

Assessment of Clinical Profile, And Treatment Outcome of Diabetic Ketoacidosis among Diabetic Children, In Two Selected Hospital, Addis Ababa, Ethiopia, 2020

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is an acute and life-threatening situation that accounts for the majority of diabetes related morbidity and mortality in children and adolescents who suffer from type 1 diabetes mellitus (T1DM). Diabetic ketoacidosis is the most severe endocrine emergency in pediatrics, which is characterized by hyperglycemia (>250 mg/dl or 14 mmol/l), metabolic acidosis (venous pH < 7.3), with associated glucosuria, ketonuria, and ketonemia.

Objective: To assess the precipitating factors, clinical presentation, and treatment outcome of diabetic ketoacidosis among diabetic patients in two tertiary hospital of Addis Ababa.

Methods: A retrospective analysis was done on the case records of 175 children with diabetic ketoacidosis admitted to our hospital from January 2015 to April 2020. They were managed using a standard protocol including intravenous fluids and insulin infusion. Blood glucose, serum electrolytes, blood urea, and urinary ketones were monitored at regular intervals. The outcomes were assessed. The data was checked for its completeness and entered into Epi version 4.6, and imported to SPSS version 25 software for analysis. The Associations between independent and dependent variables were analyzed using binary logistic regression models. Result: The median age at presentation was 8 years (range from < 6 months to 12 years with male to female ratio of 1:1.5). One hundred thirty-seven children (78.3%) were detected to have diabetes mellitus at the time of presentation. Dehydration, Polyuria with polydipsia was the commonest clinical presentation. The precipitating factor of DKA was newly diagnosed, omission of insulin and infection respectively (137, 78.3%, 33, 21.7% and 5, 2.9%). There was mortality which accounts 6.9%.

Conclusion and Recommendation: DKA were most prevalent in newly diagnosed T1DM cases. Newly diagnosed T1DM and insulin omission were the main factors associated with DKA. The age of presentation and clinical symptoms of studied subjects were similar to international studies. High frequency of DKA at presentation of T1DM requires careful attention to issues of early diagnosis before development of ketoacidosis and subsequently need prevention of DKA management complication. We recommend all the health facilities to give health education about the sign and symptoms of DM and the acute complications of DM.

Keywords: Diabetic ketoacidosis; Treatment outcome; Precipitating factors

INTRODUCTION

Diabetes mellitus is a chronic disease that occurs due to lack of insulin secondary to pancreas does not produce enough insulin or the body cannot effectively use the insulin which was produced [1]. The other definition of DM is a common endocrine disorder that results from either insufficiency or ineffectiveness insulin. DM is divided into two major types: type 1 and type 2 DM. Type 1 DM is caused due to insulin deficiency, and type 2 DM is caused

due to insulin ineffectiveness. DKA is the most common acute complication of type 1 DM in children [2], while type 2 DM occurs during stressful conditions like surgery, trauma, infections [3,4]. DKA is the most severe endocrine emergency in pediatrics, which is characterized by hyperglycemia (>250 mg/dl or 14 mmol/l), metabolic acidosis (venous pH < 7.3) with associated glycosuria, ketonuria, and ketonemia [5].

An estimated 96 000 children under 15 years old develop the disease

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each year worldwide, and the incidence continues to increase at a rate of 3% per year globally [6]. Estimates from the International Diabetes Federation [7] suggest that diabetes will expand in Africa by 98% to 28 million patients in 2030. The frequency and treatment outcome of DKA is different from country to country. The prevalence of DKA in children with newly diagnosed diabetes is 20–40% [8]. DKA has different clinical manifestations: Polyuria, polydipsia, polyphagia, vomiting, abdominal pain, dehydration; acetone breathing, fever, hypotension, coma, and confusion are the usual clinical signs and symptoms of DKA. Three Poly symptoms are presented in the majority of DKA patients. All patients in DKA are presented in the hospital with dehydration. Therefore rapid rehydration is necessary for a better outcome [8,9].

The most common risk factor of DKA is infections, insulin withdrawal, and undiagnosed T1DM [10]. There are also other factors like sex, negligence, poverty, and delay in diagnosis increase the prevalence of DKA [9]. DKA results with both short-term and long-term complications. Recent data have shown that DKA is responsible for up to 73% of the causes of deaths during the first decade of diabetes. Mortality is predominantly related to the occurrence of cerebral edema, whereas only a minority of deaths in DKA is occurred due to other causes [11].

The aim of this study was to assess the clinical profile, and treatment outcome of diabetic ketoacidosis among diabetic children of two hospitals.

MATERIALS AND METHODS

A retrospective study was done in pediatrics departments of two tertiary level care hospitals at Addis Ababa, Ethiopia. The case records of children admitted with DKA from February 2015 to April 2020 were reviewed and personal data details, presenting complaints, clinical features, family history of type 1DM, laboratory parameters, management, death certificates and outcome was recorded using a structured questioner. We called for the family if the chart was incomplete data. We had taken the family's phone number from the patient's chart.

DKA was diagnosed when blood sugar at admission was $>250\text{mg/dl}$ with poly symptoms (polyuria, polydipsia, polyphagia) and presence of ketonemia and ketonuria. Severity was graded as mild, moderate and severe depending on clinical features. Monitoring of heart rate, respiratory rate, blood pressure, level of consciousness and fluid registering was done hourly. Capillary blood glucose, urine ketones was measured hourly while serum electrolyte measured daily.

The study population consisted of children aged 0-12 years admitted with DKA at two tertiary hospitals of Addis Ababa.

Statistical analysis

Statistical analysis was performed using SPSS ver.25.0. Simple frequency, tables, and figures were used to present the processed information.

Binary logistic regression was done to see the crude significant relation (crude odds ratio with 95% CI) of each 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. A P-value less than or equal to 0.05 was taken as a cut of value to be significant. The results were displayed by using frequency tables and charts.

Ethical consideration

The present study ethical approval was secured from the department of pediatrics and child health research and publication committee (DRPC) of Addis Ababa University of Collage of Health Science with the study number of 175. For the confidentiality purpose the name of the participant has omitted and the collected data was kept locked cupboard.

RESULTS

Socio-demographic characteristics of the respondents

We studied the medical records of 175 children admitted with DKA during the 5-year period (February 2015 to April 2020) preceding the study. All children who met the eligibility criteria during the study period were recruited. The median age of children was 8 years, ranging 6 months to 12 years. The majority of children (105, 60%) were males with the male to female ratio of 1.5:1. Half of the study participant 89, (50.86%) were between the ages of 5 and 10 years.

Parent educational level were; 48 (27.4%) of mothers were can read and write, and 44 (25.1%) of them were grades 1- 8; while 76 (43.4%) of fathers were above grade 12. One hundred twenty (68.6%) of their parents were married, and fifteen (8.7%) were widowed. The occupation of the parents, 74, (42.3%) of their mother was a housewife and a small number 5, (2.9%) of the mother were students. The fathers' occupation was 76, (43.4%), civil servant 44, (25.1%), merchant and 23, (13.1%) Pensioned. The mean and standard deviation parental income was 4,663 birr and 2,273 respectively (Table 1).

Clinical feature of DKA

The commonest clinical manifestation was dehydration which accounts 158 (90.3%), polydipsia 150, (85.7%), polyphagia 30, 17.1%) and impaired consciousness 80 (45.7%) while shock was account 15 (8.6%) (Figure 1).

Precipitating factors of diabetic ketoacidosis in children

In the current study the most common 137(78.3%) precipitating factor of DKA was being newly diagnosed type 1DM. The next common 38 (21.7%) were the omission of insulin in a known T1DM. Majority of the participant 145(82.9%) had preceding signs and symptoms of DM before the onset of DKA. Almost half of them (41.7%) had a family history of DM. One third (28.6%) of the parents had knowledge of the clinical sign and symptoms of DM/DKA. Most clinical sign and symptoms which were known by the parents were polydipsia (41%), polyuria (36.2%), and weight loss (30%). Ninety-nine (56.6%) of total participant with DKA had Preceding infection before the onset of DKA (Table 2).

Treatment outcome of DKA in children

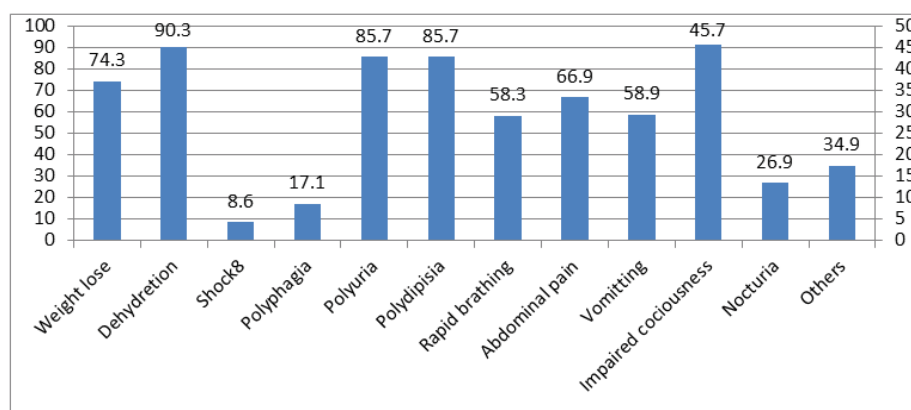
The treatment outcome of the current study was 163 (93.1%) DKA patients has improved while 12 (6.9%) has died. The mean and standard deviation of random blood sugar (RBS) at presentation were 444 and 118 respectively. The mean and standard deviation of hospital stay in days were 7 and 4 respectively (Figure 2).

Bivariable analysis of factors associated with the prevalence of DKA in children among DM children

In bivariable logistic regression analysis; the educational level of

Table 1: Socio-demographic characteristics of children and their families admitted with DKA at Tikur Anbesa specialized and Yekatit 12 hospital from February 2015 - April 2020.

Variables		Frequency (175)	Percentage (100%)
Sex	Male	105	60
	female	70	40
Age in yr/month	≤ 6 month	2	1.1
	>6 moths - 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	48	27.4
	Grade 1-8	44	25.1
	Grade 9-12	18	10.9
	Above 12	39	22.3
Father's educational level	Unable to read and write	4	2.3
	Read and write	36	20.6
	Grade 1-8	17	9.7
	Grade 9-12	42	24
	Above 12	76	43.4
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

**Figure1:** Clinical future of DKA children admitted with DKA at Tikur Anbesa specialized and Yekatit 12 hospital from February 2015 - April 2020.**Table 2:** Precipitating factors of DKA in children admitted with DKA at Tikur Anbesa specialized and Yekatit 12 hospital from February 2015 - April 2020.

Variable		Frequency(175)	Percent (100%)
Is the child known type 1 DM	YES	38	21.7
	NO	137	78.3
Preceding sign 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
Child's parents' knowledge of the sign and symptoms of DKA/DM?	Yes	50	28.6
	No	125	71.4
Omit insulin before the onset of DKA?	Yes	33	18.9
	No	5	2.9
	Missing	137	78.3
Preceding infection before the onset of DKA	Yes	99	56.6
	No	76	43.4

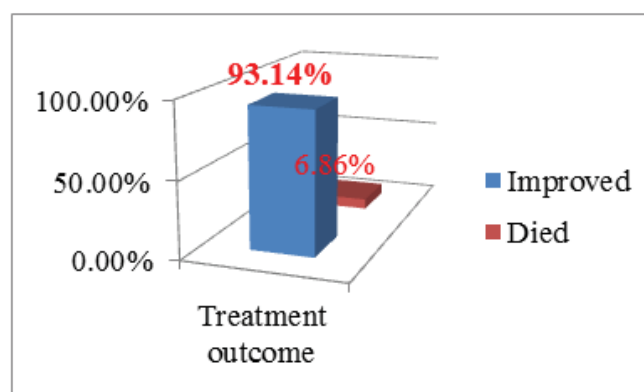


Figure 2: Treatment outcome of DKA in children admitted with DKA at Tikur Anbesa specialized and Yekatit 12 hospital from February 2015 - April 2020.

Table 3: Bivariate analysis for associated precipitating factors DKA in children admitted with DKA at Tikur Anbesa specialized and Yekatit 12 hospital from February 2015 - April 2020.

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.
Preceding S/S of DM before on set 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.
Knowledge of parent on 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 bivariable analysis. S/S sign and symptom

mother and father, occupation of mother and father, monthly income, known type 1DM, preceding infection before the onset of DKA, family history of DM, knowledge of the parent, preceding sign and symptom of DM before onset of DKA and omission of insulin were significantly associated with the prevalence of DKA in children. But some variables like sex, age and parent's marital status had no significant association by using bivariable logistic regression (Table 3).

Multivariable analysis on factors associated with the prevalence of DKA among DM children

According to the result of multivariable analysis after controlling other factors (confounders), Known type 1 DM, family history of DM, preceding infection before the onset of DKA, and omission of insulin had a statistically significant association with the magnitude of DKA in children (Table 4).

Table 4: Multivariate analysis for associated precipitating factors DKA in children admitted with DKA at Tikur Anbesa specialized and Yekatit 12 hospital from February 2015 - April 2020.

Variables	Categories	DKA		COR with 95% CI	AOR with 95% CI	P-value
		Yes	No			
Known type 1 DM	Yes	30(79%)	8(21%)	0.295(0.107-0.812)	0.051(0.003-0.898)	*0.042
	No	127(93%)	10(7%)	1	1	
Family history of DM	Yes	61(84%)	12(16%)	0.318(0.113-0.891)	0.083(0.009-0.735)	*0.025
	No	96(94%)	6(6%)	1	1	
Infection before the onset of DKA	Yes	95(96%)	4(4%)	5.363(1.687-17.045)	8.593(1.125-65.631)	*0.038
	No	62(82%)	14(18%)	1	1	
Omission of insulin	Yes	28(85%)	5(15%)	3.73 (1.124-32.470)	6.648(1.064-41.544)	*0.043
	No	3(60%)	2(60%)	1	1	

NB: *variables were significant (P <0.25) in multivariable analysis

Table 5: Bivariate and multivariate analysis for associated factors of treatment outcome of DKA in children admitted with DKA at Tikur Anbesa specialized and Yekatit 12 hospital from February 2015 - April 2020.

Variable	Categories	Treatment outcome		COR with 95% CI	AOR with 95% CI	P-value
		No \Improved	Yes/Died			
Cerebral oedema	Yes	6(40%)	9(60%)	1	1	*0.001
	No	157(98.1%)	3(1.9%)	0.013(0.003-0.059)*	0.007(0.00-0.114)**	
Pulmonary oedema	Yes	5(41.7%)	7(58.3%)	1	1	0.990
	No	158(96.9%)	5(3.1%)	0.923(0.005-0.097)*	0.042(0.003-0.700)	
Infection	Yes	43(82.7%)	9(17.9%)	0.119(0.031-0.462)*	8.085(1.016-59.67)**	*0.04
	No	120(97.6%)	3(2.4%)	1	1	
Electrolyte imbalance	Yes	29(82.9%)	6(17.1%)	0.216(0.065-0.719)*	7.754(1.054-57.059)**	*0.044
	No	134(95.7%)	6(4.3%)	1	1	
Hypoglycaemia	Yes	23(76.7%)	7(23.3%)	1		0.058
	No	140(96.6%)	5(3.4%)	0.117(0.034-0.401)*	0.042(0.003-0.715)	
Renal failure	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 bivariable analysis, **statistically significant at p-value ≤0.05 in the multivariable analysis

Bivariable and Multivariable analysis on factors associated with treatment outcome of DKA in children

In multivariable logistic regression only cerebral edema, infection, electrolyte imbalance, and renal failure had a significant association with treatment outcome of DKA in children (Table 5).

DISCUSSION

This retrospective study described the sociodemographic data and clinical profile of children with DKA in two tertiary care hospitals. The initial presentation of DKA, was encountered by the vast majority of patients. The usual symptoms of DKA are polyuria, polydipsia, abdominal pain, vomiting, and decreased level of consciousness were the presenting complaints in most cases. New onset diabetes and insulin omission in those with established T1DM were the most common precipitants of DKA this was the finding of in the current study, which is concordant with the study done in Milwaukee, Addis Ababa, Saudi Arabia and Pakistan respectively [12-15].

Approximately, half of patients (50.8%) were between 5 and 10 years old. The finding may be explained by the fact that a high number of patients were newly diagnosis of T1DM. These data were attributed to the high number of new-onset cases presenting

with DKA. The commonest age of presentation in our children was between 5 to 10 years, this was similar with the study done [16] in contrary with our study [17] reported that 55% of children presenting with DKA were above 10 years old. In the current study male is predominant than female, with male to female ratio 1.5:1 this finding is concordant with the study [18] while, discordant with study done [19,20] females were predominant.

Infection 1-2 weeks before the onset of DKA was significantly associated with the prevalence of DKA in children this finding similar with the study done in India [21-25].

The explanation can be infection cause body to produce higher levels of adrenaline or cortisol these counter regulate the production of insulin.

The most frequent clinical features of DKA in our 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 to the study conducted in Indore, India [21], Pakistan [15], Egypt [22], while discordant with Milwaukee [12] study the poly symptoms were not the main clinical manifestation.

The treatment outcome in our study was 12 (6.9%) children with

DKA have died. This finding is higher in study done in Pakistan 4% [25], and Indore, India 3.4% [21], while lower than Madras Medical College, Chennai 12.8 % [23].

In the current study cerebral edema, infection, renal failure and electrolyte imbalance were the risk factor of death this was consistent with the study conducted in Bangladesh [9], Iran [24], and the Himalayan state of north India [18].

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