

Evaluation of the Occurrence of Acute Hyperglycemia and its Association with Outcome in Patients with Severe Burns Hospitalized at KNH.

A dissertation submitted as part fulfillment of the requirements of the University of Nairobi for award of the degree of Master of Medicine (MMed) in General Surgery.

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DECLARATION

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I hereby declare that this study is my original work and has not been presented at any other university;

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DEDICATION

This work is dedicated to:

My dear wife and son for their patience during the long hours of absence as I under took this study.

My parents for their encouragement since my early childhood.

ACKNOWLEDGEMENT

This work could not have been possible without the work of the following:

The ever-supportive supervisors Dr. J. K. Wanjeri and Dr. P.W.L. Ndaguatha who tirelessly guided me throughout the period of the study - I am sincerely grateful for their support.

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My statistician, Mr. Ayeko of KEMRI for his guidance.

I cannot forget to thank the burns patients admitted at the burns unit KNH who participated in the study and for those that passed on, may God rest their souls in eternal peace.

To all those who participated in any way to the success of this study, I give my thanks to you all and may you be blessed abundantly.

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ABSTRACT

Background

Hyperglycemia is one of the most prominent features of the hyper-metabolic response among patients suffering major burn injury. It has been associated with poor outcome in patients with severe burns and other major trauma, while early recognition and treatment of this profound metabolic change has been shown to improve clinical outcome. This study aimed at evaluating whether hyperglycemia is associated with the high morbidity and mortality observed in patients with severe burns admitted at Kenyatta National Hospital (KNH), burns unit. This was with the aim of providing recommendations for glycemic control in these patient population.

Objectives

To evaluate the occurrence of acute hyperglycaemia and its association with outcome in patients with severe burn injury, hospitalized at Kenyatta National Hospital.

Materials and Methods

The study was a prospective cross-sectional descriptive study, carried out at the Kenyatta National Hospital (KNH).

The patients who met the inclusion criteria were recruited into the study for a period of 6 months, and a structured questionnaire was used to collect data. Random blood sugar samples were collected and analyzed in the first week of the study. Patients were followed-up and assessed for duration of hospital stay and mortality.

Data was analyzed using univariate and multivariate analysis methods and presented through graphs, charts and tables.

Results

The mean blood glucose increased with time from 6.4 mmol/ l on day 1 to an average of 9.6 mmol/ l on day 7. The percentage of patients with hyperglycemia increased from 9.1% to 51.1% ($p < 0.001$). Further increase in prevalence of hyperglycemia on day 7 was noted but this increase was not significant compared to day 3 ($p = 0.87$).

The case fatality for burn patients with hyperglycemia at KNH burns unit was 24%. Mortality was persistently higher among patients with hyperglycemia in all 3 days compared to the patients with normo-glycaemia, [day 1 (55.6%) v/s (20%) ($p = 0.029$), day 3 (22.9%) v/s (15.2%) ($p = 0.34$) and day 7 (19.6%) v/s (9.5%) ($p = 0.24$)]. The presence of hyperglycemia on day 1 was significantly associated with reduced duration of burns unit stay ($p = 0.026$), while the Hyperglycemia on day 3 or 7 did not predict duration of hospital stay with median duration of stay of between 10 days and 15 days.

Conclusion

From the study, it is clear that hyperglycemia is associated with increased morbidity and mortality among patients admitted with severe burns at KNH. Therefore, there is a need to institute regular monitoring of blood sugar levels among patients with severe burns and give appropriate treatment for those found with deranged blood sugar levels.

LIST OF ABBREVIATIONS/ACRONYMS

TBSA-	Total Burnt Surface Area
ABA-	American Burn Association
SIH-	Stress Induced Hyperglycemia
KNH-	Kenyatta National Hospital
IL-	Interleukin
ICU-	Intensive Care unit
NICE-SUGAR-	Normoglycemia in Intensive Care Evaluation–Survival Using Glucose Algorithm Regulation
LMIC-	Low and Moderate Income Countries
SPSS-	Statistical Package for Social Sciences
DIGAMI-	Diabetes Mellitus Insulin-Glucose Infusion in Acute Myocardial Infarction

DEFINITION OF OPERATIONAL TERMS

Counter regulatory hormones: hormones which antagonize the effects of insulin; (catecholamine, glucocorticoid, glucagon, and dopamine)

Gluconeogenesis: glucose synthesis from amino acids and lipids e.g. lactate, alanine and glycerol

Glycogenolysis: glycogen breakdown to release glucose

Intensive (tight) glucose control: target of 81 to 108 mg per deciliter (4.5 to 6.0 mmol/liter).

Conventional glucose control: target of 180 mg or less per deciliter (10.0 mmol/liter or less).

Burns: Partial or full-thickness

Young or old: <10 or >50 years old

Adults: >10 or <50 years old.

Next of kin: patient's husband or wife, parent or the guardian

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INTRODUCTION

Burn injury represents one of the most devastating conditions encountered in medicine and represents an assault on all aspects of the patient, from the physical to the psychological^(1, 2). It affects persons of all age groups, from the very young to the elderly and it is a major cause of global public health crisis. It is the fourth most common type of trauma worldwide, following road traffic accidents, falls, and interpersonal violence⁽³⁾.

Approximately 90 percent of burns occur in low to middle income countries, regions that generally lack the necessary infrastructure to adequately care for and reduce the incidence and severity of burns⁽⁴⁾. The incidence of burns injury in the low and middle income countries is 10 times higher than in high income countries⁽⁵⁾.

All trauma victims experience a hyper-metabolic response but in major burn trauma the severity, duration and magnitude of the response is uniquely severe. The hyper-metabolic response is characterized by among other features massive protein, lipid catabolism and stress induced hyperglycemia. Early recognition and treatment of these profound metabolic changes has been shown to improve clinical outcome⁽⁶⁾.

Hyperglycemia is one of the two most prominent features of the hyper-metabolic response and it invariably occurs in most patients with severe burns. Previously, this hyperglycemia was perceived to be a 'normal' response to the severe trauma and thus it was thought that intervention was not needed. Recent studies have however established that there is an association between hyperglycemia and poor outcome in patients with severe trauma including severe burns, and other critically ill patients. Therefore, the current thinking leans towards aggressive detection and management of Stress-Induced Hyperglycemia (SIH), with the aim of reducing the associated complications and improve outcome in patients with severe burns. The results so far are encouraging showing improved outcome in patients put on hyperglycemic control treatment. Nevertheless, there are still many un-answered questions regarding the management of the stress induced hyperglycemia before it can be universally accepted and adopted as a standard treatment⁽⁷⁾. Some of these un-explained questions include:

What should be the level of hyperglycemia at which intervention is necessary?

What is the optimal blood glucose control required to achieve optimal improved outcome in patients with severe burns?

Should we use intensive or conventional glyceic protocols in the management of SIH?

The use of intensive insulin is associated with increased risk of hypoglycemic events (up to 30%). Does this translate to increase in mortality and morbidity?

What is the role of oral hypoglycemic agents (e.g. biguanides, fenofibrates and glitazones) in management of SIH knowing that the risk of hypoglycemia is minimal with these agents?

STATEMENT OF THE RESEARCH PROBLEM

An average of 800 burn patients are hospitalized at the Kenyatta National Hospital (KNH) every year.

The mortality of burn patients hospitalized at the Kenyatta National Hospital (KNH) is high at 14-36% ^(14, 15). Ninety percent of the deaths occur in patients admitted with major thermal injury (KNH Medical records).

Increased morbidity and mortality in patients with severe burns has been associated with SIH in other parts of the world ⁽²⁰⁾. The study aimed at establishing whether hyperglycemia was associated with the high morbidity and mortality observed in our setting.

LITERATURE REVIEW

Epidemiology

The discovery of fire has given man great advancement in food preparation and industrial development. However, on the other hand it has brought with it a great deal of misery through thermal injury⁽⁸⁾.

Burns are a common medical problem that occur all over the world. The mean worldwide incidence of fire-related injuries in 2004 was estimated to be 1.1 per 100,000 population, with the highest rate in Southeast Asia and the lowest in the Americas⁽³⁾. The incidence of burns in low and moderate-income countries is 1.3 per 100,000 populations; this is 10 times higher compared with an incidence of 0.14 per 100,000 population in high income countries⁽³⁾.

Locally, Gome and colleagues in their study on paediatric trauma at (KNH) reported that burns accounted for the highest single cause of trauma admission at 34.8%⁽⁹⁾.

Over 1 million people in the USA have a burn injury each year but the majority are minor burns which are disabling never the less. In 2008, burns sustained at home accounted for 65.5% of all burn injuries in the United States, with a mortality rate of 4% overall. It is estimated that approximately 75% of the deaths from burns and fires in the United States occurred either at the scene of the incident or en route to medical facilities⁽¹⁰⁾.

About 90% of burns worldwide occur in developing countries and 70% of these are in children. Survival of burn injury patients with 40% Total Body Surface Area (TBSA) is rare in the developing countries⁽¹¹⁾. While in developed countries patients with burns of $\geq 90\%$ TBSA are reported to survive⁽¹²⁾.

Local studies have shown that burns constitute 3% of all injuries seen in hospital, but burn injury associated mortality rate is much higher when compared with other causes of trauma ⁽¹³⁾. In his study on outcome of moderate and severe thermal injuries at KNH, Okonjo reported a mortality rate of 36%⁽¹⁴⁾. While Nthumba, in his study on outcome of moderate and severe thermal injuries at KNH, reported mortality rate of 14.4% ⁽¹⁵⁾. In Nthumba's study, 68.9 % of deaths occurred within the first week of admission, with another 12 % dying in the second week. Those who died

had an average of 50.4% TBSA and he reported that 60 of the 85 patients admitted into the Burn Unit died.⁽¹⁵⁾ Data from medical records at KNH for last five years show mortality rate ranging between 18-20%. In his recommendations Nthumba noted the need to optimize care in patients with moderate to severe burns in order to reduce the high mortality rate⁽¹⁵⁾. These mortality rates are significantly higher compared to the 4% mortality rate in the United States (US).

Gerd et al in his report revealed a 50% decline in burn-related deaths and hospital admissions in the (US) during the previous 20 years mainly because of effective prevention strategies, decreasing the number and severity of burns. Advances in therapy strategies, based on improved understanding of resuscitation, enhanced wound coverage, more appropriate infection control, improved treatment of inhalation injury, and better support of the hyper metabolic response to injury have further improved the clinical outcome of this unique patient population⁽¹⁶⁾.

The adverse effects of severe burn injury involve many organ systems in the body leading to increase in morbidity and mortality. Among the causes of increased morbidity and mortality is the hyper-metabolic response which is similar to what occurs in other forms of trauma or major illness but the magnitude, severity and duration is unique in the severely burnt patients^(6,17).

The hyper-metabolic response is characterized by a massive protein and lipid catabolism, total body protein loss, hyper-dynamic circulation, muscle wasting, increased energy expenditure, increased body temperature, increased infection risks, stimulated synthesis of acute phase proteins located in the liver and intestinal mucosa and peripheral insulin resistance and hyperglycemia,. Early recognition and treatment of these profound metabolic changes has been shown to improve clinical outcome⁽⁶⁾.

The two most prominent components of the stress response to severe burn injury are hyperglycemia and muscle protein catabolism⁽¹⁸⁾. Raised glucose levels were first linked to trauma around 150 years ago when Claude described a state of “diabète traumatique” during hemorrhagic shock^(16,19). Ever since, multiple studies have documented hyperglycemia after severe trauma including burns, myocardial infarction, stroke or surgery. For a long time the treatment of this condition has been expectant with the belief that this is a normal physiologic fight and flight response, and therefore no treatment is required. During the past few years however, multiple studies have suggested that trauma induced hyperglycemia may be of serious

clinical concern as it has been frequently linked to increased muscle protein catabolism, impaired wound healing, increased incidence of infections and increased skin graft loss. All these factors contribute to increased morbidity and mortality⁽¹⁶⁾.

Effects of hyperglycemia in burned patients

Hyperglycemia in the burn patient was considered a physiological response to thermal injury, which should be left untreated. It was postulated that blood glucose levels usually return to normal spontaneously without any detrimental effect. This is reflected in the conventional guidelines for treatment of hyperglycemia, which include acceptance of blood glucose levels up to 215 mg/dl before insulin therapy is commenced. However, recent studies suggest that hyperglycemia and insulin resistance are harmful and that correcting blood glucose to normal levels with insulin might improve the prognosis significantly and reduce mortality rates⁽²⁰⁻²³⁾. Burn injury patients with poor glucose control have been shown to have poorer outcomes in terms of morbidity and mortality. Several studies have demonstrated an association between hyperglycemia and increased risk of infections e.g. wound infection, pneumonia, bacteremia, and sepsis^(21, 24, 25).

Evidence indicates that hyperglycemia leads to glycosylation of plasma proteins, which include the immune proteins and once glycosylated they become inactive. Hyperglycemia also impairs phagocytic action of macrophages and neutrophils. It also impairs some cytokines production and thus increasing the risk of infection and sepsis⁽²⁶⁻²⁸⁾. Hyperglycemia in major burn patients is also associated with an increase in muscle protein breakdown which also provides a possible mechanism for the observed relationship between hyperglycemia to detriments in wound healing and immune function⁽¹⁸⁾. Studies in pediatric population have also demonstrated an association of hyperglycemia with positive blood cultures, reduced graft take, prolonged hospital stay and increased mortality^(24, 25).

Hyperglycemia acutely increases circulating pro-inflammatory cytokines (plasma IL-6, TNF α , and IL-18) concentrations by an oxidative mechanism⁽²⁹⁾. These proinflammatory mediators may worsen damage to tissues. Even though the study was done in diabetics and patients with glucose intolerance, the same may apply to burns hence increasing the morbidity.

Admission hyperglycemia was also demonstrated to independently predict increased admission to Intensive Care Unit (ICU), increased hospital length of stay and mortality in the trauma population⁽³⁰⁾. It would be interesting to find out if that is also true for burns patients. It may provide a simple easily available and cheaper tool for prognosticating our burns patients.

Management options for the hyperglycemia

One of the most important advances, for the improvement of morbidity and mortality in major burn patients, has been the manipulation of the profound metabolic response to burns injury⁽¹⁰⁾.

Glycemic control is reported to lower the incidence of sepsis and bacteremia⁽³¹⁾. However, the optimal target of blood glucose control required to achieve these desired outcomes has not been determined. The looming debate is whether to institute tight glycemic control protocol, or the conventional protocol. Two landmark studies provided evidence of a marked benefit in survival outcome for ill patients with tight glucose control. Malberg et al looked at patients with acute myocardial infarction in the DIGAMI 1 trial. They found a significant reduction in the level of mortality (29% reduction, $p=0.027$)⁽³²⁾. The study could however not specifically attribute the reduction in mortality entirely on intensive insulin therapy. Van den Berghe et al looked at patients in a surgical ICU setting, and also demonstrated a remarkable improvement in outcome in terms of survival (34% mortality reduction, $p<0.04$). The authors also found reduced rates of septicemia, renal impairment requiring dialysis, transfusion requirements and length of stay in the ICU⁽²⁰⁾. The results appeared so significant that there was some extrapolation of the results and tight glucose control was recommended for different groups of critically ill patients largely based on the later study. Unfortunately, attempts to replicate the survival benefit of the original study have been unsuccessful and even achieving the recommended degree of control of hyperglycaemia has proven difficult. All of the studies have shown that attempts at strict control of glucose are associated with increased episodes of hypoglycemia and some studies have suggested a worse outcome for the patients in the intensive treatment arm. An example of such a study is the NICE-SUGAR Study, an international multi-center study involving 6104 patients at 42 centers. Patients admitted to ICUs were randomized to tight control (4.5–6 mmol/l) or conventional treatment (<10 mmol/l). Mortality rates were 27.5% in the tight group vs. 24.9% in the conventional group⁽³³⁾.

Other studies have used different blood sugar levels to assess improved outcome. These include a study by Holm et al who reported reduced mortality with glycemic control between 10 to 11 mmol/l⁽²¹⁾. Hemmila et al on the otherhand reported reduced risk of infection and morbidity with glucose control below 6.7 mmol/l and Finney et al reported reduced mortality with glucose control ≤ 7.8 mmol/l^(34, 35).

Meta-analyses regarding glucose control include the Griesdale meta-analysis and the Weiner meta-analysis^(22, 23). None of the two meta-analyses demonstrated any mortality benefit of intensive insulin therapy (tight glycemic control) over the conventional therapy group of patients and at the same time, tight glycemic control was associated with increased risk of hypoglycemia. The Griesdale meta-analysis suggested that there might be some benefit of glycemic control in surgical ICU patients, although this was largely due to the Van den Berghe study results. Subgroup analysis of other studies including the NICE-SUGAR trial did not demonstrate improved survival in surgical ICU patients receiving intensive insulin control⁽³⁶⁾.

As evidenced in the above two meta-analyses, the major concern of tight glucose control is hypoglycemia with an incidence of up to 30% in both surgical and medical critically ill patients^(22,23). Nevertheless, the severely burnt patient may be at a much higher risk of hypoglycemic events due to increased metabolic rate, frequent surgeries and dressing changes. Hence, this raises some challenges in recommending use of intensive insulin therapy on this patient population.

Beneficial effects of insulin in the body are far and beyond its role on glucose control and include positive effect on both innate and acquired immunity; protection against bacterial invasion and translocation of bacteria through the gastrointestinal mucosa and skin, thus potentially increasing infection rates. It also enhances wound healing and inhibits the production of pro-inflammatory mediators, which may delay healing by inducing prolonged inflammation⁽⁷⁾.

Metformin an oral anti-hyperglycemic agent has also been used in trials in patients with burns and in patients who are severely ill. Its mechanism of action include decreasing glucose levels by improving insulin sensitivity and decreasing hepatic gluconeogenesis by as much as 75%. Such actions are directly antagonistic to those metabolic abnormalities associated with the hypermetabolic response to injury. Thus, metformin may provide much more direct

improvement in glucose control after major injury. Studies in patients with diabetes also suggest that metformin is not associated with hypoglycemia, thus possibly eliminating this concern associated with the use of exogenous insulin. Additionally, the other advantages of metformin is that it is orally administered and its prolonged action may allow for a reduction in the frequency of glucose monitoring required⁽³⁷⁾.

In Summary, hyperglycemia in severe trauma patients including severe burn injury patients is a complex and multifaceted phenomena. There is definite association between hyperglycemia and increased mortality in major burn patients. There is also increase in morbidity associated with increased infection (local and systemic), reduced graft take, length of ICU and hospital stay in hyperglycemic patients.

The available evidence indicate possible benefit of glucose control in critically ill and severe burns patients who are hyperglycemic but there is currently no consensus on whether to use intensive or convectional glycemc control protocols. There is therefore an urgent need to do studies locally and in other developing countries to clarify these issues which are not clear and which remain unresolved. This is because developing countries shoulder most of burn injury burden with the highest mortality rate.

STUDY JUSTIFICATION

Despite aggressive and optimal resuscitation in addition to other subsequent management protocols of severely burnt patients, the mortality rate in our institutions is still very high with most deaths occurring in the acute period. Studies in burns patients that evaluate the effect of glycemic control on morbidity and mortality have yielded conflicting results. This is in relation to the level of glucose control using convectional versus tight glucose control. Due to these, burn centers around the world do not have agreed protocols on how to manage hyperglycemia in burns and other severe trauma, and our institution is no exception. Consequently, most of these looming questions need to be answered by studies done mostly in developing countries as they shoulder the majority (90%) of burn injuries. No studies have been done to assess the pattern of hyperglycemic control in burnt patients locally. Therefore, this study aims to evaluate the occurrence of early hyperglycaemia and its association with clinical outcome at KNH. The findings will provide a foundation for further interventional studies in the management of stress induced hyperglycemia.

STUDY QUESTION

Is stress-induced hyperglycemia associated with increased morbidity and mortality in patients with major burns admitted at KNH?

OBJECTIVES

BROAD OBJECTIVE

To evaluate the occurrence of acute hyperglycaemia and its association with outcome in patients with severe burn injury hospitalized at Kenyatta National Hospital.

SPECIFIC OBJECTIVES

- To assess the pattern of blood glucose levels in severely burnt patients in the acute period.
- To evaluate whether there is an association between the level of blood glucose and outcome in severely burnt patients.

METHODOLOGY/MATERIALS & METHODS

STUDY DESIGN

This was a descriptive prospective cross-sectional study, running for a period of 6 months from June 2012 to December 2012.

STUDY SITE

The study was conducted at the Kenyatta National Hospital, a National Referral Hospital and the teaching hospital of the University of Nairobi.

STUDY POPULATION

Patients with severe burns (≥ 30 % TBSA) admitted at KNH burns unit.

SAMPLING

Non-random convenient sampling of patients who met inclusion criteria until sample size was obtained.

Burns patients admitted at KNH Burns Unit who qualified to be included were required to give informed consent. However, patients who were unable to sign due to nature of injury or age had their consents taken from next of kin.

The next of kin included the patient's husband, wife, parent or the guardian accompanying the patient.

Principal investigator/trained assistants collected data and blood sample for random blood sugar testing. The trained assistants were postgraduate students in general surgery rotating in burns unit.

SAMPLE SIZE CALCULATION

Ndungu in his study on the value of abbreviated burns severity score index in predicting outcome of patients' with severe burns found that patients with more than 30% TBSA constituted 15% of all burns patients admitted at KNH ⁽³⁸⁾.

Sample size was calculated using the following formula:

$$n = \frac{t^2 \times p(1-p)}{m^2}$$

Description:

n = required sample size

t = confidence level at 95% ($t^2 = 1.96$)

p = estimated prevalence of severe burns ($\geq 30\%$ TBSA) in patients admitted at KNH = 15%

m = margin of error at 5% (standard value of 0.05)

$$n = \frac{1.96 \times 0.15(1-0.15)}{0.05 \times 0.05} = 99.96$$

The sample size was **100**.

INCLUSION CRITERIA

Patients with severe burns ($\geq 30\%$ TBSA) admitted at KNH burns unit, who signed the informed consent form.

EXCLUSION CRITERIA

Refusal of patient or patients' next of kin to sign informed consent.

Patients who were known diabetics at admission

Patients with renal disease at admission

Patients with liver disease

Patients with less than 30% TBSA

Determinant variables

Blood sugar levels.

Outcome variables

- Mortality.
- Length of burns unit stay.

Confounding factors

- Inadequate, poor or delayed resuscitation.
- Infection.
- Inhalational injury.
- Age of patient.

Biases and assumptions

- Non-randomized sampling technique.
- Patients had normal blood glucose levels before the trauma.
- Outcomes associated with the determinant variable.

Quality assurance measures

- Random blood sugar test was done using coded glucoStix strips.
- Before using a pack of glucoStix, control electrode, which comes with the specific pack, were used to calibrate the glucometer so that the control code on the glucometer matches the glucoStix code.
- Before running the test, it was confirmed that the glucoStix code matched that of the glucometer machine.

Data was collected from patients or their relatives using a structured questionnaire. (Appendix I)

Total Burnt Surface Area was determined using the Lund and Browder chart. (Appendix V)

Patients were followed up until official discharge from the burns unit: either to ward 4D or direct discharge home. They were assessed for duration of stay in burns unit and the outcome i.e. dead or alive.

DATA ANALYSIS AND PRESENTATION

Data was collected using a structured questionnaire and the collected data was entered into the Statistical Package for Social Sciences version 17.0 (SPSS 17.0). It was cleaned for errors, inconsistent (conflicting) answers, missing entries and duplicate entries to ensure high quality data.

Descriptive univariate analysis of data on socio-demographic characteristics (age, gender, educational level, marital status) was analyzed and presented using percentages, frequency tables, pie charts and graphs.

Univariate analysis on TBSA and RBS was done and the results presented by use of measures of distribution like frequency distribution tables, measures of central tendency like mean & median measure of dispersions (range and standard deviation),

Multiple linear regression analysis to compare RBS with length of hospital stay (continuous variable) was done after adjusting for age, gender and TBSA; whereas multiple logistic regression analysis was done to compare RBS with mortality (dichotomous variable) after adjusting for age, gender and TBSA.

All statistical tests were performed at 5% significance level with 95% confidence limit.

STUDY LIMITATION

There are many factors which contribute to burns morbidity and mortality and consequently it is difficult to wholly attribute the outcome to the patients' blood glucose level. Hence, the study could only establish an association.

RESULTS

One hundred burn patients admitted to KNH burns unit department between June 2012 and December 2012 were included in the analysis. The analysis of the basic characteristics of these patients are presented below:

i. Patient age

The age of the burn patients ranged from 5 months to 67 years and the average age of admissions with burns at KNH was 18.2 (± 15.6) years. Table 1 shows frequency of burn presentation among children under five, older pediatric age group (5-18 years), and adults. Most (33%) of the burn patients were children aged below 5 years. Young adults aged between 18-29 years were the second most commonly affected age group accounting for 28 (28%) of all burns admitted to KNH.

Table 1: Percent age distribution of burn patients at KNH burns unit

	Frequency (n)	Percent
Age group		
5 months - 4 years	33	33
5 - 18 years	16	16
18 - 29 years	28	28
30 - 39 years	15	15
40 years and above	8	8
	100	100.0

ii. Gender

Males accounted for 53 (53%) out of the 100 burn patients at KNH burns unit (Figure 1). The proportion of male patients 53% (95% CI 43% to 62.9%) was not significantly higher than that of female 47% (95% CI 37% to 57%), patients ($P = 0.55$) with a Male-to-Female ratio of 1: 1.1.

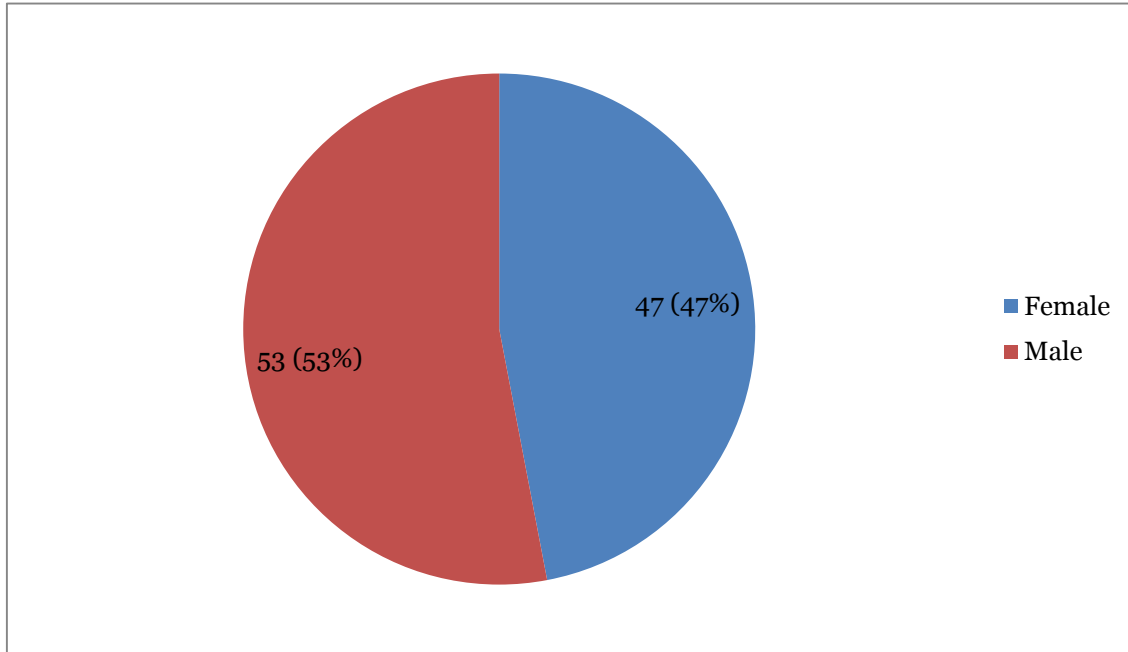


Figure 1: shows gender distribution of the burns.

iii. Education level

Figure 2 shows the percent distribution of the burn patients according to level of education. Most (49%) patients had no formal education and thirty-three (67.3%) of these patients with no formal education were aged below 5 years and had therefore not attained the age for attending formal education. Most of patients who attended formal education had basic primary level education.

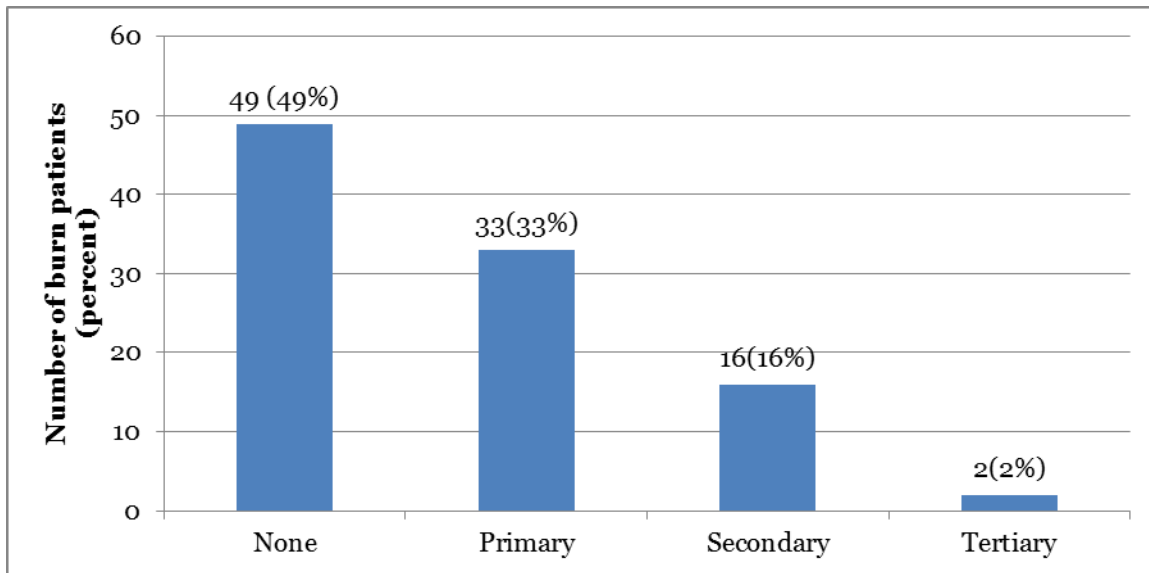


Figure 2: shows the percent distribution of the burn patients according to level of education.

iv. Extent of Burn (Body surface area Burnt)

The TBSA among burn patients ranged from 30% to 90%. The distribution of burn injury according to TBSA is presented in Figure 3. Seventy-two (72%) patients had TBSA between 30 and 40%. TBSA above 40% were less common compared to below 40%, and cumulatively 28 (28%) patients had TBSA greater than 40% (Figure 3).

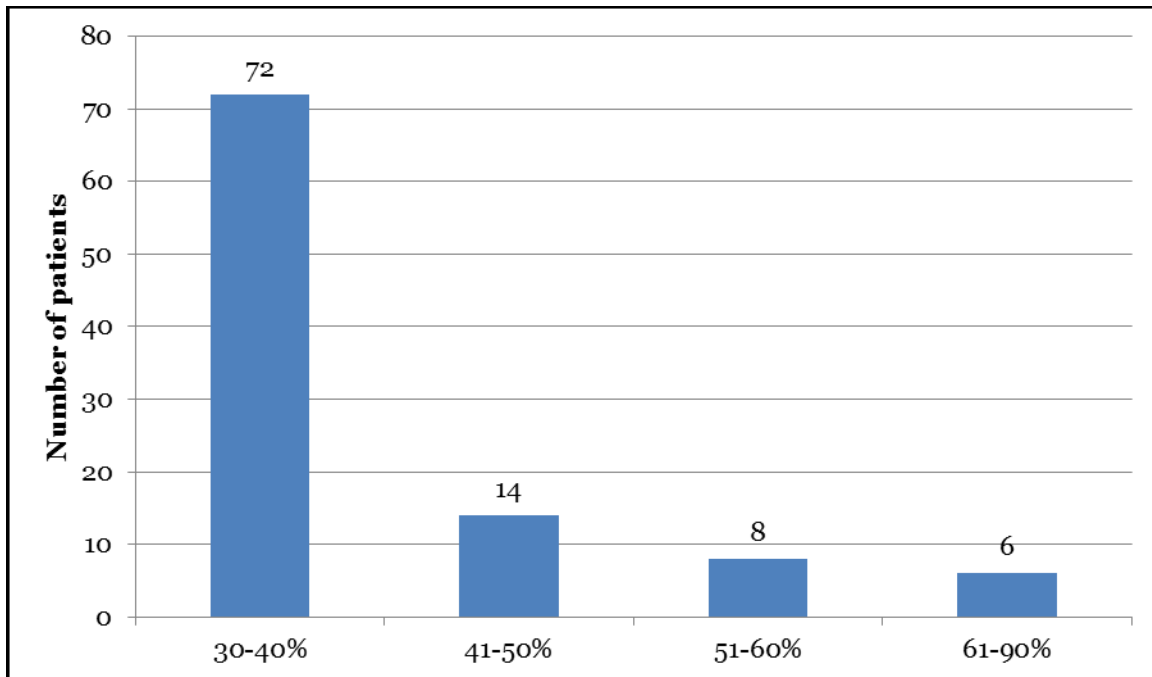


Figure 3: Distribution of burn injury based on TBSA among patients at KNH

v. Types of burn injury

Table 2 shows the type of burns injury patients presented with to hospital. The type of burn injury showed a statistically significant association with age (ANOVA $F = 33.1$, $p < 0.001$). The average age of patients with scald (4.3 years) was lower than that of patients presenting with either electrical injuries (20.8 years) or burn injuries secondary to flames (25.8 years).

The type of injury was not significantly associated with gender ($p = 0.40$) or the depth of burns ($p = 0.15$).

Table 2: Types of burn injury among patients at KNH

	N	Mean Age	SD
Type of burn injury			
Scald	33	4.3	7.3
Open flame	57	25.8	14.5
Electrical	10	20.8	10.4

vi. Other Characteristics of burn injuries among patients at KNH

Table 3 presents the additional details of burn injuries among participants. The home was the most common setting within which burns occurred with 80 (80%) of injuries occurring at home, followed by the workplace where seven (7%) of burn injuries were sustained.

According to types of burns, flames caused more than one-half (57%) of all burns and scalds accounted for one-third of all burns (33%). Inhalation injuries were reported in 56% of patients and 40% of patients had full-thickness burns.

Table 3: Characteristics of burn injuries among patients at KNH

	Frequency (n)	Percent
Inhalation injury		
Yes	56	56
No	44	44
Full thickness burn		
Yes	40	40
No	60	60
Setting of injury		
Home	80	80
Workplace	7	7
Mob justice	3	3
Blasts	2	2
Other	9	9

vii. Blood glucose levels

Table 4 shows the random blood sugar levels for all patients available during day 1, 3 and 7. The mean blood glucose increased with time from 6.4 mmol/ l on day 1 to an average of 9.6 mmol/ l on day 7.

Table 4: Random blood sugar values among burn patients at KNH

	N	Mean	SD	Minimum	Maximum
Random blood sugar					
Day 1	100	6.4	1.8	1.8	13.1
Day 3	94	8.7	2.6	2.6	17.8
Day 7	88	9.6	3.6	1.8	17.4

There was a statistically significant difference in RBS levels between day 1 and day 3 among the 94 patients with measures on both days (difference 2.3 [95% CI 1.9 to 3.0] mmol/ l, $p < 0.001$). Similarly, blood sugar levels increased significantly between day 3 and day 7 (difference 1.0 [95% CI 0.4 to 1.7] mmol/L, $p = 0.001$).

Figure four shows a significant increase in hyperglycemia (RBS > 8.4 mmol/ l) between day 1 and day3 (p < 0.001). The percentage of patients with hyperglycemia increased from 9.1% (95% CI 3.3 to 14.6) to 51.1% (95% CI 41 to 61). Further increase in prevalence of hyperglycemia on day 7 was noted but this increase was not statistically significant compared to day 3 (p = 0.87).

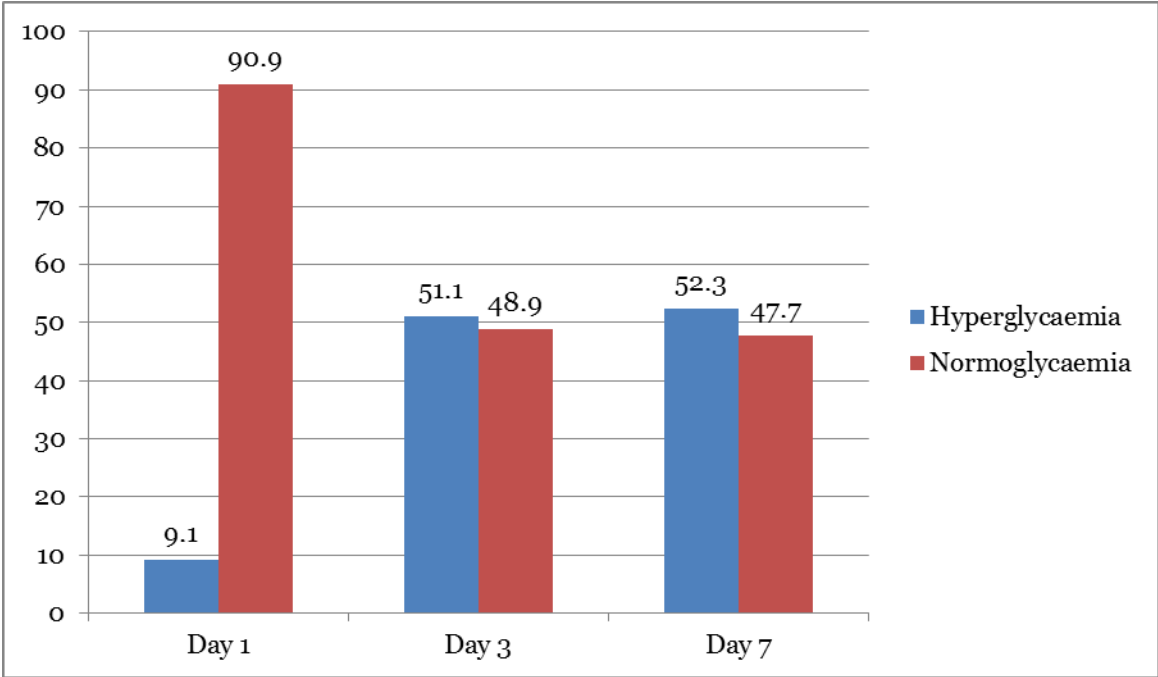


Figure 4: Prevalence of hyperglycaemia (RBS >8.4 mmol/l) in burn patients at KNH

viii. Hyperglycemia and Mortality

The case fatality for burn patients with hyperglycaemia at KNH burns unit was 24%. The mortality rate among patients with hyperglycemia on day 1, 3 and 7 was higher (55.6%, 22.9% and 19.6% respectively) than the mortality rate for patients who had normo-glycaemia (20%, 15.2% and 9.5%) (Table 5). Mortality showed statistically significant associations with hyperglycemia on day 1 ($p = 0.029$). However the higher mortality rates observed among patients with hyperglycemia on day 3 and 7 were not statistically significant [day 3 ($p = 0.34$) or day 7 ($p = 0.24$)].

Table 5: Mortality rates among burns patients at KNH according to random blood sugar levels on day 1, 3 and 7

	Alive (n = 76)	Died (n = 24)
Day 1		
Normoglycemia	72 (80%)	18 (20%)
Hyperglycemia	4 (44.4%)	5 (55.6%)
Day 3		
Normoglycemia	39 (84.8%)	7 (15.2%)
Hyperglycemia	37 (77.1%)	11 (22.9%)
Day 7		
Normoglycemia	38 (90.5%)	4 (9.5%)
Hyperglycemia	37 (80.4%)	9 (19.6%)

ix. Hyperglycemia and duration of stay in burns unit

The presence of hyperglycemia on day 1 was statistically significantly associated with duration of hospital stay ($p = 0.026$). Hyperglycemic patients on day 1 had a short duration of hospital stay (median = 4.5 days) compared to normoglycaemic patients (median = 12.5 days), Table 6. As reported in Table 5, 55.6% of hyperglycemic patients died explaining the short duration of hospital stay in this group. Hyperglycemia on day 3 or 7 taken after early deaths had occurred, did not predict duration of hospital stay with median duration of stay of between 10 days and 15 days.

Table 6: Median duration of hospital stay according to random blood glucose level in burn patients at KNH

	Median duration of stay	Interquartile range
Day 1		
Normoglycaemia	12.5 days	6-21 days
Hyperglycaemia	4.5 days	2.5-9.5 days
Day 3		
Normoglycaemia	10 days	6-20 days
Hyperglycaemia	13 days	7-22.5 days
Day 7		
Normoglycaemia	10 days	6-22 days
Hyperglycaemia	15 days	7-22 days

DISCUSSION

Stress induced hyperglycemia has been associated with increase in morbidity and mortality among patients with severe trauma and severely ill medical patients. However, most of the available literature on stress-induced hyperglycemia post- burn injury have been conducted in developed world. This study is distinct among other reports in the literature, for its setting in a developing country with unique characteristics, challenges and with the largest burden of burns injury⁽³⁻⁵⁾.

A bimodal peak pattern of burn injury was observed with the first peak being among infants and children below 5 years at 33% and the second involving young adults (18-29 years) at 28%. This is in keeping with findings from other parts of Africa and the world. A retrospective review of 139 studies on burns epidemiology over a period of 27 years showed that under 5 years children comprised a majority of all burn patients^(39, 40). Nderitu S in his study on the epidemiological pattern, risk and safety awareness at KNH reported an incidence rate of 48.6%. The percentage of burns children below 5 years is higher in Nderitu's study probably due to the inclusion of mild burns patients who were not included in this study. There is therefore a need to increase both primary and secondary prevention campaigns to reduce the high rates of burns in children in which most of the causes are preventable. The second peak in young adult is probably due to increased exposure to hazard, employment, as well as risk-taking⁽¹³⁾.

The proportion of male patients 53% (95% CI 43% to 62.9%) was not significantly higher than that of female 47% (95% CI 37% to 57%) patients ($P = 0.55$) with a Male-to-Female ratio of 1: 1.1. Other studies have reported varied gender differences, largely based on age and socio economic status. Studies from Egypt and India have reported high morbidity and mortality in women of reproductive age group, whereas higher cases are reported among males in Argentina, Thailand, Uruguay and Saudi Arabia^(41, 42, 43, 44).

Children under the age of 5 years comprised two thirds of patients with no formal education this is because they had not attained the school going age. Never the less only 16% of sampled patients had attained secondary school education and above. The low literacy level is among the low socioeconomic factors which are known to increase risk of burn injury. Other factors include; overcrowded household, unemployment, single parent and low house hold income⁽⁴⁵⁾.

As for the severity of burn injury the majority of patients (72%) had TBSA of between 30-40% while the rest burn injury of between 41-90%. Fifty six percent of patients had inhalational injury, while 40% of patients had deep burns. Extent and depth of burn injury and presence of inhalational injury are known to increase morbidity and mortality in burn patients ⁽⁴⁶⁾. Due to these factors among others only an association between hyperglycaemia and mortality could be deduced from the study rather than a cause and effect relationship.

The average age of patients with scald (4.3 years) was lower than that of patients presenting with either electrical injuries (20.8 years) or burn injuries secondary to flames (25.8 years). In Forjuoh study, scalds was also the main cause of burns in children below 5 years at 45% ⁽⁴⁷⁾. While Shields B.J. and others from US also reported similar results ⁽⁴⁸⁾. United States National burns repository report, showed that flame burn was the overall main cause of burns at 42%. This is lower than our results finding in which flame burns was the cause of 57% of all burn injury ⁽⁴⁹⁾. This is probably due to the rural setup, with more exposure to open flame and stove for cooking, candles and lanterns. Other factors that may contribute include use of flammable house materials, storage of volatile and flammable fuels and smaller housing units.

The percentage of patients with hyperglycaemia (RBS >8.4mmol/l) increased consistently from 9.1% on day 1, to 51.1% day 3, and 52.3% on day 7. While the level of hyperglycaemia ranged from a minimum of 8.4mmols/L to a maximum of 17.4mmols/L. The available studies in the literature have not documented the number of patients with hyperglycaemia but this is because any patient with glucose derangement is put on insulin or other hypoglycaemic agent. In KNH burns unit, aggressive diagnosis and treatment of stress induced hyperglycaemia has not been put in place. It is hoped that the results of this study will raise the awareness of the extent of the stress induced hyperglycaemia.

The case fatality for burn patients with hyperglycaemia was 24%. The mortality rate among patients with hyperglycaemia on day 1, 3 and 7 was higher (55.6%, 22.9% and 19.6% respectively) than the mortality rate for patients who had normoglycemia (20%, 15.2% and 9.5% respectively) These findings are consistent with findings from other studies which have reported a higher mortality rate among severely injured patients including severe burns ^(20, 22, 24, 30). Gore et al in their retrospective study “Association of hyperglycaemia with increased mortality after severe burn injury” reported a length of ICU stay and mortality rate of 27% in patients with persistent hyperglycaemia compared with only 4% in patients with adequate glucose control ($p \leq$

0.05) ⁽²⁴⁾. While Yendamuri et al reported that Hyperglycaemia was associated with increased mortality among both patients with moderate hyperglycaemia (34.1% vs. 3.7%, $p < 0.01$) and those with mild hyperglycaemia (15.5% vs. 2%, $p < 0.01$) compared with corresponding normoglycaemic groups. In the same study hyperglycaemia was an independent predictor of mortality and of hospital and intensive care unit length of stay after multiple logistic regression while controlling for age, Injury Severity Score, Revised Trauma Score, and gender ⁽³⁰⁾. The study could only establish an association between hyperglycaemia and mortality.

The study however failed to establish a positive association between hyperglycaemia and length of stay in burns unit, a fact consistently established by other studies on stress induced hyperglycaemia ^(7, 19, 22, 24). Our study showed reduced duration of stay for patients with hyperglycaemia on day 1, while Hyperglycaemia on day 3 or 7 taken after early deaths had occurred, did not predict duration of hospital stay. This was expected due to the increase in mortality rate among patients with hyperglycaemia on the first day.

Possible explanations as to why the study failed to establish increase in hospital stay in patients with severe burns include, lack of standard operative procedure on when to discharge a patient from burns unit to the general ward or a high turnover rate in the burns unit due the limited capacity of the burns unit compared to the patients load needing admission.

CONCLUSION AND RECOMMENDATION

CONCLUSION

Severe burns injury is one of the major causes of trauma and continue to be associated with increase in morbidity and mortality. Several factors have been associated with the increase in this morbidity and mortality among them is stress-induced hyperglycemia.

The study has confirmed that the problem of hyperglycemia afflict majority of patients admitted in KNH burns unit, with severe burns from the first day of admission and throughout the acute period. The same way it afflicts patients in developed world. It is also similarly and consistently associated with increase in mortality. However, there was no statistically significant increase in the length of burns unit stay among patients with hyperglycemia compared to those with normoglycemia.

RECOMMENDATION

The need to adopt and implement as a standard protocol, regular monitoring of blood sugars in patients admitted with severe burns.

Need to employ dedicated health workers to carry out the task of glucose measurement. Currently the task is done by nurses who are already over stretched due to work load hence cannot under take sugar monitoring regularly as it should be.

Need to do follow up randomized studies evaluating insulin and other oral hypoglycemic agents to establish which protocol will be more effective and suitable to our setting.

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APPENDICES

APPENDIX I: DATA COLLECTION FORM

Study no IP/ No.

Age

Sex Male..... Female.....

Date of injury Time of injury

Time of reporting to hospital

Educational level none..... Primary..... Secondary..... Tertiary.....

Place of burn: Home..... Workplace..... Others.....

Marital status Single..... Married..... Separated/Divorced.....

Abbreviated burn injury score

Variable	Patient characteristic	Score
Male		
Female		
Age in years		
Inhalational injury		
Full thickness burn		
%TBSA		
TOTAL		

Type of burn Scald..... Flame..... Electrical..... Chemical.....

Burn depth

Mostly superficial..... Mostly deep.....

Random blood sugar levels a) day 1 b) day 3..... c) day 7.....

Duration of admission in Burns unit

Outcome a) Alive..... b) Died.....

Date of discharge or death.....

APPENDIX II (A): CONSENT FORM

Evaluation of the occurrence of acute hyperglycemia in severe burn injury patients hospitalized at Kenyatta National Hospital.

Research study

You are invited to participate in a research study on Evaluation of the occurrence of acute hyperglycaemia and its association with outcome in severe burn injury patients hospitalized at Kenyatta National Hospital (KNH) being conducted by Dr. Omar Hussein, a postgraduate student at the University of Nairobi.

Purpose of the study: The purpose of the study is to assess the occurrence of acute hyperglycaemia and its association with outcome in severe burn injury patients at KNH. The results of the study are expected provide recommendations for glycemic control in these patients with the aim of improving outcome.

Risks and benefits: There will be no direct benefit to you upon participation in the study and no physical or mental harm will be imposed on you during the study.

Confidentiality: Information related to you will be treated in strict confidence to the extent provided by law. Your identity will be coded and will not be associated with any published results. The records of this study will be kept private and any written results will discuss group findings and will not include information that will identify you. Research records will be stored securely and only researchers and individuals responsible for research oversight will have access to the records.

Voluntary participation and withdrawal from the study: Your decision whether or not to participate will not prejudice you or your medical care. If you decide to participate, you are free to withdraw your consent, and to discontinue participation at any time without prejudice to you or effect on your medical care.

Types and amount of sample

Blood sample about half a teaspoon full (2mls) will be taken to test for blood sugar levels on day 1, 3 and 7.

Contacts: You should feel free to ask questions now or at any time of the study. If you have any questions about this study, you can contact Dr Omar Hussein, phone no. 0720-911 520, email omarngotho@yahoo.com. If you have any questions concerning the rights of human research participants, contact the Chairperson, the KNH Ethics and Research Committee at 020-2726300.

I have read and fully understand the consent form. I sign it freely and voluntarily.

Signature of Participant/Next of kin Date

I certify that I have personally explained this document before requesting that the participant to sign it.

Signature of Researcher Date

APPENDIX II (B): KIBALI CHA KUSHIRIKI

UCHUNGUNZI WA TATIZO LA ONGEZEKO LA SUKARI MWILINI KWA WAGONJWA WALIO CHOMEKA VIBAYA NA KULAZWA KATIKA HOSPITALI YA KENYATTA.

Utafiti: Unaalikwa kushiriki katika utafiti wa kuchunguza ongezeko la sukari kwa wagonjwa waliochomeka vibaya na kulazwa katika hospitali kuu ya Kenyatta. Utafiti unafanywa na Daktari Omar Hussein.

Lengo la utafiti: Lengo la utafiti huu ni kutafuta na kuonyesha ni wagonjwa wangapi hupata ongezeko la sukari mwilini baada ya kuchomeka na kama hilo lina athari yeyote kwa kupona kwa wagonjwa hao. Ili kama ni tatizo kubwa tuweze kutoa ushauri wa kutibu tatizo hilo ili kuboresha matibabu ya wagonjwa hawa. Hakutakuwa na majeraha yeyote kwa washirika

Siri: Maelezo yako yatakuwa siri na matokeo ya utafiti yataelezwa kwa ujumla.

Kushiriki: kushiriki kwako kwa utafiti huu ni kwa hiari yako. Una uhuru wa kukataa kushiriki, na kukataa kwako hakutatumiwa kukunyima tiba. Damu mililita mbili itatolewa siku ya kwanza tatu na saba kupima sukari mwilini mwa mgonjwa.

Maswali: ukiwa na swali lolote kuhusu utafiti huu unaweza kumuuliza Daktari Omar Hussein kwa nambari ya simu 0720-911520 au kupitia barua pepe omarngotho@yahoo.com. Ukiwa na swali kuhusu haki za mtafiti, unaweza kuwasiliana na Mwenyekiti, KNH ERC katika nambari 020-2726300

Nimesoma na kuelewa kibali hiki. Ninaweka sahihi kwa hiari yangu.

Sahihi ya mshirika/jamii ya mshirika Tarehe

Nimeeleza kwa ukamilifu lengo la utafiti kabla ya kumuomba kuweka sahihi.

Sahihi ya mtafiti Tarehe

APPENDIX III: BLOOD SAMPLING AND TESTING PROTOCOL

Capillary blood sample was obtained from the fingertip of the patient by using the following procedure:

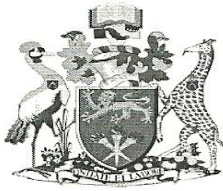
1. Explanation of the procedure and informed consent was sought from the patient.
2. Fingertip sterilized with alcohol swabs.
3. Gauge 25 needle used to prick the tip of the finger of the patient.
4. Gentle pressing of the pricked finger.
5. Blood obtained using capillary tubes.
6. Fingertip covered with dry cotton swab to control bleeding for 1 minute.
7. Blood sample analyzed by using pre-calibrated glucofix and glucometer.
8. Results recorded in the data form.
9. Same procedure repeated on day 1, 3 and 7 from the day of admission for each patient.

The blood glucose analysis was done in the wards using a glucometer provided by the researcher.

Test done by trained assistant/ principle investigator.

The normal normal reference range used was 3.5-8.3 mmol/L

APPENDIX IV: (KNH/UON- ERC APPROVAL LETTER)



UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
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Ref: KNH-ERC/A/159



KNH/UON-ERC
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Website: www.uonbi.ac.ke
Link: www.uonbi.ac.ke/activities/KNHUoN

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
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Telegrams: MEDSUP, Nairobi
13th June 2012

Dr. Omar Hussein Ngotho
Dept. of Surgery
School of Medicine
University of Nairobi

Dear Dr. Ngotho

Research proposal: "Evaluation of the occurrence of hyperglycemia and its association with outcome in patients with severe burns hospitalized at KNH"(P176/3/2012)

This is to inform you that the KNH/UoN-Ethics & Research Committee (ERC) has reviewed and **approved** your above revised research proposal. The approval periods are 13th June 2012 to 12th June 2013.

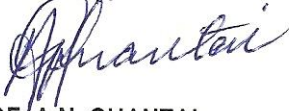
This approval is subject to compliance with the following requirements:

- a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
- b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
- c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
- d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
- e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
- f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
- g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website www.uonbi.ac.ke/activities/KNHUoN

"Protect to Discover"

Yours sincerely



PROF. A.N. GUANTAI
SECRETARY, KNH/UON-ERC

- c.c. The Deputy Director CS, KNH
The Principal, College of Health Sciences, UoN
The Dean, School of Medicine
Chairman, Dept. of Surgery, UON
Supervisors: Dr. Kimani Wanjeri, Dr. P.L.W Ndaguatha

"Protect to Discover"

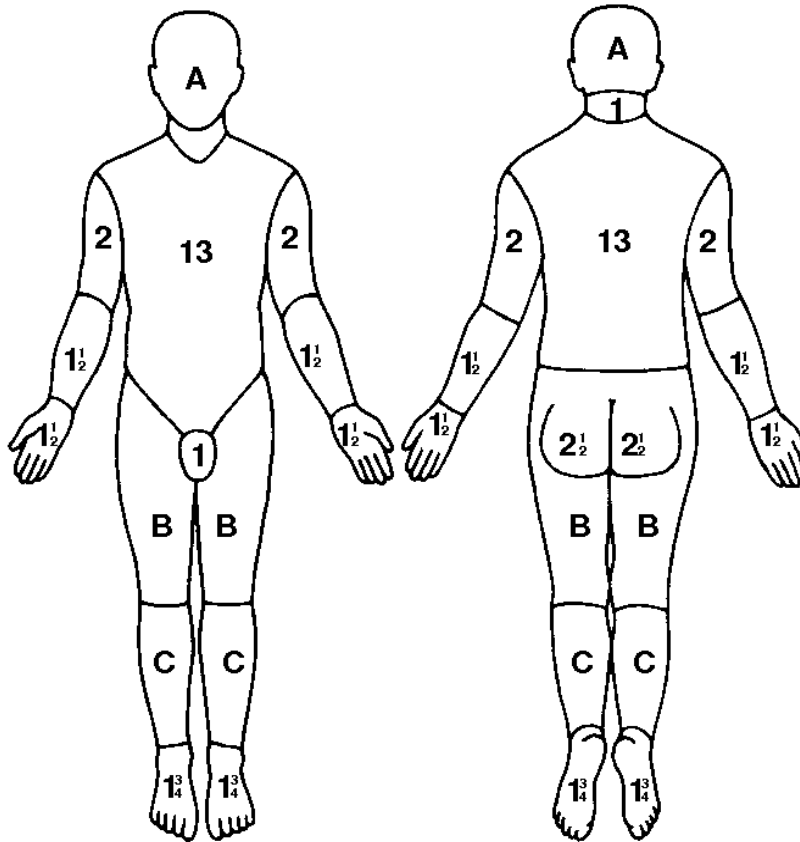
APPENDIX V: LUND AND BROWDER CHART

A BURN CHART

NAME _____ WARD _____ NUMBER _____ DATE _____

AGE _____

LUND AND BROWDER CHARTS



Ignore simple erythema.

 Superficial

 Deep

REGION	%
HAED	
NECK	
ANT. TRUNK	
POST. TRUNK	
RIGHT ARM	
LEFT ARM	
BUTTOCKS	
GENITALIA	
RIGHT LEG	
LEFT LEG	
TOTAL BURN	

RELATIVE PERCENTAGE OF BODY SURFACE AREA AFFECTED BY AGE

AREA	AGE 0	1	5	10	15	ADULT
A = 1/2 OF HEAD	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2	3 1/2
B = 1/2 OF THIGH	2 3/4	3 1/4	4	4 1/2	4 1/2	4 3/4
C = 1/2 OF ONE LOWER LEG	2 1/2	2 1/2	2 3/4	3	3 1/4	3 1/2

**APPENDIX VI: DECLARATION FORM FOR STUDENTS
UNIVERSITY OF NAIROBI**

Declaration of Originality Form

This form must be completed and signed for all works submitted to the University for examination.

Name of Student: Dr Omar Hussein Ngotho

Registration Number: H58/76616/2009

College: Health science

Faculty: Medicine

Department: General Surgery

Course Name: Mastery of Medicine in General Surgery

Title of the work: Evaluation of the Occurrence of Acute Hyperglycemia and its Association with Outcome in Patients with Severe Burns Hospitalized at KNH.

DECLARATION

1. I understand what Plagiarism is and I am aware of the University's policy in this regard
2. I declare that this thesis is my original work and has not been submitted elsewhere for examination of award of a degree. Where other people's work, or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi's requirements.
3. I have not sought or used the services of any professional agencies to produce this work
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Signature _____

Date _____

APPENDIX VII (A): DECLARATION FORM FOR STAFF

UNIVERSITY OF NAIROBI

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Name of Staff _____

Payroll Number _____

College of Health Science

School of Medicine

Department of Surgery

Title and bibliographic details of the work

Evaluation of the Occurrence of Acute Hyperglycemia and its Association with Outcome in Patients with Severe Burns Hospitalized at KNH.

DECLARATION

1. I understand what plagiarism is and I am aware of the University's policy in this regard.
2. I declare that this **Dissertation** is my original work. Where other people's work, or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi's requirements.
3. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work.
4. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

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APPENDIX VII (B): DECLARATION FORM FOR STAFF

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College of Health Science

School of Medicine

Department of Surgery

Title and bibliographic details of the work

Evaluation of the Occurrence of Acute Hyperglycemia and its Association with Outcome in Patients with Severe Burns Hospitalized at KNH.

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Date _____