ACTIVE SURVEILLANCE ON IODINATED CONTRAST MEDIA-INDUCED REACTIONS AND ASSOCIATED FACTORS AMONG PATIENTS UNDERGOING RADIOLOGY DIAGNOSTIC AND INTERVENTION AT TERTIARY HOSPITALS IN ILALA MUNICIPAL

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By

Riziki S. Shemula

A Dissertation Submitted in (Partial) Fulfillment of Requirement for the Degree of Master of Pharmacovigilance and Pharmacoepidemiology of

Muhimbili University of Health and Allied Sciences
October, 2024

CERTIFICATION

The undersigned certifies that they have read and hereby recommends for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled; **‘‘Active surveillance on iodinated contrast media-induced reactions and associated factors among patients undergoing radiology diagnostic and intervention at a tertiary Hospitals in Ilala Municipal’’,** in (partial) fulfillment of the requirements for the Degree of Master of Pharmacovigilance and Pharmacoepidemiology of Muhimbili University of Health and Allied Sciences.

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DECLARATION AND COPYRIGHT

I, **Riziki S, Shemula,** declare that this **dissertation** is my 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.

Signature…… **Date**…….

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ABSTRACT

Background: Exposure to iodinated contrast medium (ICM), particularly in high doses, poses risks of organ toxicities, especially to the kidneys and cardiovascular system, leading to acute and delayed reactions. Documenting these reactions is vital for patient safety, risk management, pharmacovigilance, and medico-legal considerations. As imaging procedures increase in sub-Saharan Africa, the risk of ICM-induced reactions may rise, yet studies on these complications remain limited in low-resource settings like Tanzania.

Objective: To assess iodinated contrast media-induced reactions and associated factors among patients undergoing radiology diagnostic and intervention at two Tertiary Hospitals in Ilala Municipal.

Methods: This observational prospective cohort study, conducted from March to May 2024 in two tertiary hospitals in Ilala Municipal, enrolled 283 patients undergoing iodinated contrast-based procedures. The study utilized the SPSS version 23D statistical package, to analyze the patients' profile, the incidence of Iodinated Contrast Media-induced reactions and to determine the risk factors associated with adverse reaction with a statistical significance set at $p < 0.05$.

Results: The study included 283 patients. The overall incidence of ICM-induced reactions was 39.2%, with acute reactions such as gastrointestinal (27.9%), neurological (18.0%), and dermatological (13.5%) being common, while delayed reactions were mainly affecting renal function (6.3%). Associated factors included normal weight (RR = 1.445, p = 0.025), overweight (RR = 1.305, p = 0.043), neurological (RR = 1.496, p = 0.007), cardiopulmonary (RR = 1.335, p = 0.045), and oncological conditions (RR = 1.350, p = 0.039), as well as a history of anemia (RR = 1.490, p = 0.003). Diabetes mellitus was protective (RR = 0.540, p = 0.033), whereas stage 2 renal failure was linked to a higher risk (RR = 2.143, p = 0.009).

Conclusion: ICM-induced reactions were common, with acute reactions more frequent than delayed ones, primarily affecting the gastrointestinal, neurological, and dermatological systems, while delayed reactions impacted renal function. Significant risk factors included BMI, specific clinical indications, and a history of anemia, while diabetes was protective.

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LIST OF ABBREVIATIONS AND ACRONYMS

ADRs	Acute Adverse Drug Reactions
ADRs	Acute Adverse Drug Reactions
BMI	Body Mass Index
CIE	Contrast-induced Encephalopathy
CRS	Common Report Standard
CIN	Contrast-induced Nephropathy
ICM	Iodinated Contrast Media
JKCI	Jakaya Kikwete Cardiac Institute
MUHAS	Muhimbili University of Health and Allied Sciences
MNH	Muhimbili National Hospital
SPSS	Statistical Package for Social Sciences
WHO	World Health Organisation

DEFINITION OF TERMS

Iodinated contrast media Are drugs containing iodine given to patients to enhance the ability to see blood vessels and organs on medical images such as X-rays or computed tomography (CT) scans. These images provide greater detail when necessary to help healthcare professionals diagnose potential problems.

Adverse reactions Are side effects or unwanted, undesirable effects possibly related to a drug. These effects can vary from minor to life-threatening events.

Acute Iodinated CMI reactions Are those reactions happening within one hour or shortly after administration of the iodinated contrast media. These reactions can range from mild (such as nausea and vomiting) to severe (such as anaphylaxis and cardiovascular collapse).

Delayed Iodinated CMT reaction Are those reactions happening one hour to more than a week after the contrast administration. They include conditions such as contrast-induced nephropathy (CIN) and thyrotoxicosis. some individuals may experience delayed hypersensitivity

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Iodinated contrast media (ICM) are among the most commonly used injectables in radiology, ICM are essential for enhancing radiological imaging by improving the visualization of internal anatomical structures (1). It is practically possible to utilize modern iodinated contrast agents wherever on the body. While they can also be given intra-arterial, intrathecal, or intra-abdominal, their most common application is intravenously (2). However, their use is associated with the risk of adverse reactions, which can vary in severity, key properties of ICMs that influence their safety profile include ionicity, iodine concentration, osmolarity, and viscosity, although adverse responses are rare and can range from minor allergy symptoms and self-limiting to severe, potentially fatal conditions (3,4). Non-ionic contrast agents are preferred over ionic ones due to their lower osmolality and viscosity, which reduce the likelihood of adverse reactions. Non-ionic agents, such as low-osmolar and iso-osmolar formulations, are less likely to disrupt cellular membranes and cause osmotic imbalances, leading to fewer adverse events compared to high-osmolar contrast media (5,6). High-viscosity contrast agents increase the risk of injection-related complications, making low-viscosity options more desirable (7). A higher osmolality is correlated with a higher iodinated concentration (mg/mL), which influences the radiopacity of ICM(8), in general, ionic monomeric ICM has a higher osmolality than non-ionic monomeric ICM (8,9).

Adverse reactions to ICM can be classified into acute and delayed types. Acute reactions, including anaphylactoid responses, contrast-induced nephropathy (CIN), and cardiovascular events, often occur within minutes to hours of administration. Studies indicate that high-osmolar contrast media are more likely to cause acute reactions due to their greater osmotic pressure, which can affect renal function and lead to conditions such as CIN, especially in patients with pre-existing kidney issues (10,11). Iodinated contrast media can precipitate both renal and cardiovascular complications, particularly in vulnerable patients. Contrast-induced nephropathy (CIN) is one of the most significant renal side effects, characterized by an acute decline in renal

function within 48-72 hours following contrast exposure (12). CIN is thought to result from a combination of renal vasoconstriction, oxidative stress, and direct toxicity to renal tubular cells, leading to decreased glomerular filtration, especially in patients with pre-existing renal disease or dehydration (13,14). Cardiovascular complications associated with ICM use range from mild symptoms such as hypotension and bradycardia to severe outcomes, including arrhythmias and cardiac arrest (2,12). These cardiovascular reactions are mediated by allergic or anaphylactoid mechanisms, as well as direct effects on vascular smooth muscle (15,16). Early detection and management of these complications, including adequate hydration and premedication with corticosteroids in high-risk patients, are essential to preventing permanent damage (17). In contrast, low-osmolar and iso-osmolar contrast agents generally result in fewer acute adverse reactions (18,19). Delayed reactions, such as hypersensitivity or persistent skin reactions, may occur hours to days after administration and are less well understood (20). These reactions are believed to be related to immunological responses to iodine or other components in the contrast medium (21,22). Studies have shown that these reactions range with an incidence of ~1 – 53.5%, 0.2 – 0.4%, and 0.04 – 0.2% in patients with mild, moderate, and severe adverse reactions, respectively (11,23).

Additionally, Health care personnel maybe faced with medico-legal issues surrounding ICM-induced reactions, Medico-legal concerns surrounding iodinated contrast media (ICM)-induced reactions have gained prominence due to the potential for litigation when adverse reactions occur (24). Healthcare providers are required to obtain informed consent from patients before administering ICM, ensuring patients are aware of both the risks and benefits associated with the procedure (24). Negligence claims may arise if adverse reactions, such as allergic or anaphylactoid responses, are not adequately managed or if appropriate pre-screening for risk factors like prior allergic reactions or renal insufficiency is overlooked (25). These complications emphasize the importance of patient safety and institutional accountability.

Contrast-based diagnostics and interventions have raised in Tanzania, as in many other sub-Saharan African nations (26,27). Studies in Tanzania have focused on specific adverse reactions like those targeting the kidney and reported a high incidence (19%) of contrast-induced

nephropathy (26). Still more work needs to be done to evaluate the responses brought on by iodinated contrast media. Therefore, the purpose of this study is to assess the factors that are associated with iodinated contrast media-induced reactions in patients receiving radiology diagnostics and intervention at two tertiary institutions in the Ilala Municipal.

1.2 Problem Statement

In developing nations, the utilization of iodinated contrast media (ICM) in imaging and interventional procedures is increasing, which heightens the risk of adverse reactions associated with these agents. If not properly reviewed and managed, the incidence of iodinated contrast-induced responses may rise significantly (28). Documenting ICM-induced reactions is crucial for ensuring patient safety, risk management, pharmacovigilance, clinical decision-making, education, and medico-legal purposes. Accurate documentation and understanding of these reactions are essential components of the overall management and safe use of ICMs.

In developing countries, including Tanzania, the reported incidence rates of ICM-related adverse drug reactions (ADRs) range between 1-19%, with the most commonly observed complications being acute renal impairment and cardiovascular issues (1,10,28). Despite this, existing studies primarily focus on the general impact of contrast media on kidney failure, often neglecting a more detailed examination of specific contrast media types and their associated risks (29,30). For instance, previous research in Tanzania has indicated a high incidence of contrast-induced nephropathy, reaching up to 19% (26). This highlights a critical gap in understanding the specific characteristics and risk factors associated with different ICM formulations and their adverse effects.

Addressing this gap is vital for improving patient safety and managing the risks associated with ICM use. This study aims to bridge this gap by investigating the incidence and types of adverse reactions to ICM, including both acute and delayed reactions, and analyzing the determinants of these reactions among patients undergoing radiology diagnostic and intervention procedures. By focusing on specific contrast media and their associated factors, this research will provide a

clearer understanding of the risks involved and contribute to the development of more effective management strategies.

1.3 Study Rationale

The study provided a better understanding of ICM induced reactions, their prevalence and severity, causes, risk factors, potential preventive measures, and interventions, which may include premedication protocols, alternative contrast agents, or modifications in administration techniques.

Study results provided a basis for healthcare providers to make informed decisions regarding the selection and administration of iodinated contrast media, thereby minimizing adverse reactions and enforcing and training the health care personnels to adhere to pharmacovigilance practice when handling ICM.

1.4 Conceptual framework

An elaboration on the relationship between occurrence of Iodinated contrast-induced Reactions and its factors is seen in Figure 1. Social demographic variables including age, weight/BMI, and sex can put the patients at risk of Iodinated contrast-induced Reaction. Iodinated contrast-induced reactions may be more likely to develop in cases of pre-existing chronic kidney disease, diabetes mellitus, anemia, heart failure, metabolic syndrome, hypoalbuminemia, and dehydration, among other clinical variables.

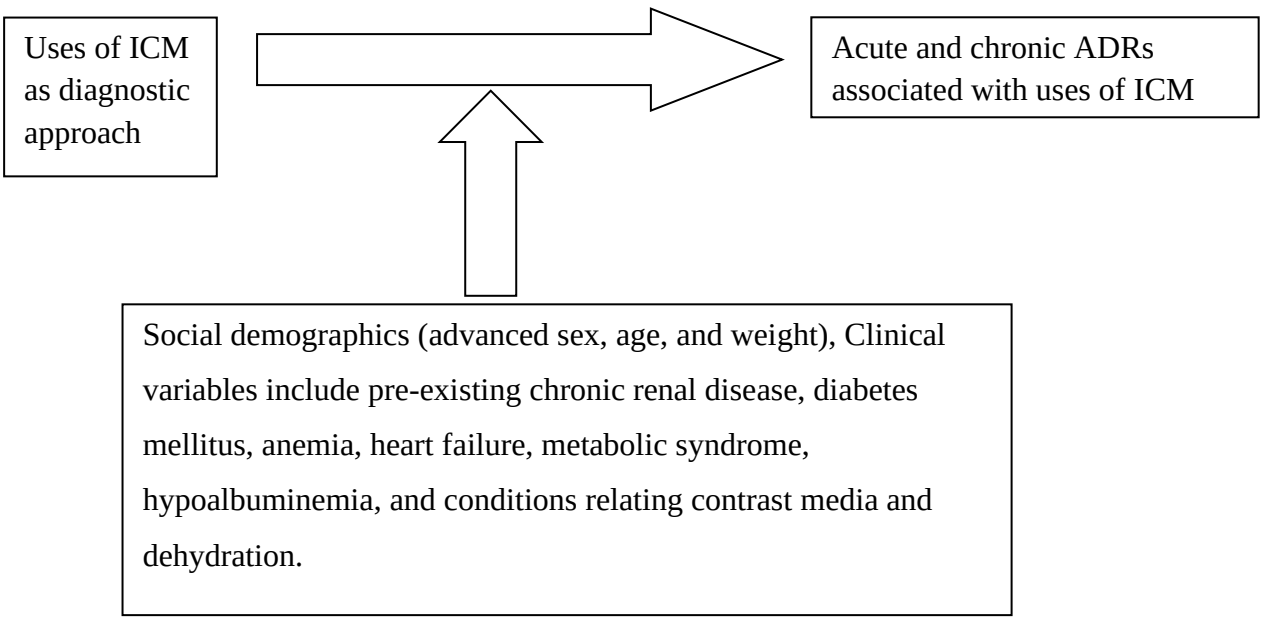


Figure 1: Conceptual framework showing the independent variables that can cause Iodinated contrast-induced reactions.

1.5 Main Research Question

What is the incidence of iodinated contrast media-induced adverse reactions and associated factors among patients undergoing radiology diagnostic and intervention from Nov 2023 to May 2024?

1.5.1 Sub-research Questions

1. What is the incidence of ICM induced reactions among patients undergoing contrast-based diagnostics and intervention from March to May 2024?
2. What are the acute adverse reactions associated with ICM intervention from March to May 2024?
3. What are the delayed adverse reactions associated with ICM interventions from March to May 2024?
4. What are the determinants of ADRs associated with the use of ICM from March to May 2024?

1.6 Research Objectives

1.6.1 Overall Objective

To assess the incidence of iodinated contrast media-induced adverse reactions and associated factors among patients undergoing radiology diagnostic and intervention from March to May 2024

1.6.2 Specific Objectives

1. To determine the incidence of ICM induced reactions among patients undergoing contrast-based diagnostic and intervention from March to May 2024.
2. To determine the acute adverse reactions associated with ICM intervention from March to May 2024.
3. To determine the delayed adverse reactions associated with ICM interventions from March to May 2024.
4. To analyze the determinants of ADRs associated with the uses of ICM from March to May 2024.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Overview of Iodinated Contrast Media (ICM) Use and Reactions

Iodinated contrast media (ICM) are indispensable in diagnostic radiology and interventional procedures, allowing for enhanced imaging clarity and detailed anatomical visualization. However, their use is associated with adverse reactions, ranging from mild to severe (22). The increasing reliance on ICM in healthcare, particularly in developing nations where healthcare systems are expanding diagnostic capabilities, underscores the need to assess the risks, benefits, and safety of these agents. Globally, the incidence of ICM-induced reactions has prompted researchers and clinicians to focus on improving contrast agent formulations, understanding the underlying risk factors, and developing guidelines to mitigate adverse effects (3).

2.2 Incidence of ICM-Induced Reactions

Globally, the incidence of ICM-induced adverse reactions varies based on the type of contrast media used (ionic vs. non-ionic), iodine concentration, and patient characteristics. Non-ionic, low-osmolar contrast agents have largely replaced high-osmolar, ionic media due to their better safety profile, with reported reaction rates of around 0.6% for mild reactions, and 0.04% for severe reactions and some as high as 6.4% (12,31). Several reports and studies have shown the incidence of iodinated contrast-induced reactions. Dermatological reactions are the most typical clinical signs of adverse responses. About 70% of negative reactions involve pruritus and urticarial (32). Flushing has also been noted in an emergency. Among the more varied spectrum of delayed symptoms that could happen include exanthema, erythema multiforme, vasculitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, and graft versus host reaction (9). Immediate signs include heart-related conditions such cardiovascular shock, arrhythmia, and cardiac arrest. (33). There is a debate over whether these cardiac symptoms are caused more directly by a cardiac mechanism (such as Kounis syndrome) or are a tributary effect of homeostatic dysfunction. There have also been reports of systemic symptoms of adverse responses which might range widely in intensity (32). Mild responses can cause arm soreness,

nausea, vomiting, and headaches. The prevalence of these symptoms increases with the use of high-osmolality drugs. Hypotension and bronchospasm can be caused by intermediate responses (32). Respiratory arrest and loss of consciousness are additional events occurring in patients who experience severe responses (11). As stated, these reactions happen in 0.2% or fewer people. Even though they are uncommon, immediate adverse effects are frequently associated with systemic symptoms (1).

In high-income regions, the incidence of ICM-related adverse reactions is well-documented due to established pharmacovigilance systems. Studies in the China, for instance, report that approximately 1-2% of patients experience adverse events after exposure to ICM, with allergic-like symptoms, contrast-induced nephropathy (CIN), and delayed reactions being the most common (34). Another most noted adverse events is acute kidney injury (26). The severe adverse outcome of ICM, also referred to as nephropathy or contrast-induced acute kidney injury (CIN), is associated with increased morbidity and death (32). It could be the supreme recognized influence for CIN is chronic renal disease. After nephrotoxic medication use and decreased renal perfusion, CIN is the third most common cause of hospital-acquired acute kidney damage in major observational studies carried out in North America (35,36). The rates range from 11 - 16% (37) to 50% in high-risk cardiac patients (38).

In Sub-Saharan Africa, there is limited but growing data on ICM use and associated reactions. However, some studies that have been done in Africa, include South Africa, Kenya, and Nigeria (29,30,39). In these studies, the incidence of iodinated contrast-induced reaction ranges from 9.9% to 35.9%. The South African study reported an association between CIN with a longer length of hospital stay and high death rates within three months, demonstrating CIN-related adverse effects in sub-Saharan Africans (29). The paucity of data from other African countries, including Tanzania, necessitates more focused studies on the incidence and risk factors of ICM reactions to establish effective safety protocols. Existing studies, such as those from Muhimbili National Hospital/Jakaya Kikwete cardiac institute in Tanzania, primarily focus on nephropathy and overlook broader adverse reaction profiles (26). This study seeks to fill this gap by systematically documenting ICM reactions in Tanzania.

2.3 Acute Adverse Reactions Associated with ICM

Acute adverse reactions to ICM are typically categorized as allergic-like or physiologic, occurring within minutes to hours of administration. Globally, mild reactions, such as nausea, vomiting, and urticaria, are reported in 1-3% of patients, whereas severe reactions, such as bronchospasm, hypotension, and anaphylaxis, occur in 0.1% of cases (12). These reactions often require immediate medical intervention and can be life-threatening. The risk is higher in individuals with a history of allergies, asthma, or previous reactions to ICM.

In Europe, where radiological practices are highly regulated, acute adverse reactions are closely monitored, and premedication strategies are employed for high-risk patients to reduce the likelihood of severe reactions. Studies have reported that premedication with corticosteroids and antihistamines could reduce the incidence of severe allergic-like reactions by 50% (40,41). However, in low-resource settings like Tanzania, access to premedication protocols may be limited, exacerbating the risk of acute reactions in high-risk populations and data is scarce.

Regionally, Despite an increase in the use of contrast media in sub-Saharan Africa, a few studies have been done in South Africa, Kenya and Nigeria, with most research focusing on contrast-induced nephropathy (CIN) rather than immediate allergic or physiologic responses (29,30,39). This study will contribute by providing detailed data on acute reactions in Tanzania, supporting better preparation for such events in resource-limited settings.

2.4 Delayed Adverse Reactions to ICM

Delayed adverse reactions to ICM, occurring 1-7 days post-administration, are less commonly studied but may include skin rashes, joint pain, fever, and nephrotoxicity (9,22). Globally, delayed reactions have been reported in 1-3% of patients, but they are often underreported due to the challenge of associating these symptoms with the contrast media after the procedure (2,12). Studies, such as those from the Japan and China, emphasize the need for long-term monitoring and patient education to identify and manage delayed reactions appropriately (5,14).

In Africa, the scarcity of follow-up data makes it difficult to establish the true incidence of delayed reactions, limited awareness among patients and healthcare workers, combined with resource constraints, means that many delayed reactions may go unreported or misattributed to other causes (26). In Tanzania, no large-scale studies have systematically tracked delayed reactions, necessitating more comprehensive research to inform clinical guidelines on post-ICM monitoring.

2.5 Determinants of ICM-Induced Adverse Reactions

The risk of adverse reactions to ICM is influenced by a range of patient- and agent-related factors. Globally, established risk factors include pre-existing renal impairment, diabetes, dehydration, cardiovascular disease, and a history of allergic reactions (18). Studies in Korea and Japan have identified contrast media osmolality and iodine concentration as key determinants of adverse reactions (42,43). Low-osmolar and iso-osmolar agents are associated with fewer adverse effects compared to their high-osmolar counterparts, while higher iodine concentrations tend to increase the risk of nephrotoxicity (18,44,45). The best of all is a previous response to ICM which has be shown to increase the risk up to 5 times (12,15,46). Those who have had an ICM reaction have a 2.5 to 44% risk of reacting. Those with a history of asthma are 10 times more likely to experience a severe reaction (17). Furthermore, the chance of a reaction is tripled in those with a history of allergies. Heart disease, dehydration, hematologic problems, metabolic problems, and extremes in age have all been connected to risk factors (12,14,17). Other danger factors include the absence of external ICM warming.(47), injection dose (48–50), injection rate (48–50), and a family history of ICM hypersensitivity (51). Specific to nephropathy, there are many risk factors now known. Age > 70 years, congestive heart failure, myocardial infarction during the previous 24 hours, diabetes mellitus, per procedural hypotension, dehydration or volume contraction, and numerous doses of contrast material are all linked to an elevated risk of CIN (52)

In Sub-Saharan Africa, studies on determinants of ICM reactions are limited, though research suggests that underlying health conditions such as hypertension and diabetes, which are prevalent in the region, may increase susceptibility to ICM-induced nephropathy (53,54). In

Tanzania, the increasing burden of non-communicable diseases such as diabetes and hypertension mean that more patients are likely to be at higher risk for ICM-induced reactions. The lack of robust screening and monitoring practices further compounds this risk.

This study aims to analyze these determinants in the local population to provide actionable insights for improving patient safety. Iodinated contrast media play a critical role in modern diagnostic and interventional radiology, but their use is not without risks. Globally, the incidence of ICM-induced adverse reactions is well-documented, particularly in high-resource settings where pharmacovigilance systems are well established. However, in developing nations, including Tanzania, there is a significant gap in the literature regarding the incidence, types, and determinants of both acute and delayed adverse reactions to ICM. This study will contribute to filling this gap by providing comprehensive data on the incidence and risk factors associated with ICM reactions in a Tanzanian context, ultimately informing local clinical practice and patient safety protocols.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Study Design

This study used observational- single baseline prospective cohort study design with analytical methodology because it enables data collection on the outcome variable (iodinated contrast-induced reactions) from march to May 2024.

3.2 Study Area

The study sites were the Jakaya Kikwete Cardiac Institute (JKCI) and Muhimbili National Hospital (MNH) at Ilala Municipal in Dar es Salaam. These locations were chosen as Tanzania's major hospitals, caring for cardiac patients as well as specialized diagnostics, treatments, and referrals from various healthcare institutes. Cardiothoracic surgery, imaging, and interventional procedures are among the services provided. With 157 beds available, the facility sees more than 1800 outpatients and 100 inpatients each week. An average of 3 patients undergoing coronary angiography or intervention daily. which makes up an average of 75 patients per month. At Muhimbili National hospital up to 4 in-patients undergo iodinated contrast media daily which makes up average of 80 patients per month.

3.3 Study Population

The study population included all patients who have received non-ionic iodinated contrast-based diagnostics and intervention. This study involved adult patients who were attending Muhimbili National Hospital and Jakaya Kikwete Cardiac Institute who were indicated for all radiological diagnosis and interventional procedures (CT, MRI and Angiography) that involve the use of iodinated contrast media, to enhance visualization and efficiency of the procedures.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

1. All patients undergoing or who have undergone non-ionic iodinated contrast-based diagnosis and intervention and whose medical records are complete
2. Patients 18 years and above
3. Patients who consented to the study

3.4.2 Exclusion Criteria

1. Patients in critical condition
2. Mentally ill patients

3.5 Sample Size Estimation

This study applied Cochran's formula to calculate the sample size required. The proportion that was used was adopted from a previous study that was done in Tanzania, which estimated the incidence of contrast media reactions to be 19% (26).

$$(n) = \frac{Z^2 p\,(1-p)}{e^2}$$

Where $\alpha=0.05$,

$z=1.96$

$p=0.19$ (incidence of contrast reactions according to a study in Tanzania (26)

so,

$$n = \frac{1.96^2 \times 0.19\,(1-0.19)}{0.05^2}$$

$n = 236$

Accounting for 20% non-response, n was 283 patients.

3.6 Sampling Procedures

Patients were enrolled conveniently until a pre-defined sample size of 283 is reached. Participants were purposely selected based on the inclusion criteria listed in section 4.3.1 of this report. Convenient sampling was ideal based on the attendance of the patients and variation in daily working hours, therefore all the participants that attended the selected departments were approached and if they consented recruitment commenced immediately.

3.7 Data Collection Tools

Interviewer administered questionnaire was utilized in collection of participants' data, including demographics (age, gender, BMI), drug currently in use, pre-existing condition, and past exposure to Iodinated contrast medium. Clients' hospital case notes were utilized to determine the current diseases, and pre-procedure client's lab results. Data obtained through patients' notes were documented in checklist. The employed a checklist was also used to gather information on complications of interest, including renal, gastrointestinal, cardiac, anaphylactic, neurological, respiratory, and dermatological complications. Patient files were reviewed at predetermined intervals of 0–60 minutes, 24 hours, 72 hours, and 7 days. Patients who were discharged from the hospital prior to the completion of the seven-day participation period were contacted using the phone numbers they provided when giving their consent and asked a series of questions pertaining to ICM-induced complications, and the information was captured in their respective individual check lists. Patients' stature and weight were documented. Height was dignified using a stadiometer where the client did not have any footwear. Weight was determined by a pneumatic weighing machine. Blood pressure was taken using an automated BP machine. Hypertension was defined as pre-procedure BP of ≥140/90 mmHg or known hypertensive on medications.

3.8 Pre-testing

The data collection tools were pre-tested in Muhimbili Hospital-Mloganzila with 47 study sample patients (20%). The patients in the pilot study were not included in the actual study. The pre-testing of the tools helped adjust the questions where necessary.

3.9 Data Collection Procedures

Research assistants received training and familiarization prior to starting the study, including instructions on how and what data to gather. Recruitment of the patients was done soon after receiving patients' consent.

3.10 Variables and Measures

Dependent:

Incidence of Iodinated contrast-induced Reactions

Independent:

Social demographic (Advanced age, weight, sex, Clinical factors include diabetes mellitus, anemia, heart failure, dehydration, and pre-existing kidney disorders and contrast medium related factors)

3.11 Data Management and Analysis

Sorting and checking of collected information were done daily to ensure completeness. In any case of discrepancies or missing data, a re-review of the patients' medical records was done to make necessary adjustments. Statistical Package for Social Sciences (SPSS) version 23D was employed for data analysis. Data was summarized in descriptive statistics; Objectives 1-3 were presented in percentages. For objective 4, the Chi-square test was employed to test at univariate level factors with a $p<0.2$ were considered fit for multivariate tests. At multivariable levels, modified poison regression analysis was employed. To elaborate the significance of test results, a p-value of less than 0.05 was used.

3.12 Ethical Issues

MUHAS Institutional Review Board granted ethical clearance before conducting the study (Reference no. MUHAS-REC-03-2024-2120). Along with that, permission was obtained from the management of the selected hospitals. Confidentiality was maintained throughout the data collection and analysis process; patient's names were not included in the data collection. Only

patients who provide consent were approached in this study as well as files with complete medical records were considered for data collection.

CHAPTER FOUR

4.0 RESULTS

4.1 Socio-demographic and clinical characteristics of the study participants

The study included 283 patients from Both Muhimbili national Hospital (MNH) and Jakaya Kikwete Cardiac Institute (JKCI), with nearly balanced gender distribution of female (51.6%) and male (48.4%) participants. The participants were categorized into three age groups. The median age was 56 years, majority (47.7%) aged 41-65. Residency-wise, 53.4% of the patients resided within Dar es Salaam [Table 1].

From the 283 patients, the median BMI was 26.84. Most patients were categorized overweight (46.6%), with obesity noted in 22.3% of participants. Allergic reactions to any medications were reported in 5.7% of patients. Conditions prompting radiological diagnosis and interventions included vascular and procedural conditions (30.0%), gastrointestinal and abdominal conditions, and cardiopulmonary conditions. Most patients received a contrast dose of less than 100 ml (86.9%) [Table 1].

Pre-existing heart problems were documented in 18.0% of cases, while thyroid disorders were present in 0.7%. History of previous contrast media use, cigarette smoking, and alcohol consumption were noted in 7.1%, 6.4%, and 13.4% of patients, respectively. Other prevalent conditions included hypertension (24.3% overall, with 10.2% at stage 2), diabetes mellitus, and renal failure (5.3% at stage 3) [Table 1].

Among the 283 participants, only 21.6% reported using diuretics. Similarly, few patients used angiotensin 2 receptor blockers (14.1%). calcium channel blockers and angiotensin-converting enzyme inhibitors were reported in less than 3% of the cases. NSAIDs were used by 7.1% of participants, while over-the-counter medications were used by 3.9%. Clopidogrel was taken by 8.8% of participants, and atorvastatin by 7.4%. [Table 1].

Table 1: Socio-demographic and clinical characteristics of the study participants (N=283)

Variable	Frequency (n)	Percent (%)
Sex		
Male	137	48.4
Female	146	51.6
Age (median = 56)		
18-40	83	29.3
41-65	135	47.7
>65	65	23.0
Residency		
Inside Dar es salaam	157	53.4
Outside Dar es salaam	126	46.6
Body Mass Index (median=26.84)		
Underweight	4	1.4
Normal weight	84	29.7
Overweight	132	46.6
Obesity	63	22.3
Allergic to any medications		
Yes	16	5.7
No	267	94.3
Condition causing radiological study		
Cardiopulmonary conditions	45	15.9
Gastrointestinal and abdominal conditions	75	26.5
Oncological conditions	53	18.7
Neurological conditions	25	8.8
Vascular and procedural conditions	85	30.0
Dose of contrast		
<100 ml	246	86.9
100-200 ml	36	12.7
>200 ml	1	0.4

Medical History		
Heart problem	51	18.0
Thyroid disorders	2	0.7
Previous use of contrast media	20	7.1
History of cigarette smoking	18	6.4
History of high cholesterol	3	1.1
History of diabetes mellitus	17	6.0
History of Asthma	5	1.8
History of alcohol consumption	38	13.4
History of anemia	10	3.5
History of hypertension		
Stage 1	21	7.4
Stage 2	29	10.2
Stage 3	19	6.7
History of renal failure		
Stage 2	11	3.9
Stage 3	15	5.3
Previous History of Medication use		
Diuretics	61	21.6
Angiotensin 2 receptor blockers	40	14.1
Calcium channel Blockers	7	2.5
Angiotensin Converting Enzyme inhibitor	2	2.5
NSAIDs	20	7.1
Over the counter /other medications	11	3.9
Clopidogrel	25	8.8
Atorvastatin	21	7.4

4.2 Incidence of Intravenous Iodinated Contrast Media Reaction

Among the 283 patients studied, 111 (39.2%) experienced a reaction to ICM. And the remaining 172 (60.8%) did not experience any ICM reactions See [Figure 2].

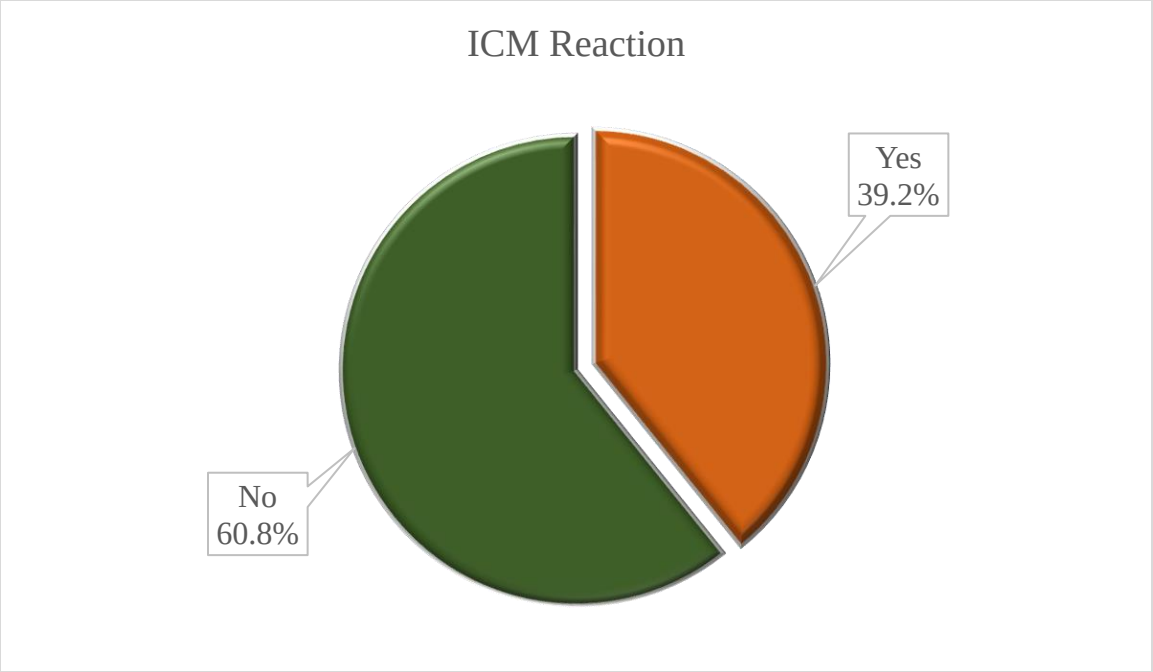


Figure 2: Incidence of ICM reaction (N=283)

Severity of experienced a reaction varied with 31 (11%) experiencing mild reactions, 47 (16.6%) had moderate reactions, and 33 (11.7%) had severe reactions. See [Table 2]

Table 2: Severity of ICM reaction among study participants (N=283)

Variable	Frequency (n)	Percent (%)
Severity of ICM reaction		
No reaction	172	60.8
Mild	31	11
Moderate	47	16.6
Severe	33	11.7

4.3 Acute Contrast Media -induced Adverse reactions.

Generally, acute onset of iodinated contrast media induced reaction were relatively higher across various categories; gastrointestinal complications were reported in 31 (27.9%), neurological 20 (18.0%), 15 (13.5%) dermatological and 10 (9.0%) anaphylaxis cases. Others occurred in smaller cases including respiratory, cardiac and renal complications. See [Figure 3]

4.4 Delayed Contrast Media-induced Adverse Reactions.

Delayed onset of iodinated contrast media induced reaction were relatively lower than acute onset and these included renal complications occurring in 7 (6.3%), dermatological complications occurring in 4 (3.6%) of the participants, followed by respiratory, anaphylactic and cardiac complications occurring in 2 (1.8%) for each. No neurological or GI complications had delayed onset. See [Figure 3]

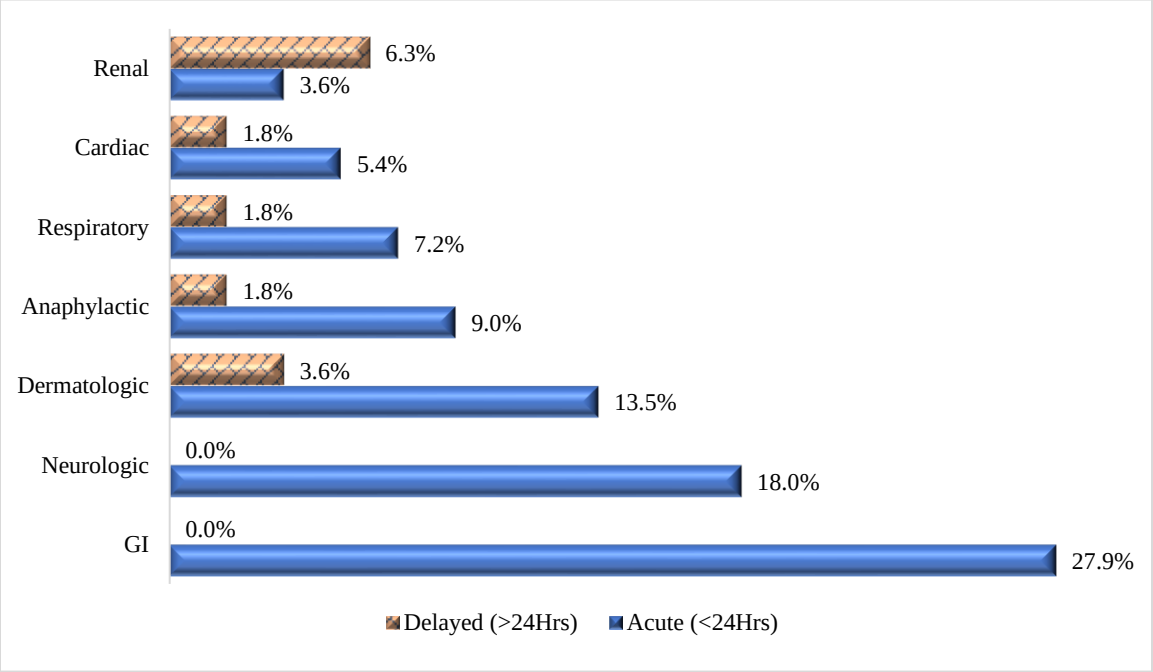


Figure 3: Acute and Delayed ICM reactions among study participants (N=111)

Overall, the most reported adverse events following ICM administration were gastrointestinal complications 31 (27.9%), which include nausea, vomiting, moderate diarrhea, and stomach pain and discomfort. The neurological effects 20 (18.0%) were headaches, dizziness, and visual disturbances. Skin peeling, urticaria, pruritus, irritation, and erythema were among the dermatological complications in 19 (17.1%). Anaphylaxis in 12 (10.8%) resulted in wheezing, angioedema, and hypotension. Respiratory adverse reactions in 10 (9,0%) included wheezing, pneumonia, and angioedema. Renal complications in 11 (9.9%) of the cases were suggested by the increased serum creatinine level that was observed in laboratory results. Cardiac complications in 8 (7.2%) included increased pulse rates and hypotension. see [Table 3]

Table 3: ICM induced complications among study participants (N=111)

Variable	Frequency	Percentage (%)
Gastrointestinal	31	27.9
Neurological	20	18.0
Dermatological	19	17.1
Anaphylaxis	12	10.8
Respiratory	10	9.0
Renal	11	9.9
Cardiac	8	7.2

4.5 Distribution of ICM occurrence across patient Characteristics.

The distribution of ICM reactions varied significantly across patient characteristics. For age, patients aged 18-40 experienced the highest reaction rate at 35 (48.6%), followed by those aged 41-65 at 54 (40.3%), and the lowest was observed in patients over 65 at 22 (28.6%). Regarding sex, females had a slightly higher frequency of reactions at 58 (39.7%) compared to males at 53 (38.7%). In terms of BMI, overweight patients had the highest reaction frequency at 70 (53.0%), followed by normal weight at 43 (51.2%), while obese patients had the lowest at 19 (20.2%). Patients with a history of allergies to medication had a reaction rate of 7 (41.2%), slightly higher than those without such allergies at 104 (39.1%). Among indications for radiological study, neurological conditions had the highest frequency of reactions at 13 (72.2%), followed by oncological conditions at 24 (53.3%) and cardiopulmonary conditions at 20 (54.1%), while vascular conditions had the lowest at 24 (21.2%). For contrast dose, those receiving 100-200 ml had a reaction rate of 16 (45.4%), while those receiving less than 100 ml had 92 (37.4%), and none of the patients receiving more than 200 ml had reactions.

Regarding hypertension, patients without hypertension experienced reactions at 91 (49.2%), while those with stage 1 hypertension had 10 (28.6%) reactions, and stage 2 hypertension had 5 (17.9%). Among those with renal failure, stage 2 patients had the highest reaction rate at 5 (71.4%), compared to stage 3 with 4 (16.7%). All patients with anemia reported reactions, 5 (100.0%), while those without anemia had 96 (34.5%) reactions. For patients with high cholesterol, all 2 (100.0%) experienced reactions, whereas those without had a reaction rate of 109 (38.8%). Diabetic patients had the lowest reaction rate at 3 (10.0%) compared to non-diabetics at 109 (43.1%). Patients with a history of alcohol consumption experienced reactions in 12 (15.5%), compared to 99 (41.9%) among non-drinkers. Asthmatic patients had reactions at 2 (28.6%), while those without asthma had a similar rate at 109 (39.5%). Lastly, patients with a history of heart problems had a reaction frequency of 18 (24.0%), whereas those without heart problems had a higher rate at 93 (44.7%). These findings highlight the variability in ICM reactions across different patient demographics and clinical histories. See summary [Table 4]

Table 4: Distribution of ICM incidence across patient characteristics (N=283)

Chi-square test				
	ICM Reaction			
Variable	**Absent (%)**	**present (%)**	**X^2**	**P-value**
Age			4.98	0.083
18-40	37 (51.4)	35 (48.6)		
41-65	80 (59.7)	54 (40.3)		
>65	55 (71.4)	22 (28.6)		
BMI			12.65	**0.005**
Underweight	2 (50.0)	2 (50.0)		
Normal weight	41 (48.8)	43 (51.2)		
Overweight	62 (47.0)	70 (53.0)		
Obese	44 (69.8)	19 (20.2)		
Sex			0.196	0.658
Male	84 (61.3)	53 (38.7)		
Female	88 (60.3)	58 (39.7)		
Allergy to medication			0.004	0.953
Yes	10 (58.8)	7 (41.2)		
No	162 (60.9)	104 (39.1)		
Indications for radiological study			23.29	**<0.001**
Cardiopulmonary conditions	17 (45.9)	20 (54.1)		
Gastrointestinal conditions	40 (57.1)	30 (42.9)		
Oncological conditions	21 (46.7)	24 (53.3)		
Neurological conditions	5 (27.8)	13 (72.2)		
Vascular conditions	89 (78.8)	24 (21.2)		
Dose of contrast			3.60	0.165
<100 ml	154 (62.6)	92 (37.4)		
100-200 ml	20 (55.6)	16 (45.4)		
>200 ml	1 (100.0)	0 (0.0)		
History of hypertension			24.37	**<0.001**
No	94 (50.8)	91 (49.2)		
Stage 0 (elevated)	30 (85.7)	5 (14.3)		
Stage 1	25 (71.4)	10 (28.6)		
Stage 2	23 (82.1)	5 (17.9)		
History of renal failure			8.36	**0.015**
Stage 1 (No)	150 (59.5)	102 (40.5)		
Stage 2	2 (28.6)	5 (71.4)		
Stage 3	20 (83.3)	4 (16.7)		
History of anemia			3.34	0.068
Yes	0 (0.0)	5 (100.0)		
No	182 (65.5)	96 (34.5)		
History of high cholesterol			0.978	0.323

Yes	0 (0.0)	2 (100.0)		
No	172 (61.2)	109 (38.8)		
History of diabetes mellitus			15.95	**<0.001**
Yes	27 (90.0)	3 (10.0)		
No	144 (56.9)	109 (43.1)		
History of alcohol consumption			3.7	0.055
Yes	35 (74.5)	12 (15.5)		
No	137 (58.1)	99 (41.9)		
History of Asthma			0.673	0.412
Yes	5 (71.4)	2 (28.6)		
No	167 (60.5)	109 (39.5)		
Heart problem			14.48	**<0.001**
Yes	57 (76.0)	18 (24.0)		
No	115 (55.3)	93 (44.7)		

4.6 Factors associated incidence of ICM reactions among patients undergoing Radiological interventions

In the univariate analysis, BMI, Indications for radiological studies, history of renal failure, the History of anemia also presented significant findings. Patients with anemia had a significantly increased risk of ICM reactions. History of diabetes mellitus was significantly associated with reactions. In the univariate analysis, the RR for patients with diabetes was higher as compared to non-diabetic patients.

In the multivariable Poisson regression analysis assessing factors associated with ICM reactions, several significant correlations were observed as shown in table 5. Participants classified as normal weight (RR = 1.445, p = 0.025) and overweight (RR = 1.305, p = 0.043) had elevated risk ratios for ICM reactions compared to those of obese. Among the indications for radiological intervention; Neurological conditions (RR = 1.496, p = 0.007), cardiopulmonary (RR = 1.335, p = 0.045), and oncological conditions (RR = 1.350, p = 0.039) were significantly associated with increased risk of ICM induced reactions. A history of anemia (RR = 1.490, p = 0.003) was also linked to higher risk, while diabetes mellitus showed a protective effect (RR = 0.540, p = 0.033) against reactions. Stage 2 renal failure demonstrated a notably higher risk (RR = 2.143, p = 0.009). whereas age, dose of contrast, history of hypertension, history of alcohol use, and history of heart problems did not show any statistical significance. see [Table 5]

Table 5: Factors associated with the incidence of ICM Reactions among patients (N=283)

	Univariate Analysis		Multivariate Analysis	
Variable	**CRR (C.I 95%)**	**P-value**	**ARR (C.I 95%)**	**P-value**
Age				
18-40	3.21 (1.21-8.75)	0.013	1.12 (0.71-1.77)	0.613
41-65	1.16 (0.90-1.49)	0.161	1.16 (0.90-1.49)	0.261
>65	Ref		Ref	
BMI				
Underweight	1.21 (1.08-5.91)	0.193	1.38 (0.74-2.59)	0.310
Normal weight	0.45 (0.05-2.20)	**0.040**	1.45 (1.047-2.0)	**0.025**
Overweight	3.15 (1.13-4.27)	**0.031**	1.31 (0.99-1.73)	**0.043**
Obese	Ref		Ref	
Sex				
Male	0.99 (0.54-2.11)	0.261		
Female	Ref			
Allergy to medication				
Yes	3.589 (1.37-8.21)	0.250		
No	Ref			
Indications for radiological study				
Cardiopulmonary conditions	1.06 (0.70-2.37)	0.104	1.36 (1.01-1.77)	**0.045**
Gastrointestinal conditions	1.25 (1.03-1.76)	0.159	1.25 (0.93-1.67)	0.138
Oncological conditions	1.20 (1.11-2.92)	0.082	1.35 (1.02-1.80)	**0.039**
Neurological conditions	2.19 (0.92-5.10)	0.013	1.50 (1.12-2.00)	**0.007**
Vascular and procedural conditions	Ref		Ref	
Dose of contrast				
<100 ml	0.77(0.28-2.74)	0.021	1.767(0.98-3.54)	0.120
100-200 ml	3.43 (1.30-6.63)	0.015	2.36 (1.00-4.68)	0.055
>200 ml	Ref		Ref	
History of hypertension				
No	0.14 (1.43-3.11)	0.017	1.34 (0.84-2.15)	0.217
Stage 1	1.24 (0.88-1.91)	0.151	0.97 (0.51-1.86)	0.925
Stage 2	2.02 (1.07-4.12)	0.011	1.27 (0.78-2.15)	0.311
Stage 3	Ref		Ref	
History of renal failure				
(stage 1) No	0.99 (0.72-2.11)	0.041	1.59 (0.91-2.79)	0.104
Stage 2	1.03 (1.01-2.50)	0.109	2.14 (1.21-3.81)	**0.009**
Stage 3	Ref		Ref	

History of anemia				
Yes	1.1 (0.95-2.23)	0.119	1.49 (1.14-1.95)	**0.003**
No	Ref		Ref	
History of high cholesterol				
Yes	0.62 (0.33-2.97)	0.351		
No	Ref			
History of diabetes mellitus				
Yes	3.15 (1.31-6.05)	0.112	0.54 (0.31-0.95)	**0.033**
No	Ref		Ref	
History of alcohol use				
Yes	1.02 (0.89-1.55)	0.178	1.02 (0.77-1.36)	0.878
No	Ref		Ref	
History of Asthma				
Yes	1.21 (1.07-2.42)	0.317		
No	Ref			
Heart problem				
Yes	2.12 (0.91-3.14)	0.106	1.02 (0.68-1.53)	0.907
No	Ref		Ref	

CHAPTER FIVE

5.0 DISCUSSION

The overall objective of the study was to evaluate predisposing factors to ICM-induced reactions, the frequency, and the nature of ICM reactions in patients undergoing radiological procedures. Generally, there was a high rate of ICM reactions in 39.2% out of 283 patients. These findings emphasize the significant incidence of complications caused by ICM. The analysis also revealed that the rate of these reactions was correlated with factors such as patient BMI, hypertension, diabetes, and other chronic diseases, as well as renal function. Based on these outcomes, some groups and health states are more vulnerable to adverse ICM reactions, which implies the requirement to introduce targeted risk management strategies during radiological procedures.

This study found an incidence rate of 39.2% for ICM adverse reactions. This recorded finding is significantly higher than the rates recorded in other studies. For instance, Recent estimates of adverse reactions to ICM range from 1% to 12% (22).In another study, the incidence of acute and delayed adverse reactions was 26.3% and 10.1% respectively (54). Therefore, the population in the tertiary hospitals in Ilala Municipal might have special predisposing factors. On the other hand, Some studies have been done in Africa, including South Africa, Kenya, and Nigeria (29,30,39). In these studies, the incidence of ICM reaction ranges from 9.9% to 35.9%. In a study done in Nigeria, among patients undergoing radiocontrast procedures, the incidence was 35.9% (55). The variation in the incidence reported could be attributed to the difference found in the health status of patients and procedures being taken in the region. This high frequency in the study could be attributed to the general practices in this region or the kind of patients that are dealt with or the types of contrast media chosen commonly.

The study found that there were higher rates of complications in various categories related to acute ICM-induced reactions. Gastrointestinal complications were the most frequent. These rates are consistent with previous studies where nausea and vomiting were commonly reported as early complications, but anaphylaxis appeared to be less frequent at 0.2% or fewer people (56). Immediate adverse effects, although uncommon, are often associated with systemic

symptoms (1). In one study, anaphylactic-type reactions to iodinated contrast agents were rare, accounting for 0.6% of cases, with only 0.04% considered severe (57). In Sub-Saharan Africa, the prevalence of acute reactions is observed to be higher due to the lack of standard monitoring and emergency response systems in radiology units (55). Data on East African populations are scarce, however, the rates obtained in the current study mandate enhanced stewardship of patient care, follow-up as well as documentation to obtain an actual picture on acute reactions.

The incidence of delayed complications was relatively low, with the majority experiencing renal, and dermatological issues. Global studies have shown varying cases of delayed reactions, suggesting that the patient population in this study may be highly sensitive or exposed differently (35). Some studies have reported delayed reactions occurring in 0.5-30% of the cases (58,59). Data is scarce in Africa, it is possible that a greater number of delayed reactions are not being fully reported in sub-Saharan follow-up, although evidence indicates gastrointestinal and dermatological effects are the most reported (32). Data on East African populations are limited; however, the rates obtained in this study highlight the need for improved patient care, follow-up, and documentation.

The analysis showed that patients with normal weight and those classified as overweight were at a significantly higher risk of experiencing ICM-induced reactions compared to obese patients. This finding is intriguing as it contradicts the conventional expectation that obesity would increase the risk of adverse reactions due to altered pharmacokinetics and increased fat tissue (49). One possible explanation for this observed trend is that patients with normal or slightly elevated body mass index (BMI) may have different hemodynamic and metabolic profiles that predispose them to enhanced vascular permeability or altered immune responses when exposed to ICM, thereby increasing their susceptibility to reactions (49,60). These results are in accordance with the literature data showing that increasing patient BMI is a known risk factor for adverse reaction to contrast media (61). In Australia, a study confirmed BMI to be a risk factor for CIN ($P = .012$). In one study conducted in Tanzania central obesity increased the risk of ICM reactions by 3.12, (95% CI 1.22 - 7.97) (26)

Patients with stage 2 renal failure were found to have a markedly increased risk of adverse reactions to ICM. Impaired renal function leads to decreased clearance of contrast agents, prolonging exposure and increasing the likelihood of contrast-induced nephropathy and other systemic toxicities (62). Additionally, the compromised renal filtration barrier can enhance the pro-inflammatory response, contributing to heightened vulnerability to contrast media reactions (52). The clinical implication is clear: patients with even mild to moderate renal impairment require careful assessment before contrast administration, including the potential use of non-contrast imaging techniques, adjustment of contrast dose, or implementation of nephroprotective measures to minimize the risk of adverse outcomes (63). In one study patients with high creatinine levels had a relative risk of developing CIN of 2.16 compared with those with normal levels ($p = 0.016$) (39). The findings also resonate with findings done in south Africa, Nigeria and Kenya on CIN (29,30,39). However this was contrary to a local study that found no association with a history of renal failure (26).

The study revealed that patients undergoing radiological interventions for neurological, cardiopulmonary, and oncological conditions were at an increased risk of ICM reactions. Neurological conditions may increase susceptibility due to compromised blood-brain barrier integrity or pre-existing cerebrovascular vulnerabilities, which could facilitate the crossing of contrast media into the central nervous system, triggering neurotoxic effects (64), Globally, similar findings have been observed, with several studies highlighting the elevated risk associated with these conditions. For instance, a systematic review reported that patients with neurological conditions, especially those with compromised blood-brain barriers, had a significantly higher likelihood of neurotoxic reactions following contrast administration (65).

Cardiopulmonary conditions, such as heart failure or pulmonary hypertension, could predispose patients to altered hemodynamics and increased vascular stress, potentially heightening the risk of adverse reactions due to contrast media (66), In cardiopulmonary patients, the heightened risk is often linked to pre-existing cardiovascular instability, as noted in studies from the United States and Italy, where hemodynamic stress during imaging was identified as a critical factor in adverse outcomes (67,68). In one study, although heart failure was significantly associated with

incidence of adverse effects, the relationship was protective at ARR of 0.69 (p = 0.0264) which was contrary to our study (67). In oncology patients, the higher risk might be attributed to the compromised immune system, pre-existing organ dysfunction, or ongoing chemotherapy, which can exacerbate the effects of contrast agents. In one study for patients with cancer, the absolute risk increase was found to vary from 0.3 to 2.3% depending on the type of cancer (69). Another study estimated that AKI due to injection of iodinated CM accounted for 11% of all cases of AKI among oncology patients (70). However, in oncological patients, PC-AKI is often multifactorial, highlighting the need to consider and weigh each of the possible causes involved (age, oncological treatments, use of other nephrotoxic agents and dehydration) (71). Also compared to these high-income settings, data from sub-Saharan Africa is scarce, with most studies primarily focusing on nephrotoxicity rather than a broad spectrum of ICM-induced reactions (72). This underscores the importance of expanding local research to validate and contextualize these findings within regional healthcare settings.

A history of anemia was associated with a significantly increased risk of ICM-induced reactions. Anemia can exacerbate oxidative stress and compromise the oxygen-carrying capacity of the blood, leading to cellular hypoxia and potential aggravation of contrast-induced nephropathy or other organ-specific toxicities. This aligns with findings from other studies globally, where anemia was linked to increased oxidative stress and cellular hypoxia, compounding the risk of contrast-induced nephropathy and other systemic toxicities, Anemia was also an independent predictor of CIN (OR 2.352, 95 % CI 1.395–3.453, P < 0.001) (72). Additionally, anemia may reflect underlying chronic conditions, such as renal disease or cardiovascular impairments, that independently contribute to adverse reactions when contrast media are used (73). Similarly, a study in Nigeria reported that anemic patients undergoing contrast-enhanced imaging had higher incidences of adverse events compared to non-anemic individuals, likely due to underlying chronic conditions such as renal impairment or cardiovascular disease, which are common in both regions (61). However, these findings are contrary to a recent study in Tanzania that found no association between anaemia and ICM reactions (26). This highlights the need for specific preventive strategies in populations where anemia is prevalent, such as pre-procedural optimization of hemoglobin levels and careful selection of contrast media to minimize risk.

Interestingly, diabetes mellitus was found to have a protective effect against ICM-induced reactions. This may be attributed to the routine use of prophylactic measures, such as hydration protocols, metformin cessation, and the administration of antioxidants in diabetic patients undergoing contrast-enhanced procedures, all of which reduce the overall incidence of adverse reactions as observed in other studies where preventive measures reduced the incidence of ICM reactions in diabetic patients (74,75). Furthermore, diabetic patients are frequently monitored for renal function, for which studies have shown may lead to early detection and management of potential complications such as CIN (38,76). This finding suggests that adherence to standardized pre-procedural care guidelines in diabetic patients may effectively reduce the risk of ICM-related reactions, serving as an exemplar for managing other high-risk populations. This finding contrasts with the majority of global literature, where diabetes is often associated with an increased risk of adverse reactions, particularly nephropathy, in studies from China, diabetes has been consistently linked diabetes to a higher incidence of contrast-related complications, largely due to pre-existing microvascular damage and chronic kidney disease (77,78) one of which reported the main high-risk subgroup, patients with elevated HbA1C levels (≥8.8%) had a higher risk of CIN disease (77). A recent study in Tanzania reported no association whatsoever with CMI reactions (26).

Implications

The results of this study align with and diverge from existing global and regional literature in significant ways, highlighting the complex interplay of patient-specific factors influencing the risk of ICM-induced reactions. The findings emphasize the importance of individualized risk assessments and proactive management strategies, particularly for high-risk groups identified through both local and international research. Understanding these factors and their implications can inform clinical practice and policy development, ultimately enhancing patient safety and the efficacy of contrast-enhanced diagnostic and interventional procedures in diverse healthcare settings.

5.1 Limitations

The generalizability of the findings should be discussed to help place the study in its proper perspective. One major limitation that can be seen is the late, small sample size in relation to the patients of the studied cohort, that just equal to 283 patients, and thus the outcomes cannot be surely generalized for more extensive categories. Another limitation was using self- reported data for some variables; for instance, smoking and alcohol use that may be subject to reporting bias. However, the findings of the present study could be beneficial in identifying the occurrence, as well as definite risk factors associated with ICM reactions within the established context to promote clinical practice and research.

5.2 Mitigations

To address the limitations of this study, future research should aim to increase the sample size, potentially through multi-center collaborations or extended study periods, to enhance the generalizability of the findings. The use of objective measures, such as biochemical markers for smoking or alcohol use, could mitigate the biases associated with self-reported data, while triangulating self-reports with medical records would further enhance data accuracy. Expanding the population to include diverse geographical or clinical settings, and stratifying results based on key demographics, would improve the relevance of the findings to broader patient populations and healthcare contexts. These steps would contribute to more robust and generalizable outcomes for future studies.

CHAPTER SIX

6.1 Conclusion

In conclusion, this study identified that the socio-demographic and clinical characteristics of patients undergoing radiological interventions at MNH and JKCI revealed a diverse patient profile with varying risk factors for ICM reactions. The incidence of ICM-induced reactions was notable, with acute reactions being more prevalent than delayed ones, highlighting the importance of vigilant monitoring during and after contrast administration. Acute adverse reactions were predominantly gastrointestinal, neurological, and dermatological, while delayed reactions mostly affected renal function. Factors significantly associated with ICM reactions included BMI categories (normal weight and overweight), specific clinical indications for radiological intervention (neurological, cardiopulmonary, and oncological conditions), and a history of anemia, which increased the risk of adverse reactions. Conversely, diabetes mellitus demonstrated a protective effect against these reactions. These findings underscore the need for personalized risk assessment and tailored contrast media management protocols to improve patient safety in radiological practices.

6.2 Recommendations

Based on this study, it is recommended that healthcare providers routinely assess risk factors such as BMI, neurological, cardiopulmonary, and oncological conditions, as well as anemia and renal function before administering iodinated contrast media. Enhanced monitoring and preventive measures should be implemented for high-risk patients, including optimized contrast dosage and close follow-up. Patient education on adverse reaction signs should be prioritized, and pharmacovigilance systems strengthened to track ICM-induced reactions. Further research is encouraged to explore protective mechanisms, such as the observed protective effect of diabetes, and to develop tailored strategies for managing high-risk patients effectively.

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APPENDICES

Appendix I: Informed consent form

TITTLE: **ACTIVE SURVEILLANCE ON IODINATED CONTRAST MEDIA-INDUCED REACTIONS AND ASSOCIATED FACTORS AMONG PATIENTS UNDERGOING RADIOLOGY DIAGNOSTIC AND INTERVENTION AT A TERTIARY HOSPITALS IN ILALA MUNICIPAL**

I am Riziki Singano Shemula, a postgraduate student pursuing Master of pharmacovigilance and Pharmacoepidemiology from Muhimbili University of Health and Allied sciences (MUHAS) conducting a research **Active surveillance on iodinated contrast media-induced reactions and associated factors among patients undergoing radiology diagnostic and intervention at Tertiary Hospitals in Ilala Municipal**

Aim of the study: This study aims at assessing iodinated contrast media-induced reactions and associated factors among patients undergoing radiology diagnostic and intervention at two Tertiary Hospitals in Ilala Municipal.

I kindly ask you to participate in this study so that the objectives of the study can be met, I kindly ask your valuable participation upon answering the questions in the questionnaire.

Confidentiality: All the information collected from the questionnaire was entered into the computerized software with only study identification number; your name will not be entered and won't appear anywhere in the research. The data was kept and observed by only authorized personnel, any unauthorized individual will not be authorized to assess it.

Compensation: Your participation is fully voluntary and there won't be any compensation whatsoever for your participation whether monetary nor materials.

Risk: I do not expect any harm to happen to you because of your participation in this study.

Right to withdrawal: Your participation in this study is voluntary, you have the right to stop answering the questions at any time even if you have already given your consent. Refusal to participate or withdrawal in the study will not involve any penalty.

Right to withdraw: Participants are free to withdraw from the study at any time during its duration.

This protocol has been reviewed by the research and publication committee of Muhimbili University of Health and Allied Sciences (MUHAS)

Whom to contact: If you have any questions and enquiries about this study you can contact;

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OR

Dr. Mathius Eulambius

Co-supervisor

OR

Mr. Manase Kilonzi

Co-supervisor

Do you agree to participate in this study? Yes……No…….

Signature of participant……. Date……...

Signature of Investigator……. Date…….

Appendix II: Fomu ya ridhaa ya kushiriki katika utafiti

SOMO: UFUATILIAJI WA KINA WA MAUDHI YATOKANAYO NA MATUMIZI YA **VITENDANISHI AINA YA *IODINATED CONTRAST*** PAMOJA NA SABABU ZINAZOHUSIANA MIONGONI MWA WAGONJWA WANAOFANYIWA UCHUNGUZI WA RADIOLOJIA NA AFUA KATIKA HOSPITALI MBILI ZA NGAZI YA JUU ZILIZOPO WILAYA YA ILALA.

Naitwa Riziki Singano Shemula ni Mwanafunzi wa Shahada ya uzamili katika programu ya *Usalama wa dawa na famakoepidemiologia* katika chuo kikuu cha Afya na Sayansi Shirikishi Muhimbili (MUHAS), kwa unyenyekevu mkubwa naomba kutumia muda wako kujibu maswali yaliyopo katika dodoso.

Lengo la utafiti: Kufanya tahmini ya maudhi yatokanayo na matumizi ya **vitendanishi aina ya *iodinated contrast*** pamoja na sababu zinazohusiana miongoni mwa wagonjwa wanaofanyiwa uchunguzi wa radiolojia na afua katika Hospitali za mbili za ngazi ya Juu zilizopo Wilaya ya Ilala.

Taarifa hizo zitasaidia kubaini ukubwa wa maudhi, viashiria vya vihatarishi kuboresha namna ya kuvizuia ama kupunguza kutokea kwa maudhi kwa watumiaji wa vitendanishi hivyo

Siri: Taarifa zote zitakazo kusanywa zitatumia namba ya utambulisho tuu, majina ya washiriki hayatahusika wala kuchapishwa sehemu yoyote. Taarifa zitaingizwa katika mfumo wa kompyuta, na kuhifadhiwa sehemu ya siri na salama na asiye husika na taarifa hizi hataweza kuzipata isipokuwa kwa idhini maalum ya wahusika.

Fidia: Kazi hii ni ya kujitolea na hakutakuwa na malipo yoyote yale.

Madhara: Kazi hii haitarajiwi kuwa na madhara yoyote yale kwa mshiriki wa utafiti huu.

Haki ya kujiondoa katika utafiti: Ushiriki wako ni wa hiari, hivyo unaruhusiwa kujitoa muda wowote katika utafiti huu hata kama umesaini makubaliano au tayari umejibu baadhi ya maswali. Kujitoa katika utafiti huu hakuna adhabu yoyote ile.

Pendekezo la utafiti huu limepitiwa na kamati ya utafiti na uchapishaji ya Chuo Kikuu cha Afya na Sayansi Shirikishi Muhimbili (MUHAS)

Mawasiliano:Kwa maswali na maoni yoyote kuhusiana na utafiti huu; unaweza wasiliana na ;

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Chuo kikuu cha Afya na Sayansi Shirikishi Muhimbili

AU

Dr. Mathius Eulambius

Msimamizi msaidizi

Unakubali kushiriki katika utafiti huu? NDIYO……HAPANA……...

Saini ya mshiriki…… Tarehe……

Saini ya mtafiti……...…... Tarehe……

Appendix III: Semi structured Questionnaire-English version



MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED HEALTH SCIENCES
SCHOOL OF PHARMACY
DEPARTMENT OF CLINICAL PHARMACY AND PHARMACOLOGY

Questionnaire No…….

Date……...

SECTION A: SOCIO-DEMOGRAPHIC, CLINICAL AND LABORATORY FINDINGS

(Please fill in the blank space and circle the most appropriate response)

1. Personal Information

    a) Initials ……
    b) Age: (years) ……
    c) Permanent Address……
    d) Weight (Kg)…….
    e) Height (Cm)……...
    f) Phone number ……

2. Gender:

    a) Male
    b) Female

If Male go to section B

3. Is the client currently pregnant or breastfeeding?

    a) Yes
    b) No

SECTION B: ALLERGIC HISTORY

4. Has the client had an allergic reaction to iodinated contrast media before?
    a) Yes
    b) No

5. Does the client have any known allergies to medications, food, supplements or other substances?
    a) Yes
    b) No

6. If yes, what was the severity?
    a) Severe
    b) Moderate
    c) Mild

7. Time the Reaction Started…….……...
8. Time the reaction ended……...
9. Was medical follow-up done for the adverse reaction
    a) Yes
    b) No

10. If yes, what was the outcome or treatment provided?

.....
.....

11. **Emergency Contact**
    - Name:
    - Relationship:
    - Contact Number:

Thank you for your participation in this questionnaire. Your feedback is valuable for improving patient care and safety

Appendix IV: Checklist-English version

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED HEALTH SCIENCES
SCHOOL OF PHARMACY
DEPARTMENT OF CLINICAL PHARMACY AND PHARMACOLOGY

Checklist No…….

Date …….

Part 1: SOCIAL DEMOGRAPHIC DATA

(Please fill in the blank space)

1. **Personal Information**

Initials ……

2. Date of iodinated contrast media administration…….

3. Reason for iodinated contrast media administration (e.g., CT scan, angiography) …… ……

4. Dose of iodinated contrast media used……...

5. Iodinated contrast media Manufacturer , address and Batch details …… …… ……

Put **(√)** to the appropriate response

Table 1: Socio-demographic, clinical and laboratory findings		
Response	**Yes**	**No**
Gender		
Male		
Female		
Age groups (years)		
18 - 40		
41 - 65		
>65		
Risk factors		
Known hypertensive		
Known diabetic		
Taking alcohol		
Cigarette smokers		
History of heart failure		
BMI		
underweight		
Normal weight		
Overweight		
Obese		
History of renal failure		
History of thyroid disorders		
History of allergy		
Previous procedure using iodinated contrast media		
History of ADE with iodinated contrast media		

Was the ADE		
Severe		
Moderate		
Mild		
History of asthma		
Medications used		
Diuretics		
ARBs		
CCBs		
ACEIs		
NSAIDs		
Over the counter /other medications		
Herbal/ supplements		
Hypertension stage		
Normal/controlled BP (120/80 mmHg)		
Stage 1(130-139/80-89 mmHg)		
Stage 2 (140-159/90-99 mmHg)		
Stage 3 (160-179/100-109 mmHg)		
Anemia (Hb<12)		
High cholesterol (Total cholesterol >200 mg/d) or 5.5 mmol/L		
Elevated FBG (>100 mg/dL or 5.6 mmol/L)		
Pre-procedure CKD stage		
eGFR		
Stage 1 (eGFR ≥90 mL/min/1.73 m²)		

Stage 2 (eGFR 60-89 mL/min/1.73 m²)				
Stage 3(eGFR 30-59 mL/min/1.73 m²)				
Experience any of the following symptoms after iodinated contrast media administration				
	0-60Min	At 24Hours	At 72 Hours	At 168 Hours
Skin rash or hives				
Itching				
severe blistering and peeling				
Anaphylaxis (Swelling of the face, throat, or tongue)				
Difficulty breathing				
Asthma, bronchitis, and pneumonia				
Nausea, Diarrhea or vomiting				
Headache				
Dizziness or lightheadedness				
Chest pain or palpitations				
arrhythmias, heart attack, and heart failure				
Nephropathy				
Other unusual symptoms				
How would you rate the severity of the reaction				
Severe				
Moderate				
Mild				

BP: blood pressure; NSAID: non- steroidal anti-inflammatory drug; ARB: angiotensin converting enzyme inhibitor; CCB: calcium Chanel blocker; ACEI: angiotensin converting enzyme inhibitor; FBG: fasting blood glucose; BMI: bodymass index; ADE: adverse event

Table 2: Trends thyroid Pannel, pause rate and blood pressure from baseline to 24-168-hours post procedure

Test	**Baseline**	**At 24hours**	**At 72 hours**	**168 hours**
Creatinine				
Thyroid-stimulating hormone (TSH).				
T3				
T4				
Pause rate				
Blood pressure				

6. Please use this space provide if there Is anything else you would like to share about your experience with iodinated contrast media?

……
……
……

Appendix V: 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/2120 Date: 12/03/2024

MUHAS-REC-03-2024-2120
RIZIKI SINGANO SHEMULA,
MUHAS.

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: ACTIVE SURVEILLANCE ON IODINATED CONTRAST MEDIA-INDUCED REACTIONS AND ASSOCIATED FACTORS AMONG PATIENTS UNDERGOING RADIOLOGY DIAGNOSTIC AND INTERVENTION AT A TERTIARY HOSPITALS IN ILALA DISTRICT.

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: 12/03/2024
EXPIRATION DATE OF APPROVAL: 12/03/2025

STUDY DESCRIPTION:
Purpose:

To determine the active surveillance on Iodinated contrast media-induced reactions and associated factors among patients undergoing radiology diagnostic and intervention at a tertiary hospital in lala district.

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-%2015363.pdf and in the MUHAS archives.

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 VI: 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.409/2022

14th March, 2024

THE EXECUTIVE DIRECTOR,
MUHIMBILI NATIONAL HOSPITAL,
P.O. BOX 65000,
DAR ES SALAAM.

RE: INTRODUCTION LETTER OF RIZIKI SINGANO SHEMULA

We would like to inform you that the carrier of this letter is Riziki Singano Shemula with registration number HD/MUH/T.409/2022 a student in the School of Pharmacy at Muhimbili University of Health and Allied Science (MUHAS), pursuing Master of Pharmacovigilance and Pharmacoepidemiology.

As part of her studies, she will be doing an elective research titled **"ACTIVE SURVEILLANCE ON IODINATED CONTRAST MEDIA-INDUCED REACTIONS AND ASSOCIATED FACTORS AMONG PATIENTS UNDERGOING RADIOLOGY DIAGNOSTIC AND INTERVENTION AT TERTIARY HOSPITALS IN ILALA DISTRICT".**

She is being supervised by Dr. Ritah Mutagonda from MUHAS and Solobi Ngasa from Muhimbili National Hospital.

The Ethical Clearance for doing the said research has been given by the University.

Kindly request your assistance and cooperation to our student.

Yours Sincerely,

Ms. Victoria Mwanilwa
For: DIRECTOR, POSTGRADUATE STUDIES

cc: Riziki Singano Shemula

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 VII: Permission to collect data at MNH and JKCI

THE UNITED REPUBLIC OF TANZANI

MINISTRY OF HEALTH

MUHIMBILI NATIONAL HOSPITAL

In reply please quote;

Ref. No.: MNH/CRTCU/Perm/2024/143 Date: 21st March, 2024

Head of Department,
Imaging Diagnostic Section
Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH

Name Student	**Riziki Singano Shemula**
Title	**"Active Surveillance on Iodinated Contrast Media-Induced Reactions and Associated Factors Among Patients Undergoing Radiology Diagnostic and Intervention Tertiary Hospitals in Dar es Salaam".**
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Dr. Ritah Mutagonda (MUHAS)
Co – Supervisor	Dr. Solobi Ngasa (MNH)
Period	21st March, 2024 to 30th May, 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. K** Solobi **Ngasa (**MNH) supervisor.

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

Sincerely,

HEAD, 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 DCSS
c.c Dr. Solobi Ngasa
c.c **Masunga R. Mkangala**

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

UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

JAKAYA KIKWETE CARDIAC INSTITUTE (JKCI)

JAKAYA KIKWETE CARDIAC INSTITUTE

In reply please quote;
Ref No: AB.123/307/01K/24 26/03/2024

Riziki Singano Shemula
HD/MUH/T.409/2022
Master of Pharmacovigilance and Pharmacoepidemiology - MUHAS

RE: PERMISSION TO CONDUCT RESEARCH AT JKCI

Reference is made to your letter requesting to do a research study entitled **"ACTIVE SURVEILLANCE ON IODINATED CONTRAST MEDIA-INDUCED REACTIONS AND ASSOCIATED FATORS AMONG PATIENTS UNDERGOING RADIOLOGY DIAGNOSTIC AND INTERVENTION AT TERTIARY HOSPITALS IN ILALA DISTRICT."** here at JKCI.

This letter serves as an official document that permits you to do the above-mentioned task as requested. However, the institution also requires you to have JKCI local co-supervisor.

It is our sincere hope that you will abide by the rules and regulations of good clinical practice. We wish you the best and hope your stay at JKCI will be fruitful.

Best Regards,

JAKAYA KIKWETE CARDIAC INSTITUTE
P. O. Box 65141
Dar-es-Salaam
JKCI

Dr. Pedro Pallangyo
Head of Research, Training and Consultancy.
CC: ALL DIRECTORATES & Head of Units