RISK FACTORS OF DIABETIC KETOACIDOSIS; CASE-CONTROL STUDY

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is a life threatening complication of Diabetes Mellitus. Diabetic ketoacidosis requires early detection, prompt assessment and immediate management. For institution of preventive measures, knowledge of risk factors present in local circumstances is pre-requisite. **Objective:** Our study was planned to identify the various risk factors of diabetic ketoacidosis and to determine outcome of patients during these episodes. **Patients & Methods:** This Case-Control Study was carried out in the Department of Medicine, Bahawal Victoria Hospital, Bahawalpur, from 1st September, 2010 to 29th February, 2012. Hundred diabetic patients aged >13 years were included. Fifty consecutive patients admitted with diabetic ketoacidosis were enrolled as cases. For each case an age and sex matched control was selected. Controls were the diabetics not having ketoacidosis. Primary end points were noted i.e. (a) Patients died in emergency room or during ward stay. (b) Patients discharged alive. The statistical analysis was done using SPSS Version 16. Multivariate analysis was carried out by comparing cases and controls. Odds ratios (ORs) for each suspected risk factor were calculated. Confidence Interval (CIs) and significance of ORs was determined through Multiple Logistic Regression Analysis. **Results:** Our study included 100 patients, 50 cases with ketoacidosis and 50 control patients. It was noted that 54% were males in each group. Maximum incidence of DKA was observed in 4th decade. 90% patients with DKA were discharged alive while 10% patients died. Cases were more likely to have infections (50 percent vs 18 percent, $P< 0.001$), poor compliance with treatment, (44 percent vs 12 percent, $P<0.001$) and newly diagnosed diabetes (16 percent vs 4 percent, $P <0.063$) as compared with controls. Other risk factors identified were trauma (2%), dehydration (2%), acute pancreatitis (2%), myocardial infarction (2%) and stroke (2%). In multivariate analysis, factors associated with a significantly increased risk of DKA were, poor compliance with treatment (Odds ratio 5.762 [95 percent confidence interval, 2.079 to 15.970]), infections (Odds ratio 4.556 [95 percent confidence interval, 1.834 to 11.316]) and recent onset diabetes (Odds ratio 4.571 [95 percent confidence interval, 0.919 to 22.729]). **Conclusion:** The risk for precipitation of Diabetic Ketoacidosis significantly increases due to infections, poor compliance with treatment and in patients with new onset diabetes.

Key words: Diabetic Ketoacidosis, Diabetes Mellitus, Risk factors

INTRODUCTION

Diabetic ketoacidosis is a major medical emergency characterized by hyperglycaemia, ketonaemia and acidosis. Ketoacidosis is caused by insulin deficiency and increase in the catabolic hormones i.e. glucagons, catecholamines, growth hormone and cortisol.[1] These lead to hepatic overproduction of glucose and the ketone bodies, impaired glucose uptake and utilization by muscle.[2] Most cases of diabetic ketoacidosis occur in patients with type 1 diabetes. It may be the presenting feature of the disease. It may occur in known diabetics who stop taking insulin or take insufficient amounts of insulin.[3]

Diabetic ketoacidosis should be suspected in any individual with mental obtundation, dehydration or acidosis. The complications of diabetic ketoacidosis include cerebral oedema, acute respiratory distress syndrome, thromboembolism, disseminated intravascular coagulation, circulatory failure, mucormycosis, and various metabolic derangements.[4,5] Mortality from diabetic ketoacidosis in developed countries ranges from 2%-5%.[6] In developing countries, diabetic ketoacidosis has 6%-24% mortality.[7] In Pakistan, two hospital based studies reported the mortality rate of 7.15% and 15.9% respectively.[8,9] Due to significant morbidity and mortality, prevention should remain the main focus in diabetic patients. Good critical care management is required when condition arises.[10]

Since no such study has been conducted in our region on risk factors of Diabetic Ketoacidosis, the present study has been envisaged to identify various risk factors of diabetic ketoacidosis and to determine outcome of the patients during episodes of diabetic ketoacidosis.

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PATIENTS AND METHOD

This case-control study was conducted in Department of Medicine, Bahawal Victoria Hospital, Bahawalpur from 1st September 2010 to 29th February 2012. Fifty consecutive patients of diabetic ketoacidosis (Cases) aged >13 years, diagnosed on the criteria (Typical clinical features e.g. dehydration, vomiting, hyperventilation, fruity smell of acetone in the breath), blood sugar level above 11.1mmol/l, ketone bodies positive in urine, blood pH < 7.3 and serum bicarbonates <15 mmol/l) were included.

For each case an age and sex matched control was selected. The controls were the diabetics not having ketoacidosis. Controls were selected from the outpatient and the emergency departments. The duration of Diabetes Mellitus was also matched to the nearest year. Consent was taken from the patients attendant and then by the patient after gaining consciousness.

Patients with evidence of other causes of metabolic acidosis and coma like Drug overdose, Hypoglycemia, Non-ketotic hyperosmolar coma, Hyponatremia, Uremia, Hepatic failure and Respiratory failure were excluded. A detailed history and thorough physical examination was done. Various investigations both laboratory and radiological were done to sought out the risk factors in the cases. Outcome (i.e. Patient died during hospital stay or the patients discharged alive) were noted. Duration of hospital stay was noted. All the above information was recorded in a pre-designed structured proforma. The statistical analysis was done on SPSS Version 16. To identify the risk factors multivariate analysis was carried out by comparing cases and controls. Odds ratios (ORs) for each suspected risk factors were calculated. Confidence Intervals (CIs) and significance of ORs was determined through multiple logistic regression analysis.

RESULTS

Characteristics of the cases

Out of totals, 54% were males 46% were females, and between 14 and 68 years of age. Mean age was 43.12 years (standard deviation $\pm$ 12.6). Maximum incidence of DKA was noted in 4th decade (44%). Thirty two patients (64%) were type-1 diabetics and ten patients (20%) were type-2 diabetics while eight patients (16%) had no previous history of diabetes. Maximum duration

of diabetes was 35 years with mean duration of diabetes of 18 years (standard deviation $\pm$12.38) (Table I). The risk factors identified among cases in our study were infections in 25 (50%), poor compliance with therapy 22 (44%) and newly diagnosed diabetics were 8 (16%).

Table I: Demographic Data

Sex	Daibetic Ketoacidosis cases		Control	
	Male	Female	Male	Female
	27(54%)	23(46%)	27(54%)	23(46%)
Age in Years (mean± 1SD)	43.12±12.6		42.56±12.8	
Type I Diabetes	32(64%)		24(48%)	
Type II Diabetes	10(20%)		26(52%)	
Newly diagnosed diabetes	8(16%)		2(4%)	

Trauma 1(2%), dehydration 1(2%), myocardial infarction 1(2%), acute pancreatitis 1(2%) and stroke 1(2%) were the other risk factors identified. More than one risk factor was identified among 10 (20%) of the cases.

Table II: Risk Factors for Diabetic Ketoacidosis

	Daibetic Ketoacidosis	Control Group	Odds Ratio	95% CI	P Value
Poor Compliance	22 (44%)	6 (12%)	5.762	(2.079-15.970)	P<0.001*
Infections	25 (50%)	9 (18%)	4.556	(1.834-11.316)	P<0.001*
Recent onset DM	8 (16%)	2 (4%)	4.571	0.919-22.7	P<0.06*
Trauma	1 (2%)	0	0.503	(0.000-4.3)	P=0.780*
Dehydration	1 (2%)	0	0.503	(0.000-4.3)	P=0.780*
Myocardial infarction	1 (2%)	0	0.503	(0.000-4.3)	P=0.780*
Acute pancreatitis	1 (2%)	0	0.503	(0.000-4.3)	P=0.780*
Stroke	1 (2%)	0	0.503	(0.000-4.3)	P=0.780*

Characteristics with P value less than 0.05, according to matched multivariate logistic regression were considered to be associated with a significantly increased risk of diabetic ketoacidosis. Fourteen (28%) of the cases developed complications during emergency management which included hypoglycemia in 8 and electrolyte imbalance in 6. Five (10%) patients developed complications during ward stay which included DVT in 1(2%), aspiration pneumonia in 1 (2%), nosocomial infections in 2 (4%) and septicemia in 1 (2%). Five patients (10%) died while 45 patients (90%) were discharge alive in stable condition.

Characteristics of controls

For each case an age and sex matched control was selected. Twenty four patients (48%) were having type 1 diabetes and 26 (52%) were type 2 diabetics

(Table-I). Risk factors for diabetic ketoacidosis present among controls were infections in 9 (18%), poor compliance with treatment in 6 (12%) while 2 (4%) patients were newly diagnosed.

Case control analysis

In multivariate analysis, three factors remained significantly associated with increased risk of diabetic ketoacidosis: Poor compliance with treatment (Odds ratio 5.762; P<0.001), infections (Odds ratio 4.556; P<0.001) and recent onset diabetes (Odds ratio 4.571; P<0.06). Trauma, dehydration, myocardial infarction, acute pancreatitis and stroke were not significantly associated with risk of diabetic ketoacidosis.

DISCUSSION

We performed a case control study to identify various risk factors of diabetic ketoacidosis. It is evident that DKA can occur both in type 1 diabetics and type 2 diabetics, but commonly in type 1 diabetics in whom there is destruction of the beta cells of the islet of pancreas.[11] It is a presenting feature in some type 1 diabetics in whom the disease was not previously detected. Though DKA is not the presenting feature in type 2 diabetics but it can be precipitated by some sort of stress like infections, trauma etc.[12]

The most common risk factors identified in our study were infections (50%), poor compliance with treatment (44%) and as a presenting feature in patients in whom diabetes was not previously diagnosed (16%). The risk factors reported in study by Naveed D et al, were infections (50%), Non-compliance to treatment (26.19%), co-morbid states (21.43%) and diabetic ketoacidosis as first presentation (2.38%).[9] Seyoum B et al, reported newly diagnosed diabetes (23%), non-compliance (59.1%), infections (16.1%) and other medical illnesses (3.5%).[13] Lin S F et al, reported infections as risk factor in 70% of their patients with diabetic ketoacidosis.[14] Ahmad F et al, reported non-compliance (54%) and infections (28%) as major risk factors.[15] Bashir T et al, reported infections (40%) as major risk factor.[16] Zafar N et al, in their study reported infections (45.5%) and non-compliance (11.4%).[8] Diabetic population neglect minor infections and minor trauma which lead to the devastating consequences. Majority have misleading concepts about the 'sick day' management. This is probably due to unawareness about the disease, lack of education, misleading by the unqualified health care providers.[17,18] Poor compliance with treatment is due to poverty, proper knowledge of dosage and administration of insulin, improper maintenance of the cold chain, and unavailability of pure form of insulin.[19,20]

The mortality in our study was 10%. Naveed D et al, reported mortality of 7.15%.[9] Zafar S et al, reported mortality of 5%.[15] Mahmood K et al, reported mortality of 11.9%.[12] Ahmad et al, reported mortality of 15%.[8] In the Western World the mortality rate due to DKA ranges between 2%-5%.[6] In the third world countries like ours the mortality ranges from 6-24%.[7] The reasons for the high mortality in our study may be delay in the start of treatment as these patients (60%) reported late for treatment i.e. after 48 hours from the onset of symptoms. Presence of sepsis in one patient (2%) and associated myocardial infarction and in one patient (2%). The limitation of our study was that the sample size was not large enough to analyze all the identified risk factors for their statistical significance. However, infections and poor compliance showed statistical significance, whereas, newly diagnosed diabetes has just significant association. Trauma, dehydration, myocardial infarction, acute pancreatitis and stroke did not show statistical significance as none of the controls has these risk factors.

CONCLUSION

Our study revealed important risk factors associated with diabetic ketoacidosis are infections, poor compliance with treatment and newly diagnosed diabetes. More than one risk factors may be present in one patient. Few cases have no obvious precipitating cause. If not properly managed, it can lead to devastating consequences and mortality rates are very high.

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