Magnitude and pattern of gastroenterological malignancies among patients at Muhimbili National Hospital, Tanzania

Mwalukombe Joseph Malingi, MD

MMed (General Surgery) Dissertation

Muhimbili University of Health and Allied Sciences

October, 2018

Muhimbili University of Health and Allied Sciences

Department of Surgery

MAGNITUDE AND PATTERN OF GASTROENTEROLOGICAL MALIGNANCIES AMONG PATIENTS AT MUHIMBILI NATIONAL HOSPITAL, TANZANIA

By

Mwalukombe Joseph Malingi, MD

A Dissertation Submitted in (Partial) Fulfillment of the Requirement for the Degree of Master of Medicine (General Surgery) of

Muhimbili University of Health and Allied Sciences

October, 2018

CERTIFICATION

The undersigned certifies that he has read and hereby recommends for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: ***"Magnitude and Patterns of Gastroenterological Malignancies among Patients at Muhimbili National Hospital, Tanzania",*** in (partial) fulfillment of requirement for degree of Master of medicine (General Surgery) of Muhimbili University of Health and Allied Sciences.

_____

Dr. Larry O. Akoko, MD, MMed

(Supervisor)

_____

Date

DECLARATION AND COPYRIGHT

I, **Mwalukombe Joseph Malingi**, I 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.

Signature: …… **Date**: …….....

ACKNOWLEDGEMENTS

First and foremost, I would like to thank The Almighty Allah; for granting me life and health throughout this study. Secondly, my supervisors, Prof. Naboth A. A. Mbembati and Dr. Larry O. Akoko; the unseen forces behind this project. And last but not least, my utmost appreciation goes to all members of staff in the Department of General Surgery MUHAS and MNH, and specifically, Dr. Hassan K. Ramadhan, Dr. Candida Moshiro, Dr. Sirili Aloyce, Dr. Abdulaziz Sheikh and Dr. Advera Ngaiza, for their input during development and follow up of this dissertation and Mr. Roland Hassani Maundu, Mrs. Hermo J. Mallya and Mrs. Agatha Swai, for their hospitality during my stay in the department, thank you.

DEDICATION

I dedicate this body of work to:

My parents; Mr. Thomas Mwagongo Mwalukombe and Mrs. Christine Phoebe Chisitsa Mwalukombe.

&

My loving wife; Dr. Leila Omar Ahmed Malingi.

ABSTRACT

Background: Gastroenterological malignancies in 2012 were highest in incidence and mortality, globally, with 4 of the top 8, and 4 of the top 6 respectively, being from this system. Developing countries including Tanzania were noted to be experiencing an increased frequency of these cancers, possibly due to adoption of a western lifestyle. There is limited data regarding the latest clinicopathological presentation and possible associated factors of these malignancies.

Objective: To evaluate the magnitude, patterns and possible associated factors of gastroenterological malignancies among patients attended at Muhimbili National Hospital, Tanzania.

Methodology: This was a cross sectional study carried out at the surgical wards and the gastrointestinal clinic at Muhimbili National Hospital, between June and December 2017. The study involved patients with malignancies in the esophagus, stomach, colon, rectum and anus. Data on the demographics, clinical presentation and exposure to suspected risk factors was collected from patients using a structured questionnaire and clinical information was sourced from their files. The data was cleaned, coded and then analyzed by SPSS computer software version 20.0.

Results: 270 participants were recruited, giving a magnitude of 15.1% all patients being attended to for a diagnosis of cancer. The participants had a male predominance of 182(67.4%) & a mean age (SD) of 56.4 (±14.6) years old. The study found that esophageal cancer 175(64.8%) was the most common gastroenterological malignancy, while Small bowel cancer was the least 4(1.5%). Alcohol consumption 211(78%) and an Age group of 40 – 70 years 194(72%), were the most prevalent associated factors of gastrointestinal cancer, while smoking was more common among patients diagnosed with esophageal cancer 96(55%) and HIV infection/AIDS was more common among patients diagnosed with small bowel 1(33.4%) and anal cancer 2(13.3%).

Conclusion: Gastroenterological Malignancies have a significant magnitude among patients at MNH and they present with a unique profile. Lack of awareness of these diseases and their associated factors poses a great challenge in the prevention and subsequent management of these patients. Addressing these challenges will help reverse the trend of an increasing incidence of these malignancies in Tanzania.

TABLE OF CONTENTS

LIST OF TABLES

ABBREVIATIONS

ART	Anti-retroviral therapy
ESCC	Esophageal squamous cell carcinoma
EAC	Esophageal adenocarcinoma
GCA	Gastric cardiac adenocarcinoma
GNCA	Gastric non-cardia adenocarcinomas
GIT	Gastro-intestinal tract
GIST	Gastrointestinal stromal tumors
HIV/AIDS	Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome
HNPCC	Hereditary nonpolyposis colorectal cancer
LMIC's	Low and middle income countries
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
SIR	Standardized incidence ratio
SOP's	Standard Operating Procedures
WHO	World Health Organization

COMMONLY USED TERM'S

Aids defining	Presence of pathology confirms a diagnosis of HIV/AIDS.
Commensal	Microorganisms including bacteria, protozoa, and fungi that are found on or in specific areas of the body.
Gastroenterological	Structures of the digestive tract and its accessory organs.
Homeostasis	the tendency toward a relatively stable equilibrium between interdependent elements, especially as maintained by physiological processes.
Immuno-suppression	The absence of adequate immunity body defenses.
Malignancy	Cancer.
Tumorigenesis	The production or formation of a tumor or tumors.
Paucity	The presence of something only in small or insufficient quantities or amounts; scarcity.

CHAPTER ONE

1.0. INTRODUCTION

1.1. Background

Efforts to reduce global cancer disparities begin with an understanding of geographic patterns in cancer incidence, mortality, and prevalence (1). The gastrointestinal tract (includes; the esophagus, stomach, small and large intestine) is a unique organ system in that it has the highest incidence of cancer and its related mortality than any other system in the body (2). The git has associated accessory organs that aid in digestion (namely; the tongue, salivary glands, pancreas, liver, and gallbladder).

The gastrointestinal tract contains trillions of commensal bacteria that aid in nutrient metabolism and help maintain mucosal homeostasis by stimulating replacement of the lining every 2 ~ 7 days. Since increased cell turnover is associated with tumorigenesis, an imbalance in epithelial cell proliferation and death may lead to the higher incidence of malignancies within the gastrointestinal tract (3). These dynamics do not apply to its accessory organs.

There are established risk factors whose distribution influences the regional variation of these malignancies, global disparities in cancer incidence and mortality are likely due to the complex interactions between modifiable and non-modifiable risk factors in these areas (1).

In 2012, globally, gastroenterological malignancies were the highest in incidence and mortality of all body systems, with 4 of the top 8, and 4 of the top 6 respectively, being malignancies of this category (4) and further showing a gender predilection of being more common among men than women. While cancers of its accessory organs had much lower rates.

Low and middle income countries, including Tanzania, are experiencing an increased frequency of these cancers, possibly because of the adoption of western behaviors and lifestyle factors known to cause cancer (2).

This increase in the rate of cancers may also be due to increased infection related cancers, Sub-Saharan Africa has the highest global burden of HIV, interestingly, in populations benefiting from ART, some non-Aids defining cancers appear to have a higher relative incidence compared with the same cancer rates seen in the general population, even after controlling for known cancer risk factors. The reasons for these increased cancer rates are poorly understood (5).

Unfortunately, early diagnosis of gastroenterological cancers is very difficult, with symptoms dependent on the site and only clearly apparent at a late stage of the disease. Early symptoms are vague and most patients are managed for other benign conditions, and subsequently discovered to have late stage cancer or one of its complications (6). In low income countries like Tanzania, patients are managed solely based on clinical examination findings due to the scarcity of radiological and endoscopic facilities in many centers, causing them to present later with advanced disease (7).

Treatment of cancer poses a challenge in resource limited settings with inadequate screening programs, late presentation, scarce endoscopic facilities, lack of adjuvant therapy, and a high morbidity and mortality being the hallmarks, in most African countries (8). Treatment depends on; the size, location and extent of the tumor, the stage of disease, the patient's age and overall health (9). The current treatment options include; surgery, chemotherapy and radiotherapy. Surgery & chemotherapy are the only option with curative potential (9,10) however they are of limited use in most developing countries due to the late presentation of a majority of patients. Thus the outcome of treatment has been poor, with commonly palliative care being offered for advanced stage disease (10). This pattern is partly due to weak health systems in LMIC's as evidenced by poor access to diagnostic tests, unavailability of national screening programs and lack of community awareness on the importance of early health seeking habits. Which can indirectly be attributed to the paucity of local data regarding these conditions (11). Thus gastroenterological malignancies excluding those of the accessory organs are a present danger worthy of being studied.

1.2. Literature Review

Gastrointestinal malignancies were highest in incidence and mortality, among all body systems, worldwide in 2012 (2). Available data elaborates that incidence rates vary internationally by more than 21-fold, the highest being in Eastern Asia and in Eastern and Southern Africa and the lowest rates being in Western Africa (2), for example esophageal cancer in Northern Iran has been noted as being common in the middle third (12), but in the distal third in Ghana (13) and again in the middle third in northern Tanzania (14) but all areas having a similar histological picture of SCC being most common (12–14). With the reported change in incidence of gastrointestinal cancers in LMIC's, it is important to evaluate whether the histopathological characteristics of these tumors have also changed. Different studies report as follows;

Soreide et al in the United Kingdom in 2016 found that gastrointestinal stromal tumors (GIST's), were most frequently located in the stomach, followed by the small bowel and colorectal but least affected the esophagus (15). Similar findings were noted by DeMatteo et al in 2000 (16) and Strickland et al 2001 (17). This being due to GISTs rarely arising outside the gastrointestinal tract (18).

Islami et al in 2004 in Northern Iran found that the esophagus was the commonest location of upper gastrointestinal tract tumors, followed by the stomach and squamous cell carcinoma was the predominant histological variation (12). Similar findings to Wakhisi et al in 2005, in the rift valley region of western Kenya (19). While Kitinya et al in 1988 in North-eastern Tanzania found that carcinoma of the stomach was the commonest gastroenterological malignancy in the Mount Kilimanjaro area of Tanzania, & the most common histopathological type being Intestinal type adenocarcinoma. Similar findings to Mchembe et al in 2012 in Northwestern Tanzania, except; generally classified the commonest histological variant as adenocarcinoma and gastric cancer represented only 4.5% of all malignancies (7). These non-uniform findings are most likely due to varying exposure to known risk factors (20), distribution of hereditary factors amongst the populations (21) and the distribution of different cell types along the different organs on which the factors act (14). Kitinya et al for example,

suspected his findings to be due to the influence of volcanic soils and Mchembe et al further suspected dietary, genetic factors and variation in the infectivity rate of H. pylori to be responsible for this regional variation (7).

Abdulkareem et al 2009 in South-western Nigeria reported that colorectal cancer was most common of all the malignant GIT tumors in the region, and the majority were of adenocarcinoma histology, followed by squamous cell (22), while Mchembe et al, in 2013 in Tanzania found that colorectal cancer represented only 4.7% of all malignancies (23). Both studies attributed the rising incidence of colorectal cancer in Africa to improved cancer awareness and a shift towards a western diet (22,23). G. A. Kumar et al, in 2015 in The United States (24), on the other hand, found that anal cancer was rare comprising 2.5% of all digestive system malignancies, yet Abdulkareem et al (22) again reported it as the second most common of all the malignant GIT tumors in South-western Nigeria but both agreed that the predominant histological variety was squamous cell carcinoma.

Also the association of cancer to infections has also now become a factor i.e. Dandapani et al in America in 2010 (25) and Bonnet et al in France in 2008 (26) reported an association between anorectal malignancy, a non – aids defining cancer, and HIV infection/AIDS, they further reported that non AIDS defining cancers have a two to three fold higher incidence in the HIV+ population (24–26). Although anorectal cancer is the only gastrointestinal malignancy with a confirmed association, this may still explain why gastrointestinal cancers are among the most frequently occurring cancers worldwide [4] and since Sub-Saharan Africa has the highest global burden of HIV, this is a factor that will mostly influence the presentation of non – aids defining cancer’s here (25).

1.3. Problem Statement

Muhimbili National Hospital is yet to establish the profile of presentation of gastroenterological malignancies in the country, while as the countries only tertiary hospital, it is the destination for thousands of patients suspected of these diseases. Also, jointly with Muhimbili University of Health and Allied Sciences, it offers training to surgical gastroenterologists, yet lacks a gastroenterology department, with the trainees nurturing their skills on a mixture of patients, denying the trainees appropriate exposure, and the patients appropriate specialized management.

1.4. Rationale

Findings of this study will provide baseline data that can be compared with that of other regions of the country and the world, it will also help relate this presentation with known predisposing factors present in the area and help formulate strategies towards lowering the local incidence.

1.5. Research Question

What is the magnitude, pattern and the possible associated factors of gastroenterological malignancies among patients attended at Muhimbili National Hospital.

1.7. Objectives

1.7.1. Broad Objective

To determine the magnitude, patterns and possible associated factors of gastroenterological malignancies among patients attended at Muhimbili National Hospital from March 2017 to December 2017.

1.7.2. Specific Objectives

1. To determine the magnitude of the different gastroenterological malignancies among patients attended at Muhimbili National Hospital.
2. To describe the characteristics of gastroenterological malignancies by organs.
3. To determine the distribution of HIV Sero-status and suspected factors of gastroenterological malignancies in our local setting.

CHAPTER TWO

2.0. METHODOLOGY

2.1. Study Design

This was a descriptive, cross-sectional, hospital-based study.

2.2. Study Area

The study was conducted in the general surgical wards and gastroenterological clinics of Muhimbili National Hospital, the National Referral hospital of Tanzania, is a facility that has a bed capacity of 1500 beds and is the main Center offering initial management of cancer related ailments for patients converging from all over the country. It has sophisticated radiological and laboratory diagnostic equipment and specialists that offer standard treatment. MNH is also the Teaching hospital of the Muhimbili University of Health and Allied Sciences (MUHAS), the countries pioneer medical school, individually and in conjunction with international institutions i.e. Harvard University, ventures into various fields of research.

2.3. Study Population

All patients attended at MNH with a suspicion to have gastrointestinal malignancies from June to December 2017.

2.4. Study Sample

All patients confirmed to have gastrointestinal malignancies attended at MNH from June to December 2017.

2.5. Inclusion Criteria

1. All patients aged 11 years and above who had a confirmed diagnosis of a gastroenterological malignancy and were being attended at Muhimbili National Hospital.
2. Patients who voluntarily gave written consent.

2.6. Exclusion Criteria

1. Patients who opted out of the study.

2.7. Sample Size

The estimated sample size was computed using the Fleiss formula (27).

A study done by Ojo J. O. et al in Southwestern Nigeria in 2016 (28), found the prevalence of gastroenterical malignancies collectively to be 12.4%, this was used as the proportion of the variable of interest in the formula above, and the Minimum sample size calculated was as 186 patients.

2.8. Sampling Method

A non-probability convenient sampling method was used, where all patients who were admitted to the general surgical wards or seen as outpatients at the gastroenterological clinic with a suspected or confirmed diagnosis of gastrointestinal malignancy during the study period were included.

2.9. Data Collection

Data on the participants'; demographics, presenting symptoms and exposure to suspected risk factors were obtained via interview administered questionnaires with the aid of two research assistants who were initially trained and familiarized on the study in order to accurately record the required patient information. Additional information on investigations i.e. HIV status (for those tested), endoscopic findings and histology results, were followed-up and gathered from their records as they were investigated and managed as per the standard operating procedures of the hospital. The information of each participant was recorded separately, coded and with no names used, it was analyzed.

2.10. Data Analysis

Data was entered and analyzed using SPSS Version 20.0 package, it was further summarized in the form of proportions and using measures of central tendency (mean and median) and measures of dispersion (range and standard deviation).

Then 2 x 2 tables of the dependent and independent variables were compiled and odds ratios were calculated for possible associations between the suspected factors and gastrointestinal malignancies, followed by binary logistic regression analysis for all independent variables found to be significant on odds ratio association, in both, a $p > 0.05$ was considered as statistically significant.

The dependent variable was a confirmed diagnosis of any of the different types of gastroenterological cancer and the independent variables were; heredity, age, a predisposing infection (Helicobacter pylori infection), smoking, exposure to industrial chemicals, exposure to ionizing radiation and obesity.

2.11. Ethical Considerations

Ethical clearance to conduct the study was sought from MUHAS Research and Publication Committee. Permission to conduct the study was obtained from Muhimbili National Hospital management to access information necessary for the study from their data base systems.

Informed written consent was obtained from all patients or from a care giver in the case of minors. The participants were assured of confidentiality, with the use of serial numbers and hospital numbers instead of names on the questionnaires. The interviews were conducted in the privacy of consultation rooms with only those the participant was comfortable with present. The participants were informed that there will be no financial gain in participating in the study & patients who refused to participate in the study would still receive standard care, and consent could be withdrawn even after initially being given. All filled questionnaires were filed and stored under lock and key and the summarized and analyzed data was stored in digital form on a backed-up, password protected database, accessible only to the researcher.

2.12. Study Limitations and Mitigations

2.12.1. Limitations

1. Some of the investigations took too long to complete i.e. histology results, thus frustrating the process of data collection.

2.12.2. Mitigations

1. Direct communication with the pathologists was occasionally necessary to aid in follow-up of results.

CHAPTER THREE

3.0. RESULTS

During the study period, 1792 patients were admitted with a diagnosis of malignant conditions to the surgical wards, with 270 confirmed histologically to have gastrointestinal malignancies, giving a magnitude of 15.1%.

Socio-demographic information

The participants had a male predominance of 181(67%), with a mean age (range) of 56.4±14.6 years (17-94 years). Most of the patients had a primary school level of education 195(72%), were unemployed or self-employed 186(69%) & had a HIV/Aids negative sero-status 195(94%). The study also found that a majority of the gastroenterological malignancy patients reported alcohol consumption 211(78.1%) & smoking 124(45.9%) as detailed in Table 1 below.

1. Determination of the distribution of the characteristics of gastroenterological malignancies among patient's at MNH.

The study found esophageal cancer to be the commonest gastroenterological malignancy 175(64.8%), followed by colorectal cancer 43(16%), while Small bowel tumors were the least common 4(1.4%) as shown in Table 1 below.

Table 1 : Socio-demographic characteristics of patients diagnosed with gastroenterological malignancies at MNH. N=270.

Demographics		Gastroenterological malignancies					Total
		Eso Ca	Gas Ca	S. B. Ca	C. R. Ca	Anal Ca	
Age	< 40	20(11.4)	1(3.2)	1(25)	9(21)	4(23)	35(13)
	40 - 70	127(72.6)	27(87.1)	2(50)	27(63)	11(65)	194(72)
	> 70	28(16)	3(9.7)	1(25)	7(16)	2(12)	41(15)
Sex	Male	124(70.9)	23(74.2)	1(25)	23(53.4)	10(58.8)	181(67)
	Female	51(29.1)	8(25.8)	3(75)	20(46.6)	7(41.2)	89(33)
Level of Education	None	9(5.1)	3(9.7)	0(0)	3(7)	1(5.9)	16(5)
	Primary	133(76)	21(67.7)	4(100)	27(62.8)	10(58.8)	195(72)
	Secondary	15(8.6)	3(9.7)	0(0)	8(18.6)	4(23.5)	30(12)
	Tertiary	18(10.3)	4(12.9)	0(0)	5(11.6)	2(11.8)	29(11)
Occupation	Unemployed	126(72)	19(61.3)	4(100)	29(67.4)	8(47)	186(69)
	Employed	49(28)	12(38.7)	0(0)	14(32.6)	9(53)	84(31)
*HIV Status	Yes	5(3.9)	2(8)	1(33.4)	3(8.1)	2(13.3)	13(6)
	No	123(96.1)	23(92)	2(66.6)	34(91.9)	13(85.7)	195(94)
Alcohol	Yes	140(80)	25(81)	3(75)	28(65)	15(88)	211(78)
	No	35(20)	6(19)	1(25)	15(35)	2(12)	59(22)
Smoking	Yes	96(55)	13(42)	0(0)	11(26)	4(24)	124(46)
	No	79(45)	18(58)	4(100)	32(74)	13(76)	146(54)
H. Pylori Infection	Yes	7(4)	2(6)	1(25)	1(2.3)	0(0)	11(4)
	No	168(96)	29(94)	3(75)	42(97.7)	17(100)	259(96)
	Total	175(64.8)	31(11.5)	4(1.4)	43(16)	17(6.3)	270

Key: * in the table stands for N = 208

2. Determination of the different histological variants of gastroenterological malignancies among patients at MNH.

Our study showed that, the different histological variants were distributed as shown in Table 2 below in the different gastroenterological malignancies.

Table 2: The distribution of different histological variants of the different gastroenterological malignancies among patients at MNH. N = 270

Gastroenterological malignancies	Histological Variants			
	Adeno (%)	SCC (%)	Others (%)	Total (%)
Esophageal cancer	9(5.1)	163(93.1)	3(1.8)*	175(100)
Gastric cancer	22(71)	4(13)	5(16)**	31(100)
Small Bowel cancer	2(50)	1(25)	1(25)***	4(100)
Colorectal & anal cancer	49(82)	8(13)	3(5)****	60(100)
Total	81(30)	176(65)	13(5)	270(100)

Key: *: represents tumors that were unclassified **: represents; GIST and MALT. ***: represents; MALT ****: represents; Metastatic secondary, Kaposi Sarcoma & Unclassified tumors.

CHAPTER FOUR

4.0. DISCUSSION

Cancer constitutes an enormous burden on society in more and less economically developed countries alike. The occurrence of cancer is increasing because of the aging population, as well as an increasing prevalence of established risk factors such as smoking, obesity, physical inactivity, and changing reproductive patterns associated with urbanization and economic development. The gastrointestinal tract has the highest incidence of cancer than any other system in the body (2) and thus it was chosen in this study to give insight on its different presentations and possible local associated factors.

For a clearer understanding of these diseases in our setting, it is important to determine their magnitude and characteristics; Gastroenterological malignancies at MNH are seen to have a magnitude of 15%, which is slightly higher than that of Ojo J. O. et al in Southwestern Nigeria in 2016, which is most likely due to a lower incidence of specifically esophageal cancer in his region (28).

The study further showed a male predominance 181(67%), of the 270 histopathologically confirmed patients studied. This was similar to other studies (13,14,19,29), meaning the distribution is regardless of geography. The reason for this predominance is unknown but the high risk behavior of men, is a likely factor, besides genetics, as men are more likely to consume alcohol and smoke cigarettes, both known risk factors towards these cancers.

These cancers also appeared to be more from the 41-70 years age group 194(72%), followed by the > 70 years age group 41(15%), a picture similar to Wakhisi et al, in western Kenya (19), Gabel JV et al, in Tanzania (29), Mchembe et al, in northern Tanzania (14) and Abdulkareem et al in Nigeria (22). A factor likely explained by advancing age being associated with increased exposure to other risk factors and inefficiency of protective mechanisms as body physiology is affected.

There was a higher occurrence of these cancers in Primary level educated patients 195(72%) and the unemployed 186(69%), two factors which are connected, and are also closely related to a low socioeconomic status which has been associated with known predisposing infections such as H. pylori, and has implications on accessibility of patients to health care facilities and

awareness of the diseases (14). Unfortunately H. Pylori sero-status was poorly tested among the participants 11(4.1%), since it is not a standard protocol for the hospital while investigating these patients and all were found to be positive. This possibly shows that there is a relationship between H. Pylori infection and gastrointestinal malignancies.

Alcohol consumption was reported among a majority of gastroenterological malignancy patients 211(78.1%), with patients diagnosed of; anal 15(88%), gastric 25(81%) and esophageal tumors 140(80%) being mostly alcohol consumers. In contrast, Singh et al in India in 2018, found that a low proportion (38.7%) of patients diagnosed with gastric cancer gave a history of alcohol consumption (30). These differences are most likely due to culture differences of the two communities and other risk factors in the area contributing to the disease.

Smoking was reported among a minority of gastroenterological malignancies 124(45.9%), but was mostly practiced by patients diagnosed with esophageal cancer 96(55%), similarly Mchembe et al in Tanzania in 2013 reported a smoking prevalence of 74.7% (14). This finding in the study is likely due to a low cultural approval of smoking as a habit and other risk factors in the area contributing to the disease.

The HIV infection/Aids prevalence 13(6.25%) in the study was similar to the national prevalence of 7% (31), hence the infection may not have a role in the general predisposition to gastrointestinal malignancies. Bonnet et al in France, in 2008 and Dandapani et al in America in 2010, reported an association between anorectal malignancy, a non – aids defining cancer, and HIV infection/AIDS (25,26), further saying that non-AIDS defining cancers have a two to three fold higher incidence in the HIV+ population. Although anorectal cancer is the only gastrointestinal malignancy with a confirmed association, there is still need to study other gastrointestinal cancers, and since Sub-Saharan Africa, has the highest global burden of HIV, this is a factor that will possibly influence the presentation of non – aids defining cancer's here (26).

Esophageal cancer was the most common GIT malignancy at 175(64.8%), in stark contrast to Abdulkareem et al in Nigeria, in 2009, who reported that colorectal cancer was the most common, and Kitinya et al, in 1988 in Northeastern Tanzania, who found that carcinoma of the stomach was the commonest malignancy in the Mount Kilimanjaro area of Tanzania (7). The histological distribution of Esophageal cancer in the study, was similar to global findings, (12,14,19,23,29), that squamous cell carcinoma (SCC) was the most common type and adenocarcinoma (EAC) was relatively uncommon, at 163(93.1%) and 9(5.1%) respectively.

Colorectal tumors were the 2nd 60(22.2%) most common gastrointestinal malignancy and the commonest histological variant was adenocarcinoma 38(88.4%) similar to Azadeh et al in Iran in 2008 and Mchembe et al in Tanzania in 2013 (23,24,32).

Gastric tumors are the 3rd 31(11.5%) most common gastrointestinal malignancy in the study & adenocarcinomas were the most common histopathological type 22(71%). Gastric squamous cell carcinoma was noted to be significantly high in the study 4(12.9%), a finding in stark contrast with global statistics (7,12,22,33), this may be explained by; errors of endoscopic result documentation, since SCC may appear both in the esophagus and the stomach or in advanced disease; where there is local spreading of distal esophageal tumors into the stomach.

Similar to global findings (2)(4)(34), small bowel tumors were the least common gastroenterological malignancy 4(1.5%). The commonest histological variant was adenocarcinoma 2(50%) and surprisingly SCC 1(25%) was also identified, while Hatzaras et al in America in 2007 found carcinoid as most prevalent (34).

CHAPTER FIVE

5.0. CONCLUSIONS AND RECOMMENDATIONS

5.1. Conclusions

Gastroenterological Malignancies have a significant magnitude among patients at MNH and they present with a unique profile. Lack of awareness of these diseases and their associated factors i.e. alcohol consumption, smoking and infections with H. Pylori and HIV/AIDS, pose a great challenge in the prevention and subsequent management of these patients. Addressing these challenges will help reverse the trend of an increasing incidence of these malignancies in Tanzania.

5.2. Recommendations

1. The current rates of gastroenterological malignancies should be communicated to the health sector and policy makers on the rising occurrences of these diseases.
2. Policy makers should lay down policies, protocols and strategies on the implementation of screening and outreach programs to encourage early diagnosis of these diseases.
3. Empowerment and improvement of health institutions should be done, to enable them to appropriately investigate and manage gastroenterological malignancies.
4. Create awareness by mobilizing communities towards the fast rising incidence of gastroenterological malignancies and their associated factors such as alcohol consumption, smoking and HIV infection/AIDS in an attempt to instill early health seeking habits.
5. Learning institutions should establish or improve training programs on gastroenterology to ensure specialists are available and competent at managing these diseases.
6. Further studies are necessary to increase our knowledge on these diseases, their risk groups and how they can be prevented.

REFERENCES

1. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: Defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol. 2006;24(14):2137–50.

2. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359–86.

3. Fukata M, Abreu MT. Role of Toll-like receptors in gastrointestinal malignancies. Oncogene [Internet]. 2008;27(2):234–43.

4. Wild CP, Stewart BW. World Cancer Report 2014. 2014. 632 p.

5. Deeken JF, Tjen-A-Looi A, Rudek MA, Okuliar C, Young M, Little RF, et al. The rising challenge of non-AIDS-defining cancers in HIV-infected patients. Clin Infect Dis. 2012;55(9):1228–35.

6. Barberis I, Martini M, Iavarone F, Orsi A. Available influenza vaccines: Immunization strategies, history and new tools for fighting the disease. J Prev Med Hyg [Internet]. 2016;57(1):E41–6.

7. Mabula JB, Mchembe MD, Koy M, Chalya PL, Massaga F, Rambau PF. Gastric cancer at a university teaching hospital in northwestern Tanzania : a retrospective review of 232 cases. World J Surg Oncol. 2012;1–10.

8. Segal I, Ally R, Mitchell H. Gastric cancer in sub-Saharan Africa. Eur J Cancer Prev [Internet]. 2001;10(6):479–82.

9. Roth AD. Curative treatment of gastric cancer: Towards a multidisciplinary approach? Crit Rev Oncol Hematol. 2003;46(1):59–100.

10. Smith JK, McPhee JT, Hill JS, Whalen GF, Sullivan ME, Litwin DE, et al. National outcomes after gastric resection for neoplasm.[Erratum appears in Arch Surg. 2009 Jul;144(7):634]. Arch Surg. 2007;142(4):387–93.

11. Khan MI, Baqai MT, Bukhari M, Hashmi RI. Original Article Gastric Carcinoma : 5 Years Survival after Gastric Surgery. 2002;(August):5–7.

12. Islami F, Kamangar F, Aghcheli K, Fahimi S, Semnani S, Taghavi N, et al. Epidemiologic features of upper gastrointestinal tract cancers in Northeastern Iran. Br J Cancer. 2004;90(7):1402–6.

13. Tettey M, Edwin F, Aniteye E, Sereboe L, Tamatey M, Ofosu-Appiah E, et al. The changing epidemiology of esophageal cancer in sub-Saharan Africa - the case of Ghana. Pan Afr Med J [Internet]. 2012;13:6.

14. Mchembe MD, Rambau PF, Chalya PL, Jaka H, Koy M, Mahalu W. Endoscopic and clinicopathological patterns of esophageal cancer in Tanzania: experiences from two tertiary health institutions WORLD JOURNAL OF SURGICAL ONCOLOGY. World J Surg Oncol [Internet]. 2013;11:257.

15. Søreide K, Sandvik OM, Søreide JA, Giljaca V, Jureckova A, Bulusu VR. Global epidemiology of gastrointestinal stromal tumours (GIST): A systematic review of population-based cohort studies. Cancer Epidemiol [Internet]. 2016;40:39–46.

16. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg [Internet]. 2000;231(1):51–8.

17. Strickland L, Letson GD, Muro-Cacho CA. Gastrointestinal stromal tumors. Cancer Control. 2001;8(3):252–61.

18. Fukasawa T, Chong JM, Sakurai S, Koshiishi N, Ikeno R, Tanaka A, et al. Allelic loss of 14q and 22q, NF2 mutation, and genetic instability occur independently of c-kit mutation in gastrointestinal stromal tumor. Japanese J Cancer Res. 2000;91(12):1241–9.

19. J WJPKBNR. Esophageal cancer in North Rift Valley of western Kenya. TT -. Afr Health Sci [Internet]. 2005;5(2):157–63.

20. Dhillon PK, Farrow DC, Vaughan TL, Chow WH, Risch HA, Gammon MD, et al. Family history of cancer and risk of esophageal and gastric cancers in the United States. IntJ Cancer [Internet]. 2001;93(1):148–52.

21. Henson DE, Dittus C, Younes M, Nguyen H, Albores-Saavedra J. Differential trends in the intestinal diffuse types of gastric carcinoma in the United States, 1973-2000: Increase in the signet ring cell type. Arch Pathol Lab Med. 2004;128(7):765–70.

22. Abdulkareem FB, Faduyile FA, Daramola AO, Rotimi O, Banjo AAF, Elesha SO, et al. Malignant gastrointestinal tumours in South Western Nigeria: A histopathologic analysis of 713 cases. West Afr J Med. 2009;28(3):173–6.

23. Chalya PL, Mchembe MD, Mabula JB, Rambau PF, Jaka H, Koy M, et al. Clinicopathological patterns and challenges of management of colorectal cancer in a resource-limited setting: a Tanzanian experience. World J Surg Oncol [Internet]. 2013;11:88.

24. Kumar A, Kumar A, Gupta A, Gupta A, Kumar P, R D. Cancers of anal canal : A review article. Int J Med Sci Res Pract. 2015;2(2):58–65.

25. Dandapani S V, Eaton M, Thomas CR, Pagnini PG. HIV- positive anal cancer: an update for the clinician. J Gastrointest Oncol [Internet]. 2010;1(1):34–44.

26. Bonnet F, Chêne G. Evolving epidemiology of malignancies in HIV. Curr Opin Oncol. 2008;20(5):534–40.

27. Eng J. Sample Size Estimation: How Many Individuals Should Be Studied? Radiology [Internet]. 2003;227(2):309–13.

28. Ojo JO, Adeola MO, Awe OO, Oluwasina YT, Akinyemi OA, Omotoso PA, et al. Analyses And Distribution Of Various Types Of Cancers Recorded In Ife-Ijesha Cancer Registry In The Five Year Period 2010 -2014. Ife J Sci. 2016;18(4):319–30.

29. Gabel J V, Chamberlain RM, Ngoma T, Mwaiselage J, Schmid KK, Kahesa C, et al. Clinical and epidemiologic variations of esophageal cancer in Tanzania. World J Gastrointest Oncol [Internet]. 2016;8(3):314–20.

30. Singh KL, Debbarma DK, Sreejith V. Original article Clinical , Endoscopic and Histological Findings of Carcinoma of Stomach. 2018;(3):125–9.

31. NBS, OCGS, ICAP, TACAIDS, ZAC, NHL-QATC, et al. Tanzania HIV Impact Survey (THIS) 2016-17: Preliminary findings. 2017;(December 2017):1–5.

32. Safaee A, Moghimi-Dehkordi B, Fatemi S, Pourhoseingholi M, Ghiasi S, Zali M. Colorectal Cancer in Iran: an Epidemiological Study Safaee. Asian Pacific J Cancer Prev. 2008;9:123–6.

33. McFarlane G, Forman D, Sitas F, Lachlan G. A minimum estimate for the incidence of gastric cancer in Eastern Kenya. Br J Cancer. 2001;85(9):1322–5.

34. Hatzaras I, Palesty A, Abir F, Sullivan P, Kozal R, Stanley D, et al. Small-Bowel Tumors. Arch Surg. 2007;142:229–35.

APPENDICES

Appendix I: Informed Consent Form (English Version)

ID No……

Consent to participate in the study on;

MAGNITUDE AND PATTERNS OF GASTROENTEROLOGICAL MALIGNANCIES AMONG PATIENTS AT MUHIMBILI NATIONAL HOSPITAL.

I am **Dr. Mwalukombe Joseph Malingi**, a postgraduate student at MUHAS, working on the research titled above.

Purpose of the study

To identify the different gastric malignancies ailing patients attending Muhimbili National Hospital, between March 2017 and February 2018.

What Participation Involves

If you agree to participate in this study, you will be interviewed using a questionnaire, detailed information on social demographic characteristics, past medical history and physical examination will be requested and a follow up of care for your condition will be done. An HIV test will be mandatory.

Confidentiality

All information collected will be entered into a password protected computer. The questionnaires will be handled in confidence. Your name will not be used anywhere through to data analysis and report development.

Risks

The researcher anticipates no harm will happen to you as you participate in this study.

Rights to Withdraw and Alternatives

Taking part in this study is completely your choice. If you choose not to participate or if you decide to stop participating, you will receive all services that you would normally get from this hospital. You can stop participating in this study at any time, even if you have already given your initial consent. Refusal to participate or withdrawal from the study will not involve penalty or loss of any benefits to which you are otherwise entitled.

Benefits

If you agree to take part in this study, you will benefit from timely explanation and follow up of investigation results and be updated on any plans regarding treatment and will be advised accordingly.

Cost

No payment will be requested from you as a fee to participate in this study.

In Case of Injury

The researcher does not anticipate that any harm will occur to you or your child as a result of participation. However, if any physical injury results from participation, we will provide you or your child with medical treatment according to the current standard of care in Tanzania.

Who to Contact

If you ever have questions about this study, you should contact the study Principal Investigator, Dr. Mwalukombe Joseph Malingi, Muhimbili University of Health and Allied Sciences, P.O. Box 65001, Dar es Salaam. E-Mail address: malingijoseph@gmail.comMobile No: 0624716896.

If you ever have questions about your rights as a participant, you may call Dr. Joyce Masalu, Chairman of the Senate Research and Publications Committee, P.O. Box 65001, Dar es Salaam. Tel: 2150302-6.

Agreement of Participation

I, ……., identification number……, have read the contents in this form and with satisfaction, agree to participate in this study.

Signature of participant/guardian…….

Signature of witness (if participant cannot read) ……..

Signature of research assistant……

Date of signing consent…….

Appendix II: Fomu ya Ridhaa (Swahili Version)

ID No……

Ridhaa ya kushirika katika utafiti juu ya.

MIENENDO NA SAMPULI ZA SARATANI YA UTUMBO KATI YA WAGONJWA WA HOSPITALI YA TAIFA MUHIMBILI.

Mimi ni **Dk. Mwalukombe Joseph Malingi**, mwanafunzi wa Shahada ya Uzamili katika Chuo Kikuu cha Afya na Sayansi za Tiba Muhimbili (MUHAS). Nafanya utafiti kwa jina, kama maelezo hapo juu.

Madhumuni ya utafiti

Kujua mienendombinu ya magonjwa ya saratani ya utumbo kulingana na hali yao ya kiafya ya ukimwi kwa wagonjwa wa Hospitali ya Taifa Muhimbili.

Jinsi ya kushiriki

Kama utakubali kushirika, utahojiwa maswali machache kuhusu matatizo yako na utaombwa kupimwa hali yako ya ukimwi, kisha ufuatiliwe katika matibabu kuangalia kama kuna uhususiano kati ya ugonjwa na hali yako ya kiafya.

Utunzaji siri

Taarifa zote zitakazo kusanywa zitatunzwa kwa usiri, na bila uwepo wajina la mgonjwa.

Madhara/Athari

Mtafiti hatarajii kutakuwa na madhara yoyote kutokana na utafiti huu.

Uhuru wa kushiriki

Kushiriki katika utafiti huu ni hiari yako. Kama utachagua kutokushiriki, utaendelea kupokea huduma zote kama kawaida kutoka hospitali hii. Unaweza kuacha kushirika katika utafiti huu wakati wowote, hata baada ya kutoa idhini yako ya awali.

Faida za utafiti

Kama utashiriki katika utafiti huu, utapewa maelezo kuhusu na kufuatiliwa majibu, na kujulishwa mipango ya tiba na kupewa ushauri utakapohitajika.

Gharama

Hakuna malipo yoyote utakayotozwa kama ada ya kushiri kikatika utafiti huu.

Taarifa/Mawasiliano:

Endapo utahitaji kupata maelezo zaidi au taarifa yoyote kuhusu utafiti huu, wasiliana na Dk. Mwalukombe Joseph Malingi, Chuo Kikuu cha Afya na Sayansi za Tiba Muhimbili, S.L.P 65001, Dar es Salaam. Barua pepe: malingijoseph@gmail.com. Simu ya Mkononi: 0624716896.

Kama utakuwa na maswali kuhusu haki yako kama mshiriki, unaweza wasiliana na Dr. Joyce Masalu, Mwenyekiti wa Utafiti, S.L.P 65001, Dar es Salaam. Simu Nambari: 2150302-6.

Idhini ya Kushiriki

Mimi……, mwenye nambari ya ushiriki……., nimeelezwa na nimesoma yaliyomo katika fomu hii, maswali yangu yamejibiwa na nikaridhika. Nimekubali kushiriki katika utafiti huu.

Sahihi ya Mshiriki/Mlezi; ……

Sahihi ya Shahidi (kamaMshiriki/Mlezi hajui kusoma); ……

Sahihi ya Mtafiti Msaidizi; ……..

Tarehe ya Ridhaa; ……..

Appendix III: Questionnaire (English Version)

TITLE: **MAGNITUDE AND PATTERNS OF GASTROENTEROLOGICAL MALIGNANCIES AMONG PATIENTS AT MUHIMBILI NATIONAL HOSPITAL, TANZANIA.**

I: IDENTIFICATION DETAILS: **S. No …….**

1. Hospital Reg. No……..
2. Date of interview…...…… Height ……
3. Weight ……..kg's BMI ……
4. Contacts …… N.O.K., contacts……

II. DEMOGRAPHIC DATA:

5. Age; ……..Years.
6. Sex; 1). MALE 2). FEMALE
7. Level of education ……
8. Occupation ……...
9. District of residence …….

III.PRESENTING COMPLAINTS:

1. Indigestion / heartburn	Yes/ No
2. Abdominal discomfort	Yes/ No
3. Loss of appetite (especially for meat)	Yes/ No
4. Weakness	Yes/ No
5. Fatigue	Yes/ No
6. Easy satiety	Yes/ No
7. Abdominal pain in the upper abdomen	Yes/ No
8. Nausea and vomiting	Yes/ No
9. Diarrhea or constipation	Yes/No
10. Weight loss	Yes/ No

11. Dysphagia	Yes/ No
12. Chest pain	Yes/ No
13. Blood in stool	Yes/ No
14. Yellow eyes	Yes/ No
15. Mass effect	Yes/ No

PHYSICAL EXAMINATION FINDINGS

……

……

……

IV. ENDOSCOPY FINDINGS:

1. Location ……
   …….
2. Appearance ……
   ……..
3. Others; ……...……
   ……..

V. INVESTIGATION RESULTS:

1. Hb. - ……
2. HIV/AIDS Sero-status 1) Positive 2) Negative
   - Last tested CD4+ count ……..
3. Histology result; - Histological tissue source …….
   - Histological type ……
4. Metastases; 1) Yes 2) No

VI. ASSOCIATED RISK FACTORS:

Risk Factor	Yes	No
Age		
Predisposing Infection		
Smoking		
Alcohol Consumption		
Radiation		
Obesity		