A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

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A dissertation submitted to the University of Zambia, School of Medicine, in partial fulfillment of the requirement for the award of Master of Medicine, Internal Medicine Degree.

The University of Zambia

Lusaka

November 2015

DECLARATION

This dissertation was written and submitted in accordance with the rules and regulations governing the award of Master of Medicine, Internal Medicine of the University of Zambia. I further declare that the dissertation has neither in part nor in whole been presented as substance for award of any degree, either to this or any other university. Where other people's work has been drawn upon, acknowledgement has been made.

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APPROVAL

This dissertation titled ‘A study to determine the clinical profile and mortality predictors of adult patients presenting with diabetic ketoacidosis at the Medicine Department of The University Teaching Hospital in Lusaka, Zambia’ by Mwanja Kakusa is approved as fulfilling the requirements of the Degree of Master of Medicine in Internal Medicine of the University of Zambia.

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To my spouse Delmer Zulu, children Lydia and Lwandile, mother Mrs Alice M. Kakusa

&

in loving memory of my late father, Judge Tamula Kakusa

.ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my supervisors Dr Brown Kamanga and Dr Soka Nyirenda for their support and professional guidance throughout the preparation of this dissertation. Through their dedication to teaching and their support I was able to find my feet in research work, a novel field to me.

I also wish to sincerely thank the project funders. This document is an output from a project funded by The Wellcome Trust through Southern Africa Consortium for Research Excellence, SACORE, for capacity building for the benefit of developing countries. The views expressed in this document are not necessarily those of the trust.

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ACRONYMS AND ABBREVIATIONS

ADA	American Diabetes Association
AMEU	Adult Medical Emergency Unit
°C	Degrees Celsius
CAT	Computerised Axial Tomography
CNS	Central Nervous System
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
GCS	Glasgow Coma Scale
HCO_3^-	Bicarbonate
HE	Hyperglycaemic emergencies
HHS	Hyperosmolar hyperglycaemic state
IDF	International Diabetes Federation
IM	Intramuscular
IQR	Interquartile range
IV	Intravenous
MAW	Medical Admission Ward
MI	Myocardial infarction
mmHg	Millimetres of mercury
mmol/L	Millimoles per litre
RBS	Random blood sugar
SC	Subcutaneous
SD	Standard deviation

SSI	Sliding Scale Insulin
Temp	Temperature
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
UTH	University Teaching Hospital
vs.	Versus
WHO	World Health Organisation

ABSTRACT

Background: Diabetes ketoacidosis (DKA) is one of the commonly encountered diabetes mellitus emergencies in hospital setups. In Zambia, there is currently no published data on DKA. This study aimed to define the clinical profile and mortality predictors of diabetic ketoacidosis at a Zambian teaching hospital.

Methods: A cross-sectional analytical study of 80 hospitalised participants with diabetes ketoacidosis at University Teaching Hospital in Lusaka, Zambia was done over a 10 month long period from October 2013 to August 2014. The data extracted included clinical presentation, precipitating factors, laboratory profile, complications and hospitalisation outcomes. Additionally, participants were dichotomised into those with coma (Glasgow Coma Scale of 8 and below) and those without coma (Glasgow Coma Scale 9 and greater). They were followed up to end of hospitalisation. Primary outcome measured was all cause in-hospital mortality. Statistical tests used were Fisher's Exact, Kruskal-Wallis and logistic regression.

Results: The participants were equally distributed by gender. The median age was 40 years (IQR 31-57). Treatment non-compliance was the single highest identified risk factor for development of DKA (42.5%) followed by new detection of diabetes (27.5%) and infection (22.5%). The prevalence of hypokalaemia was 15% while that of coma was 12.5%.

Comatose participants in the study were younger than those with higher Glasgow Coma Scale (30.0 *vs*. 42.5 years, *p*-value 0.005). They also had significantly lower baseline blood pressure readings [median systolic BP 105 mmHg *vs*. 120 mmHg (*p*-value 0.032) and median diastolic BP 60 mmHg *vs*. 77 mmHg (*p*-value 0.041)]. Additionally, comatose participants had a higher baseline respiratory rate compared to patients with higher GCS (28.5/min vs. 25/min *p*=0.031). They also had higher baseline admission random blood glucose readings compared to patients with higher coma scores (33.0mmol/L vs. 28.0mmol/L, p-value 0.012). Their baseline sodium and chloride levels were also higher [143.5 *vs*. 133 mmol/L, (p=0.006) and 4.0 *vs*. 4.2 mmol/L, (p=0.003) respectively]. The prevalences of hypokalaemia, hypernatraemia and hyperchloraemia were equally higher amongst the comatose group compared to non-comatose patients [40% *vs*. 11.4% (*p*= 0.038), 50% *vs*. 14.3% (*p*=0.017) and 40% *vs*. 10% (*p*= 0.027) respectively]. Complications identified in decreasing order of magnitude were acute renal failure, hypoglycaemia, aspiration, adult respiratory distress syndrome and seizures. Mortality rate was 7.5%. There were factors associated with

increased risk of mortality and these were development of aspiration during DKA admission, pneumonia at baseline, development of renal failure and altered mental status. Development of renal failure was independently predictive of mortality.

Conclusion: Treatment non-compliance is the commonest risk factor for development of DKA at University Teaching Hospital, Lusaka, Zambia. The mortality rate is high compared to statistics from advanced treatment centers. Development of renal failure during hospitalization with DKA is independently predictive of mortality.

CHAPTER 1

1.1 INTRODUCTION

Diabetes mellitus is one of the most common endocrine disorders in the world (Ang *et al*. 2001). It has increasingly become an important public health issue in developing countries. About 347 million people worldwide have diabetes mellitus (World Health Organisation 2012 and International Diabetes Federation 2012).

Diabetes mellitus is characterized by a myriad of metabolic abnormalities and long-term complications on various body systems. Its most serious acute metabolic complications include the two hyperglycaemic emergencies diabetic ketoacidosis and hyperosmolar hyperglycaemic state (Kitabchi *et al*. 2009). Diabetes mellitus hyperglycaemic emergencies are associated with very high mortality rates in the developing world and markedly so in the tropics (Anumah 2007).

Diabetic ketoacidosis (DKA) is a frequently encountered hospital emergency and is associated with significant morbidity and mortality. Its mortality outcome has been reported to be less than 5% in treatment experienced centres of the Americas, Europe and Asia (American Diabetes Association 2004). In Africa, mortality from hyperglycaemic emergencies is not well documented but comparatively high in published studies. A study in Libya found a mortality rate of 10% among DKA admissions, while a Kenya study showed 29% and a South African study 6.8% (Elmehdawi *et al.* 2010; Mbugua *et al*. 2005; Zouvanis *et al.* 1997).

There are a number of factors that have been found useful in predicting the outcome of this emergency in the widely varied clinical setups world over. For instance, mortality as a major adverse outcome has been associated with a number of factors such as diabetic foot, advanced age, sepsis, hypertension and hypokalaemia (Anumah 2007). Describing the clinical characteristics and outcome predictors in DKA studies is useful for guiding clinicians in managing some of these factors more aggressively to improve outcome.

In Zambia, DKA treatment outcomes were previously unknown or remained unpublished. Diabetes mellitus hyperglycaemic emergencies are frequently managed at the Medicine Department of University Teaching Hospital in Lusaka. The hospital is a tertiary care centre

which serves patients from lower level hospitals as well as the local primary healthcare centres.

The aim of this study was to establish the clinical characteristics of diabetes mellitus patients that were admitted with diabetic ketoacidosis, to describe the predictors of clinical outcomes and to determine the prognostic value of coma on treatment outcome.

CHAPTER 2

2.1 LITERATURE REVIEW

Diabetic ketoacidosis is one of the most common acute metabolic complications of diabetes mellitus (Kitabchi *et al.* 2009). It is associated with significant morbidity and mortality and is characterized by hyperglycaemia, ketone body formation and acidosis (Umpierrez *et al.* 2002).

There are many recognized precipitants of DKA with infection usually being the commonest. Others such as non-compliance with therapy, cerebrovascular accident, myocardial infarction, alcohol abuse, pancreatitis, trauma and drugs such as thiazides, corticosteroids and sympathomimetics are well recognized (American Diabetes Association 2001; Stephen *et al*. 2004; Umpierrez *et al*. 2002). According to the American Diabetes Association in 2001, morbidity and mortality risks are significantly worsened by sepsis, myocardial infarction, hypokalaemia and its associated arrhythmias, extremes of age, presence of coma, hypotension and cerebral oedema.

2.1.1 Risk factors for diabetic ketoacidosis development

2.1.1.1 Patient treatment non-compliance and DKA

Studies have shown that non-compliance to treatment is one of the commonest precipitants of DKA. A retrospective study done on a largely low income population of 80 at a tertiary care teaching hospital in southern Brazil showed that the leading precipitant of DKA at 39% was diet abuse and insulin non-adherence (Weinert 2011). This finding was similar to that from studies done largely in low income groups in Nairobi, Kenya and USA (Mbugua *et al.* 2005; Nyenwe *et al.* 2007; Musey *et al.* 1995).

A cross-sectional study done by Randall *et al*. (2011) at Grady Memorial Hospital, USA, between July, 2007 and August, 2010 to determine the factors driving insulin non-compliance in inner-city patients with recurrent DKA amongst 164 adults showed that insulin discontinuation was the leading precipitant of DKA at 68% followed by infection, new-onset diabetes, medical illness and undetermined causes in diminishing order of prevalence.

Amongst those who stopped insulin, 32% advanced no reasons, 27% lacked funds to purchase insulin, 19% felt sick, 15% were away from their supply and 5% were stretching their insulin. There was significant evidence of substance and alcohol abuse, psychiatric illness and lack of social support in the population of non-compliant patients.

A study in the UK showed that low socio-economic status was associated with a 3.5% likelihood of having DKA hospital records in the lower quintile of 35 925 study subjects compared to more affluent study subjects in the upper quintile (Wild *et al.* 2010). The commonest identified precipitant of DKA in this group of patients was treatment non-compliance.

2.1.1.2 Infection and DKA

Infection has been found to be one of the leading precipitants of DKA in some studies. In a small cross sectional retrospective study of 100 patients at a university teaching hospital setting in Libya in 2010, infection was found to be the second leading cause of DKA, accounting for 30 cases of the 100 patients with identified precipitants of DKA (Elmehdawi *et al.* 2010). The leading causes of infection in that study in decreasing order of magnitude were urinary tract infection, upper respiratory tract infection, lower respiratory tract infection, abscess, gastroenteritis, tuberculosis, diabetic foot and peritonitis.

In a small retrospective study of 21 patients in Thailand, infection was found to be the most common precipitant of DKA as well, accounting for 52% of the identified risk factors (Thewjitchaoen 2012). A 2012 published study in China showed that the major precipitant of DKA at West China Hospital was infection (Tan *et al.* 2012).

Some African studies and many more around the world reported infection as the leading risk factor for DKA development (Edo 2012; Ekpebegh 2010; Ogbera *et al*. 2009; Barski *et al*. 2011; Chung *et al*. 2006; Weinert *et al*. 2011).

2.1.1.3 DKA at diagnosis of diabetes mellitus

Some patients present with DKA as first diagnosis of diabetes mellitus. The causes and implications of this have been well studied. Studies have shown widely varied statistics of patients who present with DKA as a first evidence of diabetes mellitus (Al-Rubeaan *et al*. 2011; Estathiou *et al*. 2002; Matoo *et al*. 1991; Lee *et al*. 1987).

In a systematic review of 46 cohort studies that involved 24 000 children and young adults in 31 countries, factors associated with DKA presentation at diagnosis of DM were studied (Usher-Smith *et al.* 2011). The review compared 23 different factors. Some of the factors identified included diagnostic error, ethnic minority, lack of health insurance (in the USA), lower body mass index, preceding infection and delayed treatment. Protective factors identified included having a first degree relative with T1DM at time of diagnosis, higher parental education and higher background incidence of T1DM.

2.1.1.4 Age and gender in DKA

Many studies have shown that advanced age is associated with poorer outcomes of DKA (Kitachbi *et al.* 2009). The gender association however remains inconclusive. An interesting gendered analysis of DKA was published in 2011. This was an Israeli retrospective cohort study of 220 patients which showed that the in-hospital mortality rate was not significantly different in the sexes and neither was there a difference in the 30-day all-cause mortality nor rate of complications (Barski *et al*. 2011). This study however showed some significant difference in development of renal failure in males compared to females (16.9% vs. 3.1%). More women had received oral hypoglycaemics compared to men (19.8% vs 9.0%) and women had higher glycosylated haemoglobin A_1C before admission than males (11.9%[1.7%] vs 9.9%[2.2%]; P=0.025).

The retrospective study by Tan *et al.* in 2012 in China had an interesting finding of an enigmatic male dominance in DKA incidence with a male-to-female ratio of 1.4:1. The reasons for this male predominance and its underlying pathogenesis were not clear.

2.1.1.5 HIV and DKA

The influence of HIVinfection and its associated treatments on DKA are not well studied. Current level of evidence for association is weak. For instance, one case study published in a Danish journal reported diabetic ketoacidosis in a female, one-and-a-half years into therapy having had DKA due to her protease inhibitor-containing antiretroviral regimen. The DKA was presumed to have occurred as an adverse effect of protease inhibitor, which is known to reduce beta cell function and increase insulin resistance (Holm *et al.* 2006).

Another case study provided evidence of new onset diabetes mellitus diagnosed in the acute setting of DKA in a 49 year old HIV white male on indinavir, a protease inhibitor, for more than two years (Hughes & Taylor 2001).

2.1.2 Complications of diabetic ketoacidosis

Studies have demonstrated that DKA is associated with many complications. In the Libyan study of 100 patients with DKA, many complications were encountered. Sixty-six percent of the study subjects developed complications which included coma, iatrogenic pneumothorax and hypokalaemia (Elmehdawi and Elmagerhei 2010). Prerenal azotaemia and electrolyte disturbances were the commonly encountered complications. More rare but serious complications were upper gastrointestinal bleeding, acute gastric dilatation, acute renal failure, adult respiratory distress syndrome and disseminated intravascular coagulation.

Hypoglycaemia, hypokalaemia, hyperchloraemic non-anionic gap acidosis and cerebral oedema are some of the identified complications of DKA. A prospective cross-sectional descriptive study to determine the prevalence of hypokalaemia in DKA done in Los Angeles found a prevalence of 5.6% in a study population of 54 patients with DKA before fluid and insulin therapy (Arora *et al.* 2012).

Cerebral oedema is a rare complication of DKA in adults and has a mortality of 20-40% (Wolfsdorf, Glaser and Sperling cited in Kitachbi *et al*. 2009). Published studies of its clinical evidence are primarily case studies (Haringhuizen *et al*. 2010; Troy *et al*. 2005; Hiller and Wolf 2005).

2.1.3 Treatment outcomes of diabetic ketoacidosis and their predictors

Studies have identified factors that predict DKA outcome and most prediction models have been for factors associated with mortality. In a prospective study done in Nigeria at an urban Lagos hospital, of 111 subjects with HEs, (Ogbera *et al.* 2009) the identified predictive factors of mortality included sepsis, foot ulceration, previously undetected DM and being elderly. Eighty-one percent of the study subjects had type two diabetes. DKA accounted for 85% of the HEs in the study population. The lowest number of admissions and deaths were found in patients with long term duration of DM diagnosis. The case fatality rate for DKA was 18%.

In a retrospective Libyan study by Elmehdawi *et al.* in 2010, the mean length of hospital stay for DKA was 7.7 days (range 1-25). Mortality was high, with 12.3% loss, of which there was an insignificant male predominance. The mortality rate was significantly higher among

patients with type 2 DM than those with type 1 (40.0% *vs* 6.6%). The important co-morbidities that were associated with death included myocardial infarction, acute abdomen, pulmonary tuberculosis, acute renal failure or diabetic foot. Significantly increased mortality was more associated with age older than 40 years, type 2 DM, coma, comorbidity, pulse ≥ 115/min, diastolic BP ≤ 65mmHg, plasma glucose ≥ 525 mg/dl (29.2mmol/l), serum sodium ≥ 144 mmol/l, blood urea nitrogen ≥ 50 mg/dl≤, serum creatinine ≥ 4 mg/dl (305.04 mmol/l), arterial blood pH ≤ 7 and plasma osmolality ≥ 325 mOsm/Kg water.

A study in developing Jamaica showed multiple risk factors for increasing mortality in the univariate analyses (Chung *et al*. 2006). These included increasing age, presence of infection, increased age at onset, mixed syndrome diagnosis, presence of co-existing disease and altered mental status. In that study, altered mental status was statistically significant in multivariate analysis.

In a study done in Greece, multivariate analyses identified six variables as independent predictors of mortality in a cohort of 154 patients (Efstathiou *et al*. 2002). These included severe coexisting diseases; pH <7.0 at presentation; units of regular insulin required in the first 12 hours > 50 and serum glucose > 16.7 mmol/L, after 12 hours; depressed mental state and fever, after 24 hours.

In Thailand, a retrospective study of 83 patients with HEs showed a 5.8% DKA mortality with infection as the commonest cause of mortality and high serum sodium on admission as an independent predictor of mortality (Anthanont *et al.* 2012).

Another retrospective review Nigerian study (Edo 2012) of 84 patients with HEs, thirty-five cases (41.7%) had DKA and and 3 of these died with a low mortality rate comparable to that in advanced treatment centres. However, a study in the Eastern Cape of South Africa found an alarming high mortality of up to 37.5% in DKA (Ekpebegh *et al.* 2010).

The role of management strategies in DKA management can have a significant impact on outcome. An observational and prospective study of 153 cases of DKA over 6 years in Spain showed that management of DKA was sub-optimal in a significant number of cases and fell short below the American Diabetes Association (ADA) recommendations for treatment (Sola *et al*. 2006). There was delay in initiation of intravenous fluid therapy (70%), under-replacement of intravenous fluids (60%) and under-replacement of potassium therapy (80%) and excess use of alkali. The effect of the sub-optimal management on outcome was

unfortunately not clearly defined. A study done in 1997 found a significant number of similar management deficiencies (Singh, Perros and Frier 1997cited in Sola *et al.* 2006).

In Nairobi, Kenya Otieno et al. (2010) studied the predictors of outcomes of patients with DKA. Fourty-seven patients were studied in the final analysis of the enrolled 51 and a high mortality of 29.8% was noted and all occurred within 48 hours of hospitalization and treatment. Of the study subjects who died, 100% had altered level of consciousness while 71% had abnormal renal function and 64% were newly detected diabetes patients. Altered mental status was the major predictor of mortality. Study subjects with altered mental status also had severe systolic hypotension and severe metabolic acidosis. In an article published in 2010 by Nyenwe *et al.* which looked at acidosis as a prime determinant of altered sensorium in DKA, the biochemical combination of acidosis and hyperosmolarity was associated with increased risk of altered mental sensorium including coma. This biochemical derangement was identified in patients with severe DKA in that study.

The role of physician specialty on DKA treatment outcome was studied and significantly found that endocrinologists offered more cost-effective treatment of DKA than generalists. Patients that were managed by endocrinologists had lower hospital length of stay, lower mean hospital charges and lower readmission rates with DKA than those that were cared for by generalists (Levetan *et al*. 1999).

CHAPTER 3

3.1 STATEMENT OF THE PROBLEM

Admissions for diabetes mellitus and its associated complications are frequent at Medicine Department of University Teaching Hospital (UTH), Lusaka. According to official hospital records, there have been about 492 cases of diabetes mellitus-related admissions annually which represent an average of five percent of total admissions over the past eight years.

Currently, there is no registry to define the types of diabetes mellitus admissions. Diabetes ketoacidosis is a complication associated with significant morbidity. Its clinical characteristics, mortality statistics, and outcome predictors among adult patients had previously not been studied at UTH. An earlier pilot assessment indicated that roughly 2-3 cases of DKA are managed per week.

3.2 STUDY JUSTIFICATION

The study sought to define important clinical data regarding the profile of DKA admissions, mortality predictors and hospitalization outcomes. Patients with DKA often present with significant morbidity. Mortality outcomes in resource-limited settings have often been reported to be high compared to statistics from advanced treatment centres in the west.

Researched data on the clinical characteristics and outcome profile will help to identify problems associated with DKA admissions. The data will be useful in improving patients' quality of care and and ultimately improve survival outlook to levels comparable to the more advanced treatment centres. Detailed study of DKA in this resource challenged setting will also help clinicians and concerned policy makers to identify predictors of adverse clinical outcomes and help in improved planning for DKA patient management.

Information from this study will also be very useful in future research into various interventional strategies in the management of diabetes mellitus and its associated complications.

3.3 RESEARCH QUESTION

What were the predictors of mortality outcome among adult patients with diabetic ketoacidosis presentation at the Medicine Department of University Teaching Hospital, Lusaka?

3.4 HYPOTHESIS

Alternate Hypothesis

Coma was associated with a higher proportion of mortality in diabetic ketoacidosis presentation at the Medicine Department of University Teaching Hospital.

3.5 OBJECTIVES

3.5.1 Main Objective

To investigate the predictors of mortality outcome in diabetic ketoacidosis at UTH Medicine Department

3.5.2 Specific Objectives

1. To identify the precipitants of DKA in the study population
2. To compare the clinical profile of patients with and without coma in DKA
3. To determine hospitalisation outcomes of DKA

CHAPTER 4

METHODOLOGY

4.1 STUDY DESIGN

This was an analytical cross-sectional study on patients with DKA up to end of hospitalization; either hospital discharge or mortality.

4.2 RESEARCH SITE

Patients were recruited from all medical wards in the Medicine Department including Adult Medical Emergency Unit, Medical Admission Ward, and in-patient medical wards in E-Block and C-Block.

4.3 STUDY AND TARGET POPULATION

The target population was patients aged 16 years or older with hyperglycaemia. The study population was all adult patients who were admitted and met the eligibility criteria of DKA.

4.4 ELIGIBILITY

4.4.1 INCLUSION CRITERIA

1. Age 16 years and older
2. Patients who met the case definition based outlined below in 4.5
3. Written consent

4.4.2 EXCLUSION CRITERIA

1. Recent alcohol binge in last 36 hours Men > 10 units in 2 hours, females > 8 units in 2 hours
2. Suspected or confirmed history of poisoning with salicylate, ethylene glycol, paraldehyde, methanol, isopropanol or propylene glycol.
3. Pregnancy.

4.5 CASE DEFINITION OF DIABETIC KETOACODISIS

Adults with history, examination findings and laboratory criteria set by the American Diabetes Association and outlined below (American Diabetes Association 2003; Kitachbi, Umpierrezz & Kreisberg 2006) and defined in both I and II below:

I. Subjective evidence based on symptoms and signs of DKA

A variable history of polyuria, polydipsia, weight loss, vomiting, abdominal pain, dehydration, weakness, mental status change and coma.

Physical examination findings that may include poor skin turgor, Kussmaul respirations, tachycardia, hypotension, alteration in mental status, coma, shock, emesis (including coffee-ground vomit), abdominal pain.

II. Objective evidence of DKA based on laboratory diagnostic criteria

1. Blood glucose >13.9 mmol/L
2. Acidosis demonstrated by 1 or more of the following:
    i. pH< 7.3
    ii. HCO_3^- <18 mEq/L
    iii. High anion gap >12
3. Positive urine ketones (ketonuria 2+ or more on dip stick).

Operational definition of coma

Low admission Glasgow Coma Scale of between 3-8 (Russ, R and the University of North Carolina at Chapel Hill 2000). Table 1 below was used for scoring the GCS.

Table 1: Glasgow Coma Scale.

Eye Opening Response	Spontaneous	4 Points
	Opens to verbal command	3 Points
	Opens to pain	2 Points
	None	1 Point
Verbal Response	Oriented	5 Points
	Confused conversation	4 Points
	Inappropriate discernible words	3 Points
	Incomprehensible sound	2 Points
	None	1 Point
Motor Response	Obeys commands	6 Points
	Localises pain stimuli	5 Points
	Withdraws from pain	4 Points
	Abnormal flexion	3 Points
	Extensor response	2 Points
	None	1 Point

4.6 VARIABLES

Dependent Variables

Primary outcome was all-cause in hospital mortality

Alive: Participants who were alive at the end of hospitalization

Dead: Died during hospitalization for DKA

Independent Variables

Age, admission blood glucose readings, admission Glascow Coma Scale, blood pressure, BMI, HIV status, blood pH, serum bicarbonate, blood sodium, blood potassium, blood chloride, length of DM diagnosis

Categorical variables were sex (male, female), presence of infection (yes, no), HIV status (infected, not, declined test), coma status (present, absent), previous insulin or oral anti-diabetes therapy or combination, anti-diabetic therapy non-compliance (yes, no)

Continuous variables were age (years), admission heart rate (beats per minute), respiratory rate (breaths per minute), temperature (Celsius), Glasgow Coma Scale, blood pressure (mmHg), serum glucose (mmol/L), pH, bicarbonate (mmol/L), serum sodium (mmol/L), serum chloride (mmol/L), and potassium (mmol/L).

4.7 SAMPLING

Convenience sampling was used to maximize on recruitment rate into the study. All patients who were eligible were enrolled into the study until the desired sample size was met.

4.8 SAMPLE SIZE

The Pocock formular was used to calculate the sample size:

$$N = \frac{P_1 (100-P_1) + P_2 (100-P_2)}{(P_1-P_2)^2} \times F(\alpha, \beta)$$

Where:

N = Sample size

P_1 = Expected prevalence of 0.05 (assuming mortality prevalence in non comatose patients is low and comparable to advanced treatment centers statistics 5%)

P_2 = Expected prevalence of 0.30 (assuming mortality prevalence in comatose patients is high and comparable to statistics from resource-limited centers at 30%)

F (α, β) = is a constant fixed at 7.85 at the given significance level of 0.05 two-tailed test

Therefore:

$$N = \frac{5 (100-5) + 30 (100-30)}{(5-30)^2} \times 7.85$$

$$= 32$$

Factor in an average response rate of 80% gives (32/0.8) = 40 patients in each arm

Total sample size 80

Therefore, 80 participants were included in the final analysis

4.9 CLINIC PROCEDURE

Recruitment of study participants was done from all medical wards in the Medicine Department during working hours, Monday to Friday. Diabetic ketoacidosis patients or their surrogate decision makers were asked to participate in the study. The aims of the study and clinic procedures were fully explained. Written consent was obtained from all who met the diagnostic criteria for diabetic ketoacidosis before recruitment (Appendices 3-13).

Full history was taken by either the unit doctors or the researcher in patients who met the clinical diagnostic criteria. A physical examination was done on the recruited participants and included blood pressure, heart rate, respiratory rate and type, urinalysis and determination of ketonuria, temperature and possible infection source site determinations.

Unit doctors refers to the teams of medical doctors who were routinely assigned to care for patients when they presented to the hospital's department. The researchers had to verify as correct the history and physical examination findings before recruitment into the study.

Blood draws for glucose, pH, sodium, potassium and chloride and bicarbonate determination were done to ensure complete diagnostic criteria of DKA. This roughly translated to about 4 ml of blood samples saved in a plain serum specimen container and immediately couriered to Lancet and Sanket diagnostic laboratories. Participants were referred for diagnostic counseling and testing for HIV infection using the current practice standard set by Ministry of Health with antibody test strips (Abbot and Unigold) by qualified HIV counselors.

Each participant was followed up to the end of hospitalization (defined either as dead or alive on discharge).

The information was gathered on a data entry sheet and later entered into a Statistical Package for Social Sciences (SPSS) version 20 dataset.

4.10 STUDY PROCESS

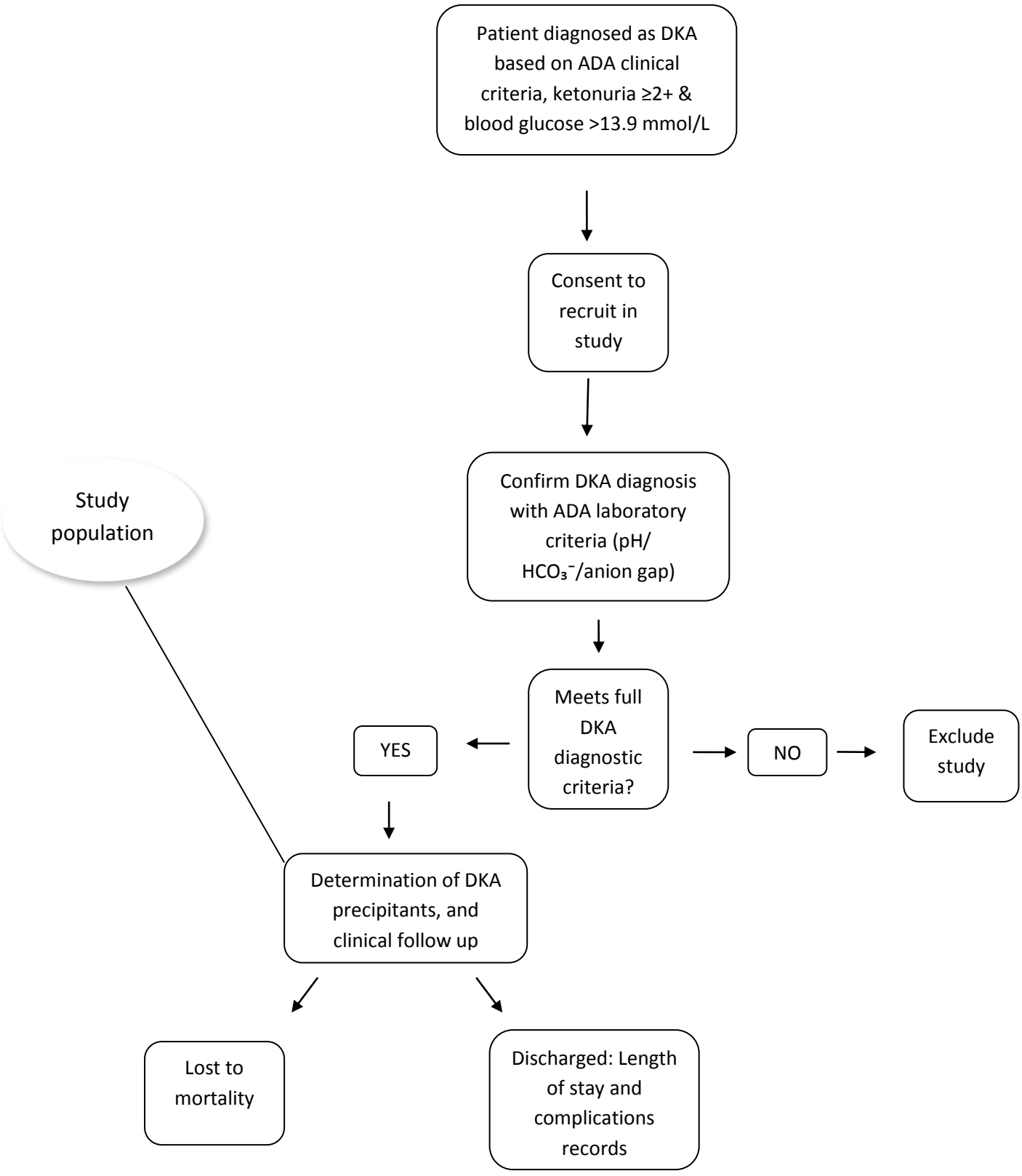


Figure1: Study process.

CHAPTER 5

5.1 DATA ENTRY

Data was collected on a hard copy using a structured data collection sheet (appendix 1). Each participant was identified by codes on these data sheets. The patient's identity code (not name) was entered on a hard copy data entry sheet for confidentiality reasons. Data collected was then entered electronically using Statistical Package for Social Sciences version 20.

5.2 DATA ANALYSIS

Frequency tables were used to describe the socio-demographic characteristics of the patients. Data was presented as medians for continuous data with percentiles. Comparisons of medians were done using Kruskal-Wallis 1-way ANOVA and Mann-Whitney U for continuous data to test for statistical significance. Categorical data was presented as percentages and proportions. Fisher's Exact test was used to examine associations between categorical data and outcome. This was because the number of participants with primary outcome was very small.

Some of the continuous data was eventually collapsed and dichotomized for the purpose of measuring their effect on primary outcome. The dichotomized data included coma state, presence of shock, respiratory rate greater than 29 per minute, young age below 35 years old, renal failure *etc*). All biochemical and baseline clinical variables were analysed to identify variables that potentially had significant association with primary outcome (mortality). All variables with p-value less than 0.20 were further subjected to binary logistic regression using backward Wald algorithm to determine adjusted odds ratios and independent predictors of mortality. These variables were elderly age greater than sixty-five, age lower than thirty-five, diastolic blood pressure, Glasgow Coma Scale, hypertension co-morbidity, coma state, tachypnea, hyperglycaemia greater than 30 mmol/L, altered mental status, hyperchloraemia, cerebro-vascular accident, pneumonia at baseline, presence of any infection, development of aspiration, development of renal failure, seizures.

A 2-sided $p < 0.05$ was considered as statistically significant.

5.3 ETHICAL CONSIDERATIONS

The research was conducted in line with Helsinki Declaration on ethics standards. Ethical approval was sought from the ethics body ERES CONVERGE. Permission was sought from the Senior Medical Superintendent of University Teaching Hospital (Appendices 14-15).

Patients were only enrolled upon consenting to participating in the study confirmed by written consent (writing or right thumb print). Patients below 18 years old were enrolled with written consent from their guardians and their express consent. Patients in coma were only enrolled if their next of kin consented to participation in the study. Patients or their next of kin, where applicable, were fully informed of the nature of the study and its purpose before they could be enrolled. Participation in the study was voluntary and patients were not coerced to give consent or receive any inducement during the study. Recruited participants were free to withdraw their participation in the study at any time without compromise to their medical management.

All procedures were carried out by qualified personnel including doctors and nurses. Participants experienced some discomfort or pain during blood draws and the finger prick glucose bedside checks. All tests done in the study were the minimum expected investigations in the standard practice of management of diabetic ketoacidosis. There were no complications reported as a result of the study.

All participants' records were kept confidential and were only used for research purposes. Information collected from the participants was kept in the Department of Medicine at the UTH under lock and key. Access to this information was restricted to the Principal Investigator, the Supervisors and Head of Department. However, any information pertinent to the participant's medical wellbeing was communicated to the unit doctors. Only participant identity codes and not their names were entered onto the data extraction sheet/database for confidentiality reasons.

There are no funding conflicts to be declared.

CHAPTER 6

RESEARCH FINDINGS

The study was conducted between October 2013 and August 2014. Ninety-four consecutive patients were assessed for eligibility. Two patients withdrew consent leaving 92 available for the study. Twelve patients were further excluded from the study due to the lack of biochemical evidence of acidosis required to diagnose DKA despite strong clinical suspicions. The total number of participants in the final analysis was 80.

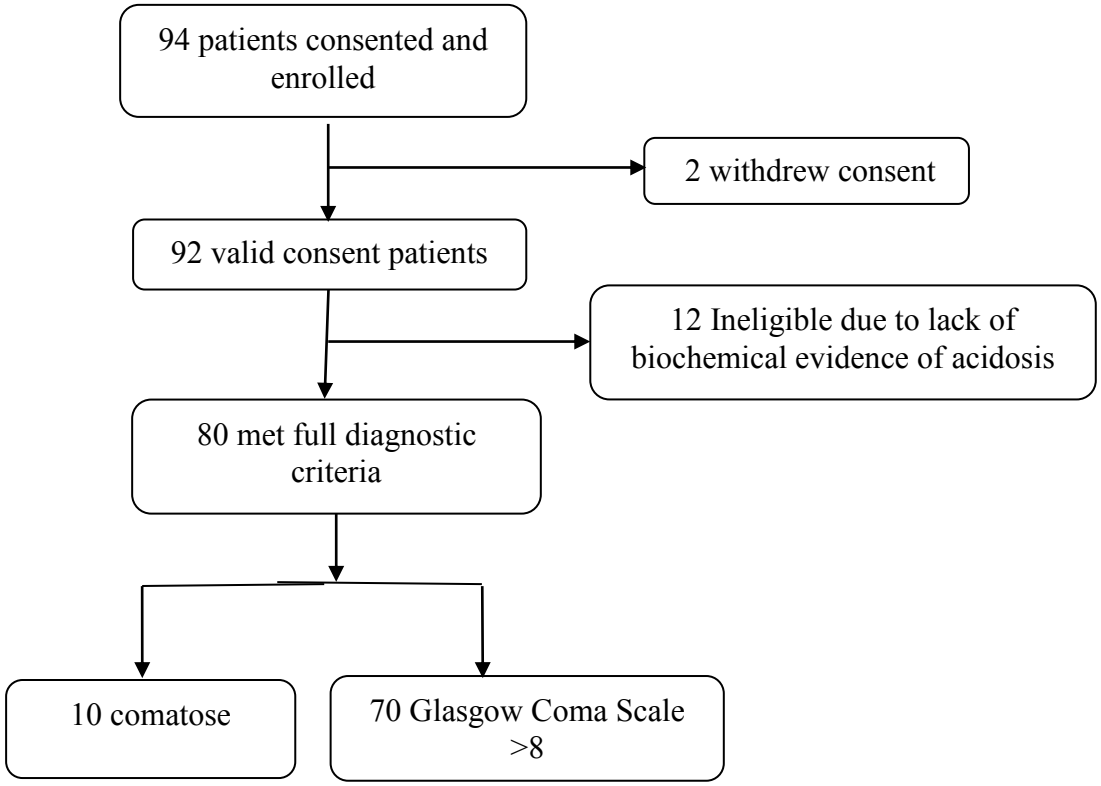


Figure 2: Randomisation into the study.

6.1 CLINICAL PROFILE

Graph 1 below shows the distribution of coma scales amongst the study participants. The prevalence of coma was 12.5%.

Graph 1: Patient distribution according to Glasgow Coma Scale.

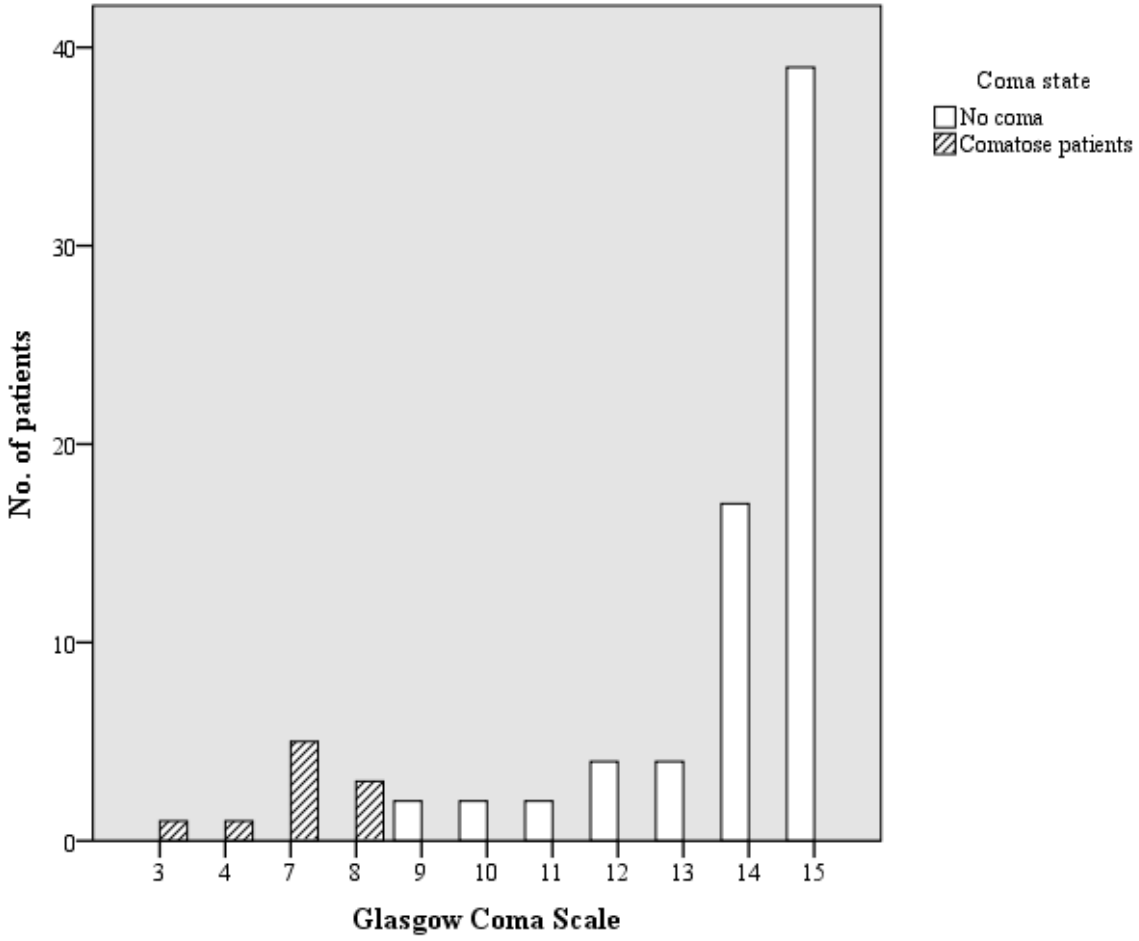


Table 2 below summarises the socio-demographic characteristics of the study participants.

Eighty percent of the participants who were comatose were younger than thirty-five years. Nearly two-thirds of the non-comatose participants were older than thirty-five years (65.7%). The ages ranged from 16 to 85 years.

Majority of the participants (72.5%) were already aware of their diabetes mellitus diagnosis at the time of presentation with DKA and most of these (93.1%) had been on some antidiabetic medications.

Table 2: Socio-demographic characteristics of the study participants.

Variable	Comatose participants = *n* (%)	Non-comatose participants = *n* (%)	*P* value
Age in years			
16-34	8 (80.0%)	24 (34.3%)	0.012
≥35	2 (20.0%)	46 (65.7%)	
Gender			
Males	5 (50.0%)	35 (50%)	>0.999
Females	5 (50.0%)	35 (50%)	
Length of DM diagnosis			
New	4 (40.0%)	18 (25.7%)	
Upto 1 month	3 (30.0%)	16 (22.9%)	0.684
>1month<1 year	1 (10.0%)	14 (20.0%)	
> 1 year	2 (20.0%)	22 (31.4%)	
Previous DM treatments			
Insulins	4 (40.0%)	18 (25.7%)	
Oral hypoglycaemics	2 (20.0%)	25 (35.7%)	
Insulin + oral hypoglycaemics	0	5 (7.1%)	-----
Not applicable	4 (40.0%)	18 (25.7%)	
Herbal treatments	0	2 (2.9%)	
Lifestyle modification	0	2 (2.9%)	
Drug adherence			
Always	3 (30.0%)	16 (22.9%)	
Poor adherence	3 (30.0%)	34 (48.5%)	0.175
Not applicable	4 (40.0%)	20 (28.6%)	
Co-morbidities			
Hypertension	4 (40.0%)	28 (40.0%)	
Tuberculosis	0	2 (2.9%)	-----
Prostate cancer	0	1 (1.4%)	
HIV status			
Negative	7 (70.0%)	53 (75.7%)	
Positive	2 (20.0%)	10 (14.3%)	0.851
Test declined/not done	1 (10.0%)	7 (10.0%)	

The baseline clinic-laboratory characteristics of the participants with DKA for both comatose and non-comatose patients were as shown in table 3 below.

Table 3: Bio-demographic baseline data of the participants.

Characteristics	Comatose (total patients= 10)	Non-comatose (total patients = 70)	*P* value
Age in Years			
Median (IQR)	30.0 (28.5-34.0)	42.5 (32.8-58.0)	0.005
Systolic BP mmHg			
Median (IQR)	105.0 (83.0-123.8)	120.5 (101.5-142.0)	0.032
Diastolic BP mmHg			
Median (IQR)	60.0 (49.0-84.3)	73.5 (60.8-90.5)	0.041
Heart Rate			
Median (IQR)	115.0 (93.0-134.0)	99.5 (87.5-111.3)	0.052
Resp rate/min			
Median (IQR)	28.5 (25.5-37.0)	25.0 (22.0-29.0)	0.031
Body temp °C			
Median IQR	36.1 (35.9-37.3)	36.2 (35.7-36.8)	0.787
GCS			
Median (range)	7 (3-8)	15 (9-15)	<0.001
RBS mmol/L			
Median (IQR)	33.0 (28.5-35.0)	27.1 (19.0-32.0)	0.012
Bicarbonate meq/L			
Median (IQR)	18.7 (15.9-20.2)	20.0 (17.1-22.0)	0.211
Sodium meq/L			
Median (IQR)	143.50 (136-150.3)	134.0 (129-138)	0.006
Potassium mmol/L			
Median (IQR)	4.0 (2.9-4.6)	4.2 (3.7-4.9)	0.190
Chloride mmol/L			
Median (IQR)	111.0 (104.8-120.8)	100.0 (92.0-108.0)	0.003
Anion gap			
Median (IQR)	15.1 (14.3-16.9)	17.2 (14.0-21.0)	0.441
pH			
Mean (SD)	7.26 (7.13-7.36)	7.32 (7.20-7.38)	0.390
Urine ketones			
Median (IQR)	3.0 (1.0-3.0)	2.00 (1.0-2.0)	0.214
Insulin & IVFs omissions &delays			
No. affected (%)	10 (100)	53 (75.7)	0.020
Hospital days			
Median (IQR)	8.0 (5.5-12.0)	6.0 (5.0-9.0)	0.268
Treatment Outcome			
Alive	8	66	
Dead (% in cohort)	2 (20)	4 (5.71)	0.133

The median GCS for comatose patients was 7 while that of their non-comatose counterparts was 15. Comatose patients were younger and had lower baseline blood pressure readings than their counterparts. They also had a higher respiratory rate and blood glucose levels at baseline. As expected, the comatose patients also had higher median blood sodium levels. The prevalence of hypokalaemia was 15%. There was no statistically significant difference in hospital length of stay between the two groups.

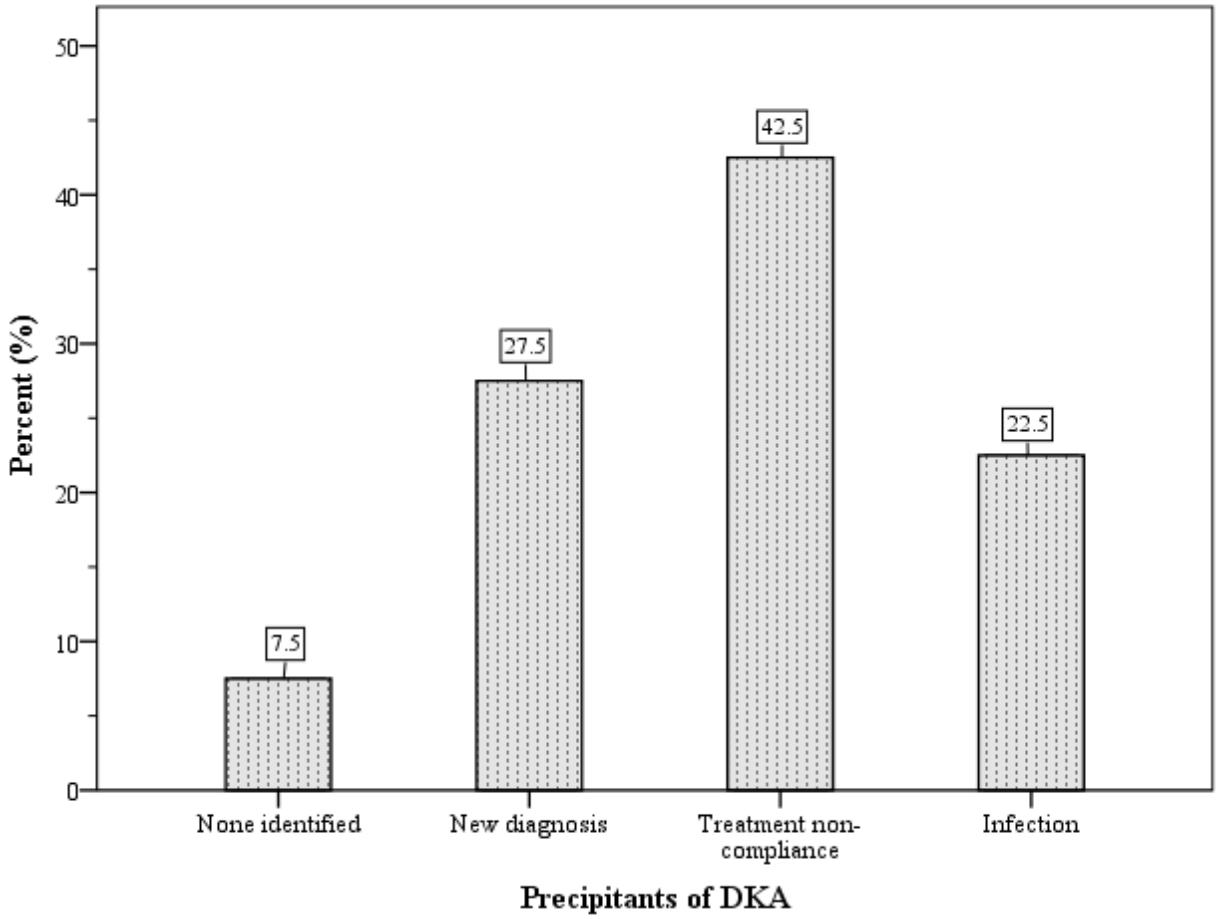
Table 4 below shows the notable differences in the clinico-laboratory derangements between the two coma groups.

Table 4: Clinico-laboratory derangements of DKA

Variable	**Comatose (total 10 patients)**	**Non comatose (total 70patients)**	***p* Value**
Systolic shock	4 (40.0%)	4 (5.7%)	0.007
Diastolic shock	5 (50.0%)	7 (10.0%)	0.005
Hypokalaemia	4 (40.0%)	8 (11.4%)	0.038
Hypernatraemia	5 (50.0%)	10 (14.3%)	0.017
Hyperchloraemia	4 (40.0%)	7 (10.0%)	0.027

6.2 PRECIPITANTS OF DIABETIC KETOACIDOSIS

Graph 2: Graph showing the frequencies of the identified precipitants of DKA



The most common identifiable factor leading to the development of DKA was problems with adhering to previously prescribed anti-diabetic treatments. Nearly a third (27.5%) of the study population was previously unaware of the diabetes diagnosis while infection accounted for 22.5% of the identifiable precipitants. Graph 2 above shows the proportions of the precipitants of DKA.

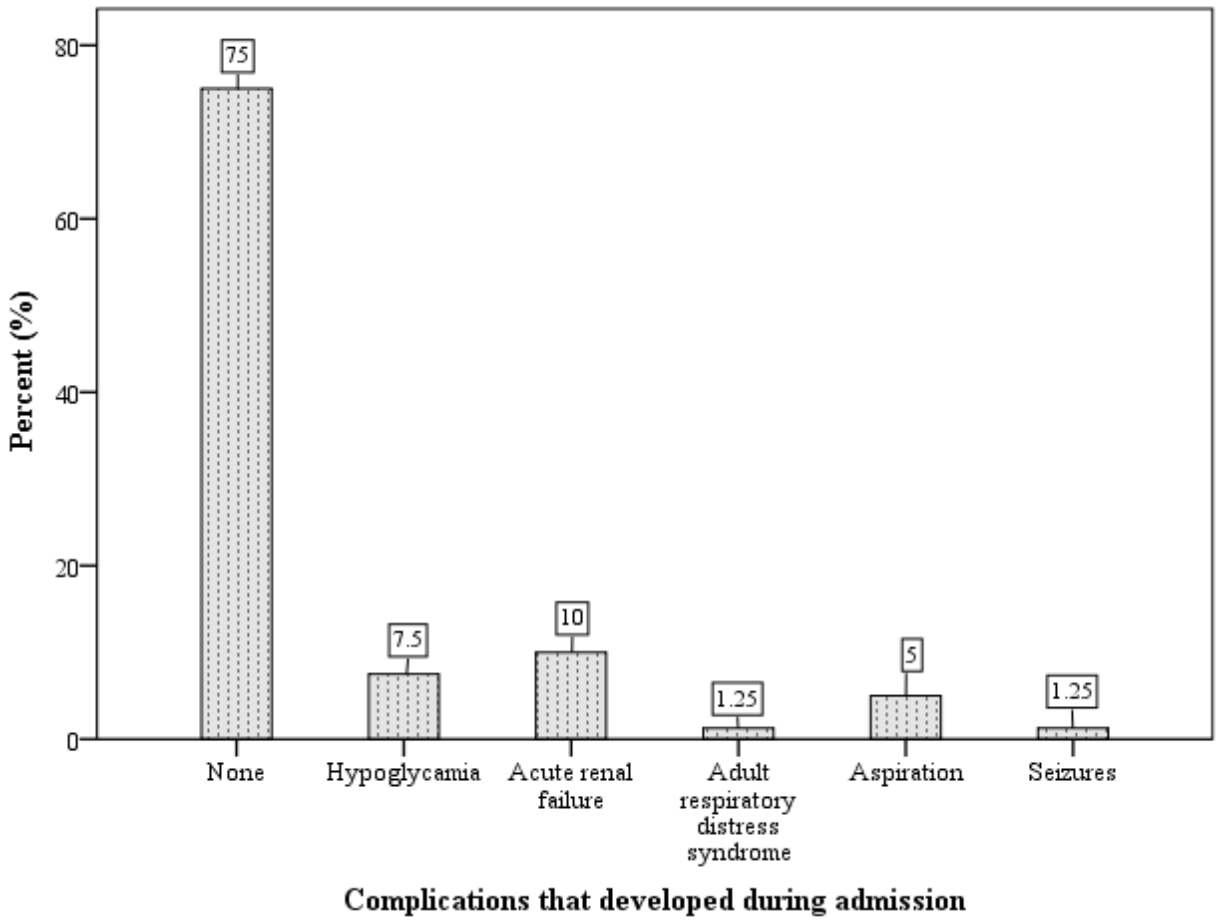
The infections associated with the development of DKA in decreasing order of magnitude were urinary tract infection, pneumonia, diabetic foot and other infected wound and upper respiratory tract infections.

Of the ten study subjects with infected wounds, diabetic foot was the most common (70%) while the remainder had decubitus ulcers (30%). The total prevalence of HIV was 15%. It was 20% amongst comatose participants and about 14.3% amongst non-comatose participants with no statistically significant difference between the two groups.

6.3 COMPLICATIONS

As shown in the graph 3 below, a number of complications were recorded in a quarter of the study participants.

Graph 3: Complications during hospitalization for DKA.



There were no obvious complications detected in 75% of the patients. Hypoglycaemia accounted for 7.5% of the complications reported during treatment and this was corrected intravenous dextrose infusion and all affected patients were eventually discharged. Ten percent developed acute renal failure while 1.25% developed adult respiratory distress syndrome, 5% had aspiration associated with comatose state and a single subject (1.25%) had a seizure.

6.4 RISK FACTORS AND PREDICTORS OF MORTALITY

Table 5: Risk factors of mortality.

Characteristics	Dead (total *n*=6)	Alive (total *n* =74)	*P* value
Age in years			
Median (IQR)	33 (30-65)	40 (32-57)	0.998
Age older than 65			
	2 (33.3%)	8 (10.8%)	0.161
Age less than 35			
	5 (83.3%)	27 (36.5%)	0.035*
Diastolic BP mmHg			
Median (IQR)	95 (61-109)	72 (60-90)	0.162
GCS			
Median (IQR)	9.5 (7-12)	15 (12-13)	0.002*
Coma			
	2 (33.3%)	8 (10.8%)	0.161
Altered mental status			
	6 (100%)	35 (47.3%)	0.015*
Hypertension			
	4 (66.7%)	25 (33.8%)	0.123
Systolic shock			
	1(16.7%)	7 (9.5%)	0.480
Diastolic shock			
	1(16.7%)	11(14.9%)	0.636
Hypernatraemia			
	2(33.3%)	13 (17.6%)	0.313
Tachypnoea			
	4 (66.7%)	23 (31.1%)	0.096
Hypokalaemia			
	1 (16.7%)	11 (14.9%)	0.636
Hyperglycaemia>30			
	5 (83.3%)	36 (48.6)	0.112
Hyperchloraemia			
	2 (33.3%)	9 (12.2%)	0.190
CVA			
	2 (33.3%)	0	-------
Pneumonia			
	4 (66.7%)	9 (12.2%)	0.006*
Infection			
	5 (83.3%)	37 (50%)	0.125
Aspiration			
	4 (66.7%)	3 (4.1%)	0.008*
Renal failure			
	4 (66.7%)	4 (5.4%)	0.001*
Seizures			
	1(16.7%)	0	-------

**Statistically significant*

Table 5 above shows that there were statistically significant associations between mortality outcome and the following variables; being younger than thirty-five years old, Glasgow Coma Scale, altered mental status, pneumonia diagnosis at baseline, renal failure and development of aspiration.

All variables in table 4 with a P value less than 0.20 were submitted to binary logistic regression using backward Wald algorithm and renal failure was found to be an independent predictor of mortality as presented in table 6 below.

Table 6: Mortality prediction.

Variable	**Unadjusted odds ratio**	**Confidence interval**	**Adjusted odds rato**	**Confidence interval**	***P* value**
Renal failure	35	4.86 - 251.96	70	6.28 - 780.82	0.001

There was a very wide confidence interval for the only independent predictor of mortality which suggests that this was very likely a pure chance finding. The positive outcomes on this analysis were too low to have a conclusive result.

Six participants (7.5%) died. Although the study found an association between altered mental status and mortality outcome, coma as a feature at admission was neither predictive of nor associated with an increased risk of mortality.

CHAPTER 7

7.1 DISCUSSION

The study showed that mortality outcome was high compared to statistics from advanced treatment centres world over. Although altered sensorium was found to have a statistically significant association with mortality outcome, the study findings suggest that comatose state on admission did not necessarily increase the risk of mortality. Development of renal failure during hospitalization was found to be an independent predictor of mortality outcome in this study with a possibility that it was a pure chance finding.

The study participants' ages ranged from 16 to 85 years. Comatose participants were significantly younger than those with Glasgow Coma Scales higher than 8 (30.0 *vs*. 42.5 years, $p = 0.005$). Although there was no statistically significant difference, the median age of those who died during hospitalisation for diabetic ketoacidosis (DKA) was equally younger compared to those who were eventually discharged (33 vs 40 years old, $p = 0.998$). This contrasts findings in other studies in both advanced and resource challenged settings including Sweden, Nigeria and Libya where mortality outcomes were higher in patients older than 65 years (Realsen *et al*. 2012, Elmehdawi *et al*. 2009 and Ogbera *et al*. 2009). A possible explanation is that younger patients in the study may have had severe insulin deficiency and hence suffered more adverse outcome compared to their older counterparts who may have had relatively higher insulin reserves or preserved beta cell fuction associated with type II diabetes. In the face of the severe insulin deficiency that afflicts the generally younger patients with type I diabetes, the younger population may have also succumbed more to adverse outcome as there were insulin administration interruptions that affected most of the patients due to frequent stock outs of essential monitoring tools and manpower shortages. Older patients who were more likely to have had type II DM may have been able to tolerate insulin dose ommissions better as long as they were getting some rehydration. Additionally, according to Welch and Zib in 2004, development of diabetic ketoacidosis is rare in type II diabetes comapared to type I which afflicts younger patients mostly. The higher prevalence of DKA in younger patients statistically increases their risk of mortality from DKA.

The factors which were associated with development of DKA in this study were treatment non-compliance, infection and new onset diabetes. These were the commonly identified

factors in similar studies (Umpierrez and Kitachbi 2003). The leading precipitant of DKA was identified as non-adherence to prescribed anti-diabetic drugs. Majority of the fifty-eight participants who were already diagnosed (93.1%) had been on anti-diabetic medications. Two participants (2.9%) reported having been exclusively on lifestyle modification strategies as advised at their primary healthcare clinics. Two others (2.9%) were using self prescribed undisclosed herbal treatments only. They however recovered without complications and were later discharged on treatment. Compliance was poor in more than half (58.6%) of the previously known diabetics but there was no significant difference in its prevalence between the comatose and non-comatose groups [30.0%. *vs*. 48.5% respectively (p = 0.175)]. This situation may be as a result of lack of basic health information and a strong primary health care establishment. Nearly a third of the participants (27.5%) were previously unaware of their diabetes and this was the second leading risk factor identified in the study. The third highest identified risk factor for development of DKA was infection at 22.5% while 7.5% of the participants did not have an obviously identifiable precipitant. The predominant identifiable infections in decreasing order of magnitude were urinary tract infection, pneumonia, infected wounds and upper respiratory tract infections.

Forty percent of the study participants had pre-existing hypertension and the prevalence was similar in the comatose and non-comatose groups (40.0% in both groups, p>0.999). This was a rather high prevalence when the median ages are considered (30.0 *vs*. 42.5 years for comatose and non-comatose groups respectively) but the study did not investigate for possible secondary causes especially in patients younger than 40 as that was beyond the scope of the study. In addition, two subjects (2.9%) who were older than 65 years had ischaemic cerebrovascular accident over three weeks prior to admission and this was confirmed on brain CAT scan. There may have been overlap of the symptoms, signs and laboratory profile with DKA but this could not be certainly established. As described by Jovanovic *et al.* (2014), CVA may have actually led to the development of DKA although the patients had had this complication for a relatively long duration.

Two participants (2.9%) were on consolidation phase of anti-tuberculous therapy and both reported marked recovery from their pulmonary tuberculosis symptoms at the time of admission with DKA. One participant (1.4%) had prostate cancer. The total prevalence of HIV infection was 15% and this is lower than the reported district prevalence of 20.8% as published by Central Statistics Office. Furthermore, there was no statistically significant difference between the coma groups [comatose 20% *vs*. non-comatose 14.3% (p = 0.851)].

The study did not demonstrate any association between HIV infection and mortality outcome. The test was not done in eight subjects. Three patients declined the test while the remaining five were affected with either test reagents stock outs or non-response from trained HIV counselors to test the patients before hospital discharge.

As expected, participants who were in comatose state were noted to have some significantly worse clinical and biochemical features than their counterparts at baseline. Comatose patients had lower median baseline blood pressures, though normal [(systolic 105 mmHg *vs*. 120 mmHg, $p = 0.032$) and (diastolic 60 mmHg vs 77 mmHg, p= 0.041)] and higher respiratory rate (28.5 per minute vs. 25 per minute, $p = 0.031$) at baseline. The prevalence of systolic shock was higher in comatose subjects compared to non-comatose ones (40.0% *vs*. 5.7%, $p = 0.007$). Comatose participants also had higher prevalence of hypokalaemia (40.0% *vs*. 11.4%, $p = 0.038$), hypernatraemia (50.0% *vs*. 14.3%, $p = 0.017$) and hyperchloraemia (40.0% *vs.* 10.0%, $p = 0.027$) than their non-comatose counterparts. There was no statistically significant difference in anion gap between the two groups ($p = 0.441$). In a similar study by Otieno *et al*. (2010), altered consciousness was associated with systolic hypotension and severe metabolic acidosis. The total prevalence of hypokalaemia from this study was 15%. Studies from around the world have reported widely varied prevalences. For instance, a low prevalence was described in a study done in a multicenter retrospective cross sectional study at emergency departments in the United States with a sample size of 155,000 adults diagnosed with DKA (Jang *et al*. 2015). Only 7 (0.0045%) of the subjects had hypokalaemia. A Nigerian study by Ogbera *et al*. (2009) reported a much higher prevalence (35%) than our findings.

The commonest complication encountered was acute renal failure followed by hypoglycaemia, aspiration, seizures and adult respiratory distress syndrome. Renal failure may have been due to prolonged pre-renal volume contraction from late hospital presentation and inadequate intravenous fluid infusion. The study noted that there were delays in infusing prescribed intravenous fluids upon admission that affected 78.7% of all the participants. All comatose participants (100%) were affected by these delays while 75.5% of the non-comatose group were affected ($p = 0.020$). Aspiration while in hospital was found in 66.7% of those who eventually died during hospitalization. All affected patients had altered mental status. Some measures such as head elevation and nasogastic tube insertion may have helped to prevent aspiration and it was noted that these were not readily available for deserving patients at all times. One participant who developed generalized tonic-clonic seizures

eventually died during admission. The participant had not been stable enough to be transported for a brain CAT scan as the machine was located far from the admission area. Although this participant had severe metabolic acidosis with pH 6.90 and severe pneumonia, aetiology of the seizures was not fully investigated and consent for postmortem was declined by family.

The mortality rate was high at 7.5% compared to the prevalence reported in advanced treatment centers (less than 5%) by American Diabetes Association (2004). It was however noted to be lower than the observations made in earlier African studies in Kenya 29.8% (Mbugua *et al*. 2005 and Otieno *et al*. 2010), Democratic Republic of Congo 27.5% (Kakoma 2014), South Africa 11.9% (Ekpebegh and Longo-Mbeza 2013) and Libya 14.4% and 11.9% (Elmehdawi *et al*. 2009, 2013). There were glaring gaps in monitoring and management that may have contributed to this high mortality rate. Most of our patients had very limited access to optimum care prescribed on admission and beyond. There was erratic administration of prescribed insulin and fluid replacements in about 78.7% of subjects enrolled into the study. This was particularly observed at the beginning of the study when the nursing staffing had dwindled as a result of an industrial strike action. Regular monitoring was hampered by frequent stock outs of basic equipment such as point of care blood glucose monitoring kits, urinalysis strips, laboratory biochemistry reagents and appropriate intravenous fluids at times. Currently, there is no point of care blood gas analyzer readily available to the department for regular monitoring to allow timely interventions.

Risk factors associated with mortality outcomes included admission with pneumonia, younger age below 35 years, development of aspiration, pre-existing hypertension, development of renal failure, and altered mental status. Coma was not necessarily associated with increased risk of mortality outcome. All participants who died had some alteration in mental status. Although there was no statistically significant difference, these participants who died had higher prevalence of hypernatraemia, hypokalaemia, high baseline blood glucose levels greater than 30 mmol/L and hyperchloraemia ($p = 0.313$, $p = 0.636$, $p = 0.112$ and $p = 0.190$ respectively). In a similar study done in Kenya, mortality was high and all patients who died had altered consciousness on admission (Otieno *et al*. 2010). In our study, the total prevalence of altered mental status on admission was 51.3% and the mortality prevalence amongst the patients with altered mental status was 14.3%.

Development of renal failure was found to be the only independent predictor mortality. Due to the small number of subjects with this primary outcome, this may have been a pure chance finding. A larger study would be necessary to study the predictors of mortality. Coma was not found to be associated with increased risk of mortality and the null hypothesis was retained.

7.2 STUDY LIMITATIONS

This was a natural non-interventional observational study that mostly relied on clinical indicators that were used by the attending clinicians to determine the resolution of DKA in patients who were eventually discharged. Many patients did not have post baseline laboratory investigations if they made marked clinical recovery within a few days and some complications may not have been adequately captured as a result.

CHAPTER 8

8.1 CONCLUSION

The mortality rate from diabetic ketoacidosis hospitalizations is high at University Teaching Hospital, Lusaka. Treatment non-compliance appears to be the single highest identifiable precipitant of DKA. Aspiration, development of renal failure, altered sensorium, young age below 35 years old, cerebrovascular accident and pneumonia at baseline are associated with an increased risk of mortality. Development of renal failure during admission is remotely predictive of mortality. Coma was not a predictor of mortality and hence the null hypothesis is retained.

8.2 RECOMMENDATIONS

1. University Teaching hospital

Many of the management gaps identified were due to understaffing and crowding in the wards. There is need to have a dedicated high dependency unit for patients presenting in DKA as they require intensive and frequent monitoring to tailor their treatments. There is also a need to assign dedicated nurses who are trained in diabetology to care for these patients. The Ministry of Health thus needs to invest in training of some nurses in diabetes care. As DKA patients require labor-intensive biochemical profile monitoring, the hospital should be equipped with point-of-care blood gas analyzers on the wards as well as uninterrupted supply of blood glucose monitoring kits, central line intravenous catheters and urinalysis strips. In view of the noted factors associated with increased risk of mortality, medical staff should aggressively manage all DKA patients admitted with altered sensorium, cerebrovascular accident and pneumonia. Consistently employing strategies such as head elevation and nasogastric tube insertion for those with altered consciousness level can help to prevent aspiration. Patients also need to have adequate and timely fluid replacement to prevent renal failure and increased nurse staffing levels may help in achieving this. Treatment protocols also need to be prepared and be made readily accessible to all health personnel managing patients on the wards.

2. Primary Health Care

There is need for Ministry of Community Development, Mother and Child Health to invest in education programs in media on diabetes mellitus and the basic lifestyle modification strategies that help to control diabetes including healthy dietary choices and routine exercise recommendations. It is also important to have routine screening for diabetes more readily available for the general population. Patients may greatly benefit from local short films on diabetes management strategies being screened in waiting rooms of public clinics and hospitals. This will improve patient awareness and hopefully treatment compliance.

3. Recommendations for future research

A study to ascertain the knowledge, attitude and practices of diabetes mellitus therapy amongst patients with diabetes mellitus may be useful in beginning to understand the problem of treatment non-compliance. A more direct study to determine the factors associated with treatment non-compliance may also help. A more detailed research into the complications associated with diabetic ketoacidosis admissions needs to be carried out. That may help to improve patient management in future and reduce mortality significantly. It would also be necessary to do a study on acute renal failure in diabetic ketoacidosis and to describe the kidney histopathological changes.

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APPENDIX 1 : DATA COLLECTION SHEET

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

Instructions : Kindly TICK or CHECK box where applicable. Data should only be collected after the consent form has been signed by the patient or next of kin where applicable.

Participant Code/Study No. **DKA** __ __ __ __

Town : _____ Residential area : _____

Phone No (1): _____ Phone No (2) :_____

Date of Admission: _____/_____/_____ Occupation_____

1. HISTORY

1. AGE: _____ yrs
2. SEX: ☐ Male ☐ Female
3. Year & month of diagnosis of DM: _____
4. Number of previous hospital admissions in the last year with diabetes mellitus complication:
   ☐ 0 ☐ 1 ☐ 2 ☐ >=3
5. Date of last admission due to diabetes mellitus-related complication: _____/_____/_____
   ☐ Not applicable
6. Drug Hx : Type of antidiabetic medication received in the last 6 months (Note: Can select more than 1 option):
   ☐ Insulins
   ☐ Oral hypoglycaemics
   ☐ Dietary control only
   ☐ None

☐ Other, specify:_____

7. Adherence to medication :

   ☐ Always ☐ Sometimes ☐ Never

   ☐ Not applicable

8. Comorbidities and drugs (List all):

   1_____

   2_____

   3_____

   4_____

   5_____

   6_____

2. PHYSICAL EXAMINATION (on admission)

1. General State:

   ☐ Coma ☐ Shock ☐ Altered mental state

   ☐ Infected wound

2. Blood Pressure: _____ mmHg
3. Heart Rate: _____ beats/min
4. Respiratory Rate: _____ breaths/min
5. Temperature: _____ ^{o} C
6. Glasgow Coma Scale_____ / 15
7. Site of wound _____

3. RESULTS (on admission)

1. Serum Glucose: _____ mmol/L
2. Serum Bicarbonate: ____ meq/L; Sodium____mmol/l; Potassium_____mmol/l; Chloride_____mmol/l
3. Blood pH: _____
4. Urine Ketostix reaction: _____
5. CD4 COUNT: _____cell/mL

4. IDENTIFIED RISK FACTORS FOR DKA DEVELOPMENT

1. Risk factors

☐ Not identified

☐ Infection;

Specify type_____

☐ Treatment non-compliance

☐ Cerebrovascular accident

☐ First time diagnosis of diabetes

Specify others _____

5. COMPLICATIONS

☐ None
☐ Cerebral oedema
☐ Adult respiratory distress syndrome
☐ Aspiration
☐ Hypoglycaemia
☐ Hypokalaemia
☐ Gastrointestinal bleed
☐ DIC
☐ Acute renal failure

Others, specify: _____

6. DISCHARGE FROM HOSPITAL:

YES ☐ NO ☐

Date of discharge from hospital: _____/_____/_____

Length of hospital stay (No. of days) _____

7. MORTALITY OUTCOME:

Outcome

Date of death: _____/_____/_____

Number of days to outcome: _____

Cause of death_____

8. MANAGEMENT GAPS IDENTIFIED:

Management gaps noted

☐ Erratic insulin administration

☐ Inadequate or delayed intravenous fluids administration (24 hourly reviews of actual implementation of fluid management plan by the attending doctors/physician, any deficit noted?)

☐ Inadequate electrolytes monitoring

☐ Others; specify_____

APPENDIX 2: PATIENT INFORMATION SHEET

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

Introduction

I, Mwanja Kakusa, an MMED student in the School of Medicine at the University of Zambia, kindly request your participation in the above mentioned study. This study is in partial fulfillment for the award of a Master of Medicine in Internal Medicine. Before you make up your mind whether to take part in the study or not, I would like to explain to you the purpose of the study and what is expected of you. If you agree to take part in this study, you will be asked to sign this consent form in the presence of a witness.

Nature and purpose of the study

This study is being conducted to ascertain how patients with the diabetic ketoacidosis, a form of diabetic emergency which you appear to have presented with, present, how they are managed and the treatment outcomes. Simply, the study will look at problems that may cause one to develop this complication, how serious the condition is upon coming into the hospital, what problems may arise due to disease and how you will fare at the end of your hospital stay. This is being done to identify some factors that can potentially be addressed to improve treatment approach.

The illness under study diabetic ketoacidosis is a known complication of diabetes which occurs when a patient has too little insulin in the body. Due to this inadequate insulin, the patient may have many complaints such as increased thirst, increased urination, dehydration and fast breathing. At times, the patients may be confused or in very serious condition of coma

Procedure of the study

If you agree to participate in this study, we will obtain information using a data entry sheet. Your contact details including phone number will be required. Samples of blood of up to 10 mls at most will be taken from you and sent to the laboratory for testing to confirm the

diagnosis. A qualified HIV counselor will counsel you before an HIV test done. The results of the tests will be communicated to you and the unit doctors if you so wish.

Possible risks and discomforts

All the laboratory tests required of you are all within the routine minimum investigations required for focused management of your condition diabetic ketoacidosis. You will not be exposed to any risks by enrolling into the study. However, you will experience discomfort during collection of blood samples and a minimal risk of infection at the puncture wound needle prick site (less than 1% risk). All other procedures during the course of treatment will be planned and followed up by your unit doctors depending on the monitoring and treatment requirements you will have.

Possible benefits

The information obtained in this study will help in improving management of other diabetic ketoacidosis presentations and reducing the risk of mortality.

Confidentiality

All the information collected is strictly confidential. Data that will be collected, analysed, and reported on will not include your name and therefore cannot be traced to you.

Consent

Your participation is strictly voluntary. You will not suffer any consequences if you decide not to participate in this study. You may also withdraw from the study at any time for any reason without consequences to you.

Thank you for considering participation in this study. If you have any questions, concerns and clarifications, please contact Dr. Mwanja Kakusa or Research Ethics committee on the following addresses;

Dr. Mwanja Kakusa,

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P/Bag RW1X,

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Mobile phone Number: +260 955 888 577

ERES CONVERGE

33 Joseph Mwilwa Road

Rhodes Park

Lusaka.

Phone +260 955 155 633/ +260 955 155 634/ +260 966 765 503

APPENDIX 3: INFORMED CONSENT

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

INFORMED CONSENT

I……
have read and been fully informed of the nature of the study and do hereby voluntarily consent to participating in the said study.

I have been given the chance to ask questions pertaining to the study and these have been addressed adequately. I am also aware of my right to withdraw from the study at any point without any negative repercussions on my treatment.

……

(Patient Signature)

……

……

(Witness signature, names & rank)

Date:

APPENDIX 4: INFORMATION SHEET FOR SURROGATE DECISION MAKER

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

Introduction

I, Mwanja Kakusa, an MMED student in the School of Medicine at the University of Zambia, kindly request your consent for your relative/spouse/ward to participate in the above mentioned study. This study is in partial fulfillment for the award of a Master of Medicine in Internal Medicine. Before you make up your mind whether to agree to take part in the study or not, I would like to explain to you the purpose of the study and what is expected of the patient. If you agree to have your relative/spouse/ward take part in this study, you will be asked to sign a consent form in the presence of a witness.

Nature and purpose of the study

This study is being conducted to ascertain how patients with the diabetic ketoacidosis, a form of diabetic emergency which your patient appears to have presented with, present, how they are managed and the treatment outcomes. Simply, the study will look at problems that may cause one to develop this complication, how serious the condition is upon coming into the hospital, what problems may arise due to disease and how the patient will fare at the end of their hospital stay. This is being done to identify some factors that can potentially be addressed to improve treatment approach.

Diabetic ketoacidosis is a known complication of diabetes which occurs when a patient has too little insulin in the body. Due to this inadequate insulin, the patient may have many complaints such as increased thirst, increased urination, dehydration and fast breathing. At times, the patients may be confused or in very serious condition of coma.

Procedure of the study

If you agree to have your patient participate in this study, we will obtain information using a data entry sheet. Your contact details including phone number will be required. Samples of blood of up to 10 mls at most will be taken from the patient and sent to the laboratory for testing to confirm the diagnosis.

Possible risks and discomforts

All the laboratory tests required of the patient are all within the routine minimum investigations required for focused management of his/her condition diabetic ketoacidosis. The patient will not be exposed to any risks by enrolling into the study. However, he/she will experience discomfort during collection of blood samples and a minimal risk of infection at the puncture wound needle prick site (less than 1% risk). All other procedures during the course of treatment will be planned and followed up by the patient's doctors assigned to care for him/her in the routine clinical work depending on the monitoring and treatment requirements the patient will have.

Possible benefits

The information obtained in this study will help in improving management of other diabetic ketoacidosis presentations and reducing the risk of mortality. This improvement may benefit your patient in the unfortunate event of a repeat of the complication in future.

Confidentiality

All the information collected is strictly confidential. Data that will be collected, analysed, and reported on will not include your patient's name and therefore cannot be traced to him/her.

Consent

Your agreeing to consent participation on behalf of your patient is strictly voluntary. Your patient will not suffer any consequences if you decide not to participate in this study. You may also withdraw from the study at any time for any reason without consequences to your patient.

Thank you for considering consenting to participation in this study on behalf of your patient. If you have any questions, concerns and clarifications, please contact Dr. Mwanja Kakusa or Research Ethics committee on the following addresses;

Dr. Mwanja Kakusa,

The University Teaching Hospital,

Department of Internal Medicine,

P/Bag RW1X,

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APPENDIX 5: SURROGATE CONSENT

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

SURROGATE CONSENT

I……
(name) have read and or been fully informed of the nature of the study and do hereby voluntarily consent

my…….(relation),
……...…….(patient's name)
participating in the said study.

I am also aware of my right to withdraw consent while I continue to be the surrogate decision maker at any point without any consequences on their medical management. I am aware of the right of my patient to make a decision to continue or withdraw from the study once they are medically determined to be able to make decisions by their assigned doctors. I have had sufficient time to ask questions and these have been addressed adequately.

……
(Surrogate's signature)

……

……
(Witness signature, names & rank)

Date:

APPENDIX 6: NYANJA INFORMED CONSENT INFORMATION SHEET

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

Chidziwitso kwa odwala pa nkhani yobvomereza utengako mbali mu kufufuza kwa ma phunziro oyangana za odwala matenda a dayabetisi ketoasidosisi (kapena kuti shuga yobvuta mu chinyanja chatsopano) mu chipatala cha uth, mu lusaka, dziko la zambia

Dzina langa ndine Dr Mwanja Kakusa, sing'anga mu chipatala cha UTH. Mbali ina, ndi phunzira pa sukulu yochedwa University of Zambia, pomwe ndiri ku mapeto a maphunziro a patsogoro yochedwa Master of Medicine ya akatswiri oyangana matenda osiyanasiyana yomwe ya gwira azimai ndi azibambo.

Ndi pempha inu kuti mu bvomereze ine kuti mutengeko mbali mu zofufuza za maphunziro za odwala matenda yochedwa mu chizungu kuti 'dayabetisi ketoasidosisi', kapena ningonena kuti shuga yobvuta kwa basi. Ndi pempha inu chifukwa mwa fika pano pa chipatala na bvuto imene imagwira anthu odwala ma tenda a shuga. Nilu pima mu zofufuza za maphunziro za umoyo zonse zimene zikhuza odwala dayabetisi ketoasidosisi. Musana bvomereze utenga mbali mu nkhani iyi ndi pempha kuti mutenge nthawi umvetsetsa bwino zimene zichitika mu nthaka iyi.

<u>Kodi lingo lake la kafukufuku wa matenda a shuga yobvuta ndi chiyani?</u>

Mu zopima zimene ndi fufudza, nifuna udziwa m'mene odwala shuga yobvuta amafikira mu chipatala ndi zooneka mthupi mwao. Ndi fufuzanso zovuta zimene zibweretsa bvutoyo mu thupi mwa odwala. Ndi yangananso m'mene matenda awa adzachira, mwina mwache zopota thupi zina zingaoneke mtsogoro ma tsiku onse omwe odwala azakhala mu chipatala.

<u>Kodi ubwino wake mu zimene izi ndi chiyani?</u>

Zokoma zake potenga mbali mu zofufudza izi ndi zambiri. Dzimene ndi zapeza mwa inu pamodzi ndi odwala ena onse a matenda awa zizatithandidza kwambiri monga chipatala, mwina mwache dziko lathu lonse udziwa bwino motsamalira onse odwala bvuto iyi. Zizathandidzanso uziwa bwino zolakwa zimene zingaoneke potsamalira odwala ndi ku sintha zolakwazo. Kuli odwala kopambana ndi zafufudza bwino uwona zopweteka zimene zipeleka matenda pa tsogoro.

Zofunika kwainu ndi zotani?

Ndi pempha kwainu kuti mundi udze zamatenda yanu uchoka pomwe muna gwiriwa ndi shuga. Nga khale kuti nuyamba ugwiriwa matenda a shuga tsiku lobwera kuno lalero chabe mwina mwache matsiku ang'ono, inu mu bvomerezedwa utengako mbali mu kafukufuku aka ngati mwandilola.

Ndiza pempha utengako magazi ang'ono osa pambana ma supuni awili akulu kapena kuti 10 mls poyamba apa. Izi ziwiri ziyenera upimiwa bwino ku labu kuti ti dziwe bwino zobvuta ndi shuga yanu no dzindikira kuti bvuto lanu ndi dayabetisi ketoasidosisi zoonadi osati matenda ena ofananako ayi. Utuluka apo, ndiza bwera uza mionani tsiku ndi tsiku ufikira pomwe mu za tulukira mu chipatala.

Nanga malipiro anu yalipo?

Kulibe kulandira malipiro andalama kapena katundu mwina mwache mphatso muka bvomeredza utenga mbali mu zofufudza izi. Zaulele zilipo ndi malipiro a magazi na mitundo yemwe yaza pimiwa ku labu mu kafukufuku aka ziliko kamodzi poyamba apa. Zonse zina zomwe a dotolo anu azafuna upimiwa ulingana na zopweteka zimene azaona mwa inu ziza lipiliwa ndi inu monga mu njira imene odwala onse ama pereka zolipira ku chipatala.

Kodi ningasinthe nzelu pa zotenga mbali mu zofufuza izi?

Inde, inu muli nawo ufulu woletsa upitiliza utenga mbali mwa izi ngakhale kuti mwa bvomereza poyamba. Ngati mwa sintha nzelu mu ndi udze mo matsuka bwino ndiponso kulibe zobvuta chifukwa inu muli nawo udindo pa za umoyo wanu. Muka chita tero, a dotolo anu azapitiliza umi tsamarani munjira imene adziwa bwino monga mwa masiku onse omwe ama sewenzerapo po ona bvuto ya shuga iyi kopanda chilango chili chonse.

Kodi kufufudza uku kunga bweretse ngozi yotani?

Kufufudza uku kulibe ngozi chifukwa tingo ona chabe m'mene muza chira ndi bvuto yamibweretsani iyi osati uyesa mankhwala yosa ziwika mwa inu ayi. A dotolo wanu aza sewenzesa mankhwala yemwe yama sewenza nthawi zonse ku bvuto lanu.

Koma zowawa pang'ono zilipo uchokera ku ka nsingano kochotsera magazi. Nchito imene iyi iza gwiriwa ndi a ka tswiri a dotolo kapena a nasi.

Mafunso

Ngati muli na mafunso yena pa izi, mungathe uni yitana pa lamya kapena ulemba kalata pa

Dr. Mwanja Kakusa,

The University Teaching Hospital,

Department of Internal Medicine,

P/Bag RW1X,

Lusaka, Zambia.

Lamya: +260 955 888 577

Akulu omwe alola zimene ndi fufudza pa phunziro imene iyi alipo. Akulu awa ama yangananso kuti zo fufudza zonse zokhudza za umoyo wa anthu a m'dziko la Zambia ndi zobvomerezeka ndi lamulo la dziko lino. Ngati mwa khudzidwa ndi zina zache mungathe ufunsa kapena ku wa dandaulira ku malo awo a:

ERES CONVERGE

33 Joseph Mwilwa Road

Rhodes Park

Lusaka.

Ma lamya: +260 955 155 633/ +260 955 155 634/ +260 966 765 503

APPENDIX 7: NYANJA INFORMED CONSENT

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

NYANJA INFORMED CONSENT

UBVOMEREZA UTENGAKO MBALI MU ZOFUFUZA ZA MA PHUNZIRO OYANGANA ODWALA MATENDA A DAYABETISI KETOASIDOSISI (KAPENA KUTI SHUGA YOBVUTA MU CHINYANJA CHATSOPANO) MU CHIPATALA CHA UTH, MU LUSAKA, DZIKO LA ZAMBIA

Ine, ochedwa…… nawerenga ndi kumvetsetsa bwino za mafufuzo aya ndiponso nda bvomera utenga mbali mu fufuzo imene iyi kopanda kakamizo. Nakhala nawo mpata woyankhidwa mokwana mafunso anga onse pa maphunziro awa.

Ndi dziwa kuti nili nawo ufulu woletsa upitiliza ukhalamo mu fufuzo imene iyi nthawi ili yonse ngati nafuna kuchita tero ndiponso uchita kulibe chilango.

……
(Siginecha)

…….

……
(Dzina, udindo, ndi siginecha ya mboni)

Tsiku:

APPENDIX 8: NYANJA SURROGATE INFORMATION SHEET

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

Chidziwitso kwa wabanja wa odwala pa nkhani yobvomereza utengako mbali mu zofufuza za ma phunziro oyangana odwala matenda a dayabetisi ketoasidosisi (kapena kuti shuga yobvuta mu chinyanja chatsopano) mu chipatala cha uth, mu lusaka, dziko la zambia

Dzina langa ndine Dr Mwanja Kakusa, sing'anga mu chipatala cha UTH. Mbali ina, ndi phunzira pa sukulu yochedwa University of Zambia, pomwe ndiri ku mapeto a maphunziro a patsogoro yochedwa Master of Medicine ya akatswiri oyangana matenda osiyanasiyana yomwe ya gwira azimai ndi azibambo.

Ndi pempha inu kuti mu bvomeredze achibanja/akazi/amuna/ana anu odwala matenda yemwe timanena mu chizungu kuti dayabetisi ketoasidosisi, kapena ningonena kuti shuga yobvuta kwa basi kuti atengeko mbali mu zofufuza za maphunziro. Ndi pempha inu chifukwa abale anu afika pano pa chipatala na bvuto imene imagwira anthu odwala ma tenda a shuga. Nilu pima mu zofufuza za maphunziro zimene zimakhalapo mu bvuto iyi ya dayabetisi ketoasidosisi. Musana bvomeredze m'bale wanu utenga mbali mu nkhani iyi ndi pempha kuti mutenge nthawi umvetsetsa bwino zimene zilu chitika mu nthaka iyi.

<u>Kodi lingo lake la kafukufuku wa matenda a shuga yobvuta ndi chiyani?</u>

Mu zopima zimene ndi fufudza, nifuna udziwa m'mene odwala shuga yobvuta amafikira mu chipatala ndi zooneka mthupi mwao. Ndi fufuzanso zovuta zimene zibweretsa bvutoyo mu thupi mwa odwala. Ndi yangananso m'mene matenda awa adzachira, mwina mwache zopota thupi zina zingaoneke mtsogoro ma tsiku onse omwe odwala azakhala mu chipatala. Nifufuzanso zonse zoipa zimene zimapeleka matenda awa pa tsogoro.

<u>Kodi ubwino wake mu zimene izi ndi chiyani?</u>

Zokoma zake potenga mbali mu zofufudza izi ndi zambiri. Zimene ndi zapeza mwa abale anu pamodzi ndi odwala ena onse a matenda awa zizatithandidza kwambiri monga chipatala, mwina mwache dziko lathu lonse udziwa bwino motsamalira onse odwala bvuto iyi. Zizathandidzanso uziwa bwino zolakwa zimene zingaoneke potsamalira odwala ndi ku sintha zolakwazo. Kuli odwala kopambana ndi zafufudza bwino uwona zopweteka zimene zipeleka matenda pa tsogoro.

Zofunika kwa abale anu ndi zotani?

Ndi pempha kwainu kuti mundi udze zamatenda ya abale anu uchoka pomwe ana gwiriwa ndi shuga. Nga khale kuti nuyamba ugwiriwa umatenda a shuga tsiku lobwera kuno lalero chabe mwina mwache ma tsiku ang'ono, abale anu abvomerezedwa utengako mbali mu kafukufuku aka ngati mwandilola.

Ndiza pempha utengako magazi ang'ono osa pambana ma supuni awili akulu kapena kuti 10 mls na mitundo poyamba apa. Izi ziwiri ziyenera upimiwa bwino ku labu kuti ti dziwe bwino zobvuta ndi shuga ya abale anu no dzindikira kuti bvuto lao ndi dayabetisi ketoasidosisi zoonadi osati matenda ena ofananako ayi. Utuluka apo, nizabwera uza waona tsiku ndi tsiku ufikira pomwe aza tulukira mu chipatala.

Nanga malipiro alipo?

Kulibe kulandira malipiro andalama kapena katundu mwina mwache mphatso muka bvomeredza kuti abale anu atenge mbali mu zofufudza izi. Zaulele zilipo nzochepekera za malipiro a magazi yemwe yaza pimiwa ku labu mu mafufuzo awa poyamba apa. Zonse zina zomwe a dotolo awo azafuna upimiwa ulingana na zopweteka zimene azaona mwa iwo ziza lipiliwa ndi banja lanu monga mu njira imene odwala onse ama pereka zolipira ku chipatala.

Kodi ningasinthe nzelu pa zotenga mbali mu zofufuza izi?

Inde, inu muli nawo ufulu woletsa m'bale wanu upitiliza utenga mbali mwa izi ngakhale kuti mwa bvomereza poyamba. Ngati mwa sintha nzelu mu ndiudze mo masuka bwino ndiponso kulibe zobvuta chifukwa inu muli nawo udindo pa za umoyo wa abale anu. Muka chita tero, a dotolo anu azapitiliza uwa tsamalira munjira imene adziwa bwino monga mwa masiku onse omwe ama sewenzerapo po ona bvuto ya shuga iyi kopanda chilango chili chonse.

Ngakhale kuti inu mwa bvomereza, abale anu ali nawo udindo woletsa upitiliza kutenga mbali mwa fufudzo iyi ngati achirako bwino ufikira pa nthano yothi adziwa zimene ziluchitka. A dotolo ao ndiwo adzawaona nthawi ndi nthawi kuti adziwe ngati odwala anga lamulile okha pa za umoyo wao.

Kodi kufufudza uku kunga bweretse ngozi yotani?

Kufufudza uku kulibe ngozi chifukwa tingo ona chabe m'mene aza chira ndi bvuto yawabweretsa iyi osati uyesa mankhwala yosa ziwika mwa iye ayi. A dotolo awo aza sewenzesa mankhwala yemwe yama sewenza nthawi zonse ku bvuto lawo mu maiko onse.

Koma zowawa pang'ono zilipo uchokera ku ka nsingano kochosera magazi. Nchito imene iyi iza gwiriwa ndi a ka tswiri a dotolo kapena a nasi.

Mafunso

Ngati muli na mafunso yena pa izi, mungathe uni yitana pa lamya kapena ulemba kalata pa

Dr. Mwanja Kakusa,

The University Teaching Hospital,

Department of Internal Medicine,

P/Bag RW1X,

Lusaka, Zambia.

Lamya: +260 955 888 577

Akulu omwe alola zimene ndi fufudza pa phunziro imene iyi alipo. Akulu awa ama yangananso kuti zo fufudza zonse zo khudza za umoyo wa anthu a m'dziko la Zambia ndi zobvomerezeka ndi lamulo la dziko lino. Ngati mwa khudzidwa ndi zina zache mungathe ufunsa kapena ku wa dandaulira ku malo awo a:

ERES CONVERGE

33 Joseph Mwilwa Road

Rhodes Park

Lusaka.

Ma lamya: +260 955 155 633/ +260 955 155 634/ +260 966 765 503

APPENDIX 9: NYANJA SURROGATE CONSENT

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

Ubvomereza utengako mbali mu kafukufuku ka ma phunziro koyangana odwala matenda a dayabetisi ketoasidosisi (kapena kuti shuga yobvuta mu chinyanja chatsopano) mu chipatala cha uth, mu lusaka, dziko la zambia

Ine, wochedwa...……

nawerenga ndi kumvetsetsa bwino za mafufuzo aya ndiponso nda vomereza kuti …….(chibale/chibululu)
……..(dzina la odwala) atenge mbali mu maphunziro awa kopanda kakakamizo.

Nakhala nawo mpata woyankhiwa mokwana mafunso onse pa maphunziro awa. Ndi dziwa kuti m'bale wanga wodwala uyu ali nawo ufulu woletsa upitiliza ukhalamo mu fufuzo imene iyi nthawi ili yonse ngati afuna kuchita tero aka dziwa bwino zimene zichitika atachirako. A dotolo wao aza wapima nthawi ndi nthawi kuti akadziwe ngati achira mokwana ufika poti angathe uzisankhila oka zopitiliza kapena kuletsa upitiliza ndi maphunziro awa.

…….

(Siginecha*)

……

……

(Dzina, udindo, ndi siginecha ya mboni)

Tsiku:

APPENDIX 10: ASSENT INFORMATION SHEET

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

My names are Dr Mwanja Kakusa. I am a Master of Medicine student at the University of Zambia. I am asking you to participate in a research which examines patients with a certain complication of diabetes called diabetic ketoacidosis. My research looks at how patients present to hospital, what leads to the problem and how they fare during their hospital stay.

I am asking you to give some information on your diabetes. I would also like to get some blood and urine for some laboratory tests that are normally used to confirm that one truly has diabetic ketoacidosis. I will continue to monitor how you will be doing as your doctors continue treating you in the ward but will not require any further tests for this research from you.

Your parents or legal guardians have already given permission for you to participate in this study, but you do not have to participate if you choose. You may quit this study at any time by simply writing on the assent form "Stop".

The findings of this research may help in improving the care of patients with this disease. You may experience some discomfort during the blood draw for the tests needed. You will not be given any money or rewards for participating in the study.

Your identity will remain protected as I will not indicate your names on the information sheet. Therefore, none of the research findings will be traced back to you specifically.

If you have any further questions about this research, please contact me on the following:

Dr. Mwanja Kakusa,

The University Teaching Hospital,

Department of Internal Medicine,

P/Bag RW1X,

Lusaka, Zambia.

Mobile phone Number: +260 955 888 577

The committee on ethics which permitted this research can be contacted on the address below if you have any concerns.

The University of Zambia Biomedical Research Ethics Committee,

Ridgeway Campus,

P.O Box 50110,

Lusaka, Zambia.

Telephone: +260-211-256067

APPENDIX 11: ASSENT FROM PATIENTS BELOW 18 YEARS OLD

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

ASSENT FROM PATIENTS BELOW 18 YEARS OLD

I……
have been fully informed of the nature of the study do hereby agree to participating in the said study.

…….

(Signature/Right thumb print)

……

……

(Witness signature, names & profession)

Date:

APPENDIX 12: NYANJA ASSENT INFORMATION SHEET

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

CHIDZIWITSO KWA ODWALA PA NKHANI YOBVOMEREZA UTENGAKO MBALI MU ZOFUFUZA ZA MA PHUNZIRO ZOYANGANA ODWALA MATENDA A DAYABETISI KETOASIDOSISI (KAPENA KUTI SHUGA YOBVUTA MU CHINYANJA CHATSOPANO) MU CHIPATALA CHA UTH, MU LUSAKA, DZIKO LA ZAMBIA

Dzina langa ndine Dr Mwanja Kakusa, sing'anga mu chipatala cha UTH. Mbali ina, ndine wa ma phunziro a Master of Medicine digiri pa University of Zambia.

Makolo anu abvomeredza kuti mutengeko mbali mu zofufuza pa za matenda anu a shuga koma inu muyenera undi udza ngati mwavomerezana nazo izi. Nayamba nda funsa makolo anu chifukwa mukalibe kufika pa musinku wa zaka 18 pomwe mungakhale na udindo wozisankhila nokha kosa phempha munthu wina.

Ndi pempha mu ni lole kuti ni pime inu kuti ni ziwe bwino za matenda anu a shuga yobvuta. Mu maphunziro aya, niwona ma bvuto m'mene yabwerera, ndi zobvuta zimene zioneka mu thupi ngati munthu adwala shuga yobvuta. Ndi yangananso m'mene odwala apolela na zobvuta zimene zibweramo kamba ka matenda pomwe muli mu chipatala.

Zimene ndi zapeza mwa inu pamodzi ndi odwala ena onse a matenda awa zizatithandidza kwambiri monga chipatala, mwina mwache dziko lathu lonse udziwa bwino motsamalira onse odwala bvuto iyi. Zizathandidzanso uziwa bwino zolakwa zimene zingaoneke potsamalira odwala ndi ku sintha zolakwazo. Kuli odwala kopambana ndi zafufudza bwino uwona zopweteka zimene zipeleka matenda pa tsogoro.

Ndi pempha kwainu kuti mundi udze zamatenda yanu uchoka pomwe muna gwiriwa ndi shuga. Nga khale kuti nuyamba ugwiriwa umatenda a shuga tsiku lobwera kuno lalero chabe, inu mu bvomeredzedwa utengako mbali mu kafukufuku aka ngati mwandilola.

Ndiza pempha utengako magazi ang'ono osa pambana ma supuni awili akulu kapena kuti 10 mls na mitundo poyamba apa. Izi ziwiri ziyenera upimiwa bwino ku labu kuti ti dziwe bwino

zobvuta ndi shuga yanu no dzindikira kuti bvuto lanu ndi dayabetisi ketoasidosisi zoonadi osati matenda ena ofananako ayi. Utuluka apo, ndiza bwera uza mionani tsiku ndi tsiku ufikira pomwe mu za tulukira mu chipatala.

Kulibe kulandira malipiro andalama kapena katundu mwina mwache mphatso muka bvomeredza utenga mbali mu zofufudza izi. Zaulele zilipo ndi malipiro a ma testi a magazi na mitundo yemwe yaza pimiwa ku labu mu kafukufuku aka ziliko kamodzi poyamba apa. Zonse zina zomwe a dotolo anu azafuna upimiwa ulingana na zopweteka zimene azaona mwa inu ziza lipiliwa ndi inu monga mu njira imene odwala onse ama pereka zolipira ku chipatala.

Inu muli nawo ufulu woletsa upitiliza utenga mbali mwa izi ngakhale kuti mwa bvomeredza poyamba. Ngati mwa sintha nzelu mu ndi udze mo matsuka bwino ndiponso kulibe zobvuta chifukwa inu muli nawo udindo pa za umoyo wanu. Muka chita tero, a dotolo anu azapitiliza umi tsamarani munjira imene adziwa bwino monga mwa masiku onse omwe ama sewenzerapo po ona bvuto ya shuga iyi kopanda chilango chili chonse.

Kufufudza uku kulibe ngozi chifukwa tingo ona chabe m'mene muza chira ndi bvuto yamibweretsani iyi osati uyesa mankhwala yosa ziwika mwa inu ayi. A dotolo wanu aza sewenzesa mankhwala yemwe yama sewenza nthawi zonse ku bvuto lanu mu maiko onse.

Koma zowawa pang'ono zilipo uchokera ku ka nsingano kochosera magazi. Nchito imene iyi iza gwiriwa ndi a ka tswiri a dotolo kapena a nasi.

Ngati muli na mafunso yena pa izi, mungathe uni yitana pa lamya kapena ulemba kalata pa

Dr. Mwanja Kakusa,

The University Teaching Hospital,

Department of Internal Medicine,

P/Bag RW1X,

Lusaka, Zambia.

Lamya: +260 955 888 577

Akulu omwe alola zimene ndi fufudza pa phunziro imene iyi alipo. Akulu awa ama yangananso kuti zo fufudza zonse zo khudza anthu a m'dziko la Zambia ndi zobvomerezeka ndi lamulo la dziko lino. Ngati mwa khudzidwa ndi zina zache mungathe ufunsa kapena ku wa dandaulira ku malo awo a:

ERES CONVERGE

33 Joseph Mwilwa Road

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Lusaka.

Ma lamya: +260 955 155 633/ +260 955 155 634/ +260 966 765 503

APPENDIX 13: TRANSLATED ASSENT FORM

A STUDY TO DETERMINE THE CLINICAL PROFILE AND MORTALITY PREDICTORS OF ADULT PATIENTS PRESENTING WITH DIABETIC KETOACIDOSIS AT THE MEDICINE DEPARTMENT OF THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

NYANJA ASSENT FROM PATIENTS BELOW 18 YEARS OLD

Ine..……..

na vomera utenga mbali mu mafufuzo awa

……...

(Siginecha)

……

……

(Dzina, signature ndi udindo wa mboni)

Tsiku:

APPENDIX 14: ETHICS COMMITTEE APPROVAL

ERES CONVERGE

33 Joseph Mwilwa Road
Rhodes Park, Lusaka
Tel: +260 955 155 633
+260 955 155 634
Cell: +260 966 765 503
Email: eresconverge@yahoo.co.uk

I.R.B. No. 00005948
F.W.A. No. 00011697

25th September, 2013

Ref. No. 2013-Aug-001

The Principal Investigator
Dr. Mwanja Kakusa
University Teaching Hospital
Dept. of Medicine
P/Bag RW 1X
LUSAKA.

Dear Dr. Kakusa,

RE: A study to determine then chemical profile and mortality predictors of adult patients presenting with Diabetic Ketoacidosis at the Medical Dept. of the UTH in Lusaka, Zambia.

Reference is made to your corrections dated 16th September, 2013. The IRB members resolved to approve this study and your participation as Principal Investigator for a period of one year.

Review Type	Ordinary	Approval No. **2013-Aug-002**
Approval and Expiry Date	Approval Date: 25th September, 2013	Expiry Date: 24th September, 2014
Protocol Version and Date	Version-Nil	24th September, 2014
Information Sheet, Consent Forms and Dates	• English, Nyanja.	24th September, 2014
Consent form ID and Date	Version-Nil	24th September, 2014
Recruitment Materials	Nil	24th September, 2014
Other Study Documents	Data Collection Sheet.	24th September, 2014
Number of participants approved for study	80	24th September, 2014

Specific conditions will apply to this approval. As Principal Investigator it is your responsibility to ensure that the contents of this letter are adhered to. If these are not adhered to, the approval may be suspended. Should the study be suspended, study sponsors and other regulatory authorities will be informed.

Conditions of Approval

- No participant may be involved in any study procedure prior to the study approval or after the expiration date.
- All unanticipated or Serious Adverse Events (SAEs) must be reported to the IRB within 5 days.
- All protocol modifications must be IRB approved prior to implementation unless they are intended to reduce risk (but must still be reported for approval). Modifications will include any change of investigator/s or site address.
- All protocol deviations must be reported to the IRB within 5 working days.
- All recruitment materials must be approved by the IRB prior to being used.
- Principal investigators are responsible for initiating Continuing Review proceedings. Documents must be received by the IRB at least 30 days before the expiry date. This is for the purpose of facilitating the review process. Any documents received less than 30 days before expiry will be labelled "late submissions" and will incur a penalty.
- Every 6 (six) months a progress report form supplied by ERES IRB must be filled in and submitted to us.
- ERES Converge IRB does not "stamp" approval letters, consent forms or study documents unless requested for in writing. This is because the approval letter clearly indicates the documents approved by the IRB as well as other elements and conditions of approval.

Should you have any questions regarding anything indicated in this letter, please do not hesitate to get in touch with us at the above indicated address.

On behalf of ERES Converge IRB, we would like to wish you all the success as you carry out your study.

Yours faithfully,
ERES CONVERGE IRB

Dr. E. Munalula-Nkandu
BSc (Hons), MSc, MA Bioethics, PgD R/Ethics, PhD
CHAIRPERSON

APPENDIX 14: HOSPITAL MANAGEMENT APPROVAL OF RESEARCH

REPUBLIC OF ZAMBIA

MINISTRY OF HEALTH
University Teaching Hospital

P/Bag Rw 1X
Lusaka - Zambia
Tel: +260 211 253947 (Switch Board)
+260 211 251451

Fax: +260 211 250305
e-mail: mduth@yahoo.com

OFFICE OF THE SENIOR MEDICAL SUPERINTENDENT

Our Ref: UTH/HCC/9/8
Your Ref:

9th September, 2013

Dr. Mwanja Kakusa
Department of Medicine
University Teaching Hospital
LUSAKA

Dear Doctor

RE: PERMISSION TO CONDUCT RESEARCH AT THE UNIVERSITY TEACHING HOSPITAL

Reference is made to your letter of 22nd July, 2013 regarding the above subject.

I am pleased to inform you that management has approved your permission to conduct research at University Teaching Hospital in the department of Medicine on the topic:" patients presenting with Diabetic Ketoacidosis at the department of Medicine".

Please liaise with the Head of Department Medicine.

Yours faithfully.

Dr. KOR. Chiyenu
A/Head - Clinical Care
For/ Senior Medical Superintendent
UNIVERSITY TEACHING HOSPITAL

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