Mortality and Prognostic Indicators in Children with Diabetic Ketoacidosis: A Study in Central India

Puja Rawat[1], Manjusha Goel[2], Sharmila Ramteke[3], Rajesh Patil[4], Rishi Dhurve[5]

1Senior Resident, Department of Pediatrics, GMC Bhopal, India
2Professor and Head, Department of Pediatrics, GMC Bhopal, India
3Associate Professor Department of Pediatrics, GMC Bhopal, India
4Assistant Professor Department of Pediatrics, GMC Bhopal, India
5JR-3, Department of Microbiology, Mahatma Gandhi Memorial Medical College, Indore, India

Corresponding Author: Rishi Dhurve

ABSTRACT

Background: Diabetic ketoacidosis is one of the most common causes of hospitalisation in children with Type I DM and the leading cause of Mortality among them. Due to limited literature and higher morbidity, this study aimed to analyse prognostic factors associated with DKA. The objective was to study the Factors determining outcomes in children presenting with Diabetic Ketoacidosis in Central India.

Methods: Thirty-nine children aged between 1 month to 12 years presenting with Diabetic Ketoacidosis were enrolled in this Study. Sociodemographic Profile, Clinical Features, Laboratory Parameters and Outcomes were recorded using a pre-tested proforma. Data was evaluated using the SPSS-PC-25 version.

Results: Poor outcome was recorded as death. A total of 7 deaths occurred out of 39 cases. Six (85.7%) out of 7 deaths occurred in patients residing in rural areas. Children aged < 2 years accounted for a total of 42.8% of deaths. Undernutrition was observed in 6 deaths (85.7%). GCS<8 was noted in 6 deaths (85.7%). Laboratory analysis showed that 6 (85.7%) out of 7 deaths had severe acidosis (pH<7.1) at admission.

Conclusion: Poor availability and accessibility of health facilities in rural areas leads to delayed diagnosis and treatment of type I Diabetes Mellitus and its complications. Nutrition is an important modifiable prognostic factor in the outcome of DKA. Cerebral oedema, shock and sepsis are more frequently associated with mortality in children with DKA.

Keywords: Undernutrition, Cerebral Edema, Shock, Sepsis.

INTRODUCTION

Diabetic ketoacidosis is an acute life-threatening complication of type I Diabetes Mellitus, leading to frequent hospital admissions. The global prevalence of type I DM ranges from 3.5-12.2 cases/100,000 children in various regions[1,] and it is 10.2 cases/100,000 children in India[2]. The prevalence of DKA at diagnosis of Type I DM is 13-80%, and in established cases, it ranges from 6-28% around the globe[3]. This large variation around the globe may be accounted for by the difference in the quality of healthcare facilities and the socio-economic circumstances of different countries. Risk factors among the newly diagnosed children are young age at presentation, delayed diagnosis, belonging to lower socio-economic status and residing in a country with a low prevalence of Type I DM, whereas risk factors among the previously diagnosed cases are omission of insulin, previous episodes of DKA and limited access to medical facilities[4].

DKA is the leading cause of morbidity and mortality in children suffering from Type I DM, with a case fatality rate of 0.15-0.35% in developed countries[5] and 3.4-13.4% in developing countries[6,7,8]. Cerebral oedema is the most dreaded complication of DKA, with an incidence as high as 26%[9] and a mortality of 43%[10] in developing countries.

Due to the large variation of clinical characteristics and outcomes of DKA worldwide and the limited literature on DKA among Indian children, this study aimed to analyse the clinical profile and risk factors associated with the immediate outcome of children with DKA in the Tertiary CARE Hospital of Central India.

METHOD

This was an observational cross-sectional study conducted in the Department of Pediatrics from December 2019 to January 2021 in children aged between 1 month to 12 years admitted with diabetic ketoacidosis. Children with ketoacidosis other than diabetes and whose parents were not giving consent were excluded. A written informed consent was taken from parents/ guardians. A detailed clinical examination and recording of baseline vitals were done at the time of admission. Information regarding sociodemographic profile, clinical features and laboratory parameters were noted in a pre-tested proforma. The modified Kuppuswamy scale was used for evaluating socio-economic status, WHO criteria for nutritional status and the Glasgow Coma Scale for the level of sensorium.

All patients were monitored for heart rate, respiratory rate, blood pressure, level of consciousness, urine output and random blood sugar hourly and serum electrolytes and arterial blood gas analysis every 4 hours. Milwaukee protocol was followed. Children presenting with shock were given a 10 ml/ kg bolus of normal saline. Insulin infusion was started at a

rate of 0.1 units/kg/h and was titrated accordingly. Insulin infusion was replaced by subcutaneous insulin once the child was alert, metabolically stable and accepting oral feeds. Methods and treatment protocols were the same for malnourished children. The resolution of DKA was based on the resolution of acidosis on ABG (pH >7.3), normalisation of blood sugar level, and stabilisation of clinical condition. The final outcome was noted as discharge or death.

Statistical analysis
The collected data was transformed into variables, coded and entered in Microsoft Excel. Data was analysed and statistically evaluated using the SPSS-PC-25 version. Quantitative data was expressed in mean±standard deviation. The difference between two comparable groups was tested by student's t-test (unpaired) or Mann Whitney 'U' test, while for more than two groups, a comparison Kruskal Wallis H test was used. Qualitative data were expressed in percentages, and statistical differences between the proportions were tested by the chi-square test or Fisher's exact test. P' value less than 0.05 was considered statistically significant. Multivariate logistic regression analysis was applied to all the factors that were found significant in univariate analysis.

RESULT
A total of 39 children with DKA were enrolled in the study. The mean age of presentation was 7.48+3.85 years, with a female: male ratio of 1.29:1. 66.6% of cases belonged to rural areas, and the rest, 33.3%, belonged to urban areas. 43.6% of cases belonged to lower Socio-Economic classes. A majority of patients presented with DKA as the first clinical manifestation of type I DM, accounting for 69.2% of total cases. Among previously diagnosed cases, 83.3% cases had poor compliance to insulin therapy and all of these cases belonged to rural areas. HbA1c level of > 8% was found in 38 cases (97.4%). Poor nutrition was recorded in 46.1% of the patients. GCS <8 was seen in 25.6% of cases, and severe acidosis at admission was seen in 28.2% of cases. Blood culture-positive sepsis was reported in 23% of cases, and urine culture-positive sepsis was reported in 10.2% of cases.

Figure 1 : Presenting symptoms in study subjects (n=39)
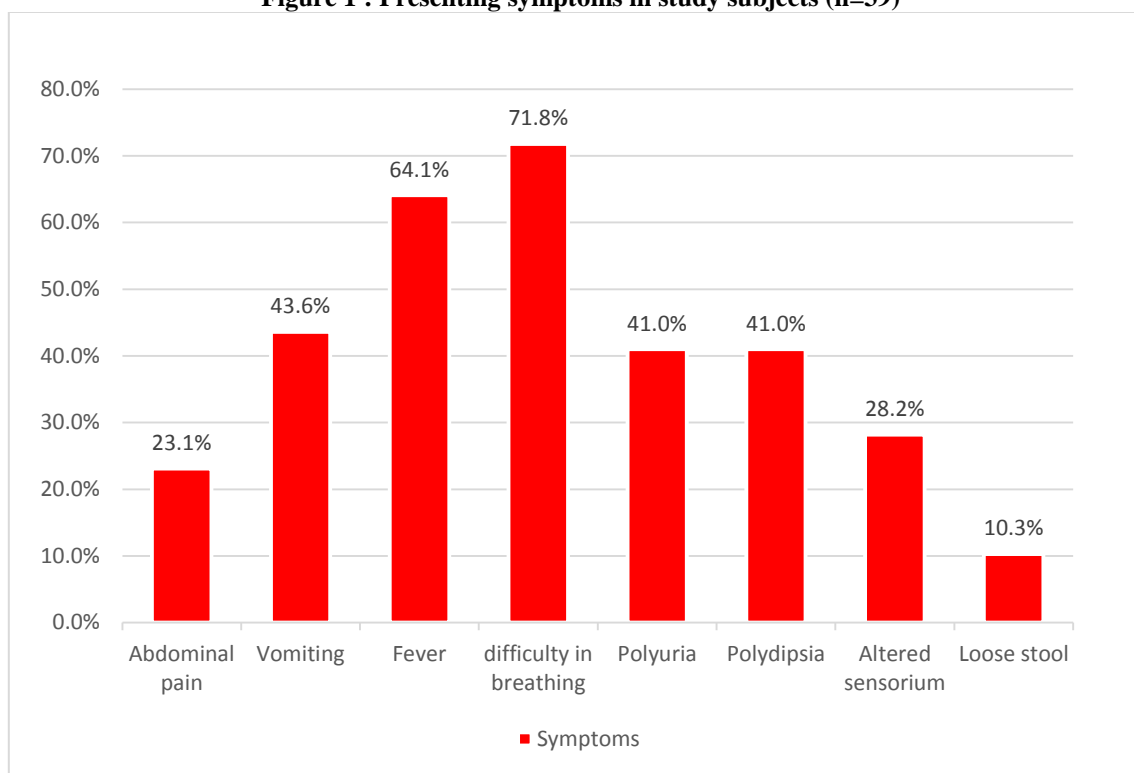
Hyperkalemia was the most common complication seen in 12 cases (30.76%), followed by cerebral oedema and shock in 10 cases (25.6%). All the cases of hyperkalemia and shock were observed at the time of admission. Two out of 10 cases of cerebral oedema presented at the time of admission, and 8 cases resulted during the treatment course. Among these 8 cases, cerebral edema was observed within 6-12 hours of admission.

Out of 39 cases, 32 cases (82.1%) were discharged successfully with a favourable outcome with an average duration of stay of 8.35 days.

Death occurred in 7 cases (17.9%). In all 7 deaths, cerebral oedema and shock were the common causes, and in 5 cases, sepsis and hyperkalemia were also present. Mortality among undernourished children was 50%, whereas it was 4.7%

among well-nourished children. Mortality in cases less than 2 years of age was 42.8%, and it was 12.5% in children aged more than 2 years. Mortality in primary cases of DKA was 14.8%, and it was 25% in secondary cases.

Risk factors that were found to be significantly associated with mortality were Chronic undernutrition (p-value 0.021), SAM (p-value 0.029), GCS<8 (p value<0.001), Ph<7.1 (p value<0.001), cerebral oedema (p value<0.001), shock (p value<0.001), hyperkalemia (p-value 0.02) and sepsis (p-value 0.03).

Table 1: Risk factors associated with the outcome of study subjects

Risk factor	Outcome		p-value
	Death	discharge	
Age <2 years	3 (42.9%)	4 (57.1%)	0.09
Nutrition			
Chronic undernutrition	2 (15.4%)	11 (84.6%)	0.021
MAM	1 (50.0%)	1 (50.0%)	1.00
SAM	3 (100%)	0	0.029
GCS<8	6 (60.0%)	4 (40.0%)	<0.001
pH<7.1	6 (54.5%)	5 (45.5%)	<0.001
Cerebral edema	7 (70.0%)	3 (30.0%)	<0.001
Shock	7 (70.0%)	3 (30.0%)	<0.001
hyperkalemia	6 (50.0%)	6 (50.0%)	<0.01
Sepsis	5 (38.46%)	8 (61.53%)	<0.03

Underlying factors	Percentage
Residence in rural areas	66.7%
Female sex	56.4%
Belonging to a low socio-economic class	43.6%
Poor nutrition	46.2%
Poor compliance	83.3%
Symptoms >14 days	10.3%
Lack of parental awareness and education about symptoms	59.4%
Seeking treatments from quacks	28.2%

Table 2: **Underlying factors responsible for the increased incidence of DKA**

DISCUSSION

This observation cross-sectional hospital-based study reported female preponderance (56.7%), which is similar to a study conducted by Dr Raghunandan Choudhary et al. [11], which also reported 55% female preponderance. The mean age of presentation was 7.48+/- 3.85 years. Sandeep Kumar Kanwal et al. [12], in their study, found a similar result with a mean age of presentation of 7.4+/-3.9 years. Socio-demographic distribution reported that 66.7% of cases resided in rural areas and 33.3% in urban areas. Forty-three percent of cases belonged to the lower socio-economic class, 38.5% belonged to the upper lower socio-economic class, and the rest belonged to the upper middle class. The majority of the cases belonged to rural areas and lower socio-economic strata, which suggests that there is a need to provide adequate and affordable health facilities to people belonging to these areas. Dipak Mukatan et al. [13], in their study, found that 72% of cases belonged to rural areas and 72% belonged to lower socio-economic status, which is comparable to our study.

DKA was seen as the first manifestation of Type I DM in 69.2% of the total cases. This could be due to delayed diagnosis or misdiagnosis of the symptoms. Ali et al. [14], in their study, observed that 30% of newly diagnosed children had at least one related medical visit prior to diagnosis, suggesting the condition is being missed by doctors. Poor compliance to insulin followed by infections were the most common causes reported in our study to be the precipitating factors in known cases of Type I DM. Educating parents and older children about the timely administration of insulin is of utmost importance to prevent further episodes of DKA. Availability and affordability of insulin is a limiting factor in reducing the incidence of DKA. Ninety-seven percent of cases had HbA1c>8% showing long-term poor glycemic control, which is supported by Kompally Vasudev et al. [15]

Difficulty in breathing (71.8%) followed by fever (64.1%) and vomiting (43.6%) were the most frequent presenting complaints. Similar results were observed in a study conducted by Kavitha Shanigaram et al. [16]. Whereas Dipak Mukatan et al. [13] in his study reported polyuria (92%) followed by polydipsia (88%) and weight loss (68%) as the most common presenting complaint.

It was observed in this study that higher mortality (42.9%) occurred in cases <2 years of age. Six out of 7 deaths were undernourished. There was 60% mortality in cases who had GCS<8 at admission. Aymar Pierre Gildas Oko *et al*. [17] also reported younger age, undernutrition and GCS<9 as risk factors for mortality in DKA. Cerebral oedema, sepsis and shock were found to be significantly associated with mortality among DKA cases. Poovazhagi V. [10] also identified these factors for increased mortality among DKA cases.

Notably, little study is still being done in India's centre area. This study sought to fill this gap by conducting a thorough analysis of the sociodemographic and clinical traits of children with DKA in Central India. The study was particularly concerned with identifying risk factors, contributing factors, and direct effects in this population. It is important to emphasise that cerebral oedema emerges as the most common consequence and a major cause of mortality among children with DKA. The results of this inquiry, however, cannot be generalised due to the small sample size used, highlighting the need for larger studies. Furthermore, it is emphasised that the outcomes of children with DKA are significantly influenced by modifiable prognostic variables, such as nutritional status and adherence to recommended regimens.

CONCLUSION

The prevalence of diabetic ketoacidosis (DKA) and its associated consequences reveals significant variation between developed and developing nations. The mortality risk factors exhibit variability, indicating that the treatment recommendations for diabetic ketoacidosis (DKA) should not be uniform between developed and developing nations. There exists a pressing requirement to enhance the efficacy and quality of medical practices in rural areas and peripheral regions. Furthermore, it is crucial to prioritise the education of parents regarding the symptoms and early indicators of diabetic ketoacidosis (DKA).

REFERENCES

1. Mobasseri M, Shirmohammadi M, Amiri T, Vahed N, Hosseini Fard H, Ghojazadeh M. Prevalence and incidence of type 1 diabetes in the world: a systematic review and meta-analysis. Health Promot Perspect. 2020 Mar 30;10(2):98-115. doi: 10.34172/hpp.2020.18. PMID: 32296622; PMCID: PMC7146037.
2. Kalra S, Dhingra M. Childhood diabetes in India. Ann Pediatr Endocrinol Metab. 2018 Sep;23(3):126-130. doi: 10.6065/apem.2018.23.3.126. Epub 2018 Sep 28. PMID: 30286567; PMCID: PMC6177665.
3. Cohen M, Shilo S, Zuckerman-Levin N, Shehadeh N. Diabetic Ketoacidosis in the Pediatric Population with Type 1 Diabetes. Major Topics in Type 1 Diabetes. InTech; 2015. Available from: http://dx.doi.org/10.5772/60592.
4. Wolfsdorf JI, Glaser N, Agus M, Fritsch M, Hanas R, Rewers A, *et al*. ISPAD clinical practice consensus guidelines 2018: Diabetic ketoacidosis and the hyperglycaemic hyperosmolar state. Pediatric Diabetes 2018; 19: 527.
5. Curtis JR, To T, Muirhead S, Cummings E, Daneman D. Recent trends in hospitalization for diabetic ketoacidosis in ontario children. Diabetes Care. 2002;**25**:1591–1596.
6. Syed M, Khawaja FB, Saleem T, Khalid U, Rashid A, Humayun KN. Clinical profile and outcomes of paediatric patients with diabetic ketoacidosis at a tertiary care hospital in Pakistan. J Pak Med Assoc. 2011;**61**:1082–1087.
7. Jayashree M, Singhi S. Diabetic ketoacidosis: predictors of outcome in a pediatric intensive care unit of a developing country. Pediatr Crit Care Med. 2004;**5**:427–433.
8. Kanwal SK, Bando A, Kumar V. Clinical profile of diabetic ketoacidosis in Indian children. Indian J Pediatr. 2012;**79**:901–904.
9. Tiwari LK, Jayashree M, Singhi S. Risk factors for cerebral edema in diabetic ketoacidosis in a developing country: role of fluid refractory shock. Pediatr Crit Care Med. 2012;**13**:e91–e96.
10. Poovazhagi V. Risk factors for mortality in children with diabetic keto acidosis from developing countries. World J Diabetes. 2014 Dec 15;5(6):932-8. doi:10.4239/wjd.v5.i6.932. PMID: 25512799; PMCID: PMC4265883.
11. Choudhary R, Prasad K, Kumar A, Chaudhary A. DIAGNOSIS AND TREATMENT OF DIABETIC KETOACIDOSIS IN CHILDREN AND ADOLESCENT. INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH. 2021;6(2).
12. Kanwal S, Bando A, Kumar V. Clinical Profile of Diabetic Ketoacidosis in Indian Children. The Indian Journal of Pediatrics. 2011;79(7):901-904.
13. Muktan D, Tamang Ghising L, Singh R. Clinical Profile of Diabetic Ketoacidosis among Children in Eastern Nepal. Journal of College of Medical Sciences-Nepal. 2019;15(4):226-229.
14. Ali K, Harnden A, Edge JA. Type 1 diabetes in children. BMJ. 2011;342:d294.
15. Vasudev K, Mothilal S, Vijaykumar G. CLINICODEMOGRAPHIC PROFILE OF DIABETIC KETOACIDOSIS AND ITS MANAGEMENT IN HOSPITALIZED CHILDREN – A PROSPECTIVE STUDY. Indian Journal of Child Health. 2020;07(04):152-155.
16. Shanigaram K, Polanki R, Varahala A. Clinico-Epidemiological Study of Type I Diabetes Mellitus in Children in a Tvertiary Care Center. Journal of Evidence Based Medicine and Healthcare. 2020;7(22):1073-1079.

17. Gildas AP, Zaharo FK, Missambou Mandilou SV, Kambourou J, Letitia L, Yolaine Poathy JP, *et al*. Acidocétose diabétique chez l'enfant: aspects épidémiologiques et pronostiques. Pan Afr Med J 2018;31. https://doi.org/10.11604/pamj.2018.31.167.14415.