

## Assessment of clinical profiles, and treatment outcomes for children with diabetic ketoacidosis, in two hospitals selected from Addis Ababa, Ethiopia, 2020.

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### Abstract

**Background:** Type 1 diabetes mellitus (T1DM) is a common autoimmune disorder that often presents in children. In these patients, diabetic ketoacidosis (DKA) is one of the most common and serious acute complications, which is associated with significant morbidity and mortality. The study aimed to assess the clinical profiles and outcomes of children admitted with DKA.

**Objective:** To assess the clinical manifestations and treatment outcomes of DKA patients in two tertiary hospitals in Addis Ababa.

**Methods:** A hospital-based retrospective analysis was conducted on 175 pediatric diabetic ketoacidosis children, who were admitted to the emergency units of two hospitals in Addis Ababa from September 2015 to February 2020 and whose medical records contained complete pertinent data. Patients were between the ages of 0 to 12 years. Proportional samples were taken from each hospital and data was collected retrospectively using a formatted checklist. The data was checked for its inclusiveness and entered Epi Info. version 4.6 and then transferred into SPSS version 25 software for further analysis.

**Result:** DKA was the presenting manifestation of Diabetes in 78.3% of patients and 21.7% were already known cases of Diabetes. Half (50.9%) of the study participants were diagnosed with DKA in the age range of 5 to 10 years and almost one-third (30.9%) were above the age of 10. A high-income level of the caretakers was found to be protective against DKA during the diagnosis of T1DM. Out of the 175 children admitted, 12 passed on, resulting in a mortality rate of 6.9%.

**Conclusion:** The majority of the known DM patients presented with DKA after the omission of insulin and a newly diagnosed T1DM at first presentation. The age of presentation and clinical symptoms of the studied participants were like other international studies. Community education regarding the signs and symptoms of childhood DM can further prevent the development of DKA. [*Ethiop. J. Health Dev.* 2022; 36(2):000-000]

**Keywords:** Diabetic ketoacidosis, Treatment outcome, and precipitating factors.

### Introduction

Diabetic Ketoacidosis (DKA) is an acute metabolic dysfunction caused by absolute or relative insulin deficiency in the body for the absorption of glucose, which is characterized by hyperglycemia (>250 mg/dl or 14 mmol/l), metabolic acidosis (venous pH < 7.3) with associated glycosuria, ketonuria, and ketonemia (1). Globally, known pediatric DM patients having repeated episodes of DKA remain a relevant problem. The risk of DKA in a known diabetic child account for 1-10% per patient, per year according to the international society of pediatric and adolescent diabetes. An estimated 96,000 children under 15 years of age develop the disease every year worldwide, and the incidence continues to increase at a rate of 3% per year globally (2).

Children and adolescents aged between 0 to 19 years, more than 1.2 million are living with type 1 diabetes. Approximately one in six live births are affected by diabetes during fetal life (3). The treatment outcomes and frequency of DKA are different from one country to another. In the developed world the incidence ranges from 0.7- 8% while in Africa there was a scarcity of studies done but the incidence ranges from 62 – 92%. (4,5,6,7). In Ethiopia there is no study at the national level, however from the few one to two center studies conducted DKA ranges from 35.8 - 80%. (8,15). In a study conducted in Addis Ababa, children whose parents knew about the signs and symptoms of

DM/DKA were 49% less likely to develop DKA at first presentation (8).

A study which was conducted in Gojjam (9), has found that one of the precipitating factors of DKA was inappropriate storage of insulin and poor adherence. A retrospective cross-sectional study conducted in Jimma (10), has found that the family history of DM and the first episode of DM are the precipitants of DKA. In the same study, the clinical manifestation of DKA was the poly symptoms. In both the Addis and Jimma studies, there were no records of death. In industrialized countries death associated with DKA is lower, accounting for 0.15-0.31% while, in developing countries, the risk of death from DKA remains high at 3.4-13.4%, the mortality may occur before or while receiving the treatment (11,12).

The study, which was conducted in Kenya and Himaia, had found that patients who had AKI and altered levels of consciousness had a high risk of mortality (13,14). Due to a lack of awareness of the signs and symptoms of diabetes, children presented to the hospital after they had developed complications. Studies that have been conducted so far in Ethiopia were mostly about the clinical profile of DKA, while studies which were about the outcome of DKA and the risk factors of mortality were very limited in number. Therefore, this study was conducted to describe the clinical profiles and outcomes of children admitted

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with Diabetic Ketoacidosis in two tertiary care hospitals in Addis Ababa.

### Materials and Methods

A retrospective cross-sectional study was conducted in the pediatrics departments of Tikur the Anbesa Specialized and the Yekatit 12 hospital. Patient Case records were studied and details about demographics, clinical presentation, and predisposing factors were recorded using a predesigned data collection tool. Confidentiality of the collected data was maintained by omitting the name of the participants.

### Inclusion and exclusion criteria

Children aged less than 12 years of age, who were diagnosed with DM and had follow up care from February 1, 2015, to April 1, 2020, were included while, charts that were lost and transferred to another hospital during the study period were excluded from the study.

### Sample size

To calculate the adequate minimal sample size, this research utilized the magnitude of DKA from the study conducted in Tikur Anbesa Specialized hospital which was 80% (15). This research utilized a 95% confidence interval level with a 5% margin of error (d). Based on this calculation the sample size was 246. Since the total number of DKA patient seen during the study period were 590 which was less than ten thousand. Corrective formulas were used, and the calculated sample size was 174 with a 10% non-response rate. Accordingly, the minimum calculated sample size was 192 children, of these 175 met the inclusion criteria.

### Sampling procedure

Proportional samples were taken from each hospital. The data was collected using systematic random sampling every second patients' records were taken for analysis.

The charts of the study participants admitted with DKA from February 2015 to April 2020 were reviewed. The personal details, presenting complaints, clinical features, family history of the T1DM, laboratory parameters, management, death certificates, and the outcome was recorded using a structured questionnaire. Researchers had taken the family's phone number from the patient's chart in case there was an incomplete chart and the parents had to be contacted. The diagnosis of DKA was made when blood sugar levels at admission were  $>250\text{mg/dl}$  with poly symptoms (polyuria, polydipsia, polyphagia) and when there was a presence of ketonemia and ketonuria. Severity was graded as mild, moderate, and severe depending on clinical features. All patients were monitored for heart rate, respiratory rate, blood pressure, level of consciousness, and fluid with registrations conducted hourly. Capillary blood glucose and urine ketones were measured hourly while serum electrolytes were measured daily.

### Study outcomes

A proportion of children admitted with DKA passed on Risk factors of mortality in DKA patients

### Operational definitions and measurements

- **Children:** the child being 12 years of age or younger.
- **Preceding infection:** any infection 1-2 weeks prior to the onset of DKA.
- **First-degree relatives with DM:** child's mother, father, or sibling with DM.
- **Preceding signs and symptoms of DM/DKA:** a child who had polyuria, polydipsia, and weight loss 1-2 weeks prior to DKA.
- **Knowledge of the signs and symptoms of DM/DKA:** parents who know about the three poly symptoms and weight loss will be considered knowledgeable.
- **3P symptoms:** polyuria (frequent urination), polydipsia (Frequent thirst), polyphagia (excessive hunger) for a day, or more than a day.
- **Dehydration:** signs like dry buccal mucosa, lethargy, sunken eyes, skin pinch goes back slowly
- **Decreased level of consciousness:** patients who provide a response for verbal or painful stimuli only.

### Statistical Analysis

Statistical analysis was performed using SPSS ver. 25.0. Binary logistic regression was done by using the crude odds ratio to see the crude significant relation (crude odds ratio with 95% CI) of the association of the independent variable with dependent variables. All variables with  $P < 0.25$  at a 95% confidence level during the bivariate analysis were included in the multivariate analysis to control all possible confounders. P-value less than or equal to 0.05 was considered as a significant cut value. Categorical variables were expressed as frequencies and percentages. The results of the study were displayed using frequency mean, median, tables, and figures.

### Ethical consideration

The ethical approval was obtained from the department of pediatrics and child health research and publication committee (DRPC) from the Addis Ababa University, College of Health Science. For confidentiality purposes, the names of the participants were omitted, and the collected data was kept in a locked cupboard.

### Results

**Socio-demographic characteristics of the respondents:** Out of the 192 participants, 175 medical records with DKA were reviewed, the rest of the records 17 (8.8%) had incomplete data. The median age of children was 8 years, the participants ages ranged from 6 months to 12 years. 50.9% of the participants were between the ages of 5 and 10 years. 60% of the children were males, with a male to female ratio of 1.5:1. 27% of the participants' mothers were able to read and write, and 25.1% of them had a grade 1- 8 level education, while 43.4% of fathers had an above grade 12 level of education. 68.6% of parents in this study were married, while 8.7% were widowed. 42.3% of mothers were housewives and 2.9% of the mothers were students, while for the fathers' occupation 43.4% were civil servants, 25.1% were

merchants, and 13.1% were pensioners. The parental monthly income means, and standard deviations were 4,663 birrs and 2,273 birrs respectively (Table1).

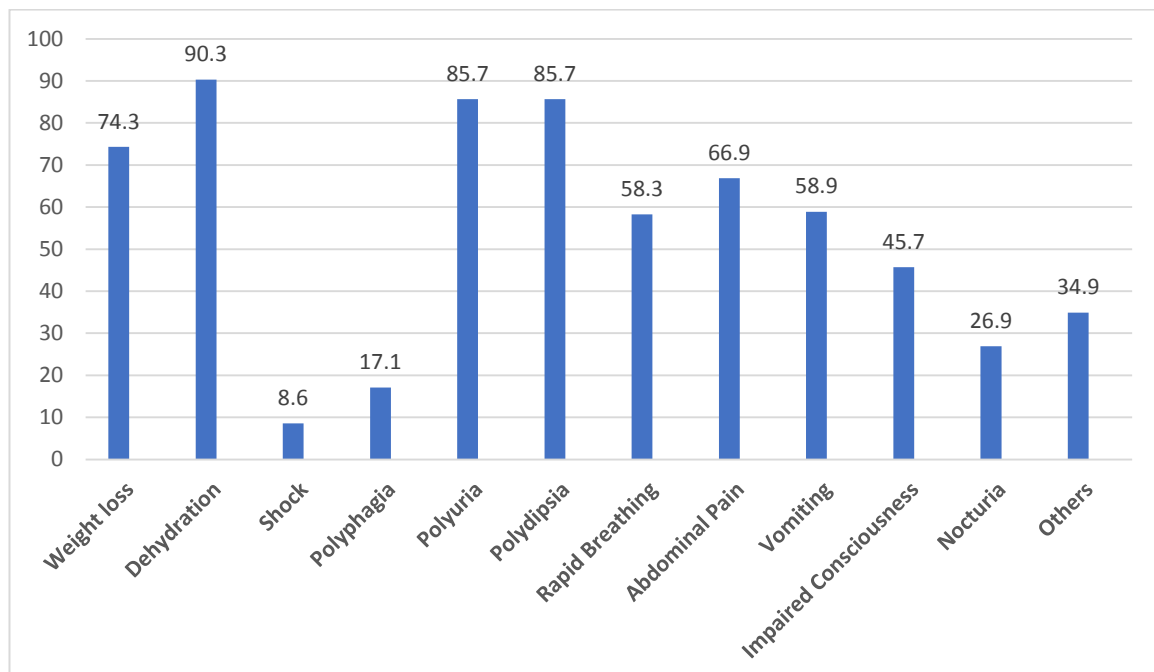
Variables		Frequency (n=175)	Percentage (100%)
Sex	Male	105	60
	female	70	40
Age in yr./month	≤ 6 months	2	1.1
	>6 months - 1years	14	8
	>1 -5 years	16	9.1
	>5-10 years	89	50.9
	> 10 years	54	30.9
Mother's educational level	Unable to read and write	26	14.3
	Read and write		
	Grade 1-8	48	27.4
	Grade 9-12	44	25.1
	Above 12	18	10.9
Father's educational level	Unable to read and write	4	2.3
	Read and write		
	Grade 1-8	36	20.6
	Grade 9-12	17	9.7
	Above 12	42	24
Occupation of father	Civil servant	76	43.4
	Daily labourer	32	18.3
	Pensioned	23	13.1
	Merchant	44	25.1
Family income per month	≤2628 Birr	55	31.4
	2629-4446 Birr	61	34.9
	4447-6264 Birr	42	24
	>6264 Birr	17	9.7

**Table 1 Socio-demographic characteristics of children and their families admitted with DKA**

**Clinical features of DKA**

Out of the 175 patients, this research found that 90.3% had signs of dehydration while the least clinical presentation was shock which accounted for 8.6%. The most frequent clinical findings were polyuria and polyphagia each accounting for 85.7% of the

symptoms. In this study Nocturia and polyphagia were presented as rare manifestations. Almost half of the patients presented with loss of consciousness. 74.3% of the participants had weight loss, and 58.9% of the participants had vomiting.



**Figure 1. Clinical future of DKA in children admitted with DKA****Precipitating factors of diabetic ketoacidosis in children**

Out of the 175 participants, 21.7% had a previous diagnosis of diabetes (prior to the current admission), while 78.3% were newly diagnosed. The most common (n = 137, 78.3%) precipitating factor of DKA was being newly diagnosed with T1DM. The next common (n = 38, 21.7%) was the omission of insulin in a known T1DM. Most of the participants (n = 145, 82.9%) had

preceding signs and symptoms of DM before the onset of DKA. Less than half of the participants (41.7%) had a family history of DM. Almost one-third (28.6%) of the parents knew the clinical sign and symptoms of DM/DKA. Most of the clinical signs and symptoms of which were known by the parents were polydipsia (41%), polyuria (36.2%), and weight loss (30%). Of the total of 175 participants, 56.6% with DKA had a preceding infection before the onset of DKA (Table 2).

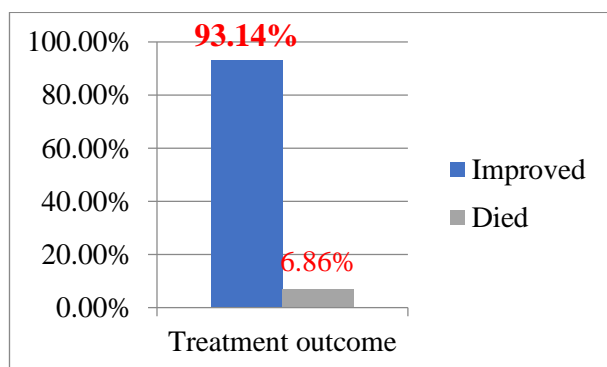
**Table 2. Precipitating factors of DKA in children admitted with DKA**

Variable		Frequency (n=175)	Percent (100%)
Is the child known as a type 1 DM	YES	38	21.7
	NO	137	78.3
Preceding signs and symptoms of DM before the onset of DKA	Yes	145	82.9
	no	30	17.1
First-degree relatives with DM?	Yes	73	41.7
	no	102	58.3
Parents' knowledge of signs and symptoms of DKA/DM?	Yes	50	28.6
	No	125	71.4
Omit insulin before the onset of DKA?	Yes	38	21.7
	No	137	78.3
Preceding infection before the onset of DKA	Yes	99	56.6
	No	76	43.4

**Treatment outcome of DKA in children**

Out of the 175 participants, 12 passed away, resulting in a mortality rate of 6.9%. The mean and standard

deviation of hospital stays in days was 7 and 4 respectively (Figure 2).

**Figure 2. Treatment outcome of DKA in children admitted with DKA****Bivariate analysis of precipitating factors of DKA among children with DM**

Bivariate logistic regression analysis was conducted to identify the relationship between DKA and the associated risk factors. According to this analysis the educational level of the parents, occupation of the mother, family monthly income, prior infection before the onset of DKA, knowledge of the parents in relation

to the symptoms, preceding signs, and symptoms of DM before the onset of DKA, and the omission of insulin were significantly associated with the prevalence of DKA in children. However, some variables like sex, age, family history of DM, known T1DM, and parent's marital status had no significant association according to the bivariate logistic regression (Table 3).

**Table 3: Bivariate analysis of the educational and economic status of the parent as precipitating factors of DKA in children**

Variable	Categories	DKA		COR with 95% CI	P-value
		Yes	No		
Mother educational level	Unable to read and write	25(96.2%)	1(3.8%)	2.083(0.25-21.199)	0.535
	Read and write	45(93.8%)	3(6.3%)	1.250(0.238-6.569)	0.792
	Grade 1-8	34(77.3%)	10(22.7%)	0.283(0.72-1.118)	0.072*
	Grade 9-12	17(94.4%)	1(5.6%)	1.417(0.137-14.641)	0.770
	Above grade 12	36(92.3%)	3(7.7%)	1	
Father educational level	Unable to read and write	3(75%)	1(25%)	0.508(0.048-5.332)	0.572
	Read and write	35(97.2%)	1(2.8%)	5.923(0.734-47.790)	0.095*
	Grade 1-8	15(88.2%)	2(11.8%)	1.269(0.254-6.336)	0.771
	Grade 9-12	39(92.9%)	3(7.1%)	2.200(0.578-8.376)	0.248*
	Above grade 12	65(85.5%)	11(14.5%)	1	
Mother occupation	Unemployed	16(88.9%)	2(11.1%)	0.421(0.035-5.083)	0.496
	Civil servant	32(91.4%)	3(8.6%)	0.561(0.054-5.789)	0.628
	Student	2(40%)	3(60%)	0.035(0.002-0.518)	0.015*
	Housewife	67(90.5%)	7(9.5%)	0.504(0.058-4.352)	0.533
	Daily labourer	18(90%)	2(10%)	0.474(0.039-5.688)	0.556
	Merchant	19(95%)	1(5%)	1	
Occupation of father	Civil servant	64(84.2%)	13(15.8%)	2.812(0.592-13.364)	0.193*
	Daily labourer	30(93.8%)	3(6.3%)	1.969(0.407-9.520)	0.400
	Pensioned	21(91.3%)	2(8.7%)	3.937(0.838-18.491)	0.082*
	Merchant	42(95.5%)	2(4.5%)	1	Ref.
Income per month	≤2628	49(89.1%)	6(10.9%)	2.513(0.616-10.243)	0.199*
	2629-4446	56(91.8%)	5(8.2%)	3.446(0.811-14.642)	0.094*
	4447-6264	39(92.9%)	3(7.1%)	4.000(0.789-20.278)	0.094*
	>6264	13(76.5%)	4(23.5%)	1	Ref.
Signs and symptoms of DM before the onset of DKA	Yes	134(92.4%)	11(7.6%)	3.708(1.303-10.550)	0.014*
	No	23(76.7%)	7(23.3%)	1	Ref
Parent Knowledge of S/S of DM/DKA	Yes	42(84%)	8(16%)	0.457(0.169-1.234)	0.122*
	No	115(92%)	10(8%)	1	Ref

**NB: \*variables were significant (P <0.25) in bivariate analysis. S/S sign and symptom**

#### **Multivariate analysis precipitating factors of DKA among DM children:**

According to the results of the multivariate analysis of newly diagnosed patients, DM had a high chance of having DKA with a statically significant P-value <

0.048. Prior infection was independently associated with an eightfold higher risk for DKA in our study OR (8.593[1.125-65.631], in a known DM patient's omission of insulin, the risk was six-fold higher for developing DKA OR (6.648[1.064-41.544]. (Table 4).

**Table 4. Multivariate analysis for associated precipitating factors of DKA**

Variables	Categories		COR with 95% CI	AOR with 95% CI	P-value
Is the child Known as type 1 DM	Yes	38(22%)	0.295(0.107-0.812)	0.051(0.003-0.898)	*0.042
	No	137(78%)	1	1	
Family history of DM	Yes	73(41.7%)	0.318(0.113-0.891)	0.083(0.009-0.735)	*0.025
	No	102(58.3%)	1	1	
Infection before the onset of DKA	Yes	99(56.5%)	5.363(1.687-17.045)	8.593(1.125-65.631)	
	No	76(43.5%)	1	1	*0.038
Omission of insulin	Yes	38(22%)	3.73 (1.124-32.470)	6.648(1.064-41.544)	
	No	137(78%)	1	1	*0.043

NB: \*variables were significant ( $P < 0.05$ ) in multivariable analysis.

#### Factors associated with treatment outcomes of DKA in children

Multivariate logistic regression analysis was conducted to identify the treatment outcomes of DKA in relation

to cerebral edema, prior infection, electrolyte imbalances, and acute kidney injury, which have a significant association with the mortality of DKA patients. (Table 5).

**Table 5. Bivariate and Multivariate analysis of factors associated with mortality of children admitted with DKA**

Variable	Categories	Treatment outcome		COR with 95% CI	AOR with 95% CI	P-value
Cerebral oedema		No\Discharged	Yes/Died			
	Yes	6 (40%)	9 (60%)	1	1	*0.001
Pulmonary edema	No	157 (98.1%)	3 (1.9%)	0.013(0.003-0.059)*	0.007(0.00-0.114)**	
	Yes	5 (41.7%)	7 (58.3%)	1	1	0.990
Infection	No	158 (96.9%)	5 (3.1%)	0.923(0.005-0.097)*	0.042(0.003-0.700)	
	Yes	43 (82.7%)	9 (17.9%)	0.119(0.031-0.462)*	8.085(1.016-59.67)**	*0.04
Electrolyte imbalance	No	120 (97.6%)	3 (2.4%)	1	1	
	Yes	29 (82.9%)	6 (17.1%)	0.216(0.065-0.719)*	7.754(1.054-57.059)**	*0.044
Hypoglycaemia	No	134 (95.7%)	6 (4.3%)	1	1	
	Yes	23 (76.7%)	7 (23.3%)	1		0.058
Renal failure	No	140 (96.6%)	5 (3.4%)	0.117(0.034-0.401)*	0.042(0.003-0.715)	
	Yes	20 (69%)	9 (31%)	1	1	*0.001
	No	143 (97.9%)	3 (2.1%)	0.947(0.012-0.187)*	0.018(0.002-0.203)**	

NB: \*variables having a ( $P < 0.25$ ) in bivariate analysis, \*\*statistically significant at  $p$ -value  $\leq 0.05$  in the multivariable analysis

#### Discussion

In the current study, the sociodemographic data, clinical profiles, and outcomes of DKA patients from two tertiary care hospitals were analyzed. In this study,

the first presentation of DM was DKA in 78.3% of the participants. This finding is different from studies conducted in three hospitals selected from Addis Ababa, as well as the Kenyan and Himalayan studies

where DKA was seen in 34.7%, 35%, and 48% of newly diagnosed patients respectively (10,13,14). This discrepancy might be due to this study being conducted in a tertiary hospital where there is an organized diabetic clinic, where patients and caregivers were exposed to education about DM which might have made the occurrence of DKA less likely in known DM patients.

The most frequent clinical features of DKA in this study were dehydration (90.3%), polydipsia (86.9%), polyuria (85.7%), weight loss (74.3%), abdominal pain (66.9%), vomiting (58.9%), and rapid breathing (58.3%). This is consistent with the study conducted in Tigray (16), Pakistan (17), Saudi (18), and Egypt (19), while discordant with an earlier study conducted in the Sri Aurobindo Institute (20) where the poly symptoms were not the main clinical manifestation (16.6%) because the main precipitating factors were infections. Less than one third (28.6%) of the parents in this study knew about the signs and symptoms of DM/DKA which is discordant with a study conducted in Addis Ababa hospitals (43%) (21, 8) with this discrepancy being because of most of the patients being newly diagnosed.

Approximately, half of the patients (50.8%) were between the ages of 5 and 10 years, this was different from a study conducted in Spain (40.8%) (21) and in Iraq (22), which reported that 45.5% of children who presented with DKA were above 10 years of age. The median age in this study at first presentation was 8 years as in previous studies conducted in Tigray and India where children presented at 11 and 9 years of age (16, 20). Though the literature suggests equal prevalence in both sexes, in this study the male was predominant, with a male to female ratio of 1.5:1. This finding is different from studies conducted in the Middle East and Asia (Iraq, Southern India, Chennai, and Iran) (22, 23, 24, 25), where females were predominant but there was no explanation with regards to this finding.

The presence of infection 1-2 weeks prior to the onset of DKA was significantly associated with the occurrence of DKA in children this finding is like a study conducted in Southern India (24). The presence of infection can cause the body to produce higher levels of adrenaline or cortisol which counter-regulate the production of insulin.

There were 12 instances of mortality with DKA in this study bringing the mortality rate to 6.9%. This finding is consistent with a Kenyan study (6.9%) (13), however this is higher than a study conducted in Pakistan (4%) (16) and lower than a study conducted at the Madras Medical College, Chennai (12.8 %) (24). In two different studies conducted earlier in Ethiopia and India, there were no instances of mortality reported (9,19). This may be due to the small sample size in both those studies.

Acute renal failure occurred in 16.5% of these participants and the overall mortality rate was 31% in this study. This is different from studies conducted in

India Chennai and Iran where it was 3.7% and 4.7% respectively (24,25). In this study, most patients presented with dehydration which had predisposed them to pre-renal azotemia.

Cerebral edema in this study was seen in 15 of the patients, of which 9 passed on, this is higher than the previous study 21-24%. (26)

Infections were found in in 52 participants in this study, this is a bit higher than a previous study from Egypt (21.9%) (27).

In the current study, 17.1% of participants with electrolyte imbalance passed away. This was consistent with studies conducted in Iran and Bangladesh (25, 28). While is discordant with studies conducted in the developed world where infection and renal failure were not identified as major risk factors for both mortality and morbidity (29, 30, 31). The presence of type 1 diabetes in a first-degree relative (FDR) is associated with a decreased risk of DKA at diagnosis. DKA occurred less in children with at least one FDR affected by T1D (13.0 vs 37.4%,  $P < 0.001$ ) (32,33). This is like in this study, the explanation could be the signs and symptom of DM, which were known by the family and therefore decreased the risk of DKA at diagnosis.

This study has limitations because the analysis was done retrospectively and as such follow-ups with the patients were not possible.

### Conclusion

Diabetic ketoacidosis is an acute metabolic disease resulting in hospital admissions and 78% of newly diagnosed diabetics presented with DKA. Awareness among the community about the signs and symptoms of DM by primary healthcare workers can reduce the occurrence of DKA. Early diagnosis and management can prevent 6.9% of deaths annually.

### Contributions of the Authors

K.G: proposal development and manuscript writing

M.T: advised on proposal development, oversaw study implementation, and manuscript writing

B.M: data collection

S.Y: revision of the proposal and support in manuscript editing

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