UNIVERSITY of RWANDA

THE EPIDEMIOLOGY, RISK FACTORS AND OUTCOMES OF HYPERGLYCEMIC EMERGENCIES AT UNIVERSITY TEACHING HOSPITAL OF KIGALI IN EMERGENCY DEPARTMENT

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine in Emergency Medicine and Critical Care, School of Medicine and Pharmacy, College of Medicine and Health Sciences, University of Rwanda

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DECLARATION

I, Dr. François Régis TWAGIRUMUKIZA, declare that this dissertation entitled **"The epidemiology, risk factors and outcomes of hyperglycemic emergencies at University Teaching Hospital of Kigali in Emergency Department"** is the result of my own research and it has not been submitted for any other degree in the University of Rwanda or any other institution.

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ABSTRACT

Background

Diabetes mellitus (DM) is a chronic condition that occurs when there is a high level of glucose in the blood. This can be due to total lack or insufficiency of the hormone called insulin produced by the body or when it is ineffectively used by the body. Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are two main serious complications of decompensated diabetes, and they are potentially fatal. However, there is limited data about diabetic complications in Rwanda, which is vital to help inform the Ministry of Health about effective health policies to prevent complications. The objective of this study was to evaluate the epidemiology, risk factors and outcomes of hyperglycemic emergencies at University Teaching Hospital of Kigali (CHUK) in the Emergency Department.

Methodology

This was a single-centered cross-sectional study evaluating epidemiology, risk factors, and outcomes of hyperglycemic emergencies at University Teaching Hospital of Kigali at Emergency Department from 1st September 2020 to 28th February 2021. Variables of interest included patient demographics such as gender, material status, ubudehe category, health insurance, medical histories including time since DM diagnosis, and type of hyperglycemic emergencies. Patient outcomes were retrospectively abstracted from Open Clinic, an online electronic database for patient history files. Data processing and analysis were carried out with the help of Microsoft Excel 2013 and StataSE 15.

Results

The total number of patients enrolled in this study was 44, with a female predominance (61.4%). Age ranged between 18 and 81 years, with the median age of 43.5 (IQR: 33, 61.5) years. The majority of patients came from home (50%) and most patients were using Mutuelle de Santé as medical insurance (77.3%). Considering the time of DM diagnosis, the majority were newly diagnosed with DM (36.4%), followed by those diagnosed with DM in less than five years (27.3%). This study showed that DKA was seen in 23 patients (52.3%) while HH) was seen in 21 patients (47.7%).

This study showed that the most common risk factor of hyperglycemic emergencies is infection (33.3%) and the other common risk factors are newly diagnosed DM (20%) and the combination of newly diagnosed DM and infection (20%). Mortality was 34.1% and was more prevalent in DKA compared to HHS patients. The median length of stay in the hospital was 11 (IQR: 6.5, 17.5) days for survived patients and 4 (IQR: 2, 10) days for died patients. In unadjusted analysis, HHS patients had lower odds of dying from a hyperglycemic emergency compared to DKA patients (OR = 0.27, 95% CI 0.07-1.00, p = 0.05). Mortality was found to be significantly associated with type of medical insurance (p = 0.005).

Conclusion

This study showed that the most common risk factors of HEs are infections and newly diagnosed DM. Overall, mortality was high among this cohort. Given that those risk factors are preventable, measures should be put in place to educate the community about the routine screening of DM and early consultation. This may be able to reduce the prevalence and outcome of hyperglycemic emergencies in Rwanda.

Keywords: Diabetic ketoacidosis, hyperosmolar hyperglycemic state, diabetes mellitus, University Teaching Hospital of Kigali, hyperglycemic emergencies.

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ABBREVIATIONS AND ACRONYMS

CHUK: University Teaching Hospital of Kigali

CMHS: College of Medicine and Health Sciences

DKA: Diabetic Ketoacidosis

DM: Diabetes Mellitus

ED: Emergency Department

GDM: Gestational Diabetes Mellitus

HEs: Hyperglycemic Emergencies

HHS: Hyperosmolar Hyperglycemic State

IQR: Interquartile range

IRB: Institutional Review Board

LMICs: Low- and middle-income Countries

LOS: Length of Stay

MI: Myocardial Infarction

MOH: Ministry of Health

MUSA: Mutuelle de Santé

OR: Odds Ratio

PID: Pelvic inflammatory Disease

RSSB: Rwanda Social Security Board

T1D: Type 1 Diabetes

T2D: Type 2 Diabetes

UR: University of Rwanda

UTI: Urinary Tract Infection

ACKNOWLEDGEMENTS

DEDICATION

To the Almighty God for his love and blessings upon us

To my Beloved Wife and lovely Children

To my Beloved Parents, Brothers and Sisters

To my Dear Classmates, Friends and Relatives

To my Supervisors

To my Patients

This work is dedicated with great pleasure

CHAPTER ONE: INTRODUCTION

1.1 Background

Diabetes mellitus (DM) is a chronic condition that occurs when there is a high level of glucose in the blood. This can be due to total lack or insufficiency of the insulin produced in the body or when it is ineffectively used by the body. (1) The prevalence of DM is rapidly increasing globally and it is expected that there will be a rise in number from 425 million in 2017 to 629 million in 2045, and 79% of this increase will affect low-and middle-income countries (LMICs). In Rwanda, the prevalence of diabetes is about 3.16% of the population with 1,918 diabetes related deaths per year.(1)

Two prevailing serious complications of DM include diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS), both of which can be fatal. Based on data from 2005, in the USA, DKA and HHS accounted for more than 120,000 hospital admissions per year compared to 62,000 hospital admissions in 1980. (2) These two hyperglycemic emergencies occur when there is ineffective insulin circulating together with a concomitant elevation of counter-regulatory hormones. (3)

DKA is commonly seen in type 1 diabetes mellitus (T1D), while HHS is frequently seen in type 2 diabetes mellitus (T2D). However, there are reports of ketosis-prone type T2D where patients can discontinue insulin therapy and remain insulin-independent. (4) Even if DKA and HHS are often discussed separately, they are all hyperglycemic emergencies due to poorly controlled diabetes. (5)

Previous literature has found multiple risk factors for hyperglycemic emergencies including, infections, a new diagnosis of diabetes, poor adherence to treatment, myocardial infarction (MI), trauma, abdominal crisis, and some drugs like antipsychotics, antiarrhythmics, corticosteroids and immunosuppressive agents. (6) Among the precipitating factors of DKA and HHS, infections are the most common. (2)(5)

1.2 Statement of the problem

Complications from DM are prevalent in both high and low and middle-income countries and have been progressively increasing in recent years. Despite the growing concern and compelling problems of DM complications, there have been limited studies on epidemiology, risk factors, and patient outcomes with DM complications in a low and middle-income context.

Therefore, this study will be carried out to establish and summarize the epidemiology, risk factors, and outcomes of hyperglycemic emergencies at CHUK in the ED.

1.3 Research objectives

1.3.1 Primary objective

➢ To determine epidemiology and mortality of hyperglycemic emergencies at CHUK ED

1.3.2 Secondary objectives

➢ To describe patient demographic information: age, sex, marital status, medical insurance used, ubudehe category, origin (rural or urban) and the referral system.

➢ To describe precipitating factors of HEs

➢ To describe the outcome of HEs in terms of length of stay in the hospital.

1.4 Research question

What are the epidemiology, risk factors and outcomes of hyperglycemic emergencies presented at University Teaching Hospital of Kigali at Emergent Department?

1.5 Rationale

This study will help to identify different risk factors for mortality associated with hyperglycemic emergencies and this will help the Ministry of Health (MOH) to put in place appropriate public health strategies and education to reduce the incidence of HEs in the Rwandan population.

1.6 Hypothesis

Hyperglycemic emergencies are not uncommon in our settings. The most common risk factors are infections, poor adherence to treatment and newly diagnosed diabetes mellitus. The mortality of hyperglycemic emergencies is high.

1.7 Structure of the study

This study entitled "Epidemiology, risk factors and outcomes of hyperglycemic emergencies at CHUK in ED" contains a title page, acknowledgements, dedication, abstract, and table of contents in the beginning, followed by six chapters: Introduction, Literature Review, Methodology, Results, Discussions, Conclusion and Recommendations.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

Diabetes mellitus is a burden worldwide because its complications are usually associated with disability, reduced life expectancy, and significant health costs for every society, including in Rwanda. (7) Therefore, looking at the epidemiology, risk factors and outcomes of hyperglycemic emergencies is very important to better understand the problem and to create preventive measures and or policies. In this chapter we will present the epidemiology of hyperglycemic emergencies, risk factors, and outcomes in different regions in the world.

2.2 Theoretical Literature

2.2.1 Definitions

Diabetes mellitus is a chronic condition that occurs when there is a high glucose level in the blood. This can be due to total lack or insufficiency of the hormone insulin produced in the body or when it is ineffectively used by the body.(1) Diabetic ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS) are two serious and potentially fatal hyperglycemic emergencies. HHS is a metabolic condition characterized by severe hyperglycemia, hyperosmolarity, and dehydration in the absence of ketoacidosis. DKA is a complication of uncontrolled DM and it is associated with a high mortality rate especially in developing countries. This condition is characterized by hyperglycemia, ketonemia and metabolic acidosis. (8)

Both DKA and HHS can occur in type 1 diabetes (T1D) and type 2 diabetes (T2D). However, DKA is more frequent in young people with T1D. Whereas HHS is more frequently reported in adult and elderly patients with T2D. (5) Its exact incidence is not known, but it is estimated to account for 1% of hospital admissions in patients with diabetes worldwide. (9)

2.2.2 Risk factors

Prior literature has found multiple risk factors for hyperglycemic emergencies. These risk factors include a new diagnosis of diabetes, poor adherence to treatment, myocardial infarction (MI), trauma, abdominal crisis, and some drugs like atypical antipsychotics, such as alpha-interferon and cocaine. (6) The most common risk has been found to be infections. (11)

2.2.3 Pathophysiology of DKA and HHS

The figure (Figure 1) below summarizes the pathophysiology of HEs. (6)
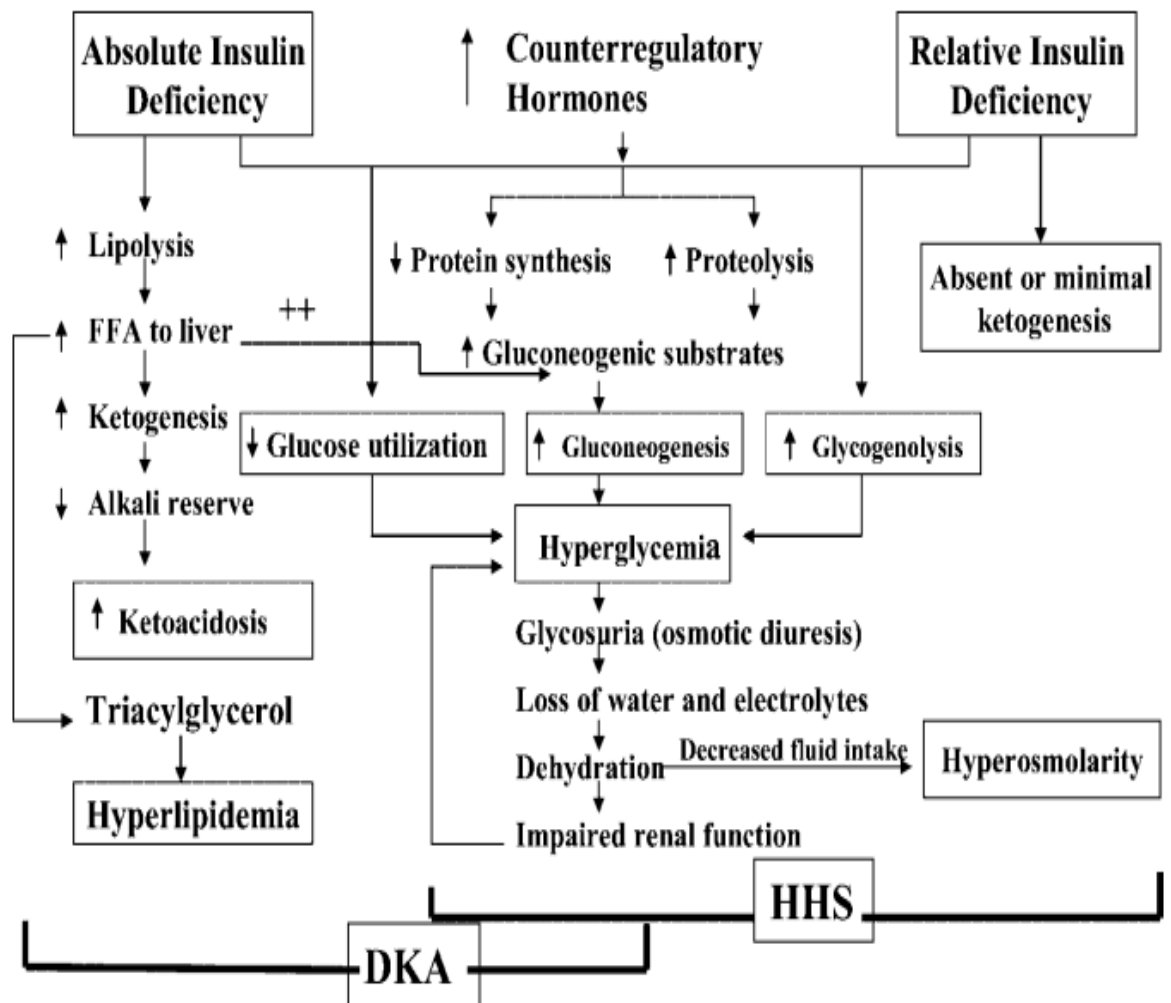
Figure 1: Pathophysiology of DKA and HHS

2.2.4 Diagnosis of DKA and HHS

The diagnosis of DKA and HHS is made using both clinical presentation and laboratory findings. The symptoms of DKA develop more rapidly over hours to days compared to those of HHS which develop insidiously over days or weeks. These symptoms include those associated with hyperglycemia such as polyuria, polydipsia, malaise, weight loss and signs of dehydration (Table 1). Laboratory diagnostic criteria are summarized Table 2.

For DKA in addition to the above mentioned symptoms, kussmaul breathing, nausea, vomiting and abdominal pain may occur. Altered mental status can occur on both DKA and HHS depending on the severity of the condition. Dehydration is more profound in HHS than in DKA. (2)

Table 1: Clinical presentation of HEs

Type of HE	Symptoms	signs	Presentation
DKA	Polydipsia	Hypothermia	Acute onset (Hours-days)
	Polyuria	Tachycardia	More common in T1D
	Weakness	Tachypnea	
	Weight loss	Kussmaul breathing	
	Nausea	Ileus	
	Vomiting	Acetone breath	
	Abdominal pain	Altered sensorium	
HHS	Polydipsia	Hypothermia	Gradual onset (Days-weeks)
	Polyuria	Hypotension	More common in T2D
	Weakness	Tachypnea	
	Weight loss	Altered sensorium	

Table 2: Laboratory diagnostic criteria for DKA and HHS on presentation

	Mild DKA	Moderate DKA	Severe DKA	HHS
Glycaemia (mmol/L)	>13.88	>13.88	>13.88	> 33.8
pH	7.25-7.30	7.0 to <7.24	<7.0	>7.3
HCO_3^-	15-18	10 to < 15	<15	> 15
S_{osm} (mmol/kg)	Variable	Variable	Variable	>320
Ketones	Positive	Positive	Positive	Small
Dehydration	6L			9L
Anion gap	>10	>12	>12	Variable
Mental status	Altered	Altered/drowsy	coma	coma

2.2.5 Treatment of Hyperglycemic emergencies

The management of DKA and HHS aims at replacing fluid loss, correcting electrolytes disturbances, correcting acid-base derangement, controlling glycaemia and managing the underlying precipitating factors. (2)

2.3 Empirical research

While limited, few studies have been conducted on hyperglycemic emergencies performed in various countries in Africa. In Ethiopia, a study done showed that the most common precipitating factor were infections (59%). (7) The mortality rate of HEs in this study was 9.8%. In a study conducted in Tanzania, in an ICU of a tertiary hospital in Mwanza, the most common precipitating factor of DKA was infection, followed by newly diagnosed DM. The mortality rate was 24.1%. (9)

2.4 Critical Review and Research Gap identification

In Rwanda, most patients with HEs are managed in referral hospitals and tertiary hospitals. Research on epidemiology of hyperglycemic emergencies in all referral hospitals can show different risk factors associated with those HEs and then recommendations can be made to the Ministry of Health to put in place strategies to decrease their prevalence.

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This study is on epidemiology, risk factors and outcomes of hyperglycemic emergencies at University Teaching Hospital of Kigali (CHUK). In this chapter, details about study design, population, sampling, ethical considerations, data collection, analysis and final data dissemination will be provided.

3.2 Study design

This is a single-centered cross-sectional study evaluating the epidemiology, risk factors and outcomes of hyperglycemic emergencies at CHUK ED.

3.3 Study period

This study covered six months from 1st September 2020 to 31st February 2021.

3.4 Study site and settings

This study was conducted at University Teaching Hospital of Kigali (CHUK) in the Emergency Department (ED). CHUK is a referral and tertiary health facility located in Kigali city. It serves the Northern Province, a part of Southern Province, a part of Western Province and Kigali city. The Emergency Department has a capacity of 26 beds. CHUK ED receives patients from home, private clinics, District hospitals, and Provincial Hospitals and these includes trauma patients and adult patients with different medical and surgical conditions. The ED is covered by General Practitioners (GPs), Emergency Medicine and Critical Care (EMCC) residents and Emergency Medicine and Critical Care Specialists. After initial evaluation and stabilization in emergency, different departments are consulted for further management and disposition.

3.5 Study population

Our study population included all adult hyperglycemic emergencies patients received at CHUK ED from 1st September 2020 to 28th February 2021.

3.5.1 Inclusion criteria

➢ All adult patients above 18 years with DKA or HHS received at CHUK ED during the study period and signed the consent form were enrolled in this study.

❖ Diagnostic criteria for DKA:

- Blood glucose >13.88 mmol/L
- Positive ketones on urine dipstick

❖ Diagnostic criteria for HHS:
  • Blood glucose > 33.8 mmol/L
  • Negative ketones on urine dipstick

3.5.2 Exclusion criteria

➢ All patients who didn't sign the consent form.
➢ All patients who were unable to give the consent due to the severity of the illness and didn't have the next of kin to sign the consent form.

3.6 Sampling

3.6.1 Sample size

The study aimed to include all patients with DKA and HHS arriving at the CHUK ED during the six-month study period. This study being an exploratory analysis aimed at understanding baseline characteristics of the population of interest to inform future research, no formal sample size was calculated.

3.6.2 Sampling strategy

Dedicated research personnel trained in standardized protocols collected data using structured case reporting forms were present 24/7 over the study period. All patients presenting for care to the CHUK ED were continuously screened for hyperglycemic emergencies. To identify those with HEs, we used history taking, physical examination, bedside glycaemia, urine dipsticks and the admitting physician were consulted as well to confirm the diagnosis. After obtaining the consent form the patients or caretakers, the research personnel used a structured data collection form to fill the required information. For the patient mortality, we retrospectively assessed patients' files from the medical records department/archives and Open Clinic after obtaining the permission to consult those files.

3.7 Validity and reliability of research instruments

A used data collection form was developed after consulting different literatures. After its elaboration, it was reviewed by my supervisors who are emergency medicine and critical care physicians before being used.

3.8 Data collection

Data was collected using the validated data collection form continuously by the primary investigator and four research assistants during the six months of study period.

Variables of interest included patient demographics such as gender, material status, ubudehe category, health insurance, medical histories including time since DM diagnosis, and type of hyperglycemic emergencies. The primary outcome was hospital-based mortality.

3.9 Data analysis

Data processing and analysis were carried out with the help of Microsoft Excel 2013 and StataSE 15. Descriptive statistics were summarized using frequencies and percentages for categorical variables and median and interquartile ranges (IQR) for continuous variables.

Patients were stratified by the primary outcome of mortality, and differences in characteristics were assessed using χ^2 or Fisher's exact tests for categorical variables or an independent t-test for normally distributed continuous variables. A univariate logistic regression was employed to calculate odds ratios (ORs) with associated 95% confidence intervals (CIs). A significance level of $p<0.05$ was utilized for all analyses.

3.10 Ethical considerations

The permission to conduct this study was obtained from the CMHS Institutional Review Board (IRB) No 304/CMSH IRB/2020 and the CHUK ethics committee EC/CHUK/053/2020. Patients' files numbers were used instead of names for confidentiality.

3.11 Data management

All data collection sheets were kept in a locked cupboard that is only accessible by study investigators. Electronic data were kept in a folder secured with a password.

3.12 Data dissemination

After completion of this study, data will be submitted for journal publication and then will be presented as a thesis for the master program of Emergency Medicine and Critical Care.

CHAPTER IV: RESULTS

4.1 Introduction

The total number of patients with hyperglycemic emergencies received at CHUK ED during six months study period was 44 patients. All patients who presented with a hyperglycemic crisis, who met inclusion criteria and consented were enrolled.

4.2 Presentation of results

2.2.1 Patient's socio-demographic characteristics

The results presented below show the socio-demographic characteristics of the study population.

Table 3: Patients socio-demographic characteristics

Characteristics	n (%) median(IQR)
Gender	
Male	17 (38.64)
Female	27 (61.36)
Age (Years)	
Median	43.5 (33, 61.5)
Civil status	
Single	12 (27.27)
Married	25 (56.82)
Divorced	1 (2.27)
Widowed	6 (13.64)
Ubudehe category	
Category I	4 (9.09)
Category II	12 (27.27)
Category III	26 (59.09)
Unknown	2 (4.55)
Medical insurance	
MUSA	34 (77.27)
RSSB	6 (13.64)
AHA	2 (4.55)
None	2 (4.55)
Origin	
Rural	18 (40.91)
Urban	26 (59.09)
Referral	
Home	22 (50.00)
Private clinics	3 (6.82)
District hospital	18 (40.91)
Provincial hospital	1 (2.27)

Table 3 above shows that the majority of our study population were female (61.4%). The age ranged from 18 to 81 years with the median age of 43.5 years.

The majority of patients were married (56.8%). Many patients came from urban areas (59.1%). The majority of the patients in this study came from home (50%) followed by those referred from different district hospitals (40.9%). Few patients came from provincial hospitals (2.3%) and private clinics (6.8%).

Most of the patients in this study were using Mutuelle de Santé as medical insurance (77.3%) followed by those using RSSB (13.6%) and many were in ubudehe category III (59.1%) and 12 patients (27.3%) were in category II.

2.2.2 Type of hyperglycemic emergencies

DKA and HHS were almost equally distributed with 23 patients (52.3%) having DKA and 21 patients (47.7%) with HHS.
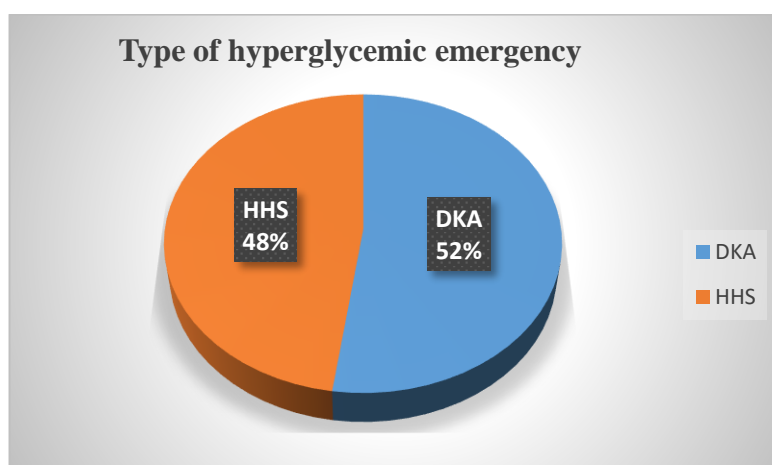
Figure 2: Distribution of patients according to type of HEs

2.2.3 Time of DM diagnosis

Most patients, 16 (36.4%), were newly diagnosed with DM followed by 12 patients (27.3%) diagnosed with DM in less than five years. Only one patient (2.3%) couldn't remember when DM was diagnosed.
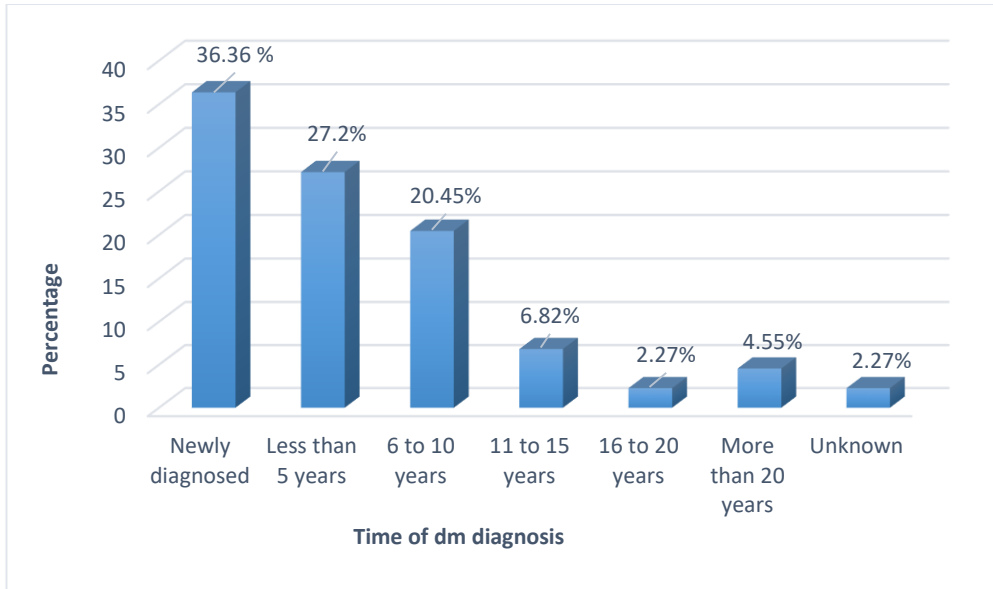
Figure 3: Distribution of patients according to time of DM diagnosis

2.2.4 Risk factors of hyperglycemic emergencies

The figure 4 below shows that the most common precipitating factor of hyperglycemic emergencies is infection (36.4%) followed by newly diagnosed DM and combined newly diagnosed DM and the presence of infection (18.2%).
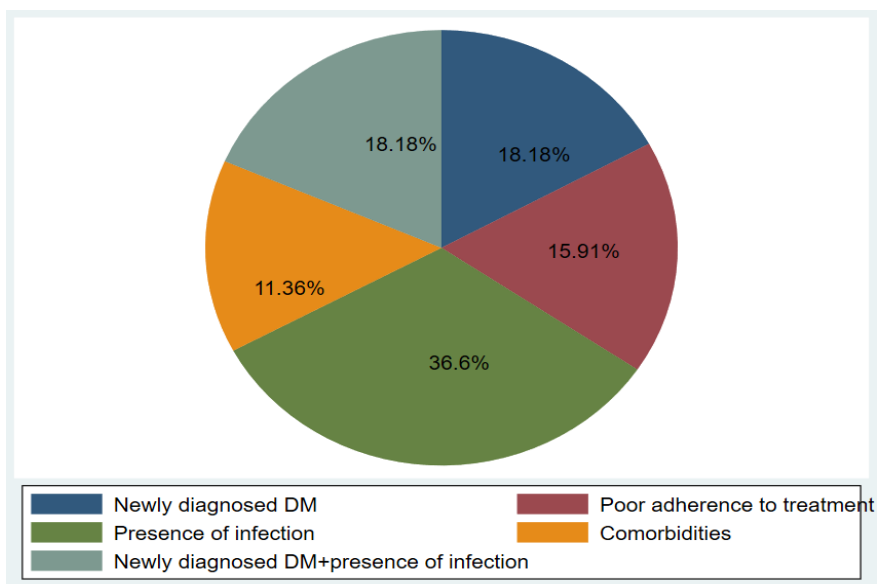
Figure 4: Distribution of patients according to risk factors

2.2.5 Categorical variables according to mortality

The table below describes the difference in categorical variables stratified by mortality along with an unadjusted univariate analysis with the associated ORs.

Characteristics	Survived n (%) median(IQR) (n=29)	Died n (%) median(IQR) (n=15)	P value	Univariate OR (95%CI)	P
Gender				0.60 (0.17-2.14)	
Male	10 (34.48)	7 (46.67)	0.431		
Female	19 (65.52)	8 (53.33)			0.43
Age (Years)				0.99 (0.95-1.02)	
Median	46 (33, 65)	38 (33, 57)	0.524		0.52
Ubudehe category				2.05 (0.85-4.92)	
Category I	4 (13.79)	0			
Category II	7 (24.14)	5 (33.33)	0.112		0.11
Category III	18 (62.07)	8 (53.33)			
Category IV	0	0			
Unknown	0	2 (13.33)			
Medical insurance					
MUSA	26 (89.66)	8 (53.33)		3.35 (0.65-17.32)	
RSSB	3 (10.34)	3 (20.00)	0.005*		0.15
AHA	0	2 (13.33)			
None	0	2 (13.33)			
Civil status					
Single	8 (27.59)	4 (26.67)		0.85 (0.42-1.71)	
Married	16 (55.17)	9 (60.00)	0.535		
Divorced	0	1 (6.67)			0.64
Widowed	5 (17.24)	1 (6.67)			
Origin				0.70 (0.20-2.47)	
Rural	11 (37.93)	7 (46.67)	0.576		0.58
Urban	18 (62.07)	8 (53.33)			
Referral					
Home	15 (51.72)	7 (46.67)		0.97 (0.52-1.81)	
Private clinics	1 (3.45)	2 (13.33)	0.709		0.92
District hospital	12 (41.38)	6 (40.00)			
Provincial hospital	1 (3.45)	0 (00.00)			
Type of Hyperglycaemic emergencies				0.27 (0.07-1.00)	
DKA	12 (41.38)	11 (73.33)	0.060		0.05
HHS	17 (58.62)	4 (26.67)			
Length of stay in hospital				0.93 (0.85-1.03)	
Median	11 (6.5, 17.5)	4 (2, 10)	0.143		0.15

Table 4: Categorical variables according to mortality with univariate analysis

Table 4 shows that there were 15 (34.1%) deaths in total. There was no statistical difference between among those who died and gender as 46.7% were males and 53.3% were females (p = 0.431). No statistical difference between, age (p = 0.524), ubudehe category (p = 0.112) civil status (p = 0.535), origin (p = 0.576) and referral status (p = 0.709). The median length of stay in the hospital was 11 day for those who survived compared to four days for those who died. Although this was also found to not be statistically different (p = 0.143).

Mortality was significantly associated with the type of insurance (p = 0.005). Among those who died eight patients (53.3%) were using Mutuelle de Santé (MUSA) as medical insurance compared to 26 patients (89.7%) who survived. Patients who had MUSA for health insurance had higher odds of dying from a hyperglycemic emergency compared to other health insurance companies (OR = 3.35, 95% CI 0.65-17.32, p = 0.15).

2.2.6 Mortality according to risk factors

Figure 5 below shows that infection is the most common precipitating factor among those who survived and those who died (37.9% vs. 33.3%). The average number of all patients with poor treatment adherence was higher among those who died compared to those who survived (20.0% vs. 13.8%).
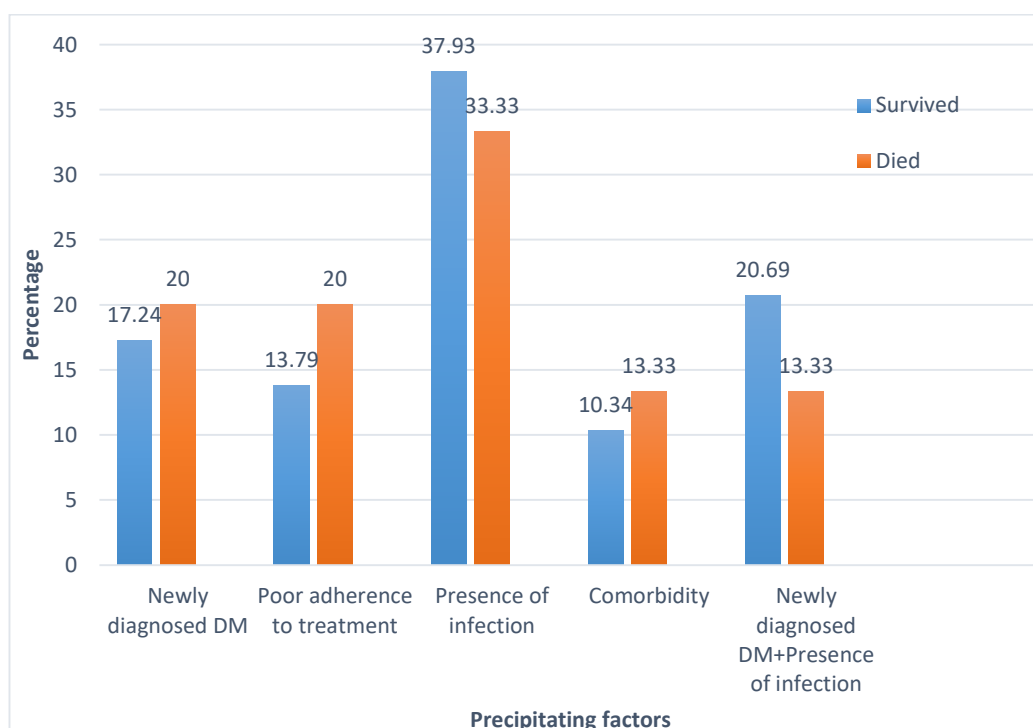
Figure 5: Mortality according to risk factors

2.2.7 Mortality according to type of HE

The figure below shows mortality according to hyperglycemic emergencies. Among those who died 11 (73.3%) were a DKA compared to 4 (26.7%) patients with HHS, although this difference was statistically insignificant (p = 0.06). In unadjusted analysis, HHS patients had lower odds of dying from a hyperglycemic emergency compared to DKA patients (OR = 0.27, 95% CI 0.07-1.00, p = 0.05).

	Survived	Died
DKA	41.38	73.33
HHS	58.62	26.67
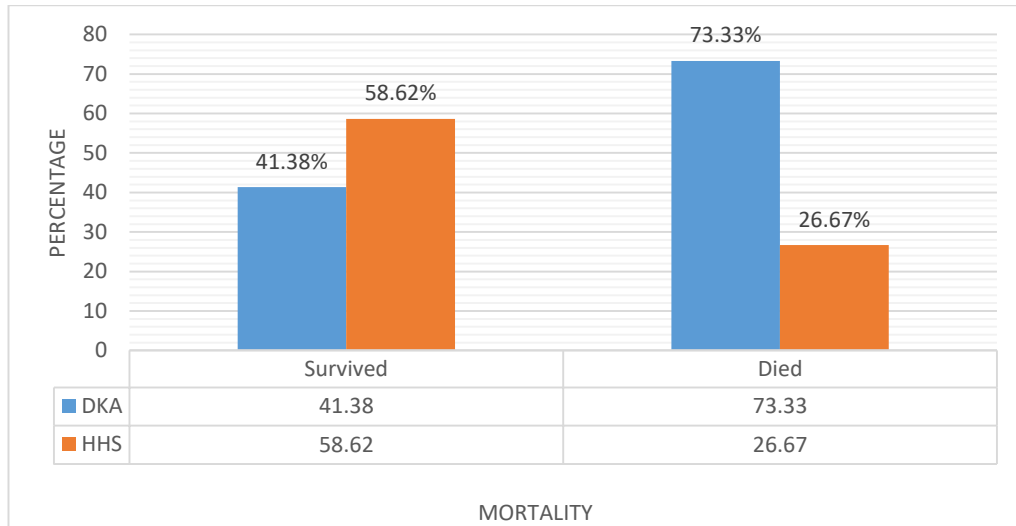
MORTALITY

Figure 6: Mortality according to type of HEs

CHAPTER FIVE: DISCUSSION

In this study, the total number of patients who presented with hyperglycemic emergencies at CHUK ED over a study period of six months was 44. This sample study is comparable to a study done in Johannesburg in South Africa, where during one year study period, the sample study was 82. (10) The age ranged from 18 to 81 years with the mean age of 46.2 years, and this is comparable to the study done in southeast Nigeria. (11)

The majority of our study population came from an urban area which is similar to another study performed in Ethiopia at Jimma University Specialized Hospital. (7) This may be because CHUK is located in Kigali City, and the majority of our study population came from their home. Females were more affected by hyperglycemic emergencies compared to males. This female predominance is similar to other studies done in Nigeria (4) and South Africa. (12)

About three-quarters of the patients in this study were using Mutuelle de Santé as medical insurance. MUSA, is a public medical insurance and accessible to every Rwandan, while others are private medical insurances or are provided by the company someone is working for. The other reason for MUSA predominance is that the study site is a public hospital accessible to everyone, and MUSA covers the bill at different percentages depending on ubudehe category. Patients who use private insurance tend to consult private health facilities.

The majority of the patients with hyperglycemic emergencies had newly diagnosed DM, which is similar to the study conducted in Ethiopia, where 45.4% were newly diagnosed with DM.(13) This is probably due to the fact that people do not do regular health status screening and do not consult until they get sick. Therefore, education about routine screening for DM and early consultation are the key in preventing DM complications. Slightly more than half of our study population had HHS, which is consistent with what was found in Nigeria. (4) This is different from what was found in a study conducted in South Africa where there were a predominance of patients with DKA. (10)

In this study, the most common risk factor of hyperglycemic emergencies was infections. Other risk factors were newly diagnosed DM and the combination of newly diagnosed DM and infection. Similar findings have been seen in many studies conducted worldwide widely like in South Africa (10), in Ethiopia (7), Nigeria (4), and in other countries. The rate of poor adherence to medications (15.9%) found in our study is lower compared to studies done in America, Thailand and Kenya, where the rate of poor adherence was ranging between 34 to 69%. (7)

In this study, the overall mortality rate of patients with HEs is 34%. This rate is higher compared to other studies done in Thailand (9.8%) (13), in Nigeria (20%) (14), and in Pakistan (21%). (15) The mortality was higher in DKA patients compared to those with HHS, and this is different from what was found in Thailand, where the highest rate was seen in HHS than that of DKA (13) and in Ethiopia. (16) In this study, mortality was significantly associated with the type of insurance with p = 0.005 (Table 4) and those with MUSA had higher odds of mortality compared to other insurance companies. This warrants further investigation and it may be associated with other key health system barriers. There were no other studies found comparing mortality according to types of medical insurance.

The explanation of the high mortality rate found in this study may be due to delayed consultation, poor initial management before the transfer, or delayed transfer to tertiary hospitals. The other reason may be that those patients referred to tertiary level hospitals are very sick, and the mortality is already high.

Study limitations and Challenges
The sample was small due to a short period of study and the data is from a single centered urban tertiary care center and may therefore represent a subset of patients with greater severity of illness. Being a single centered study we do not have a picture about hyperglycemic emergencies in Rwanda.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

Overall, there were a total of 44 patients enrolled into the study which had a female predominance 61.36%. DKA and HHS were almost equally distributed with 52.27% and 47.73% respectively. The most common risk factor of hyperglycemic emergencies is infection with 36.36% followed by newly diagnosed DM and the combination of infection and newly diagnosed DM with 18.18%. Overall, mortality was high (34%) compared to other studies in similar settings and this mortality was found to be significantly associated with the type of insurance.

6.2 Recommendations

- ➤ The MOH should elaborate the strategies to educate the patients about Diabetes Mellitus and its complications and encourage them to do routine screening. In addition to that, people should be educated about early consultation in case they don't feel well in order to be treated as soon as possible as well as how to prevent infection. These measures could improve the outcomes of the patients with DM and its complications.
- ➤ Given that the most common risk factor of HEs is infection, I recommend CHUK ED to screen every septic patient for DM.
- ➤ I also recommend conducting a multicenter study about clinical manifestations, management and outcome of hyperglycemic emergencies for a longer period of study in order to have a clear picture of hyperglycemic emergencies in Rwanda and elaborate other recommendations from that study.

REFERENCE

1. International Diabetes Federation, IDF Diabetes Atlas 8th edition. Eighth edition 2017. IDF Diabetes Atlas, 8th edition. 2017. 1–150 p.

2. Chaithongdi N, Subauste JS, Koch CA, Geraci SA. Diagnosis and management of hyperglycemic emergencies. Hormones. 2011;10(4):250–60.

3. Brenner ZR. Management of Hyperglycemic Emergencies. 2006;14621.

4. Edo AE. Clinical profile and outcomes of adult patients with hyperglycemic emergencies managed at a tertiary care hospital in Nigeria. :121–6.

5. Fayfman M, Pasquel FJ, Umpierrez GE. Management of Hyperglycemic Crises Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. Med Clin NA [Internet]. 2017;101(3):587–606. Available from: http://dx.doi.org/10.1016/j.mcna.2016.12.011

6. Goguen J, Gilbert J. Hyperglycemic Emergencies in Adults. Can J Diabetes [Internet]. 2013;37(SUPPL.1):S72–6. Available from: http://dx.doi.org/10.1016/j.jcjd.2013.01.023

7. Desse TA, Eshetie TC, Gudina EK. Predictors and treatment outcome of hyperglycemic emergencies at Jimma University Specialized Hospital , southwest. BMC Res Notes. 2015;1–8.

8. Nyenwe EA, Kitabchi AE. The evolution of diabetic ketoacidosis: An update of its etiology, pathogenesis and management. Metabolism [Internet]. 2016;65(4):507–21. Available from: http://dx.doi.org/10.1016/j.metabol.2015.12.007

9. Iddi S, Francis B, Jaka HM, Mirambo MM, Mushi MF. Clinical presentation and precipitating factors of diabetic ketoacidosis among patients admitted to intensive care unit at a tertiary hospital in Mwanza, Tanzania. Tanzan J Health Res. 2017;19(1):1–5.

10. Zouvanis M, Pieterse AC, Seftel HC, Joffe BI. Clinical characteristics and outcome of hyperglycaemic emergencies in Johannesburg Africans. Diabet Med. 1997;14(7):603–6.

11.   Nkpozi M, Ohagwu K, Chapp-Jumbo A, Unachukwu C, Chinenye S. Precipitating Factors of Hyperglycaemic Emergencies in a Tertiary Health Facility, South East, Nigeria. Int J Med Sci Diagnosis Res [Internet]. 2019;3(4):159–66. Available from: https://www.researchgate.net/profile/Kenneth_Ohagwu/publication/332967471_Precipitating_factors_of_hyperglycemia_emergencies_in_a_tertiary_health_facility_southeast_Nigeria/links/5cd42863299bf14d95836e56/Precipitating-factors-of-hyperglycemia-emergencies-

12.   Ekpebegh CO, Longo-Mbenza B, Akinrinmade A, Blanco-Blanco E, Badri M, Levitt NS. Hyperglycaemic crisis in the Eastern Cape province of South Africa: High mortality and association of hyperosmolar ketoacidosis with a new diagnosis of diabetes. South African Med J. 2010;100(12):822–6.

13.   Incidences and Outcomes of Hyperglycemic Crises : A 5-Year Study in a Tertiary Care Center in Thailand. 2012;95(8):995–1002.

14.   Ogbera AO, Awobusuyi O, Unachukwu C, Fasanmade OA. Clinical features, predictive factors and outcome of hyperglycaemic emergencies in a developing country. 2009;(February).

15.   Jabbar A, Farooqui K, Habib A, Islam N, Haque N, Akhter J. Clinical characteristics and outcomes of diabetic ketoacidosis in Pakistani adults with Type 2 diabetes mellitus. 2004;920–3.

16.   Gebremedhin G, Enqueselassie F, Yifter H, Deyessa N. Hyperglycemic crisis characteristics and outcome of care in adult patients without and with a history of diabetes in tigrai, Ethiopia: Comparative study. Diabetes, Metab Syndr Obes Targets Ther. 2021;14:547–56.

APPENDICES

A. DATA COLLECTION FORM

I.   PATIENT IDENTIFICATION

- ➢ ID number: ………
- ➢ Sex:
  - o Male ☐
  - o Female ☐
- ➢ Age: ………

II.   SOCIO-ECONOMIC STATUS

A. Ubudehe category: ☐

B. Medical insurance: …….

C. Civil status:
- ➢ Single ☐
- ➢ Married ☐
- ➢ Widowed ☐

D. Origin:
- ➢ Rural ☐
- ➢ Urban ☐

III.   REFERRAL

- ➢ Home ☐
- ➢ Private clinics ☐
- ➢ District Hospital ☐
- ➢ Provincial Hospital ☐

IV.   BEDSIDE TESTS:

- ➢ Blood glucose: ………
- ➢ Urine ketones: ………

V.   TYPE OF HYPERGLYCEMIC EMERGENCIES

- ➢ DKA ☐
- ➢ HHS ☐

VI.   TIME OF DIABETES DIAGNOSIS

- ➢ Newly diagnosed DM ⬜
- ➢ Less than 5 years ⬜
- ➢ 6 to 10 years ⬜
- ➢ 11 to 15 years ⬜
- ➢ 16 to 20 years ⬜
- ➢ More than 20 years ⬜

VII.   DIFFERENT RISK FACTORS (Select 1 or more)

- ➢ Newly diagnosed DM ⬜
- ➢ Poor adherence to treatment ⬜
- ➢ Presence or suspected infection ⬜
- ➢ Trauma ⬜
- ➢ Myocardial Infarction (MI) ⬜
- ➢ No identified risk factor ⬜
- ➢ Comorbidities (other diseases) ⬜
- ➢ Number of crisis ⬜

VIII.   OUTCOME

❖ Length of stay in hospital (in days)…..

❖ Mortality
- ➢ Dead ⬜
- ➢ Cured ⬜

B. INFORMED CONSENT FORM IN KINYARWANDA

Urupapuro rwemeraruhare mu bushakashatsi

Iriburiro

Muraho, nitwa TWAGIRUMUKIZA François Régis nkaba ndi umuganga wimenyereza umwuga w'ubuvuzi bwihuse no kuvura indembe muri kaminuza y'u Rwanda/Ishamiry' ubuganga n'ubuvuzi, nkaba ndigukora ubushakashatsi:"**Ingano n'ibyaba bitera ingaruka mbiz'isukari nyinshi mumubiri, kubitaro bikuru bya Kaminuza bya Kigali muri serivisi yakira inkomere n'indembe"**.

Ndagusaba kugira uruhare muri ubu bushakashatsi tugasangira amakuru yose ajyanye n'ubu bushakashatsi. Ndakubaza ibibazo uhitemo niba wemera uruhare mu bushakashatsi cyangwa utarugira.

Integoy'ubushakashatsi

Ubu bushakashatsi bugamije kureba ingano ndetse n'ibintu byaba bitera ingaruka mbi z'isukari nyinshi mu mubiri kubitaro bikuru bya Kaminuza bya Kigali muri serivisi y'inkomere n'indembe.

Ibanga

Amakuru yose uduha araba ibanga hagati y'abakora ubushakashatsi. Nta bimenyetso bikuranga byandikwa, tuzakoresha uburyo kuburyo nta myirondoro yawe igaragara. Amakuru yose azakoreshwa mubushakashatsi kugeza burangiye.

Ingarukan'inyungu

Nta ngaruka mbi nini ziri mu kujya muri ubu bushakashatsi, uretse ko ibibazo twakubaza bishobora kukubangamira. Ingaruka tuzazigabanya tugira ibanga ku makuru yose uduha. Amakuru yose azaba ari hagati y'abakora ubushakashatsi. Ntamakuru azahabwa abantu bo hanze.

Inyungu irimo ni ugufasha abaganga kumenya neza ingano n'icyaba gitera ingaruka mbiz'isukari nyinshi mu mubiri bityo bikazabafasha kwitaho neza abarwayi ba diyabeti ndetse banabasobanurira ukobagomba kwitwara.

Uburenganzira bwo kwanga cyangwa kuva mu bushakashatsi

Buri wese yemerewe kwanga cyangwa kwikura mu bushakashatsi igihe cyose kandi nta ngaruka bimugiraho.

Abo wabaza mu gihe ubuvuyemo:

Imyirondoro

Ushaka ibindi bisobanuro cyangwa afite ikibazo, ushaka kuva mu bushakashatsi wabaza aba bakurikira:

 -**Dr TWAGIRUMUKIZA François Régis**, Nimero za telephone: +250783290516

-**Dr NDEBWANIMANA Vincent**, Nimero za telephone: +250788634804

- **Prof GAHUTU Jean Bosco**, vice chair IRB, Nimero za telephone: +250783340040

- **Dr RUSINGIZA Emmanuel:** Nimero za telephone: +250785466254

Uruhushya rwo kuba mu bushakashatsi

Uremera ko wumvise neza uruhare rwawe muri ubu bushakashatsi, urahabwa ibyangombwa byo muri ubu bushakashatsi. Niba wemera kugira uruhare byemere mu magambo ushyireho umukono.

Izinaryawe cg umurwaza: …………………………………………………………….......

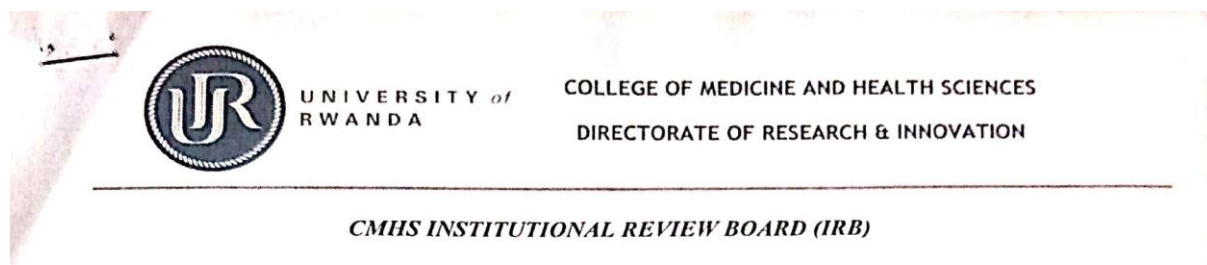Igisubizo utanze: …………………………………………………………………………

Umukono wawe…………………………………………   Italiki………/…..../……...........

Umukono w''ukora ubushakashatsi …………………   Italiki: …… /…… /…………..

Izinary'ubaza mu bushakashatsi: …………………………………………………………

C. CMHS IRB

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 18th/ March /2020

TWAGIRUMUKIZA François Régis
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 052/CMHS IRB/2020

Your Project Title *"Epidemiology, Risk Factors and Outcome of Hyperglycemic Emergencies at Kigali University Teaching Hospital in Emergency Department"* has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Yes	Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

The header "Involved in the decision" spans the Yes/No columns; "No (Reason)" spans the Absent and Withdrawn columns.

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 12th March 2020, **Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 18th March 2020

Expiration date: The 18th March 2021

Professor GAHUTU Jean Bosco
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

D. CHUK REVIEW APPROVAL NOTICE

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

13,Jul,2020   Ref.:EC/CHUK/053/2020

Review Approval Notice

Dear TWAGIRUMUKIZA FRANCOIS REGIS ,

Your research project: **"Epidemiology, risk factors and outcome of Hyperglycemic Emergencies at Kigali University Teaching Hospital iat Emergency Department "**

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 13,Jul,2020 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=127&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Dr Emmanuel Rusingiza Kamanzi
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali

ETHICS COMMITTEE
CHUK