to facilitate glucose utilization but adequate to prevent fatty acid lipolysis. HHS differs from DKA in degree of ketosis and magnitude of dehydration¹.

As DKA is a preventable complication of diabetes, it is essential that risk factors should be clearly identified in the local population. The present study is undertaken to evaluate the magnitude of DKA in Saudi population with specific emphasis on clinical laboratory characteristics over 20 years in a tertiary hospital (referral hospital) in Saudi Arabia.

Patients and Methods

This study is a prospective observational study conducted between December 1985 and 2005 in King Khalid University Hospital, King Saud University, Riyadh, Kingdom of Saudi Arabia. Hospital records of 240 patients admitted due to DKA were maintained. Patient's demographic data were collected using specially designed computer form. Clinical data were also included namely symptoms of DKA, diabetes history and treatment regimen. DKA precipitating factors namely missing insulin dose and respiratory infections were reported. Biochemical parameters including pH, blood glucose, bicarbonate, potassium levels were measured. All the data has been collected by trained physicians.

Inclusion criteria in the study were DM patients of both genders aged from 13 to 40 years, who required inpatient admission for DKA with positive urine ketosis dipstick test. Patients treated in the Emergency room were excluded from the study.

Statistical Analysis

Continuous variables are represented as means \pm SD and percentages. Unpaired t test was used to analyze the difference between means. Statistical Package for Social Sciences (SPSS) for windows version 12 (Chicago, IL, USA) was used for statistical analysis.

Results

Total number of patients with DKA who were admitted in to the Hospital was 240 during the period from 1985 to 2005. There were 150 (62.5%) males and 90 females (37.5%) and the mean age was found to be 21.7 ± 7.2 years. The educational background of the patients were intermediate 41 (17%), secondary school 102

(42.2%), university 51 (21.2%) and other educational level 46 (19.3%). Their average body mass index (BMI) was 22.8 ± 5.01 kg/m². About 40 (16.6%) patients with no history of diabetes presented with DKA as the first presenting episode of diabetes. The average duration of diabetes among diabetic patients was 5.02 ± 4.8 years.

For majority of the patients (73.7%) precipitating factor for DKA was identified clearly. Precipitating factors were missed insulin dose in 123 (51.2%) patients and infections in 54 (22.5%) patients. Total insulin requirement at presentation was 45 ± 23.9 Units/day (0.72 ± 0.23 U/kg/day).

The presenting symptoms included vomiting in 148 (61.6%) cases, polyuria in 137 (57%) cases, abdominal pain 136 (56.6%), polydipsia 130 (54.1%), fever 30 (12.5%), dehydration 30 (12.5%) and altered consciousness 13 (5.4%) (Table I). The mean blood sugar (venous plasma glucose) at presentation was 23.49 ± 8.34 mmol/L. The mean presenting pH was 7.21 ± 0.14 and mean bicarbonate value was found to be 14.7 ± 4.3 meq/l. The mean potassium level was 4.4 ± 0.67 mmol/L.

In males the mean blood pH was 7.23 ± 0.12 and in females it was found to be 7.16 ± 0.20 that was significantly lower ($P < 0.01$) than males. The mean blood bicarbonate and potassium levels in males were found to be 13.87 ± 6.11 meq/l and 4.55 ± 0.76 meq/l and in females 12.02 ± 6.14 meq/l and 4.34 ± 0.80 meq/l respectively. Blood bicarbonate and potassium levels were found to be significantly lower ($P < 0.02$ and $P < 0.04$ respectively) in females when compared with males. All the other parameters such as duration of diabetes, number of hospital days, BMI, blood pressure, blood glucose levels and insulin requirement per day were not significantly different between males and females in the study.

Table I. Presentation of DKA.

Presenting characteristics	Number (percentage)
Abdominal pain	136 (56.6%)
Polyuria	137 (57%)
Polydipsia	130 (54.1%)
Vomiting	148 (61.6%)
Fever	30 (12.5%)
Dehydration	30 (12.5%)
Altered consciousness	13 (5.4%)

Average duration of hospital stay was 6.56 ± 3.4 days while number of patients requiring intensive care unit (ICU) admission were 14 (5.8%). No death due to DKA was recorded during the study. Table II gives an overview of gender differences among the age groups in the characteristics of DKA.

Discussion

The male to female ratio of DKA patients is found to be 1.6:1. However, findings from other studies in Saudi population indicate the higher incidence of DKA among female patients. Yousuf and Chaudhry⁶ reported a male to female ratio of 1:2 among Saudi population. In a study in Saudi children⁷, a higher prevalence of DKA among female patients was reported with male to female ratio 1:1.4. In another study with Saudi population, an equal male to female ratio was reported⁸. However, studies in other populations reported a higher incidence of DKA among male patients⁹⁻¹¹. It appears that the gender difference may not be a significant factor in the prevalence of DKA.

16.6% of patients were newly diagnosed as having diabetes. Most of the patients presented with vomiting, abdominal pain and polyuria. However, the number of patients (5.4%) with altered consciousness was found to be lower than the previous studies¹². The clinical picture of DKA typically presents with polyuria, polydipsia, weight loss, weakness, vomiting and abdominal pain. The symptoms such as polyuria, polydipsia, polyphagia and weight loss are related to hyperglycemia. The symptoms of nausea, emesis and abdominal pain are more related to the ketonemia.

Results indicate that younger age group is at higher risk of DKA. The intermediate and secondary schools students comprise about 59.2% of total number of DKA patients studied. Other studies report a relatively higher age^{12,13}. At the same time, several studies indicate that incidence of childhood DKA is on the rise^{14,15}.

The blood sugar at presentation was 23.4 ± 8.3 mmol/l which is close to what is reported by other authors¹⁶. About 5.8% of patients required ICU admission. Majority of the patients reported of discontinued insulin therapy as precipitating factor. A similar precipitant profile was observed in previous studies¹⁷.

Table II. Gender difference among the age groups in the characteristics of DKA patients.

Characteristics	Age below 20 years mean \pm SD			Age above 20 years mean \pm SD			
	Total (N = 127)	Males (N = 72)	Females (N = 55)	Total (N = 113)	Males (N = 78)	Females (N = 35)	p value
Age	16.1 \pm 2.3	15.9 \pm 2.2	16.4 \pm 2.4	29.4 \pm 6.8 ^a	29.3 \pm 6.5	29.5 \pm 7.5	0.92
Duration of diabetes	3.3 \pm 3.2	3.5 \pm 3.3	3.1 \pm 3.0	6.9 \pm 6.6 ^a	6.1 \pm 5.5	8.8 \pm 8.3*	0.04
Hospital days	5.7 \pm 2.7	5.7 \pm 3.0	5.8 \pm 2.2	7.2 \pm 3.7 ^a	7.3 \pm 3.6	7.0 \pm 3.9	0.74
BMI	21.7 \pm 4.9	21.7 \pm 4.1	21.8 \pm 5.8	23.7 \pm 5.1 ^a	22.7 \pm 3.5	25.7 \pm 7.1*	<0.01
BP (systole)	113.7 \pm 14.0	114.4 \pm 14.4	112.7 \pm 13.5	120.8 \pm 15.8 ^a	120.8 \pm 15.3	120.9 \pm 17.1	0.97
BP (diastole)	71.8 \pm 9.3	73.0 \pm 8.8	70.2 \pm 9.8	76.1 \pm 10.2 ^a	76.62 \pm 10.19	75.0 \pm 10.3	0.45
Blood glucose	22.1 \pm 8.3	22.3 \pm 8.4	21.8 \pm 8.3	24.3 \pm 9.4 ^b	24.9 \pm 9.7	23.0 \pm 8.5	0.31
Blood pH levels	7.2 \pm 0.1	7.2 \pm 0.1	7.1 \pm 0.1*	7.2 \pm 0.1	7.2 \pm 0.1	7.1 \pm 0.2*	0.03
Blood bicarbonate levels	13.0 \pm 6.1	14.0 \pm 6.0	11.7 \pm 6.2*	13.3 \pm 6.1	13.7 \pm 6.2	12.3 \pm 6.0	0.28
Blood potassium levels	4.4 \pm 0.7	4.5 \pm 0.7	4.3 \pm 0.8	4.5 \pm 0.8	4.5 \pm 0.7	4.3 \pm 0.8	0.24
Insulin requirement per day	0.7 \pm 0.5	0.7 \pm 0.4	0.8 \pm 0.5	0.7 \pm 0.4	0.7 \pm 0.4	0.6 \pm 0.4	0.15

^ap<0.01; ^bp<0.05, significantly different when compared with respective characteristic of patients with age below 20 years; *Significantly different when compared with the corresponding characteristics of males.

Blood pH and bicarbonate levels were found to be lower. These are consistent with values that would be expected for DKA. Absolute or relative insulin deficiency combined with counter-regulatory factors such as glucagon, cortisol and catecholamines are involved in the pathogenesis of DKA. Metabolic acidosis results from the accumulation of ketoacids such as acetoacetic acid and β -hydroxy butyric acid in plasma. However, surprisingly the mean potassium levels were found to be within the normal range. In many of the reported cases of DKA the potassium levels were found to be high.

Blood pH was found to be significantly lower in females when compared with that of males while bicarbonate levels, potassium levels were similar. Duration of diabetes, hospital days, BMI, blood pressure (BP) and blood glucose levels were significantly higher in patients with age above 20 years when compared with patients aged below 20 years. Among patients below 20 years of age, females had significantly lower blood pH when compared with males. And blood bicarbonate levels were also found to be significantly lower in females among patients below 20 years indicating that the ketoacidosis was severe among females when compared to male patients.

In patients aging above 20 years, females had significantly longer duration of diabetes. Females also had a significantly higher BMI when compared with that of males of same age group. Females had significantly lower blood pH and a lower but not a significant decrease in blood bicarbonate levels when compared with males. Overall, DKA is more severe in female patients compared to males among both the age groups.

The DKA was reversible in all the patients and no event of death was recorded among patients during the DKA episode while other studies from Saudi Arabia reported mortality rates 3.5% and 2.9%^{6,9}. This improvement could be attributed to the highest level of medical care at the University Hospital. As infections and missed dose of insulin were found to be the most frequent precipitating factors in Saudi population in this study, prevention of DKA can be achieved by better access to medical care, effective communication with patients by health care provider and creating awareness among diabetic patients through patient education and counseling.

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