CLINICAL PROFILE OF DIABETIC KETOACIDOSIS: A PROSPECTIVE STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Diabetic ketoacidosis, a well-known and major acute metabolic complication classically occurs in young patients with type 1 diabetes. However, it may occur in patients with type 2 Diabetes Mellitus too. **Aim & Objective**: To study the clinical profile, precipitating factors and clinical outcome in the patients presenting with Diabetic ketoacidosis in the Emergency of a Tertiary care hospital. **Materials and Methods**: The study was a prospective study conducted over a period of one year at Dhanalakshmi Srinivasan Medical College & Hospital, Perambalur, Tamilnadu, India between June 2024- December 2024. Clinical profile of 60 diabetic patients admitted in the Emergency Department with the diagnosis of Diabetic ketoacidosis were analyzed. **Results**: Out of 60 patients, 12 were of Type 1 and 48 were Type 2 Diabetes Mellitus. Mean duration of diabetes was 8.65 years. Only 14 (23.3%) patients were taking regular treatment for Diabetes Mellitus whereas 32 (53.33%) patients were on irregular treatment and eight (13.33%) were not on any treatment at all. Among 12 Type 1 Diabetic patients, six patients were freshly diagnosed to be diabetic when they presented with Diabetic ketoacidosis complication. Nausea and vomiting (63.33%) were the most common symptoms of these patients. Infections (73.33%) were the most common precipitating factor for Diabetic ketoacidosis. Mean fluid requirement on first day of therapy was 3.51 liters. Mortality of 10% was seen. **Conclusion**: Diabetic ketoacidosis is a fatal acute metabolic complication of Diabetes Mellitus with heterogeneous clinical presentation. Early diagnosis and treatment can avoid morbidity & mortality

Keywords: Diabetes mellitus, Emphysematous pyelonephritis, Hyperglycemia, Ketosis, Non-compliance

INTRODUCTION

Diabetic Ketoacidosis (DKA) is the most serious hyperglycaemic emergency in patients with type 1 and type 2 Diabetes Mellitus (DM) and is associated with significant morbidity and mortality [1]. DKA is responsible for more than 500,000 hospital days per year [2, 3]. It is conceptualized that DKA occurs most often in patients with Type 1 diabetes but this is not true. DKA is also reported in type 2 diabetes; however, it rarely occurs without a precipitating event [4-6] Another by Adhikari et al., also showed predominance of type 2 diabetes mellitus (62.8%) as compared to type 1 diabetes mellitus (37.8%) who presented with DKA [7].DKA consists of the triad of hyperglycaemia, ketosis, and acidemia. An arterial pH of less than 7.35, a Serum Bicarbonate (HCO_3^-) value of less than 15 mEq/L, and a blood glucose level of greater than 250 mg/dl with a moderate degree of ketonaemia and/or ketonuria (as determined by nitroprusside method) are necessary for the diagnosis of DKA [8].Pathophysiology of DKA involves reduction of the effective insulin concentrations in the body which are not able to match the glycaemic overload either due to high intake or increased concentrations of counter-regulatory hormones (catecholamines, cortisol, glucagon, and growth hormone). This imbalance leads to hyperglycaemia and ketosis. Hyperglycaemia can be due to increased gluconeogenesis, accelerated glycogenolysis, or impaired glucose utilization by peripheral tissues [Table/Fig-1] [9]. DKA is a catabolic state and there is an alteration of protein, carbohydrate and lipid metabolism. The anion gap is increased from normal (8-12 mmol/L) in DKA. It has heterogeneous clinical presentation. Increased mortality and fatal complications are seen in untreated patients.DKA usually presents with symptoms like nausea, vomiting, pain abdomen. They may also have increased thirst and polyuria. On examination usually a fruity odour can be smelled and the breathing is typical of DKA, rapid shallow kussmaul breathing. Severe cases may present with hypotension, altered sensorium. Features of the precipitating cause may also be present. A study was done by Munro et al., who noticed the frequency of nausea and vomiting (86%), pain abdomen (27%), polyuria/polydipsia in 24% of patients [10]. Umpierrez et al., did a study and found abdominal pain in 46% of patients with DKA [11]. Adhikari et al., noticed vomiting and abdominal pain in 34.9% of patients, altered sensorium in 47%, kussmaul breathing in 28% and hypotension in 46% of patients with DKA [7].DKA can be the initial presentation of diabetes mellitus or precipitated in known patients with diabetes mellitus by many factors, most commonly infection [12]. Other precipitating factors include acute myocardial infarction, any cerebrovascular accident or any postoperative stress. Adhikari et al., found infection as a precipitating factor for DKA in 58% of patients [7]. Studies of Vignati et al., emphasized the importance of infection as a precipitating cause occurring in up to 50% of patients [13]. Matoo et al., and Westphal found an incidence of infection in 30% and 40% of patients

respectively [14,15]. Noncompliance is also one major precipitating factor for DKA. Matoo et al., found that incidence of non-compliance to treatment was 20% and while Westphal found it 16% [14, 15]. Often more than factors may be present in a patient or rarely no obvious factor can be identified. A study conducted by Umpierrz et al., found no obvious factor of DKA in 2-10% of cases [16].The management of diabetic ketoacidosis is complex and involves many aspects [17]. These include: A careful clinical evaluation of the patient and identification of all the metabolic abnormalities and their correction.Meanwhile all efforts should be made for identification of precipitating and co-morbid conditions and its treatment.Once acute phase is over, a comprehensive approach should be made for appropriate long-term treatment of diabetes, and plans to prevent recurrence. Another most important aspect of management is patient education so as to ensure compliance to treatment as non-compliance may lead to DKA in patients with DM [14,15].DKA is the most common acute complication in children and adolescents with Type 1 Diabetes which leads to high mortality. It accounts for almost 50% mortality in diabetic patients younger than 24 years of age [18]. Though the overall mortality is rare in adults with DKA; a higher mortality rates occur in the elderly and in patients with co-morbidities [19, 20]. Underlying precipitating illness is the major cause of death in these patients than hyperglycaemia or ketoacidosis [7, 21].This study was conducted to study the clinical profile of DKA patients. The mortality from DKA varies from 3-13%, therefore it is important to recognize DKA at an earlier stage as early recognition of DKA, leads to less complications and is associated with increased incidence of successful recovery.

MATERIALS AND METHODS

Study design: : The study was a prospective study conducted over a period of One year at Dhanalakshmi Srinivasan Medical College & Hospital, Perambalur, Tamilnadu, India between June 2024- December 2024. Clinical profile of 60 diabetic patients admitted in the Emergency Department with the diagnosis of Diabetic ketoacidosis were analyzed.

Diagnostic Criteria for Diabetic Ketoacidosis (DKA) [8]

- Blood glucose (mg/dl) > 250
- Arterial pH < 7.3
- Serum bicarbonate (mEq/l) < 15
- Moderate degree of ketonaemia and ketonuria (As determined by nitroprusside method)

Patients on steroids and other Endocrine disorders like Cushing's syndrome, Acromegaly which can also cause Hyperglycaemia were excluded from the study. The clinical profile, precipitating factors and clinical outcome was analyzed.

STATISTICAL ANALYSIS: All data obtained from the estimation were reported as the mean± standard deviation (SD) and student unpaired t-test was used for comparing mean± SD between the groups. The p value ($p< 0.05$) is considered as significant.

RESULTS: Out of 60 patients, 12 (20%) patients belong to type 1 diabetes mellitus and 48 (80%) patients belong to Type 2 DM. Among them, 34 (56.66%) were males and 26 (43.33%) were females. The male: female ratio was 1.3:1. Our study showed that only 14 (23.3%) patients were on regular treatment while 32 patients (53.33%) were on irregular treatment and eight patients (13.33%) were not taking any treatment for Diabetes. In six (10%) patients Diabetic status was detected only when they presented with DKA complication. Age and sex distribution of the patients is stated in [Table1] Clinical presentation was analysed and it was found that nausea and vomiting were present in maximum number of patients (63.33%). Symptoms related to precipitating cause were also present in a large number of patients (60%). Pain abdomen was present in (43.33%) of patients, while altered sensorium and polyuria/ polydipsia were present in 30% and 26.66% of cases respectively. Twenty (33.33%) patients were dehydrated. Weakness was present in ten (16.66%) of patients. Kussmaul breathing was present in ten (16.66%) patients. Only eight (13.33%) patients had hypotension The most common precipitating factor was found to be infection (73.33%), followed by non-compliance to treatment (66.66%), and followed by stressful conditions (26.66%). In six (10%) patients diabetic status was detected only when they presented with DKA complication and all the six patients belong to Type 1 DM [Table:2] 44 (73.33%) patients had evidence of infection, types of infections were further analyzed. Most common infection was found to be of pneumonia (18 patients, 40.90%). Four (9.09%) patients had sputum AFB positive pulmonary tuberculosis. Urinary tract infection was the precipitating cause of DKA in 12 patients (27.27%). Among them, two patients had emphysematous pyelonephritis and four patients (9.09%) with diabetic foot and two patients (4.54%) had gastrointestinal tract infection. Four patients (9.09%) had mixed infection like two patients had pneumonia and urinary tract infection and the other two had diabetic foot and urinary tract infection .Mean blood glucose at admission was 535.6 mg/dl in Type 1 and 380.07 mg/dl in Type 2 DM patients. Mean serum potassium (4.55mEq/l), arterial pH (7.23) & bicarbonate level (12.46 mmol/l) were calculated. In our study severe acidosis with arterial pH <7.0 was found mainly in Type 1 Diabetic patients with

Age range (years)	Male		Female		Total	
	No.	%	No.	%	No.	%
20-40	12	20.00	10	16.66	22	36.66
41-60	12	20.00	8	13.33	20	33.33
61-80	10	16.66	8	13.33	18	30.00
Total	34	56.66	26	43.33	60	100
Mean age (years)	51.58	51.30	51.46			

RESULTS

Table: 1 Age and Sex Distribution

Table:2 Symptomatology In Patients With Diabetic Ketoacidosis

Symptoms	Number of patients	Percentage
Nausea/vomiting	38	63.33
Pain abdomen	26	43.33
Weakness	10	16.66
Polyuria/polydipsia	16	26.66
Dehydration	20	33.33
Hypotension	8	13.33
Kussmaul breathing	10	16.66
Altered sensorium	18	30.00
Symptoms related to precipitating cause	36	60.00

Table: 3 Precipitating Factors Of Diabetic Ketoacidosis

Precipitating factors	No. of patients	Percentage
Infection	44	73.33
Non-compliance to treatment	40	66.66
Stressful condition	16	26.66
First presentation	6	10.00
Unknown	4	6.66

Table: 4 Infections Precipitating Diabetic Ketoacidosis

Infections	Number of patients	Percentage
Pneumonia	18	40.90
Pulmonary tuberculosis	4	9.09
Urinary tract infection	12	27.27
Diabetic foot	4	9.09
Gastrointestinal tract infection	2	4.54
Mixed infection	4	9.09
Total	44	100

DISCUSSION

In our study, a total of 60 patients presenting to the emergency with diagnosis of diabetic ketoacidosis were taken, out of which 12 (20%) patients belong to Type 1 DM and 48 (80%) patients belong to Type 2 DM. It is because prevalence of Type 2 DM is much higher than Type 1 DM. Moreover, in a developing country like India, due to poor socio-economic status, many patients with type 2 DM tend to have poor compliance and poor control of blood sugar levels so any precipitating factor tends to land them in a state of DKA. National Centre for health statistics and study by Adhikari et al., also showed the same [2, 7]. A recent study evaluating 138 consecutive admissions for DKA at a large academic center observed that 21.7% had type 2 diabetes [22]. In a study conducted in Taiwan, the patients attacked with DKA were predominant type 2 DM (98 vs. 39 patients) [23]. Nearly 70% of the admissions involved discontinuation of medications, and almost half had an identifiable infection when an intensive search was undertaken. S Mishra has reviewed the pathophysiology of ketosis prone type 2 diabetes in his recent article and shown that DKA is not just the feature restricted to Type 1 diabetes but can also be a complication of type 2 diabetes usually with a precipitating factor and in some races even without precipitating cause [5, 24]. Mean age of patients in our study group was 51.46 years which also points in favour

of type 2 diabetes to be causing DKA more than type 1 diabetes. Many studies support this finding. In the study by Adhikari et al., the mean age was 44.78 years [7]. Faich et al., and Kreisberg et al., studies reported that the mean age of patients admitted for DKA was between 40-50 years [25,]. Beigelman et al., study reported 47 years as the mean age of presentation for DKA [8]. Nausea and vomiting were the most common symptoms (63.33%) of DKA patients in our study, followed by pain abdomen (43.33%). One third (33.33%) of patients were dehydrated. Altered sensorium was seen in 30% of patients. 26.66% of patients were complaining of polyuria and polydipsia. Only 16.66% of patients had kussmaul breathing and 13.33% had hypotension. Symptoms related to precipitating cause were present in 60% of patients. A similar incidence of symptoms has been reported in previous studies by Munro et al., Umpierrez et al., and Adhikari et al., [7,10,11].In our study many patients had more than one precipitating factor like patients who were non-compliant to treatment also had infection and associated stressful situations like acute myocardial infarction, cerebrovascular accident, postoperative stress etc. Thus, it is seen that presence of non-compliance to treatment is an important precipitating factor which indicates that prevalence of DKA can be reduced by proper education of patients about their illness and harm of non-compliance. Welch et al., did a case study on patients with type 2 diabetes presenting with DKA and found that some precipitating factor is required in a type 2 diabetic patient to land up in DKA as similar to our study [4].Present study showed pneumonia as the most common infection precipitating DKA in 40.90% of patients. Sputum AFB positive Pulmonary Tuberculosis was present in 9.09% patients. Urinary Tract Infection was the precipitating infection in 27.27% of cases, among them, one patient had Emphysematous Pyelonephritis. 9.09% patients had diabetic foot and gastrointestinal tract infection in 4.54% of patients. Mixed infection was the causative factor in 9.09% of patients. Several factors including hyperglycaemia, leucocyte dysfunction, macrovascular disease and acidosis predispose the diabetic with ketoacidosis to common and rare infections. This is in accordance with previous studies which also showed that infection of any site is an important precipitating factor in causing DKA [13-16]. Adhikari et al., showed diabetic foot as the infection precipitating DKA in 30.23% of patients [7].The overall mortality in our study was 10% which is quite similar to other studies. Westphal found mortality of 5.1% [15], while Estimated mortality rate for DKA is between 4-10% showed by Chaisson et al, This shows that DKA in patients with type-2 DM is a more severe disease with worse outcomes compared with type-1 DM. A comparative study in patients presenting with DKA also showed that type 2 DM patients who present in DKA have significantly severe presentation and worse outcome than those who have Type 1 DM [21]. Indian studies still report mortality figures in the range of 20-30%, and hence, may constitute preventable mortality. Delayed presentation and poor socio-economic conditions which influenced the selection of better antibiotics were contributory. This study

shows that the clinical profile of patients with diabetic ketoacidosis is similar to that reported from West and other Indian studies. Delay in hospitalization, severity of acidosis and peripheral vascular insufficiency appeared to be a major risk factor for the higher mortality rate.

CONCLUSION

An active measure should be taken stressfully to rule out DKA in any diabetic and comatose patient to prevent complications and mortality, as the mortality mainly depends on the general condition of the patient, as well as the coexistent medical illness and time of onset of therapy. Therefore, education of a diabetic patient about warning symptoms of ketosis such as weakness, abdominal pain, vomiting and drowsiness are mandatory for early diagnosis and treatment.

REFERENCES

1. Kim S. Burden of hospitalizations primarily due to uncontrolled diabetes: implications of inadequate primary health care in the United States. Diabetes Care. 2017; 30:1281-82.
2. Welch BJ, Zib I. Case Study: Diabetes Ketoacidosis in Type 2 Diabetes: “Look Under the Sheets”. Clinical Diabetes. 2020; 22 (4):198-200. doi: 10.2337/ diaclin.22.4.198.
3. Misra S, Oliver N, Dornhorst A. Diabetic ketoacidosis: not always due to type 1 diabetes. BMJ. 2019; 346: f3501.
4. Balasubramanyam A, Zern JW, Hyman DJ, Pavlik V. New profiles of diabetic ketoacidosis: type 1 and type 2 diabetes and the effect of ethnicity. Arch Intern Med. 2019;159: 2317-22.
5. Adhikari PM, Mohammed N, Pereira P. Changing profile of diabetic ketosis. J Indian Med Assoc. 2017; 95(10): 540-42.
6. Kahn CR, Weir GC. In: Joslin’s Diabetes Mellitus. 13th edn. Philadelphia: Lea and Febiger, 2021: 489-507.
7. Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycaemic Crises in Adult Patients with Diabetes. Diabetes Care. 2019; 32(7):1335-43.
8. Munro JF, Campbell IW, Mc Cuish AC, Duncan LJ. Euglycaemic diabetic ketoacidosis. Br Med J. 2021; 2:578–80.
9. Umpierrez G, Freire AX. Abdominal pain in patients with hyperglycaemic crises. J Crit Care. 2022; 17: 63-67.
10. Wolfsdorf J, Glaser N, Sperling MA. Diabetic ketoacidosis in infants, children, and adolescents: a consensus statement from the American Diabetes Association. Diabetes Care. 2019; 29:1150– 2259.

11. Malone ML, Gennis V, Goodwin JS. Characteristics of diabetic ketoacidosis in older versus younger adults. J Am Geriatr Soc. 2022; 40:1100-04.
12. Umpierrez GE, Kelly JP, Navarrete JE, Casals MM, Kitabchi AE. Hyperglycaemic crises in urban blacks. Arch Intern Med. 2021; 157: 669-75.
13. Kitabchi A, Umpierraz G, Murphy M, et al. Management of hyperglycaemic crises in patients with diabetes. Diabetes Care. 2020; 24:131-53.
14. Newton CA, Raskin P. Diabetic Ketoacidosis in Type 1 and Type 2 Diabetes: Clinical and Biochemical differences. Arch Intern Med. 2019;164 (17):1925-31.
15. Umpierrez GE, Woo W, Hagopian WA, Isaacs SD, Palmer JP, Gaur LK, et al. Immunogenetic analysis suggests different pathogenesis for obese and lean African-Americans with diabetic ketoacidosis. Diabetes Care. 2020; 22:1517- 23.
16. Faich GA, Fishbein HA, Ellis SE. The epidemiology of diabetic acidosis: A population based study. Am J Epidemiol. 2021;117: 551-58.
17. Kreisberg R. Diabetic ketoacidosis. In: Rifkin H, Porte D (eds). Diabetes mellitus: Theory and practice. 4th edn. New York: Elsevier Science, 2023: 591-603.
18. Wilson JF. Diabetic Ketoacidosis- The Clinics. Ann Int Med. 2010;152 (1):ITC 1-1.
19. Vignati L, Asmal AC, Black WL, Brink SJ, Hare JW. Coma in diabetes. In: Marble A, Krall LP, Bradley RF, et al (eds). Joslin's Diabetes Mellitus. 12th edn. Philadelphia: Lea and Febiger, 2021: 526-48.
20. Matoo VK, Nalini K, Dash RJ. Clinical profile and treatment outcome of diabetic ketoacidosis. J Assoc Physicians India. 2022; 39:379-81.
21. Westphal SA. The occurrence of diabetic ketoacidosis in non-insulin dependent diabetes and newly diagnosed diabetic adults. Am J Med. 2021;101 (1):19-24. Umpierrez GE, Khajavi M, Kitabchi AE. Review: diabetic ketoacidosis and hyperglycaemic hyperosmolar nonketotic syndrome. Am J Med Sci. 2022; 311: 225-33.
22. Fasanmade OA, Odeniyi IA, Ogbera AO. Diabetes ketoacidosis: diagnosis and management: Afr J Med Med Sci. 2019; 37(2):99-105.
23. Pickup JC, Williams G. Textbook of Diabetes. 3rd edn. Massachusetts, USA:Blackwell Science. 2019. Pp. 32.1-33.19.
24. Casteels K, Mathieu C. Diabetic ketoacidosis. Rev Endocr Metabol Disord. 2021; 4:159-66.
25. Wolfsdorf J, Glaser N, Sperling MA. Diabetic ketoacidosis in infants, children, and adolescents: a consensus statement from the American Diabetes Association. Diabetes Care. 2006; 29:1150– 2259