LEVELS AND SIGNIFICANCE OF SERUM CARDIAC TROPONIN T *(cTnT)* IN BURN PATIENTS

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DECLARATION

Student's declaration

This dissertation is my original work and has not been submitted to any other university to obtain a degree.

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DEDICATION

I dedicate this work to my lovely wife Monicah, son Rueben and Dad Kimani

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LIST OF ABBREVIATIONS AND ACRONYMS

ACS	Acute Coronary Syndrome
CHS	College of Health Sciences
cTn	Cardiac Troponin
cTnT	Cardiac Troponin T
CV	Coefficient of Variation
FAB	Fragment Antigen Binding
hs-cTnT	High Sensitivity Cardiac Troponin T
IgG	Immunoglobin G
KNH	Kenyatta National Hospital
KNH/UoN/ ERC	Kenyatta National Hospital / University of Nairobi Ethics and Research Committee
LMIC	Low and Middle Income Countries
LoD	Limit of Detection
MI	Myocardial Infarction
NSTEMI	Non-ST Elevation Myocardial Infraction
ROS	Reactive Oxygen Species
TBSA	Total Burn Surface Area
TGF	Tissue Growth Factor
TNF-α	Tissue Necrosis Factor-alpha
UoN	University of Nairobi
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Burns

Burns are injuries to tissues, primarily caused by heat, but can also be due to radiation, radioactivity, electricity, friction, or contact with chemicals. While most burns cause injuries, inhalation of smoke is also considered as burns. (WHO)

Acute Myocardial Injury

Myocardial injury according to the Fourth Universal Definition of myocardial infarction is defined as an elevation of cardiac troponin (cTn) value without ischemia, frequently encountered clinically with adverse prognosis. It reflects an elevated cTn value above the 99^{th} percentile upper reference unit. (Thygesen K. A., Jan 2019)

Wallace Rule of Nines

This is a tool used by trauma and emergency medicine providers to assess the Total Body Surface Area (TBSA %) in burn patients

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ABSTRACT

BACKGROUND

Burns are a public health problem globally. It is estimated to cause 265,000 deaths from fires alone. Burns trauma are a major cause of injury in Low and Middle-Income Countries (*LMIC*). Fatal fire-related burns accounts for 95% according to 2015 Global Health Estimates. Kenya, an LMIC has significant burns cases with a study by Saidi in Nairobi indicating a prevalence of 25.9% of all injuries. Hospital burns deaths were at 1.7% compared to pre-hospital deaths at 5.9%.

Burns are also known to cause neuroendocrine derangement, hypovolemia and induce different inflammatory cytokines. The three can singly cause myocardial injury, thus, an amplified effect when the three are present.

Cardiac Troponin T (cTnT) levels, a myocardial injury biomarker helps in evaluating the extent and significance of burns as a stress factor for myocardial injury. The elevation of levels of troponins in patients with burns corresponds to the myocardial injury.

OBJECTIVE

To determine the levels and significance of cTnT in burn patients admitted at Kenyatta National Hospital (KNH).

METHODOLOGY

The study was a descriptive, cross-sectional study done at KNH. All 91 study participants were patients admitted with burns. Serum was analyzed using a calibrated Cobas 6000 platform using the chemiluminescent immunoassay technique. Chi-square and Spearman's Correlation were used to statistically analyze the data.

RESULTS

Thermal burns contributed to 81.3% while electrical burns contributed to 18.7% of all burns where 72.5% (*n*=66) of serum cardiac troponin T were normal while 27.47% (*n*=25) were high. There was a weak positive correlation between High Sensitive - cTnT and Burn Types, but it was not statistically significant ($r = 0.106$, $p = 0.320$). There was a significant relation between Hs-cTnT and Total Burn Surface Area (TBSA %) with $p = 0.023$, as well as a negative correlation between Hs-cTnT and TBSA% with $r = -0.238$ and $p = 0.023$.

CONCLUSION

This study has demonstrated that burns patients have elevated serum cardiac troponin T compared to the general population. The prevalence of myocardial injury was 27 % as diagnosed by hs-cTnT.

CHAPTER 1: INTRODUCTION

BACKGROUND

Burns are a devastating serious public health problem globally with fire contributing to an estimated 265,000 deaths. Other forms of burns from other causes lack data due to the failure of reporting or unavailable data. Burns trauma are a major cause of injury in Low and Middle-Income Countries (LMIC). Fatal fire-related burns accounts for 95% according to 2015 Global Health Estimates. (WHO)

Kenya, a LMIC has significant burns cases with a study by Hassan in Nairobi indicating a prevalence of 25.9%. (Hassan, 2016) The rate of burn injury is higher in males than females at 81.2% and 18.8% respectively. Females have a 16% rate of death from burns, slightly higher than males' 4.7%. Hospital deaths were at 1.7% compared to pre-hospital deaths at 5.9%, showing significant importance of hospitalization for burns. They are the 5th most common cause of trauma in Kenya after Traffic, assault, fall, and gunshots respectively. (Hassan, 2016) (Wanjeri, 2018) (World Health Organization, 2018)

Burns are traumas with unimaginable severity and often quantified differently compared to other traumas. They are known to cause morbidity and mortality resulting from hospitalization, disability, stigma, rejection, and death. They are also known to cause neuroendocrine derangement, hypovolemia and induce different inflammatory cytokines. The three can singly cause myocardial injury, thus, an amplified effect when the three are present.

Following excessive stress by burns, organ damage can be evident especially when the Total Burn Surface Area (TBSA %) is high. The rise or fall of Hs-cTnT above the 99th percentile indicates a myocardial injury used in risk stratification of myocardial infarction. Cardiac Troponin T (cTnT),

a myocardial injury biomarker has gradually been studied leading to the development of assays with high detection specificity and sensitivity.

The scrutiny and elucidation of the levels of cTnT, which reflects even microscopic zones of injuries and necrosis will help in the characterization of its significance and possibly infer advanced burn injury management.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

Burn injuries present complex pathophysiology following immediate cell injuries, late cell damage or cell death. They are known to cause circulatory, physiological, catabolic and immune system alterations common in all traumas but severe in burns. Studies are constantly uncovering different complex mechanisms involved which infer the management.

2.2 Zones of burn injury

There are three burn injury zones:

- Zone of coagulation: these are necrotized tissues destroyed at the time of burn
- Zone of stasis: it surrounds necrotized tissues with widespread inflammation and low perfusion which ends up necrotizing within the first 48 hours post-burn, expanding the area and depth of the burn.
- Zone of hyperaemia: perfused and non-impaired microvasculature (Bohr S, 2013)

2.3 Pro-inflammatory phase

Macrophages, the tissue major pro-inflammatory mediators of inflammation leads to a systemic inflammatory syndrome, by biochemical cytokines, the TNF-α inducing apoptosis, and IL-6 (Colton B. Nielson, Jan/Feb 2017)

Reactive Oxygen Species (ROS) results from profound hyper-metabolism. The products of ROS are associated with inflammation at the site of production. They lead to systemic inflammatory syndrome and when they are not excreted or transformed, they lead to tissue damage and death. Tissue death leads to a widespread multiple organ failure which leads to death. (Horton, 2003).

ROS has also shown a deleterious effect on the cell membrane, thus, the mast cell mediators' vasoactive actions could damage the burn injury area. (Santos FX, 2000)

2.4 Anti-inflammatory phase

This phase is mediated by T lymphocytes helper type-2, mediated by cytokines, interleukin 4, interleukin 10 and tissue growth factor (TGF). The endothelial junction in the microvasculature widens the cell junctions' leading to leakage. Bradykinin, a vasoactive mediator cytokine causes venule to dilate, an inflammatory process. (Vaughn L, 2012)

2.5 Wallace rule of nines

This is an emergency medicine scoring tool used in burns trauma. It helps in assessing the Total Burn Surface Area % of burns aiding the health care provider determine the severity and chat the intravenous fluid resuscitation need. Fluid resuscitation is critical in burns due to hypovolemia. The algorithm is used in second and third-degree burns with consideration of paediatrics and obese patients due to body mass index as a major factor for fluid resuscitation. (Moore, 2019)

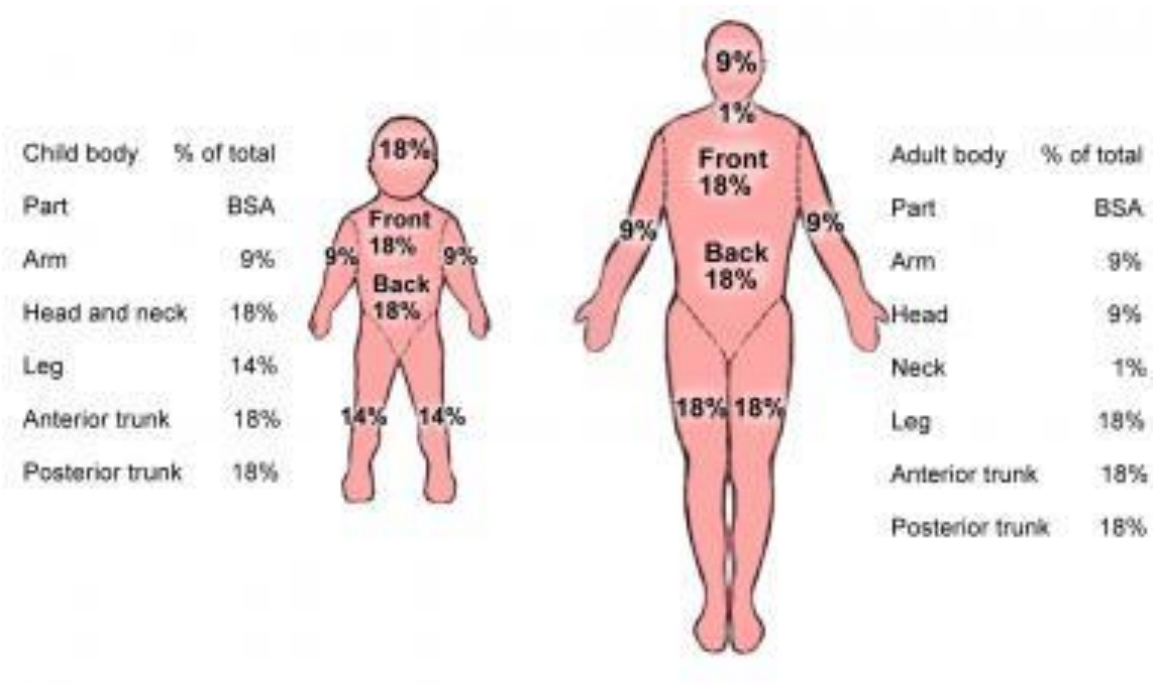


Figure 2.1 Wallace Rule of Nines for evaluating TBSA%

2.6 Burns and organ systems

Burns affect almost all organ systems with a pathophysiological response known to change the metabolism. This has been studied and shown to remain for several years. They are characterized by inflammation, hyper-metabolism, insulin resistance and muscle wasting. (Porter C, 2013)

They are characterized by two phases:

- Resuscitation: this is the first phase to occur and lasts approximately 24 to 72 hours. There is an increase in vascular permeability, fluid shift leading to intravenous fluid depletion and edema formation. The phase restore and preserve tissue perfusion. These helps the body in overcoming ischemia and hypovolemic and cellular shock of the burn area. (Porter C, 2013). However, this does not always happen due to mismanagement or failure in recognizing it during patient management.

- Hyper dynamic and hypermetabolic: this phase involves a decrease in vasculature permeability, increase in heart rate following neuroendocrine system activation and decrease in peripheral vascular resistance following inflammation cytokines resulting in to increase in cardiac output, 1.5 times of fit non-burned person. (Porter C, 2013)

2.7 Troponin: Cellular

Troponins are calcium-mediated proteins that regulate the interaction of myosin and actin, which causes striated muscles to contract and relax. The troponin complex is made up of three subunits which include Troponin C for binds calcium; Troponin I which inhibits actin-myosin interactions; Troponin T which binds to tropomyosin and attaches the troponin complex, facilitating contraction. (Missov ED, 1999).

With the similar amino acid sequences, troponin C is expressed by skeletal muscle cells as well as cardiac cells. Immunologically, this gives the same antibody, the basis of in vitro immunoassay, making it non-specific due to lack of differentiation. Troponins I and T contain unique amino acid sequences in myocardiocytes. This isolation of their specificity has led to the development of diagnostic qualitative and quantitative immunoassay techniques. Their high sensitivity and specificity as analytes have allowed detection of myocardial injury and stratification of myocardial infarction. (Missov ED, 1999)

Apoptosis of cardiomyocytes leads to the release of Troponin, a cellular protein. This leads to an estimated 0.1–0.2 ng/L normal reference range (Missov ED, 1999). The majority of cardiac troponin is structurally bound in the myofibril's cytoplasmic contractile apparatus at the cellular level. However, in the cytoplasm, only 3%–5% of troponin I and 7%–9% of troponin T are free.

(Wu AH, 1998). The diagnostic criteria for myocardial infarction uses cardiac troponins to define myocardial injury resulting from myocardial necrosis. (Thygesen K, 2012)

2.8 Mechanism of troponin elevation in burns

Troponin leakage in burns results from inflammation, hypovolemia shock and hypoxic effects on cardiomyocytes. During burn injury TNF alpha, an inflammatory marker is elevated. The degree of elevation was shown to be related to TBSA% of the burn. (Herndon, 1996) Burn injuries are known to cause hypovolemia which correlates with TBSA% leading to decreased cardiac output leading to compensation through tachycardia. Tachycardia compensates for hypoxia through rapid contraction of muscles. This leads to ischemia resulting from myocardial hypoperfusion due to decreased myocardial oxygen supply, predominantly by reduced diastolic time. (Jeremias A, 2005)

Tachycardia is caused by any increase in oxygen demand without coronary stenosis. (Patane S, 2009) Cardiac troponin elevation is caused by supraventricular or ventricular tachycardia, atrial fibrillation with a high ventricular response, or any other tachycardia. This is caused by temporary myocyte injury spurred on by hemodynamic compromise.. (Neumayr G, 1997)

2.9 Cardiac troponin in burns patients

Cardiac troponins are released early in the course of myocardial injury where even minimal elevations are considered significant. In exclusion of ACS and other Non-ACS which equally elevates cardiac troponins, burns have over time been characterized though scarcely published but have shown significant elevations.

Acute burns of ≥15% TBSA were associated with elevation of troponin levels where a positive troponin test strongly correlated with increased risk of acute cardiac complication and death. A

positive increase in cardiac troponins affected cardiac and survival outcomes. (American Burn Association, 2006)

Cardiac troponin I in burn patients without ACS with ≥15% TBSA had raised cardiac troponin I irrespective of age. Chen et al showed all patients had increased cTnI on two or more occasions. The mean cTnI concentration was significantly higher in patients with TBSA of burn > 30%. They concluded that burned patients have varying degrees of non-ischaemic cardiac injury, manifesting as leakage of cTnI from myocytes into the circulation. (Chen YN, 2000)

There was a significant correlation between a positive troponin test and increased risk of acute cardiac complication and death, as did burns greater than 15% total body surface area (%TBSA) and age. Acute burns of ≥15% TBSA are associated with elevated troponin levels. (William Alexander, 2018)

2.10 Cardiac troponin kinetics

Serum cardiac troponin rise in phases following cardiomyocyte damage from any aetiological cause including burns which occurs in two phases. The initial phase involves the leakage of free cytoplasmic cardiac troponin following the alteration of the cell membrane. The second phase involves the release of cardiac troponin complexes bound to the myofibril. This however occurs gradually and is equivalent to the extent of cardiomyocyte damage. This gives a constant and sustained troponin release until the healing of myocytes (Higgins JP, 2003).

Approximately 2-4 hours after the commencement of myocardial damage, cardiac troponin is first detectable; adequate diagnostic sensitivity and specificity are attained by 9 hours. It however doesn't allow early detection compared to other cardiac biomarkers such as myoglobulin due to its kinetics. (Jaffe AS, 2006). It has been shown the sensitivity of troponin T at the time of hospital

admission ranges from 25%–65%, and increases to 59%–90% at 2 to 6 hours after the presentation (Panteghini M, 1999). The sensitivity approaches 100% by 6 to 12 hours after admission. (Panteghini M, 1999)

2.11 Sample collection

The diagnostic and clinical sensitivity of a biomarker defines its clinical use and choice. Due to its high tissue specificity, hs-cTnT proves to be the biomarker of choice in the detection of myocardial damage. Technological advancement has also led to the development of a new generation of assays with fewer false positives.

Blood samples for cardiac troponin based on its kinetics should be collected between 6 hours and 9 hours. This optimizes both analytical and clinical sensitivity and specificity for determining myocardial injury which helps in the stratification of Myocardial infarction. (Thygesen K. e., 2007). Serum cardiac troponin levels remain elevated for between 4–7 days for troponin I, and 10–14 days for troponin T which gives a broad analytical time with samples collected on different days. (Adams JE, 1993).

2.12 Troponin clearance

Hs-cTnT has a large molecular size and it can be complexed with cTnI. Studies have shown that it is cleared in the reticuloendothelial system. (Freda BJ, 2002). According to Diris et al., troponin T is broken up into molecules small enough to be excreted by the kidneys. This explains the high prevalence of troponin T elevation in patients with renal failure (Diris JH, 2004).

2.13 Troponin assays

The cTnT assays have gone through a cyclic development by different developers for diagnosis of AMI with or without ischemia. This is through the definition of presence or absence of myocardial injury which must be present for stratification of myocardial infarction. There have been four generations of assay development where:

- **First generation:** bovine cTnT was used as the standardization reference material. It did, however, exhibit non-specific binding to human skeletal muscle protein, which reduced its sensitivity and specificity as a diagnostic test.
- **2nd generation:** it was refined further with the introduction of the detection antibodies.
- **3rd generation:** using recombinant technology, a human cTnT was developed and used for standardization
- **4th generation:** this generation led to more modifications where:
    - The use of antibodies' Fragment Antigen Binding *(FAB)* region was utilized. Two cTnT specific mouse monoclonal antibodies in a sandwich format where cTnT was used as an antigen.
    - The antibody was directed at recognizing an epitope located in the central part of cTnT *(Amino Acid 125 – 131)* and *(135 - 147).*
    - Tris (Bipyridyl) ruthenium (II) was used as the probe in an electrochemiluminescence immunoassay..

A 2007 consensus lead to the standardization of cardiac troponin as an assay for the diagnosis of myocardial injury for stratification of myocardial infarction. (Thygesen K. e., 2007). Myocardial injury occurs when the concentration of cardiac troponin exceeds the upper reference range's 99th

percentile. This can however be measured serially for the rise and/or fall to define whether it's a chronic or an acute scenario. (Thygesen K. e., 2007).

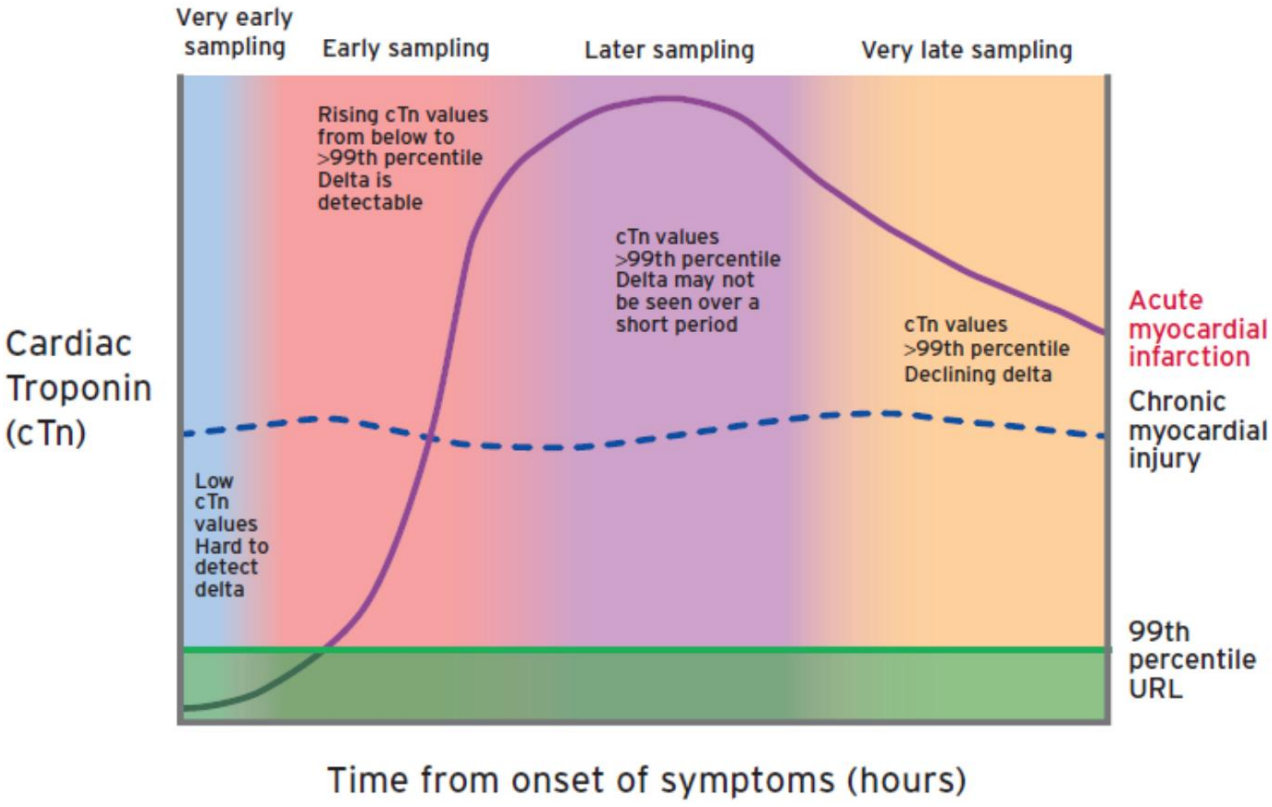


Figure 2.2: cTnT dynamics-Fourth Universal Definition of myocardial infarction

The 4th generation analytical properties:

- The Limit of Detection: 0.01 ng/ml
- Normal population 99th percentile cut-off point: 0.01 ng/ml
- 10% coefficient of variation: 0.03 ng/ml

2.14 High sensitive cardiac troponin assay

The 4th generation immunoassay showed reduced precision shown to be significantly affected by heterophile antibodies. Due to this susceptibility, the constant region of the antibody has been further modified, resulting in the design of the High Sensitive Cardiac Troponin T (hs-cTnT) assay. The biotinylated capture antibody was preserved in this experiment. Genetic engineering has been used to modify the detecting antibody. A mouse-human chimeric detection antibody was created by swapping out the constant C1 region in the monoclonal mouse FAB fragment with a human IgG C1 region. (Giannitsis E, 2010)

The analytical sensitivity was improved by increasing the sample volume from 15 µL to 50 µL, increasing the ruthenium concentration of the detection antibody, and lowering the background signal via buffer optimization. (Giannitsis E, 2010)

The hs-cTnT assay's analytical performance was greatly enhanced where:

- The Limit of detection was improved to 0.003 ng/mL (3 ng/L)
- 99th percentile cut-off point improved to 0.014 ng/mL (14 ng/L)
- Coefficient of Variance of 10%: 0.013 ng/mL (13 ng/L). (Giannitsis E, 2010)

With a lower LoD and an increased precision due to reduced heterophile antibodies interference, the hs-cTnT assay can detect more subtle elevations indicative of cardiac injury. Reichlin et al demonstrated that high-sensitive cardiac troponin T assay is a superior diagnostic biomarker with precision in the detection of acute Myocardial Infarction (MI). This was contrasted to a traditional troponin assay, particularly in individuals who came within three hours of the onset of symptoms. (Reichlin T, 2009)

Quality and accurate diagnosis of myocardial injury using hs-cTnT allow timely and rapid patient management (Reichlin T, 2009). The identified patients would then be assessed, diagnosed further for Acute Myocardial Infarction, monitored and then guided on the need for early invasive procedures. This would reduce morbidity and mortality for burn patients.

PROBLEM STATEMENT

Burn injuries are a public health problem globally with LMIC having a bigger burden due to low literacy levels, insufficient resources and poor prevention and management of burns. Different preventive measures have been embraced in different setups, with developed countries being a notch higher than developing countries like Kenya.

The management of burn patients has significantly been researched and improved. However, complex burns pathophysiology still demands more research since much is still uncovered. In doing more research, the cost of patient management and mortality shall be reduced.

The main purpose of the study was to measure the levels of cTnT as a preferred myocardial injury biomarker and characterize it for its significance in burn patients.

RATIONALE

Cardiac Troponins are biomarkers that have over time revolutionized the prognosis, diagnosis and management of myocardial injury. Burns is associated with increased Troponins, which can be used to improve myocardial risk stratification.

Despite the use of cTnT as a biomarker for MI, it has not been studied for its significance for advancing the management of burn patients. This study will assist in enhancing or changing the management.

Measuring the levels of cTnT will help in evaluating the extent and significance of burns to myocardial injury. Early recognition of myocardial injury can be diagnosed through the measurement of cardiac troponins which would infer stratifying and treatment of myocardial infarction. This would improve clinical outcomes by reducing morbidity and mortality associated with cardiac dysfunction in burn patients.

Given myocardial dysfunction is one of the outlined causes of mortality in burn injury patients, measuring cTnT for its significance will help in enhancing and adding to the body of knowledge for burns care. This will help in combating organ or life-threatening consequences in burn injuries based on the biomarker.

RESEARCH QUESTION.

Do burns patients at Kenyatta National Hospital have elevated serum cardiac Troponin T levels?

OBJECTIVES

BROAD OBJECTIVE

To determine the levels and significance of serum cardiac troponin T in burn patients at Kenyatta National Hospital

SPECIFIC OBJECTIVES

1. To determine the number of patients admitted with burns at Kenyatta National Hospital.
2. To determine serum levels of cardiac troponin T (cTnT) in patients admitted with burns injury at Kenyatta National Hospital.
3. To correlate serum cardiac troponin T (cTnT) with the type of burn.
4. To correlate serum cardiac troponin T (cTnT) with Total Burn Surface Area (TBSA %).

CHAPTER 3: METHODOLOGY

3.1 STUDY DESIGN

The study was a descriptive, cross-sectional study.

3.2 STUDY AREA

The study was done at Kenyatta National Hospital burns ward which has a 70 bed capacity of burn patients with an average admission of 2 patients per day. There is an additional 18-bed capacity burns unit for the severely burnt patients

3.3 STUDY POPULATION

The study population involved the selection of burn patients received at the burn unit *(severe burns)* and burns ward Kenyatta National Hospital.

3.3.1 INCLUSION CRITERIA

- Patients who were admitted with burn injuries within the first 48 hours after the burn
- Patients who consented or whose next of kin have consented for them
- Assented patients for those aged between 8 and 17 but have to be consented by next kin
- Any age group
- Any gender

3.3.2 EXCLUSION CRITERIA

- Patients from whom written informed consent shall not be obtained.
- All patients with any known cardiac disease
- End-Stage Renal Disease with eGFR of less than 15.
- Patients with known neuromuscular disease
- Patients on a biotin supplement

3.4 SAMPLE SIZE CALCULATION

The Fischers' formula was used to calculate the sample size of patients with burns to participate

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where n = sample size,

Z = Normal deviation at the desired confidence interval. In this study, a Z value at 95% CI will be 1.96

P = Proportion of the population with the desired characteristic

d = Degree of precision = 0.05

Since the proportion of the population with myocardial injury in burns is not known, a 50% P-value was used to maximize the sample size of the study

$$n_1 = \frac{1.96^2 * 0.5(1-0.5)}{0.05^2} = 384.14 = 384$$

The sample size was adjusted due to the study timeline and resources available using the equation below

$$\mathbf{n_2 = n_1\ N/\ (N + n_1)}$$

(Survey methods and practices statistics Canada 2010)

Where:

- n_1 = sample size at the expected prevalence
- N = Total number of patients admitted at KNH with burns is estimated to be 2 per day, with the study being descriptive with an estimated time of 2 months. 2 * 60 = 120

$$\mathbf{n_2 = \frac{384 * 120}{120 + 384}}$$

$$\mathbf{= 91}$$

3.5 RECRUITMENT AND CONSENTING

A screening questionnaire based on the study with the help of qualified clinical staff was used to recruit study participants. Those fitting the inclusion and exclusion criteria were consented or assented with the help of their next of kin. Clinical and demographic data of the study participants was collected with the help of a research assistant from the patient's files.

3.6 SAMPLING TECHNIQUE

A non-random consecutive sampling of all consented and assented patients at KNH

3.7 DATA COLLECTION PROCEDURES

3.7.1 QUESTIONNAIRE

A qualified research assistant used a screening questionnaire to recruit all study participants by filling and signing the consent form. This helped in the collection of clinical and demographic data.

3.7.2 CLINICAL DATA

TBSA percentage, degree of burns and creatinine levels for calculation of eGFR to rule out renal failure were collected from the consented and assented file in consultation with the attending nurse in charge or doctor.

3.7.3 SAMPLE COLLECTION

All samples were collected on or after 9 hours from the time of burns and before 12 days from the day of burns for analytical sensitivity and specificity based on cTnT kinetics.

A 3 milliliters blood sample for determination of cTnT in burn injuries was collected by the attending physician or the principal investigator in a non-anticoagulated vacutainer.

Clinicians will help in the collection of samples for the severely burnt patients during the insertion of the central line

3.7.4 SAMPLE TRANSPORTATION

The samples were transported in a cool box at between 4^0C and 8^0C to the laboratory for separation and analysis

3.7.5 SAMPLE STORAGE

The samples were stored at 4^0C after analysis for analytical or clinical queries that may arise within the study time frame. The samples were however not used for any other purpose or study. The samples were discarded appropriately on completion of the study.

3.7.6 SAMPLE ANALYSIS

The blood sample was centrifuged for separation after clotting. Upon separation, the serum was analyzed using a calibrated Cobas 6000 platform at KNH, after the running of 'pathological low', and 'pathological high' controls. The results were produced and a copy submitted to the attending physician for consideration and filing.

3.7.7 INTERPRETATION OF cTnT AND REFERENCE RANGES

Any study participant having cTnT above the 99th percentile cut-off point (male: 14 ng/L, female 10 ng/L) was deemed to have a high cTnT and a lower value had a normal cTnT. A high cTnT was reported as a myocardial injury. For all high levels of cTnT, a serial estimation of cTnT was advised for the rise and fall.

3.8 QUALITY CONTROL AND ASSURANCE

A new batch of cTnT reagent was procured with its calibrators and standards. The analyzing platform was calibrated before the samples were run and the controls were run before running of study participant's serum.

3.8.1 PRE-ANALYTICAL ERRORS MINIMIZATION

1. Specimen type:

   Three milliliters of blood sample were collected using a syringe and needle and transferred to a non-anticoagulated vacutainer. On clotting, serum was separated by centrifugation and transferred to a cuvette before analysis.

2. Haemolysed, icteric and lipemic specimens:

   All haemolysed, icteric and lipemic samples were rejected

3. Biotin supplementation

   All patients on biotin supplement were excluded from the study

4. Stability:

   Upon collection, blood samples were transported to the laboratory at 4^0C for specimen stability.

5. Exclusion criteria

   All patients with ESRD, neuromuscular disease and on biotin supplementation,

3.8.2 ANALYTICAL ERRORS MINIMIZATION

1. Heterophile antibodies

   They usually cause elevations in immunoassays. A standardized cTnT Roche assay kit was used whose interferences are controlled. This is through directing recognition of an epitope located in the central part of cTnT.

2. Calibration and quality control

   Before running the samples, the calibrator was run and its controls (low and high) run to detect shifts near diagnostic thresholds

3.8.3 POST-ANALYTICAL ERRORS MINIMIZATION

1. Myocardial injury diagnostic threshold

   The 99^{th} percentile of the healthy reference population was used.

2. Reporting units

   Consistency of international standardized units (ng/ml) was used for ease of assessing the magnitude of myocardial injury.

3.8.4 STANDARD OPERATING PROCEDURES

All the KNH Standard Operating Procedures for receiving the sample, sample separation, sample processing and analysis, results interpretation and result dispatch were followed. The manufacturer's sample processing and analysis guidelines were followed.

Internal Quality Control

Internal quality control was checked for drifts and shifts before running the patient's sample.

External Quality Assurance

Standardization and harmonization of results was considered with reference to participation in external quality assurance programs (RIQAS – Appendix 4)

3.9 ETHICAL CONSIDERATIONS

3.9.1 APPROVAL

Approval was sought from KNH/UoN - ERC for review, consideration and authorization. The study commenced soon after approval (Appendix 3)

3.9.2 CONFIDENTIALITY

The highest level of secrecy was maintained at all times when collecting data for this study. Throughout and after recruiting, respect was extended to every study participant. The information gathered was utilized only for this study and was only shared if it was in the patient's best interest, with that patient's consent, or via KNH/UoN- ERC.

The screening questionnaire did not include the patient's name. For simplicity of reporting the patient's results and storing a copy in their files, the study research assistant kept a study logbook with the patient's name and IP number.

3.9.3 CONSENT

Written informed consent had been prepared for recruiting study participants. A research assistant was trained on recruiting procedures using the prepared questionnaire. The study participants were told what the study entails, its benefits and risks. They were also free to withdraw from the study should at any point of the study, where the study won't jeopardize the treatment or management during their stay in the hospital. There was an adult consent form for the adults and parents for children aged below 6 years and child assent form for children aged 6 to 17years.

3.9.4 BENEFITS

The study participant did not pay for the cTnT test or any other study material. The results were communicated to the attending physician through a copy of the printed interpreted result of the sample.

CHAPTER 4: RESULTS

4.1.1 INTRODUCTION

The levels of cTnT were measured using the Cobas 6000 platform after running and passing the Quality Controls (QC) and External Quality Control (EQA)

4.1.2 INTERPRETATION OF cTnT AND REFERENCE RANGES

Any study participant hs-cTnT that was above the 99th percentile cut-off point male - 14 pg/ml female -10 pg/ml was termed as high cTnT and a lower value was termed as normal cTnT. A high cTnT was reported as a myocardial injury. This was a survey type of investigation targeting all burns patients admitted at KNH to determine the levels of serum cardiac troponin T.

4.1.3 GENDER DISTRIBUTION

A total of 91 participants (*N=91*) admitted with burns were recruited as study subjects to participate in this study. Out of the total samples, 57.1% (*n=52*) were males while 42.9% (*n=39*) were female.

Table 4.1 ***Gender distribution***

Gender

	Frequency	Percent	Valid Percent	Cumulative Percent
Male	52	57.1	57.1	57.1
Female	39	42.9	42.9	100.0
Total	91	100.0	100.0	

4.2 AGE AND TBSA% DISTRIBUTION

The age was between 19 days and 56 years with a mean age of 20.63, *SD* of 15.30 with an age skewness of 0.476. Age grouping comprised of those below 1 year 4.4% (*n*=4), 1-10 years comprising of 28.6% (*n*=26), 11-20 years 19.8% (*n*=18), 21-30 years 20.9% (*n*=19), 31-40 years 12.1% (*n*=11), 41-50 years 12.1% (*n*=11), and those above 50 years consist of 2.2% (*n*=2).

The TBSA% ranged from a minimum of 3.0 to the highest of 60.0 with a mean of 25.0, median of 22.0, and standard deviation of 14.11 with skewness of 0.315.

Table 4.2: **Age and TBSA% distribution**

Descriptive Statistics

	Age	TBSA%
Mean	20.6269	25.001
Median	19.0000	22.000
Std. Deviation	15.30408	14.1140
Variance	234.215	199.204
Minimum	1 month	3.0
Maximum	56 years	60.0

4.3 Type of Burn

During the study period, only two types of burns were encountered. Thermal burns were 81.3% (*n*=74) while electrical burns were 18.7% (*n*=17).

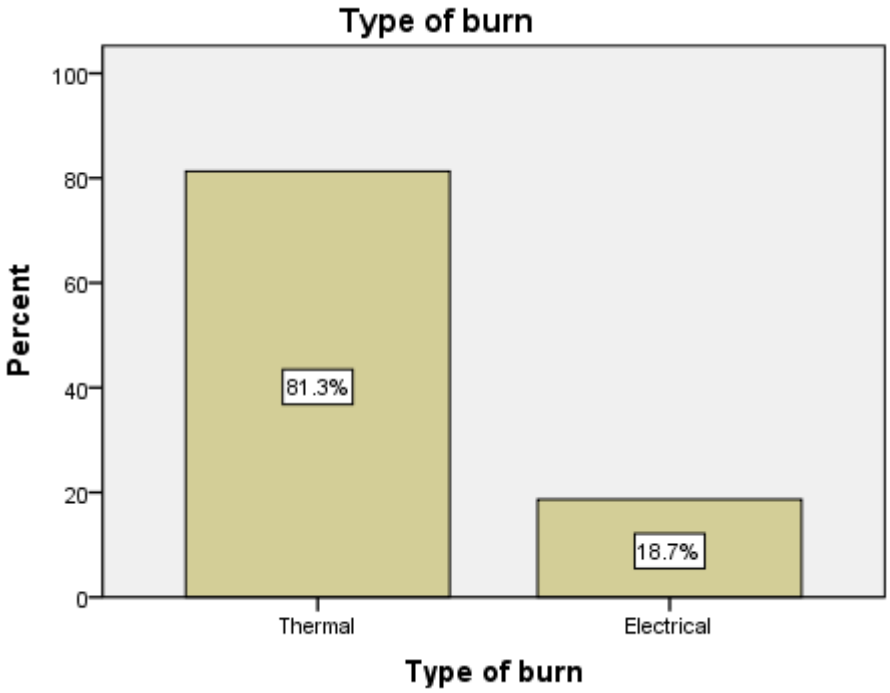


Figure 4.1: ***Type of burns proportions***

Distribution of TBSA% among burn patients

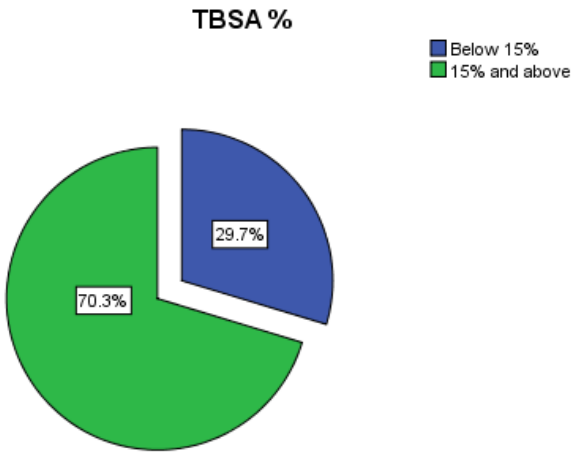


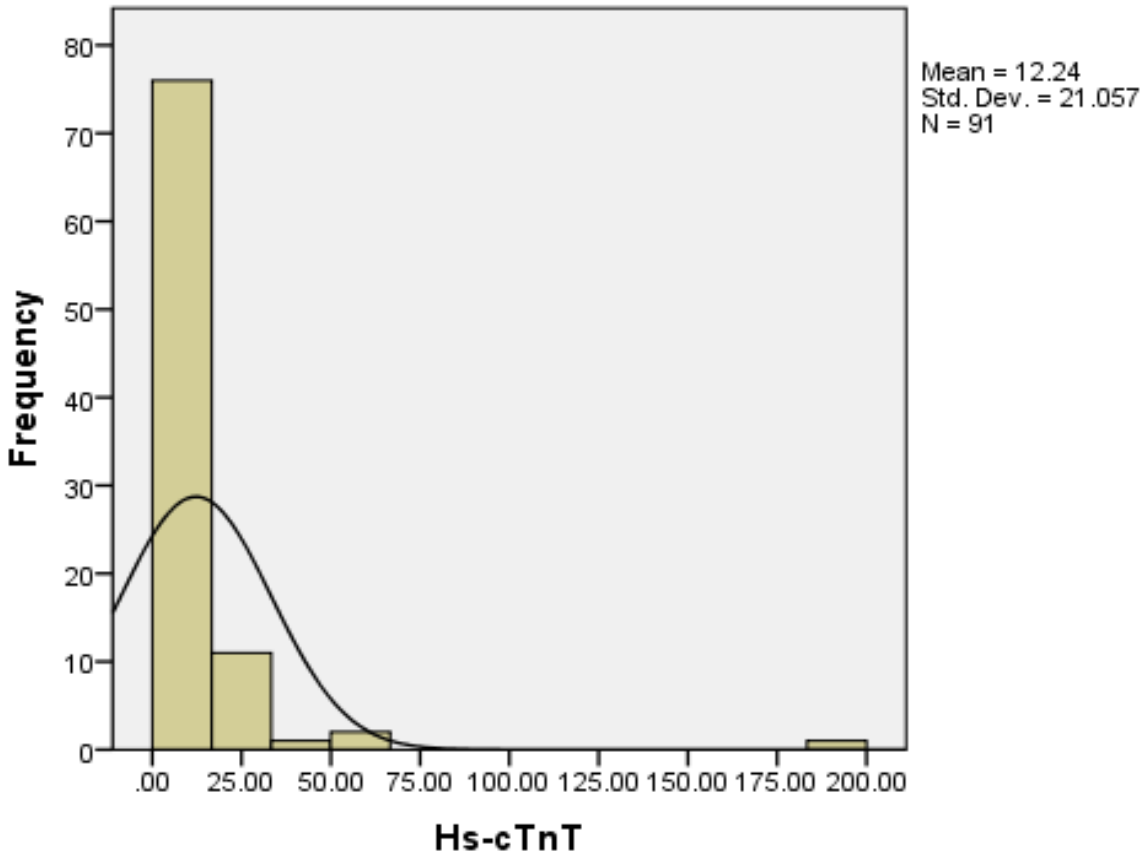
Figure 4.2: ***TBSA% severity***

In this study, 70.3% (*n*=64) of the burn patients had a TBSA of 15% and above whereas 29.7% (*n*=27) had TBSA % of below 15%.

Table 4.3: *cTnT distribution* (pg/ml)

Hs-cTnT distribution (pg/ml)	
Mean	12.2444
Median	6.7200
Mode	3.00
Std. Deviation	21.05736
Minimum	1
Maximum	186.50

Figure 4.3 ***hs-cTnT distribution (pg/ml)***



4.3: *cTnT distribution*

The cut-off point of hs-cTnT in males was 14 pg/ml while females were 10 pg/ml. The hs-cTnT output was skewed towards the right (6.73). The lowest measure concentration hs-cTnT levels was 1 *pg/ml* while the highest was 186.50 *pg/ml.* The mean hs-cTnT levels was 12.24 while the standard deviation was 21.06 with a median of 6.72.

Prevalence of myocardial injury in burns patients by use of cTnT

Of the total Hs-cTnT tests, 72.5% (*n*=66) were normal while 27.47% (*n*=25) were high. The prevalence of myocardial injury using high-sensitive cardiac troponin T as a biomarker in burns patients was 27.47%

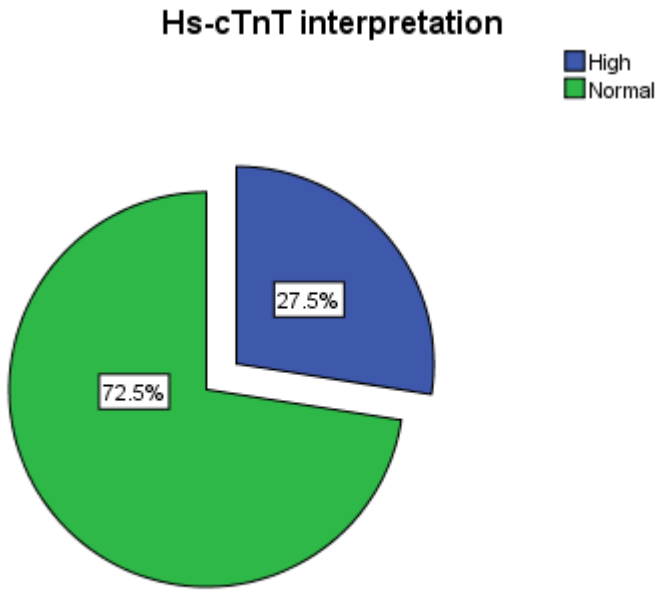


Figure 4.4: ***hs-cTnT prevalence in burns patients***

4.5 Relationship between cTnT and 'Type of burn'

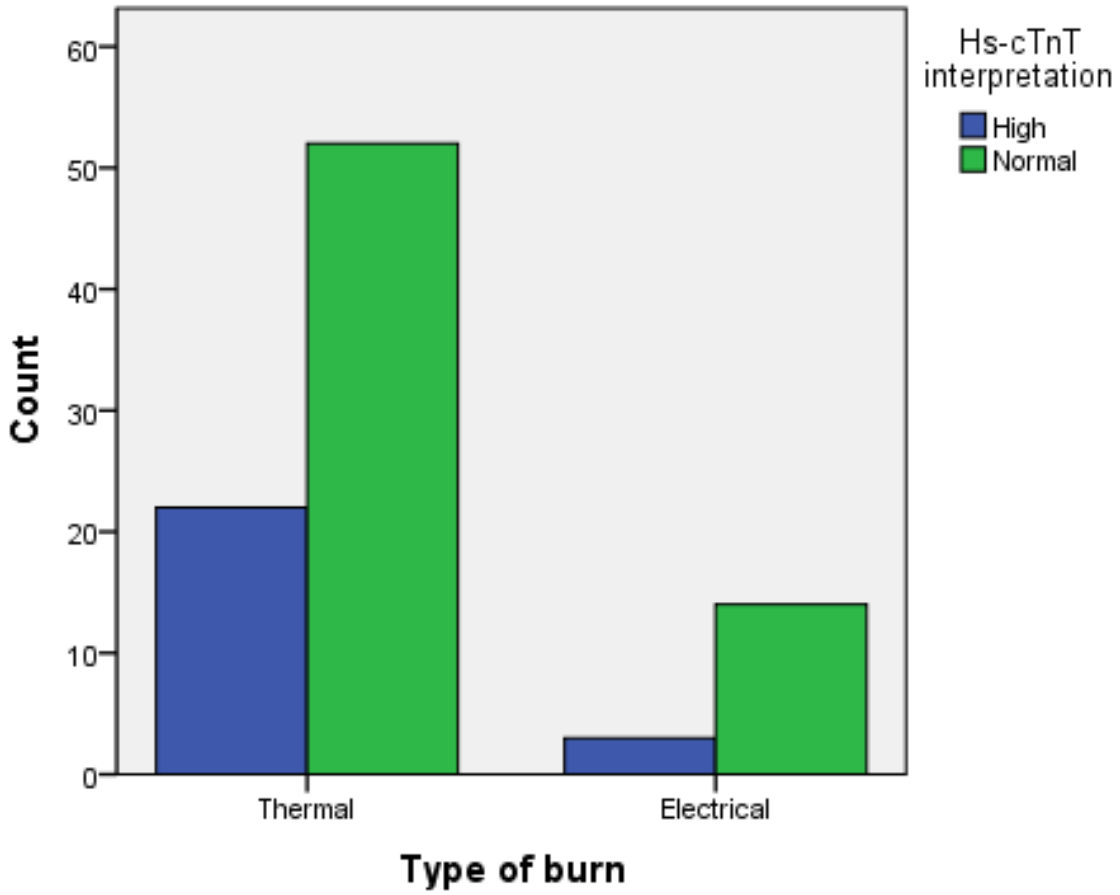


Figure 4.5: ***correlation between the type of burns and hs-cTnT***

Both electrical and thermal burns had raised serum cardiac troponin T. This study found no significant difference between the type of burns and hs-cTnT where $p = 0.314$. There was a weak positive correlation between Hs-cTnT and Types of burn which was not statistically significant with $r_s=0.106$ and $p = 0.320$.

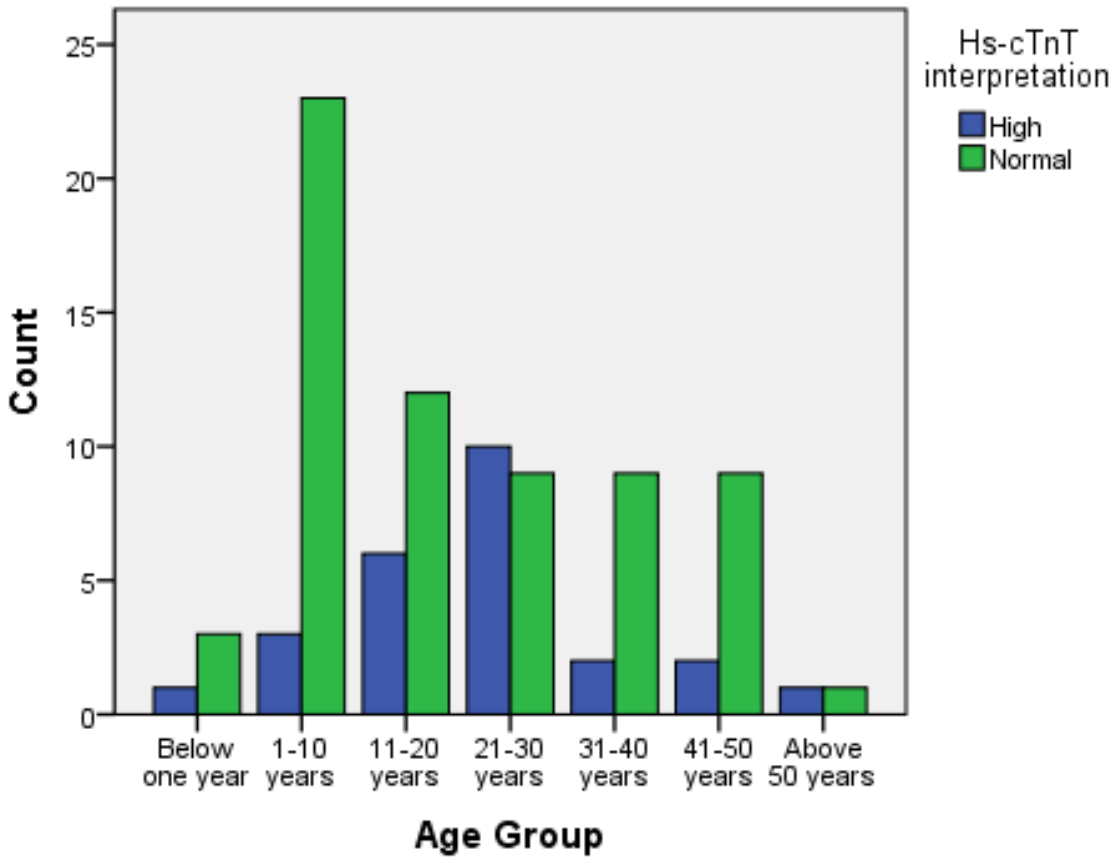


Figure 4.6: ***Distribution of hs-cTnT amongst different age groups***

Among the study participants, ages 1 to 10 years had more admissions, however, most had normal hs-cTnT levels. The age group with the highest hs-cTnT levels was 21 to 30 years followed by 11 to 20 years.

Relationship between cTnT and TBSA%

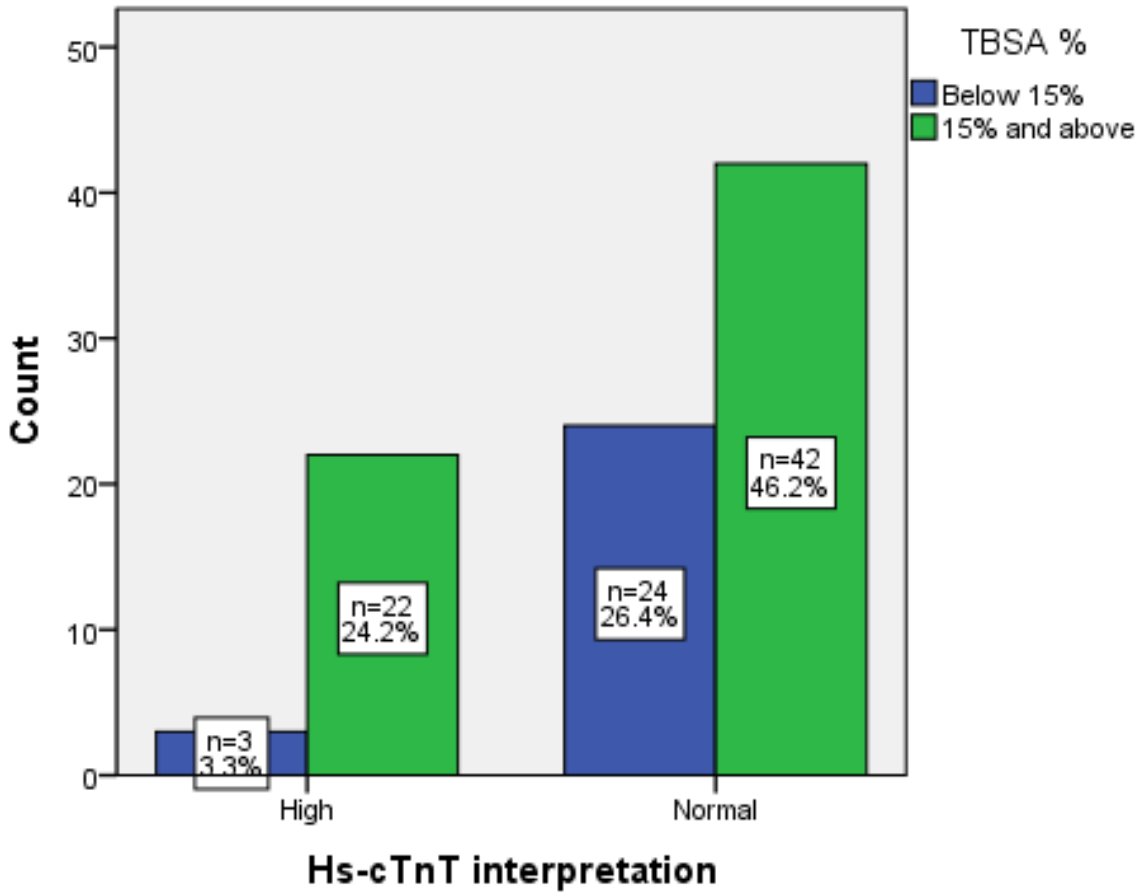


Figure 4.7: ***correlation between cTnT and TBSA%***

24.2% of patients with high hs-cTnT had TBSA% greater than 15% compared to 46.2% patients with normal hs-cTnT who had TBSA% greater than 15%. This study found a significant relationship between serum hs-cTnT and TBSA% where p = 0.023. There was a negative correlation between serum hs-cTnT and TBSA% with r_s= -0.238 and p = 0.023.

CHAPTER 5: DISCUSSION

Demographics (Age, Gender, TBSA% and type of Burns)

This was a descriptive, cross-sectional study on a non-randomized sample of patients with no previous known cardiac, neuromuscular or kidney pathology. This was to ensure that the data collected gave reliable, accurate and non-biased results due to known causes of troponin elevation.

This study evaluated 91 burns patients, most of who were male 57.1% while 42.9% were female. The rate of burn injury did not compare to the previous local study carried out at the same hospital by Hassan et al which gave an 81.2% and 18.8% for males and females respectively. This possibly was attributed to the study duration of four years compared to this study which was done over two months. This might also have been due to the study design where Hassan et al was observational compared to this descriptive study. (Hassan, 2016)

The age distribution in this study was between a 19 days old neonate to 56 years with a mean age of 20.63, *SD* of 15.30 with an age skewness of 0.476. Age grouping comprised of those below 1 year 4.4% (*n*=4), 1-10 years comprising of 28.6% (*n*=26), 11-20 years 19.8% (*n*=18), 21-30 years 20.9% (*n*=19), 31-40 years 12.1% (*n*=11), 41-50 years 12.1% (*n*=11), and those above 50 years consist of 2.2% (*n*=2). The age group distribution was concurrent with a study done by Wanjeri et al (Wanjeri, 2018)

The TBSA% ranged from a minimum of 3.0 to the highest of 60.0 with a mean of 25.0, median of 22.0, and standard deviation of 14.11 with a distribution skew of 0.315. (Moore, 2019)

During the study period, thermal burns contributed to 81.3% (*n*=74) while electrical burns were 18.7% (*n*=17). The distribution concurs with the findings of studies done in LMIC where 95% of burns are fire-related as per 2015 Global Health Estimates. (World Health Organization, 2018)

Serum cardiac troponin T (cTnT) levels in burns injury patients at KNH

The lowest value of hs-cTnT was 1 pg/ml while the highest was 186.50 pg/ml. The mean hs-cTnT levels was 12.24 while the standard deviation was 21.06 with a median of 6.72. The Hs-cTnT output was skewed towards the right (6.73) where total hs-cTnT tests, 72.5% (*n*=66) were normal while 27.5% (*n*=25) were high. The prevalence of myocardial injury using high-sensitive cardiac troponin T as a biomarker in burns patients was 27.47%. The finding in this study is in concurrence with a study done in 2000 by Chen et al. The study showed all patients had increased (serum cardiac troponin I) cTnI on two or more occasions where the mean cTnI concentration was significantly higher in patients with TBSA of burn > 30%. They concluded that burned patients have varying degrees of non-ischaemic cardiac injury, manifesting as leakage of cTnI from myocytes into the circulation. (Chen YN, 2000)

Correlation between the type of burns and serum cardiac troponin T (cTnT)

Burns are categorized by their causes which include thermal, electrical, radiation and chemical burns. During the study timeframe only two types of burns were encountered, thermal and electrical burns. Thermal burns contributed to the highest proportion of burns patients (81.3%) compared to electric burns (18.7%) of the sample size. This is in concurrent with Global health estimates of LMIC that have fire-related burns as a major cause of burn injury (World Health Organization, 2018)

This study found a significant relationship between the type of burn and hs-cTnT, with no significant difference between the variables (p=0.314). There was a weak positive correlation between hs-cTnT and burn types, but it was not statistically significant (r = 0.106, p = 0.320).

Serum cardiac troponin T (cTnT) and TBSA% correlation

The severity of burns is measured using TBSA % and degree of burns. In this study, TBSA% was used where it was categorized into two to quantitatively define and compare the research findings. Of the 91 study participants, 70.3% (*n*=64) had a TBSA of 15% and above whereas 29.7% (*n*=27) had TBSA % of below 15%.

The relationship between hs-cTnT and TBSA% was significant ($p = 0.023$). Hs-cTnT and TBSA% had a negative correlation with $r = -0.238$ and $p = 0.023$. This differs from the findings of William et al which demonstrated a significant correlation with a positive troponin test. Burns that affected more than 15% of the total body surface area (%TBSA) demonstrated an elevated risk of acute cardiac complications and death. There was an association between higher troponin levels and acute burns with TBSA% more than 15%. (William Alexander, 2018)

CONCLUSION

This study has demonstrated that burns patients have elevated serum cardiac troponin T compared to the general population. The rise in serum cardiac troponins was shown to be dependent on TBSA%. The rise in cardiac troponin T is a direct measure of myocardial injury caused by burns which can lead to potential AMI which can cause death. Therefore, a proportion of burns patients on the study population are likely to have myocardial ischaemia.

The prevalence of myocardial injury in burn patients using serum cardiac troponin T as a biomarker was 27%. Of these, a significant proportion (81.3%) of all burns was contributed to by thermal burns as opposed to electrical burns (18.7%). There is therefore a need for routine assessment of all burns patients using cardiac troponin to help in the early identification and stratification of patients at risk of AMI. This would help in early intervention to prevent morbidity and mortality associated with myocardial dysfunction due to burns.

RECOMMENDATIONS

1. A rise in serum cardiac troponin T has been demonstrated in burns patients at Kenyatta National Hospital implying the possible presence of myocardial injury in burns patients. This suggests that burn patients should be assessed by measuring the levels of a preferred and recommended biomarker such as cTnT. This would assist in the early identification and stratification of patients at risk and allow for early intervention to reduce the morbidity and mortality associated with myocardial injury.
2. Future studies should be done to further elucidate the correlation of serum cardiac troponin T and different types of burns.
3. A diagnostic serum cardiac troponin cut-off point should be established to ease the interpretation of different troponins levels in different burns. This would impact diagnostic workup on myocardial injury in burn patients and its outcome in different types of burns.

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APPENDICES

INFORMED CONSENT FORM

English version

This informed consent form was for patients hospitalized at KNH with burns during the study period. We requested these patients to participate in the research project whose title was, "levels and significance of cTnT in burn patients", a cross-sectional descriptive study.

1. **Adult consent form: for enrolment in the study (*over 18 years*)**
2. **Child assent document: for enrolment in the study (*aged 6 to 17 years*)**
3. **Statement of consent**
4. **Statement of witness**
5. **Statement by the researcher.**

PARTICIPANT INFORMATION AND CONSENT FORM

ADULT CONSENT FOR ENROLLMENT IN THE STUDY

Title of Study:

LEVELS AND SIGNIFICANCE OF SERUM CARDIAC TROPONIN T *(cTnT)* IN BURN PATIENTS

Principal Investigator\and institutional affiliation:

Principal researcher

Kimani Geoffrey Warui

Masters of Science in Clinical Chemistry

Department of Human Pathology

University of Nairobi

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MB ChB, MMed (H Pathology)

Lecturer, Department of Human Pathology, College of Health Sciences - University of Nairobi

Dr. Wanjeri, Joseph Kimani

MB ChB, MMed (Surg), MPH, Ph.D. candidate

Lecturer, Department of Surgery, College of Health Sciences - University of Nairobi

Dr. Caroline Njeru

MB ChB, MMed (H Pathology)

Lecturer, Department of Human Pathology, College of Health Sciences - University of Nairobi

Introduction:

I would like to tell you about a study being conducted by the above-listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in medical research:

i) Your decision to participate is entirely voluntary

ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal

iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities.

We will give you a copy of this form for your records.

May I continue? YES ☐ NO ☐

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No: P56/02/2020

WHAT IS THIS STUDY ABOUT?

The researchers listed above are interviewing individuals who have burns. The purpose of the interview is to seek consent to recruit you as a participant in the study to investigate the level and significance of cardiac troponin T *(cTnT)*. Participants in this research study will be asked questions about burns they experienced leading to admission. Participants will also have the choice to undergo test cardiac troponin T *(cTnT)*.

There will be approximately 91 participants in this study randomly chosen. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:

You will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately five minutes. The interview will cover topics on how you got burns, date of burns and span of admission and whether you have any known body disease or condition.

After the interview has finished, we shall seek to know whether you have understood and given a chance for any question. Upon consent, we shall collect three milliliters of blood using a needle and a syringe or through the central line already inserted by the attending doctor.

We will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. The reasons why we may need to contact you include:

i) Informing you that your results are out and delivered to your attending doctor

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Efforts should always be put in place to minimize the risks. One potential risk of being in the study is the loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

It may be ironic to give three milliliters of blood when you best need it during your healing process. We will however do everything we can to ensure that this is done professionally and in private. Furthermore, all study staff and interviewers are professionals with special training in these interviews, phlebotomy, analysis and reporting of your results.

You may feel some discomfort or pain when we shall be collecting blood, however, it is more of what you might have experienced during routine blood collection. Professional care shall be in

place in case of any eventuality. In case of an injury, illness or complications related to this study, contact the study staff right away at the number provided at the end of this document. The study staff shall coordinate with the attending doctors and nurses to give you immediate help.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

You may benefit by receiving free cardiac troponin T *(cTnT)* testing and reporting. We will deliver a report of the results for filing. Also, the information you provide will help us better understand myocardial injury in burns patient. This information is a contribution to science and the community at large in enhancing and adding to the body of knowledge for burns care. This will help in combating organ or life-threatening consequences in burn injuries based on the biomarker.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

You are not required to pay any money towards the research for any utility pertaining to cardiac marker sample collection, running the test, results production or any other utility whatsoever. You are requested to communicate to the Principal researcher in case of such an eventuality in course of your management

WILL YOU GET REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

The research team does not expect you to incur any expense in course of the study, however, in any scenario that this may arise, we shall request you to communicate to the principal investigator for an action or a refund of the same.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call, email or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

CHILD ASSENT DOCUMENT *(aged 6 to 17 years)*

Project Title

LEVELS AND SIGNIFICANCE OF SERUM CARDIAC TROPONIN T *(cTnT)* IN BURN PATIENTS

Investigator

GEOFFREY WARUI

We are doing a research study about how the heart responds in the event of a burn accident. Permission has been granted to undertake this study by the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC Protocol No. P56/02/2020

This research study is a way to learn more about people. At least all the admitted children with burns who accept a blood collection will be participating in this research study with you.

If you decide that you want to be part of this study, you will be asked to allow the doctor to collect a blood sample using a three milliliters syringe where it will be analyzed and results returned. There are some things about this study you should know. This is the collection of a blood sample which involves a needle or collection through the already inserted central line. This comes with minimal or no pains.

Everyone who takes part in this study will benefit. A benefit means that something good happens to you. These benefits will be producing a report of your cardiac status based at the time of sample collection at no cost to your bill.

If you do not want to be in this research study, your treatment plan shall continue as scheduled.

When we are finished with this study we will write a report about what was learned. This report will not include your name or that you were in the study.

You do not have to be in this study if you do not want to be. If you decide to stop after we begin, that's okay too. Your parents know about the study too.

If you decide you want to be in this study, please sign your name.

I, _____, want to be in this research study.

_____ _____

(Signature/Thumb stamp) (Date)

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study: Yes ☐ **No** ☐

I agree to have my blood sample collected for the study: Yes ☐ No ☐

I agree to provide contact information for follow-up: Yes ☐ No ☐

Participant printed name:.....

.....

Signature (*participant/Next of Kin***)**

Thumb print of participant if illiterate

(*A witness must sign below*)

.....

Date: day ☐☐ **month** ☐☐ **year** ☐☐☐☐

Statement by the witness if the participant is illiterate

I have witnessed the accurate reading of the consent form to the participant and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely

Name of witness .....

Signature

.....

Date: day ☐☐ **month** ☐☐ **year** ☐☐☐☐

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name: .....

Date: .....

Signature .....

Role in the study: Research Assistant ☐

Name .....

Contact information .....

Signature /Thumb stamp: .....

Date: .....

For more information contact:

Principal Investigator

Kimani G. Warui

P.O. Box 14188 - 00100

Nairobi, Kenya

Email: drkgwarui@gmail.com

At:

Mob No: +254 727 656 282

From:

8 00 am to 5 00 pm

Co-Investigators and institutional affiliation:

Dr. Julius Gikonyo Kuria

MB ChB, MMed (H Pathology)

Lecturer, Department of Human Pathology, College of Health Sciences - University of Nairobi

P.O. Box 19676 – 00202

KNH, Nairobi

Tel +254 20 276300

Email: dept-hpathology@uonbi.ac.ke

Dr. Wanjeri, Joseph Kimani

MB ChB, MMed (Surg), MPH, Ph.D. candidate

Lecturer, Department of Surgery, College of Health Sciences - University of Nairobi

P.O. Box 19676 – 00202

KNH, Nairobi

Dr. Caroline Njeru

MB ChB, MMed (H Pathology)

Lecturer, Department of Human Pathology, College of Health Sciences - University of Nairobi

P.O. Box 19676 – 00202

KNH, Nairobi

Tel +254 20 276300

Email: dept-hpathology@uonbi.ac.ke

KISWAHILI CONSENT FORM

FOMU YA ITHINI

Mtafiti Mkuu

Kimani G. Warui

Saduku la Posta 7894-00300

Nairobi, Kenya

Nambari ya rununu: 0727656282

Katibu wa utafiti, Hospitali kuu ya Kenya na Chuo kikuu cha Nairobi

Saduku la posta 20723 - 00202

Nairobi

Nambari ya simu: 726300-9

Msimamizi mkuu, Sekta ya Magonjwa, chuo kikuu cha Nairobi

Saduku la posta 19676 – 00202

Nairobi

Nambari ya simu +254 20 276300

Ningetaka kukueleza kuhusu utafiti tunaoufanya. Umuhimu wa fomu hii ya idhini ni kukupa yote unayohitaji kujua kabla kutupa kibali cha kukuhusisha. Unaweza kuuliza swali lolote lile wakati wowote kwa kile usichokifahamu, umuhimu wa utafiti huu kwako na kwa jamii, utakavyo kuadhiri na swali lingine ili kuhakikisha umeelewa. Tutakapomaliza kukuelimisha, tutakuomba udhibitishe kwa kutia sahihi kwa karatasi tutakayokupa kama dhibitisho ya kuwa unajua kile kinachoendelea. Kabla kuendelea, ni muhimu ujue yafuatayo:

i. Kuhusika kwako kwa utafiti huu ni kwa kujitakia
ii. Unaweza amua kutojihusisha ama utake wakati wowote bila hata kupeana sababu
iii. Kutojihusisha kwa utafiti huu hakutaadhiri kwa njia yoyote ile matibabu unayopata kwa hospitali hii

Ningalitaka kuendelea NDIO ☐ LA ☐

Utafiti huu umeithinishwa nambari P56/02/2020

UTAFITI HUU UNAHUSU NINI

Utafiti huu unahusisha wagonjwa wowote wa kuchomeka. Tutakuwa tunaangalia uhusiano war oho na kuchomeka tukitumia kipimo cha damu. Kuhusika kwako kwa utafiti huu kutakuwa kukuuliza maswali kwanza ya vile ulivyochomeka kasha tukutoe damu ambayo tutapima bila kukugarimu chochote. Utafiti huu unahusisha wahusika takribani tisini na moja ambao tutawachagua bila kubagua.

NINI KITAKACHOFANYIKA UKIAMUA KUJIHUSISHA NA UTAFITI HUU

Baada ya kuamua kujihusisha na utafiti, utaulizwa maswali na msaidizi mmoja wa utafiti ambapo utakuuliza tu yale yanayotusaidia na kuhusisha uchunguzi. Baada ya maswali, utaulizwa ama umeelewa kasha kuridhika kwako kutawaruhusu kukutoa damu milimita tatu tu.

Utaombwa kutia sahihi kijikaratasi kama dhibitisho ya kuhusika kwa utafiti hii na endapo utahitaji kujua majibu yakitoka, utaombwa upeane nambari yako ya simu utakayopokea ujumbe mfupi.

MWILI NA MAISHA YANGU

Kuhusika kwako kwa utafiti kutabidi upeane habari ama ujumbe ambao kwa wengi ama hata kwako ungaliona ngumu kupeana. Hata hivyo, kuna hakikisho la kurinda maneno yote utakayotupa kwa utafiti huu peke yake. Kuhakikisha tumeiweka salama, anayekuhoji amehitimu kama muuguzi na kisha tukamfunza mengi kuhusu utafiti na kuweka maneno ya utafiti kuwa ya utafiti bila ya kuyaeneza. Endapo ungehisi mambo yako yataenda nje ya utafiti, una uhuru wa kuuliza na kusema kwa mtafiti mkuu.

Utafiti huu unatumia kipimo cha damu na kwahivyo tutakuomba kutoa damu kindogo ambayo utaskia uchungu kidogo ka ya hizo sindano zingine. Haya yote yanafanywa na wauguzi na madaktari waliohitimu.

NITAFAIDIKAJE KUTOKANA NA UTAFITI HUU

Utafiti huu unahusu kipimo cha roho ambacho kwa kawaida kingekugarimu pesa. Kujihusisha na utafiti kwa hicho kipimo hakutakugarimu chochote kwa bili yako ya hospitali. Endapo ugalimiwe, unastahili kupigia mtafiti mkuu ili husuruhisha.

Majibu ya utafiti yatakapotoka yatawezesha daktari kukutibu kulingana na yatakavyotoka na kisha baada ya utafiti, wagonjwa wote wa kuchomeka watafaidika na matokeo ya utafiti huu ili kuwezesha watibiwe vizuri kwa hii nchi yatu na mbali Zaidi ya nchi.

GHALAMA

Utafiti huu haukughalimu chochote kwa njia ya pesa. Endapo ujipate ukigharimika, tunakuomba uwasiriane na mtafiti mkuu wa utafiti huu ili kusuruhisha jambo lolote.

MASWALI BAADA YA KUJIHUSISHA NA UTAFITI

Kuwa mhusika katika utafiti kunakupa kibali cha kuuliza maswali wakati wowote ila tu iwe inahusu utafiti. Kupitia nambari ambazo tumepatiana kwa kijikaratasi hiki, unaweza kuwasiliana na yeyote na ungalikuwa na swali la uhalisia wa utafiti huu, piga nambali ya No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke Hospitali kuu ya Kenyatta (KNH) na Chuo Kikuu cha Nairobi (University of Nairobi).

UHURU WA MAAMUZI MENGINE

Una uhuru wa kujitakia wewe mwenyewe bila kusinikizwa na yeyote na uko na uhuru wa kujitoa ama kujiuzuru bila kuulizwa na yeyote. Una uhuru na haki ya kupata matibabu yako kawa kawaida ukiwa kwa utafiti au nje ya utafiti na kwa hivyo usishinikizwe kuwa mmoja wa wahusika wa utafiti.

FOMU YA IDHINI KWA WATOTO WA MIAKA SITA HADI KUMI NA SABA

MTAFITI MKUU

Geoffrey Warui

Ninafanya utafiti wa kuchunguza vile roho huadhirika mtu anapochomeka. Nitatumia damu kama kipimo kuangalia chemikali inayotolewa na roho mtu achomekapo na kuilinganisha na ukubwa wa kuchomeka. Hii inaweza tumika kusaidia matibabu ya aliyechomeka.

Ningependa kukuchagua wewe kama mhusika katika utafiti huu wangu ili kufanikisha lengo kuu. Utafiti hutusaidia kujua mengi kuhusu mwli na hunufaisha katika kufanya maamuzi mazuri kwa daktari anayekutibu.

Kuitikia kwako kuwa mhusika katika utafiti huu kutakuwa kwa manufaa kwako na kwa jamii ya leo nay a siku za usoni. Utaulizwa maswali ya ulivyopata majeraha ya moto kasha tutaomba kukutoa damu milimita tatu tu ambazo tutapima kwa maabara. Baada ya kupima, tutarejesha majibu kwa daktari anayekutibu. Haya yote tutayafanya bila gharama kwa wazazi wako. Utafiti huu ni wa hiari kwa wahusika wote ambako kutaka kwako kujihusisha au kutojihusisha hakukugharimu chochote na hakuadhiri unavyotibiwa.

Kama umeamua kuwa katika utafiti huu, tafadhari tia sahihi hapa

JINA:.....

TAREHE:.....

SAHIHI:.....

Kwa swali lolote lile baadae

Dr. Julius Gikonyo Kuria

Mwalimu msimamizi, Chuo kikuu cha Nairobi

Saduku la posta 19676 – 00202

Nairobi

Nambari ya simu +254 20 276300

Dr. Wanjeri, Joseph Kimani

Mwalimu msimamizi, Chuo kikuu cha Nairobi

Saduku la posta 19676 – 00202

KNH, Nairobi

Dr Caroline Njeru

Mwalimu msimamizi, Chuo kikuu cha Nairobi

Saduku la posta 19676 – 00202

Nairobi

Nambari ya simu +254 20 276300

SEHEMU YA PILI: IDHINI

Mimi *(jina)* ..... kwa hiari yangu ama kwa hiari ya mgonjwa wangu *(jina la mgonjwa)* ..... nimekubali kushirikishwa katika utafiti huu unaofanywa na Kimani G. Warui wa chuo kikuu cha Nairobi kutokana na hali ambazo zimeelezwa na si kwa malipo ama shurutisho lolote.

Nimeelewa kwamba naweza kujiondoa wakati wowote nitakapo na hatua hii haitahatarisha matibabu ninayopewa ama anayoipata mgonjwa wangu. Matokeo ya utafiti yaweza kuwa ya manufaa kwangu ama kwa wagonjwa wengine kwa jumla na yanaweza kusaidia kwa matibabu ya wengine wanaopata ajari na majeraha ya kuchomeka

.....

Sahihi / kidole cha gumba (*mhusika/msimamizi wake*)

.....

Kidole cha gumba kwa asiyejua kuandika

(*shahidi atie sahihi hapa chini*)

☐ ☐ ☐

Tarehe: siku mwezi mwaka

SHAHIDI

.....

Sahihi / kidole cha gumba

.....

☐ ☐ ☐

Tarehe: siku mwezi mwaka

DATA COLLECTION INSTRUMENTS

QUESTIONNAIRE

Study Unique No.: | | | |

(Please tick or fill where appropriate)

1. Patient details

1.1. Name of the hospital ***(Kenyatta National Hospital)*** .....

1.2. Admitting ward ..... | | | |

1.3. Date of admission ..... | | date | | month | 2019 | Year |

1.4. Age ***(if less than 5 years, please fill in months)*** ..... | | | |

1.5. Gender ..... | | male | | female | | others |

2. Residence of the patient

2.1. county .....

2.2. constituency .....

3. Clinical details

3.1. Cause of burn injury:

3.1.1. thermal *(specify)* ..... |

3.1.2. electrical *(specify)* ..... |

3.1.3. chemical *(specify)* ..... |

3.1.4. radiation *(specify)* ..... |

3.1.5. others *(specify)* .....

3.2. Burn site:

3.2.1. Head ..... |

3.2.2. Trunk .....

3.2.3. Limbs .....

3.2.4. Groin .....

3.2.5. Combination *(specify)* .....

3.3. Burn severity:

3.3.1. 1st Degree .....

3.3.2. 2nd Degree .....

3.3.3. 3rd Degree .....

3.4. TBSA% ..... **%**

4. Where did the victim sustain the burn injury

4.1. home *(specify)* .....

4.2. place of work *(specify)* .....

4.3. institution *(specify)* .....

4.4. in a vehicle *(specify)* .....

4.5. others *(specify)* .....

5. Time

5.1. how long did it take for you to get to the hospital .....

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/157

21st May 2020

Kimani Geoffrey Warui
Reg. No. H58/8197/ 2017
Dept. of Human Pathology
School of Medicine
College of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL
APPROVED
21 MAY 2020
KNH/UoN-ERC
P.O. BOX 20723 - 00202 NAIROBI

Dear Geoffrey

RESEARCH PROPOSAL – LEVELS AND SIGNIFICANCE OF SERUM CARDIAC TROPONIN T *(cTnT)* IN BURN PATIENTS (P56/02/ 2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 21st May 2020 – 20th May 2021.

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 serious 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. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. 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*).
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**http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

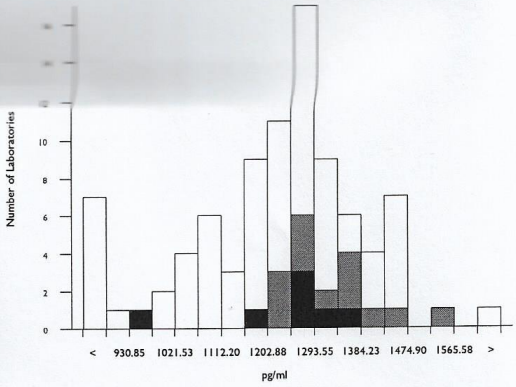
c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Human Pathology, UoN
Supervisors: Dr. Julius Gikonyo Kuria,Dept. of Human Pathology, UoN
Dr. Wanjeri Joseph Kimani, Dept.of Surgery, UoN
Dr. Caroline NJeru, Dept.of Human Pathology, UoN

Troponin T, pg/ml

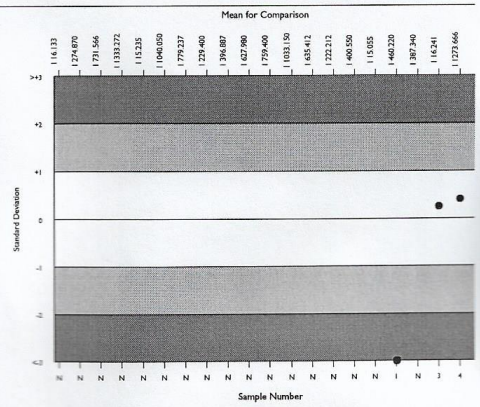
	N	Mean	CV%	U_m	SDPA	Exc.
All Methods	79	1248.221	9.7	17.00	132.80	10
Roche cobas Troponin T hs kits	18	1299.277	5.8	22.20	138.20	2
Roche Cobas c501/502/503 e601/602	6	1273.666	5.4	35.30	135.50	1

Your Result	1327.000	SDI	0.39
		RMSDI	Too Few
Mean for Comparison	1273.666	TS	112
		RMTS	Too Few
		%DEV	4.2
		RM%DEV	Too Few

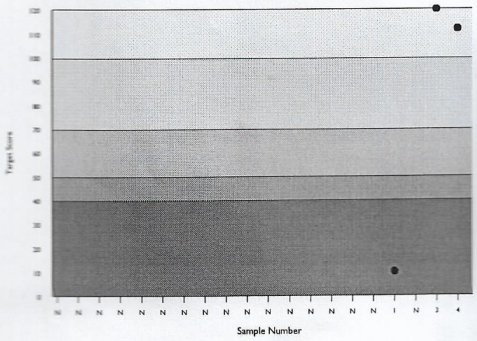
Acceptable limits derived from Biological Variation	N/A
Acceptable limits of performance for RIQAS	17.50%

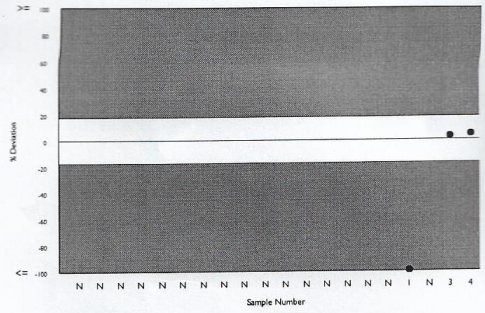


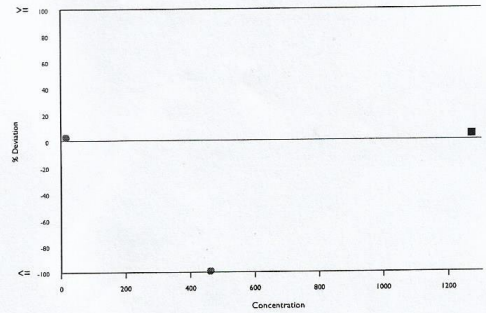
Method	N	Mean	CV%	U_m
Roche cobas Troponin T hs STAT	50	1231.920	9.7	21.00
Roche cobas Troponin T hs kits	18	1299.277	5.8	22.20
Roche h232	5	773.000	27.2	117.30
Roche cobas e801 TnT hs kits	4	1478.000	6.5	59.60
Roche cobas e801 TnT hs STAT	4	1252.750	9.2	71.60



TDPA = 17.5%







RIQAS

UKAS

STUDY BUDGET

ITEM	**ESTIMATED COST**
1. Stationary, photocopying, printing and binding	**10,000**
2. Computer and internet	**5,000**
3. Research assistant	**10,000**
4. Statistician	**15,000**
5. Vacutainers	**3,000**
6. Syringes with needles	**3,000**
7. Cool box	**5,000**
8. cTnT calibrator, controls and reagents (*100 tests*)	**90,000**
9. Final document preparation	**5,000**
10. Miscellaneous	**5,000**
Estimated total	**151,000**

STUDY TIME FRAME

ACTIVITY	**TIMEFRAME**
1. Preparation of proposal	**October 2018 to August 2019**
2. Presentation to the department of Human Pathology	**August 2019**
3. Submission to KNH / UON Ethics and Research Committee	**February 2020 to May 2020**
4. Sample collection and analysis	**June 2020 to November 2020**
5. Data analysis and results presentation	**June 2021**
6. Report writing and dissertation submission	**July 2021**
7. Dissemination and utilization of results	**September 2021**