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Original Research Paper

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TRENDS OF VARIOUS PRESENTATIONS AND PRECIPITATING FACTORS OF DIABETIC KETOACIDOSIS

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ABSTRACT

Background: Diabetes Mellitus a chronic disease resulting from hyperglycemia and diabetic ketoacidosis. Diabetic ketoacidosis (DK) is a deadly complication characterised by increase in plasma glucose levels with dehydration, acidosis and ketone bodies in urine. The aim is to study various presentations, seasonal variation and precipitating factors attributing to diabetic ketoacidosis. **Materials and methods:** This is a prospective observational study of 290 consecutive patients admitted in a tertiary care hospital of Government Medical College, Aurangabad, MS, India. **Results:** According to the study, Out of 290 patients, 147 patients were females and 143 being males; Male to female ratio is almost 1:1. The most common symptom at the time of admission was nausea/vomiting in 157 patients (54%) followed by fever found in 122 patients (42%). Most common risk factor for diabetic ketoacidosis surveyed was infections in 137 patients (46%) followed by non-compliance of medications in 76 patients (26%). There was no significant seasonal variation found in incidence of ketoacidosis. **Conclusion:** Diabetic ketoacidosis is a deadly syndrome of symptoms if not attended timely. The sizable patients of 290 nos. helped in the current study to understand the various expression of the disease. The most common symptom found was nausea or vomiting. Risk factor found to be commonest was infections. The study may help to counsel patients about importance of treatment adherence and early detection of symptoms.

KEYWORDS :

INTRODUCTION

Diabetes is a silent killer, it has an ability to eat a human alive. Diabetes is characterised by chronic hyperglycemia which is either due to pancreas not producing enough insulin or impaired functioning of insulin. Diabetes Mellitus is classified into type 1 and type 2 diabetes. Type 1 results due to autoimmune destruction of pancreatic beta cells and Type 2 is due to insulin resistance mostly seen in adult population.[1]

The etiopathology lies in 14 players recently discovered as Dirty Dozen Treacherous 13 Faithless 14. Dirty Dozens include the pathophysiology of liver, muscle, adipose tissue, pancreas, kidneys (SGLT2 receptors), gut (decreased in incretin), brain (neurotransmitter dysfunction), gonads (decreased testosterone), decreased dopaminergic activity and decreased vitamin D levels, increased RAS activity. 13th player is serotonin and 14th includes iron overload in beta cells.[2]

Diabetic ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS) are dangerous complications of diabetes mellitus. Diabetes ketoacidosis symptoms can often occur quickly, sometimes within 24 hours. In some cases, being thirsty, frequent urination, stomach pain, feeling weak or tired, shortness of breath, fruity-scented breath, and being confused may be the first signs of onset of diabetes.

According to a recent survey 50% of youth is being hospitalized at the onset of diabetes. In Type 2 Diabetes 40% of all newly diagnosed diabetes are in the age group of 10-20 years among Asians. Almost 30% children which are newly diagnosed with diabetes, present with diabetic ketoacidosis. Prevalence of ketoacidosis at diagnosis was 29.4% in type 1 and 97% in youth with type 2 diabetes mellitus.[3,4]

Diabetic Ketoacidosis is an acute, life-threatening complication characterized by hyperglycemia, dehydration, acidosis and ketonuria.[5] Diagnosis of diabetic ketoacidosis is done based on plasma glucose concentration of more than 250mg/dl, pH less than 7.3, bicarbonates less than or equal to 18mEq per L and positive urine ketone test.

Diabetes ketoacidosis is classified as mild when blood pH ranges between 7.25 to 7.30 and serum bicarbonate is decreased to 15- 18 mmol/L; moderate when pH ranges between 7.0 to 7.25 and serum bicarbonate decreased to 10-15 mmol/L; severe when pH goes below 7.0 and serum bicarbonate below 10 mmol/L.[6]

Table no. 1 – American Diabetes Association diagnostic criteria for DKA severity.

	Mild	Moderate	Severe
Plasma glucose	>250mg/dl	>250mg/dl	>250mg/dl
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00
Serum bicarbonate (mEq/1)	15–18	10 to <15	<10
Urine ketones	Positive	Positive	Positive
Serum ketones	Positive	Positive	Positive
Anion gap	>10	>12	>12
Mental status	Alert	Alert/drowsy	Stupor/coma DKA, diabetic ketoacidosis

Precipitating factors for pathogenesis of DKA are sub optimal insulin dose, insulin or oral antidiabetic drugs omission, respiratory tract infections, genito-urinary tract infections and other triggering infections and cerebrovascular accidents such as ischemic stroke and hemorrhagic stroke. These infections act like a trigger for diabetic ketoacidosis precipitation.[7]

Patients suffering with symptoms of polyuria, thirst, generalized tiredness, weight loss, nausea and vomiting,

blurring of vision and abdominal discomfort. Patient may have signs of dehydration like hypotension, cold extremities, peripheral cyanosis, may have tachycardia, acidotic breathing causing air hunger, hypothermia, smell of acetone, confusion, irritability, drowsiness and coma.[7]

Diabetic ketoacidosis is a recoverable complication when treated promptly and if left untreated patient may land up in complications such as cerebral edema, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), electrolyteabnormalities, throm boembolism, infections, myocardial infarction, and acute circulatory failure.

There is paucity of information on seasonal variation associated with diabetic ketoacidosis. Considering the void of information, this study was undertaken with the aims to study various risk factors associated with diabetic ketoacidosis to evaluate common presentation of diabetic ketoacidosis and to study seasonal variation of diabetic ketoacidosis.

MATERIALS AND METHODS

This is a prospective observational study of 290 consecutive patients admitted in a tertiary care hospital of Government Medical College, Aurangabad, MS, India.

The patients with known diabetics type 1 or type 2 with ketoacidosis, diabetic ketoacidosis as the first presenting symptom without any history suggestive of diabetes and accidental detection of diabetic ketoacidosis but primarily admitted for some other diseases were included in the study. Criteria for diabetic ketoacidosis was followed for the admission with hyperglycemia of more than 250mg/dl, urine ketones positive, serum bicarbonate less than or equal to 18mEq/L and blood pH less than 7.3.

Upon admission, detailed clinical history and examination was conducted with relevant investigations like complete blood count, blood sugar levels, serum electrolytes, arterial blood gas analysis, urine sugar level, urine ketone level, urine microscopy, chest Xray, ECG, and Glasgow coma scale were also analyzed.

Inclusion criteria includes patients above 12 years of age and who have given informed written consent with diabetic ketoacidosis admitted in a tertiary care hospital of Government Medical College, Aurangabad, MS, India, irrespective of type of diabetes except of gestational diabetes mellitus. Exclusion criteria include gestational diabetes mellitus, hyperosmolar hyperglycemic states, non ketotic coma and no informed written consent received.

The data was collected and analysed using one tailed Student's 't test for continuous variables and the Chi square test for categorical data. Data analysis was done by appropriate statistical method with statistical software SPSS ver.20.

RESULTS

Age distribution

In the study, minimum age and maximum age of patients observed is 13 year and 80 year, respectively. Sixty-one cases were observed in the age group of 31-40 years and 32 cases were in the age group between 51-60 years. Findings of this study are consistent with the study conducted by Balasubramanyam et al. (1999).[8]

Distribution of patients according to Sex

Out of 290 patients, 147 patients are females and 143 being males. Male to female ratio is almost 1:1

Distribution of patients according to Age of onset duration of diabetes and incidence of DKA.

Table no. 2 - Age of onset duration of diabetes and DKA incidence

Sr. No.	Duration of diabetes in years	No of DKA patient	Percentage
1.	0-5	189	65%
2.	6-10	69	23%
3.	11-15	23	8%
4.	16-20	9	3%

Mean 56.33 month; S.D.53.74 month; Range 0-240 months.

Various presentations of DKA

The most common symptom at the time of admission was nausea/vomiting in 157 patients (54%), fever in 122 patients (42%), abdomen pain/loose motion in 116 patients (40%) and shortness of breath was found in 116 patients (40%), drowsiness at the time of admission in 49 (17%) patients, polydypsia and polyuria in 20 patients (7%). Three patients were in coma. Findings of this study are consistent with study done by Rajasoorya et al.(1990).[9]

Table no.3- Clinical profile of DKA patients various presentations of DKA.

Sr. No.	Presentation	No of DKA patient	Percentage
1.	Nausea/Vomiting	157	54%
2.	Fever	122	42%
3.	Thirst/Polyurea	20	7%
4.	Abdomen Pain/Loose Motion	116	40%
5.	Shortness Of Breath	116	40%
6.	Mental Confusion	49	17%
7.	No Symptoms	0	

Precipitating Factors of DKA

Risk factors play pivotal role and need to be probed for advancing the strategies for control for the disease.

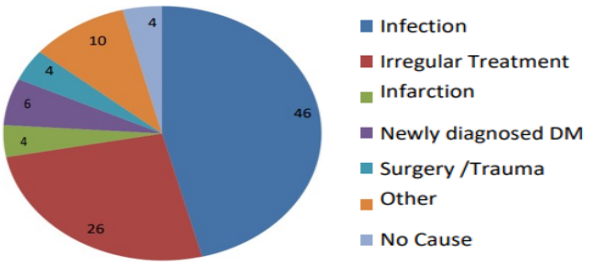
Most common risk factor for diabetic ketoacidosis surveyed was infections in 134 patients (46%), Majority of patients had respiratory tract infections (36) and urinary tract infections (27). Seventy six patients (26%) either omitted treatment or were on irregular treatment. Seventeen patients (6%) of diabetes ketoacidosis were due to onset diabetes. Infarction was seen in 12 patients (4%). Trauma or surgery was seen as a cause in 11 patients (4%). Out of thirty patients (10% of total 290 patients), 7 patients had AKI, 7 patients presented with metabolic encephalopathy, 4 patients with alcohol intoxication, 3 patients with hyponatremia, 3 patients were pregnant and 3 patients were detected with malignancy. Idiopathic or no cause was seen in 12 (4%) population.

Table no. 4 – Precipitating Factors of DKA

Sr. No.	Precipitating factors	No of patient	Percentage
1	**Infection**	134	46
	LRTI	36	
	UTI	27	
	Sepsis	24	
	Pancreatitis	9	
	Cholecystitis	3	
	Acute Gastroenteritis	6	
	Abscess	6	
	URTI	15	
2	**Irregular Treatment**	76	26
3	**Infarction**	12	4
	CVA	4	
	IHD	4	
4	**Newly Diagnosed DM**	17	6

5	**Surgery /Trauma**	11	4
6	**Other**	30	10
	AKI	7	
	Alcohol Intoxication	4	
	Hyponatremia	3	
	Pregnancy	3	
	Metabolic Encephalopathy	7	
	Malignancy	3	
7	**NO Cause**	12	4

These results were comparable with results of studies done by Matoo, (1991).[10] There was no significant seasonal variation in incidence of ketoacidosis.



Precipitating factors of DKA

DISCUSSION

Diabetes Ketoacidosis is a life threatening condition, Mastering and timely noticing the warning signs helps in creating cognition of disease symptoms and successfully treating the disease. By studying the clinical profile, risk factors, seasonal variation and precipitating factors will help in better understanding of the disease and its course.

Age distribution

Various studies have been conducted to determine the at-risk age group.

According to study done by Gaikwad (2013) [11], clinical features and risk factors of DKA in type 1 DM in tertiary care hospital in Maharashtra, India; the mean age of the patients in the study was 25.17±8.74yrs. The maximum number of patients were found in the age group 10- 20 yrs.

Table no. 5 - Age distribution of DKA in various other studies.

Sr. No.	Author	Year	No of Patients	Age Range	Mean Age
1.	Matto [10]	1991	143	8-70 yrs	21.5±4.2
2.	Balasubramanyam [8]	1999	75	<40yrs	35.5±10.1
3.	Levy-Marchal [12]	2001	1260	Below 15	8.25±4.17
4.	Neu [13]	2003	2121	Below 15	7.9 yrs
5.	Christopher	2004	108	15-66 yrs	35±12.1
6.	Lin [15]	2005	132	16-60 yrs	43.1±14.9
7.	Elmehdawi [16]	2010	81	15-68 yrs	29.2±11.6
8.	Zahara Razavi [17]	2010	48	Below 15	7.3±5.15
9.	Gaikwad [11]	2013	77	12-40 yrs	25+_8y
10.	Present Study	2019	290	13to80 yrs	40+-16.89y

As per the study the mean age of the patients being studied was 25, maximum number were from age group of 10 – 20 years. Study depicted 57.35% as males and 42.67% as females, discrepancies were multifactorial.

Sex distribution

There had been multiple gender based study to establish the disease prevalence. According to study done by Gaikwad (2013) [11], clinical features and risk factors of DKA in type1 DM in a tertiary care hospital in Maharashtra, India, females were 42.67% while the males were 57.35%.

Table no. 6 - Sex distribution of DKA in various other studies.

Sr. No.	Author	Year	No of Patients	M:F
1.	Matto [10]	1991	143	60-83
2.	Pinkney [18]	1994	230	130-100
3.	Balasubramanyam [8]	1999	75	43-32
4.	Christopher [14]	2004	108	80-28
5.	Lin [15]	2005	132	58-74
6.	Gaikwad [11]	2013	77	44-33
7.	Present Study	2019	290	143-147

The discrepancy in sex ratio was seen to be multifactorial and depends on genetic, environmental and social differences in various groups that were studied. However in this study the male to female ratio was 1:1.

Duration of diabetes and seasonal trends.

In one study the duration of diabetes varied in the following manner: Up to 1 year incidence of diabetic ketoacidosis was 2.2%, whereas in 1- 5 yrs. it was 2.8%, in 6-10yrs. it was 2.9% and >10 yrs. it was 4.3%. There was no significant seasonal variation in incidence, according to descriptive study from Maharashtra. Most of the cases of ketoacidosis occur in autumn season (19.65%), in late summer (16.55%), in spring (16.55%), (16.20) in early spring, (15.51%) in high summer and hibernal period.

According to a descriptive study by Gaikwad (2013) [11] from Maharashtra, seasonal trends and laboratory markers of DKA in type1 DM, cases of DKA were more common in spring and summer especially high summer 15.51%

Precipitating factors

According to study done by Gaikwad (2013) [11], clinical features and risk factors of DKA in type 1 DM in a tertiary care hospital in Maharashtra, India most common risk factor for Diabetic Ketoacidosis was infection followed by omission of treatment or irregular treatment. In the present study, the most common precipitating factors were infection (46%) i.e 134 cases followed by omission of treatment or irregular treatment (26%). Among infections the commonest of all infection was respiratory tract infections (36 patients), urinary tract infections (27 patients) and acute gastroenteritis (6 patients). Noncompliance i.e discontinuation of medications was observed in 76 patients.

Table no. 7 - Risk Factor of DKA in various other studies

Sr. No.	Author	Year	No of PTS	Infection	Non Compliance	Other
1.	Matto [10]	1991	143	42(30%)	29(20%)	
2.	Christopher A [14]	2004	138	21.6%	85%	
3.	Lin [15]	2005	132	47(31.7%)	41(27.7%)	24(16.2 %)
4.	Elmehdawi [16]	2010	100	30%	38%	3%
5.	Rao [19]	2012	27	60%	20%	
6.	Gaikwad [11]	2013	77	47%	44%	9%
7.	Present Study	2019	290	47%	44%	9%

Clinical Features

Clinical features are the symptoms seen in diabetic ketoacidosis with which a patient presents to emergency room. They vary from person to person and patients may come up with one or the other symptoms. In one of the study conducted by Chaisson, et al (2003) [20]. cases were observed

with symptoms of nausea (83.4%), vomiting (78.5%) polyuria (75.2%), polydipsia (74.4%), abdominal pain (51%) and polyphagia (33%). These findings were consistent C Rajasoorya et al. (1993).[9] In the study of Shaaron (2018)[21], altered sensorium occurred in 20% of population, being commonest following vomiting which occurred in 26% of diabetic ketoacidosis population. GCS calculated initially affected the outcome significantly. The worst outcome was with GCS less than 8 score.

In present study, most common symptoms at the time of admission were nausea /vomiting seen in 157 (54%) patients and fever observed in 122 (42%) patients. Abdomen pain/loose motion was found in 116 (40%) patients whereas 116 ie 40% patients experienced shortness of breath and 49 (17%) patients were drowsy at the time of admission. Polydypsia and Polyuria was found in 20 (7%) patients whereas 3 patients were in coma.

CONCLUSION

By studying the various presentations, seasonal variation and precipitating factors, patients could be diagnosed and managed properly. This also helps to counsel patients about importance of treatment adherence and early detection of symptoms.

In the present study, maximum number of cases i.e 61 cases (21%) were from age group 31- 40 yrs. Minimum number of cases i.e. 32 (11%) were from age group 51-60 years. Male to female ratio was almost 1:1. Incidence of ketoacidosis in 189 patients out of 290 were within 5 years of onset of diabetes. Duration was 2-5 years in majority of cases.

In the present study, commonest of all symptoms was nausea/vomiting in 157 (54%) patients and fever in 122 (42%) patients. Abdominal pain or loose stool was seen in 116 (40%) patients; whereas; 49 (17%) patients were found drowsy and disoriented at the time of admission. Three patients were found in coma in emergency room. Polyuria and polydypsia was found in 20 (7%) patients. Thus, most common presentations are nausea, vomiting, fever, abdominal pain and, shortness of breath.

Risk factors found in the study was infections in 137 (46%). Among infections, 51 had respiratory tract infection in majority of them and 27 had urinary tract infections. Seventy-six (26%) patients were non-compliant to medications or were on irregular treatment.

Therefore, infection was the most common precipitating factor followed by irregular treatment. Other causes include head injury, cerebrovascular accidents, ischemic heart disease and surge.

Appropriate counselling and education of patients and relatives is a keystone to prevent diabetes and related complications.

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