Kurabachew Mengistu, Dereje Geleta. *Ethiop Med J, 2020, Vol. 58, No. 3*

ORIGINAL ARTICLE

OCCURRENCE AND FACTORS ASSOCIATED WITH DIABETIC KETOACIDOSIS AMONG CHILDREN SEEN AT HAWASSA UNIVERSITY, COMPREHENSIVE PECIALIZED HOSPITAL: A CROSS-SECTIONAL STUDY

Kurabachew Mengistu, Msc[1], Dereje Geleta, MPH[2]

ABSTRACT

Introduction: *Diabetic ketoacidosis is a medical emergency that requires prompt hospital admission and treatment. It contributes significantly to morbidity and mortality in children with type 1 diabetes mellitus. Diabetic Ketoacidosis is a result of an absolute or relative shortage of insulin deficiency, resulted in hyperglycemia, ketonemia, acidemia, and systemic inflammation.*

Objective: *To study the prevalence of diabetic ketoacidosis and associated factors among the pediatric diabetic age group in Hawassa University teaching hospital from September 2014 to August 2019.*

Methods: *The research area is in a pediatric clinic, Hawassa University teaching hospital. This study is a retrospective cross-sectional study of 150 cases who had diabetes mellitus. Data were collected from patient records by trained data collectors. Data intended for our study that consists of the patient's history, physical examination, progress notes, treatment results, and a summary of deaths from September 2014 to August 2019.*

Results: *Of the 150 patients, 108 (72%) had diabetes ketoacidosis. The condition was common (28.7%) among patients in the age group 10 to 14 years. The majority (98.7%) had type 1 diabetes mellitus. Of patients with diabetes ketoacidosis, 50 (46.2%) were on drug treatment for diabetes, of which 48 (96%) used insulin and two (4%) were on oral hypoglycemic agents.*

Conclusion: *Diabetic ketoacidosis was common among patients with Type diabetes mellitus. Most patients with diabetes ketoacidosis presented with symptoms of polyphagia, polydipsia, and polyuria. Early recognition of warning symptoms of ketosis such as weakness, abdominal pain, vomiting and drowsiness are required to make diagnosis early and provide treatment.*

Keywords: *Diabetic ketoacidosis, Hyperglycemia, Cerebral oedema, Ketonemia, Ethiopia*

INTRODUCTION

Diabetic ketoacidosis (DKA) occurs most commonly in patients with type-1diabetes mellitus (DM), but also may occur in patients with type 2 diabetes, and is most often triggered by omission of treatment, occurrence of infection, or alcohol abuse (1). The diagnostic criteria of DKA issued by the International Society for Pediatric and Adolescent Diabetes consists of blood glucose > 11 mmol/L, blood pH<7.3, serum bicarbonate <15 mmol/L, ketonemia and ketonuria, and a high anion gap (2,3).

Differential diagnosis of DKA consists of alcoholic ketoacidosis, starvation ketosis, and conditions causing metabolic acidosis such as lactic acidosis, chronic renal failure and ingestion of drugs such as salicylate, methanol, ethylene glycol, and paraldehyde (4).

The risk of DKA in young patients with established Type-1 diabetes mellitus (TIDM) is 1% - 10% per patient per year (5).

Clinical decision must be taken to decide optimal treatment for the individual patient, and appropriate adjustments to treatment must be made based on meticulous clinical and biochemical monitoring of the patient's response (6). The true incidence of DKA in tropical Africa is unknown, but has been estimated at 24% (International Diabetes Federation 2011), suggesting that many cases are underreported or misdiagnosed (7).

The incidence of DKA at the onset of DM may be due to parents' unawareness of symptoms of hyperglycaemia. Having a first degree relative with DM is associated with a decreased risk of DKA. However, the degree of awareness of DM symptoms among medical care providers seems to be crucial in DKA prevention (8). Incidence rates of DKA vary and are influenced by demographic, socio-economic, and clinical and laboratory service settings in each area (9).The prevalence of DKA among newly diagnosed patients remains unacceptably high, even among the nations with a highly developed system of medical care (10).

[1] Hawassa University, facility of Medicine, Department of Aneasthia.
[2] Hawassa University, facility of Health science, School of public Health
*Corresponding Author E-mail: darajegalata@gmail.com

Therefore, our aim of the study was to identify the occurrence and associated risk factors of DKA in children at Hawassa University Teaching Hospital (HUTH) in Southern Ethiopia.

PATIENTS AND METHODS

Study area

This was study conducted at HUTH located in Hawassa town, southern Ethiopia. It is located 273 km south of Addis Ababa. The hospital has more than 68 units and serves more than 18 million people in Southern Nations and Nationalities People's Regional State of Ethiopia and neighboring regions such as of Oromia and Somali..

The hospital has 528 beds and provides the public with service in various specialized area, including dental, dermatology, laboratory, pathology, clinical psychiatry, ear, nose and through (ENT), physiotherapy, surgery (general surgery, neurosurgery, and orthopedic, urological and plastic surgery), and subspecialty (cardiology, neurology, ophthalmology, radiology, anesthesia, oncology, gynecology and obstetric, and pediatric services.

Of the total number of beds, 78 were for pediatric department, 40 for newborns. Currently, there are a total of 58 senior physicians, 34 residents and 19 general practitioners; among these eight senior physicians, 18 residents and four general practitioners working in the department of pediatrics. The average monthly delivery in the hospital is 380 per month. The number of patients admitted to the hospital pediatrics' ward is 147 per month, of which 75 are neonates covering 51% of pediatric admissions.

Study design

This was a cross-sectional study with data collected retrospectively at Hawassa University Comprehensive Specialized Hospital (HUCSH) from September 2014 until August 2019. All pediatric patients treated at the hospital for a specified period. All pediatric diabetic patients treated at the hospital during the study period were included

Inclusion and exclusion criteria

All pediatric diabetic patients who were being treated at HUCSH with complete records were included. Pediatric patients with DM and treated at the hospital during the study period, but had incomplete (unknown age and type of diabetes treatment and treatment outcome) records in the study period were excluded.

Sampling size

We identified a total of 173 records of patients treated for DKA. Of these, 150 medical records with complete information were included in the study.

Data collection and analysis

Checklist prepared by reviewing the different literature and previous studies conducted to review the patient's records. The checklist consists of the data in question from the history, physical examination, progress notes, and the results of treatment, and a summary of death.

Data were collected included patient's age, gender, treatment adherence, education level of parents, family history, type of medication, precipitating factors, other chronic diseases, drug withdrawal, body mass index, whether previously known or newly diagnosed DM, type of DM, presenting signs and symptoms, place of residence, treatment given and outcome of treatment. The contents of the checklist was pre-tested before the actual data collection process in 5% of the patient records. Based on the result of pretest the necessary changes were made to improve the quality of the tool. the collected data for on each participant was checked for completeness and a code provided prior to data entry. The data were cleaned and entered onto SPSS version 20 and cleaned before data analysis. Frequency distribution, proportion and descriptive summaries were used to describe the study variables.

Ethical Considerations

Ethical clearance was obtained from Hawassa University, College of Medicine and Health Sciences Internal Review Board, and Hawassa Teaching Hospital. Consent from patients was not obtained since the study involved retrospective data in patietn records.

RESULTS

One hundred and fifty patients who had 148 types 1 and type 2 DM studied at HUCSH during the five-year study period from September 2014 to August 2019. One hundred and eight patients (72%) had DKA. The demographic data of the 150 patients are shown in Table 1. There were 56 (51.9%) males and 52 (48%) females, with a male-to-female ratio of 1: 1.1. A majority 31 (28.7%) of the patients were in the age group 10-14 years. Of the total patients who had DKA 73 (67.6%) were underweight and 35 (32.4%) were within the normal range.

Patients from urban residence accounted for 61 (56.48%), while those from rural area accounted for 47 (43.52%).

Table 1: Sociodemographic data of patients with type 1 and type 2 diabetes mellitus Hawassa University, Teaching Hospital, September 2014 to August 2019.

Variables		Frequency	Percent
Age	<1 year	2	1.3
	1-4 yrs.	32	21.3
	5-9 yrs.	38	25.3
	10-14 yrs.	46	30.7
	15-18 yrs.	32	21.3
Gender	Male	81	54
	Female	69	46
BMI	Underweight	93	62
	Normal	56	37.3
	Overweight	1	0.7
Residence	Urban	88	58.7
	Rural	62	41.3
Type of DM	Type-1	148	98.7
	Type-2	2	1.3

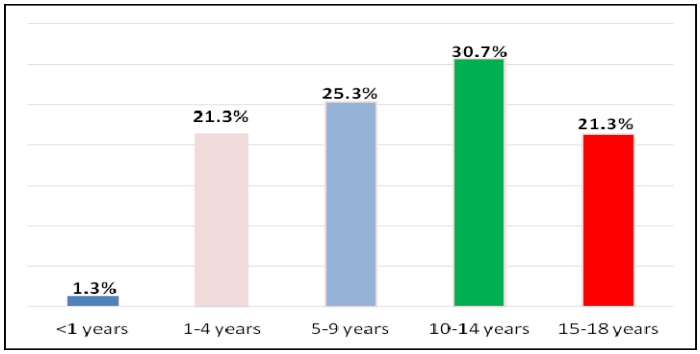

Figure 2: Distribution of Diabetic ketoacidosis among pediatric patients in HUTH from September 2014-August 2019.

In our study, 148 (98%) of the patients were type 1 DM, and 2 (1.3%) of the were type 2 DM. Eighty (53.3%) of the patients were newly diagnosed DM and 70 (46.7%) were known cases of DM. Of the known diabetic patients, 68 (97.1%) had type-1 DM and two (2.9%) had type 2 DM. From a total of 148 patients with type 1 DM, 106 (71.6%) presented with DKA. Among them, 58 (54.7%) were newly diagnosed with type 1 DM.

Of the known diabetic patients, 50 (45.7%) developed DKA, of which 48 (96%) were type 1 and two (4%) type 2 DM patients. Among patients who developed DKA, 30 (27.8%) had a family history and 21 (19.4%) did not have a family history of diabetes and the remaining 57 (52.8%) had no known family history DM.

Among the 108 children who presented with DKA, 27 (25%) had a history of DKA, and 29% of the patients with DKA were between 10 to 15 years of age. Of the 108 DKA patients, 52 (48.1%) had mild, 37(34.3%) had moderate and the remaining 19 (17.6%) had severe DKA of whom 11 (57.9%) had urinary ketone level +3. Sixty-five percent of DKA patients had random blood sugar (RBS) between 250mg/dl and 500mg/dl and t22% had over 500mg/dl.

Of the 108 patients with filed outcomes, 105 (97.22%) improved after treatment, whereas three (2.8%) died in hospital. The cause of death was severe DKA in two patients and moderate DKA in one patient. (Table-2)

Table 2: Clinical Characteristics of diabetic ketoacidosis in children in Hawassa University Teaching Hospital, September 2014 -August 2019.

Variable		Percent of DKA		Total
		Yes	No	
Age at Diagnosis of DM	less than 5 year	30	10	40
	5 to 10 year	38	10	48
	10 to 15 year	36	19	55
	15 to 18 year	4	3	7
Previous history of DKA	Yes	27	0	27
	No	81	42	123
Age at first DKA diagnosis	less than 5 year	26	1	27
	5 to 10 year	24	0	24
	10 to 15 year	31	0	31
	15 to 18 year	12	1	13
	Mild	52	1	53
Current grade of DKA	Moderate	37	0	37
	Severe	18	0	18
The current blood glucose level	RBS less than 250mg\dl	16	26	42
	RBS 250mg\dl to 500 mg\dl	70	15	85
	greater than 500mg\dl	22	1	23
Onset of DM	Known DM patient	50	20	70
	Newly diagnosed	58	22	80
Family history of DM	Yes	30	8	38
	No	21	13	34
	Unknown	57	21	78

Of the 108 DKA patients, 56 (51.8%) had precipitating factors, either preceding infections (n=55), of which 24 (41.3%) had respiratory tract infections (RTI), 18 (31%) urinary track infection (UTI), three (0.1%) gastroenteritis, and 13 (22.4%) infections of other organ systems.

Regarding their treatment regimen of 50 (46.2%) of patients with DKA, 48 (96%) were on insulin, two (4%) were taking oral hypoglycemic agents and, of these 21 (42%) discontinued medication for unknown reasons. Twenty (23.1%) of the patients were not taking their meals regularly (Table-3).

Table 3: Characteristics of factors associated with Diabetes ketoacidosis in children, Hawassa University Teaching Hospital, September 2014 -August 2019.

Variables		Presence of DKA		Total
		Yes	No	
Pre-Medication history	Yes	50	20	70
	No	58	22	80
	Total	108	42	150
Type of Medication	Insulin	48	19	67
	Oral hypoglycemic agent	2	0	2
	Total	50	19	69
Medication Discontinuation	Yes	21	3	24
	No	29	17	46
	Total	50	20	70
Patients who take their meal properly	Yes	83	35	118
	NO	25	7	32
	Total	108	42	150
Chronic illness other than DM	Yes	7	1	8
	No	101	41	142
	Total	108	42	150
Precipitating factor	Yes	56	3	59
	No	52	39	91
	Total	108	42	150
Presence of infection	Yes	55	4	59
	No	53	38	91
	Total	108	42	150

In this study, the frequently reported presenting symptoms of DKA were poly symptoms (polyphagia. Polydipsia, polyuria) 84 (77.8%), and nausea and vomiting 66 (61%), tachypnea and easy fatigability 57 (52.8%), abdominal pain 51 (47.2%), and loss of consciousness 15 (13.9%) (Table 4).

Table 4: Clinical Presentations of children with diabetic ketoacidosis, Hawassa university Teaching Hospital, September 2014 - August 2019.

Variables		Presence of DKA Yes	No	Total
Nausea and vomiting	Yes	66	8	74
	No	42	34	76
Abdominal pain	Yes	51	2	53
	No	57	40	97
Loss of consciousness	Yes	15	3	18
	No	93	39	132
Poly symptoms	Yes	84	36	120
	No	24	6	30
Other symptoms	Yes	57	15	72
	No	51	27	78

There was a significant association between DKA and preceding infections X^2 =21.7 ($p<0.0001$), medication discontinuation X^2=4.622 ($p=0.05$) and BMI X-=7.024 ($p=0.03$). Patient's sex, parental education status, family history of diabetes, the onset of diabetes, type of diabetes, not taking food well, and other chronic diseases besides diabetes do not have a significant relationship with the occurrence of DKA.

DISCUSSION

Ketoacidosis is an acute complication of DM, especially type 1 DM, demonstrating a severe insulin deficiency (11). DKA results from both absolute or relative insulin deficiency, and elevated counter-regulatory hormones (glucagon, catecholamine, cortisol and growth hormone (12,13). DKA in children with recognized T1DM can be the result of non-compliance with insulin therapy, insulin pump failure, or intercurrent illness (14).

In our study, the prevalence of DKA among pediatric age group was 72%, which is comparable with the study conducted at Tigray region hospitals and the overall prevalence Ethiopia is 80% (15). A study in the Sudan reported the prevalence of 81.2% newly diagnosed DM patients with DKA (16). Research done in a different countries have reported relatively similar figures with our study, which have shown a high facility prevalence of DKA among the pediatric age group worldwide (15). In contrast, low occurrences have been reported from Finland (22%), Iran (24%), Sweden (14%) (16).

In our series, we found a significant association between DKA and preceding infection, discontinuation of medication, and patient's BMI. This is similar to a study conducted by Smith JA, et.al., which indicated a strong effect of preceding infection on the development of DKA. Similar observations have also been reported from Mekele Teaching Hospital and by research done in Addis Ababa Hospitals (16-18). Another study (19), has also shown that the combination of inadequate insulin administration, the presence of infection, and other clinical conditions such as myocardial infarction, cerebrovascular accidents, pulmonary embolism, pancreatitis, illegal drug use, and alcohol abuse predispose patients with DM to DKA.

There was a family history of DM in 27.8% of our patients, which was slightly higher than the 23.3% reported from Mekele Teaching Hospital (17). Family history is an important risk factor for the development of T1DM (18). This was also been demonstrated in our study, where family history of DM is in the order of 27.8% and 28.7% of DKA occurred in the age group 10 to 14 years higher than the age group 0-14 years, an observation also corroborated by other studies (20).

The commonest presenting symptoms in our study were poly symptoms (61%), which is also common presenting symptoms (98%) at the Tikur Anbesaa Hospital (16) in Addis Ababa. There were three deaths, which accounted for a 2.8% case fatality rate, and of two among the deaths presented with severe DKA.

Our study showed 52 (42%) of the children presented with mild DKA followed by moderate which was seen in 37 (34%) of them and severe 19 (17.6%). This finding is comparable to the reports of studies done in a tertiary care hospital (22). Weight loss before a diagnosis is a usual sign of metabolic imbalance, with a greater risk of developing DKA, and which has also been affirmed by a report form Nepal (23). In industrialized countries, the death associated with DKA in children is in the order of 0.2% to 0.3% (24), whereas in our study the corresponding figure much higher (2.8%).

In sub-Saharan Africa, in particular, there are many challenges regarding patients with DM, because of the lack of effective management systems, including timely awareness of its complications and prevention of DM (25). Improving awareness among parents and clinicians about the early symptoms of DM through diabetes education programmes - such as community intervention in Italy, which reduced the prevalence of DKA at diagnosis from 78% to 12.5% (26).

Conclusion

DKA is the most common complication of type 1 DM and cause of morbidity in the pediatric age group with DM. It commonly occur in newly diagnosed type 1 DM patients. Most patients with DKA present with poly symptoms.

In most patients, a precipitating factor is preceding infections (like UTI, URTI and acute gastroenteritis), although drug discontinuation is one of the precipitating factors. As most of the risk factors associated with DKA among children from developing countries are pretreatment factors, the primary goal of future programmes should be focused on the prevention of DKA in children. Early awareness and prompt commencement of treatment with reevaluations and adjustments of care plans are so important to decrease complications and death.

ACKNOWLEDGMENT

We thank all study participants for generous collaboration and participation in this study.

Conflict of interest

The authors have declared that no competing interests exist.

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