DIABETIC KETOACIDOSIS- A STUDY OF 33 EPISODES

C Rajasoorya, S F Wong, L S Chew

ABSTRACT

Twenty-six patients presenting with 33 episodes of Diabetic Ketoacidosis (DKA) and managed on a protocol oriented system were analysed. Diabetes mellitus was newly diagnosed at presentation in 18% of the 33 episodes. The presenting symptoms were polyuria and polydipsia (58%), nausea and vomiting (52%), change in sensorium (24%), hyperventilation (24%), and abdominal pain (18%). The main clinical findings at admission were dehydration (97%), acidotic respiration (67%), coma and confusion (61%), a clinically detectable source of sepsis (49%), fever (33%) and hypotension (9%). Blood sugar levels at admission ranged between 351 mg/dl and 1200 mg/dl (mean = 633 mg/dl). The mean serum potassium at diagnosis was 5.1 mmol/l and the mean calculated serum osmolality was 320 mOsm/kg. The mean serum osmolality was higher in those with disturbed conscious level. Infections, particularly those of the urogenital tract, were the main precipitating cause for the DKA. Only 12 of the 19 patients with sepsis had fever. Eight of the episodes were attributed to patients' non-compliance with insulin. Four patients died during the 33 hospitalisations, giving a mortality rate of 10%. Death occurred despite glucose control and stabilisation of the ketoacidotic state and was due to uncontrolled septicaemia. The mean duration of hospitalisation was 11 days. The ketoacidosis state was reversed after a mean duration of 9.5 hours, with an average soluble insulin requirement per patient of 52.4 units.

Keywords: *diabetes mellitus, ketoacidosis, glucose, insulin, infections, treatment*

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INTRODUCTION

Diabetes mellitus is common in Singapore with a prevalence in the adult population of 4.7%[1] and is a leading cause of mortality and ill health. Despite the widespread use of Insulin for Insulin Dependent Diabetes Mellitus, Diabetic Ketoacidosis (DKA) continues to present in substantial numbers with its resultant mortality and morbidity. The diagnosis of DKA requires rapid recognition and prompt attention. In contrast with other emergencies in clinical medicine, DKA can be easily missed. Whilst the insidious onset and slow progression of symptoms often deceive the patient into complacency, it can sometimes even fool the physician. Hence a high index of suspicion is required. A study to assess DKA in one medical unit in a General Hospital in Singapore was done to document the clinical characteristics amongst a sample of the local population. No previous local studies have documented the profile of patients presenting with DKA. Patients presenting with diabetic ketoacidosis were analysed on their clinical characteristics, investigations at presentation, hospitalisation course and final therapeutic outcomes.

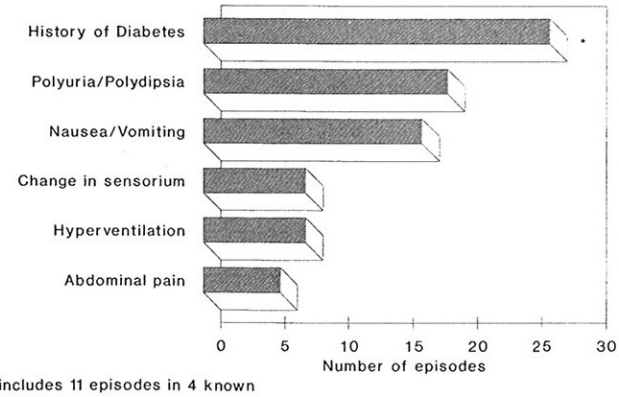
METHODS

For this study, an episode of diabetic ketoacidosis was defined as a clinical state in which a patient has uncontrolled hyperglycaemia (blood sugar more than 300 mg/dl) in association with metabolic acidosis (serum standard bicarbonate value of 15 mmol/l or less) and ketonuria requiring rapid fluid and insulin therapy[2,3]. Ketonuria was defined when urinary dipstix was ketone positive. This definition does not take into account the extent of serum ketones[2] as this was not routinely available at the time of the study.

The patients were managed by a protocol oriented approach. Fluid replacement was initiated with normal saline at the rate of aproximately 1 litre per hour in the first two hours. Thereafter the replacement was titrated according to age, clinical status, hydration status and clinical response. After a bolus intravenous insulin administration of 10 units insulin, continuous intravenous insulin was infused through an infusion pump at the rate of approximately 0.1 U/kg until 1 hour after a blood sugar level of 250 mg/dl was achieved. The time since admission to achieve this blood sugar level was documented. Potassium was routinely administered at a rate inversely proportionate to the serum potassium level, as long as the serum potassium was less than or equal to 6 mmol/l. Careful attention was paid to the urinary output and need for close clinical and laboratory monitoring. This protocol-oriented system was newly introduced in our hospital in 1986. [Details of the protocol are directly available from the authors]. This is a retrospective analysis over an 18-month period in which patients with documented diabetic ketoacidosis had their hospital records retrieved.

Grouped data were tested for statistical significance using the Mann-Whitney (Wilcoxon) Non-Parametic Statistic. The relationship between a set of two variables was assessed using regression analysis. Probability levels greater than 0.05 are described as not statistically significant.

Fig 1 - Symptoms at presentation



•includes 11 episodes in 4 known diabetics

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Fig 2 - Signs at examination

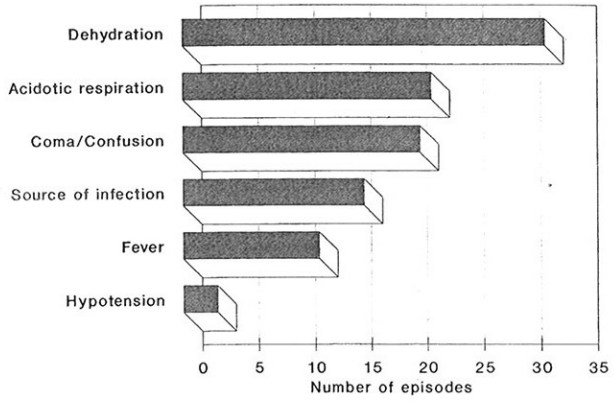
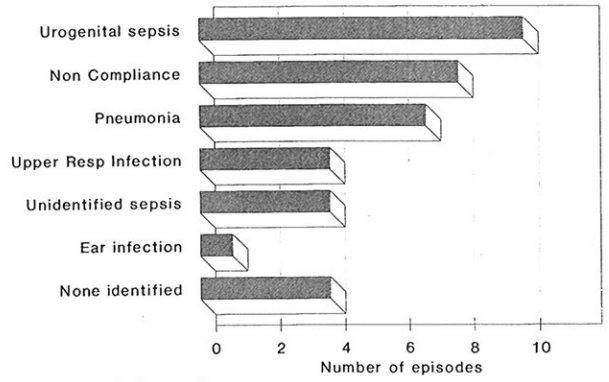


Fig 3 - Precipitating Cause(s)*



*Some patients had more than one contributory cause

RESULTS

Clinical characteristics

Over an 18-month period, 33 episodes of diabetic ketoacidosis occurred in 26 patients. Of these 26 patients, 11(42.3%) were male and 15(57.7%) were female. The ethnic distribution amongst those with DKA were 10 Malays (38.5%), 3 Indians (11.5%) and 13 Chinese (50%). The patients' age ranged between 12 to 77 years with a mean age of 52.6 years (1 SD = 17.3). Of these 26 patients, 34.6% were aged 65 years or more.

Symptomatology

Fig 1 shows the most common symptoms that were elicited in patients either just prior or at the time the diagnosis of ketoacidosis was made. Diabetes mellitus was newly diagnosed at presentation in 18% of the 33 episodes. The presenting symptoms were polyuria and polydipsia (58%), nausea and vomiting (52%), change in sensorium (24%), hyperventilation (24%), and abdominal pain without any specific underlying cause (18%).

Clinical findings

Fig 2 shows the clinical findings at admission which were dehydration (97%), acidotic respiration (67%), coma and confusion (61%), a clinically detectable source of sepsis (49%), fever (33%) and hypotension (9%) - hypotension was defined as a systolic blood pressure below 90 mmHg.

Laboratory investigations

Blood sugar levels at admission varied between 351 mg/dl and 1200 mg/dl. The mean blood sugar was 633mg/dl (1SD = 233.1). The mean blood sugar level in those who had coma/confusion compared to those who did not, was 730 and 460 mg/dl respectively. This difference was statistically significant ($p<0.0002$). The blood sugar level did not correlate with any other clinical or laboratory parameter.

The mean serum potassium at diagnosis was 5.1 mmol/l 1SD = 1.1. Only two patients had a serum potassium level below 3.5 mmol/l. There was a trend for serum potassium levels to be lower in those with nausea compared with those without (ie 5.4 vs 4.7 mmol/l), and the difference was statistically significant ($p<0.05$).

Blood gas analysis revealed the mean pH to be 7.15 (range 6.67 - 7.43, 1SD = 0.16), the mean bicarbonate was 8.7 mmol/l (range 1.9 - 15, 1SD = 4.1). Again there was a trend for those with clinically suspected acidosis to show a lower mean standard bicarbonate level (7.7 mmol/l) compared to those deemed not to have acidotic respiration (10.1 mmol/l). However, this difference was not statistically significant ($p=0.17$).

The calculated anion gap and serum osmolality were respectively 26.6 mmol/l (1SD = 6.9) and 319.6 mOsm/kg. These showed no correlation with any other biochemical parameter. However the serum osmolality showed marked difference in those with altered conscious levels. Patients with disturbed conscious level or confusion had a mean serum osmolality of 334 mOsm/kg while those who did not manifest this sign had a mean osmolality of 295 mOsm/kg. This difference showed high statistical significance ($p<0.0005$). The relationship between the first serum glucose and serum bicarbonate levels was analysed using simple regression analysis. There was no statistically significant correlation between the two ($r=0.15$, $p=0.40$).

The mean initial haemoglobin and initial leucocyte count were 14.8g/dl (1 SD = 1.8) and 15,982/mm^3 (1 SD = 7,648) respectively. The haemoglobin and leucocyte count did not show any significant correlation with the serum osmolality or any other clinical or biochemical parameter.

In the search for a precipitating cause for the DKA (Fig 3) it was noted that infections dominated the clinical picture. Eight episodes were attributable to the patients themselves stopping their insulin. The patients had stopped insulin for a variety of reasons including depression, being "fed-up" and a feeling that they were well enough not to require insulin. Amongst infections, uro-genital tract infections predominate. It was present in nearly a third of the patients.

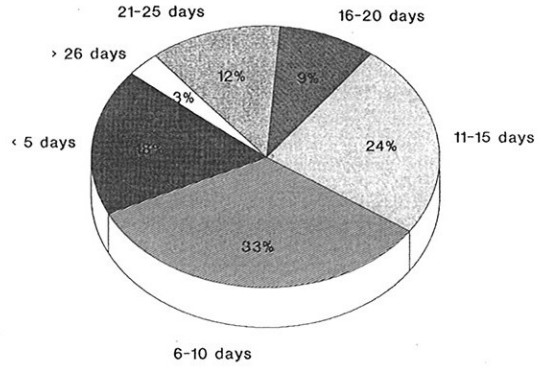
Outcome of Treatment

Of 33 hospitalisations, 4 patients succumbed to death. Death was due to uncontrolled septicaemia despite good glucose control and stabilisation of their ketoacidotic state. The mean duration for the blood sugar level to reach value of less than 250 mg/dl was 9.5 hours (1SD = 4.4). The mean insulin requirement to achieve this target value was 52.4 units (1SD = 29.6). The duration of hospitalisation for the episodes of diabetic ketoacidosis is shown in Fig 4. The mean duration of hospitalisation was 11 days. All patients who were discharged from hospital showed no evidence of complications of ketoacidosis.

DISCUSSION

Diabetic ketoacidosis continues to be common with a relatively constant incidence in the western countries despite an improvement in general medical care[4]. While this is not an epidemiological study, the incidence of 33 episodes over a 18-month period seen in one medical unit certainly highlights the extent of the problem. It must be borne in mind that this represents only small proportion of patients admitted for diabetes mellitus and its related complications[5]. As in other studies the incidence of ketoacidosis was higher in the elderly[6]. The

Fig 4 - Duration of Hospitalisation*



* inclusive of 4 patients who died at 2,4,10 and 11 days respectively

higher representation of females presenting with ketoacidosis is true of most series as in this one[7]. The higher proportion of Malays presenting with ketoacidosis cannot be accounted for purely by the increased number of Malay patients seen in this hospital. A subsequent study[5] of 135 diabetic patients (57 males and 78 females) admitted over a 2-month period to the same medical unit revealed an ethnic distribution of 64.4% Chinese, 18.5% Indians and 17.5% Malays.

In this series 18.1% of our patients never knew they had diabetes mellitus and were diagnosed for the first time during an acute presentation. This figure is probably diluted by the fact that this analysis takes into account only patients above the age of 12 years - as those younger would have been admitted to the paediatric wards. The typical symptoms related to uncontrolled hyperglycaemia dominate the clinical presentation. We believe that this figure may actually be higher as a high proportion of patients (60.6%) on clinical examination are found to be confused or comatose. Even if the patients recover from their ketoacidotic state, they may be unable to recall all their symptoms. Slightly more than half of our patients had nausea and vomiting. These are the individuals who require more than their daily requirements of insulin. This point is worth reminding our patients when talking to them about sick days. Abdominal pain as presenting feature in diabetic ketoacidosis is not uncommon, occurring in about 15% of episodes[8-10]. The complaint is present in 18% of our patients. The pain has been attributed to gastric distention or stretching of the liver capsule. Occasionally, it can even simulate an acute abdomen, as in one of our patients who was admitted to the surgical wards. Where the index of suspicion is high, this helps in preventing unnecessary surgery. Hyperventilation could reflect one of two possibilities - one of compensation for metabolic acidosis or as in 7 DKA episodes, a pneumonia. The presence of clinically detectable dehydration in almost all the episodes of the diabetic ketoacidosis is not surprising. In DKA, patients may lose fluid easily throgh osmotic diuresis, vomiting, fever and hyperventilation. They may easily have a deficit of between 5 to 10 litres[11].

The lack of biochemically demonstrable hypokalaemia in patients with DKA is not unexpected. Despite their total body potassium deficit, studies have shown that only in 4-10% of patients is the plasma potassium less than normal[12,13]. The apparent normokalemia is thought to be primarily due to shift of potassium extracellularly in response to the acidotic state.

Only in two-thirds of the DKA episodes was acidotic respiration detectable. One should therefore not be led into a false sense of complacency. The degree of acidosis seen in our group of patients are similar to those documented previously[14-16]. If the severity of hyperglycaemia is directly related to the severity of acid-base disturbance a correlation would be expected between the initial plasma glucose and serum bicarbonate. However, in this series, as well as a recent one from the Mayo Clinic[17], no correlation exists. This observation is of clinical significance in that, it highlights the variability that exists in the glucose concentration in patients with established DKA. It may also account for the observations in literature of diabetic patients with ketoacidosis but blood sugar levels below 300 mg/dl; an entity termed "euglycaemic ketoacidosis"[18]. Although, by definition, our criterion for diagnosis of DKA excluded patients with euglycaemic ketoacidosis, we did not encounter any such patients during the study period.

The high mean serum osmolality at presentation is not surprising in view of the marked dehydration in most of these patients. This study also documents previous observations that disturbance of consciousness is most closely linked to the degree of dehydration[3,19].

Another pitfall for the unwary is the absence of fever in proven sepsis - fever was present in only 12 patients of the 19 shown to have sepsis of some sort or another. Several studies have emphasised the importance of infection as the precipitating cause of DKA since signs of infection have been observed in more than 50% of cases[20-22]. Eight of the episodes could probably have been prevented if those patients had not stopped their regular insulin injections. The morbidity and mortality from diabetic ketoacidosis continues to be disturbing. During the 33 episodes of DKA, the average duration of hospitalisation was 11 days - this is about double the average duration of hospitalisation in Singapore. We had a mortality of 12.1% which compares with the average mortality of about 0-20% described in the diabetic literature[10]. Despite achieving good blood sugar levels and correction of metabolic acidosis we lost these patients to uncontrolled sepsis.

CONCLUSION

Definitions of DKA vary. Even with all the clinical and biochemical data available it is an arbitrary definition. Inevitably different definitions have been used in different studies so it is important to appreciate the severity of the ketoacidosis when interpreting results from different centres. Diabetic ketoacidosis is not uncommon. One should not be led into a false sense of complacency even if symptoms and signs are absent. A high index of suspicion is necessary both on the part of the patient and his doctor. Prevention is the main key towards reduction of mortality and morbidity in diabetic ketoacidosis. The cornerstone of prevention should be achievement of euglycaemia, guided by adequate monitoring. However, despite good control some patients react differently to stressful situations like a florid infection, in which case the diabetes should not be neglected - it is important to control the hyperglycaemia and be on the lookout for a developing emergency as well as to get the infection treated. Once ketoacidosis is diagnosed a vigorous search should be made for a source of sepsis and if infection is identified aggressive antimicrobial treatment is warranted. A study of this nature cannot address the question on the routine use of broad spectrum antibiotics and if the use could have prevented the mortality. But losing four of the patients to septicaemia does prompt the need for further studies on this aspect. The institution of continuous intravenous insulin is safe and effective in the control of hyperglycaemia.

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