**ADDIS ABABA UNIVERSITY**

**COLLEGE OF HEALTH SCIENCES**

**SCHOOL OF NURSING AND MIDWIFERY**

**DEPARTMENT OF NURSING**

**POST-GRADUATE PROGRAM**

# TIME TO RECOVERY FROM DIABETIC KETOACIDOSIS AND ITS PREDICTORS AMONG CHILDREN WITH TYPE 1 DIABETES AT SELECTED GOVERNMENTAL HOSPITALS IN ADDIS ABABA, ETHIOPIA, 2023: RETROSPECTIVE FOLLOW-UP STUDY

**PRINCIPAL INVESTIGATOR: SHIMELES TEFERA (BSc)**

**A RESEARCH THESIS TO BE SUBMITTED TO THE POST GRADUATE STUDIES SCHOOL OF NURSING AND MIDWIFERY, COLLEGE OF HEALTH SCIENCE, ADDIS ABABA UNIVERSITY FOR THE PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF SCIENCE IN PEDIATRICS AND CHILD HEALTH NURSING**

**JUNE, 2023**

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**JUNE, 2023**

**ADDIS ABABA, ETHIOPIA**

## APPROVAL SHEET

I, the undersigned MSc student, declare that I have submitted my original work entitled time to recovery from diabetic ketoacidosis and its predictors among children with type 1 diabetes at selected governmental hospitals in Addis Ababa, Ethiopia, 2023: retrospective follow-up study for examination.

Submitted by:

Shimeles Tefera (BSc) _____ _____

Name of student Signature Date

This thesis by Shimeles Tefera is accepted in its present form by the board of examiners as satisfying thesis for degree of masters in pediatrics and child health nursing.

Approved by

EXAMINER: _____ _____

Signature Date

ADVISORS:

Name of major advisor Signature Date

Tigistu Gebreyohannis (Ass. Prof.) _____ _____

Name of co -Advisor Signature Date

Sr. Feven Mulugeta (BSc, MSc) _____ _____

DEPARTMENT HEAD

Name Signature Date

Dr. Girum Sebsibe (PHD) _____ _____

## STATEMENT OF DECLARATION

By my signature below, I confirm that this thesis is my own novel work. I have followed all ethical principles of research in the preparation, data collection, data analysis and compilation of this thesis. Any scholarly matter that is included in the thesis has been given recognition through citation. I endorse that I have cited and referenced all sources used in this document.

This thesis is submitted in partial fulfillment of the requirements for a master's degree of pediatrics and child health nursing at Addis Ababa University. The thesis will deposit in the Addis Ababa University library and will make available to borrowers under the rules of the library. I seriously declare that this thesis has not been submitted to any other institution anywhere for the award of any academic degree, diploma, or certificate.

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## ACRONYM AND ABBREVIATION

| | |
|---|---|
| CE | Cerebral Edema |
| CI | Confidence Interval |
| DKA | Diabetic Ketoacidosis |
| DM | Diabetes Mellitus |
| HCO3 | Bicarbonate |
| ISPAD | International Society for Pediatric and Adolescent Diabetes |
| IV | Intravenous |
| NaCl | Sodium Chloride |
| NT1D | Newly Diagnosed Type 1 Diabetes |
| PICU | Pediatrics Intensive Care Unit |
| PT1D | Previously Diagnosed Type 1Diabetes |
| T1DM | Type One Diabetes Mellitus |
| T2DM | Type Two Diabetes Mellitus |
| TASH | Tikur Anbessa Specialized Hospital |
| USA | United States of America |
| VBG | Venous Blood Gas |
| ZMH | Zewditu Memorial Hospital |

Table of contents Page number

## LIST OF TABLES

## LIST OF FIGURES

## ABSTRACT

**Background:** Diabetic ketoacidosis (DKA) is one of the most severe clinical features of diabetes mellitus, which can result in morbidity and mortality. The prevalence of DKA is increasing worldwide and nationwide. There is a discrepancy of time to recovery from DKA between developed and developing country. The Ethiopian government aims to decrease premature mortality from noncommunicable diseases, including diabetes, by one-fourth by 2025. To achieve this target plan, more research should be conducted in this area.

**Objective:** To assess time to recovery from DKA and its predictor among children with diabetic ketoacidosis at selected governmental hospitals in Addis Ababa, Ethiopia, 2023

**Methods:** A five years retrospective follow-up study design was employed among 391 children admitted with DKA to selected governmental hospitals in Addis Ababa, Ethiopia from January 1, 2018 to December 30, 2022. Simple random sampling technique was used to select the hospitals and participants. Preliminary survey of the study hospitals was done to determine flow and the sample was proportionally allocated. Structured data collection checklist was adapted from similar studies in the literature. Data was checked for completeness, and exported into Stata version 16 for analysis. A variable with P value < 0.05 in the multivariate Cox proportional hazards model was considered as significant predictors of time to recovery from DKA.

**Results:** a total of 391 (92.4%) children with DKA were included in the final analysis**.** Out of these 370, recovered and discharged. The left 21 cases were censored. The overall median time taken for resolution of DKA was 27hrs, IQR (16-38). DM history (AHR=0.41, 95% CI:0.30-0.56), severity of DKA (AHR=2.35, 95% CI:1.36-4.1), presence of comorbidity (AHR=1.76, 95% CI:1.37-2.26), and blood sugar level were (AHR= 0.61, 95% CI:0.39-0.96) all independent predictors of time to recovery from DKA.

**Conclusion:** Though the total median time to recovery from DKA was in the accepted range (<36hrs), it was significantly associated by the identified predictors in this study. Thus, increasing public awareness on symptoms of DKA, giving emphasis, enhancing quality of care, prioritize and treating children with identified predictors is important.



**Keywords:** Diabetes, diabetic ketoacidosis, recovery time, children

# 1. INTRODUCTION

## 1.1. Background

Diabetes mellitus is a prevalent, persistent metabolic disorder with elevated blood glucose as a key biochemical feature due to impaired insulin secretion, sensitivity, or both. Diabetes can be classified into different types, depending on the etiology of the disease. Type 1 and Type 2 diabetes mellitus (DM) are the two most prevalent variations of the illness (1, 2). Most children with diabetes are type 1 and require exogenous insulin for the rest of their lives (3).

Diabetic ketoacidosis is among the most severe clinical features of diabetes mellitus, which can result in dehydration, unconsciousness, and mortality (4). Absolute or relative insulin insufficiency is the primary cause of diabetic ketoacidosis (DKA). The continuous loss of beta cell reserve and function in a person with newly diagnosed diabetes is what leads to insulin insufficiency. The main factor causing diabetic ketoacidosis in those with preexisting diabetes is insulin omission (5).

The metabolism of carbohydrates, proteins, and lipids is significantly altered in DKA. Generally, the body undergoes a significant catabolic state with the breakdown of glycogen stores, hydrolysis of triglycerides from adipose tissues, and mobilization of amino acids from muscle (6). According to the International Society for Pediatric and Adolescent Diabetes( ISPAD), presence of blood sugar >200 mg/dL ( hyperglycemia),Venous pH less than 7.3 or serum bicarbonate less than 15 mEq/L (metabolic acidosis), having ketones in the blood (>3 mmol/L beta-hydroxybutyrate) or urine (ketosis) are required for diagnosis of DKA in children (7). However, in rare cases DKA may occur with slightly increase or normal blood glucose level which is known as euglycemic DKA(8). Although ketone bodies are normally present in the blood, when the body cannot use blood sugar, their levels rise to pathogenic levels (e.g., starvation, fasting, as a result of a defect in insulin synthesis, or vigorous exercise) (9, 10).

Depending on the bicarbonate (HCO3) level in the blood and the PH venous level, diabetic ketoacidosis can be categorized as mild, moderate, or severe. It is said to be mild DKA if the serum level of HCO3 falls below 15mmol/l and venous PH is between 7.2 and 7.3. If the venous PH level falls between 7.1 and 7.2 and the amount of serum bicarbonate falls below 10 mmol/l, moderate ketoacidosis develops. It is referred to as Severe DKA if the concentration of bicarbonate in the serum drops below 5mmol/l and venous PH descends under 7.1 (11).

In settings with limited resources like Ethiopia, the diagnosis of DKA mostly depends on the clinical features, existence of hyperglycemia, ketonuria, and glycosuria (12, 13). The other way of assessing the severity of DKA is using clinical condition of the child. In mild DKA the child is alert, and oriented but fatigued with no or some dehydration sign; moderate sign includes presence of kussmaul respiration, sleepiness, and dehydration; and patient with severe DKA exhibits kussmual's or depressed breathing, and shows sign of shock or severe dehydration plus sensorium depression to coma (1, 14).

Individuals who have diabetes are at the greatest risk of dying from DKA, which is the most frequent hyperglycemic emergency (15). It typically affects individuals with type 1 diabetes, although it has also been seen in persons with type 2 diabetes, typically under situations of significant physical stress like trauma, surgery, or illness (16). Having one episode of moderate or severe diabetic ketoacidosis at diagnosis is linked to worse cognitive scores and stunted brain development in children, with potential long-term consequences on neurocognitive function (17). Early diagnosis, comprehensive biochemical and clinical examination, and proper management is vital for successful recovery from DKA (6) .

The introduction of insulin to end ketosis and lower hyperglycemia, restoration of dehydration with intravenous (IV) fluids, and correction of electrolyte imbalances with electrolyte replenishment are all part of the management of DKA. Rehydrating children with DKA can be done carefully using a variety of IV fluid methods (18). Healthcare professionals and families need to be more aware of DKA prevention at the time of diagnosis. In order to avoid repeated DKA in the future, a parent must be informed, actively involved, and have access to proper and routine medical care (19). Implementation of any protocol should be cautiously performed as reversal of DKA is associated with risks such as hypokalemia, cerebral edema (CE) and hypoglycemia (1).

## 1.2. Statement of problem

In the 21st century, diabetes is one of the health crises with the fastest global growth. Every year, the number of childhood diabetes is increasing around the globe with rising cost of treatment for diabetes related illness. Type 1 diabetes (T1D) is estimated to affect over 1.2 million children, and adolescents under the age of 20 and around 108,200 of children below 15 years per year worldwide (20). Up to 80% of children under fifteen years diagnosed with diabetes are presented with DKA every year (21). In Africa, 59,500 children and adolescents have diabetes and 19700 are newly diagnosed each year (20).

DKA is the important cause of hospitalization among children with diabetes, globally. It is widely seen in everyday clinical practice, both in newly diagnosed cases (up to70%) and in known T1D patients (rate, 1-10% for every case each year) (11). DKA prevalence amongst children and adolescents with T1D varies significantly around the globe. In wealthy nations, the yearly incidence of DKA in children with known T1D receiving insulin therapy ranges from 5% to 7.1% (22) . The prevalence of DKA among T1D youth at diagnosis of DM was 35.3% in US, and 28.7% in India (23).

The majority of youngsters in Sub-Saharan Africa arrive at healthcare centers with DKA at initial diagnosis after a mild DM diagnosis was missed (24). Even though there is no study at national level in our country, according to some studies, the prevalence of DKA in Addis Ababa in newly diagnosed DM children ranges 35.8%-78.3% and 21.7%-64.2% in established DM (25, 26). In Tigray the prevalence of DKA in children with newly diagnosed T1D was 78.7% (27) , and the incidence of DKA in established T1D and T2D was 58.5% in East Gojjam (28).

With an average hospitalization rate of 16.5-78%, DKA is the leading cause of acute morbidity and death in children with T1DM (29),and the median period to recover from DKA ranges from 24hrs-8 days according to some studies (30, 31). In emerging nations, DKA associated death rates varies from 6% to 24% while in western nations it is 0.15% to 0.31% (32). This discrepancy may be due to poor management system in low-income countries. Both in wealthy and emerging nations, there have been reports of higher rates of death among children hospitalized with DKA along with an increase in cerebral edema (CE), shock, sepsis, altered level of consciousness, cerebral injury, renal failure, respiratory failure, and delayed diagnosis (32-35). Death form CE accounts 0.5-0.9% for all episodes of diabetic ketoacidosis (36). Due to these severe sequelae, DKA patients need to be closely monitored and receive sensitive, balanced therapy, most likely in ICU with aim of rehydrating, correction of acidosis and

disappearing of ketosis (11). In addition to this having a significant financial impact on healthcare systems, DKA also places an additional financial burden on patients and their families. As an example DM-related costs for young patients with DKA in Germany were up to 3.6 times greater than for those without DKA (37).

Studies showed time to recovery from DKA is affected by; severity of DKA, biochemical parameters such as blood glucose, serum creatinine, and serum electrolytes (38-44). With appropriate management children with DKA may recover in 10-36 hours depending on its severity (1). Different countries have implemented various methods and preventative measures, including diabetes self-management ,education, and adopting or establishing DKA treatment standards, to enhance DKA recovery and reduce mortality (45). There was not standard of practice in our country that focus on the management of DKA until 2014, when the federal ministry of health adopted DKA treatment protocol from ISPAD, the international guideline and standard text books. However due to poor healthcare system in our setup, the risk of mortality from DKA is high (26, 27, 46). By 2025, the Ethiopian government aims to decrease premature mortality from noncommunicable diseases, including diabetes, by one-fourth (47). Achieving this target plan needs conducting more research in this area.

Improving time taken to correct the acidosis with respect to time of initiating treatment of DKA in children is vital to reduce or prevent risk of morbidity and mortality as well as decrease the high expenses associated with treating the severe long-term effects of cerebral edema and other complications that may arise throughout the course of treating DKA. Beside to this, in countries like Ethiopia where there is limitation of pediatric intensive care unit (PICU) access, it decreases avoidable PICU admission due to DKA complication that occurs after starting treatment at pediatrics emergency unit. Most of previous studies in our country were focused on the prevalence, incidence, and determinant of frequency and outcomes of DKA, but not on the recovery time from diabetic ketoacidosis and factors affecting it among children with diabetes. Therefore, this study aimed to assess time to recovery from DKA and its predictors among children with diabetes at selected governmental hospitals in Addis Ababa, Ethiopia, 2023.

### 1.3. Significance of the study

Identifying time to resolution and factor affecting it among children with diabetic acidosis would be decisive for many stakeholders

It can help healthcare providers to identify high-risk patients who may require more intensive management to achieve timely recovery and to create efficient plans for enhancing the standard of care, for reducing errors associated with treatment, and for delivering quality care services to reduce time for correction of DKA. Shortening time to recovery from DKA can result in cost savings and can lead to better outcomes for children with DKA and potentially reduce the risk of long-term complications. Shorter hospital stays and reduced need for intensive care can translate to lower medical expenses, which can be particularly important for families of children with diabetes which may face significant financial burden.

The findings of this study can help generate new hypotheses and lead to further research, ultimately advancing the field of endocrinology and improving patient care.

Beside to this, for future investigators who are interested in conducting follow-up or metanalysis study on the area, the finding of this study would be used as input and framework by giving relevant evidence on factor associated with time of resolution from diabetic ketoacidosis in children.

Finally for ministry of health and policy makers it will give information to do nationwide research similar to this topic so that they establish DKA treatment protocol and regularly modify it based on researches finding.

# 2. LITERATURE REVIEW

This review of literature is organized into two parts. The literature on recovery time from DKA in children is discussed in the first section. The literature on factors that affect the time to recovery is described in the second part.

## 2.1. Time to recovery from DKA

As per studies conducted in various nations, the time duration taken for diabetic ketoacidosis to resolve in the pediatric population starting from initiation of treatment varies. In some studies, the median time taken to resolve from DKA was relatively shorter. In studies done in USA (40), Japan (41) and Turkey (48) the median time taken to resolve from DKA was 8.4hrs, 10 to 11hrs, and 14.30±6.43 hours respectively. In contrast, in studies done in India (49), Indonesia (50) , Iran (51), and China (52) the median time taken to resolve from DKA was relatively longer (26hrs, 28.8 ± 14.5, 21hrs (4-75hrs), and 41.72hrs respectively).

According to study conducted in Israel the median time to resolve from DKA among newly diagnosed DM was significantly longer than in established diabetes children (13 versus 8.5) (53). Correspondingly a multicenter retrospective cohort study conducted in Colombia revealed that duration of DKA ranges from 16 to 19hrs in NT1D and 8 to 16hr in PT1D (54).

Another prospective study done in Cipto Mangunkusumohe hospital; Indonesia shows that the median time of DKA resolution was 21 (9-52) hours (55). According to prospective hospital based comparative study conducted in children from 4 month to 13 years in India the average recovery time from diabetic ketoacidosis was 23.15hrs (56).

## 2.2. Predictors of time to recovery from DKA

### 2.2.1. Socio-demographic characteristics

Even though only few researches were found on factors that affects time to recovery from DKA in pediatrics population; socio demographic factors such as age, and sex, were not significantly associated with recovery time from DKA (30, 48, 57). Study done in India among adult DKA patients revealed that, male patients recover from DKA more rapidly than females (42).

### 2.2.2. Clinical characteristics

#### 2.2.2.1. Severity of DKA

Severity of DKA was found to be the significant predictor of time to recovery from DKA. According to study done in USA, in comparison to moderate and severe DKA, children presented with mild DKA recovered more quickly (40). Another study conducted in China showed that children admitted with mild DKA has short recovery time than moderate and severe DKA (39). Moreover, retrospective study in China revealed children with severe DKA at admission had 5.9hrs longer recovery time than mild DKA ($P < 0.001$) (38).

#### 2.2.2.2. Diabetic history

History of DM was also one of the significant factors that determine the time to recover from DKA. For instance, the study conducted in Colombia revealed that children presented with established T1D as compared to new onset of T1D had quick recovery time (54). Similarly a retrospective cohort study done in Japan on children with DKA described that child with new onset of T1D had prolonged recovery time than established one (41). Another study conducted in turkey has shown that new onset of DM was independent risk factor for recovery of DKA (48). Likewise, study carried out in Israel has shown children admitted with new onset of diabetes with DKA presentation had long recovery time than those with known type diabetes admitted with DKA ($P < 0.001$) (53).

#### 2.2.2.3. Comorbidity

Children with DKA may have additional illness that can precipitate the condition during admission to hospitals. A retrospective cohort study conducted in Japan has shown there was delay in DKA correction time in children with gastroenteritis (41).

Another retrospective study conducted in India revealed that correction time of diabetic ketoacidosis was significantly longer in children with acute kidney injury (AKI) than those without ($P=0.006$) (58).

### 2.2.3. Biochemical profile

According to retrospective cohort study conducted in Israel there was positive correlation between time of recovery from DKA and higher value of sodium and chloride, and there was negative correlation between bicarbonate level, potassium level, phosphorus level and PH value at presentation and recovery time of DKA (53). In contrast study done in Turkey has

shown there is no association of recovery time from DKA and serum sodium, chloride, potassium, and phosphorus at admission (48).

A study conducted in USA at Boston Children's Hospital has shown that HCO3>15 mmol/ accurately predicts the resolution of pediatrics DKA, and addressed that in limited setup where venous blood gas (VBG) is unavailable, electrolyte parameters alone could predict the resolution time of DKA (40). Another study done in USA at Miami children's hospital revealed that delta gap and base excess had negative association with time to recovery from DKA (57).

Study conducted in India addressed that, there was association between prolonged acidosis (lasting> 24 hrs.) and low PH, and high total leukocyte count at admission (30). A ten years retrospective study conducted in Japan has shown that there was a significant correlation between blood 3-hydroxybutyrate on admission and recovery time from DKA (correlation coefficient =0.72 ,P=0.005) (41). Moreover study conducted in turkey has shown that blood HCO3, base excess, and blood gas PH had negative correlation with DKA resolution time, whereas, calculated osmolality, serum creatinine, serum glucose, and anion gap were positively associated with time to resolve from DKA (48).

### 2.2.4. Treatment related factors

Colombian retrospective cohort study found that children with DKA treated with greater volume of intravenous fluid with larger sodium chloride content (0.9% normal saline, (Nacl 154 mEq/L) needed longer time of recovery than children managed with ringer lactate (Nacl 130 mEq/L) (54). A randomized control study conducted on children with DKA in USA shown children who received high volume of IV fluid (bolus (20 mL/kg) + 1.5 × maintenance rate) had significantly shorter recovery time from metabolic acidosis when compared to those received low volume of IV fluid (10ml/kg+1.25 × maintenance) ( [HR] = 2.0;95%, [CI] 1.0–3.9; P= 0.04) (43). Studies conducted on children showed slow rate of isotonic fluid for the management of DKA causes rapid resolution of DKA (P=0.01) (44).

### 2.3. Conceptual framework

By considering on the preceding review, time to recovery from diabetic ketoacidosis and its predictors among children admitted with DKA, the following conceptual framework has been summarized. This conceptual framework is built on the assumption that the time to recovery from diabetic ketoacidosis and its predictors is correlated to those factors as collected from various literatures. Besides new variables are added by hypothesizing that sociodemographic characteristics at admission will affect recovery time from DKA.

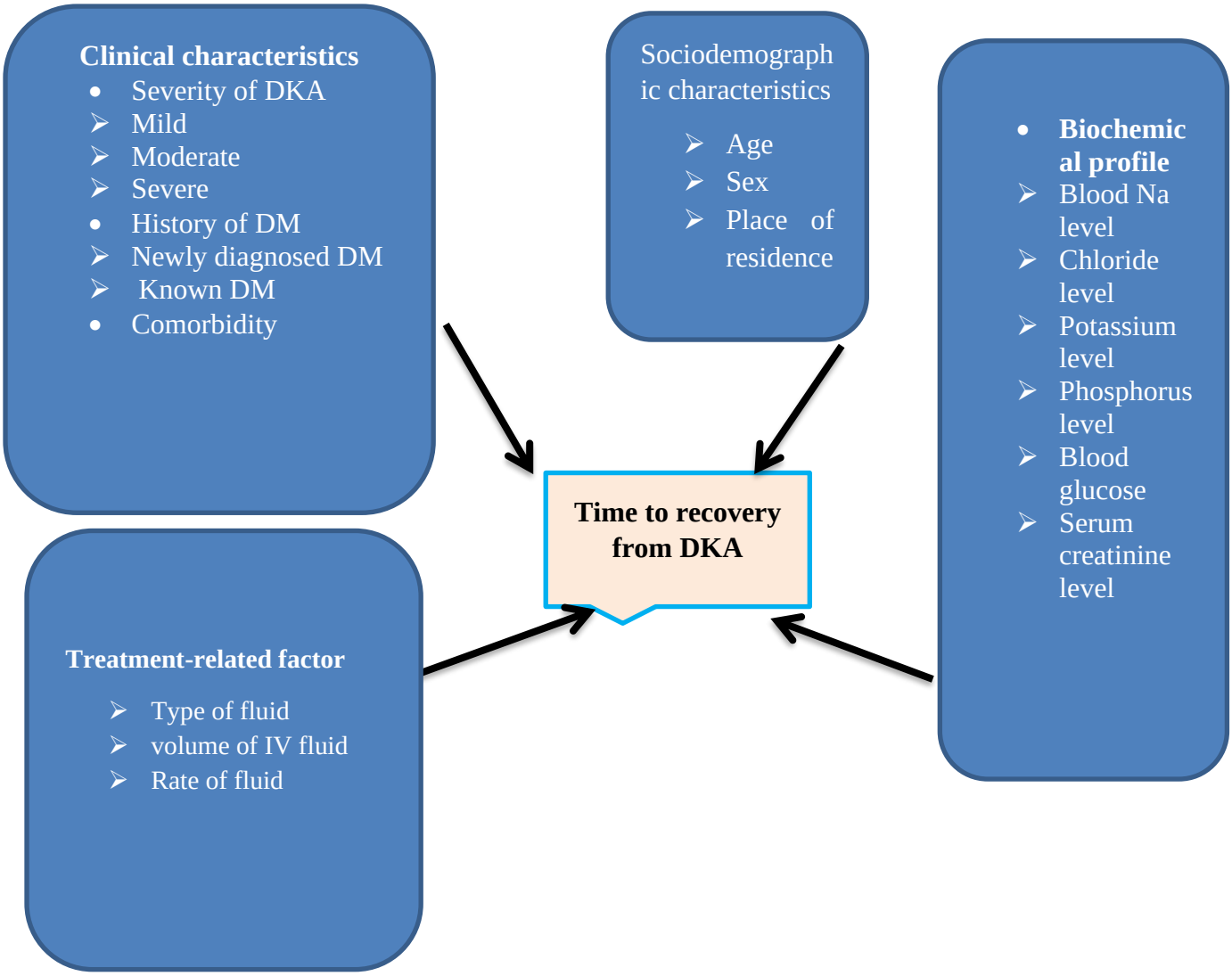


**Figure 1** Conceptual framework to determine time to recovery from diabetic ketoacidosis and its predictors among children with diabetic ketoacidosis admitted to selected governmental hospital from 2018-2022, Addis Ababa, Ethiopia, 2023 (30, 38, 40, 41, 43, 44, 48, 53, 54, 58)

# 3. OBJECTIVES

## 3.1. General objective

To assess time to recovery from DKA and its predictors among children with type 1 diabetes at selected governmental hospitals in Addis Ababa, Ethiopia, 2023

## 3.2. Specific objectives

- To determine time to recovery from DKA among children with type 1 diabetes at selected governmental hospitals in Addis Ababa, Ethiopia, 2023
- To identify predictors of time to recovery from DKA among children with diabetic ketoacidosis at selected governmental hospitals in Addis Ababa, 2023

# 4. METHODS AND MATERIALS

## 4.1. Study setting

The study was conducted at selected governmental hospitals in Addis Ababa, Ethiopia, among children aged from 1 month to ≤15 years and diagnosed with DKA who have been admitted to pediatric emergency, ward and PICU. Addis Ababa is the most populous and capital city of Ethiopia. According to United nation World population prospects, in 2023, it is estimated that over 5.4 million people live in the city, which has a total area of 527 square kilometers, and officially divided into eleven sub-cities and 121 districts. The city's population is growing at a rate of 4.46% (59) . There are 13 government hospitals in the city, distributed throughout 11 sub-cities. Among them, six are governed by the Addis Ababa health bureau, five of them are federal hospitals, one is owned by the military, and one is run by the police force (60). The study was done in Tikur Anbessa Specialized Hospital, Zewditu memorial Hospital, Saint Paul medical millennium college Hospital, Saint Peter specialized Hospital, and Yekatit 12 Hospital.

## 4.2. Study design and period

An institution-based retrospective follows up study was conducted on children with diabetic ketoacidosis who attended care, and treatment at the selected governmental hospital from March 16, 2023--April 16, 2023 in Addis Ababa, Ethiopia.

## 4.3. Population

### 4.3.1. Source of population

All children admitted and treated for DKA at all governmental Hospitals in Addis Ababa from the first of January 2018 to 31$^{th}$ of December 2022.

### 4.3.2. Study population

All children admitted and treated for DKA at the selected governmental Hospital from the first of January 2018 to 30$^{th}$ of December 2022.

### 4.3.3. Sample population

All children admitted and treated for DKA that fulfill inclusion criteria at selected governmental Hospitals in Addis Ababa who have been recorded from January 1, 2018 to 30$^{th}$ of December of 2022.

### 4.4. Eligibility criteria

#### 4.4.1. Inclusion criteria

- All children aged from 1 month to ≤15 years, and were admitted with DKA to each selected governmental Hospital in Addis Ababa.

#### 4.4.2. Exclusion criteria

- Incomplete or unavailable medical records of children who were admitted with DKA to each selected governmental Hospital in Addis Ababa was excluded.

### 4.5. Sample size determination and sampling procedure

#### 4.5.1. Sample size determination

A single population proportion formula was employed to calculate the sample size by considering the following statistical assumptions:

P = 0.5 since there is no study done in our country on time to recovery from DKA in children.

By considering 95% confidence interval (CI) with level of precision $Z\alpha_{/2}$= 1.96, margin of error 0.05.

$$n= \frac{Z\,(a/2)^{2}\,P\,(1-P)}{d^{2}}$$

$$n= \frac{(1.96)2\,(0.5)\,(0.5)}{(0.05)^{2}}$$ **n= 384**. By adding 10% for missing or incomplete data, (38.4), giving final total sample sizes of = **423.**

#### 4.5.2. Sampling technique and procedure

Among 13 governmental hospitals located in Addis Ababa, 5 hospitals were selected randomly by using simple random sampling technique. In order to identify study participants, the total number of children hospitalized with DKA from January 1, 2018 to the 31$^{th}$ of December 2022 was identified using list of medical records of children with DKA that recorded on health management information system (HMIS)) of each institution. By proportionally dividing the total sample, sampling units was chosen from each institution. Finally using random sampling technique, the study participants was selected from each selected hospitals as shown in figure 2.

Proportional sample size allocation = $\frac{\boldsymbol{nf \times Nj}}{\boldsymbol{N}}$

Where, N = total number of children admitted with DKA in the selected hospitals

nf =final sample size of the study

Nj =number of children admitted with DKA in each hospital

After the total children DKA cases of each 5 five years in each 5 selected hospitals was taken, for each year, the final sample was calculated as

Sy = $\frac{Y \times nf}{N}$

Where Sy= is the number of children DKA cases that was selected from each five-years, Y= the number of children DKA cases of each 5 year, and nf= final sample size of the study, and N = total number of children admitted with DKA in the selected hospitals

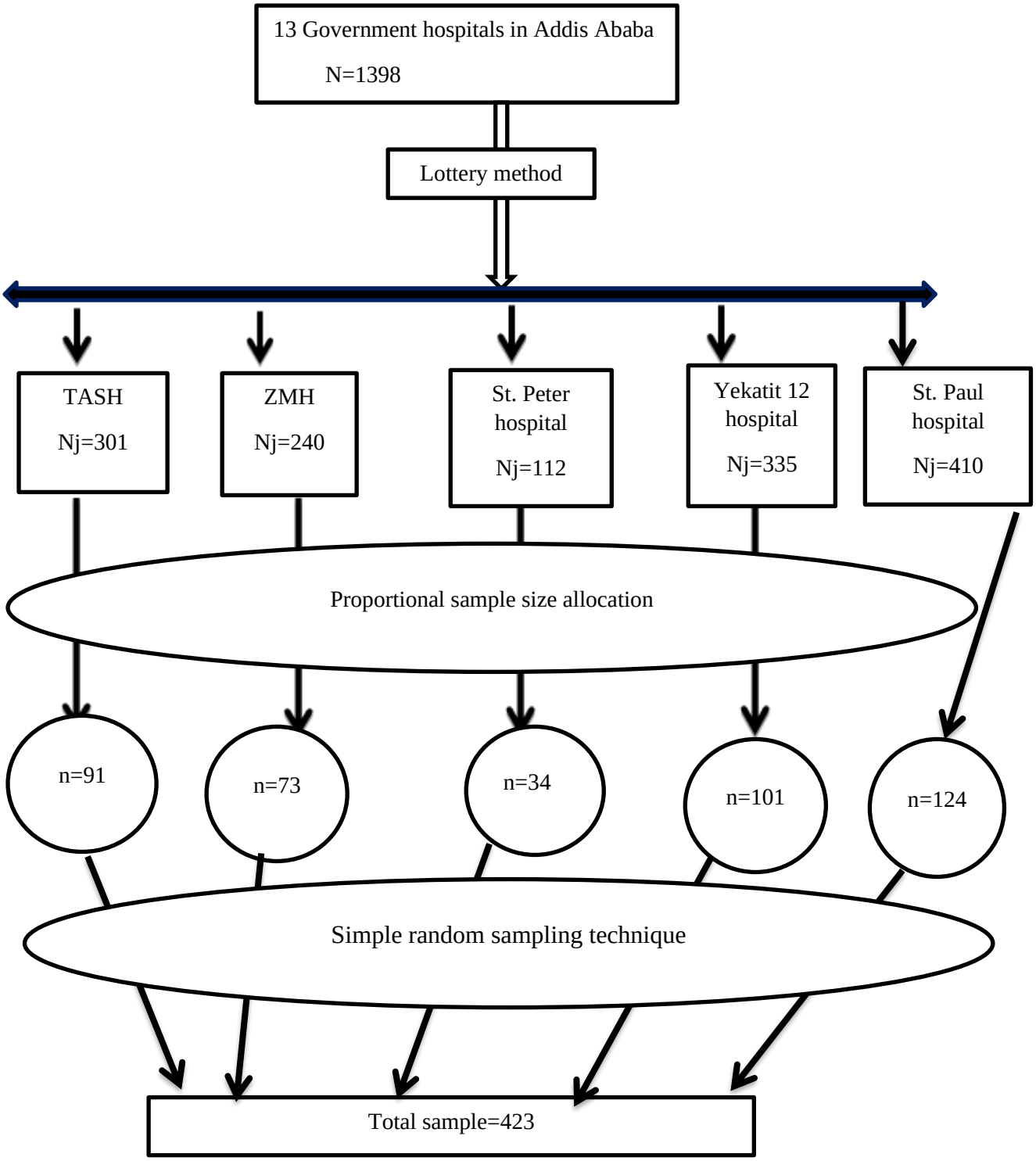


Figure 2 Schematic presentation of sampling procedure to assess time to recovery from DKA and its predictors among children admitted with DKA at governmental hospitals in Addis Ababa,2023.

### 4.6. Variables

#### 4.6.1. Dependent variable

Time to recovery from diabetic ketoacidosis

#### 4.6.2. Independent variables

Socio demographic characteristics

- Age, sex, place of residence

Clinical characteristics

- Severity of DKA (mild, moderate, severe)
- History of DM (newly diagnosed or established)
- comorbidities (AKI, gastroenteritis, others.)

Biochemical profile

- Blood Na level, chloride level, potassium level, phosphorus level, blood glucose level, creatinine

Treatment related factors

- Type of fluid, volume of IV fluid, rate of fluid

### 4.7. Operational definition

**Event:** Children recovered from DKA before discharge or transferred to other facility for any reason.

**Censored:** Children transferred to other facility, discontinuation against therapy of DKA, or died for any reason before recover from DKA, and children with unknown status.

**Newly diagnosed DM**: children diagnosed with DM for the 1st time in patient with previously no history/ unknown status of DM.

**Established DM**: patient with previous history of DM or known DM patient on follow up.

**Euglycemic DKA:** blood sugar level<250 mg/dl, positive for urine ketone and symptoms of metabolic acidosis

**Mild DKA:** Patient who meet DKA criteria, and who are alert, and oriented but fatigued with no or some dehydration sign(1)

**Moderate DKA:** A patient who meet DKA criteria and has kussmaul respiration, is lethargic and exhibits shock or dehydration sign(1).

**Severe DKA:** patient who fulfills DKA criteria and exhibits kussmaul's or depressed breathing, and shows sign of shock or severe dehydration plus sensorium depression to coma (1)

**Index cases of DKA:** the first DKA episode admitted and recovered or not recovered at selected hospitals in patients with previous history of DKA at others health institution or newly diagnosed at study areas.

**Time interval:** time period in hours from fluid management of DKA started to the occurrence of event or censored

**Time to recovery from DKA:** time period in hours from which fluid management of DKA is started until absence of two consecutive ketone in the urine (13).

**Resolution of DKA (Recovery from DKA):** absence of two consecutives ketone in the urine since the beginning of DKA therapy (13, 61).

**Prolonged recovery**: if overall median time to recover from DKA is >36hrs, for mild and moderate DKA>24hrs, and for severe cases >36hrs (1).

### 4.8. Data collection tools and procedures

The tool was prepared, adopted and modified according to Ethiopian context from available information on patient's medical chart, and from previous related literature (41, 48, 54). The checklist was prepared in English language, it consists of four parts; Part one -socio demographic characteristics of study participants, part-two- participants clinical characteristics on admission, part three biochemical profile, and part four treatment-related factors. After getting approval letter from responsible bodies template of checklist was prepared in Kobo Toolbox and shared through cell phones URL and given for three trained BSc nurses. Data was collected from medical records like patient's electronic records and charts. Only index cases were included and recurrent cases of DKA episodes were excluded to avoid selection bias. The medical records were retrieved using the client's registration numbers which was identified in the registration books. The starting point for retrospective follows up is the time from which the patient's started treatment of DKA and end point is the time at which patients recovered

from DKA. The study participants records were assessed to exclude ineligible cases before starting collection of data.

### 4.9. Data quality assurance

To assure the quality of the data, the checklist was assessed for its completeness and coherence and pretest was done on 5% (21 charts) of study samples at Tirunesh Beijing hospital 15 days prior to data collection date. The validity of the checklist was checked by experts. The suggestion and comments of the experts was recorded and revision was made. Then crucial modification was done to warrant comprehensiveness and clarity of the tool. Data was collected and supervised by BSc nurses. Training was given for data collectors and supervisor. On each day of data collection, the collected data was checked for completeness. The principal investigator was meticulously entered and properly clean the data before starting the analysis. Data cleaning was done using Stata version 16 statistical software.

### 4.10. Data processing and analysis

The data was collected using kobo Toolbox, and exported to Stata version 16 software for cleaning, categorizing and analysis. The clinical and sociodemographic characteristics of the study participants was described by descriptive statistics such as median, percentage and frequency. To calculate the DKA mean free survival time, Kaplan Meier survival curve was utilized. The DKA-free survival time was compared between several categorical explanatory variables by log-rank test using chi square and p-value. A Cox proportional hazard model with a hazard ratio, 95% CI was used to analyze the predictors of DKA recovery time. Variables with p-value of less than 0.25 in the bivariate analysis was added to the multivariate Cox proportional hazards model, and variables with p-value $< 0.05$ in the multivariate Cox proportional hazards model was considered as significant predictors of time to recovery from DKA. The proportional hazard assumption was assessed graphically using log-log plot, and goodness of model fit was tested based on Schoenfeld residual (phtest) test. The overall global test p-value was 0.0507. To calculate recovery time, hours was utilized as time scale. The status of study participants was dichotomized as either event or censored.

### 4.11. Ethical consideration

Ethical clearance was obtained from research ethical review board of Addis Ababa University, College of Health Science, School of Nursing and Midwifery, Department of Nursing, and distributed separately to selected hospitals (Ref. No pm 23/681). The supportive letters were obtained from Department of Nursing. The copy of ethical clearance and supportive letters was taken directly to tertiary hospitals governed by ministry of health and to Addis Ababa health bureau for hospitals under control of Addis Ababa health bureau. Then the permission letter was written to each selected hospital. The information gathered was held confidentiality; names and any other personal identifiers was not used during data collection and analysis. The data collectors were informed to keep the patient's information confidentially. Security of the data was maintained using secret code after exported into computer.

### 4.12. Dissemination of the result

The result of this study was submitted and presented to Addis Ababa University, School of Health Sciences, Department of Nursing and Midwifery as a partial fulfillment of post graduate program in child health nursing. It will so be disseminated to those hospitals where the research was conducted. Moreover, efforts will be made to present the finding at national and international conference. Lastly, we will attempt to publish the findings of this study on reputable and peer- reviewed international journals

# 5. RESULTS

## 5.1. Sociodemographic characteristics of study participants

Of 1398 DKA admission from January 1st, 2018 to January 30th, 2022, 423 charts were randomly selected for this study. Three charts were absent, and twenty-nine charts were incomplete and excluded from this study. Three hundred ninety-one (92.4%) fulfills the inclusion criteria.

The median age of the participants were 8 years with an interquartile range (IQR) of 3.5-11 years. More than half (56.3%) of the study participants were males. More than two-third (69.6%) of the patients were from Addis Ababa. Majority (60.4%) of children were from Addis Ababa

Table 1: Socio-demographic characteristics of children admitted with DKA at selected public hospitals in Addis Ababa from January, 2018 to December, 2022, (n=391).

| Variables | Category | Survival status | |
|---|---|---|---|
| | | Recovered n (%) | Censored n (%) |
| Age in years | Under five | 115(94.3%) | 7(5.7) |
| | 5-10 | 128(92) | 11(8) |
| | >10 | 127(97.7) | 3(2.3) |
| Sex | Male | 206(93.6) | 14(6.4) |
| | Female | 164(96) | 7(4) |
| Residence | Addis Ababa | 263(96.7) | 9(3.3) |
| | Out of Addis Ababa | 107(90) | 12(10) |
| Family history of DM | Yes | 138(94) | 9(6) |
| | No | 224(95) | 12(5) |
| | Unknown | 8(100) | 0(0) |

### 5.2. Clinical Characteristics and Patient baseline information

More than half (51.2%) of the participants had no previous history of DM before admission. The median duration of illness in previously diagnosed DM subjects was 2 years. Most of the participants (93.7 %) admitted with known diabetes were on mixed (NPH and Regular) insulin. Non-compliance to insulin was the most common (51.3%) precipitating factor in known DM patients, followed by infection (26.2%). The most frequently diagnosed acute comorbid illness was respiratory tract infection (11.5%), followed by urinary tract infection 21 (5.4%). The others nineteen (4.9%) had gastroenteritis, and seventeen (4.3%) came with other illnesses. Around three-fourth of the study subjects (74.4%) had a history of polysmptoms. All study subjects presented with a history of polysmptoms had a history of polyuria. Sixty-one (15.6%) of study participants were presented with shock. Regarding to severity of DKA, 180 (46%), were mild, 140 (35.8%) moderate, and 71 (18.2%) were severe. (Table 2)

Table 2: Clinical characteristics of children admitted with DKA at selected governmental hospitals in Addis Ababa from January 2018 to December, 2022, (n=391).

| Clinical characteristics | Categories | Survival status | |
|---|---|---|---|
| | | Recovered n (%) | Censored n (%) |
| History of DM | Newly diagnosed | 187 (93.5) | 13 (6.5) |
| | Known | 183 (95.8) | 8 (4.2) |
| Type of insulin (n=191) | Mixed (NPH and regular insulin) | 171(95.5) | 8 (4.5) |
| | NPH | 11(100) | 0 (0) |
| | Regular and Lente | 1(100) | 0 (0) |
| Precipitating factor among known DM children (n=191) | Total omission of insulin | 79(95.2) | 4(4.8) |
| | Inadequate dosage of insulin | 15(100) | 0(0) |
| | Infection | 47(94) | 3(6) |
| | Consumption of high carbohydrate content food and fluid | 22(95.7) | 1(4.3) |
| | Others | 3(100) | 0(0) |
| | Unknown | 17 (100) | 0(0) |
| Poly-symptoms | Polyuria | 275 (94.5) | 16(5.5) |

Table 2 continued

| | | | |
|---|---|---|---|
| | Polydipsia | 260 (95.0) | 14(5.0) |
| | Polyphagia | 60(87.0) | 9(13.0) |
| Nausea/vomiting | Yes | 224(93.7) | 15(6.3) |
| | No | 146(96.0) | 6(4.0) |
| Abdominal pain | Yes | 169(93.0) | 13(7.0) |
| | No | 201(96.2) | 8(3.8) |
| Fever | Yes | 108(94.7) | 6(5.3) |
| | No | 262(94.6) | 15(5.4) |
| Weight loss | Yes | 171 (94.5) | 10(5.5) |
| | No | 199 (94.8) | 11 (5.2) |
| Kussmual breathing | Yes | 176 (92.6) | 14(7.4) |
| | No | 194 (96.5) | 7(3.5) |
| Changed in mentation | Yes | 164 (93.7) | 11(6.3) |
| | No | 206 (95.4) | 10(4.6) |
| Shock | Yes | 59 (96.7) | 2(3.3) |
| | No | 311(94.2) | 19(5.8) |
| Dehydration | Yes | 183 (93.4) | 13(6.6) |
| | No | 128(95.5) | 6(4.5) |
| Severity of DKA | Mild | 174(96.7) | 6(3.3) |
| | Moderate | 127(90.7) | 13(9.3) |
| | Severe | 69 (97.2) | 2 (2.8) |
| Comorbidity | Yes | 98(96.0) | 4(4.0) |
| | No | 272 (94.0) | 17(6.0) |
| Types of comorbidities | Respiratory tract infection | 43(95.6) | 2(4.4) |
| | Urinary tract infection | 21(100) | 0(0) |
| | Gastroenteritis | 18(94.7) | 1(5.3) |
| | Others | 16(94) | 1(6) |

Others= stress, trauma

### 5.3. Biochemical profiles of study participants

Three hundred seventy (94.6%) children were hyperglycemic, and twenty-one (5.4%) were euglycemic. The majority of urine glucose (30.9%) at arrival was plus three (+3). About half

of the study subjects were presented with ketonuria plus three. One hundred sixty-nine (43.2%) had blood sodium of below 135 mmol/l. Twenty-two (5.6%) had hypernatremia. The median chloride level, and potassium level on admission were 100.4 (68-137) mmol/l, 4.54 (2.3-7.69) mmol/l respectively. (Table 3)

Table 3:Biochemical characteristics of children admitted with DKA at selected public hospitals in Addis Ababa from January 2018 to December, 2022, (n=391).

| Variable | Category | Survival status | |
|---|---|---|---|
| | | Recovered n (%) | Censored n (%) |
| RBS | Hyperglycemic | 349(94.3) | 21(5.7) |
| | Euglycemic | 21(100) | 0 (0) |
| Urine glucose | Negative | 46 (100) | 0 (0) |
| | +1 | 81 (97.6) | 2 (2.4) |
| | +2 | 103 (95.4) | 5 (4.6) |
| | +3 | 114 (94.2) | 7 (5.8) |
| | +4 | 26 (78.8) | 7 (21.2) |
| Urine ketone | +1 | 15(100) | 0(0) |
| | +2 | 106(96.4) | 4(3.6) |
| | +3 | 186(95.9) | 8(4.1) |
| | +4 | 63(87.5) | 9(12.5) |
| Sodium (mmol/l | Below 135 | 160 (94.7) | 9 (5.30) |
| | 135-145 | 189 (94.5) | 11(5.5) |
| | >145 | 21 (95.5) | 1(4.5) |
| Chloride (mmol/l) | Low | 106 (93) | 8(7) |
| | Normal | 204 (95.8) | 9(4.2) |
| | High | 60(93.8) | 4(6.3) |
| Potassium (mmol/l) | Below 3.5 | 32 (94.1) | 2 (5.9) |
| | 3.5-5.5 | 292 (94.8) | 16 (5.2) |
| | >5.5 | 46 (93.9) | 3(6.1) |
| Age-specific creatinine level mg/dl | Normal | 267 (94) | 17(6) |
| | High | 103(96.3) | 4(3.7) |

### 5.4 Treatment-related characteristics of study subjects

Among a total of 391 children with DKA, 278 (71.10%) were treated with IV fluid. All children were injected with regular insulin. Two hundred eight six (73.1%) taken IV boluses. RBS was checked every one hour, and urine ketone was assessed every two hours. Potassium (KCL) was added for 237 (60.61%) of the study subjects. The most frequently used fluid was NS and DNS. Children with comorbid illnesses were managed with specific treatments for each disease. (Table 4)

Table 4:Treatment related characteristics of children admitted with DKA at selected governmental hospitals in Addis Ababa from January 2018 to December, 2022. (n=391)

| Variable | Category | Survival status | |
|---|---|---|---|
| | | Recovered n (%) | Censored n (%) |
| Fluid management | Iv fluid | 262 (94.2) | 16 (5.8) |
| | Oral fluid | 92 (95.8) | 4(4.2) |
| | Both iv and oral | 16 (94.1) | 1 (5.9) |
| IV bolus | Received | 270(94.4) | 16 (5.6) |
| | Not received | 100 (95.2) | 5 (4.8) |
| KCL | Added | 224 (94.5) | 13 (5.5) |
| | Not added | 146(94.8) | 8 (5.2) |
| Other medication | Antibiotics<br>Others<br>Both antibiotics and others | 64 (98.5)<br>14 (82.4)<br>9 (81.8) | 1 (1.5)<br>3 (17.6)<br>2(18.2) |

IV fluid= Normal saline, DNS, ringer lactate. Oral fluid= ORS, water. KCL=potassium chloride

### 5.5. Time to recovery from diabetic ketoacidosis and overall Kaplan- Meier survivor function

Among a total of 391 study subjects 370 (94.6%) were recovered and discharged from hospital, whereas 21(5.4%) were censored. More than half (11) of censored case were unknown status, one was gone against medical therapy, six were absent on call, two were transferred to other facility, and one was died. The median length of stay in hospitals was 4 days. There was a total of 11,289 analysis time at risk and under observation. As shown in figure 3 the overall median time to recovery from ketosis was 27hrs, IQR (16-38). The median time was prolonged in moderate and severe DKA, (30 and 42 hrs. respectively).

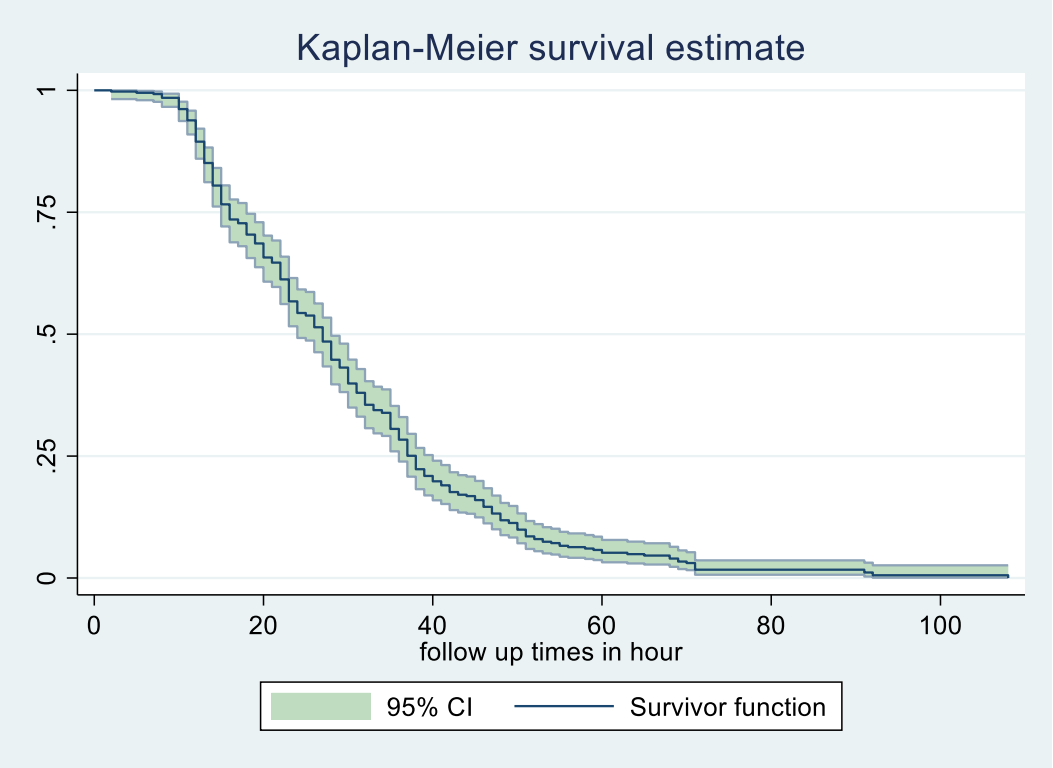


Figure 3**:**Overall Kaplan-Meier estimation of survivor functions of children with diabetic ketoacidosis followed at selected governmental hospitals, Addis Ababa, Ethiopia, from January 2018 to December 2022, (n=391)

### 5.6 Comparison of survival status

The Log-Rank test was performed to assess survival time between predictor groups. Based on this test, survival time was significantly different across several groups of predictors such as diabetes history, severity of DKA, presence of comorbidities, blood glucose level at a 5% level

of significance. The median time to resolve from DKA varied across independent categorical variables. As shown in figure 4 the median time to recover from diabetic ketoacidosis in children with newly diagnosed type 1 DM was longer than that of previously diagnosed DM, 32, and 23hrs respectively.

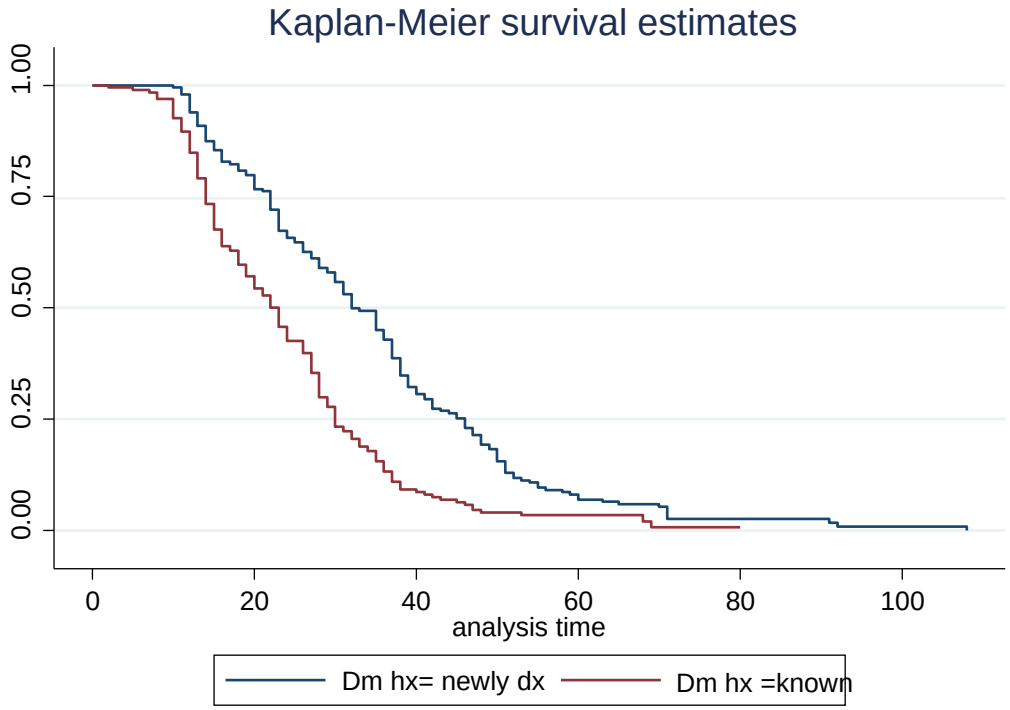


Figure 4. The Kaplan-Meier survival curves showing the survival status of children with DKA at selected governmental hospitals by history of diabetes, Addis Ababa, Ethiopia from January 2018 to December 2022, (n=391).

There was also variation of median time among children admitted with DKA regarding the severity of DKA. Children with mild DKA had a quick median recovery time which was 19hrs than moderate (30hrs) and severe (42hrs) DKA.

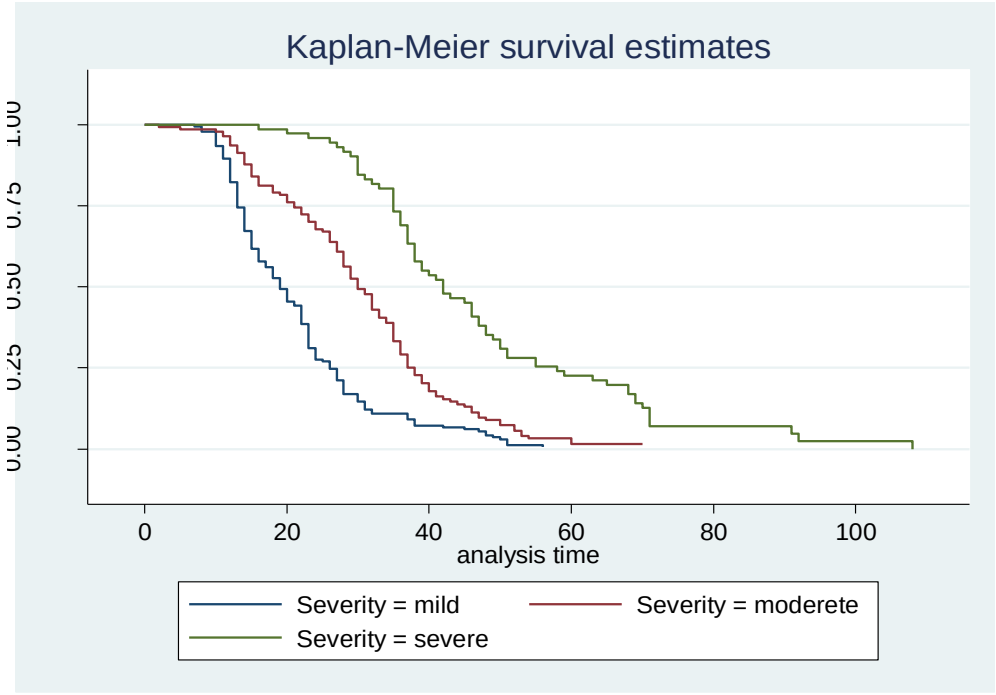


Figure 5: The Kaplan-Meier survival curves showing the survival status of children admitted with DKA at selected governmental hospitals by severity of DKA, Addis Ababa, Ethiopia from January 2018 to December 2022, (n=391).

Besides this, in comparison with children presented without acute comorbid illness, children with acute comorbid illness were delayed in median recovery time from DKA (23, 36hrs respectively), as shown in figure below.

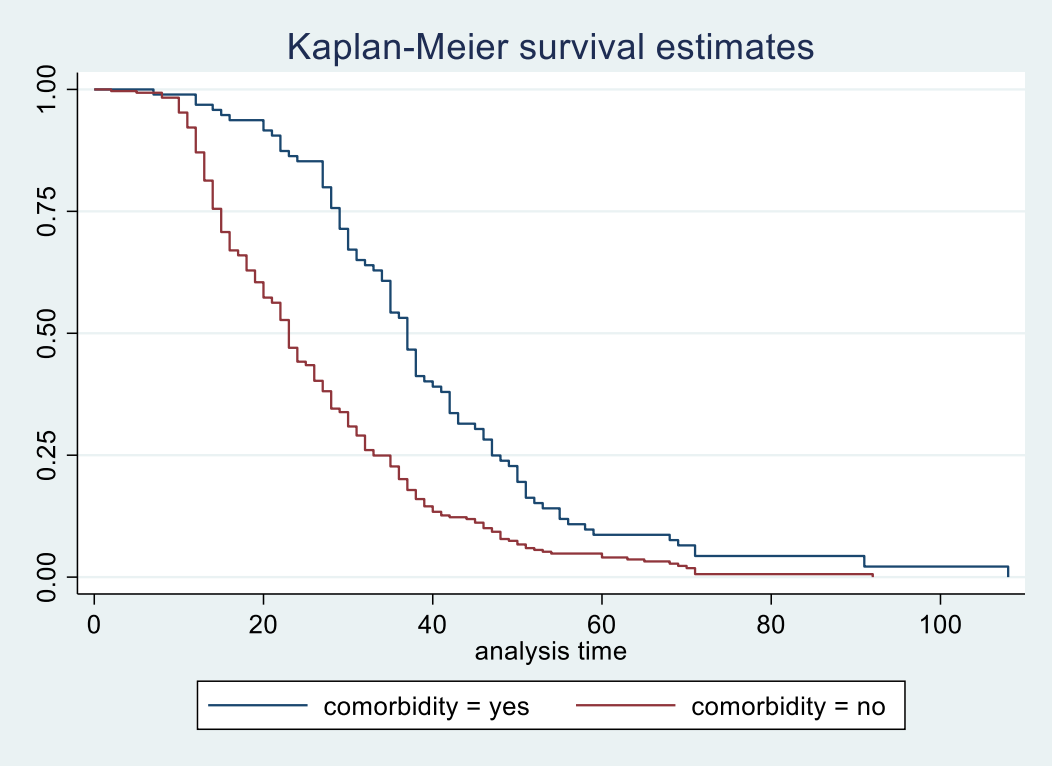


Figure 6: The Kaplan-Meier survival curves showing the survival status of children admitted with DKA at selected governmental hospitals by presence of comorbid diseases, Addis Ababa, Ethiopia from January 2018 to December 2022, (n=391).

In addition to this, children admitted with high blood sugar (>250mg/dl) had longer time to recovery when compared to their counterparts.

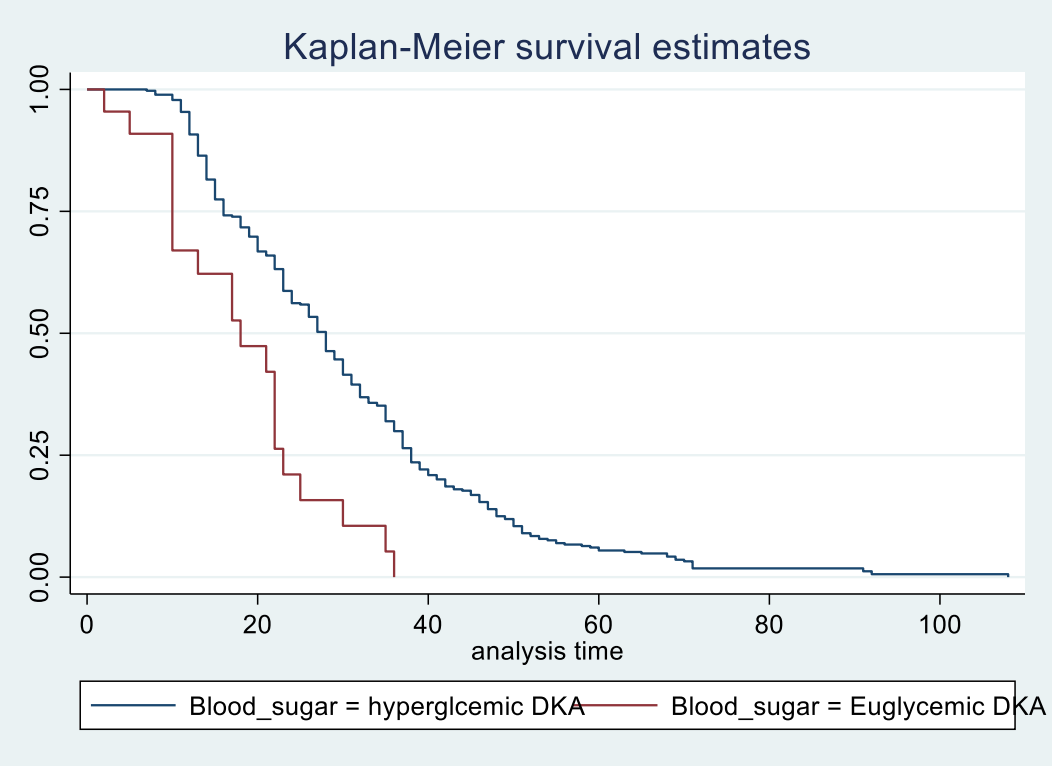


Figure 7. The Kaplan-Meier survival curves showing the survival status of children admitted with DKA at selected governmental hospitals by blood glucose level Addis Ababa, Ethiopia from January 2018 to December 2022, (n=391)

The following table also shows the comparison of median time to recovery from DKA within each group of explanatory variables by p-value and chi$^2$ log rank test. There was statistically significant difference in time to recovery between each group of predictors as log- rank test p-value was less than 0.05 (See table 5)

Table 5: Median time to recovery and log rank test according to different characteristics of children admitted with diabetic ketoacidosis at selected governmental hospitals from January 2018 to December2022, Addis Ababa, Ethiopia (n=391)

| Variables | Category | Median time to recovery (95%CI) | Log-rank test | |
|---|---|---|---|---|
| | | | p-value | $X^2$ |
| Diabetic history | Newly dx | 32 (30-36) | 0.000 | 41.75 |
| | Known DM | 23 (19-24) | | |
| Polysypmtoms | Yes | 28 (26 -31) | 0.0001 | 15.43 |
| | No | 23 (18-27) | | |
| Nausea and vomiting | Yes | 30 (28-32) | 0.0001 | 16.29 |
| | No | 22(24-28) | | |
| Weight loss | Yes | 31(28-36) | 0.0000 | 26.24 |
| | No | 23(21-26) | | |
| Abdominal pain | Yes | 30(28-33) | 0.0000 | 21.82 |
| | No | 23(21-24) | | |
| Kussmual breathing | Yes | 35(32-37) | 0.0000 | 83.55 |
| | No | 27(24-28) | | |
| Shock | Yes | 42(37-47) | 0.0000 | 42.03 |
| | No | 23(22-26) | | |
| Severity | Mild | 19(17-22) | 0.0000 | 121.95 |
| | Moderate | 30(28-33) | | |
| | Severe | 42(38-47) | | |
| Comorbidity | Yes | 36(31-38) | 0.0000 | 22.84 |
| | No | 23(22-26) | | |
| Blood glucose level | Hyperglycemic | 28(26-39) | 0.0000 | 18.98 |
| | Euglycemic | 17(13-22) | | |
| Fluid mgt | Taken Iv fluid | 31(29-35) | 0.0000 | 93.56 |
| | Taken oral fluid | 15(13-19) | | |
| | Taken both | 28(14-31) | | |
| Iv bolus | Yes | 31(29-34) | 0.0000 | 72.50 |
| | No | 16(14-19) | | |

### 5.6. Predictors of recovery time from DKA

In the Bivariate Cox Proportional Hazards regression model; diabetic history, Polysymptoms, nausea and vomiting, weight loss, abdominal pain, Kussmaul breathing, presence shock of on admission, severity of DKA, Presence of comorbidity, blood glucose level, fluid management and Iv bolus were significantly associated with time to recovery from DKA among children at p-value less than 0.25.

After controlling for possible confounders Multivariable Cox-proportional hazard regression analysis showed that diabetic history, severity of DKA, presence of comorbidity, and random blood glucose level were all found to be the significant predictors of time to recover from DKA among children at $p$-value $\leq 0.05$.

This study revealed that time to recovery from DKA in children with new onset diabetes was delayed by about 59% (AHR=0.41, 95% CI: 0.30-0.56) compared with children with known (established) diabetes. Children admitted with mild and moderate DKA was 2.35 and 1.73 times more likely to recover from DKA than those with severe DKA., (AHR=2.35, 95% CI: 1.36-4.10), and (AHR=1.73, CI:1.13-2.63) respectively. The recovery time was 1.76 times faster in children without another comorbid diseases when compared to those presented with other comorbid illness. (AHR=1.76, 95% CI:1.37-2.26). Children with hyperglycaemic DKA was 39% less likely to recover from DKA compared to euglycemic DKA. (AHR=0.61, 95% CI: 0.39-0.96).

Table 6: Bivariable and Multivariable cox proportional hazards regression analysis of time to recovery from DKA among children admitted with diabetic ketoacidosis at selected governmental hospitals in Addis Ababa from January, 2018 to December, 2022 (n=391)

| Variables | Categories | Survival status | | CHR (95%CI) | AHR (95%CI) | P-value |
|---|---|---|---|---|---|---|
| | | Recovered (%) | Censored (%) | | | |
| Diabetic history | New onset | 187(93.5) | 13(6.5) | 0.51(0.42-0.63) | 0.41 (0.30-0.56) * | 0.000 |
| | Known DM | 183(95.8) | 8 (4.2) | 1 | 1 | |
| Polysymptoms | Yes | 275(94.5) | 16(5.5) | 0.63 (0.50-0.80) | 1.1 (0.81-1.45) | 0.598 |
| | No | 95 (95) | 5 (5) | 1 | 1 | |
| Nausea and vomiting | Yes | 224 (93.72) | 15 (6.28) | 1 | 1 | |
| | No | 146(96.05) | 9 (3.95) | 1.52(1.23-188) | 1.14 (0.87-1.50) | 0.341 |
| Weight loss | Yes | 171(94.48) | 10 (5.52) | 1 | 1 | |
| | No | 199 (94.76) | 11 (5.24) | 1.70(1.38-2.10) | 0.99 (0.73-1.36) | 0.992 |
| Abdominal pain | Yes | 169(92.86) | 13(7.14) | 1 | 1 | |
| | No | 201(96.17) | 8(3.83) | 1.62 (1.31-20) | 1.3(1.0-1.64) | 0.055 |
| Kussmaul breathing | Yes | 176(92.63) | 14(7.37) | 1 | 1 | |
| | No | 194(96.52) | 7 (3.48) | 2.61(2.10-3.25) | 1.40(0.95-2.0) | 0.09 |
| Shock on admission | Yes | 59(96.72) | 2(3.28) | 0.41 (0.31-0.54) | 0.88 (0.60-1.32) | 0.529 |
| | No | 311(94.24) | 19(5.76) | 1 | 1 | |
| Severity of DKA | Mild | 174(96.67) | 6(3.33) | 4.86 (3.55-6.65) | 2.35 (1.36-4.1) * | 0.002 |
| | Moderate | 127(90.71) | 13(9.29) | 2.36 (1.72-3.24) | 1.73 (1.13-2.63) * | 0.011 |
| | Severe | 69(97.18) | 2(2.82) | 1 | 1 | |
| Presence of comorbidity | Yes | 98 (96.1) | 4 (3.9) | 1 | 1 | |
| | No | 272(94.12) | 17 (5.88) | 1.73 (1.37-2.20) | 1.76(1.37-2.26) * | 0.000 |
| Blood glucose level | Hyperglycaemic | 349 (94.32) | 21(5.68) | 0.39 (0.25-0.61) | 0.61 (0.39-0.96) * | 0.033 |
| | Euglycemic | 21(100) | 0 (0) | 1 | 1 | |
| IV bolus | Taken Iv bolus | 270(94.41) | 16 (5.59) | 1 | 1 | |
| | Not taken Iv bolus | 100 (95.24) | 5(4.76) | 2.65 (2.10-3.37) | 0.74 (0.39-1.43) | 0.376 |
| Fluid management | Iv fluid | 262 (94.24) | 19 (6.7) | 1 | 1 | |
| | Oral fluid | 92(95.83) | 4(4.17) | 3.18(2.47-4.08) | 2.0 (1.0-3.92) | 0.051 |
| | Both | 16(94.12) | 1(5.88) | 1.53 (0.92-2.54) | 1.14(0.66-1.95) | 0.639 |

### 5.7 Multicollinearity test

Multicollinearity test was checked using variance inflation factor (VIF) for each predictor's variables. There is no clear agreement on its normal value. Some experts recommend a value of VIF less than 10 is acceptable whereas others authors state it should be less than 4. The table below shows the multicollinearity test done for variables that had a p value of less than 0.25 in binary cox regression using VIF. As it is shown in the table all listed variables has a value of VIF less than 4. From this we can concluded that there was no collinearity between each explanatory independent variable.

**Table 7**: Multicollinearity test on predictors of time to recovery from diabetic ketoacidosis in children admitted with diabetic ketoacidosis in selected governmental hospitals from January 2018 to December 2022, Addis Ababa, Ethiopia

| Variables | VIF | 1/VIF (Tolerance) |
|---|---|---|
| Diabetic history | 2.22 | 0.45 |
| Polysmptoms | 1.60 | 0.62 |
| Nausea and vomiting | 1.40 | 0.71 |
| Weight loss | 2.14 | 0.45 |
| Abdominal pain | 1.18 | 0.85 |
| Kussmaul breathing | 2.91 | 0.34 |
| Presence of shock | 1.64 | 0.61 |
| Severity of DKA | 3.93 | 0.25 |
| Comorbidity | 1.13 | 0.88 |
| Blood glucose level | 1.05 | 0.95 |
| Fluid management | 2.16 | 0.46 |
| Iv bolus | 2.46 | 0.41 |

VIF = variance inflation factor

### 5.8 Proportional hazard assumption test

Among regression method used in survival analysis cox proportional hazard is the commonly utilized technique. In survival analysis there are different approaches used for assessing the proportionality of hazard assumption. As it is mandatory and crucial to test for proportional hazard assumption to know whether its key assumption is violated or not, we assessed the hazard assumption based on Schoenfeld residual test (phtest). According to this assumption a P value of each covariate and the overall global test should be insignificant, which makes the test non subjective unlike that of judging the assumption graphically. Table below shows all covariates and global test has a P value of > 0.05 which indicates the assumption is satisfied.

Table 8: Schoenfeld residual for cox proportional hazard assumption of variables for children admitted DKA at selected governmental hospitals from January 2018 to December 2022, Addis Ababa, Ethiopia.

| Variables | RHO | $Chi^2$ | P-value |
|---|---|---|---|
| Diabetic history | 0.06207 | 1.42 | 0.2341 |
| Polysymptoms | 0.02612 | 0.25 | 0.6154 |
| Nausea and vomiting | -0.03105 | 0.41 | 0.5220 |
| Weight loss | 0.08036 | 2.50 | 0.1137 |
| Abdominal pain | -0.00258 | 0.00 | 0.9585 |
| Kussmaul breathing | 0.05670 | 1.07 | 0.3004 |
| Shock on admission | 0.01078 | 4.15 | 0.4160 |
| Severity of DKA | 0.00496 | 0.01 | 0.9186 |
| Comorbidity | -0.01269 | 5.87 | 0.1540 |
| Blood glucose level | -0.03674 | 0.51 | 0.4745 |
| Fluid management | 0.03080 | 0.40 | 0.5266 |
| Iv bolus | -0.05628 | 1.35 | 0.2448 |
| Global test | | 23.63 | 0.0507 |

## 6. DISCUSSION

The aim of this retrospective follow-up study was to ascertain the time to recovery from diabetic ketoacidosis and its predictors in children with type one diabetes who were admitted to a public hospital in Addis Ababa. This study revealed the median survival time to recover from DKA at the end of the study was 27hrs with an IQR of 16-38. The median survival time is almost similar with study conducted in India (49) , and extended in comparison with study done in USA(40), Japan(41),and at Cipto Mangunkusumo Hospital, Indonesia (55). In contrast the finding of this study is shorter than study conducted in China (52). The possible reason for the variation of the results may be due to the variation in definition of DKA free time, and the criteria used for the definition of DKA resolution. The other possible justification for this discrepancy may be due to the variation of DKA severity across the studies, or it may be because of the design of the study or sample size variation. Furthermore, it could be as a result of using different treatment protocol.

Regarding predictors of time to recovery from DKA, the present study showed children with new onset DM have slower recovery time compared with children with established diabetes (32 vs 23hrs), which is comparable with studies conducted in Colombia (54), Israel (53), and Japan (41). This may be due to lower index of suspicion in newly diagnosed type 1 children and subsequent delaying of seeking medical attention. As a result, they exposed to extended period of insulin deficiency, which result in severe DKA. Besides newly diagnosed children may not tolerate or resistance to exogenous insulin used to treat DKA.

The current study revealed the time to resolve from DKA in children with other comorbid illness was significantly longer than those admitted with DKA alone, which is supported by study conducted in Japan (41) in which children with gastroenteritis had prolonged recovery time from DKA when compared to others without the condition. Likewise, study done in India (58) showed children with AKI had prolonged recovery time from DKA than without AKI. The possible scientific explanation may be acute comorbid illness may markedly increase the amount of counterregulatory hormone which result in decrease the action of insulin by increasing blood sugar through promoting gluconeogenesis and glycogenolysis, and ketogenesis, which in turn worse DKA.

The present study further revealed that children with mild and moderate DKA had rapid recovery time than those admitted with severe DKA which is comparable with two studies done in China (38, 39), and USA (40).

The possible scientific explanation could be in severe DKA the body experience more extensive metabolic abnormalities and has undergone significant alteration because of insulin deficiency and hyperglycaemia. Consequently, the body needs longer time for gradual replacement of fluids, and electrolytes as well as insulin to correct metabolic abnormality. On the other hand, as compared to severe DKA in mild and moderate DKA, the metabolic derangement is insignificant, which takes fewer time to rebalance and recorrect the acidosis.

Blood glucose level was another predictor of time to recovery from DKA. Children with blood glucose level below 250 had rapid recovery time. The finding is supported by study done in Turkey(48). The reason behind this may be in high blood sugar there may be higher osmotic diuretics which result in severe dehydration, severe electrolyte derangements and severe acidosis which takes longer time to recorrect. Previous study showed high blood glucose can result in hyperinflammation condition and this in turn causes insulin resistance(62).

# 7. STRENGTH AND LIMITATION OF THE STUDY

## 7.1. Strength

The study includes five hospitals, which is multicenter and it is more representative than single center study. In addition to this in our knowledge this is the first study conducted in Ethiopia using Cox regression analysis to determine factors affecting recovery time from DKA in children with type 1 diabetes.

## 7.2. Limitation

The main limitation of this study was using of urine ketone free time as a criterion of DKA resolution time to calculate DKA free survival time as there is unavailability of laboratory investigation such as blood ketone, blood PH, and bicarbonate in our setup. This study used secondary data which imposed us to exclude undocumented children's and children's family information that may affect the time to recovery from DKA, and the factors mentioned in this study are only those that were recorded.

# 8. CONCLUSION AND RECOMMENDATION

## 8.1. Conclusion

The overall median time to recovery from DKA in children admitted with type 1 DM was 27hrs, which is in line normal range. Diabetic history, severity of DKA, presence of comorbidity, and blood glucose level on admission were statistically significant predictors of time to recovery from DKA in children.

## 8.2. Recommendation

Based on the finding of this study we would like to recommend the following concerned body.

**Federal ministry of health**

Screening for DM, increase public health awareness on clinical sign and symptom of DKA, and the advantage of adherence to insulin by promoting health education at community level as well as by using mass media, so that family and care givers of children, especially those presented with new onset of DM may recognize its signs and symptoms and early seek health facility, and will get treatment as this decrease associated costs too.

Investigate more studies on factors that affect DKA recovery time, establish DKA treatment guideline line, and regularly modify it depending on best practices and latest research finding

**Hospitals**

Give priority for children admitted with DKA with identified predictors.

**Researchers**

Conduct further studies through prospective follow-up study by including additional significant variables that were not included in this study.

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# 10. ANNEXES

**Annex 1: information sheet**

**Title of research project:** time to recovery from diabetic ketoacidosis and its predictors among children with type 1 diabetes at selected governmental hospitals in Addis Ababa Ethiopia 2023. Retrospective follows up study.

**Name of investigator:** Shimeles Tefera (BSc, candidate of MSc)

**Name of organization:** Addis Ababa University, College of health science, School of nursing and midwifery, Department of nursing.

**Name of sponsor:** Madda walabu University

**Introduction:** This information sheet was prepared for administrators and pediatric emergency unit coordinators offices, PICU coordinators office, and pediatric ward coordinators office of selected governmental hospitals of Addis Ababa. The aim of the form was to make the above-concerned offices clear about the purpose of research, data collection procedures and get permission to conduct the research.

**The purpose of research project:** was to assess time to recovery from diabetic ketoacidosis and its predictors among children admitted with DKA to selected governmental hospitals in Addis Ababa Ethiopia,2023. Retrospective follows up study.

**Procedure:** to achieve the above objective first information regarding the total number of children with DKA and the medical registration number of each patient was obtained from the health information and management system (HIMS) of each public hospital. Then detailed information about each patient was extracted from each selected patient chart.

**Risk and /or Discomfort:** Since the study was conducted by taking appropriate information from medical chart, it did not inflict any harm on the patients. The name or any other identifying information was not recorded on the questionnaire and all information was taken from the chart was kept strictly confidential and in a safe place. The information retrieved was only use for the study purpose.

**Benefits:** the research has no direct benefit for one whose document/ record was included in this research. But the indirect benefit of the research for the participant and other clients in the program. This is because if program planners/caregivers prepare predicted plans there will be a benefit for clients in the program of getting appropriate care and treatment services. In all, the research work has a paramount direct benefit for health care planners and managers.

**Confidentiality:** To reassure confidentiality the data on the chart was collected without the name of the clients and the information collected from this research project was kept confidential and stored in a file cabinet. In addition, it was not be revealed to anyone except the investigator and it was kept in a key and locked system with computer pass ward.

**Person to contact:** This research project was reviewed and approved by the institutional review board of Addis Ababa University College of Health Science, school of nursing and midwifery and department of nursing. If anyone have any doubt, questions or any unclear information, he/she can contact any of the following individual's (Investigator and Advisors) and she/he may ask at any time she/he want.

1. Shimeles Tefera: Addis Ababa University, College of Health Science, school of Nursing and midwifery and Department of Nursing: principal investigator

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**Annex 2: Data collection tool (checklist)**

This tool was prepared for the collection of socio-demographic characteristics of the children, disease factors of diabetic ketoacidosis, and other related information that is important for the assessment of time to recovery and its predictors of diabetic ketoacidosis among children with diabetic ketoacidosis patients at selected governmental hospitals in Addis Ababa, Ethiopia,2023. This information is collected by BSc Nurses.

Data collection date----------month----------Year----------
Name of data collector---------- signature----------
Name of supervisor----------signature----------
Code no----------

Table 9: A checklist to assess time to recovery from diabetic ketoacidosis and its predictors among children admitted with DKA to selected governmental hospitals in Addis Ababa Ethiopia, 2023.

| **Q .no** | **Part I: Socio-demographic characteristics** | | |
|---|---|---|---|
| 101 | Age | (--------) years / (-------) Months | |
| 102 | Sex | 1. Male. 2. Female | |
| 103 | Place of residence | 1. Rural. 2. Urban | |
| | **Part II: Clinical characteristics** | | |
| 104 | Date of admission | ___day-------month-------yr**.** | |
| 105 | Date of discharge | -------day------month------yr. | |
| 106 | Date and time of starting treatment of DKA | Date __/__/__ Time_____ | |
| 107 | Time of absence of ketone in urine | Date __/__/__ Time_____ | |
| 108 | Date and time of censored occurred | Date__/__/__ | |

| | | | |
|---|---|---|---|
| 109 | Reason for censoring | 1 Transfer to other facility<br>2 Went against medical mgt<br>3 Death<br>4 Absent on call<br>6 unknown status | |
| 110 | Diabetic history | 1 New onset<br>2 Known | Skip to Q.no 112 if new onset |
| 111 | If known diabetic: | | |
| | 1 Duration of illness | _____in year/s | |
| | 2 Insulin type | _____ | |
| | 3 Triggering factor of DKA | _____ | |
| 112 | DM history in the family | 1. Yes 2. No | |
| 113 | Poly symptoms | 1. Yes 2. No | Skip to Q.no 115 if no |
| 114 | If yes which Polystmptom | 1. polyuria<br>2. polydipsia<br>3.polyphagia | |
| 115 | Nausea/Vomiting | 1. Yes 2. No | |
| 116 | Kausmaul breathing | 1. Yes 2. No | |
| 117 | Mental status on admission | 1. Alert<br>2. lethargic<br>3. obtunded<br>4. comatose | |
| 118 | Shock on admission | 1. yes<br>2. No | |
| 119 | If no shock had child had sign of dehydration | 1. Yes<br>2. No | |
| 120 | Severity of DKA | 1 Mild | |

| | | | |
|---|---|---|---|
| | | 2 Moderates<br>3 Severe | |
| 121 | Had child had comorbidity | 1. yes 2. No | |
| 122 | If yes what type of illness | 1. Gastroenteritis | |
| | | 2. renal disease | |
| | | 3. others, specify_____ | |
| | **Part III Biochemical profile (laboratory investigation)** | | |
| 123 | Blood Na level at admission | _____mmol/L | |
| 124 | Chloride level at admission time | _____ mmol/L | |
| 125 | Potassium level at admission | _____mmol/L | |
| 126 | Phosphorus level at admission | _____ mg/dL | |
| 127 | Blood glucose level at admission | FBS_____ mg/dl<br>RBS _____ mg/dl | |
| 128 | Urine glucose at admission | Negative. +1. + 2. +3. +4. | |
| 129 | Urine ketone at admission | 1+ 2+ 3+ 4+ | |
| 130 | Creatinine level at admission | _____ mg/dL | |
| | **Part IV: Treatment-related factor** | | |
| 131 | Type of fluid | 1. NS 2. Ringer lactate 3 DNS 4 ORS 5 water | |
| 132 | IV bolus | 1 Taken 2 not taken | |

| | | | |
|---|---|---|---|
| 133 | Volume of IV fluid | _____ | |
| 134 | Type and dose of insulin | _____,_____ | |
| 135 | Kcl | 1 Added 2 Not added | |
| 136 | Medication other than insulin | _____ | |