Original Research Paper

Volume - 13 | Issue - 04 | April - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Medicine

CLINICO-BIOCHEMICAL PROFILE AND HOSPITAL BASED OUTCOME OF PATIENTS WITH DIABETIC KETOACIDOSIS ADMITTED IN A TERTIARY CARE INSTITUTE IN ASSAM

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ABSTRACT **BACKGROUND** Diabetes mellitus is a metabolic disorder which is characterized by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. Globally, the prevalence of diabetes among adults is estimated to be 537 million in 2021 and is expected to be 783 million by 2045. Most patients with DKA recover when treated appropriately but if remained untreated, may lead to complications and rise in mortality and morbidity. Hence, early identification of ketoacidosis and aggressive management with insulin, intra-venous fluids and electrolytes replacement may change the outcome of the disease. **METHODOLOGY** A hospital based observational study recruited 60 patients of age more than 12 years admitted under the Department of Medicine, GMCH with Diabetic Ketoacidosis from 1stJuly 2020 to 31st June 2021. **RESULTS** DKA was seen in all the age groups but predominantly in middle-aged patients in 41-50 years age group (28%) with male predominance (Male:Female ratio =1.7:1). The incidenceof DKA was more among Type 2 Diabetes (76.7%) than with Type 1 Diabetes (23.3%) . Mortality of patients in the study was found to be 18.3%, which was higher in comparison to standard literature. Most of the patients in the study presented with nausea, vomiting and pain abdomen (28.30%). Sepsis and inadequate therapy (31.6% and 20.0%) were the leading precipitating cause of DKA Among the patients, 33.33% presented with severe DKA at the time of presentation and it was also observed that there is significant correlation between severity of the disease and mortality ($P < 0.05$). Patients with Poor GCS, raised serum creatinine, blood urea, serum calcium, alanine transaminase, aspartate transaminase and total serum bilirubin has significant correlation with mortality (P value <0.05). However, the body mass index, blood sugar, pH, serum bicarbonate, sodium, potassium, magnesium, albumin, triglyceride, glycosylated haemoglobin, total leucocyte count and haemoglobin levels at the time of presentation do not have a significant correlation with mortality (P value >0.05). **CONCLUSION** It was observed from our study that contrary to standard literature, the incidence of DKA is more common in adults than children. DKA was significant in patients with type 2 diabetes in our series of patients and hence further studies are necessary to re-evaluatethis observation. **CONFLICT OF INTEREST** None

KEYWORDS : Diabetes, Diabetic ketoacidosis

INTRODUCTION

Diabetes mellitus is a metabolic disorder which is characterized by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both leading to disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both [1].

Globally, the prevalence of diabetes among adults aged 20-79 years is estimated to be 537 million (10.5% of all adults in this age group) in 2021. The number of diabetics is increasing globally with each decade and is expected to be 783 million by 2045 2. The burden of the disease is also increasing in India over the years. Data obtained from various cross-sectional studies conducted in various parts of the country reports that Diabetes is becoming more prevalent in India [3].

A state level report on the disease burden in India stated that among all ages from 1990 to 2016, the percentage change in prevalence was 64.3%, whereas the age-standardised prevalence was 29.3% 4. Another study on the prevalence and number of people with diabetes in India reported a rise from 5.5% and 26.0 million in 1990 to 7.7% and 65.0 million in 2016 [5].

Diabetic Ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS) are two states of severe hyperglycemia (> 250 mg/dL) associated with both Type 1 and Type 2 Diabetes Mellitus (DM)[1].

The precipitating factors for pathogenesis of DKA are sub optimal insulin dosage, insulin or oral anti-diabetic drugs omission, infections like respiratory tract infections, genito-urinary tract infection, etc, myocardial infarction and cerebrovascular accidents such as ischemic and haemorrhagic stroke [6].

Patients with DKA usually presents with symptoms of polyuria, thirst, reduction in weight, generalized tiredness, nausea, vomiting, blurring of vtld extremities, peripheral cyanosis, tachycardia, air hunger (Kussmaul's breathing), smell of acetone, hypothermia, confusion, drowsiness, and coma at the time of presentation [7].

Most patients with DKA recover when treated appropriately but if untreated, patients may develop complications such as cerebral oedema, electrolyte abnormalities, thromboembolism, acute respiratory distress syndrome (ARDS), disseminated intra vascular coagulation (DIC), myocardial infarction, infections, and acute circulatory failure.

Hence, early identification ketoacidosis and aggressive management with insulin, intra venous fluids and electrolytes replacement may change the outcome of the disease.

METHODOLOGY

This study is a single centred, prospective study on 60 patients of age 12 years and above who presented with diabetic ketoacidosis in the Department of Medicine, Gauhati Medical College and Hospital, Guwahati, Assam during a period of 12 months (1st July 2021 to 30th June 2022).

The diagnosis of DKA was made in the emergency department by the presence of 3 laboratory findings: plasma glucose level of 250 mg/dL or higher, serum bicarbonate level of 15 mEq/L or lower and arterial blood pH of 7.30 or lower, or/ and moderate or large urinary ketones. Inclusion criteria included atients who were admitted in the study centre with age of above 12 years and were diagnosed to have diabetic ketoacidosis at the time of presentation. Exclusion criteria icluded post-cardiopulmonary resuscitated patients, late stages of chronic kidney disease, severe left ventricular dysfunction, terminal stages of cancer, decompensated chronic liver disease, ketotic states such as alcoholic ketosis and starvation ketosis, lactic acidosis, hyperchloremic acidosis, drug or toxin Induced acidosis, COVID-19 patients The patients were documented at the time of examination through history and clinical examination under the following headings :- Age, Sex, Glasgow coma scale of patients at the time of presentation was recorded and divided into severity of brain injury (Mild, Moderate and Severe), type of diabetes, duration of Diabetes Mellitus, treatment history, previous episodes , comorbidity, clinical Features, severity of diabetes, BMI and precipitating factor.

The following initial biochemical investigations sought on admission:- Random blood sugar, Serum Elecrolytes (Sodium, potassium, Calcium, Magnesium, Phosphate), Urine Acetone, Blood urea and Serum creatinine, ABG, routine blood investigation (Total

Count, Haemoglobin, Platelet), Lipid profile and Liver function test (AST, ALT, Total bilirubin)

Data was entered into Microsoft Excel. Statistical analysis was done using software IBM SPSS-version 26. Data were expressed as mean with standard deviation. Categorical values were reported using number and percentage and statistical analysis performed. Probability value (p valve) less than 0.05 was considered as statistically significant.

RESULTS

DKA was seen over all the age groups but predominantly in middle-aged patients 28% in 41-50 years age bracket, male participants (Male:Female ratio =1.7:1)and among type 2 DM (76.7%) . Among this study population, elder patients had significant mortality.

The mean duration of diabetes of the study population is 5.05±4.72 years and most of the participants in our study population was previously treated with oral hypoglycemic agents (36.7%). It was observed that hypertension (26.7%) was the most common comorbidity followed by coronary artery disease (5.0%). The average BMI of patients was 25.71+4.71 but it has no significant correlation with outcome.

Most of the patients in the study presented with nausea, vomiting and pain abdomen (28.30%). Sepsis and inadequate therapy (31.6% and 20.0%) were the leading precipitating cause of DKA Among the patients, 33.33% presented with severe DKA at the time of presentation and it was also observed that there is significant correlation between severity of the disease and mortality (P <0.05).

Mortality of patients in the study was found to be 18.3%, which was higher in comparison to standard literature.

Initial presentation among patients with DKA		
Presentation	Frequency	Percentage
Altered mental status	14	23.3
Diarrhoea	5	8.3
Fever	9	15
Nausea, vomiting and pain abdomen	17	28.3
Seizures	4	6.7
Shortness of breath	11	18.3
Total	60	100

Correlation between the severity of Diabetes and death as outcome			
DKA Severity	Discharged	Deaths	Total
Not severe DKA	38	2	40
Severe DKA	11	9	20
Total	49	11	60
P value = 0.0001			

	Mean value of discharged patients	Mean value of expired patients	P value
BMI	25.71±4.71	27.55±3.83	0.231
Random Blood Sugar	431.31±106.13mg/dL	467.36±98.45mg/dL	0.307
pH	7.15±0.11	7.10±0.10	0.224
Serum bicarbonate	8.81±3.39mmol/L	10.07±3.13mmol/L	0.262
Blood urea	38.55±18.65 mg/dL	82.00±18.41 mg/dL	<0.001
Serum creatine	0.88±0.44 mg/dL	1.79±0.32 mg/dL	<0.001
Sodium	134.961±7.01 mg/dL	137.73±11.36mg/dL	0.300
Potassium	4.37±1.12 mg/dL	3.99±1.02 mg/dL	0.311
Calcium	8.20±0.55 mg/dL	7.81±0.71 mg/dL	0.048
Magnesium	2.90 ±1.07 mg/dL	2.43±0.81 mg/dL	0.170
Aspartate transaminase	38.10 ±14.14 mg/dL	152.55±132.34 mg/dL	<0.001
Alanine transaminase	41.76 ±16.94 mg/dL	151.45±135.04 mg/dL	<0.001
Total serum bilirubin	0.72±0.39 mg/dL	1.25±0.70 mg/dL	0.001
Serum albumin	3.98±0.80 mg/dL	4.31±1.19 mg/dL	0.268
Triglyceride	171.41±110.04 mg/dL	185.64±89.64 mg/dL	0.691
HbA1c	9.95±2.57%	10.17±2.95%	0.798
Total leucocyte count	10393.88±3922.55 cells/mm3	12963.64±5364.94 cells/mm3	0.072
Hemoglobin	12.48±1.89 g/dL	11.46±1.48 g/dL	0.102

Poor GCS has a significant correlation with outcome. The mean RBS and HbA1c level of the participants in our study was 437.92+104.89 mg/dL and 9.98+2.28% respectively but they have no significant correlation with mortality. it was observed that there is significant correlation of increased serum osmolality (>320mOsm/L) and mortality as outcome. The mean blood pH and serum osmolality among the patients with DKA is 7.14+0.11 and 9.04+3.35 mmol/L respectively but they have no significant correlation with mortality.

In this study, the mean blood urea and serum creatine levels among the patients with DKA is 46.52+25.05 mg/dL and1.05+0.55 mg/dL respectively, and they have a significant correlation with mortality. The mean Serum sodium and potassium in the study was 135.46+7.94 mg/dL and 4.29+1.10 mg/dL respectively, and they have a significant correlation with mortality. The mean Serum calcium in the study was 8.13+0.59 mg/dL. The mortality in DKA have a significant correlation with the serum calcium levels of the patient in our study. The mean Serum magnesium in the study was 2.81 +1.04 mg/dL and the mortality in DKA does have a significant correlation with the serum magnesium levels. In our study, the mean serum AST, ALT and total bilirubin is 59.08+71.59 mg/dL, 61.87+71.80 mg/dL and 0.81+0.49 mg/dL, and they have a significant correlation with the outcome. In this study, the mean serum albumin and triglyceride among the patients with DKA is 4.04+0.88 mg/dL and 174.02+106.03 mg/dL. However, they have no significant correlation with mortality. The mean Total leucocyte count and hemoglobin count among the patients with DKA is 10865.00 + 4289.71 cells/mm3. And 12.29+1.85 g/dL respectively but they have no correlation with mortality in this study.

DISCUSSION

In this study, majority of the patients (28.30%) presented with nausea, vomiting or pain abdomen, followed by altered mental status(23.30%). Sepsis is the most common precipitating factor (31.6%) followed by inadequate therapy (20%) and poor compliance (16.7%)and the results were comparable with results of studies done by Dhatariya KK et al 6, George JT et al, 2018 8, Ahuja W et al, 2019 9 and Almalki MH et al, 2016 10 in which the two foremost precipitating cause was infection and poor adherence to therapies.

The mortality of patients (18.3%) in this patient is much higher compared to many other similar studies like Wu XY et al, 2020 11 who had zero mortality among DKA patients.

The possibilities for higher mortality could be that, in our study most of the participants were of older age group and being an apex institute in the region, many of the patients were referred late in the course of disease. However, further studies are necessary in this regard to ascertain the higher cause of mortality in the study. 33.33% of the patients had severe DKA at the time of presentation while 66.76% did not have severe DKA, which correlates with the study conducted by George JT et al, 2018 8. The severity of Glasgow Coma Scale has a significant correlation with mortality in our study (p= <0.001). This is however, not consistent with the study conducted by Agarwal A et al, 2016 (p = 0.076) 12.

The HbA1c and Random blood glucose, blood pH and serum bicarbonate level of the participants in our study has no correlation with mortality,which is consistent with the study conducted by Agarwal A et al, 2016 (p = 0.716), Gibb et al, 2016 (p=0.220), Ooi E et al, 2021 (p = 0.4496) 12, 13, 24. Trends similar to Agarwal A et al, 2016 (p = <0.001) 12 and Gibb et al, 2016 (p=0.002) 13 was observed in our study in which there is significant correlation between blood urea, serum creatinine and mortality. Among serum electrolytes, sodium, potassium and magnesium has no correlation with mortality, however elevated calcium levels in serum has.

The mean serum aspartate transaminase, alanine transaminase and serum bilirubin derangements have significant mortality which is consistent with a study conducted by Agarwal A et al, 2016 ($p < 0.001$) 12 but not with serum triglyceride, hemoglobin levels and total leucocyte count.

In this study, the mean Hemoglobin among the patients with DKA is 12.29+1.85 g/dL. Hemoglobin levels of the patient does not have significant correlation with mortality in this study (p value = 0.102), which is consistent with a study conducted by Agarwal A et al, 2016 (p=0.437) 12.

CONCLUSION

The present study was an initiative to know the clinical and biochemical profile of patients presenting with diabetic ketoacidosis and their hospital-based outcomes in terms of mortality in this part of India, where a pilot study is still lacking. The demographic profile of the patients; clinical presentation and biochemical reports were assessed.

It was concluded from our study that contrary to popular belief, the incidence of DKA is more common in adults than children. There is also a significant proportion of patients with type 2 diabetes who presented with DKA. Hence, a re-evaluation might be necessary regarding the popular belief that DKA is more common in young T1 DM patients Patient counselling is also necessary to prevent DKA as the two most frequent precipitating cause is found to be sepsis and inadequate or noncompliance to therapies. Mortality in DKA has a significant correlation with increased age, severity of DKA, BMI, Glasgow Coma Scale, Serum osmolality, urea, creatinine, Serum calcium, AST, ALT and total bilirubin at the time of presentation; but has no correlation with gender, RBS, pH, bicarbonate, sodium, potassium, magnesium, phosphate, albumin, triglyceride, total leucocyte count, haemoglobin, or HbA1c at the time of presentation of the patient.

Therefore, while evaluating a patient of DKA the clinician should not only restrict himself to the management of the hyperglycaemic crisis only but also keep an watchful eyes on the biochemical parameters to reduce in-patient mortality in DKA.

Our study was a small sample sized hospital based observational study, which by default carries some inherent fallacies from statistical point of view. In future, we hope a prospective randomized controlled study will help in better understanding of this complex disease process and would improve the diabetic patient care to a greater level.

Another limitation was that, this study was done during the COVID-19 pandemic which led to reduction of sample size and may have an impact on the sample size and the results generated from our data.

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