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MEDICINE AND HEALTH SCIENCES

**CLINICAL PROFILE AND HOSPITALIZATION OUTCOME OF PATIENTS
ADMITTED WITH HYPERGLYCEMIC EMERGENCIES AT TERTIARY
HOSPITALS IN RWANDA.**

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Kigali, August 2021

DECLARATION

I, NDIZIHIWE Eulade, to the best of my knowledge hereby declare and certify that the work presented in this dissertation entitled "CLINICAL PROFILE AND HOSPITALIZATION OUTCOME OF PATIENTS ADMITTED WITH HYPERGLYCEMIC EMERGENCIES AT TERTIARY HOSPITALS IN RWANDA." is entirely my own and original, and it has never been presented or submitted in whole or in part to any other university.

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Signature:



Date: 01/09/2021

I, hereby declare that this dissertation has been submitted with my approval as the supervisor.

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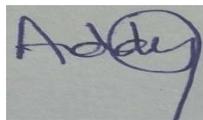
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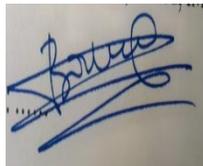
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ABSTRACT

Objective: This study aims to evaluate the clinical profile and hospitalization outcome of patients admitted with hyperglycemic emergencies at tertiary hospitals in Rwanda.

Materials and Methods: This was a prospective observational study conducted from November 2019 to November 2020. Data on socioeconomic status, demographics, clinical profile, type of diabetes and duration, prior treatment, laboratory data, precipitating factors if known were recorded. Outcome measures were length of hospital stay and inhospital death.

Results: One hundred forty-three patients were included in the study, seventy-nine (55%) were female, thirty-five (25.2%) had type 1 diabetes mellitus, one hundred and five (73.4%) had type 2 diabetes and two (1.4%) patients were unclassified. Most of the study subjects were middle-aged (56%) and most of them originated from Kigali city and southern province 40 (28%), 63(44.1%) respectively.

Of 143 patients, 85 were diagnosed with DKA, 51 were diagnosed with HHS, and 7 were unclassified, sixty-seven patients (46.9%) were newly diagnosed with diabetes mellitus (DM). abdominal pain and kussmal breathing were most observed in DKA in relation to HHS patients 26 (78.8%) vs 6 (18.2%) and 41 (48.2%) vs 4 (7.8%) with significant p values ($p = 0.035$, $p < 0.001$) respectively. There was a statistically significant difference between DKA and HHS in median of serum blood sugar, mean serum Potassium and median serum Chloride (447 vs 635), (4.1 ± 1.0 vs 4.1 ± 0.9), (105.1 vs 97.0) with p values ($p = < 0.001$, $p = 0.034$, $p = 0.019$) respectively. The leading precipitating factors were infections 56(34.5%) newly diagnosed DM 48 (29%) and poor drug adherence 31 (19%).

Having infections at admission, raised serum creatinine, comatose state, history of poor drug adherence and hypernatremia were independent predictors of mortality, the overall mortality rate among recruited patients was 27.9%(40 /143).The median hospital stay was 11 days ranging from less than 1 day to 103 days.

Conclusion: Nearly half of the patients who presented with DKA and HHS had no previous diagnosis of DM; most of the patients come from urbanized areas. Infection, poor drug adherence, and newly diagnosed DM were the leading precipitating factors, the mortality rate was high.

Keywords: Hyperglycemic emergencies; clinical profile; tertiary hospital; Rwanda.

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ACRONYMS

ABG: Arterial blood gaz

BUTH: Butare University teaching hospital

CMHS: college of medicine and health sciences

DH: district hospital

DKA: diabetic keto acidosis

DM1: Diabetes mellitus type 1

DM2: Diabetes mellitus type2

HEs: Hyperglycemic emergencies

HHS: hyperosmolar hyperglycemic state

IDF: International Diabetes Federation

IRB: institutional review board

IV: Intravenous Fluid

KUTH: Kigali University teaching hospital

LMIC: Low-and middle-income country

NCD: Non communicable diseases

P: P-value

PH: hydrogen potential

RMH: Rwanda military hospital

SPSS: Statistical package for the social sciences

UT I: Urinary tract infection

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Last but not least, my gratitude is presented to all my colleagues, friends, and relatives for their endurance and charity throughout my life, and particularly through my studies "May the Almighty God bless you".

NDIZIHIWE Eulade, MD

DEDICATION

To God the Almighty

To my wife UWIMANA Nadia

To my children:

NDIZIHIWE HIRWA Edwin

NDIZIHIWE INEZA Nancy

To my relatives and parents

To my classmates and other people who contributed
to my studies

I dedicate this work

Chapter I. Introduction

I.1. Background

Diabetes mellitus (DM) is a life long disease that occurs when the pancreas produces very little or no insulin at all or when the body's ability to respond to insulin is impaired resulting in hyperglycemia [1]. Most of the untreated or inadequately treated patients develop acute metabolic complications such as Diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state (HHS), which are life threatening if not managed urgently and adequately. These complications are associated with high morbidity and mortality[2]

A pooled analysis of the worldwide trend in DM since 1980 showed that a growing population and increasing life expectancy made the number of affected adults four times high since that year and this rate is faster in low-and middle-income countries (LMIC)than in high income countries[3].DKA and HHS globally contribute significantly to mortality, financial burden, and poor quality of life of patients and their families [4]

In Rwanda, the overall prevalence of DM was 3.2% in 2015 [5] and diabetes related death was estimated to be 2% of total death in 2016[6].To my knowledge, there is no available data about the burden of hyperglycemic emergencies and outcomes in Rwanda to date.

I.2.Problem statement

Even if there is no published evidence, based on my own clinical experience and observation, the number of people with diabetes mellitus might be increasing in Rwanda. We frequently admit patients with hyperglycemic emergencies at Butare University Teaching Hospital (BUTH), Kigali University Teaching Hospital (KUTH), and Rwanda Military Hospital (RMH). Some of those admitted patients were previously on blood glucose lowering medications and others are newly diagnosed with different health outcomes. To date, no studies have evaluated the clinical profile, precipitating factors, and treatment outcome of DKA and HHS to guide clinicians and stakeholders on adequate and evidence based decisions to improve the management and prevention of those serious acute complications.

I.3. Research question

This study was designed to respond to the following clinical questions:

1. What are the demographic and clinical characteristics of patients with HHS or DKA?
2. What are the identified precipitating factors for HHS or DKA in patients admitted at tertiary hospitals?
3. What is the management outcome of DKA or HHS patients at tertiary hospitals and what are the associated risk factors to death and long duration of hospital stay?

I.4. Objectives

I.4.1. General Objectives

To determine the clinical profile and hospitalization outcome of patients with hyperglycemic emergencies at the three referral hospitals in Rwanda.

I.4.2. Specific objectives

- To determine the socio demographic characteristics of patients with DKA and HHS admitted in KUTH, RMH, and BUTH wards
- To reveal the clinical profile of patients admitted with hyperglycemic emergencies.
- To point out the most common precipitating factors of hyperglycemic emergencies of patients admitted at KUTH, BUTH, RMH
- To determine the inhospital DKA and HHS related mortality rate and associated risk factors, the duration of hospital stay and risk factors for a long hospital stay.

Chapter II: Literature review

II.1. Introduction

There are acute non metabolic and metabolic complications of diabetes. Metabolic complications include Diabetic ketoacidosis and hyperosmolar hyperglycemic state, which are life threatening complications commonly known as hyperglycemic emergencies[7] These account for most indication of admission of patients with diabetes [8] and are the leading causes of loss of life in patients with diabetes [9].

These metabolic complications result from a combined effect of total or relative lack of insulin and a surge in counterregulatory hormones notably catecholamines, glucagon, growth hormone, and cortisol.

DKA is mostly observed in patients who have autoimmune type 1 diabetes; however, it can also develop in patients with type 2 diabetes in case of catabolic stress such as infections, surgery, or trauma [7]. The three main distinguishing features of DKA are metabolic acidosis hyperglycemia, and increased total body ketone production; whereas hyperosmolality, severe hyperglycemia, profound dehydration without significant ketoacidosis characterize HHS.

The most prominent symptoms in DKA, as well as HHS, are polydipsia, polyuria, vomiting, loss of weight, dehydration, altered mental status, and weakness. Physical findings are a decrease in skin turgor, Kussmaul breathing (more seen in DKA), hypotension, and tachycardia. Mental status can vary from full consciousness to coma; the latter is commonly seen in HHS. Seizures and focal neurologic signs are mostly found in HHS[10] and altered sensation has been the distinguishing feature of patients with HHS[11]

Nausea, vomiting, dizziness, and abdominal pain are significantly observed in type 1 DM patients with DKA [12] normally those symptoms resolve after initial treatment. When the gastrointestinal symptoms are not resolved after one day following initialization of treatment of DKA other potential causes should be promptly investigated [13] It was found that abdominal pain correlates with the severity of acidosis[14] and hypothermia was found as a poor prognostic factor for DKA[15]

II.2.Precipitating factors

Infections, poor adherence to blood glucose lowering drugs, and newly diagnosed diabetes were the major precipitants of hyperglycemic emergencies [16]. Some of the reasons for non adherence to diabetes treatment include non affordable cost, ignorance, fearing weight gain due to insulin[17], fear of hypoglycemia, defiance of medical advice. Depression was particularly found to be the cause of non adherence to treatment in adolescents [10].

Among infections urinary, respiratory tract infections, and malaria were found to be the most common precipitating factors[18]

The surge of counter regulatory hormones caused by concurrent medical conditions such as myocardial infarction, trauma, stroke, severe dehydration can result in HHS [19]. Elderly patients being water restricted due to other comorbidities, being bedridden or restrained with underlying impaired thirst response are at high risk of developing HHS[20].Some drugs which alter the metabolism ofcarbohydrates such as thiazides,corticosteroids,sympathomimetic drugs can be triggers of DKA[17].

II.3.Mortality rate and hospital stay

A bunch of studies found that a higher mortality rate is reported in individuals with HHS than in those with DKA[21][22][23]

DKA and HHS occupied the 3rd position of diabetic complications requiring long hospital stay after congestive heart failure and diabetic foot syndrome[8]. In Nigeria Ezeani et al [24] in their study found that the duration of hospital stay was 24.2 ranging from 0.5 days to 88 days.

In Ethiopia, higher mortality rate was recorded in males than in females 11.8% and 6.6% respectively with P value ($P = 0.286$), most of the deaths cases occurred within the first week of admission[16]

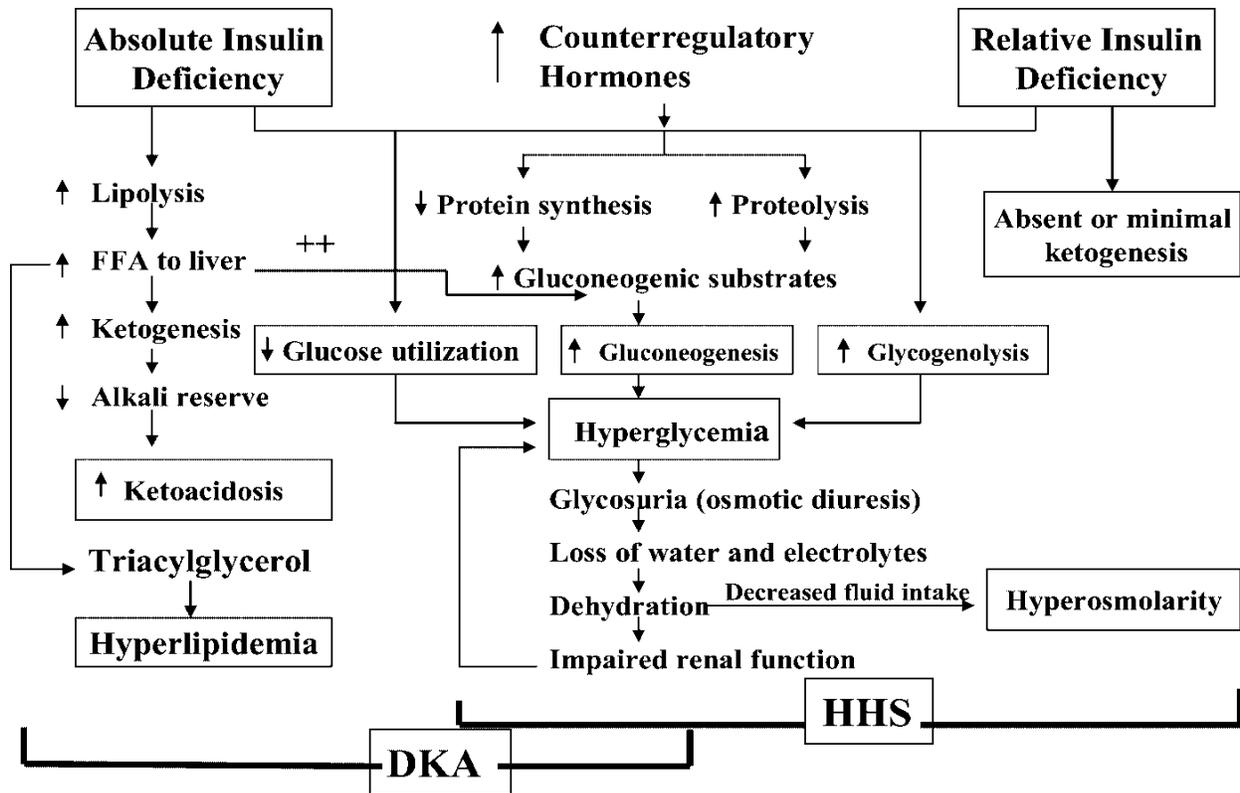


Figure 1: The pathogenesis of DKA and HHS

Adapted from: Statements ADA. Hyperglycemic Crises in Adult Patients with diabetes. 2009;32(7). doi:10.2337/dc09-903

Table 1: Biochemical difference between DKA and HHS

Parameter	DKA			HHS
	Mild	moderate	severe	
Plasma glucose,mg/dL	>250	>250	>250	>600
Arterial pH	7.25-7.3	7.0-7.24	<7.0	>7.30
Serum bicarbonate, mmol/L	15-18	10 to <15	<10	>18
Serum ketones	Positive	Positive	Positive	Small
Urine ketones	Positive	positive	Positive	small
Effective serum osmolality, mOsm/kg	Variable	Variable	Variable	>320
Anion gap	>10	>12	>12	Variable
Alteration in sensoria or mental obtundation	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

Calculation: $2[\text{measured Na}^+ (\text{mEq/L})] + \text{glucose (mg/dL)}/18$.

Nitroprusside reaction method.

Calculation of anion gap: $(\text{Na}) - (\text{Cl} + \text{HC03}) (\text{mEq/l})$.

Adapted from: A. D. A. Statements, “Hyperglycemic Crises in Adult Patients with diabetes,” vol. 32, no. 7, 2009, doi: 10.2337/dc09-9032.

II.4.Biochemical profile

A study done by Ezeani I.U et al[23] concluded that initial blood glucose, serum osmolality, electrolytes were highest in HHS compared to other patients and was lowest in DKA patients.

The most common electrolyte derangements in hyperglycemic emergencies are hyponatremia, 31 (36.9%) and hypokalemia 21 (25%)[25]. In a study done by Guillermo et al [22] on urban blacks found that the level of consciousness correlated well with serum osmolality than it is with age or degree of metabolic acidosis in both hyperglycemic emergencies.

Ahmed in Saudi Arabia[12] found that there is a statistically significant difference of biochemical data of studied population with the HES with the mean blood Sugar ($p=0.00$) and plasma osmolality ($p=0.05$).

It was observed in this study that there was more acidosis in DKA patients than in HHS patients with a mean pH of (7.2 ± 0.1) and (7.3 ± 0.1) respectively. It was also noticed that sodium level was low in HHS patients with a mean of (129.6 ± 6.0) compared to DKA patients who had a mean sodium level of (131.9 ± 5.4) but there was no statistical significance found.

However, hypokalemia was more seen in DKA patients than in HHS with a mean potassium level of (4.5 ± 0.9), (4.6 ± 1.1) respectively. There was a statistical difference in bicarbonate level between HHS and DKA patients with a P value of 0.01

Leukocytosis is commonly found in patients with hyperglycemic emergencies [10]. Its diagnostic utility in hyperglycemic emergencies is very limited [26]because white cell count can be often raised without infection[27] due to dehydration and /or increased catecholamines.

It has been shown by Corey et al[28] that elevated band is the only marker of occult infection among other variables in DKA patients and its presence suggests the ultimate necessity of antibiotics but again leukocytes greater than 25,000 / μ L should alert the clinician to a higher likelihood of infection and further workup should be done [21]

II.5. Management of DKA and HHS

The successful management of HHS and DKA follows this order: correction of dehydration, initiation of insulinotherapy taking into account electrolyte imbalances, recognition and management of precipitating causes, and then close monitoring of patient.

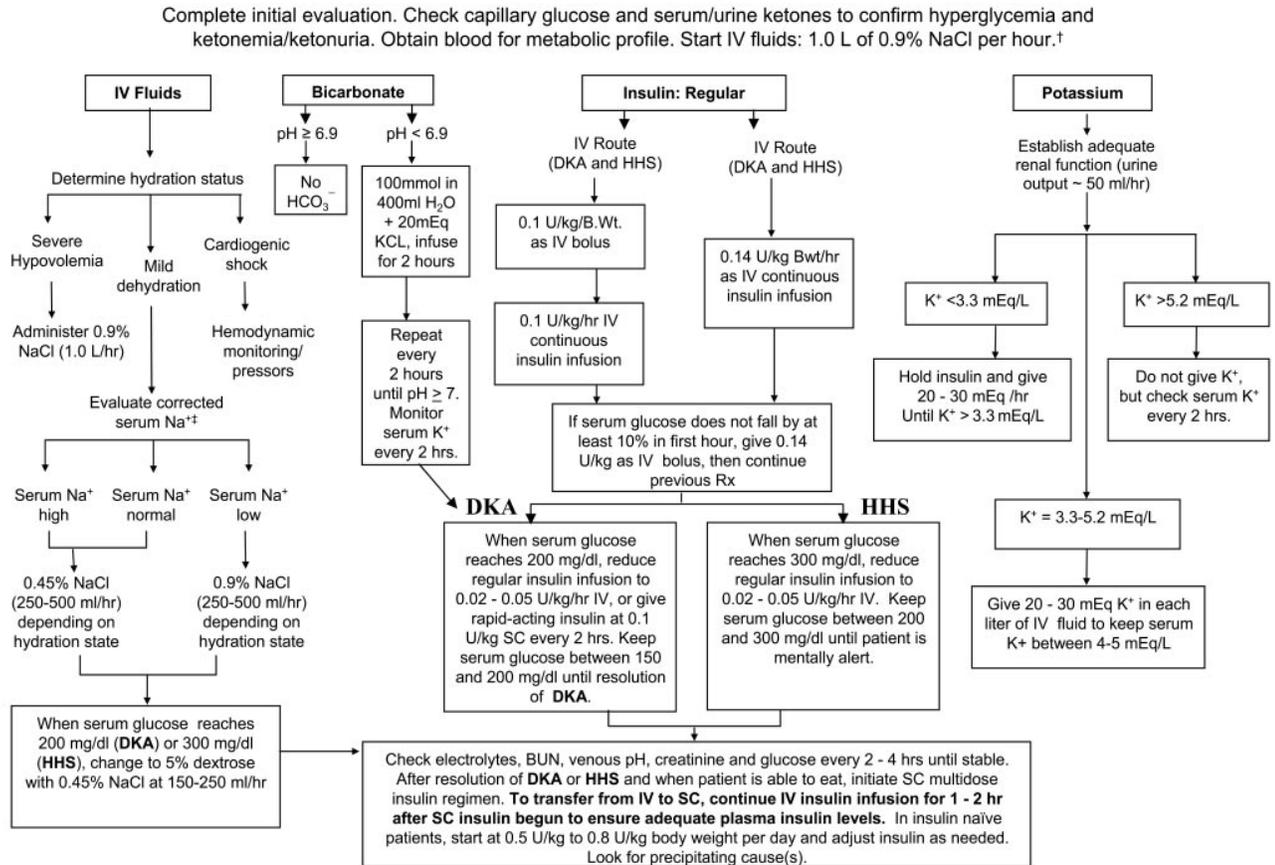


Figure 2: Management of hyperglycemic emergencies

Adapted from: Statements ADA. Hyperglycemic Crises in Adult Patients with diabetes. 2009;32(7). doi:10.2337/dc09-903

II.6. Prognostic factors

It was found by Ogbera et al that the duration of DM was a predictive factor of mortality most of the deaths occurred in a patients with short term duration of DM (less than 10 years) as defined in this study, including newly diagnosed cases[18].

Advanced age was also seen as an independent predictor of mortality[29].This was found in a study conducted in Nigeria and predictors of mortality were sepsis, DM foot ulcers, and hypokalaemia [18]

II.7. Contribution of socio economic status to the incidence of hyperglycemic emergencies

Ahmed found that in the Middle East and Saudi Arabia diabetes and its complications are one of the most expensive disorders to treat.[12]

Global report on diabetes 2016 states that the increase in total global diabetes health expenditure is expected to grow as diabetes incidence increases. This economic loss will be more pronounced in low-and middle -income countries where insulin is not constantly present in hospital pharmacy. Lack of health insurance, lack of injection and self monitoring devices predispose patient with diabetes to have hyperglycemic emergencies[4].

It is worth generating local evidence to guide clinicians and health decision makers for evidence based practice in the management of HEs.

Chapter III Methodology

III.1. Study design

This was a prospective observational study conducted from November 2019 to November 2020.

III.2. Study site and period

This study was conducted mainly at the emergency wards and intensive care units at KUTH, RMH, and BUTH located in Kigali City and Butare (South Rwanda) respectively. Included participants were followed up from admission to hospital to discharge or death.

III.3. Study population

All patients admitted from the emergency department, ICU or medical wards that are diagnosed with diabetic ketoacidosis or hyperosmolar hyperglycemic state by the treating doctor.

III.3.1. Inclusion criteria

All adult patients aged fifteen years and above diagnosed with hyperglycemic emergencies were recruited.

III.3.2. Exclusion criteria

- Patients who refused to consent
- Pregnant women
- Patients with heart failure, end stage renal disease and liver failure were excluded from this study because they may be affected by aggressive administration of intravenous fluid given in the management of hyperglycemic emergencies.

III.4. Sample size

A prospective registry of all participants was recruited consecutively as received at the Emergency department at KUTH, BUTH, and RMH from Nov 2019 to Nov 2020.

III.5.Data collection

This is a prospective observational study carried out at KUTH, BUTH, and RMH for already diagnosed and newly diagnosed patients with DM aged fifteen years or above presenting with hyperglycemic emergencies will be recruited for the study. Data was recorded on age, sex, education level, duration of DM, or (whether newly diagnosed) signs and symptoms, plasma glucose, electrolyte levels, urea and creatinine at presentation, previous treatment type before admission, precipitating factor if known, length of hospital stay, and inhospital mortality rate.

III.6.Definition of terms

Duration of DM was classified into:

Newly diagnosed DM: Patients without a previous diagnosis of DM

Short term duration: This refers to have DM for: <10 years

Medium term duration: This refers to have DM for: 10–19 years

Long term duration: This refers to have DM for: 20 years and more

Type 1 DM: Refers to DM patients who have been insulin dependent since diagnosis and absolutely require insulin injection to live.

Type 2 DM: Refers to patients with DM who at the beginning were managed with only lifestyle change, blood sugar lowering agents, or patients requiring insulin who at diagnosis were not insulin dependent.

III.7.Ethical consideration

Ethical approval was obtained from CMHS/IRB and institutional review by KUTH, BUTH, and RMH IRB. Participants were free to consent and only those who provided the consent to participate were included. The reports of laboratory investigations were kept in the patients' charts

III.8. Data recording and Analysis

The study data were collected using a data collection sheet and were entered into the Excel sheet for database creation .Collected data were cleaned and entered into Epidata version 3.1 and then exported to IBM SPSS version 25 for analysis. Descriptive categorical data were presented using frequencies and percentages in tables and continuous data were summarized using mean and median depending on their distribution.

The difference in mean and/or median scores among groups was tested using t-test and ANOVA test for normally distributed data and by nonparametric test (Mann Whitney U test for binary outcomes and Kruskal Wallis test for the outcomes with more than 2 categories) for skewed data. Chi-square test and logistic regression analysis (Odds ratios and their 95% confidence intervals) were used to study the relationship between the predictors and outcomes. Statistical significance for the associations was taken at the level $p < 0.05$. The results of the research will be kept in a confidential, password protected electronic file accessible only by the investigator.

Chapter IV: Results and Interpretation

4.1. Socioeconomic and demographic characteristics of participants

The majority of the participants were female (55%), married (59%). Most of the participants were middle-aged 80(56%). Health insurance was covered in 95.1% of participants. Around half of the participants (51.7%) had a primary level of education. Most of the patients were originating from Kigali city and southern province 28%, 44.1% respectively

Table 2: Socioeconomic and demographic characteristics of participants

Characteristics	Frequency	%
Age in years		
≤35(young)	45	31.5
36-65(middle-aged)	80	56
>65(Elderly)	18	12.6
Gender		
Female	79	55.2
Male	64	44.8
Education		
No formal education	10	7.0
Primary	74	51.7
Secondary	47	32.9
University	12	8.4
Marital status		
Married	85	59.4
Single	39	27.3
Widow	18	12.6
Divorced	1	0.7
Economic category (ubudehe)		
Cat 1	22	15.5
Cat 2	37	26.1
Cat 3	83	58.5
Insurance		
CBHI	117	81.8
Premiums	19	13.3
No insurance	7	4.9
Province		
Southern	63	44.1
Kigali City	40	28.0
Eastern	24	16.8
Western	10	7.0
Northern	5	3.5
DRC	1	0.7

CBHI: Community based health insurance; DRC: Democratic Republic of Congo

4.2. Clinical characteristics of study participants

Type of diabetes, treatment and duration.

Most of the participants had type 2 diabetes mellitus compared to type 1 105(73.4%) vs 36(25.2%) respectively whereas two cases were unclassified, Majority of those who were recruited with a previous diagnosis of diabetes were on oral medications followed by those taking insulin alone and a small number were combining the two (47%,46%,6.5%) respectively. Among recruited patients with a known diagnosis of DM a big number of them 58 (40.6%) had diabetes lasting less ten years.

Medication adherence, admission room, and hospital stay.

A big number of participants had poor adherence to drugs (41%), the most common reason for stopping meds was running out of medication, followed by fear of hypoglycemia, most of the patients admitted were admitted to the emergency department with a non negligible proportion of admission in a general ward, only a few numbers of them accessed either ICU or HDU 15(10.5%), 13(9.1%) respectively, the median hospital stay was 11 days ranging from less than 1 day to 103 days. The longest hospital stay was observed in patient with infected diabetic foot.

Precipitating factors

The three major precipitating factors of HEs were infection, poor adherence to medication, and a new diagnosis of diabetes in decreasing order.UTI and pneumonia being the most common infection. There was only one case of trauma and one case of cerebral vascular accident triggering HEs.

Table 3: Clinical characteristics of study participants

Characteristics	Frequency	%
Type of Diabetes Mellitus		
Type 1	36	25.2
Type 2	105	73.4
Unclassified	2	1.4
Admission room		
Emergency	85	59.4
General ward	30	21.0
ICU	15	10.5
HDU	13	9.1
Diabetes duration		
Newly diagnosed	67	46.9
<10 years(short term duration)	58	40.6
10 -19 years(medium term duration)	7	4.9
≥20 years (long term duration)	11	7.6
Symptom duration(days) prior consultation		
Median (Q1-Q3)	7 (4-13)	
Treatment		
Insulin alone	35	46
Oral medications	36	47
Insulin and oral medications	5	6.5
Drug compliance		
Good	44	58.7
Poor	31	41.3
Raison to stop drugs		
Fear of hypoglycemia	8	22.8
Runs out of medication	15	42.8
Poor understanding of disease	7	20
Depression	2	5.7
Side effects	3	8.5
Precipitating factors		
At least 1 type of infection	56	34.5
Poor adherence to treatment	31	19
Corticosteroids	2	1.2
Gastroenteritis	2	1.2
Newly diagnosed	48	29
Trauma	1	0.6
Cerebral vascular accident	1	0.6
Unidentifiable	22	13.5
Hospital stay in days [Median (Q1-Q3)]		11 (6-18)

Q1: Quartile 1 (25th percentile); Q2: Quartile 3 (75th percentile); ICU: Intensive care unit; HDU: High Dependency Unit

4.3. Clinical and laboratory presentation of participants with hyperglycemic emergencies

Clinical presentation of participants

Patients with DKA were more likely to present with shortness of breath, polyuria, abdominal pain, and Kussmaul breathing compared to those with HHS with statistically significant P values (see table 4). Comatose status and convulsions were most seen in DKA than in HHS patients however P values were not statistically significant (P:0.199, P: 0.738) respectively.

Laboratory profile of participants

There was a significant difference in blood sugar median values at admission where patients with HHS showed to have a high level of blood sugar. Patients with HHS had low serum chloride measurements compared to patients with DKA ($p=0.019$). There was a statistically significant difference in mean serum potassium measurements with DKA patients having high median potassium level ($p=0.034$). There was no statistically significant difference in glycated hemoglobin level, sodium, creatinine, urea, and serum osmolality between DKA and HHS patients.

Table 4: Clinical and laboratory presentation of participants with hyperglycemic emergencies

Presentation	Hyperglycemic emergency type		P value
	DKA (N=85)	HHS (N=51)	
Signs and symptoms			
Convulsions (n=11)	8 (9.4%)	3 (5.9%)	0.738
Shortness of breath (n=41)	32 (37.6%)	9 (17.6%)	0.031
Nausea and vomiting (n=42)	29 (34.1%)	13 (25.5%)	0.205
Weight loss (n=39)	27 (31.8%)	12 (23.5%)	0.415
Weakness (n=89)	50 (58.8%)	39 (76.5%)	0.088
Polyuria (n=19)	16 (18.8%)	3 (5.9%)	0.012
Abdominal pain (n=32)	26 (78.8%)	6 (18.2%)	0.035
Dehydration (n=88)	58 (68.2%)	30 (58.8%)	0.506
Lethargy (n=49)	28 (32.9%)	21 (41.2%)	0.576
Kussmal breathing (n=45)	41 (48.2%)	4 (7.8%)	<0.001
Coma status (n=12)	10 (11.8%)	2 (3.9%)	0.199
Biochemical measurements			
Blood sugar [Median (IQR)]	447 (325-634)	635 (572-739)	<0.001
HbA1c [Median (IQR)]	13.0 (11.0-15.9)	12.9 (10.4-15.6)	0.286
Potassium (Mean \pm SD)	4.1 \pm 1.0	4.1 \pm 0.9	0.034
Sodium (Mean \pm SD)	165.2 \pm 144.1	135.3 \pm 11.6	0.508
Chloride [Median (IQR)]	105.1 (95.0-120.3)	97.0 (92.0-106.7)	0.019
Creatinine [Median (IQR)]	145.0 (97.2-218.6)	95.3 (78.5-168.8)	0.087
Urea [Median (IQR)]	7.9 (4.2-13.2)	5.9 (4.1-8.8)	0.799
Serum osmolarity [Median (IQR)]	309.0 (287.5-333.0)	293.0 (272.2-317.7)	0.13

IQR: Interquartile range [Q1: Quartile 1 (25th percentile)-Q2: Quartile 3 (75th percentile)]; SD: Standard Deviation; DKA: Diabetic Ketoacidosis; HHS: Hyperosmolar Hyperglycemic state

4.4. Diagnosis and general in-hospital outcomes among patients with hyperglycemic emergencies in Rwanda

The general hospital outcomes among patients with hyperglycemic emergencies. HHS patients had a high discharge rate of 76.5% than DKA patients 65%, $p < 0.001$, DKA patients presented a high mortality rate of about 30.5% than HHS patients 23.5%, $p < 0.001$.

Forty (27.9%) patients died.

Three patients were counter transferred to the nearest DH for continuation of care; one military patient was transferred to a military hospital.

Table 5: Diagnosis and general in-hospital outcomes among patients with hyperglycemic emergencies

Outcome	DKA	HHS	unclassified	Total
Counter transferred	3 (3.5%)	0 (%)	0	3
Discharged to home	55 (65%)	39 (76.5%)	5 (71%)	99
Transferred	1 (1%)	0 (%)	0 (%)	1
Died	26 (30.5%)	12 (23.5%)	2 (29%)	40
Total	85	51	7	143

DKA: Diabetic Ketoacidosis; HHS: Hyperosmolar Hyperglycemic state

4.5. Predictors of mortality among patients presenting with hyperglycemic emergencies

The mortality rate was high in males than in females 19 (29.7%) vs 21 (26.6%) however the difference was not statistically significant (OR=1.16; 95%CI: 0.56-2.42; P=0.681)

Patients who presented with at least one type of infection were 3 times more likely to die compared to the patients without triggering infections (OR=3.11; 95% CI: 1.43-6.74; P=0.004). Patients admitted with acute kidney injury were 4 times more likely to die compared to those without acute kidney injury (OR=4.03; 95% CI: 1.85-8.77; p<0.001). Furthermore, those with poor adherence to their treatment were 3.34 times more likely to die than those who were adherent to their treatment (OR=3.34; 95% CI: 1.13-9.87; P=0.029). On hospital admission patients who presented with shortness of breath, impaired respiration (Kussmaul breathing and shortness of breath), unconsciousness (Coma), and hypernatremia had high odd of dying.

Table 6: Predictors of mortality among patients presenting with hyperglycemic Emergencies

Predictors	Admission outcome		OR (95% CI)	P value
	Died (n:40)	Survived(n:103)		
Gender				
Female	21 (26.6%)	58 (73.4%)		
Male	19 (29.7%)	45 (70.3%)	1.16 (0.56-2.42)	0.681
Type of Diabetes Mellitus				
Type 1	10 (27.8%)	26 (72.2%)	0.96 (0.41-2.23)	0.927
Type 2	30 (28.6%)	75 (71.4%)		
Duration of diabetes				
Newly diagnosed	20 (29.9%)	47 (70.1%)		
<10 years	13 (22.4%)	45 (77.6%)	0.66 (0.22-1.97)	0.466
≥10 years	7 (38.9%)	11 (61.1%)	1.47 (0.65-3.31)	0.348
Infections at admission				
Yes	19 (45.2%)	23 (54.8%)	3.11 (1.43-6.74)	0.004
No	21 (21.0%)	79 (79.0%)		
Acute kidney injury at admission				
Yes	27 (43.5%)	35 (56.5%)	4.03 (1.85-8.77)	<0.001
No	13 (16.0%)	68 (84.0%)		
Presence of comorbidities				
Yes	14 (26.9%)	38 (73.1%)	0.91 (0.42-1.94)	0.802
No	26 (28.9%)	64 (71.1%)		
Drug compliance				
Good	7 (15.9%)	37 (84.1%)		
Poor	12 (38.7%)	19 (61.3%)	3.34 (1.13-9.87)	0.029
Shortness of breath				
Yes	19 (45.2%)	23 (54.8%)	3.14 (1.45-6.83)	0.004
No	21 (20.8%)	80 (79.2%)		
Dehydration				
Yes	27 (29.3%)	65 (70.7%)	1.21 (0.56-2.63)	0.623
No	13 (25.5%)	38 (74.5%)		
Kusmall breathing				
Yes	23 (50.0%)	23 (50.0%)	4.7 (2.16-10.26)	<0.001
No	17 (17.5%)	80 (82.5%)		
Coma state				
Yes	9 (75.0%)	3 (25.0%)	9.6 (2.46-37.98)	0.001
No	31 (23.7%)	100 (76.3%)		
Sodium blood concentration				
Hyponatremia	8 (14.8%)	46 (85.2%)		
Normal sodium level	14 (35.0%)	26 (65.0%)	1.19 (0.49-2.87)	0.693
Hypernatremia	18 (39.1%)	28 (60.9%)	3.69 (1.42-9.61)	0.007

OR: Odd Ratio, CI: confidence interval

Chapter IV: Discussion

This study intended to assess the clinical profile and hospitalization outcome of patients with hyperglycemic emergencies in three tertiary hospitals. 143 participants were enrolled, seventy-nine (55%) were female, majority of included participants were diagnosed with type 2 DM (73.4%). This is in line with other studies which showed that globally type 2 DM accounts for 90% of diabetes [30]. Most of the participants were in the middle age group (56%) this is similar to CDC's national diabetes report where type 2 diabetes is found in middle-aged and older adults [31]. However there was no statistically significant difference in admission outcome across gender of participants and type of diabetes mellitus as found in other studies [16].

Most of the patients were originating from Kigali city and southern province 28%, 44.1% respectively; this can be explained in part by the fact that those places are hubs of tertiary hospitals where the study was conducted and possible reluctance and/or difficulty of health professionals to transfer patients living far away from tertiary hospitals. But again those hospitals are situated in urban areas are frequently visited by urban population who have a high prevalence of diabetes compared to rural population [32]

The hyperglycemic emergencies (DKA, HHS) were an index diagnosis in 67 (47%) cases that are newly diagnosed DM. This finding implies that many Rwandans remain undiagnosed of DM as showed in IDF (International Diabetes Federation), where undiagnosed DM in low income countries compared to high income countries is (66.8%) vs (38.3%) respectively[30]. This highlights the need to raise public awareness about DM signs, symptoms, and screening for DM. This number is higher compared to the one reported in a study done by Guillemo et al (17%) [22] who found that newly diagnosed DM accounted for 17% but low compared to another study done in Nigeria (55.2%) [25]

Weakness, dry throat, and polydipsia were the most prevalent symptoms in both DKA and HHS whereas nausea and vomiting were most observed in DKA patients 29 (34.1%) vs 13 (25.5%) in HHS patients though it was not statistically significant with P value of 0.205).

Abdominal pain was seen more in DKA with a statistically significant difference with a P value: 0.035. These findings are similar to the one found in Saudi Arabia [12] Connecticut USA [13] and Syria [33].

Abdominal pain encountered in DKA is not clearly understood, possible explanations are dehydration of the abdominal muscle, prolonged gastric emptying, and ileus caused by electrolyte derangement and metabolic acidosis. In some circumstances, abdominal pain in DKA has been misdiagnosed as surgical abdomen [34] hence abdominal pain plus classic symptoms of diabetes can be used for public awareness to decrease the late presentation of patients, severity and misdiagnosis of DKA. Eleven patients had seizures in this study with more cases in DKA than in HHS (8 vs 3) respectively however P value was not statistically significant (P= 0.738). This is an infrequent finding as most other studies reported seizure in HHS patients [18][22][35]. However it is not a surprising result as an almost equal number of seizures in both HEs was also found in a study done by Edo in Nigeria [25]

In the present study, the median hospital stay was 11 days ranging from less than 1 day to 103 days. Patient with abscess, cerebral vascular accident, infected diabetic foot had a longer hospital stay than others with the latter being associated with the longest hospital stay. This finding is consistent with what was found in a study done in Nigeria [8][36] because wounds took longer to heal and close.

The leading precipitating factors in our study were infections 56(34.5%) newly diagnosed DM 48 (29%), and poor drug adherence 31(19%). Pneumonia and UTI were on top of other infections, similar results were found in other studies [16][19]. In the present study twenty two precipitating factors (13.5%) were not identified and are among the top five precipitating factors similar results were found in other studies [16][18][25] [37]. This highlights the need for extensive laboratory workup and imaging to hunt the underlying triggering factor as part of the management of HEs. However, in this study, the HEs precipitated by malaria were few compared to other studies which reported malaria among the common precipitating factors [25] this is attributed to the effort made by Rwanda in putting in place measures to decrease malaria related death [38].

Poor drug adherence seen in this study was mostly due to medication discontinuation the main reason being running out of meds. This can be attributed to ignorance since more than half of patients (52%) had only primary education level and not due to the high cost of drugs as was

found in other studies[18] because 95% of patients were health insured which imply a low cost of drugs. However poor adherence may be partly explained by total lockdown during covid 19 pandemic during which this study was conducted as there were population travel restrictions and it was required to have a private way of transport to go to the hospital.

In the present study though there was a statistically significant difference in blood sugar between DKA and HHS ($p < 0.001$) there was no statistically significant difference in sodium, creatinine, urea, and serum osmolality between the two. These results do not accurately reflect the reality because most of the patients received treatment including fluids and insulin prior the transfer which can alter the laboratory profile at admission and this result is similar to what was found in other studies[16][25].

The most deranged electrolytes were sodium and potassium with more hyponatremia cases mostly seen in HHS than DKA 135.3 ± 11.6 vs 165.2 ± 14.1 respectively. This is in agreement with another study done in Ethiopia[12]. This can be explained by the osmotic shift of intracellular water to outside in presence of hyperglycemia. Patients who presented with hypernatremia probably due to severe dehydration were 3.69 times more likely to die compared to those who presented with hyponatremia (OR=3.69; 95% CI: 1.42-9.61; P=0.007).

The overall mortality of both HEs in the current study is 27.9%; this mortality is higher than the one reported in other studies done in countries of Africa including Ethiopia [16] Nigeria [18] and South Africa [37][39]. This can be explained by insufficient nurses, doctors, unavailability of HEs treatment protocol, lack and/or inadequate laboratory investigations, late hospital presentation, long turnaround time of results for monitoring of treatment response, lack of bed in ICU and HDU where close monitoring would be expected to be adequate, in this study only 15 out 143 got ICU bed.

DKA is most associated with most of the death cases than HHS 30.5% Vs 23.5% respectively with a significant P value of $p < 0.001$; this is in opposition with other studies where DKA related mortality rates were low Tanzania[40], Canada [41], Australia[29] and Nigeria[18] This may be explained by the fact that in this study comatose state and Kussmaul breathing were found to be an independent predictor of mortality and were mostly seen in DKA but again may be due to lack of laboratory test like serum PH, serum bicarbonate, which would have informed clinicians to adjust medications like supplementation of bicarbonate in severe acidosis.

In the current study, most of those recruited with a known diagnosis of DM had short term duration of DM (i.e less than ten years) and similar result was found in other studies[12][18][23][24]. However contrary to previously cited studies the mortality rate was higher in those with long term duration compared to those with short duration (newly diagnosed cases excluded). This can be explained by differences in patients' characteristics, comorbidities, the severity of underlying precipitating factors and overall life expectancy.

Patients who developed acute kidney injury at admission were 4 times more likely to die compared to patients who did not have acute kidney injury with a statistically significant difference (OR=4.03; 95% CI: 1.85-8.77; $p<0.001$). This can partly explain the reason why most of the death cases were seen in DKA patients as most AKI cases were observed from this category of patients. This is in line with other studies done in Pakistan where higher mean serum creatinine was seen in patients who died compared to those who survived [42] and in study done in Ethiopia where creatinine >1.2 mg/dl was an independent predictor of mortality[16].

In study patients low level of consciousness (comatose state), Kussmaul breathing (i.e rapid and deep breathing) were 9.6 and 4.7 times (OR=9.6; 95% CI: 2.46-37.98; $P=0.001$), (OR=4.7; 95% CI: 2.16-10.26; $P<0.001$) respectively more likely to die compared to those who did not present in those states and this is contrary to other studies[10].

The comatose state in this study was most seen in DKA patients compared to those of HHS this is attributed to the fact that Kussmaul breathing i.e acidotic breathing in these patients reflects severe acidosis complicated into a comatose state which heralded poor hospital outcome.

Three patients in this study were counter transferred to the nearest DH for palliative care because they were in a vegetative state associated with poor prognosis.

This study had several limitations the fact that enrolled patients passed through a channel of health system notably from the health center to district hospitals up to the tertiary hospital could confound some laboratory values at admission such as glycemia, electrolytes and serum osmolarity because patients were treated with insulin and IV Fluids before being transferred.

In this study, the classification of type 1 and type 2 diabetes mellitus were done according to patients' characteristics and biochemical data, based on antibody testing or C Peptide levels measurement was not done.

Due to lack of funding, some laboratory investigation of HEs was not exhausted as some tests including serum PH, ABG, serum ketones which would have helped clinicians in accurate stratification of patients in distinct entities of HEs namely DKA, HHS, and mixed states were not done.

Although this study was conducted in three big tertiary hospitals in Rwanda with a large catchment area comprising all districts hospitals, which reflects a high diversity of study participants, it is worth noting that only complicated cases were transferred whereas mild cases were managed at district hospital levels. Hence this hospital based study outcome mainly mortality rate cannot be extrapolated to an entire country as a whole.

Chapter VI: Conclusion and Recommendation.

Our study showed that hyperglycemic emergencies account for the initial presentation of diabetes mellitus which highlights much effort to be put into diabetes screening and raising population awareness about diabetes. Infections, newly diagnosed diabetes, and poor drug adherence were the most precipitating factors of HEs whereas comatose state, elevated serum creatinine, history of poor drug adherence, and having triggering infections were independent risk factors for mortality.

This study showed that among recruited patients with a known diagnosis of diabetes, majority of them had diabetes for less than ten years and the mortality was higher among patients with diabetes for more than 10 years. However, there was no statistically significant difference in admission outcome across gender of participants and type of diabetes mellitus.

The mortality rate was high in this study, this shows a big gap existing in the management of patients with hyperglycemic emergencies hence strong measures have to be taken including availing enough nursing, laboratory and doctors staff. Putting in place diagnostic tests, treatment protocols of hyperglycemic emergencies, proper and prompt monitoring of treatment response of patients should be advocated for. The median hospital stay was eleven days which was longer compared to other studies this warrants more studies to investigate the reasons.

There is a need to raise public awareness about diabetes signs, symptoms, and its complications together with education of patients with diabetes about infection prevention, good drug adherence, foot care and diabetes self care as those are focus points for clinicians in preventing the most common triggering factors of hyperglycemic emergencies because they are preventable. This can be done through mass communication in community gatherings and media (Radio, TVs.)

The cause of death was not investigated in this study hence future studies are needed to explore deeply patients' management, treatment complications, and the real cause of death.

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ANNEXES

Annexe1: Data collection tool

**CLINICAL PROFILE AND HOSPITALISATION OUTCOME OF PATIENTS
ADMITTED WITH HYPERGLYCEMIC EMERGENCIES AT TERTIARY
HOSPITALS (KUTH, BUTH, RMH), RWANDA.**

1. Questionnaire number:
2. Hospital ID:
3. Phone N°:
...../.....
.....
4. Enrollment date
DD/_MM_/_YYYY_
5. Enrolled from: 1.OPD/ 2. Inpatient
6. Hospital: **KUTH** **BUTH**, **RMH**

SECTION A: SOCIO DEMOGRAPHIC CHARACTERISTICS

1. Names:
2. Age:
3. Sex: F/M
4. Address: District.....Province.....
5. Transferred from DH: Home : other:
6. Marital Status: 1.Single 2.Married 3.Widow Divorced:
7. Education level: 1. Nil 2.Primary 3. Secondary 4.More than 2ndary
8. Ubudehe category: 1. I 2.II 3.III 4.IV
9. Health insurance: 1. Community based insurance 2.Premiums 3.none

Clinical profile at Admission

Was the patient known with diabetes yes? or no

If yes duration of diabetes: less than 10 years ,10–19 year 20 years and above

Was the patient on anti diabetic drugs?

Lifestyle change alone oral drugs alone oral drugs plus Insuline

Insulin alone stopped the medication, **why medication stopped :**

Financial problem poor understanding of the disease, depression, weight control

When the patient took the last dose?

Who gives drugs to the patient: her/himself, family member, Others

Drug compliance: bad, good, very good Excellent

When the symptoms started prior to arrival at tertiary hospital: Days weeks:

Where the patient is followed, HC NCD Clinic, DH , Tertiary hospital, other

Patient doctor relationship: was the patient told/educated about the prevention of hyperglycemia

yes, told but forgotten not told /educated

if Yes how often: at every visit, once 3 months, once a year, other

Presenting signs and symptoms

Symptoms		Signs	Precipitating Factors	
Shortness of breath		Alert	Pneumonia	
Convulsion		obtunded	Poor drug adherence	
Cough			Malaria	
Nausea/Vomiting/ Diarrhea		drowsy	UTI	
Abdominal pain		Agitated	Diabetic foot infection, Infected wound	
Irrational speech		Coma	Abscess	
Nocturia/ Polydipsia/dry throat		Tachycardia	Gastroenteritis,	
Weakness		Dehydration	Cerebral vascular accident	
Fever		Tachypnea/kussmal breathing/resp distress	Sepsis	
Headache		Abdominal tenderness	Intoxication	
Weight loss		Lethargic	Drugs eg: corticosteroids	
Other		Other	Other	

Comorbidities		Blood and Biochemical test						
Hypertension		To		Blood sugar		PH		Wbc:
HIV		RR		Potassium(k)		Pco2		Hb:
Kidney disease AKI/CKD		PR		Sodium(Na)		Po2		Plt:
Heart disease		BP		creat		Bicarbonat e		N:
Hepatitis B				Anion gap		A ₁ C		L:
Hepatitis C								
Other diabetes complications Retinopathy, neuropathy		Sp O ₂		Urea		Serum osmolality		M: E:
Other				Cl		Ketonuria		B:

Diagnosis made DKA, HHS, not clear

Type of DM diagnosed: type 1 , type 2 , not clear

Where the patient is hospitalized in ICU , HDU , at emergency, public ward

Hospital stay: number of days : hospitalization outcome: discharged

Discharged against medical advice, transferred Died

Annexe2: Consent form / English version

EXPLANATIONS ABOUT THIS STUDY

My name is NDIZIHIWE Eulade, I am a medical doctor in postgraduate studies I am researching the **clinical profile and hospitalization outcome of patients admitted with hyperglycemic emergency at tertiary hospitals KUTH, BUTH, RMH in Rwanda**, I am requesting your consent because you are eligible for this study.

Diabetes mellitus is a condition characterized by hyperglycemia due to absolute or relative impairment in insulin secretion or peripheral resistance to it.

In some instances, the glycemia goes high and the patient may be diagnosed to have hyperglycemic emergency, the signs and symptoms of this patient include altered mental status coma, severe body weakness, polyuria, polydipsia and can cause death if not promptly treated.

This study aims at looking for clinical profile, the precipitating factors, and the hospitalization outcome of patients diagnosed to have hyperglycemic emergencies. After being well explained about this study and you consent to participate in it you will be requested to put names and signature at the end of this consent form.

OBJECTIVES OF THIS STUDY

Hyperglycemic emergencies include diabetic ketoacidosis and hyperosmolar hyperglycemic state

The patient diagnosed to have one of the above mentioned conditions is considered a medical emergency and should be rapidly and promptly treated

A recent study shows that the prevalence of diabetes in RWANDA is 3% and is increasing as time goes on. There is no study done about a patient diagnosed to have hyperglycemic emergencies their clinical presentation, precipitating factors, and hospitalization outcome.

This study will also reveal any eventual gap in taking care of such patients and make ways to improve our current practices.

METHODOLOGY

If you consent to participate in this research you will put your signature at the end of this sheet, then you will be or your official next of kin asked questions including your identifications, and your laboratory data will be recorded then you will be followed up in hospital till you are discharged.

Potential harmful effects of this study

You may experience mild and self subsiding pain where your peripheral venous blood will be drawn it is mild short time pain and goes away without treatment.

The benefit of study participant

No money will be paid to the participant; the findings from this study will help us to know clinical presentation, precipitating factors, how to prevent and how to improve taking care of patients coming to KUTH, BUTH, RMH diagnosed to have hyperglycemic emergencies.

Rights of study participants

To participate in this study is voluntary no coercion, no penalties for refusal, any question you may have will be answered to your satisfaction, you have the right to discontinue participating in this research at any time and it will not affect your medical care.

For more information about this research call

Dr. NDIZIHIWE Eulade 0788775907

Director of IRB: 0788490522

Vice director: 0783340040

Consent form

After the explanation, I got about this study, benefits, potential harm, and my rights
I voluntarily agree to participate in this study.

The participant

First Name:

Last name :

Date of birth :

Signature:

date :

The principal investigator / Helper

First Name:

Last name :

Signature:

date:

Annexe3: Consent form/ Kinyarwanda version

Ibisobanuro kubushakashatsi

Nitwa NDIZIHIWE Eulade, ndi umuganga uri kwiga mu kiciro cya gatatu cya kaminuza ndigukora ubushakashatsi ku barwayi ba diabetes baje kwa muganga bafite ibipimo byisukari mu maraso biri hejuru. Wasabwe kwitabira ubu bushakashatsi kuko wagaragaweho ubwo burwayi.

Indwara ya diabetes ni indwara irangwa no kugira isukari nyinshi mu maraso aho bitewe nimpamvu zitandukanye, uyirwaye ashobora kugira ibipimo byisukari biri hejuru cyane, bene uyu murwayi bimwe mu bimenyetso bimiranga harimo kuba yata ubwenge cg akajya muri koma kugira inyota ikabije, kwihagarika bidasanze gucika ntege bikabije, ndetse iyo adahise avurwa byihuse byamuviramo nurupfu.

Ubu bushakashatsi bugamije kureba uko aba barwayi baza kwa muganga bameze, igituma isukari iba yazamutse no kumenya uko bigenda nyuma yo kwitabwaho nabaganga, Numara kumva ibijyanye n'ubu bushakashatsi kandi ukemera kubwitabira turagusaba gushyira amazina n' umukono kuri aya masezerano.

Intego y'ubu bushakashatsi.

Indwara ya diabetes ni indwara irangwa nisukari nyinshi mu maraso harigihe ibipimo by'isukari bishobora kujya hejuru cyane nukuvuga hejuru ya 250 mg/dl kuzamura icyo gihe uyu murwayi aba arembye cyane ndetse aba akeneye kwitabwaho byihuse mu cyumba cyindembe.

Ubushakashatsi buheruka mu Rwanda bugaragaza ko indwara ya diabete iri ku kigero cya 3% kandi ikaba ikomeje kwiyongera ntabushakashatsi burakorwa bugaragaraza umubare wabafite uburwayi bwavuzwe haruguru baza muri KUTH,BUTH,RMH, ibimenyetso baza bafite ndetse nikiba cyateye izamuka rikabije ryisukari yo mu maraso, bizadufasha kumenya niba impanvu zizwi zibitera ahandi arinazo zibitera hano mu Rwanda.

Ubu bushakashatsi bugamije kumenya uko abarwayi ba diabetes baza bafite isukari iri hejuru ibimenyetso baza bafite, ikiba cyabiteye nukumenya ikivamo nyuma yo kwitabwaho nabaganga. ndetse bizadufasha kumenya niba hari icyuho gihari mukuvura aba barwayi bidufashe kubitaho byisumbuye.

Uko ubu bushakashatsi buzagenda

Niba wemeye kuba muri ubu bushakashatsi, uzasabwagushyira umukono kuri iyinyandiko. Nyumay'umukono,uzabazwa ibibazo cyangwa umurwaza wawe wemewe tuzafata umwirondoro wawe , tuzareba ibisubizo byawe bya laboratwari hanyuma dukomeze kugukurikirana igihe cyose uri mu bitaro kugeza usezerewe .

Ingaruka zishoboka

Kubera amaraso azafatwa muri ububushakashatsi,uzaba aburimo ashobora kubabazwa n'urushinge ruzakoreshwa. Gusa ni ububare bw' akanya gato kandi buhita bushira hatagombye guhabwa umuti

Inyunguz'ububushakashatsi

Nta nyungu y' amafaranga uwemeye kujyamuri ububushakashatsi azabona. Ubumenyi tuzakura muri ubu bushakashatsi buzadufasha kumenya ibitera umurwayi wa diabetes kugira isukari iri hejuru bidufashe kumenya uko tubyirinda no kuvura birushijeho uwagize ubu burwayi.

Uburenganzira bw'uwitabiriye ubushakashatsi.

Ntabwo ukwiye guhatirwa kwemera kwitabira ububushakashatsi. Ibibazo byose waba ufite bikwiye gusubizwa neza kuburyo wumva unyuzwe. Niba wumva udashaka kuba muri ubu bushakashatsi ufite uburenganzira bwo kuba wahindura icyemezo cyawe igihe icyoaricyo cyose ubu bushakashatsi buzaba bukorwa kandi ntangaruka bizakugiraho.

Niba umaze kumva ibijyanye n'ububushakashatsi kandi ukemera kubwitabira , turagusaba gushyira amazina n' umukono kuri ayamasezerano

Ushaka ibindi bisobanuro kubijyanye nubu bushakashatsi wahamagara

Dr NDIZIHIWE Eulade 0788775907

uhagarariye ikigo gishinzwe ubushakashatsi 0788490522

umwungirije 0783340040

Inyandiko y' amasezerano yo kwitabira ubushakashatsi kubushake.

Nyuma yogusobanurirwa ibijyanye n'ubushakashatsi , ingaruka zishobora kubaho n' uburenganzira mfite, niyemeje ntagahato kwitabira ububushakashatsi.

Uwemeye Kwitabira ubushakashatsi

Amazinayombi:

Italiki y' amavuko:

Umukono:

Italiki:

Uhagarariye ubushakashatsi wayoboye igikorwa

Amazinayombi:

Umukono:

Italiki:

Annexe 4 : IRB Approval



UNIVERSITY of
RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES
DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 15th /October/2019

Dr NDIZIHIWE Eulade
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 478/CMHS IRB/2019

Your Project Title *“Clinical Profile And Hospitalization Outcome Of Patients Admitted With Hyperglycemic Emergencies At Tertiary Hospitals In Rwanda (CHUB, CHUK, RMH)”* has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			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		

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 14th October 2019, **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 15th October 2019

Expiration date: The 15th October 2020


Professor GAHUR W. BOSSO
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
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