PROGNOSTIC VALUE OF IONISED MAGNESIUM IN PREDICTING OUTCOME OF ADULT PATIENTS WITH SEPSIS ATTENDING THE EMERGENCY MEDICINE DEPARTMENTS IN TANZANIA

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MMed (Emergency Medicine) Dissertation
Muhimbili University of Health and Allied Sciences
October, 2024

Muhimbili University of Health and Allied Sciences

Department of Emergency Medicine

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By

Jaimini K.K Popat

A Dissertation Submitted in Partial Fulfilment of the Requirements for the Degree of Master of Medicine (Emergency Medicine) of

Muhimbili University of Health and Allied Sciences
October, 2024

CERTIFICATION

The undersigned certifies that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled**: "Prognostic value of ionised magnesium in predicting outcome of adult patients with sepsis attending the emergency medicine departments in Tanzania"** in (partial) fulfilment of the requirement for the degree of Master Medicine (Emergency Medicine) of Muhimbili University of Health and Allied Sciences (MUHAS), Dar es Salaam, Tanzania.



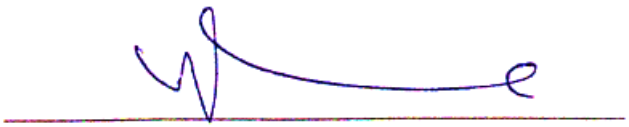
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DECLARATION AND COPYRIGHT

I, **Jaimini K.K Popat**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

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ACKNOWLEDGMENT

I am eternally grateful to the Almighty God for His grace, love, and mercy in supporting me to complete my dissertation. I am uttermost thankful to my supervisor's Dr Said S Kilindimo, Dr Alphonce Simbila, Dr Shaffin Rajan, Prof Henry Sawe and Prof Ellen Weber for being tolerant of me and for giving me their time and guidance throughout the proposal development, research implementation, data analysis, and report writing. It feels special for me to work under their supervision. I would like to thank the Department of Emergency Medicine MUHAS for their advice during the development of this research.

I would like firstly and foremostly to extend my gratitude to Dr Juma Mfinanga and to thank Emergency Medicine staffs from Muhimbili National Hospital, my fellow residents, registrars and research assistants for their support; for being cooperative and enabling me to conduct this study.

I would like to extend my gratitude to all academic staff and clinical staff of the Department of Emergency Medicine at the Muhimbili University of Health and Allied Sciences (MUHAS) and Muhimbili National Hospital (MNH) for their kindness throughout my training

With love of God, I am utmost grateful to my beloved husband, mummy and daddy, mummy-in-law and friends for their support during my entire academic and dissertation journey.

DEDICATION

To my loving parents, Kailesh Kantilal Popat and Ritaben Kailesh Popat, my lovely mother-in-law, Nirmala Borhara and my beloved husband, Sagar Borhara.

ABSTRACT

Background: Serum Lactate is used as an indicator of sepsis in critically ill patients and is alternatively compared with qSOFA. Magnesium is the second most abundant intracellular ion which plays an essential role in enhancing host immunity against sepsis. To date, there is no literature from Tanzania evaluating the association between ionized magnesium and mortality from sepsis. This study aimed to determine the performance of ionized magnesium in predicting the mortality of patients with sepsis attending emergency medicine department in Tanzania.

Methodology: From February 2024 to April 2024 314 patients were consecutively enrolled at the emergency medicine department (EMD) of Muhimbili National Hospital (MNH) and Shree Hindu Mandal Hospital (SHMH) in Tanzania prospectively. Adults (≥18 years old) suspected having sepsis who met the qSOFA score≥2 were included and followed up for 24 hours to assess mortality. The primary outcome was the prognostic ability of ionized magnesium to predict 24 hours mortality at the EMD. At EMD ionized (iMg) and total magnesium (tMg) levels were classified as normal and abnormal based on cut-off values of 0.4-0.6 mmol/L and 0.7-1.0 mmol/L, respectively. Sensitivity, specificity, positive and negative predictive values, and area under the curve (AUC) were evaluated of hypermagnesemia and hypomagnesemia to determine their ability to predict 24 hour's mortality among critically ill adult patients with sepsis.

Results: 314 patients met the inclusion criteria and were enrolled. iMg had an AUC=0.549 (95% CI, 0.439-0.659). Sensitivity and specificity of iMg were 66.67% (95% CI, 46.50-86.83) and 41.05% (95% CI,35.34-46.76) respectively. Hypermagnesemia was 40.9% sensitive and 73.2% specific whereas hypomagnesemia was 4.5% sensitive and 78.7% specific.

Conclusion: Our study showed that total magnesium had the ability to predict mortality in the emergency medicine departments. While ionised magnesium had no prognostic value among adult patients with sepsis in Tanzania. However, lack of standardization of diagnostic reference levels was the reason for the seldom identification of iMg in sub-Saharan Africa.

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ABBREVIATIONS

A&E	Accidents and emergency
ABG	Arterial blood gases
ACLS	Advanced Cardiac Life Support
AHA	American Heart Association
ATP	Adenosine triphosphate
AVPU	Alert Voice Pain Unresponsive
BP	Blood pressure
CPR	Cardiopulmonary resuscitation
DAMP	Damage Associated Molecular Patterns
DIC	Disseminated Intravascular Coagulation
DNA	Deoxyribose-nucleic Acid
ECG	Electrocardiogram
EMD	Emergency Medicine Department
ERP	Enterprise Resource Planning
ESICM	European Society of Intensive Care Medicine
ETS	Emergency Triage Score
EWS	Early Warning Scores
FN	False negative
FP	False positive
GCS	Glasgow Coma Score
Hb	Hemoglobin
HIC	High income countries
HR	Heart Rate
HDU	High Dependency Unit
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
IL	Interleukin
IMAI	Integrated Management of Adolescent and Adult Illness

IRB	Institution Research Board
LIC	Low-income countries
MEWS	Modified Early Warning Score
Mg	Total Magnesium
MIC	Middle income countries
iMg	Ionized Magnesium
MIC	Middle Income Countries
MODS	Multi-organ Dysfunction Syndrome
MNH	Muhimbili National Hospital
NPV	Negative predictive value
PPV	Positive predictive value
POC	Point Of Care
RBG	Random blood glucose
RR	Respiratory rate
SHMH	Shree Hindu Mandal Hospital
SOFA	Sequential Organ Failure Assessment
qSOFA	Quick Sequential Organ Failure Assessment
SCCM	Society of Critical Care Medicine
SPO2	Saturation of oxygen
SSC	Surviving Sepsis Campaign
TN	True negative
TNF	Tumor Necrosis Factor
TP	True positive
UPT	Urine pregnancy test

DEFINITION OF KEY TERMS

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection.

Organ dysfunction can be identified as an acute change in total qSOFA score≥2 points consequent to the infection which includes 2 of the 3 criteria which are altered mental status=1, respiratory rate≥2 and SBP≥100mmHg.

Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.

MEWS score is a score which determines physiological parameters to identify patients that are at increased risk of catastrophic deterioration, resulting in ICU admission or death.

Infection is the invasion of microorganisms into sterile host tissue.

Cardiopulmonary resuscitation is a resuscitative procedure that can be performed by laypeople as well as medical personnel involving repeated cycles of compression of the chest and artificial respiration. It is performed to maintain blood circulation and oxygenation in a person who has suffered cardiac arrest.

Multiple Organ Dysfunction Syndrome is a syndrome associated with the failure of more than one organ system.

Total magnesium is the level of magnesium in blood that is bound to albumin.

Ionized magnesium is the level of magnesium in blood in an unbound state which is expressed as a cation.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. (1)It is the body's systemic immune reaction to an infectious process that may result in end-stage organ malfunction and death. Despite significant advancements in understanding of the pathogenesis of this clinical condition, sepsis remains a major source of morbidity and mortality in critically ill patients. (2) . Magnesium (Mg), also known as "the forgotten electrolyte", is the fourth most abundant cation overall and the second most abundant intracellular cation in the body.(3)

Magnesium is a very crucial electrolyte for optimal body function. Apart from influencing signal transduction, energy metabolism, and cell proliferation such as the transfer of potassium and calcium ions, it also includes mechanisms of magnesium's cellular uptake and efflux, as well as its intracellular transport, intestinal absorption, renal excretion, and hormone-related effects on these processes.(4) Magnesium also is required for protein synthesis, muscle contraction, nerve function, blood sugar regulation, blood pressure regulation and hormone receptor binding, heart rate variability, ion flux transmembrane. Along with this, energy generation involves magnesium which is essential for adenylate cyclase metabolism (ATP metabolism) and oxidative phosphorylation hence glycolysis and energy production. (5)

Magnesium plays a significant role in SIRS and sepsis, particularly in patients who are critically ill. Deficiency of magnesium leads to an increased release of several cytokines, which causes significant inflammation and raises the risk of death. A number of factors contribute to magnesium depletion in septic patients, including decreased magnesium absorption, inadequate nutrition intake and the use of medications such as diuretics, gentamycin, amikacin, and amphotericin B, which cause magnesium loss via the kidneys. Numerous studies have shown that low serum magnesium levels are linked to longer hospital stays, higher fatality rates, longer stays on mechanical ventilation, and longer stays on mechanical ventilator support among patients with severe sepsis. (7)

In critically ill patients, sepsis and septic shock continue to be the major causes of death. The syndrome's heterogeneity makes it difficult to generate reliable mortality risk estimates. In research conducted by Bauer et al., observed 30-day mortality rates of sepsis patients were 24.39%, whereas observed 90-day mortality of sepsis patients was 32.24%, despite extensive efforts to combat sepsis-related mortality. (6) Because critically ill patients are more likely to experience symptomatic or asymptomatic magnesium deficiency, which can have serious clinical consequences (such as hypokalemia, cardiac arrhythmias, hypocalcemia, neurotoxicity, and psychiatric issues) and ultimately increase morbidity and mortality, total magnesium monitoring may have prognostic as well as therapeutic implications.(7) Whereas the sole measure that can distinguish between critically sick patients with reduced magnesium status and surgical patients who need to have their perioperative consequences from magnesium deficit reduced is ionized magnesium.(8,9)(11)

On the other hand, a study done on children with sepsis admitted to the pediatric ICU revealed that when total magnesium levels reached 1.0 mmol/L which was high, children with sepsis had a considerably greater risk of inpatient mortality. This demonstrated a significant correlation between hypermagnesemia and elevated inpatient mortality in children with sepsis. Among them, 151 had hypermagnesemia and 352 had hypomagnesaemia, both of which had death rates of 36.9% and 6.3%, respectively. From the available data, it was observed that high magnesium increased rates of mortality among children.(10)

Despite the fast-rising prevalence of sepsis in developing nations, the majority of sepsis research is carried out in wealthy nations. Data on the general clinical profile, outcome, and its outcome predictor are particularly scarce in developing nations such as those in Tanzania. All in all, there is paucity of literature stating the relationship of magnesium whether ionized or total in predicting the outcome of patients with sepsis depicted in Tanzania. In context to this, the main goal of conducting this research is to determine the performance of magnesium both total and ionized in predicting the all-cause mortality of adult patients with sepsis in Tanzania.

1.2 Problem statement

Sepsis is a serious clinical illness that affects the body's biochemical and physiological processes. Sepsis is currently described as "organ dysfunction caused by a dysregulated host response to infection". Sepsis is one of the leading causes of mortality, leading to an estimated 48.9 million cases worldwide and contributed to 11 million sepsis related death in 2017.(11) Like any other developing countries, the burden of sepsis is high in Tanzania(12) as it has been shown in various small-scale studies.(13) qSOFA has been proposed as a predictor of mortality in sepsis, but it is poorly sensitive and can delay initiation of intervention known to improve sepsis related outcome.

It is estimated that there are about 19 million instances of sepsis each year, with 5 million deaths attributable to sepsis; most of these deaths occur in low- and middle-income countries (LMICs). Acute infection risk in LMIC like Tanzania is increased by poverty-related factors like inadequate preventive healthcare, low vaccination rates, malnutrition, poor living conditions as well as exposure to environmental which might contribute to abnormal electrolyte and poor outcome.(14) The ability of healthcare and public health delivery systems to care for septic patients varies greatly between and within LMICs hence different burden seen in different context.

Hypermagnesemia was strongly correlated with an increased risk of inpatient death in children with sepsis. Despite the fact that numerous research have looked at the relationship between ionised and total magnesium in patients with sepsis, no information has been found to suggest that ionised magnesium is particularly important in predicting mortality among patients with sepsis. (16, 17). These findings will advance knowledge of numerous risk factors for unfavourable outcomes in adult patient with sepsis in Tanzania.

Sepsis and electrolyte abnormalities are common in Tanzania(15); however, the relationship between these two illnesses and magnesium is not well discussed in Tanzanian and East African publications and local literature.

1.3 Conceptual Framework

The above framework aims at determining the relationship of magnesium levels i.e., total or ionized magnesium in patients suspected to have sepsis by qSOFA to predicting mortality at the emergency department and at 24 hours. To date, serum lactate and physician gestalt is the standard of care in prediction of mortality at EMD, but ionized magnesium is not tested on its predictability to mortality in septic patient. However, age, sex, comorbidities, and severity of illness (MEWS score) can be confounders to the mortality.

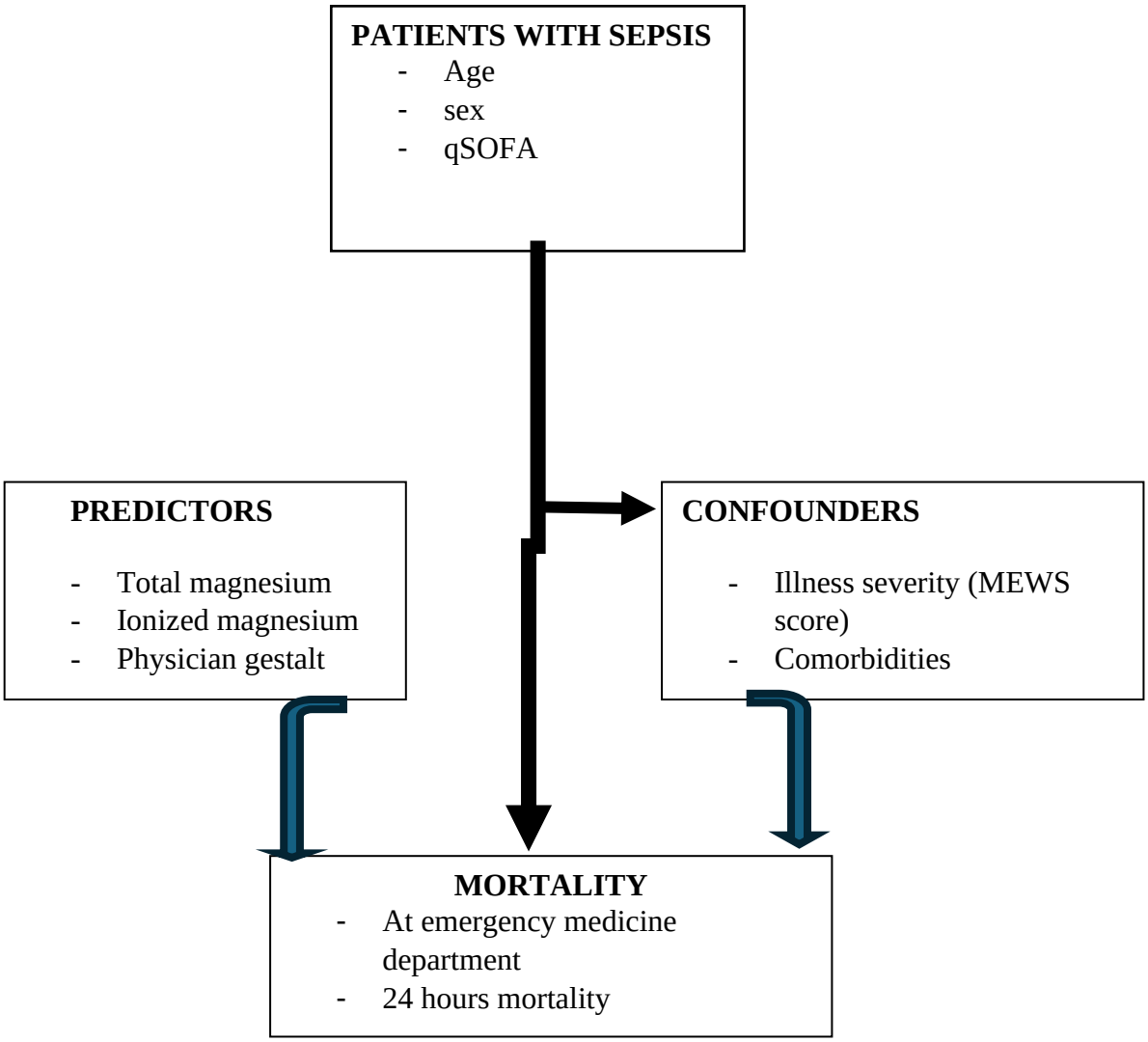


Figure 1: A conceptual framework

1.4 Rationale

This study provided an opportunity to understand whether total magnesium or ionized magnesium was a good prognostic marker of mortality in patients with sepsis at the departments of emergency medicine in Tanzania.

Understanding the performance of ionized magnesium in predicting the mortality of patients with sepsis helped to provide an alternative prediction that no previous studies of this kind have been carried out in Tanzania. In addition, this study also determined the relationship between patient outcomes in terms of all-cause mortality and the emergency and urgent care that was offered at the EMD. Furthermore, this study assisted in locating potential gaps in patient as far as ionized magnesium was concerned.

1.5 Research question

In adult patient with sepsis attending emergency department in Tanzania, what is the performance of ionized magnesium in predicting the mortality in 24 hours?

1.5.1 Specific Research questions

1. For patients with sepsis attending the EMD of Tanzania what proportion have an abnormal ionized magnesium?
2. In patients with sepsis attending the EMD of Tanzania, what is the accuracy of ionized magnesium with comparison to total magnesium in predicting the mortality?
3. For patients who have sepsis at the EMD of Tanzania, what is the role of hypermagnesemia in comparison to normal magnesium levels in determining the all-cause mortality?
4. For patients who have sepsis at the EMD of Tanzania, what is the role of hypomagnesemia in comparison to normal magnesium levels in determining the all-cause mortality?

1.6 Objectives

1.6.1 Broad objective

To determine the performance of ionized magnesium in predicting the mortality of patients with sepsis attending emergency medicine departments of Tanzania.

1.6.2 Specific Objectives

1. To determine the proportion of patients with abnormal ionized magnesium in predicting mortality in sepsis.
2. To determine the accuracy of ionized magnesium with comparison to the accuracy of total magnesium in predicting mortality in sepsis.
3. To determine the role of hypermagnesemia in comparison to normal magnesium levels in determining the all-cause mortality.
4. To determine the role of hypomagnesemia in comparison to normal magnesium levels in determining the all-cause mortality

CHAPTER TWO

2.0 LITERATURE REVIEW

Prevalence of sepsis in patients at the emergency department

Sepsis continues to be a concern for healthcare providers and administrators worldwide. Numerous countries have significant population-based prevalence of sepsis, according to recent studies. Sepsis is a major public health concern in the United States accounting more than $20 billion hospital costs in 2011.(16)

In three critical care units 3700 people were screened for sepsis and septic shock. 2016 (44%) and 110 (4%) of the SIRS patients experienced sepsis and septic shock, respectively. A study which was a one-day prevalence study performed between March 28 and 29, 1995 in adult ICUs. 895 patients were enrolled, 521 of whom had sepsis. In 23 closed multi-disciplinary ICUs of 21 hospitals in Australia and New Zealand. A total of 691 patients, 11.8 per 100 ICU admissions were diagnosed with 752 sepsis patients.(16)

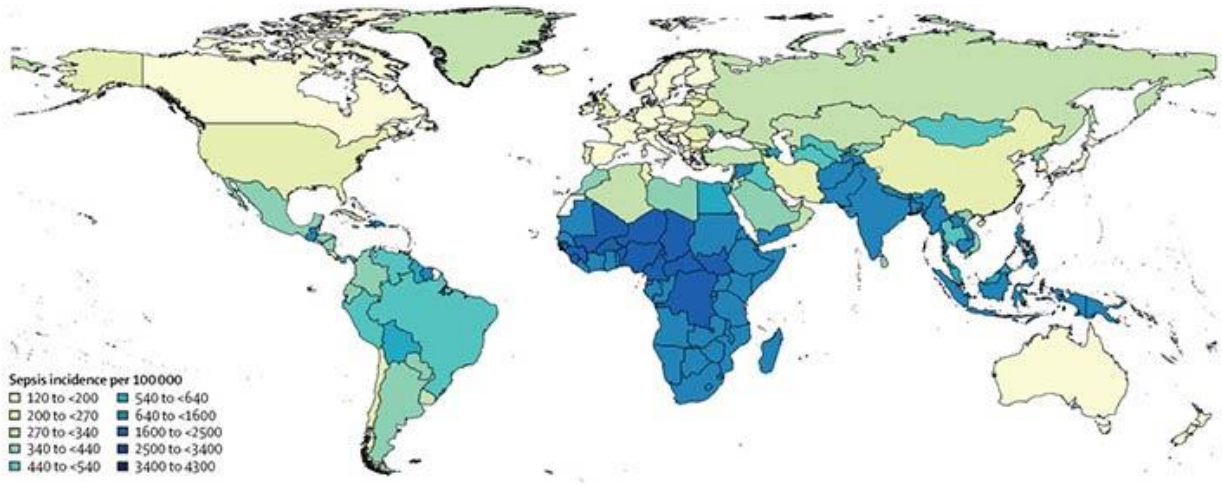
In 2018, a study conducted in Dublin whereby an overall, 42 of 3585 ED patients met the criteria for sepsis or septic shock. This represents 11.7 patients with sepsis or septic shock per 1000 ED attendances. Since most patients with sepsis are admitted to ICUs from the ED. The epidemiology of sepsis in the ED setting has been reported in the USA and Brazil in 2007 which reported that of 331.1 million adult ED visits in the United States over four years, approximately 2.3 million visits (571,000 annually) were for suspected severe sepsis.(17)

In Malawi, a single-center study found that at admission, 29% of medical patients had sepsis as defined by a suspected infection and qSOFA 3. Another study done which was a two centered study in Malawi it was found that the prevalence of sepsis among in patients in two hospitals was 9.3%..(19) Another study done in Kiruddu National Referral Hospital in Kampala, Uganda between December 2018 and July 2019 whereby 1,657 patients screened during the study period, 243(14.7%) had sepsis. This shows high prevalence of sepsis in the sub-Saharan Africa.(19)

One of the studies conducted in St Francis Referral Hospital, Ifakara, United Republic of Tanzania in 2018 which suggested onto the diagnosis made at the emergency department involving a total of 35,903, the most common disease groups were of infectious origin (46.3%).(20)

Mortality of sepsis in patients at emergency department

According to a recent scientific study, sepsis caused 11 million deaths worldwide in 2017 and 48.9 million cases, accounting for nearly 20% of all fatalities worldwide. There are regional differences in sepsis incidence and mortality; globally, low- and middle-income countries accounted for around 85% of sepsis cases and sepsis-related fatalities. Every year, hundreds of millions of patients around the world are affected by healthcare-associated infections, one of the most common forms of adverse events that can happen during the provision of care.(14,21) In a recent study conducted in 2020, it was estimated that the burden of sepsis worldwide has doubled in comparison to 2017.



Sources: Figure 3 (map) and Supplementary appendix (data) , Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study, The Lancet, January 18-24, 2020

Figure 2: World Map of Sepsis Incidence by Location

Emergency departments serve as the initial medical point of contact for patients who are critically ill and are crucial in the early detection of sepsis patients at high risk. Even for seasoned ED clinicians, identifying those patients early on might be difficult since it's not always as simple as it seems. Retrospective cohort research was carried out at a district general hospital and a sizable metropolitan teaching hospital on adult ED patients with sepsis who were admitted to the hospital. Data were gathered between January 1, 2006, and January 31, 2007. A total of 308 ED patients with sepsis were eligible for inclusion, of which 307 had complete records and were included in the study. Among these were 72 deaths (23%). (22)

There is a dearth of information regarding the prevalence and consequences of sepsis in emergency rooms from sub-Saharan Africa. Data were gathered for patients attended in a rural Ugandan emergency room between 2010 and 2019. Out of 48,653 patient visits between 2010 and 2019, 17,490 interactions involved patients who were 18 years of age or older and had a suspected illness, of which 3,323 involved sepsis. The observed mortality rates for non-malarial sepsis climbed from 6.3% to 14.9% and expected mortality rates increased from 8.8% to 12.0% between 2012 and 2019.(23)

In comparison to those from high-income countries (HIC), people in low- to middle-income (LMIC) regions of the world and particularly in Tanzania suffer from disproportionately high mortality rates. Data are few in low-resource areas, especially SSA, however several studies have found high mortality rates.(12,24)In contrast to HIC, sepsis is a significant source of morbidity and mortality in SSA.

According to the Surviving Sepsis Campaign (SSC) and Intergraded Management of Adolescent and Adult Illnesses (IMAI) guidelines, prompt identification, empirical antibiotics, resuscitation, and adequate source control constitute the fundamental elements of sepsis management. The SSA has not yet undergone a systematic evaluation that looks at these procedures.(25)(7)

According to a recent study conducted in 2022 by Mehrunnissa Taj et al., patients with a diagnosis of sepsis spent an average of 7 days in the hospital, and the yearly sepsis-related mortality rate in Tanzania accounted to 41%.(15)

Mortality in sepsis in relation to magnesium

A deficit in magnesium causes endothelial cells to become more vulnerable to oxidative stress, endothelial dysfunction, decreased fibrinolysis, and increased coagulation. Additionally, animals and humans with low magnesium levels exhibit weakened immunological responses; nevertheless, partial or complete recovery of the immunodeficiency can be achieved with magnesium supplementation. Furthermore, the cytotoxicity of CD8 killer T cells and natural killer cells is regulated by intracellular free magnesium levels. Mg deficiency may result in increased oxidative stress and low-grade inflammation, which may be linked to several age-related diseases, including higher predisposition to infectious diseases. (26)

Low intracellular free magnesium levels in NK and CD8+ T cells reduces their cytotoxicity. Patients with genetically low intracellular free magnesium, who are supplemented with magnesium, have a partial or near complete reversal of dysfunctional NK and CD8+ T cells and a reduced viral load. Dysfunctional CD8+ T cell cytotoxicity leads to increased proinflammatory death in virally infected cells and healthy bystander cells, as opposed to silent apoptotic death, increasing the risk of cytokine storm in the lungs. (26)

Magnesium activates vitamin D into the hormone calcitriol. Magnesium deficiency slows fibrinolysis and increases coagulation and thrombosis. Low magnesium status increases damage to tissues and cellular membranes and reduces antioxidant defense systems leading to increased oxidative stress and damage. (27)

Mortality is subjected widely as a state of being subjected to death. Sepsis plays a huge impact as a causative of mortality in wide aspects. Studies of magnesium supplementation in critically ill patients have reported conflicting results regarding mortality.

A study finding suggested a relationship between magnesium sulphate administration and a decreased 28-day all-cause mortality in sepsis patients in severe condition. The robustness of the conclusion was demonstrated by the association's stability in sensitivity analyses and consistency across subgroup analyses. Use of magnesium sulphate was also linked to

decreased rates of renal replacement therapy use, ICU mortality, and in-hospital mortality.(28)

In a study conducted by Cirik et al in USA December 2020, it found that no significant differences between hypo- and normomagnesemia had outcome of mortality in sepsis. However, hypermagnesemia, an electrolyte imbalance that is typically observed in elderly individuals and those with significant comorbidities, is linked to mortality as well Furthermore, during the ICU follow-up, patients with hypermagnesemia had greater mortality rates than the other groups.(29)

In between the juggle which exists to whether hypo- or hypermagnesemia has relation to mortality in sepsis, yet no studies as present shows the correlation between sepsis, mortality and magnesium ion in the continent and region respectively. In addition to this, this study could be of great benefit in determining this correlation in Tanzania and would serve to be a future refence for new researchers.

Ionized Magnesium as a predictor of adverse events in critically ill patients with sepsis

Ionized magnesium constitutes about 50% of the total magnesium and represents the active portion. The remaining forms of magnesium are either bound to protein or to anions such as phosphates, bicarbonate and citrate. Ionized magnesium is rarely measured in the clinical setting because of its specialized equipment of whole blood measuring.(9)

The only specific marker that can be used to identify critically ill patients with poor magnesium status is ionized magnesium. iMg cannot be computed; instead, it must be physically measured in order to improve measurement reliability. iMg is rarely assessed in this clinical environment, despite the fact that critically sick patients are among those most susceptible to dysmagnesemia. For iMg measurement, specialized tools are required, and full blood analysis is necessary right away.(8)

Lately, no promising literature suggests the role of magnesium in predicting sepsis in critically ill patients especially adults with sepsis in the sub-Saharan Africa. However, there exists a study done in South Africa by James et all in 1988 which was an

experimental study in baboons receiving adrenaline infusion, it was observed that magnesium infusion abolished arrythmias, increased cardiac output and stroke volume and reduced systolic vascular resistance. Magnesium had an antiarrhythmic and alpha-adrenergic effect on baboon. Nevertheless, this correlation is yet to be explained in sub–Saharan Africa.(30)

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

This was a prospective cohort study of prognostic value of ionised magnesium in predicting outcome of sepsis in adult who presented to Muhimbili National Hospital (MNH-EMD) and Shree Hindu Mandal Hospital's Emergency Medicine Department (SHMH- EMD) between February 2024 and April 2024.

3.2 Study Setting

This was a two-centred study conducted in a period of 3 months at the EMD of MNH and Shree Hindu Mandal Hospital.

MNH is a tertiary hospital situated along United Nations Road, Upanga, in the Dar es Salaam neighbourhood of Ilala. It is a 1500-bed facility that serves as Tanzania's national hospital and the primary destination for most referrals from the country's many regions. The emergency medicine department in Tanzania was first established in 2010 with assistance from the Abott Fund Tanzania. At MNH, the emergency room is a full-service EMD and serves as a training facility for the emergency medicine residency program. Medical and nursing students, as well as volunteers, rotate through the EMD throughout these rotations.

The MNH EMD serves to attend all patients with emergencies and transfers from tertiary hospitals. The EMD at MNH has 7 sections which includes the triage, resuscitation room, treatment rooms and corridors, paediatric wing, VIP area, mass causality area, an ultrasound room and emergency theatre.

The EMD at MNH is well equipped in terms of its POC and medications. POC which are readily available at the EMD includes arterial blood gases (ABG), cardiac troponins, electrolytes such as sodium, potassium, chloride and calcium, random blood glucose (RBG), renal function tests such as urea and creatinine, urine dipstick, urine pregnancy test (UPT), determine HIV-1/2, an ECG machine and POC ultrasound machine. All patients

are triaged using a locally derived 3-tier triage system, adapted from the Emergency Severity Index (ESI). Any critically ill patients arriving by ambulance or who walk in are brought to the resuscitation area and are triaged at the triage area or in the resuscitation room. The EMD has six areas.

1. Triage area, where all referral and emergency cases are received and rapid assessment and transfer to respective area depending on patient condition is done.During the day, all the emergency cases are received through ambulance bay entrance.
2. Treatment area where priority and queued triaged patients are seen.
3. A resuscitation room (also known as resus) – is a room designated for the care of the patient with respiratory or circulatory compromise and patients who go into cardiac arrest. The minimum requirement for equipment in a resus room includes cardiac monitors/ defibrillator with sync mode and pacer if available, airway equipment from basic to advanced airways, crash cart with the emergency medications which are needed in different critical interventions such as intubation, ACLS medications, inotropic support
4. A dedicated room for bedside ultrasound with 3 ultrasound probes. The room is equipped with a Siemens-ultrasound machine with 3 functioning probes: a cardiac (phased array), curvilinear and linear probe, the room has oxygen supply and a crash cart present when needed.
5. Mass casualty area where all causalities from the site of accident are received and triaged to respective areas.
6. Emergency theater for both minor and major operations needed on an emergent basis

The emergency medicine specialists that oversee the MNH EMD are trained locally and work there 24 hours a day, seven days a week. The EMD at MNH is staffed by locally qualified EM specialists who monitor patient care and instruct interns, registrars, and EM residents. The EMD is open twenty-four hours a day, seven days a week. An average of 50,000 patients are seen in the ED each year, with a 50% admission rate. Data at MNH is obtained from Well soft system.

Shree Hindu Mandal hospital started as a dispensary in 1919 and currently operates a 53 bedded regional private hospital. It is located at Ilala district at Shree Hindu Mandal Street in the city of Dar es Salaam, Tanzania. It encompasses 6 bedded emergency medicine, high dependency unit and intensive care unit respectively. The EMD at Shree Hindu Mandal started in 2013. SHMH EMD has 6 beds. Before a patient enters the emergency room, a triage nurse assesses the patient and triages to either the emergency department or outpatient department. Along with this SHMH also consists of a 3 bedded HDU and 5 bedded ICU. Currently, it sees an average of 2000 patients annually. Data at SHMH is obtained using the ERP system.

The department of emergency medicine at both the facilities receives patients with sepsis diagnosed using qSOFA. Samples are then collected from patients who meet the qSOFA score of 2 or more in 2 green vacutainers. One of these sample is sent to the main laboratories of either SHMH or MNH respectively depending on where the samples were collected from. These samples are sent for total magnesium analysis.The second vacutainer from MNH was sent to SHMH for iMg analysis using the table top machine located at SHMH. Samples from MNH were transported in a special transport specifically arranged for this purpose by research assistants at the end of each shift which lasts 12 hours or less.

At SHMH, samples are analysed using critical care blood gas analyzer, branded as STAT profile prime + by NOVA biomedical. This tabletop machine measures ph, PCO2, PO2, Na, K, Cl, iCa, IMg, glucose, hematocrit, lactate, TCO2, BUN, creatinine, tHb, O2Hb, COHb, MetHb, HHb and SO2%. This machine has the ability to self-calibrate and the samples do not use catridges.

The data is then entered into red cap by the PI or the research assistants. The laboratory at MNH and SHMH operate 24 hours, seven days a week. The EMD at MNH has facility to measure total magnesium at the main laboratory. However, ionized magnesium is a tabletop point of care investigation measured using a blood gas analyser. This investigation is currently available at SHMH and was effectively used.

Ionized and total magnesium at the emergency medicine department were determined as normal and abnormal based on the cut off values which included 0.4-0.6 mmol/L and 0.7-

1.0 mmol/L respectively. Alongside, lactate value of >2 was considered critically ill based per previous studies conducted at the emergency medicine setting.

3.3 Study population

All adult patients suspected of having sepsis and consented were seen in the emergency rooms of Shree Hindu Mandal Hospital and Muhimbili National Hospital.

3.4 Sampling Design

We used the consecutively convenient enrollment strategy to enroll all adult critically ill patients coming to the EMD of MNH and SHMH who met inclusion criteria during the time the research assistant or the main investigator were available.

3.5 Study subjects

3.5.1 Inclusion criteria

1. All adult with suspected to have sepsis >18 years of age and meet qSOFA criteria which includes any two of the following parameters: -
    - altered mental status.
    - RR ≥22breaths per minute
    - SBP ≤100mmHg

3.5.2 Exclusion criteria

1. Patient with solid tumors.
2. Patients who had cardiac arrest and attained ROSC.
3. Patients with missing information i.e., no data on magnesium levels, no diagnosis of sepsis in the electronic record.
4. Patients who have not consented to the study.

3.6 Variables of interest

3.6.1 Independent variables

1. Demographic data

These included date and time, age in years, date of birth, gender, visit type, insurance status, insurance company and qualification of the doctor treating the patient.

2. Clinical profile

   This included the presenting complaints such as difficulty in breathing, fever, chills, altered mental status, decreased urine output and others

3. Comorbidities

   These included hypertension, diabetes, Human immunodeficiency virus, malignancy (any), end stage renal disease, chronic obstructive lung diseases, end stage liver diseases, malignancy, prior intubation, old and new stroke and heart diseases.

4. Initial vitals (blood pressure, heart rate, respiratory rate, SPO2, RBG, Temperature and AVPU)
5. Initial POC (lactate, ionised magnesium and total magnesium)
6. Disposition point (ward or ward/ICU/HDU/discharge/DAMA/mortuary)

3.6.2 Dependent variables (Adverse events)

1. Magnesium sulphate initiated.
2. Fluid resuscitation and type and amount of fluid used.
3. Vasopressors/inotropes used.
4. Airway compromise and intubation done.
5. Cardiac arrest at EMD
6. Mortality at EMD

Outcomes

The primary outcome was 24-hour mortality from the time of arrival to EMD to disposition until 24 hours of follow up. The secondary outcome was determined by the proportion of abnormal ionized magnesium.

3.7 Sample Size estimate

The proportion adult patients with sepsis who are critically ill and died in 24 hours of admission with abnormal magnesium will be used to calculate sample size. A study in China by Pan Jiang et had the 24-hour mortality rate of 24.3%. (31)

From, $n=Z\alpha^2 P(1-P)/d^2$

Whereby, n=sample size; Z=confidence level statistic, P=expected prevalence, and d=precision (effect size matching to precision).

Therefore:

$n=1.96^2x0.24(1-0.24)/0.05^2$

n=280

Keeping the 10% (28 individuals) buffer in the sample size calculation

n=308

Therefore, the required sample size that will be used in this study is 308 patients.

3.8 Data management

3.8.1 Data collection

Screening and enrolment

Every patient attended in the emergency departments of Muhimbili National Hospital and Shree Hindu Mandal Hospital had have their electronic medical records checked by the principal investigator and/or research assistant whenever they were available. Those who satisfied the inclusion requirements were further assessed for eligibility to participate in the study.

Standardized data collection tools

Data collection was done whenever available to consecutively enroll patients every 24 hours. This was done in two parts, clinical profile as well as blood sample analysis. All eligible patients at the emergency medicine department (EMD) were asked to sign consent to participate in the study, A standardized case report form was filled out by the primary investigator or a qualified research assistant to gather data from the treating physician as well as and electronic medical record (well soft). To ascertain in-hospital death rates and

the length of stay for those who survive to discharge, the enrolled patients were followed up for 24 hours.

Blood samples for labs and point of care were taken by the primary medical doctor attending the patient. Sample for Magnesium level (both total and ionized) were collected in 2 green vacutainer bottles per each patient. One of the green vacutainer bottles of the sample was sent to main laboratory of MNH and SHMH respectively to analyze total magnesium levels while the second one was used to analyze ionized magnesium levels at SHMH. Analysis for ionized magnesium levels at SHMH was done as a POC test using a tabletop machine called stat profile prime + machine by nova biomedical.

The analysis of POC test of ionized magnesium levels was carried out by the research assistants or the nurses in charge of the analyzer. Blood samples were inserted into the machine which was consisting of cartridges that are capable of determining ionized magnesium levels along with POC electrolytes such as sodium, potassium and chloride and lactate. The number of patients who failed to meet the requirements for inclusion of requirement were not enrolled.

For admitted patients follow up was done and data was collected to determine their respective admission units such as general wards or ICU/HDU.

Pre-testing of the tool

In order to get ready to use a Case Report Form that were transformed into Redcap, the online platform used to acquire the required data, two research assistants went through training for three days. The Case Report Form were pre-tested to gather data from patients who conveniently appeared at the ED after the research assistants had successfully finished training and comprehended how to use the Case Report Files.

Three sections which made up the standardized data gathering form:

Section I: Patient evaluation on compliance with inclusion criteria using a questionnaire.

Section II: Evaluation and Reporting of Cases

Patients who were part of the study had their demographics, clinical presentation, vital sign which included the BP, point-of-care venous blood gases, electrolyte, urea, creatine, and lactate levels recorded.

For each patient suspected to have sepsis, blood was drawn after cannulation and samples were taken in green bottles for testing total magnesium and ionized magnesium as a point of care investigation in the critical care blood gas analyzer which is the stat profile prime + machine by nova biomedical which is located in SHMH.

Section III: A case's progress: The principal investigator and research assistant followed up all enrolled patients for 24 hours in the appropriate setting, such as an ICU, HDU, or EMD to document the outcome.

3.8.2 Data management and analysis

After data cleaning, data was analyzed using SPSS software with $p<0.05$ taken as significant. Continuous data was presented as mean$\pm$ Standard deviation (SD or median (interquartile range) as appropriate and categorical data as proportion. The predictability of magnesium in determining mortality was done using relative risk and hence comparing the ROC curves based on the magnesium levels in each respectively to mortality.

3.9 Ethical considerations

The MUHAS IRB was asked for ethical approval before this study was conducted and permission for collection was given by MNH and SHMH. We reached out to Muhimbili National Hospital responsible personnel to get their permission to collect data. A formal consent was required from the patient before data collection commencement and if a patient was confused or unconscious, consent from the patient's relative was requested for. Data collection was not started until a patient, or a patient's proxy, had consented to take part in the study.

The questionnaire and blood sample were identified by serial numbers, not by the patient's name or identifier was kept. The filled questionnaires were not made available to anyone, rather kept by principal investigator in password encrypted computer.

CHAPTER FOUR

4.0 RESULTS

During the study period, 610 patients were triaged to resuscitation as patients with sepsis. Of these, 314 (52%) patients met the inclusion criteria and were therefore recruited as study

participants, while 296 (48%) patients were not included in the study. Of those included, magnesium total or ionized was not done in 6(2%) patients. Among 162(53%) total normal magnesium, 71(23%) had normal ionized magnesium and 91(30%) had abnormal ionized magnesium and among 146(47%) total abnormal magnesium 93(30%) had normal ionized magnesium while 53(17%) had abnormal ionized magnesium as seen in figure 4.

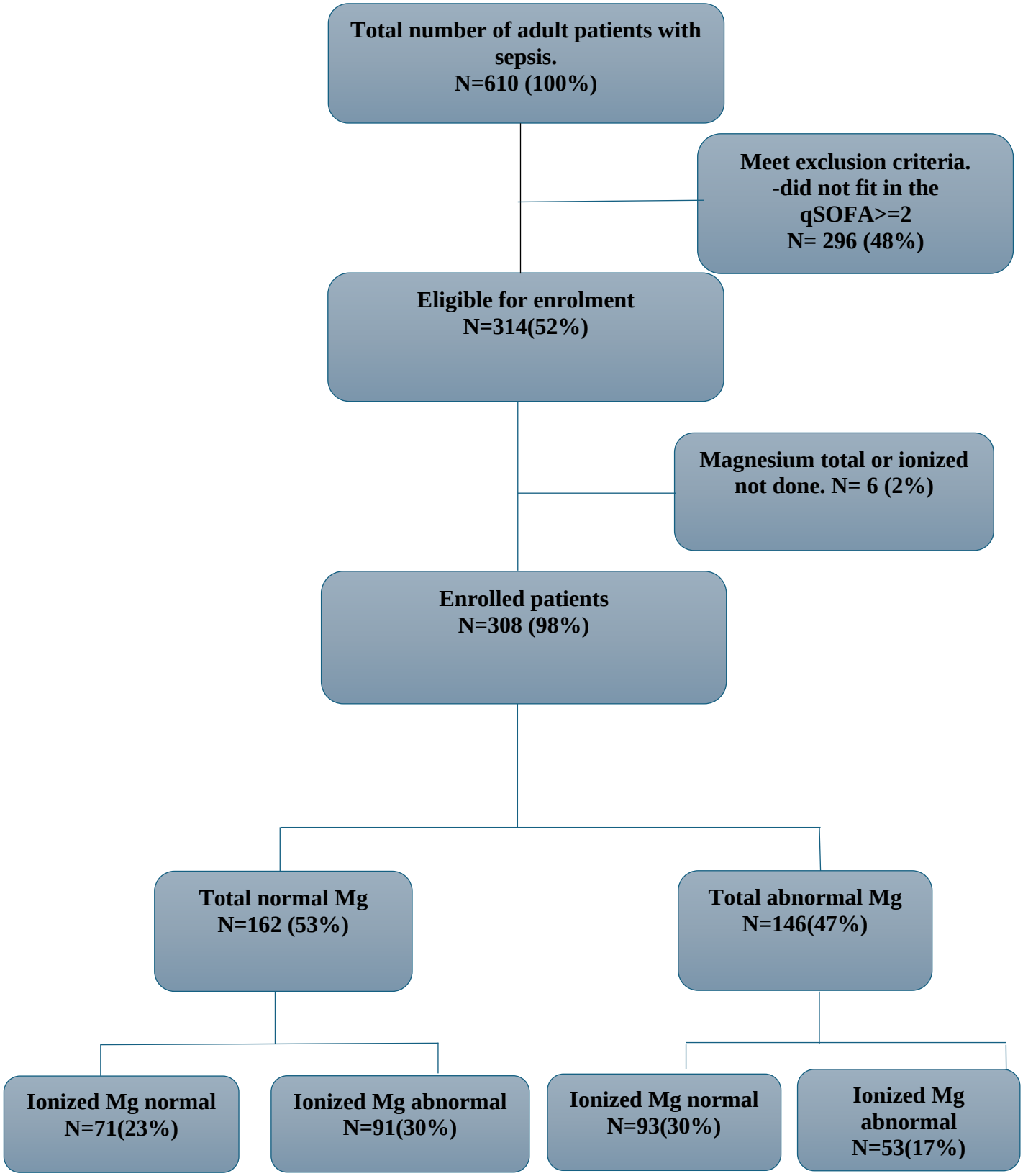


Figure 3: A Flow Diagram

Socio-demographic characteristics of study participants

We enrolled 314 patients from February 2024 to April 2024 demographically, 57% were male and 43% were female, with a median age of 55 years (Range of 39-68 years) by qSOFA score ≥2. The majority of the patients were seen by residents (71.3 %) during the study period as shown in table 1.

Table 1: Socio-demographic characteristics of the study participants N = 314

Variable	Frequency (n)	Percent (%)
Age group (years)		
18–29	40	12.7
30–39	40	12.7
40–49	53	16.9
50–59	44	14.0
≥ 60	137	43.6
Median age in years (IQR)	55 (39, 68)	
Gender		
Male	179	57.0
Female	135	43.0
Visit type		
Self-referral	141	44.9
Referred from other facilities	173	55.1
Qualification of treating doctor		
Intern doctor	8	2.5
Registrar	70	22.3
Resident	224	71.3
Specialist	12	3.8

Patients clinical profile

Among 314 study participants, Hypertension 28%, diabetes 12.1%, HIV 7.6 % and other 40.4% were the leading comorbidities in the study population. Of the complaints that brought the patient to the ED, altered mental status 39.5 % and difficulty in breathing 33.8% were the most commonly reported. The median systolic blood pressure, respiratory rate, heart rate, oxygen saturation and temperature were 99 (88, 126), 23.0 (22.0, 26.0), 98.0 (81.0, 115.0), 98.0 (96.0, 100.0) and 36.8 (36.5, 37.0) respectively. The median lactate level was 8.22 (4.22, 13.55), the median ionized magnesium was 0.62 (0.54, 0.75) and the median total magnesium was found to be .84 (0.72, 1.02). Of the 314 study participants 311 (99%) had a QSOFA score ≥ 2 and 240 (77.2%) had a MEWS score of ≥ 4 as shown in table 2.

Table 2: The clinical characteristics of the study participants N = 314

Variable	Frequency (n)	Percent (%)
Presenting complaints *		
Difficulty in breathing	106	33.8
Fever, Chills	43	13.7
Altered mental status	124	39.5
Decreased urine output	14	4.5
Comorbidities		
PUD	11	3.5
ARDS	5	1.6
Hepatic injury	7	2.2
Renal insufficiency	19	6.1
Hematological change	3	1.0
Skin lesions	1	0.3
Diabetes mellitus	38	12.1
Hypertension	88	28.0
Malignancy	3	1.0
HIV	24	7.6
Others	127	40.4
Vital signs, index tests		
Systolic blood pressure, Median (IQR)	99 (88, 126)	
Median respiratory rate (IQR)	23.0 (22.0, 26.0)	
Median heart rate (IQR)	98.0 (81.0, 115.0)	
Median oxygen saturation (IQR)	98.0 (96.0, 100.0)	
Median temperature (IQR)	36.8 (36.5, 37.0)	
Median lactate (IQR)	8.22 (4.22, 13.55)	
Median ionized magnesium (IQR)	0.62 (0.54, 0.75)	
Median total magnesium (IQR)	0.84 (0.72, 1.02)	
AVPU		
Alert	144	45.9
Pain	74	23.6
Voice	70	22.3
Unresponsive	26	8.3
QSOFA score		
≥ 2	311	99.0
MEWS Score		
1–2	4	1.3
3	67	21.5
≥ 4	240	77.2

**Others: Headache, diarrhoea, generalized body weakness, vaginal bleeding, yellowish discoloration of the
eye, abdominal swelling, easy fatigability, limb weakness, passing melena, back pain, neck swelling, foot ulcers, trauma, breast pain, constipation, breast swelling, urine incontinence, hiccups, dysphagia, haemoptysis.

Treatment received at emergency department

Fluids were given to 70.4% patients, and normal saline was used in 176 (56.1%) of these patients, ringer's lactate in 74 (23.6%) and other types of fluid in 38 (12.1%). Most patients received 1000-2000mls 159 (71.9%). Patients who had NGT placement, central line placement, inotropy/vasopressor support, endotracheal intubation and blood transfusion were 282(89.4), 290 (92.4), 277 (88.2), 276 (87.9) and 283(90.1) respectively.

Table 3: Treatment received at Emergency department N = 314

Variable	Frequency (n)	Percent (%)
Fluid resuscitation		
Yes	221	70.4
No	93	29.6
Type of fluid		
Normal saline	176	56.1
Ringer lactate	74	23.6
Other	38	12.1
Volume of the fluid given (mL) (n = 221)		
<1000	31	14.0
1000–2000	159	71.9
3000–4000	21	9.5
>4000	10	4.5
NGT placement		
Yes	32	10.2
No	282	89.8
Central line placement		
Yes	24	7.6
No	290	92.4
Inotropy/ vasopressor support		
Yes	37	11.8
No	277	88.2
Endotracheal intubation		
Yes	38	12.1
No	276	87.9
Blood transfusion		
Yes	31	9.9
No	283	90.1
Number of units (n = 31)		
1 – 2	23	76.7
3 – 4	5	16.7
>4	2	6.7
Magnesium sulphate replacement		
Yes	11	3.5
No	303	96.5

Disposition

Of the 314 study participants, majority of the patients were disposed to general ward 227 (72.3%) while ICU 56 (17.8%) were admitted to the ICU, 16 (5;1%) were discharged and 4 (1.3%) patients left against medical advice (DAMA) 4 (1.3). There were 11 (3.5%) deaths in the ED.

Table 4: Disposition

Disposition	Frequency (n)	Percent (%)
General ward	227	72.3
ICU	56	17.8
Discharged	16	5.1
DAMA	4	1.3
Mortuary	11	3.5

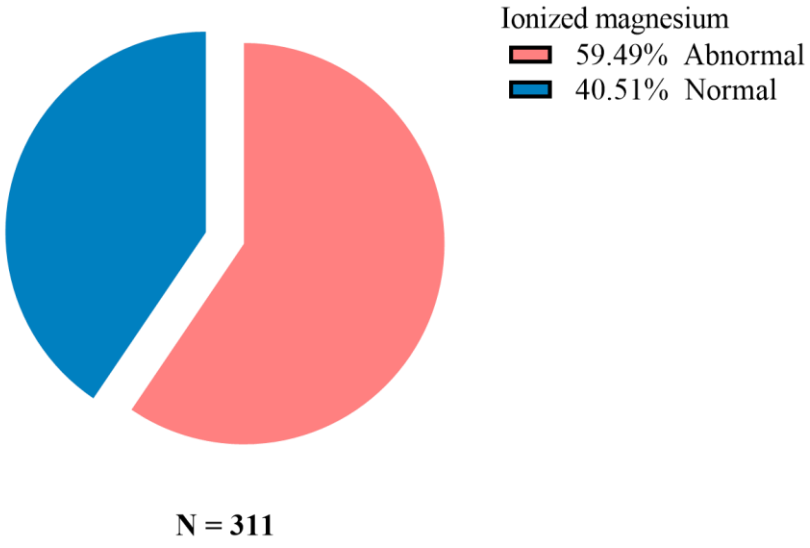


Figure 4: A pie chart showing proportion of abnormal versus normal ionised magnesium

From the study conducted, showed that 92.4% patients enrolled had abnormal ionized magnesium This proportion indicates that 59.49% of the tested population has abnormal levels of ionized serum magnesium.

ROC curve for ionized and total magnesium on prediction of mortality

The AUROC curve for total magnesium was 64.2% (95% CI, 0.538-0.746) with ability of predicting mortality which was statistically significant different from prediction by chance (p value-0.008). In comparison to ionized magnesium the AUROC was 54.9% (95% CI, 0.439-0.659) with ability of predicting mortality which was not statistically significant different from prediction by chance (p value- 0.379). Total magnesium to ionized magnesium was found to have area difference under the curve -0.92 (95% CI, -0.209-0.024) which is not statistically significant as shown in figure 5

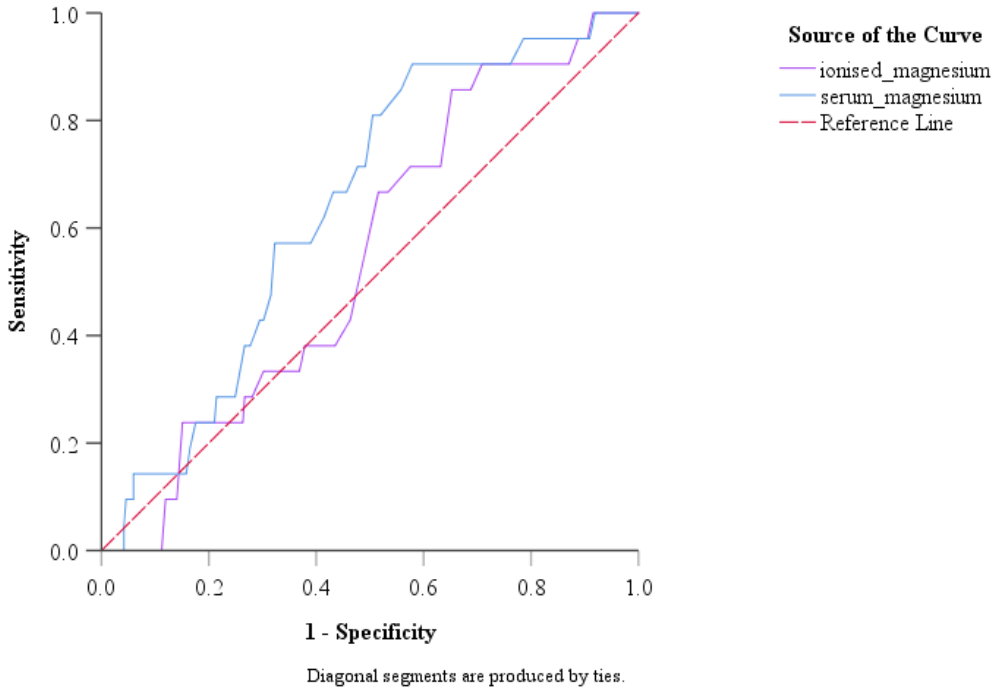


Figure 5: ROC curve for total and ionized magnesium on predicting mortality

Note: BLUE LINE; total magnesium PURPLE LINE; ionized magnesium

Diagnostic characteristics of total magnesium in predicting mortality

The sensitivity and specificity of total magnesium on prediction of mortality among adult patients with sepsis were 42.86% (95% CI, 21.69-64.02) and 51.93% (95% CI,46.13-57.73) respectively with a positive predictive value of 6.16 % (95% CI, 2.26-10.07) and negative predictive value of 92.50% (95% CI, 88.42-96.58). Furthermore, total magnesium

was found to have a positive and negative diagnostic likelihood ratio 0.89 (95% CI,0.54-1.48) and 1.10 (95% CI, 0.75-1.62) as shown in table 5

Table 5: Diagnostic characteristics of the total magnesium in predicting mortality

			95% Confidence Interval	
	Estimates	**Standard Errors**	**Lower CL**	**Upper CL**
Sensitivity	42.86 %	10.80 %	21.69 %	64.02 %
Specificity	51.93 %	2.96 %	46.13 %	57.73 %
PPV	6.16 %	1.99 %	2.26 %	10.07 %
NPV	92.50 %	2.08 %	88.42 %	96.58 %
PDLR	0.89	0.26	0.54	1.48
NDLR	1.10	0.20	0.75	1.62

PDLR- Positive Diagnostic Likelihood Ratio

NDLR- Negative Diagnostic Likelihood Ratio

Diagnostic characteristics of ionized magnesium in predicting mortality

The sensitivity and specificity of ionized magnesium on prediction of mortality among adult patients with sepsis were 66.67% (95% CI, 46.50-86.83) and 41.05% (95% CI,35.34-46.76) respectively with a positive predictive value of 7.69 % (95% CI, 3.82-11.56) and negative predictive value of 94.35% (95% CI, 90.29-98.42). Furthermore, ionized magnesium was found to have a positive and negative diagnostic likelihood ratio 1.13 (95% CI,0.82-1.55) and 0.81 (95% CI, 0.44-1.51) as shown in table 6.

Table 6: Diagnostic characteristics of the ionized magnesium in predicting mortality

			95% Confidence Interval	
	Estimates	**Standard Errors**	**Lower CL**	**Upper CL**
Sensitivity	66.67 %	10.29 %	46.50 %	86.83 %
Specificity	41.05 %	2.91 %	35.34 %	46.76 %
PPV	7.69 %	1.98 %	3.82 %	11.56 %
NPV	94.35 %	2.07 %	90.29 %	98.42 %
PDLR	1.13	0.16	0.82	1.55
NDLR	0.81	0.32	0.44	1.51

Comparison of sensitivity and specificity between ionized magnesium and total magnesium

The sensitivity of ionized magnesium and total magnesium are 66.67% (95% CI,46.50-86.83) and 42.86% (95% CI, 21.69-64.02) respectively with a difference of 23.81 and a p-value of 0.132 which is not statistically significant. The specificity of ionized magnesium and total magnesium are 41.05% (95% CI, 35.34-46.76) and 51.93% (95% CI, 46.13-57.73) respectively with a difference of -10.88 and a p-value of 0.007 which is statistically significant as shown in table 7.

Table 7: Comparisons of sensitivity and specificity between ionized magnesium and total magnesium

	Serum magnesium				
	Total	**Ionized**	**Difference**	**Test statistics**	**p - value**
Sensitivity	42.86%	66.67%	23.81	2.2727	0.132
Specificity	51.93%	41.05%	-10.88	7.3359	0.007

Comparisons of predictive values and diagnostic likelihood ratios between ionized and total magnesium

The positive predictive values of total and ionized magnesium are 6.61% (95% CI, 0.71-2.18) and 7.69% (95% CI,0.71-2.18) with a p value of 0.437 and negative predictive values of total and ionized magnesium are 92.5% (95% CI,1.07-0.399) and 94.35% (95% CI, 0.97-1.07) with a p value of 0.399. The positive diagnostic likelihood ratios of total and ionized magnesium are 0.89 (95% CI,0.43-1.43) and 1.13 (95% CI, 1.43-0.435) with a p value of 0.435 and the negative diagnostic likelihood ratio of total and ionized magnesium are 1.10 (95% CI, 0.65-2.81) and 0.81 (95% CI, 0.65-2.81) with a p value of 0.414 from table 8.

Table 8: Comparisons of predictive values and diagnostic likely ratios between ionized magnesium and total magnesium

	Serum magnesium			95% Confidence Interval		
	Total	**Ionized**	**Ratio**	**Lower CL**	**Upper CL**	**p - value**
PPV	6.16%	7.69%	1.25	0.71	2.18	0.437
NPV	92.5%	94.35%	1.02	0.97	1.07	0.399
PDLR	0.89	1.13	0.7883	0.43	1.43	0.435
NDLR	1.10	0.81	1.3552	0.65	2.81	0.414

The sensitivity and specificity of hypermagnesemia

Comparison of hypermagnesemia to normal magnesium level in predicting mortality

Using the hypermagnesemia estimate cut off of 1 mmol/L,86 patients were thought to have hypermagnesemia in the ED and 9 among them died of hypermagnesemia. Of 223 patients who were not having hypermagnesemia, 210 patients did not die of hypermagnesemia as shown in table 9.

Table 9: Comparisons of hypermagnesemia and mortality

	Death		
Hyper magnesium	**Yes**	**No**	**Total**
Yes	9	77	86
No	13	210	223
Total	22	287	309

Performance characteristics of hypermagnesemia in predicting mortality

Using mortality as the predictor of adverse outcome, the sensitivity and specificity of hypermagnesemia were 40.9% (95% CI, 20.7-63.6) and 73.2% (95% CI, 67.6-78.2) respectively with a positive predictive value of 10.5 % (95% CI, 4.9-18.9) and negative predictive value of 94.2% (95% CI, 90.2-96.9). Furthermore, hypermagnesemia was found to have positive and negative likelihood ratios of 1.25 (95% CI, 0.90-1.72) and 0.72 (95%

CI, 0.39-1.33) respectively with a diagnostic accuracy of 70.9% (95% CI,65.5-75.9) as shown in the table 10

Table 10: Performance characteristics of hyper magnesium in predicting mortality

		95% Confidence Interval	
Decision Statistics	**Estimate**	**Lower**	**Upper**
Test sensitivity	40.9 %	20.7 %	63.6 %
Test specificity	73.2 %	67.6 %	78.2 %
Diagnostic accuracy	70.9 %	65.5 %	75.9 %
Positive predictive value	10.5 %	4.9 %	18.9 %
Negative predictive value	94.2 %	90.2 %	96.9 %
Likelihood ratio of a positive test	1.25	0.90	1.72
Likelihood ratio of a negative test	0.72	0.39	1.33
Diagnostic odds ratio	1.74	0.68	4.44

Comparison of hypomagnesemia to normal magnesium level in predicting mortality

Using the hypomagnesemia estimate cut off of 0.7 mmol/L ,62 patients were thought to have hypomagnesemia in the ED and 1 among them died of hypomagnesemia. Of 247 patients who were not having hypomagnesemia, 226 patients did not die of hypomagnesemia as shown in table 11.

Table 11: Comparisons of hypo-magnesium and mortality

	Death		
Hypo-magnesium	**Yes**	**No**	**Total**
Yes	1	61	62
No	21	226	247
Total	22	287	309

Performance characteristics of hypomagnesemia in predicting mortality

Using mortality as the predictor of adverse outcome, the sensitivity and specificity of hypomagnesemia were 4.5% (95% CI, 0.1-22.8) and 78.7% (95% CI, 73.6-83.3) respectively with a positive predictive value of 1.6 % (95% CI, 0.0-8.7) and negative predictive value of 91.5% (95% CI, 87.3-94.7). Furthermore, hypomagnesemia was found to have positive and negative likelihood ratios of 0.21% (95% CI, 0.03-1.47) and 1.21 (95% CI, 1.09-1.35) respectively with a diagnostic accuracy of 73.5% (95% CI,68.2-78.3) as shown in the table 12

Table 12: Performance characteristics of hypo-magnesium in predicting mortality

		95% Confidence Interval	
Decision Statistics	**Estimate**	**Lower**	**Upper**
Test sensitivity	4.5 %	0.1 %	22.8 %
Test specificity	78.7 %	73.6 %	83.3 %
Diagnostic accuracy	73.5 %	68.2 %	78.3 %
Positive predictive value	1.6 %	0.0 %	8.7 %
Negative predictive value	91.5 %	87.3 %	94.7 %
Likelihood ratio of a positive test	0.21	0.03	1.47
Likelihood ratio of a negative test	1.21	1.09	1.35
Diagnostic odds ratio	0.18	0.02	1.34

CHAPTER FIVE

5.0 DISCUSSION

The aim of this study was to predict the prognostic value of ionized magnesium in adult patients with sepsis attending the emergency medicine departments of Tanzania. Patients with risk of clinical deterioration were identified using the qSOFA score and those who scored greater than or equal to 2 of qSOFA were enrolled into the study, initial point of care lactate and point of care ionized magnesium and laboratory total magnesium were drawn. After identification of critically ill patients, aggressive resuscitation, disposition and mortality at the EMD and 24 hours were determined.

A study conducted by Maria Paz Escuela et al. in Spain over a 6-month period showed enrollment of 144 patients were the study (98 men, 46 women; mean age 60.6+- 15.4 years). Of the 314 participants enrolled demographically, 57% were male and 43% were female, with a median age of 55 years (Range of 39-68 years). This was statistically significant.

Sepsis being the main cornerstone of our study suggested at early recognition and management for better outcome of adult patients in our settings. According to a systemic review and meta-analysis done by Ben Morton in Sub Saharan African countries guidelines have been adopted into sepsis management components of the World Health Organization (WHO), Integrated Management of Adolescent and Adult Illness (IMAI) guidelines in low-resource settings. The core components of early management for sepsis shared by the SSC and IMAI guidelines include rapid identification, empirical antibiotics, resuscitation and adequate source control. This was in support of our study whereby we observed majority of treatment initiated in patients enrolled with sepsis included fluid administration which was 70.4% patients whereby normal saline was used in 56.1% of these patients, ringer's lactate in 23.6% and other types of fluid in 12.1%. Most patients received 1000-2000mls 71.9%. However, other measures of resuscitation such as early inotropy support was observed in only 11.8%.

Regarding disposition from the EMD, ICU admission for patients with sepsis is typically necessary due to the need for intensive monitoring, advanced treatments, potential for rapid deterioration, specialized care, and the ability to provide a prompt and coordinated response to critical changes in the patient's condition. From a study done by Shannon M. Fernando suggested that 51.4% patients with sepsis were disposed to ICU while 37.4% patients were disposed to the wards. while from our study, it was suggested that 72.3% patients with sepsis were admitted to the wards while 17.8% patients with sepsis admitted to ICU.

Total magnesium was able to correctly predict mortality in 42.86% patients, and correctly identifies those who did not die 51.93% of the time with the AUC=0.642. Ionized magnesium was able to correctly predict mortality in 66.67% patients, and correctly identifies those who did not die 41.05% of the time with the AUC=0.547. Using ionized magnesium verses total magnesium in a study done by Scarpati et al in Europe showed that in critically ill patients, the correlation between iMg and total Mg has been demonstrated to be poor 69-85% of critically ill patients with low total Mg results have been found to have normal iMg levels. And that iMg is only a marker that specifically identifies patients with dysmagnesemia. Henceforth, iMg still remains a poor prognostic marker of sepsis.

According to the results of this study, the sensitivity and specificity for hypermagnesemia were 40.9% and 73.2%, respectively, whereas the corresponding values for hypomagnesemia were 4.5% and 78.7%. This magnesium was found to be more specific than sensitive in both hypo- and hypermagnesemia, with no discernible differences. Huabin Wang et al. report that there was no difference in the overall survival rate between the hypomagnesemia group and the normal group, but that there was a decrease in the hypermagnesemia group's survival rate compared to the normal group (P <0:001). This study demonstrated a substantial correlation between higher inpatient mortality in children with sepsis and hypermagnesemia.

Hypomagnesemia has been found to be common in critically sick patients, with a prevalence as high as 50%, according to a study by Dimitrios Velissaris et al. In contrast, our study found that hypomagnesemia was prevalent in 20% of individuals with sepsis.

Conversely, our research revealed that hypermagnesemia was prevalent in 27.8% of study participants, a finding that shows no discernible shift.

Overall, according to the study conducted, ionised magnesium did not play a major role as prognostic value in adult patients with sepsis attending the emergency departments of Tanzania.

CHAPTER SIX

6.0 LIMITATION, CONCLUSION AND RECOMMENDATIONS

6.1 Limitations

1. The fact that this was a two-centred study may have limited how broadly the findings can be applied since EMD-MNH treats patients from all over the nation, the sample under study may be typical of the sickest individuals across all demographic regions.
2. Although the sampling strategy was based on sequential convenient sampling, there was not round-the-clock coverage, so it's possible that some patients who would have matched the inclusion criteria were overlooked. Because the researcher and research assistant alternated between day and night shifts, a representative sample ought to have been produced.
3. There was no literature providing data on the relationship between ionized magnesium and mortality related to sepsis in the sub-Saharan Africa which could have led to the poor comparison on information since majority of the patients are of different clinical and demographic background in the sub-Saharan Africa.

6.2 Conclusion

The rare detection of iMg in clinical practice is due to lack of standardization of diagnostic reference levels. The correlation between ionised magnesium and total magnesium concentrations in sub-Saharan Africa, as well as the proportionate increase in iMg after reintegration, are not well understood. According to this study, ionised magnesium does not serve as a reliable predictor of sepsis in adult patients seen in the emergency departments of MNH and SHMH.

6.3 Recommendations

Due to the excessive volume of critically sick patients presenting at emergency departments and the limited resources available in our scenario.

I recommend the ionised magnesium not be used as a marker of sepsis in adult patients at the emergency medicine department.

I recommend more studies in the upcoming future which shall enlighten longer duration of follow up after disposition from the emergency medicine department and the enrolment of a greater number of patients with various age differences including the paediatric population.

We further recommend the study shall be performed in more peripheral settings in country since many patients with sepsis arrive in these centres primarily and are missed due to the delays on arrival at the tertiary centre while majority simultaneously die before arrival to a well-resourced emergency department.

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APPENDICES

Appendix I: Questionnaire/Case Report Form

This is the data collection checklist which will be used for each participant with sepsis, meeting the inclusion criteria for the study. Please fill all the details mentioned in the checklist.

Code no:
Medical record no:
Date of EMD visit:
Time of EMD visit:
Date of EMD discharge:

Patient's contact no:
1st of kin contact:
2nd of kin contact:

1.DEMOGRAPHICS

Birth date:
Age _____

Age group:
□ 18-29
□ 30-39
□ 40-49
□ 50-59
□ >60

Sex:
□ Male
□ Female

Visit type
□ Self-referral
□ Referred from other facilities

Insurance status.
□ Insured
□ Self payment

Qualification of the doctor treating the patient

□ Medical student

□ Intern doctor

□ Registrar

□ Resident

□ Specialist

2. CLINICAL PROFILE

Presenting complaints

□ Difficulty in breathing

□ Fever, chills

□ Altered mental status

□ Decreased urine output

Others_____

Comorbidities

□ H/o cardiac failure

□ H/o PUD

□ H/O ARDS

□ H/O hepatic injury

□ H/O renal insufficiency

□ H/O Haematological change

□ H/O skin lesions

□ H/O diabetes

□ H/O hypertension

□ H/O malignancy

□ HIV

□ H/O prior intubation

Others _____

Initial vitals

BP: _____ HR: _____ RR: _____ SPO2: _____

RBG: _____ Temp:_____

SBP (mmHg):

□>100

□<100

RR (breaths/minute)

□>22

□<22

AVPU

□Alert

Initial POC/Lab results

Lactate: _____

□Voice
□Pain
□Unresponsive

Ionised magnesium _____
Total Magnesium_____

Clinical Severity

qSOFA score: _____

□<2

□>2

MEWS score: _____

□1-2

□3

□>4

3.ED MANAGEMENT:

Fluid resuscitation:	Type of fluid	Volume of fluid
□Yes	□ NS	□ <1000mls
□No	□ RL	□ 1000-2000mls
	Other: _____	□ 3000-4000mls
		□ >4000mls

Magnesium sulphate given:

□ Yes

□ No

ED length of stay: _____ hrs

□<1hr

□1-2 hrs

□3-4 hrs

□>4hrs

DISPOSITION

□ Admitted to ward specify which ward: _____

□ Admitted to ICU

□ Discharged

□ DAMA

DISPOSITION FROM ED:

□Died in ED

□Ward

□ICU

OUTCOME:

Time from ED arrival to discharge: _____ hrs

□Within 24 hrs

□>24hrs

Time from ED arrival to death: _____hrs

□Within 24 hrs

□>24hrs

PHYSICIAN LIKELIHOOD OF ADVERSE EVENTS

What is the likelihood of an adverse event (mechanical ventilatory support, vasoactive drug use, cardiac arrest, mortality at the ED)? (To be answered by attending physician)

□ Low

□ Moderate

□ High

What parameters did you use to guide your gestalt? (To be answered by attending physician)

……

Appendix II: Informed Consent Form (English Version)

Greetings, my name is Dr Jaimini K.K Popat, I am a postgraduate student in the department of emergency medicine at Muhimbili National hospital. I am conducting research on prognostic value of ionised magnesium in patients with sepsis in the department of emergency medicine. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study. Please take time to review this information carefully. If you have any queries, please do not hesitate to consult me. Once you understand the information in this form, please sign below if you agree to take part in the study.

Study title: Prognostic value of ionised magnesium in predicting outcome of emergency department patient with sepsis in Tanzania.

Researcher: Dr. Jaimini K.K Popat, Department of Emergency Medicine Muhimbili National Hospital.

Purpose of this study: Sepsis is a life-threatening organ dysfunction caused by dysregulated host response to infection. Sepsis is one of the leading causes of mortality world-wide and magnesium plays an essential role in predicting the outcome of mortality in patients suspected with sepsis in the department of emergency medicine. This study is aimed at comparing ionised and total magnesium in patients suspected with sepsis and predict the outcome of the patient. With this information we may be able to manage you and any other patient that may present with sepsis to our department.

Who can take part in this study? This study is for all patients above the age of 18 years who are seen at the emergency department with sepsis. Participation in this study is entirely voluntary. You may also leave this study at any time without any harm on you. You will not lose any benefits, nor you will be given improper treatment if you decide not to take part in this study.

What will happen in this study? When you agree to be part of this study you will be asked a few questions about your demographic characteristics. We will also look at your blood investigations results, and the management provided to you. All this will be done to identify which factors can affect the prognosis of patients with sepsis. You will be given all the information regarding your results during this study. You will also receive the standard of care that is appropriate for you, as per the hospital policies.

Are there any risks of taking part in this study? There are no risks for you for participating in this study. The laboratory / Point of care investigations that will be done are the same routing ones that are done for all patients with sepsis. You will not be given any experimental medication, nor will any additional test be done on you as part of the research.

Are there any benefits of taking part in this study? You may not receive any personal benefits from being in this study. However, any new information that will be learned in this study will be used to manage your condition better.

Are there any costs or fees for entering this study? There will be no additional costs to you or your family for being in this study. You will only pay for all the things that you would have paid for if you were not in the study.

Is there confidentiality in this research project? The information gained in this study about you will only be known to you and the researcher. No other person will be given open access to the information. If your information is needed in the future by another doctor for your treatment, it will be made available to him. The results of this study could be published in an article for other researchers to read but would not include any information that would let others know who you are.

Your signature below means you have read that the above information, understood it well and are voluntarily ready to participate in this study.

Signature of Participant Date

_____ _____

Thank you for agreeing to participate in the study. Please do not hesitate to contact me for any clarification should need arise.

Contact Information

Dr Jaimini K.K Popat
Principal Investigator
Mobile No: +255789783678
Email: jaimini_znz@hotmail.com

Dr Bruno Sunguya
Director of Research and Publications,
Research and publications Committee,
Muhimbili University of Health and Allied Sciences
P.O Box 65001, Dar es Salaam.
Telephone number: +255713250074

Appendix III: Consent Form (Swahili Version):

Kwa majina ninaitwa Dr Jaimini K.K Popat, ni mwanafunzi wa udaktari bingwa wa magonjwa ya dharura . Nina fanya utafiti kuhusu wagonjwa maambukizi ya mkondo wa damu. Unaweza kuwa na haki ya kushiriki katika mradi huu wa utafiti. Hati hii inakupa Habari muhimu kuhusu utafiti. Inaelezea mud awa kupitia taarifa hii kwa makini . Kama una maswali yoyote , tafadhali usisite kuwasiliana na mimi. Baada ya kuelewa Habari katika fomu hii, tafadhali Saini hapa chini kama utakubali kushiriki katika utafiti.

Mada: Thamani ya ubashiri ya magnesiamu ioni kwa wagonjwa wazima walio na maambukizi waliolazwa katika idara ya dharura ya magonjwa ya dharura na ajali.

Mtafiti: Dr Jaimini K.K Popat, Idara ya tiba ya dharura, Chuo Kikuu cha Afya na Sayansi Muhimbili

Lengo la utafiti: Maambukizi yam kondo wad amu ni hali ambayo inaathiri watu wengi katika jami yetu. Ugonjwa huu unaweza kusababisha matatizo mbalimbali Pamoja na vifo. Matibabu sahihi ya tatizo hili itasababisha matokeo bora kwa wagonjwa. Lengo la utafiti huu ni kuangalia sababu ipi inaweza kutusaidi kutabiri matokeo na matibabu sahihi ya wagonjwa wanaolazwa na ugonjwa huu. Kwa utafiti huu, tunaweza kuwa na uwezo wa kutibu wewe na wagonjwa wengine ambao wana ugonjw wengine ambao wana ugonjwa huu.

Nani anaweza kushiriki katika utafiti huu? Utafiti huu ni kwa ajili ya watu wazima wote juu ya umri wa miaka 18 ambao wamelazwa katika wodi ya dharura na ugonjwa wa maabukizi ya mkondo wad amu. Kushiriki katika utafiti huu ni hiari kabisa. Unaweza pia kuacha utafiti huu wakati wowote bila ya madhara yoyote kwako . Huwezi kupoteza faida yoyote , wala hautapewa matibabu yasiyofaa kama wewe hutoamua kushiriki au kuacha utafiti huu.

Nini kitatokea katika utafiti huu? Utaulizwa maswali kadhaa kuhusu tabia yako binafsi. Pia tutakuwa tunaagalia matokeo yako yad amu na matibabu utakayopewa. Wewe utapewa taarifa zote kuhusu matokeo yako wakati wa utafiti huu. Pia utapata huduma sahihi kulingana na hali yako , kwa mujibu wa sera za hospitali.

Je, kuna hatari yoyote kwa ajili ya kuhiriki katika utafiti huu? Hakuna hatari kwako kwa kushiriki katika utafiti huu.Vipimo vya maabara ambavyo vitafanyika nis aa na vipimo kwa wagonjwa wote wa maambukizi yam kondo wad amu. Hautapewa dawa yoyote ya majaribio , wala vipimo vyovyote vya ziada havitafanyika kwasababu ya kushiriki katika utafiti.

Je, kuna faida yoyote ya washiriki katika utafiti huu? Hutapata faida yoyote ya kibinafsi kutoka kuwa katika utafiti huu. Hata hivyo, taarifa yoyote mpya ambayo kitatokea katika utafiti huu kitatumika kutibu hali yako bora.

Je,kuna gharama yoyote au ada kwa ajili ya kushiriki katika utafiti huu? Hakutakuwa na gharama za ziada kwa wewe au familia yako kwa kuwa katika utafiti huu. Wewe utalipa kwa ajili ya huduma zote ambazo ungepewa usingekuwa katika utafiti.
Je, kuna usiri katika utafiti huu? Taarifa zitakazopatikana katika utafiti huu kuhusu wewe zitabaki na wewe na mtafiti. Hakuna mtu mwingine atapewa uwezo wa kujua taarifa hizo. Kama taarifa yako zitahitajika katika siku zijazo na daktari mwengine kwa ajili ya matibabu yakom zitatolewa kwake. Matokeo ya utafiti huu inaweza kuchapishwa katika Makala kwa ajili ua watafiti wengine kusoma lakini taarifa itakuwa bila ya taarifa yoyote ambayo ingeweza kuruhusu wengine kujua wewe ni nani.

Saini yako chini ina maana umesoma Habari hapo juu, huelewa vizuri na unashiriki katika utafiti huu kwa hiari.

Saini ya mshiriki Tarehe

_____ _____

Ahsante kwa kukubali kushiriki katika utafiti huu. Tafadhali usisite kuwasiliana na mimi kwa maswali yoyote.

Mawasiliano

Dkt Jaimini K.K Popat
Mtafiti Mkuu.
Namba ya simu: +255789783678
Barua pepe: Jaimini_znz@hotmail.com

Dkt Bruno Sunguya
Mkurugenzi wa Utafiti na Machapisho,
Kamati ya Utafiti na Machapiso,
Vhuo Kikuu Cha Sayansi na Tiba Cha Muhimbili.
S.L.P 65001, Dar es salaam.
Namba ya simu: +255713250074

Appendix IV: Approval for ethical clearance

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATION

Ref. No.DA.282/298/01.C/2051 Date: 19/02/2024

MUHAS-REC-02-2024-2051
JAIMINI KAILESH KANTILAL POPAT
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: PROGNOSTIC VALUE OF IONISED MAGNESIUM IN PREDICTING OUTCOME OF ADULT PATIENTS WITH SEPSIS ATTENDING THE EMERGENCY MEDICINE DEPARTMENTS IN TANZANIA.

Reference is made to the above heading,

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 19/02/2024
EXPIRATION DATE OF APPROVAL: 19/02/2025

STUDY DESCRIPTION:
Purpose:

The purpose of this prospective cohort study is to determine the performance of ionised magnesium in predicting the mortality of patients with sepsis attending emergency medicine department of Tanzania.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided: https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2015245.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain Data Transfer Agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain Material Transfer Agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country.
8. Apply for and obtain permission to publish the results from National Institute for Medical Research. The application should be before submitting to a publisher and not concurrently through the email publications@nimr.or.tz.
9. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
10. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
11. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.



Dr. Nahya Salim Masoud,
CHAIRPERSON, MUHAS RESEARCH AND ETHICS COMMITTEE

Appendix V: Introduction letter

UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;
Ref. No. HD/MUH/T.49/2021

26th February 2024

The Executive Director,
Muhimbili National Hospital,
P.O. Box 65000,
DAR ES SALAAM

Re: INTRODUCTION LETTER

We would like to inform you that the bearer of this letter is Jaimini Kailesh Kantilal Popat with Reg. No. HD/MUH/T.49/2021 is a student at Muhimbili University of Health and Allied Sciences (MUHAS) pursuing MMed. Emergency Medicine.

As part of her studies, she will be doing an elective research titled: **"PROGNOSTIC VALUE OF IONISED MAGNESIUM IN PREDICTING OUTCOME OF ADULT PATIENTS WITH SEPSIS ATTENDING THE EMERGENCY MEDICINE DEPARTMENTS IN TANZANIA"**
She is being supervised by Dr. Said Kilindimo from MUHAS and Dr. Alphonce Simbila from MNH.

The research has been approved by the Chairman of University Senate.

Kindly provide her with the necessary assistance to facilitate the conduct of her research.

We thank you for your cooperation.

Ms. Victoria Mwanilwa
For: DIRECTOR, POSTGRADUATE STUDIES
c.c. Jaimini Kailesh Kantilal Popat

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam: Tel. G/Line: +255-22-2150302/6; Ext. 1015; Direct Line:+255-22-2151378;Telefax:+255-22-2150465;E-mail:dpgs@muhas.ac.tz;Web:https://www.muhas.ac.tz

Appendix VI: Permission letter MNH

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

MUHIMBILI NATIONAL HOSPITAL

In reply please quote:

Ref. No.: MNH/CRTCU/Perm/2024/108 Date: 28th February, 2024

Head of Department,
Emergency Medicine
Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH

Name of Student	**Jaimini Kailesh Kantilal Popat**
Title	**"Prognostic Value of Ionised Magnesium in Predicting Outcome of Adult Patients with Sepsis Attending the Emergency Departments in Tanzania"**
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Dr. Said Kilindimo (MUHAS)
Co – supervisor	Dr. Alphonce Simbila (MNH)
Period	28th February, 2024 to 30th April, 2024

Approval has been granted to the above principal investigators to collect data at MNH. Dissemination of study findings at MNH shall be overseen by **Dr. Alphonce Simbila** (MNH) supervisor.

Kindly ensure the named principal investigator abide to the ethical principles and other conditions of the research approval.

Sincerely,

H.D. TEACHING, RESEARCH & CONSULTANCY UNIT * P. O. Box 65000 DAR-ES-SALAAM * MUHIMBILI NATIONAL HOSPITAL

Dr. Charles K. Pallangyo
For: Head of Clinical Research, Training and Consultancy Unit

c.c DMS
c.c Dr. Alphonce Simbila
c.c **Jaimini Kailesh Kantilal Popat**

Upanga West, Kalenga Street, Plot No. 10480/3, P.O. BOX 65000, Dar es Salaam, Tanzania.
Telephone: +255-22-2151367-9, Telephone: +255-22-2151351-2
Email: info@mnh.or.tz, Website: www.mnh.or.tz

Appendix VII: Permission letter SHMH

SHREE HINDU MANDAL
DAR ES SALAAM
HOSPITALS | SCHOOLS | WELFARE
RESEARCH & TRAINING

RESEARCH

Date: 12th April 2024

Ref: RNT/KR/24/006

Name: Dr. Jaimini Popat
Address: MUHAS

Dear Dr. Popat,

RE: ACCEPTANCE OF CONDUCTING A RESEARCH.

In reference to the above subject. Please be duly informed that your request for conducting research at Shree Hindu Mandal Hospital (SHMH) titled "**Prognostic value of ionised magnesium in predicting outcome of adult patients with sepsis attending the emergency medicine departments in Tanzania"** has been approved. Below are the details.

Subsidiary:	SHMH	Department(s):	Emergency
Reporting to:	Dr. Esmail Sangey	Designation:	HOD - CCU
Start Date:	01/04/2024	End Date:	31/03/2025

Your research project period with our hospital will deal with important and sensitive information, records and other matters of the hospital. You will, therefore, be required to sign our Research projects Terms of Reference and research agreement attached.

You are also reminded that the grant shall be received via the following back account and you will be required to request for any expenses 1 week prior and submit all receipts after payments.

Account Name: SHREE HINDU MANDAL HOSPITAL DSM
Bank Name: NMB Bank Plc
Currency: USD
SWIFT Code: NMIBTZTZ
Branch Name: OHIO STREET

Kindly sign and send back the attached documents as acceptance to the terms and conditions mentioned.

Yours sincerely,

SHREE HINDU MANDAL
DAR-ES-SALAAM
RESEARCH & TRAINING

Prof. Kaushik Ramaiya
Research & Training Convener
Shree Hindu Mandal Research and Training