ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING AND MIDWIFERY

SURVIVAL AND PREDICTORS OF DIABETIC KETOACIDOSIS AMONG CHILDREN WITH DIABETES IN WEST AND EAST GOJJAM ZONE REFERRAL HOSPITALS NORTH WEST ETHIOPIA, 2019: A RETROSPECTIVE COHORT STUDY

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A RESEARCH PROPOSAL SUBMITTED TO SCHOOL OF NURSING AND MIDWIFERY, COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY FOR THE PARTIAL FULFILMET OF THE REQUIREMENTS FOR DEGREE OF MASTERSOF PEDIATRICS AND CHILD HEALTH NURSING

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MASTER OF SCIENCE RESEARCH PROJECT SUBMISSION FORM

Name of Investigator	**Birtukan Assefa**
Name of advisors	**1) Mrs. Rajalakshmi Murugan (Asst. professor)** **2) Kalkidan Wondwossen(Lecturer)**
Title of the research	**SURVIVAL and predictors of diabetic ketoacidosis among children with DM in west and east Gojjam zone referral hospitals north west Ethiopia,2019: A retrospective cohort study**
Duration of the study	**From march1st, 2019 to 28th of April, 2019**
Study area	**Referral hospitals in east and west Gojjam zones**
Total cost	**28065.88 ETB**
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ABBREVIATIONS AND ACRONYMS

COPD	CRONIC OBSTRACTIVE PULMONARY DISEASE
DKA	DIABETICKETOACIDOCIS
DM	DIABETUS MELLITUS
DMRH	DEBRE-MARKOS REFERAL HOSPITAL
FHRH	FELEGE-HIWOT REFERAL HOSPITAL
FBGL	FASTING BLOOD GLUCOSE LEVEL
HTN	HEYPER TENTION
ISPAD	INTERNATIONAL SOCIETY OF PEDIATRICS AND ADOLECENT DIABETICS
OPD	OUT PATIENT DEPARTMENT
RBGL	RANDOM BLOOD GLUCOSE LEVEL
T1DM	TYPE 1 DIABETUS MELLITUS
UK	UNITED KINGDOME
USA	UNITED STATES OF AMERICA

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SUMMARY

Background; Diabetic mellitus is one of the most common chronic diseases of childhood disease, with a global incidence of 5% or above per year in children. If the condition is left untreated, children will suffer by Diabetic ketoacidosis. Diabetic ketoacidosis represents a state of acute metabolic stress, when the body suffers due to absolute or relative insulin deficiency for metabolism of glucose. Recurrent- Diabetic ketoacidosis in patients with already diagnosed diabetic mellitus remains a relevant problem in pediatric with incidence of 1–10% per patient. the overall incidence of DKA in Ethiopia is not known but some studies from different part of the country indicates prevalence of DKA in Addis Ababa , Dessie, Jimma were 62.2%,19.9%, 34% respectively. These shows the incidence of DKA increasing in Ethiopia and Diabetes is becoming public health problem in Ethiopia due to increasing prevalence and related complications spatially DKA. So, this study aims to determine the incidence rate of DKA and identify its predictors among DM diagnosed children.

Objective: To assess incidence and predictors of diabetic ketoacidosis among children diagnosed with diabetes at east and west Gojjam referral hospitals, North West Ethiopia, 2019

Methods: Institution based retrospective cohort study will be conducted among diabetic mellitus diagnosed children who were registered from January 1, 2014 to January 1, 2018 using pre-structured check list that measures socio-demographic characteristics, disease factors of Diabetic ketoacidosis and other clinical information regarding time duration to develop Diabetic ketoacidosis to gather the information. To select the study subjects' first total diabetic mellitus caseload will be assessed in the data base on the electronic system from medical record office then; simple random method will be applied to select the required sample size 389. The collected data will be coded and entered in Epi data version 4.2 and will be transferred to SPSS 21.0 for further analysis. The Kaplan Meier estimator will be used to estimate median time to develop DKA during the treatment period and log rank tests, to compare survival curves. To investigate predictors of DKA will be analyzed by Cox proportional hazard model. Hazard ratio, 95% CI and $P \leq 0.25$ level in the bivariable analysis will be entered in the final Cox-regression analysis. Statistical test will consider significant at P level less than 0.05.

Budget: to conduct this research it needs 28065.88 Ethiopian Birr.

1. INTRODUCTION

1.1 Background

Diabetic mellitus (DM) is a chronic endocrine disorder that leads for multiple complication as well as death. When, there is rising of blood glucose level above the physiologic limits Diabetic Ketoacidosis (DKA) can occur[1]. DM is one of the most common chronic diseases of childhood disease, with a global incidence of 5% or above per year in children[2, 3]. If the condition is left untreated, children will suffer by DKA. DKA is a life-threatening medical emergency caused by sever insulin deficiency which usually results in hyperglycemia[4]. it is predominantly a complication of type 1 diabetes, but it may occur in type 2 when precipitated by major surgery, severe illness such as myocardial infarction, or severe infection (sepsis) since, these conditions are associated with increase in stress hormones which oppose the action of insulin and exacerbating the relative insulin deficiency [5].

DKA represents a state of acute metabolic stress, when the body suffers due to absolute or relative insulin deficiency for metabolism of glucose[6].Farther lack of insulin and excess of counter regulatory hormone result in osmotic diuresis, prerenal azotemia, ketone formation and metabolic acidosis. People suffering from DKA usually have severe dehydration and significant alterations of the body's blood chemistry[7, 8]. If glucose elevation and dehydration are severe and persist for several hours, the risk of cerebral edema increases particularly in children. Also children with DKA are vulnerable to other complications such as hyper- or hypokalemia with arrhythmias, Sepsis, acute respiratory distress syndrome, pneumonia, pulmonary edema, and alveolar rupture [9]. During absence of insulin, there is no uptake of glucose by tissues like muscles, fat and liver, then the counter regulatory hormones such as glucagon, growth hormone and catecholamine enhance triglyceride breakdown into free fatty acids and gluconeogenesis cause for elevation in serum glucose. Thus, the oxidation of free fatty acids leads to increased formation of ketone bodies [10].

Globally, recurrent-DKA in patients with already diagnosed DM remains a relevant problem in pediatric. The risk of DKA in established diabetes is 1–10% per patient per year in children[11]. Also, frequency of DKA widely vary with geographical variation.it was 7.1% in U.S, 5.0% in Austria and Germany and 6.4% in, England and Wales [12]. The true incidence

of DKA in tropical Africa is unknown but according to International Diabetes Federation 2011 it has been estimated as 24%.

Also, the overall incidence of DKA in Ethiopia is not known but some studies from different part of the country indicates prevalence of DKA in Addis Ababa , Dessie, Jimma were 62.2%,19.9%, 34% respectively. These shows the incidence of DKA increasing in Ethiopia and Diabetes is becoming public health problem in Ethiopia due to increasing prevalence and related complications spatially DKA[13].

According to ISPAD 2014 guidelines Risk factors for DKA in patients with known diabetes were insulin omission, poor metabolic control, previous episodes of DKA, gastroenteritis with persistent vomiting and inability to maintain hydration, psychiatric (including eating) disorders, challenging social and family circumstances, peri-pubertal and adolescent girls, limited access to medical services[11]. The aim of this study is to determine the incidence rate of DKA and identify its predictors among DM diagnosed children.

1.2 Statement of the problem

Diabetes is one of the largest global health emergencies of the 21st century. Globally more than 96,000 children and adolescents under15 years are estimated to be diagnosed with type1 diabetes annually. The overall annual increase is estimated to be around 3% with strong indications of geographic differences. Currently, 50,600 children and adolescents under the age of 20 are living with type 1 diabetes in Africa and in Ethiopia (2.6 (1.1-3.8)) million people estimated to be living with DM [14]. The incidence of DKA varies with geographical variation. The incidence of DKA at diagnosis of T1DM in the UK was 25% [15] and in study of Amirkola Children's Hospital in Iran in 2005-2013 the incidence of DKA was 55.5% [16]. In Africa the data on incidence of DKA is scarce, but some studies report the frequency of DKA in north-western Nigeria 62.2% [17], in South Africa 69.8% [18]. Also in Ethiopia the incidence of DKA is not well studied but a study in Addis Ababa, showed that the prevalence of DKA is 35.8% [19] . DKA is the most common cause of death among children and is associated with an increased risk of cerebral edema and cognitive deficits[20, 21].A study showed that risk of developing cerebral edema was 12.4 per 1000 episodes of DKA which was higher than Non DKA DM patients (3.8 per 1000). It had a significant mortality (24%) and morbidity (35%)[22].

The burden of DKA also presents a crisis in terms of health care costs, both direct and indirect, ranging from individual to national economy. for example one DKA-related hospital admission from US$4125 to US$11 196 cost it had, in addition to the familial and societal costs associated with missed work and school days was observed [23]. The mortality of DKA high in developing than developed countries[24]. The consequences of poor public healthcare delivery systems in Africa like Ethiopia have impacted negatively on the management of patients with diabetes thus intern may have impact on the existence of DKA .

Lack of proper public health education[25]and challenge in self-care because of they are children (seek assistance from family) may have contribution to a high incidence of DKA in Ethiopia. Thus, Self-care of Glycaemic control can have a great impact on DKA existence in many patients and contribute to most of the increased morbidity and premature mortality[26, 27]. Even, many patients seek alternative treatments such as consulting traditional healers,

using herbal remedies[28], prayers and rituals that further complicating the disease process[29].

Because symptoms exist before the onset of DKA, a delay in the diagnosis and treatment of diabetes can be a risk factor for DKA. Other factors, such as younger age (< 5 yrs), lower socioeconomic status and lower parental education, also confer an increased risk of DKA at onset of diabetes [30]. Generally, the most mentioned trigger of DKA was an illness with infections, inadequate insulin therapy and newly diagnosed or previously unknown diabetes. Various other causes like stress, heavy use of concentrated carbohydrate, Physical or emotional trauma, Surgery contribute to DKA [30-32]. Infection is the most common factor for DKA from this urinary tract infection and pneumonia account for the majority factor[33].Ethnic variations in diabetes-related complications like DKA had been recognized [34, 35]. As far as I get there is no study done in Ethiopia on the incidence and predictors of DKA among diabetes diagnosed children, this study aims to fill these gap. Efforts will be also made to examine whether there is age, sex and other socio-demography variables differences in the incidences of ketoacidosis and to determine the time duration to develop diabetic ketoacidosis.

2. LITERATURE REVIEW

2.1 Incidence of DKA

Globally, recurrent-DKA in patients with already diagnosed DM remains a relevant problem in pediatric. The risk of DKA in established diabetes is 1–10% per patient per year in children(13) also, Diabetic ketoacidosis is a global health emergency, the incidence was s studied both in developed and developing countries. A retrospective cohort study which was conducted on youth in US population showed that DKA at the diagnosis was 25.5%. It decreased with age from 37.3% in children aged 0 to 4 years to 14.7% in those aged 15 to 19 years. And also, it was significantly higher in patients with type 1 (29.4%) rather than in those with type 2 diabetes (9.7%)(36). A longitudinal population-based study in Italian children under 15 years of age replied that DKA frequency was 40.3%. Even there was a significant trend toward an increase in the incidence of severe DKA over time with an average increase of about 3% per year during the study period (37). A retrospective review of children aged < 15 years with newly diagnosed type 1 diabetes mellitus (T1DM) in the Auckland Region (New Zealand) in 1999–2013, showed that, 27% of had DKA at diagnosis(38). In addition, study in US youth indicated that with type 1 diabetes, the prevalence of DKA was 30.2% in 2002–2003, 29.1% in 2004–2005, and 31.1% in 2008–2010 And with type 2 diabetes , DKA prevalence decreased from 11.7% in 2002–2003 to 5.7% in 2008–2010 (39).

In other study done in southern Iraq, 400 patients with T1DM enrolled reviled that the incidence of DKA was 40%. (40). A study conducted at Poland indicated that the incidence of DKA were 25% to 28 % in 2006-2007 and 2013-2014 respectively(41). Twenty years prospective Population based study done in Austrian children revealed that the incidence of DKA was 37.2% and the incidence rate of DKA was 8.4 to 18.4 per 100,000 during the observation period (42).

In a study at Saudi Arabia showed that about 6.5% from all cases admitted to PICU and 0.94% from total children admitted to Pediatric Department in the same period developed DKA. (43). In another six year retrospective review at Saudi Arabia indicates the incidence of DKA was 6.2% per year (44)

Another retrospective study conducted in Benin found the frequency of DKA in newly diagnosed children was 77.1% which is higher(45). The study conducted in Ethiopia at TikurAbesa specialized hospital , 80 % of patients from the newly diagnosed type I DM patients were DKA cases (46).

2.2 Precipitating factor of DKA

2.2.1 Socio-demographic characteristics

A study conducted at US (36), Italy (37) ,Southern Iraq (47) and Austria (48) reviled younger age at diagnosis (0-4 years) were predictors of DKA. In other study conducted in New Zealand increasing age at diagnosis in children aged 2 to 14 years was associated with greater likelihood of being in DKA at presentation (38). A study conducted at Poland a 2-fold increase in DKA was noted in children under the age of 3 years (41).

Area of residence were identified as predictors of DKA. A study conducted in Italian children (37), Southern Iraq (47) reviled that children from rural area was associated with DKA. Also, studies in Italy (37), Southern Iraq (47), reviled that parental educational status and family income were identified as predictors of DKA. in studies done at US (39) , Benin(45) Italy reviled that family history of DM was predictors of DKA. Studies carried out at US(39), New Zealand (38) reviled that ethnicity were identified as predictors of DKA. lack of private health insurance identified as predictors of DKA in US(39) and a decreased risk of DKA was associated with having a usual provider of care in Canada (32). Gender were identified as predictor of DKA. Male gender were identified as predictors of DKA in T2DM in US(39)and female gender were more affected for DKA in Iran (47), and Austria (48)

2.2.2 Clinical characteristics

A study done at US reviled that type 1 of DM was predictors of DKA (36). A study in Southern Iraq indicates presence of acute recent illness and previous DKA attacks were predictors of DKA.

Infections were identified as predictors of DKA. In Saudi Arabia childhood infections were the commonest and leading precipitating factor, reported infections included upper respiratory infections, bronchopneumonia and tonsillitis. But, urinary tract infection and vaginal candidiasis were rare causes(43). in Malaysia Sepsis was recorded as the foremost cause

which was followed by respiratory tract infection(49). in patients in sub-Saharan Africa (50)and north India Infections were identified as predictors of DKA(51). A 10 years retrospective study conducted in, Nigeria showed that 172 patients admitted because of DKA precipitated by septicemia and DKA patients precipitated by meningitis (52). A cross sectional study carried out in Ethiopia at TikurAbesa showed that upper respiratory tract infection and urinary tract infection being two of the most common causes of DKA(53), (54). In study conducted in England, Wales, U.S, Austria, and Germany reviled that children with HbA1c >7.5% were more likely to develop DKA(11). In other study at Poland higher HbA1c levels were predictors of DKA (41)

2.2.3 **Treatment factors of DKA**

In studies done at Saudi Arabia (43), Grand Memorial Hospital Atlanta Georgia in US (55), patients in sub-Saharan Africa (50), Saudi Arabia(44)and north India (51) identified poor compliance with omission of insulin was predictors of DKA. In the study conducted at Southern Iraq, missing insulin doses and frequency of the dose missing, number of previous DKA attacks, using of syringes or pens as a tool of insulin delivery, source of insulin supply to patients, presence of glucometer at homes and frequency of its uses were predictors of DKA (47) In the study carried out in Ethiopia at TikurAmbesa showed that the most common precipitating factor for DKA was treatment non-adherence

2.3 Conceptual frame work

The following conceptual framework shows association between independent variables with dependent variable which is developed after reviewing many literatures (32, 36-39, 43, 46, 47, 49, 50, 52-56). The dependent variable (incidence rate of DKA) is affected by socio-demographic characteristics; clinical characteristics and treatment factors of the child which are described in the figure: 1below.

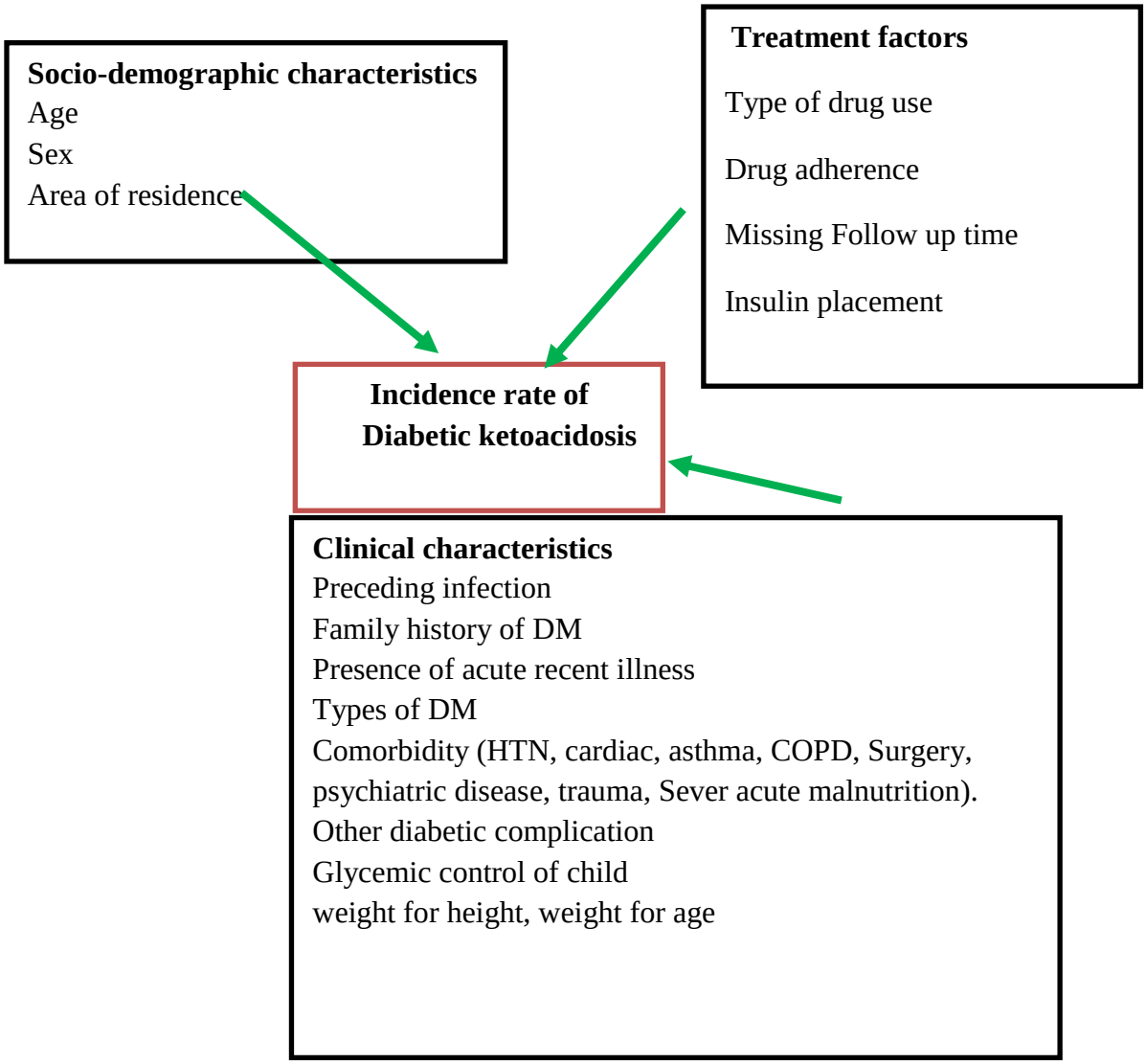

Figure 1: Conceptual frame work of incidence and predictors of DKA among DM diagnosed children East and West Gojjam zone referral hospitals, Ethiopia, 2019.

3. JUSTIFICATION OF THE STUDY

Poor understanding about the nature of DM by patients, and/or insufficient information given by diabetic clinics contributes for rising of magnitude as well as severity of DM in Ethiopia which result in short and long-term complications of DM spatially DKA. These complications intern results in related DM morbidity and mortality. Also, the community has no a culture of checkup for sugar level in the nearby health institute, most patients visit the hospital after developing life threatening complications like DKA.

Most DM patients especially in none-developed countries have low educational status which created a problem in communication with the health professional. As a result, most patients discontinued the drug for different reason; adjust the dose and the schedule without the order of the physician to make it convenient for their fasting, work and other social reason. This all put them at the expense of acute complication (DKA). There is also a gap in diabetic education, the way to administer DM drugs at home and put the drug in a safe place, the way to act when concomitant disease like acute fever illness occurred, how to adjust the drug during strenuous exercise and work, the way the type of diet they used. This put a huge burden economically, socially and politically on the family, the community, the hospital and the country at large. These conditions are more devastating in children due to they are dependent on their care giver. Therefore, this study is designed to assess incidence and risk factors of diabetic ketoacidosis among children attending referral hospitals in west and east Gojjam zones, North West Ethiopia, 2019.

4. SIGNIFICANCE OF THE STUDY

Studying the incidence and predictors of DKA is vital for developing preventive strategies as well as treatment protocols to minimize the impact of its complication. The final result of the study will be helpful for the patient & care givers by providing Knowledge about predictors of DKA that guides them to plan preventive methods that maximize their quality of life. Also for health professionals this study will tell about incidence and predictors of DKA and then, important for the development of interventions to reduce the occurrence of DKA. This in turn decrease bed occupancy in the hospital and reduce the amount of human and material resource needed to control it as well as its complications.

The finding of this study also used as a base line data for those who are interested in carrying out further. It will also be helpful for health policy makers as input to document gaps and in designing possible interventions to combat DKA and related consequences.

5. OBJECTIVES

5.1 General objective

To assess survival and predictors of diabetic ketoacidosis among Diabetics diagnosed children at Gojjam referral hospitals, North West Ethiopia, 2019.

5.2 Specific Objectives

To determine the incidence rate of DKA among DM diagnosed children attending east and west Gojjam referral hospitals, North West Ethiopia, 2019.

To identify predictors of DKA among DM diagnosed children attending at east and west Gojjam referral hospitals, North West Ethiopia, 2019.

6. METHODS AND MATERIALS

6.1 Setting/Study area

The study will be conducted in the two referral hospitals (Debre-Markos referral hospital and Felege-Hiwot referral hospital) of East and West Gojjam zones in Amara regional state. Debre- Markos referral hospital is found in Debre -Markos, the town of East Gojjam Administrative Zone. Whereas, Felege-Hiwot referral hospital found in west Gojjam zone in Bahir- Dar, the town of Amhara regional state. These hospitals are found in Northern direction 565 Kilometers and 299 Kilometers far from Addis Ababa (capital City of Ethiopia) respectively.

Debre -Markos referral hospital is located 256 Kilometer from Bihar Dar to south direction. Debre-Markos is found 265 Km from Bahir-Dar and 300 kilometers from Addis Ababa.it has an altitude of 2450- 2520 m above sea level and average temperature ranging from 15-22 ^{o}C. The hospital which is 30, 020 km^2 wide, provides health service to more than 3.5 million population. Currently about 100 health centers and 9 district hospitals are available in the catchment area of the referral hospital. The hospital has a total of 315(205 male, 110 female) clinical staffs[55, 56].

According to information obtained from administrative offices of these hospitals, Debre-Markos and Felege-Hiwot referral hospitals serve for more than 3.5 million and 5 million population in their catchment area respectively. Apart from other services, both referral hospitals provide Diabetic treatment services. Currently, 777 and 898 patients had Diabetic follow up in Debre Markos referral hospital and Felege Hiwot referral hospital respectively.

6.2 Study period

This study will be conducted from March 1, 2019, to April 30, 2019.

6.3 Study design

Institution based retrospective cohort study will be conducted.

6.3 Population

6.3.1 Source Population

All DM diagnosed children medical records from January 1, 2014 to January 1, 2018 in Gojjam referral Hospitals

6.3.2 Study Population

The study population will be randomly selected children diagnosed with DM and who had follow up from January 1, 2014 to January 1, 2018 in Gojjam referral Hospitals.

6.4 Eligibility Criteria

6.4.1 Inclusion criteria

The inclusion criteria will be children age less than 15 years and diagnosed with DM with follow up care from January 1, 2014 to January 1, 2018 at Gojjam Referral hospital.

6.4.2 Exclusion criteria

Child who was developing DKA at the first diagnosis of DM will be excluded from the study.

6.5 Sample Size and Sampling Procedure

6.5.1 Sample Size Determination

For the first objective, a single population proportion formula will be used to calculate the sample size by considering the following statistical assumptions.

P = proportion of DKA among children with DM 35.8% from study done in Addis Ababa selected hospitals; Black Lion, Yekatit and Zewditu hospitals [19].

Z α/2 = the corresponding Z score of 95% CI

d= Margin of error (5%)

N= Sample size

$$N= \frac{Z\,(a/2)^2\,P\,(1-P)}{d^2} = (1.96)^2*0.358*0.642/0.05^2=0.8829379776/0.0025$$

=353.175~353.2

10% missing data=35.32

There for, the sample size calculated with 10% missing data is 389

For the second objective, the sample size will be determined using double population proportion formula by considering recent acute illness and missed insulin dose as predictor variables of DKA based on study done in Southern Iraq [45]by using Epi info version 7 statistical package. It is calculated by taking two-sided significant level (α) of 5 %, power (ZB) 80 % and 1:1 ratio of non-exposed to expose.

Table 1: Shows sample size calculation for predictors of DKA among children in east and west Gojjam Zone Referral Hospitals, North West Ethiopia 2019.

Variables	Assumptions	Total sample size	After adding 10%
Recent acute illness	P1=50.9% P2=27.4%	150	165
Missed insulin dose	P1=48.8% P2=33.7%	358	386.8

- P1: is percent of exposed with the outcome
- P2: is percent of non-exposed with the outcome

Finally, the largest sample size (N= 389) will be selected as the final sample size for the study.

6.5.2 Sampling technique and procedure

The two referral hospitals (Debre-Markos referral hospital and Felege-Hiwot referral hospital) are selected. Then to select the study participants from each hospital, the proportional allocation formula will be used based on caseloads. There about 842 children with DM between January 1st, 2014 to January1st, 2018 in both East and West Gojjam Zone Referral Hospitals, 322 are from DMRH and 520 are from FHRH. After that, medical records of children diagnosed with DM will be isolated. From the isolated cards in each hospital, simple random sampling technique will be applied to select the study participants.

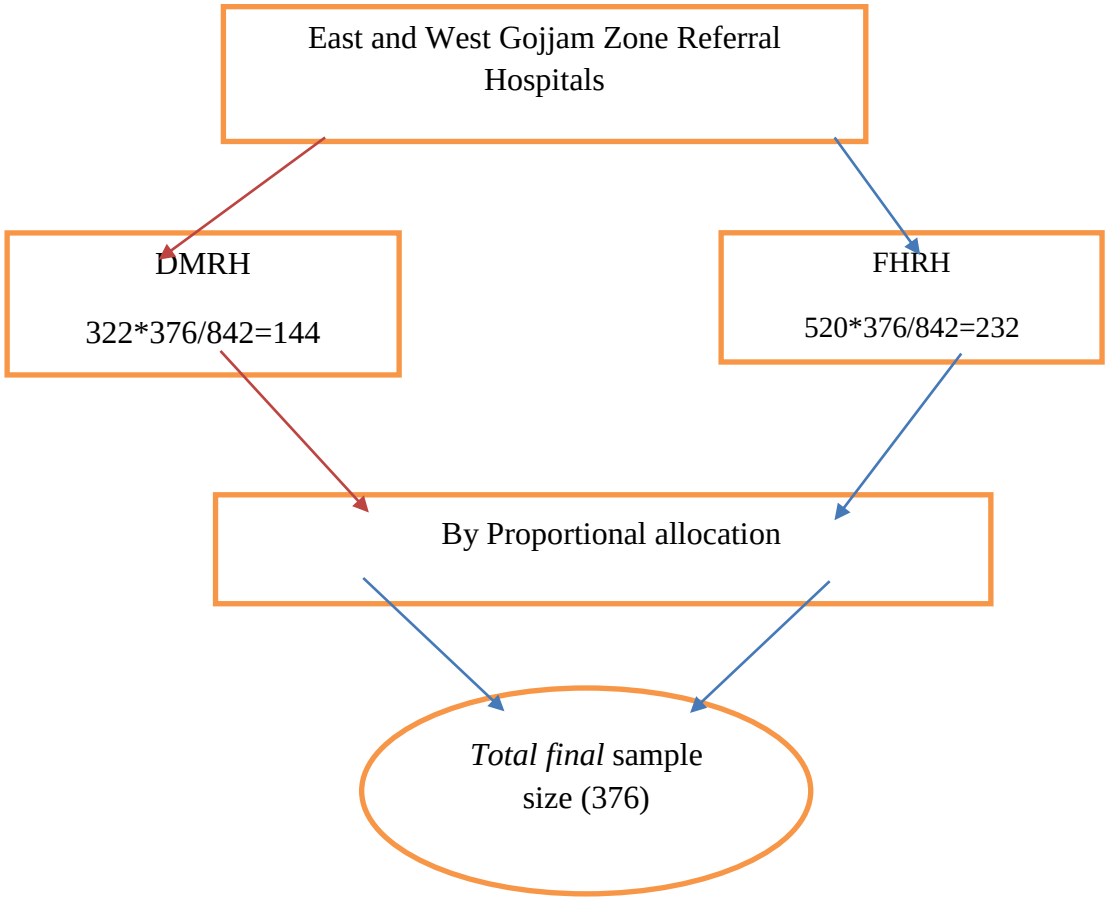

Figure 2 Schematic presentation of sampling procedure to assess the incidence and predictors of DKA among children in east and west Gojjam Zone Referral Hospitals, North West Ethiopia 2019

6.6 Variables of the Study

6.6.1 Dependent Variable

Incidence rate of Diabetic ketoacidosis

6.6.2 Independent Variables

Socio-demographic factors

- Religion, age, sex, body mass index**,** residence**.**

Disease factors

- Family history of DM, Preceding infection of DKA, presence of acute illness on DKA

Types of DM, presence of Comorbidity (HTN, cardiac, asthma, COPD, Surgery, psychiatric disease, trauma) and other diabetic complication (peripheral neuropathy, retinopathy, foot ulcer, Hypo-glycaemia, Acute or chronic kidney injury and retinopathy)

Treatment factors

- Follow up frequency, type of drug use ,medication adherence, and Frequency of the dose of drug missed

Glycemic control of child

- HbAc1 or average measurement of FBGL or RBGL

6.7 Operational Definitions of Variables

Diabetic ketoacidosis: will be considered on the basis of the clinical diagnosis made by a health care provider.

Glycemic control of child; Hbac1 or average measurement of FBGL or RBGL

Incidence of DKA: Total number of children who develop DKA among the study per 1000 patients

Classification of diabetes type: it will be determined on the basis of the clinical diagnosis made by a health care provider (type -1 diabetes and type -2 diabetes).

Time to develop DKA: it will be the time in which when the diabetes children develops DKA after the diagnosis of DM.

Censor: Children who did not develop DKA and children died or transfer out to other health institutions before developing DKA will be considered censored.

Co-morbidities: **c**hildren with DM and will have other medical, surgical or psychiatric diseases

Event: DM children who develop DKA

6.8 Data Collection Procedure

6.8.1 Data collection tool and procedure

Pre structured questionnaire will be used to assess the incidence and predictors of diabetic ketoacidosis. A checklist that measures the socio-demographic characteristics, clinical information, and time to develop DKA will be used.to collect the study participant's total DM caseload will be assessed in the data base on the electronic system from the discharge catalog of admitted patient's pediatric ward and in emergency, OPD from January 1, 2014 to January 1, 2018. Then medical registration number (MRN) of all diabetic pediatric patients will be sorted. After this, simple random method will be applied to select the study subject. Finally the selected medical registration number will pick out the medical card of each DM patient. Two BSC Nurse for supervision and two BSC Nurse for data collection will be recruited. One day training will be given to data collectors and supervisors regarding purpose of the study and correct completion of the checklist and ethical considerations to standardize the data collection. The supervisors will monitor the data collection process.

6.8.2 Quality Assurance

To keep data quality supervisor and data collectors will be trained on how and what information they should collect from the targeted data sources. Data extraction forms will be checked prior to data collection. Completeness of the collected data will be checked onsite daily basis during data collection and give prompt feedback by the supervisor and the principal investigator. Besides this, the principal investigator will carefully enter and thoroughly clean the data before the commencement of the analysis. Pretest will be done on 5% of the study samples in finote- selam hospital. After the pretest necessary corrections will be done on the check list.

6.9 Data Processing and Analysis

The collected data will be coded and entered in Epi data version 4.1 and will be transferred and cleaned to SPSS 21.0 (Statistical Package for the Social Sciences) for analysis.

Descriptive and inferential statistics will be used to present the data. Descriptive statistics like frequency and percentage will be used to summarize the socio-demographic characteristic of the study participants and also clinical characteristic.

Descriptive characteristics will be reported as follows: normally distribute continuous data will be reported as means with standard deviation (SD); non-normally distributed continuous data will be reported as medians with interquartile range (IQR); categorical data will be reported as proportions (frequency and percent). The incidence densities of DKA (per 1000 person-years) will be estimated by each predicator variables.

The Kaplan Meier estimator will be used to estimate median Time to develop DKA during the treatment period and log rank tests, to compare survival curves. To investigate predictors of DKA will be analyzed by Cox proportional hazard model. Hazard ratio, 95% CI and P-value will use to assess the strength of association and statistical significance, Variables significant at $P < 0.25$ level in the bivariable analysis will be entered in the final Cox-regression analysis to identify independent predictors of DKA. Statistical test will consider significant at P level less than 0.05. Covariates will be checked for interaction effect, the Cox regression model for its fitness to the data and proportional hazard assumptions will be checked using log-log plot and goodness of fit by Schoenfeld Residuals.

6.10 Dissemination of Results

The results of the study will be submitted to School of Medicine and allied Health Science College, Addis Ababa University. The finding will be distributed to East Gojjam zone health bureau and other organizations working on related area to be used as a baseline for intervention. The study abstract will be submitted to associations like Ethiopian Nursing Association, Ethiopian Public Health Association and other international associations to present the results of the research during continuous medical education events or conferences organized by those associations. The result will be submitted to the international or national peer reviewed journal for publication.

6.11 Ethical Consideration

Ethical clearance will be obtained from school of nursing and midwifery, college of health sciences, Addis Ababa University. After the approval of the proposal the letter will be obtained from the school of nursing and midwifery to Amhara zone health bureau, and then permission letter will be written to debre-markos and felege-hiwot referrals hospitals for data collection. To keep the confidentiality all collected data will be coded and locked in a separate room before entered in to the computer. after entered to the computer the data will be locked by password, names and unique card numbers will not include in data collection format and the data will not disclosed to any person other than principal investigator. All information collected from patients' cards will be kept strictly confidential.

7. WORK PLAN

No	Activities	Responsible person	Time period 2018/2019 of Activities									
			Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun
1	Title selection	PI										
2	Title defense	PI										
3	Proposal writing	PI &Advisers										
4	Proposal defense	PI										
5	Submission of proposal	PI										
6	Ethical clearance	PI										
7	Recruitment and training of data collectors	PI										
8	Data collection	PI, DC & SP										
9	Data entry and analysis of data	PI										
10	Report /thesis writing	PI										
11	Submission of drafted thesis$ mock defense	PI										
12	Submission of the first thesis	PI and adviser										
13	thesis defense	PI										
14	Submission of the final thesis	PI										

Figure 3 GANNT chart of work plan to assess the incidence and predictors of DKA among children in east and west Gojjam Zone Referral Hospitals, North West Ethiopia 2019

Key: PI: Principal investigator

DC: Data Collector

SP: Supervisor

8. BUDGET BREAK DOWN

Table 2 shows budget breakdown for personal, stationary and logistic to assess the incidence and predictors of DKA among children in east and west Gojjam Zone Referral Hospitals, North West Ethiopia 2019

Personal

For Training					
Title	No. of participant	Qualification	No. of days	Cost in E. birr	Total
Data collectors	4	BScN	2	200	1600
Supervisors	2	MSc/BScN	2	250	1000
Total					***2600***
For Data Collection					
For card extractor	2	Diploma/BSc in HIT	12	200	4800
Data collectors	4	BScN	14	200	11200
Supervisors	2	BScN	10	300	6000
Total					***22200***

Stationary and logistics

Item	Quantity	Unit price	Total
Questionnaire duplication	3*600 pages	.5	900
Print (proposal & thesis)	6 copies*30 pages	3	540
Paper	4 ream	200	800
Pen	12	5	60
Pencil	12	1	12
Eraser	12	3	36
Binder	8	15	120
Note pad	12	10	120
Mobile card	12	50	600
Total			***3188***

Budget summary for the project.2

Item1	Cost in Ethiopian BIRR
Personnel Cost	24600
Stationary and logistics	3188
Sub- total	27788
Contingency 10%	277.88
Total cost	28065.88 Ethiopian birr

Therefore, to conduct this research it needs 28065.88 **ETB** Ethiopian Birr.

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APPENDIX

Annex: data extraction form (Checklist)

This tool is prepared for the collection of socio-demographic characteristics of the child, disease factors of DKA and other related information that is important for the assessment of Incidence and predictors of DKA among children with DM at Gojjam referral hospitals, Amhara Regional State, 2018/2019. All this information will be retrieved from individual patient card without mentioning the name of clients. This information will be collected by health care providers (BSc Nurses) possibly working in Debre-Markos and Felege-Hiwot referral hospitals.

Contact information: Birtukan Assefa Cell phone+251966305871, Mrs Rajalakshmi Murugan Cell phone: +251-911721193, Kalkidan Wondosen Cell phone: +251-913634088.

Data collection date----------month----------Year----------

Name of the Hospital ----------

Name of data collector---------- signature----------

Name of supervisor----------signature----------

Code no----------

PART-I SOCIO DEMOGRAPHIC CHARACTERISTICS

	Socio-demographic characteristics	Possible answers	Skip
1.	Age	(--------) years / (-------) months	
2.	Sex	1. Male, 2. Female	
3.	Residence	1. Urban 2. Rural	
PART-II Clinical characteristics			
4.	Weight of the child	_____kg	
5.	Height of the child	_____ m2	
6.	Weight for height of the child	_____	

7.	Weight for age of the child	_____	
8.	Child's Family history of DM	1. Yes 2. No	
9.	child had developed DKA	1. Yes 2. No	If no skip to Q 13
10.	Date of DM diagnosis	—day—month——Year	
11.	Date of first DKA occurred?	——da—month——Year	
12.	Date of last observation?	——da—month——Year	
13.	Types of DM the child diagnosed for?	Type 1 Type 2 Other type————	
14.	Child had got preceding infection before DKA developed?	1. Yes 2. No	Skip if no to Q18
15.	If yes, what had Child got preceding infection before DKA developed? If no	☐Respiratory infections ☐ Pneumonia ☐ TB ☐ Tonsillitis ☐ Gastrointestinal ☐ Urinary tract ☐ Hepatitis ☐ Otitis media ☐ Chickenpox ☐ mengitis ☐ fungal skin infection ☐Other Specify _____	
16.	Child had got acute recent illness at DKA developed?	1. Yes 2. No	Skip if no to Q20
17.	If, yes what type of acute recent illness child had up to the first DKA developed? Clink in the box	☐Respiratory infections ☐ Pneumonia ☐ TB ☐ Tonsillitis ☐ Gastrointestinal ☐ Urinary tract ☐ Hepatitis ☐ Otitis media ☐ Chickenpox ☐ mengitis	

		☐ fungal skin infection ☐Other Specify _____	
18.	Child had Co- morbidity of DM up to the first DKA developed?	Yes No	If no skip to Q 22
19.	If, yes what Co-morbidity child got up to the first DKA developed the child had? Clink in the box	☐ Hypertension ☐ Asthma ☐ COPD ☐ Other cardiac disease ☐ Renal disease ☐ Trauma ☐ Surgery ☐ Psychiatric ☐ sever acute malnutrition Others ----------	
20.	Child had diabetic complication up to the first DKA developed?	Yes No	If no skip to Q 24
21.	If yes, what diabetic complication the child had up to the first DKA developed?	☐ Acute Renal injury ☐Chronic kidney injury ☐Peripheral neuropathy ☐ Foot ulcer ☐ Retinopathy ☐ Hypoglycemia	
GLYCEMIC CONTROL OF THE CHILD			
22.	hemoglobin A1C	_____%	
	FBGL (the average of three consecutive measurement))	_____mg/dl	
PART-III TREATMENT FACTORS OF DKA			
23.	What Type of drug the child used to treat DM up to the first DKA developed?	1.Not take any drug 2.Hypoglycemic drugs	

		3. Insulin 4. Both	
24.	Was the child adhere to the medication given for DM treatment?	1. Yes 2. No	
25.	Was child miss follow up for DM?	1. Yes 2. No	
26.	How insulin was placed at home?	1. Appropriately 2. inappropriately	

APPROVAL SHEET

ADDS ABABA UNIVERSITY

COLLEGE HEALTH SCIENCE

SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING AND MIDWIFERY

I, the undersigned MSc student, declare that I have submitted my original work on the title of incidence and predictors of diabetic ketoacidosis among children with diabetes in east and west Gojjam zone referral hospitals, North West Ethiopia, 2019: a retrospective cohort study, for the examination.

Submitted by:

Birtukan Assefa _____ _____

Name of student Signature Date

This thesis work has been submitted for examination with my approval as an advisor.

Approved by:

1. Mrs. Rajalakshmi Murugan (Asst. professor) _____ _____

Name of major advisor Signature Date

2. Kalkidan Wondwossen (Lecturer) _____ _____

Name of co -Advisor Signature Date