CLINICAL PRESENTATION, INVESTIGATIONS, AND TREATMENT MODALITIES OF GASTRIC CANCER AT MUHIMBILI NATIONAL HOSPITAL: A RETROSPECTIVE REVIEW

David Moses Antanamsu, MD

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By

David Moses Antanamsu

A Dissertation Submitted in (partial) Fulfillment of the Requirements of the Degree of Master of Medicine (Surgery) of

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled; **"Clinical presentation, investigations, and treatment modalities of gastric cancer at Muhimbili National Hospital",** in (partial) fulfilment of the requirements for the degree of Master of Medicine (Surgery) of Muhimbili University of Health and Allied Sciences.

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Dr. Larry O. Akoko

(Supervisor)

Date: _____

_____

Dr. Kitembo S. Kibwana

(Supervisor)

Date: _____

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I, **Dr. David Moses Antanamsu,** 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**………………………………….

ACKNOWLEDGMENT

DEDICATION

To Moses and Mary Maro

ABSTRACT

Background: Gastric cancer is the 7th most diagnosed malignancy in Tanzania and the 6th cause of cancer-related deaths in 2018. The disease is associated with a high mortality rate in the country. This is partially attributed to the fact only a small proportion of patients with gastric malignancies undergo gastric resection in Tanzania.

Objective: To investigate patient social demographic and clinical characteristics in relationship to treatment modalities pursued in patients with gastric cancer at Muhimbili National Hospital.

Materials and Methods: A retrospective analytical study was conducted at MNH involving patients treated between 2015 and 2019 with gastric adenocarcinoma. Patients' case record files were accessed, and demographic and clinical data were extracted. Data were entered into SPSS and analyzed. Association was tested using the chi-square method with a p-value of 0.05 accepted for significance.

Results: There were 122 patients with gastric adenocarcinoma who were reviewed. The mean age of respondents was 59.3±14.27 years with a male to female ratio of **1.5:1.** Most patients presented with symptoms of advanced disease with a median duration of symptoms of 4 months. Most tumors were in the distal stomach. About 60% of the respondents had metastatic disease at the time of diagnosis with the liver and peritoneal surfaces being the commonest sites for metastasis. About 30% of the patients underwent gastric resection. Having medical insurance or making private payments, age between 50 and 70 years and polypoid tumors positively influenced patients to undergo gastric resection.

Conclusion: Gastric cancer mostly affects people in the 5th and 6th decades of life. Most of the patients have advanced disease at the time of diagnosis. Only a small proportion of patients undergo gastric resection. Having advanced disease and young age at diagnosis are associated with low gastric resection rates.

Recommendations: Studies to investigate factors that lead to late presentation of patients with gastric cancer. Primary care health facilities should build the capacity of diagnosing gastric cancer to enable early diagnosis and referral to tertiary facilities.

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LIST OF ABBREVIATIONS

AJCC	:	American Joint Committee on Cancer
CT	:	Computed tomography
GERD	:	Gastroesophageal reflux disease
H. pylori	:	*Helicobacter pylori*
GC	:	Gastric Cancer
GFT	:	Gastrostomy feeding tube
GIST	:	Gastrointestinal stromal tumor
MNH	:	Muhimbili National Hospital
MRI	:	Magnetic resonance imaging
MUHAS	:	Muhimbili University of Health and Allied sciences
PET	:	Positron emission tomography
TNM	:	Tumor, Node, Metastasis
WHO	:	World Health Organization

DEFINITION OF TERMS

Clinical characteristics: Refers to patients' demographic characteristics, presenting symptoms, physical findings, and disease stage at presentation.

Gastric cancer: Refers to malignant neoplasm of the stomach. It is being used interchangeably with gastric adenocarcinoma.

Gastric resection: This refers to the removal of the distal, proximal, or total removal of the stomach.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Gastric cancer is the 5th most diagnosed cancer and the 3rd contributor to cancer-related mortality in the world. The burden of the disease is the highest in East Asia countries (1). In Africa, gastric cancer ranks 9th contributing to 3% of all cancer diagnoses. It also makes 4.1% of cancer deaths making it the 7th cause of cancer deaths in Africa in 2018(2). In East Africa, the estimated incidence of gastric cancer in 2018 was 4.7 per 100,000 in men and 4.0 per 100,000 in women. In Tanzania, Gastric cancer is the 7th most diagnosed cancer responsible for 3.2% of cancer diagnoses in 2018. It was the 6th cause of cancer-associated deaths(3).

Most gastric cancers are adenocarcinoma(4). Anatomically, gastric cancer is classified as cardia and non-cardia gastric cancer (5). The two anatomical sites present a potential for different etiologies, presentation, and disease outcomes (6). Cardia gastric cancer is associated with obesity, long-standing gastroesophageal reflux, and possibly tobacco smoking. Non-cardia gastric cancer is associated with *Helicobacter pylori* infection, tobacco smoking, and high dietary salt intake(7).

There is a discrepancy in the incidence of gastric cancer in different geographical regions. The incidence of the disease is higher in high-income countries compared to low-income countries. There is also a discrepancy in sex predilection. In developed countries, the male predilection of gastric cancer is more pronounced than in developing countries(4).

The outcomes of patients with gastric cancer also show variations. There is better survival in Japan compared to North America and European countries(7,8). This is explained by the practice of screening for gastric cancer in Japan which is not practiced in North America and Africa where the disease is diagnosed after it has developed symptoms(9). In Africa, there is unclear information on cancer survival. However, the number of cases diagnosed in a year is close to mortality figures indicating a high mortality rate (10).

In Tanzania, there were 1,353 cases of gastric cancer diagnosed in 2018. In that same year, there were 1,323 mortalities attributed to gastric cancer (3). Moreover, only a small proportion of gastric cancer patients undergo gastric resection(11) which is the mainstay treatment. Despite this dismal outlook, the epidemiology of gastric cancer is still not well documented in the country. Also, the factors determining the type of treatment these patients receive are not known. We are therefore unable to explain the cause of this dire situation or what needs to be done to improve the situation.

1.2 Literature review

1.2.1 Patients' demography

Age at Presentation

Gastric cancer shows a wide age variation, with some countries reporting younger age while others reporting older age groups. In North America, gastric cancer presents at a mean age of 69 to 70 years(12). This is like East Asia where the mean age at presentation is 67 years(13). In Africa, most studies report gastric cancer occurs almost two decades earlier at a mean age of 50 years (14,15). With the global trends in gastric cancer changing, the current age at presentation of gastric cancer in Tanzania is not known.

Sex distribution

Gastric cancer is more common in males compared to females. However, the male-to-female ratio is different in different areas of the world. In East Asia, the ratio is high with studies reporting ratios ranging from 2.18 to 3.2(16,17). In Europe, the male to female ratio is 2.5(18). In Africa, male predominance is slightly less pronounced with the male to female ratio being 1.8(10,18). With changing times, the gender disparity seems to be narrowing over decades(19).

Urban versus rural disparity

In most regions of the world, the incidence of gastric cancer is more in urban settings than in rural areas (12). However, most studies demonstrate that patients in rural areas had worse outcomes compared to patients in urban areas(20–22). This discrepancy is in part attributed to early diagnosis in urban settings and hence earlier initiation of treatment(22). There is no information on the differences in the presentation and treatment of gastric cancer in rural and urban areas in Tanzania.

1.2.2 Clinical presentation

Presenting symptoms

In areas where gastric cancer screening is conducted, such as Japan, patients are diagnosed with subtle or no symptoms(13). In areas where their diagnosis occurs after the development of symptoms, patients are diagnosed with advanced disease(23). Studies profiling gastric cancer patients in Africa show that patients in this region present with symptoms consistent with advanced disease such as palpable epigastric mass and features of gastric outlet obstruction (15,24).

Duration of symptoms at presentation

Patients in low-income countries show the longest duration from the onset of symptoms to presentation to a healthcare facility (25). A review of studies showed most patients present at a duration ranging from 3 weeks to 3 years. The studies showed the average duration of symptoms varies from 6 months, 9 months, and 16 months(11,14,26). The duration of symptoms shows a close correlation to the countries' level of development, with patients from developed countries presenting earlier compared to patients from developing countries(27,28).

Disease stage at presentation

There is a great variation in disease stage at diagnosis around the globe. In Japan, diagnosis commonly occurs through screening, and hence it is detected at an earlier stage. A study in Japan showed 60% of gastric cancer cases were detected at stage 1(13). In Africa, most gastric cancer patients are diagnosed at advanced stages(25). In studies in Nigeria, Ethiopia, and Rwanda all show that more than 50% of gastric cancer patients are diagnosed at stage IV(24,29,30).

Anatomical tumor location

There is uniformity in most world regions concerning tumor location. In most areas, distal gastric tumors are the most common form. In Japan, 74% of tumors were in the distal stomach. Studies were done in Iran and India; similar results were found(26,31). Studies conducted in Africa show the same trend with studies in Uganda and Tanzania showing the commonest tumor location being in the antrum(11,15).

1.2.3 Treatment of Gastric Cancer

The mainstay treatment of gastric cancer is surgical resection of the tumor and lymph node dissection. This can be achieved when patients are diagnosed in the early stages of the disease. In Japan and China, between 80 and 95 percent of gastric cancer patients have operable tumors at the time of diagnosis (13,32). In Africa there is some variability, In Nigeria, more than half of patients with gastric cancer have gastric resection(14). In other African nations, only a minority of patients can undergo gastric resection(14,33,34). In general, most patients in Sub-Saharan Africa are usually undergoing non-curative procedures.

In Tanzania, it is known that only small proportions of gastric cancer patients undergo gastric resection (11). However, it is not known how the patient's demographics and disease stage determine which patients have operable or inoperable tumors.

1.3 Problem Statement

Gastric cancer has persistently ranked the 7th commonly diagnosed cancer in Tanzania and the 6th contributor of cancer-related mortality over the last decade. Recent data from 2018 and 2020 shows the disease has been diagnosed in 1353 (3.2%) and 1091 (3.5) patients respectively. It has also resulted in 1323 (4.6%) and 947 (3.5%) deaths during the same period respectively (1,35). Despite being a common disease, the exact reason for this dismal picture is not properly discerned. There is a paucity of data regarding the demography, clinical presentation, and their relationship with the treatment of gastric cancer patients in Tanzania. This has left patients, their families, and the healthcare systems overwhelmed by a disease with a poor prognosis despite promising outcomes reported in the literature from other countries around the globe.

1.4 Study Rationale

This study has identified the factors that influence the treatment modalities of gastric cancer at Muhimbili National Hospital. This information has identified areas that can be modified to increase the proportion of patients with gastric cancer who can undergo curative resections. Such an understanding will be vital to design interventions that will aim at optimizing gastric cancer outcomes in Tanzania.

1.5 Conceptual Framework

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┌─────────────────────────┐              ┌─────────────────────────────────┐
│       DEMOGRAPHY        │              │       CLINICAL FEATURES         │
│          Age            │   ══════>    │          Symptoms               │
│          Sex            │              │  Physical Examination Findings  │
│    Insurance Coverage   │              │           Stage                 │
│    Area of Residency    │              │          Histology              │
└─────────────────────────┘              │        Tumor location           │
                                         └─────────────────────────────────┘

              ┌─────────────────────────────────┐
              │        TREATMENT DONE           │
              └─────────────────────────────────┘

     ┌──────────────────┐          ┌──────────────────┐
     │    No GASTRIC     │          │     GASTRIC      │
     └──────────────────┘          └──────────────────┘

              ┌──────────────┐      ┌──────────────────────────┐
              │    TOTAL     │      │  SUBTOTAL GASTRECTOMY    │
              └──────────────┘      └──────────────────────────┘
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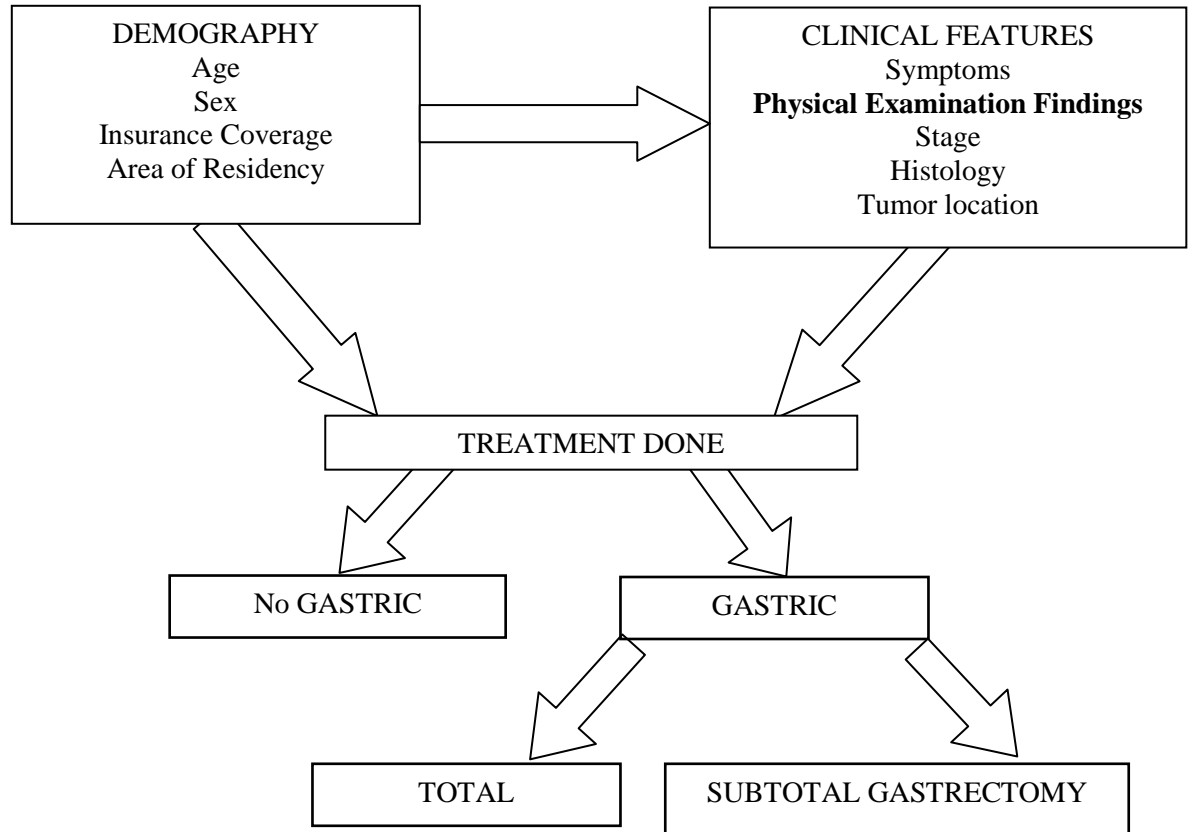
Figure 1: Conceptual framework

Patients' demographic characteristics such as age, sex, area of residency, and whether they have medical insurance may have an influence on the disease characteristics the patient will present with. Moreover, both patient's demographic characteristics and disease characteristics will influence whether the patient receives gastric resection or not. While for the patients who will undergo gastric resection, there are different extents of resection as shown in figure 1 above.

1.6 Research Question

What are the factors determining treatment modalities of gastric malignancies at Muhimbili National Hospital?

1.7 Study Objectives

1.7.1 Broad Objective

To investigate patient social demographic and clinical characteristics in relationship to treatment modalities pursued in patients with gastric cancer at Muhimbili National Hospital.

1.7.2 Specific Objectives

1. To document clinical presentation of patients with gastric malignancies at MNH.
2. To evaluate the diagnostic and treatment modalities of gastric cancer patients at MNH.
3. To assess the relationship between social-demographic and clinical characteristics of participants and treatment modalities provided.

CHAPTER TWO

2.0 MATERIALS AND METHODS

2.1 Study design

This was a retrospective analytical hospital-based study involving gastric cancer patients attended at MNH between January 2015 and December 2019.

2.2 Study setting

The study was conducted at the Department of Surgery of the Muhimbili National Hospital. This is a public hospital, in Dar es Salaam the commercial capital of Tanzania. The hospital serves as the last referral point for the country which has a population of 56 million people. The hospital thus enjoys receiving referrals from all over the country, including patients with gastric cancer. MNH can investigate, stage, and offer surgery for patients with gastric cancer. It has a state-of-the-art endoscopy suite where diagnostic biopsies are collected. It also has 128 multi-slice Computed tomography which can offer reliable TNM staging. Laparoscopic facilities are also available to be used for staging purposes where a CT scan is not reliable. Pathology services and laboratory services are available with capabilities for performing histology, tumor markers, *H. pylori* tests, and immunohistochemistry of HER-2 status. The hospital has two surgical firms that take care of gastric cancer patients, with surgical gastroenterology training.

2.3 Study Population

The study involved all patients admitted at the Department of Surgery at Muhimbili National Hospital treated for an intra-abdominal malignancy between January 2015 and December 2019.

2.4 Study sample

Patients diagnosed with gastric malignancy.

2.5 Inclusion and exclusion criteria

Inclusion Criteria

i. Diagnosed and or treated during the study period.

ii. Histologically confirmed diagnosis of gastric adenocarcinoma.

iii. Patients of all ages and sex.

iv. Have retrievable case notes from the medical records of the hospital.

Exclusion Criteria

Patients with incomplete information from the case notes were excluded in the analysis.

2.6 Sample Size

In a study done in Nigeria, 56% of patients with gastric malignancies underwent gastric resection. A sample of 98 patients with gastric cancer was required an operability rate of 56% at type one error of 5% and type 2 error of 80% at 95% CI(36).

Sample size calculation was based on the formula below

$$N = \frac{[Z_\alpha\sqrt{P(1-P)(1/q_1 + 1/q_2)} + Z_\beta\sqrt{P_1(1-P_1)(1/q_1) + P_2(1-P_2)(1/q_2)}]^2}{(P_1 - P_2)^2}$$

Where

N= Sample size

Z_α = the standard derivate of α = 1.96

Z_β = the standard derivate of β = 0.8416

q_1 = Proportion of patients who undergo gastric resection = 0.56

q_2 = Proportion of patient who did not undergo gastric resection = 0.44

Therefore, the minimal sample size required in the study is 98 patients.

2.7 Study variables

Patients' demography included age that was calculated from the date of birth registered with the hospital case notes. Sex was categorized as male or female. Region of residency was extracted from medical records and further classification into geographical zones was done. Clinical information on the stage of the tumor was considered as documented in the case notes by the managing clinician. This included information on the local extent of the disease, invasion of adjacent structures, metastasis to distant organs (to be mentioned, including peritoneal seeding), and lymph node involvement. This was used to provide the best estimate of TNM staging. Presenting symptoms at the time of initial diagnosis at MNH were recorded. Tumor histology type was obtained from a signed MNH histology report. Tumor location was obtained from the endoscopy report. All diagnostic investigations are done, and treatment offered at MNH were recorded from the case notes.

2.8 Data collection methods

A search was made in the hospital medical records system to identify patients with a recorded diagnosis of gastric malignancy. Their medical record numbers were captured, and a search was made in the pathology records to identify those with histological diagnoses of gastric adenocarcinoma. Case notes of the patients who had a confirmed diagnosis were retrieved from the hospital medical records.

An electronic data abstraction spreadsheet available online, KoBo collect®, was utilized for real-time quality checks. Then the information in the checklist was codified then entered in SPSS for analysis.

2.9 Data analysis

Data were analyzed using the Statistical Product and Services Solution (SPSS) version 23. Categorical variables were summarized into the frequency with proportions while continuous variables were summarized into means with standard deviation and range. Pearson Chi-square

test was used to identify factors predicting resectability by using a p-Value of < 0.05 to indicate statistical significance.

2.10 Ethical Consideration

The study proposal was submitted to MUHAS IRB for ethical review and consideration and a letter upon approval to the MNH directorate of research and training for permission to use hospital patients' medical records. Direct patient identifiers used during data abstraction will be de-identified during data transfer into SPSS software to keep the anonymity of the patients.

2.11 Study Limitations and Mitigation

The retrospective nature of the study demonstrated incomplete variables such as patients' functional status, nutritional status, occupation, and level of education were missing from most patients' case notes, and thus analysis was not conducted on those variables.

CHAPTER THREE

3.0 RESULTS

A total of 122 patients with histology-proven gastric adenocarcinoma were identified. Among them 74 (60.7%) were males with a male to female ratio of 1.5:1. The mean age was 59.29±14.27 (29 – 95) years. The median duration of symptoms to presenting to the hospital was 4 months (1 – 36 months). There were 74 (60.7%) patients who were in the public cost-sharing category, with the rest having medical insurance or making private payments. Most of the tumors were situated in the antrum followed by the body, with a polypoid appearance at endoscopy. Histologically, intestinal tumors were predominant.

Table 1: Clinical and pathological characteristics of 122 patients with gastric cancer at MNH

Variable	Frequency (%)
Sex	
Male	74 (60.7%)
Female	48 (39.3%)
Age groups	
< 50	35 (28.7%)
50 – 70	63 (51.6%)
> 70	24 (19.7%)
Payment category	
Public cost-sharing	74 (60.7%)
Private/Insurance	48 (39.3%)
Duration of Symptoms (Months)	
0 – 6	84 (68.9%)
7 – 12	26 (21.3%)
> 12	12 (9.8%)
Tumor location	
Antrum	60 (49.2%)
Body	26 (21.3%)
Proximal stomach	23 (18.8%)
Diffuse	3 (10.7%)
Bormann classification	
Polypoid	76 (62.3%)
Ulcerative/Fungating	24 (19.7%)
Diffuse	22 (18.0%)
Lauren Classification (N=90)	
Intestinal type	63 (70%)
Diffuse type	27 (30%)

Gastric cancer patients were analyzed by their origin from the seven zones of Tanzania's mainland. Most of the patients had a coastal zone as their origin as was in 81 (67%) patients, followed by Northern and central zones each having 10 (8%) patients.
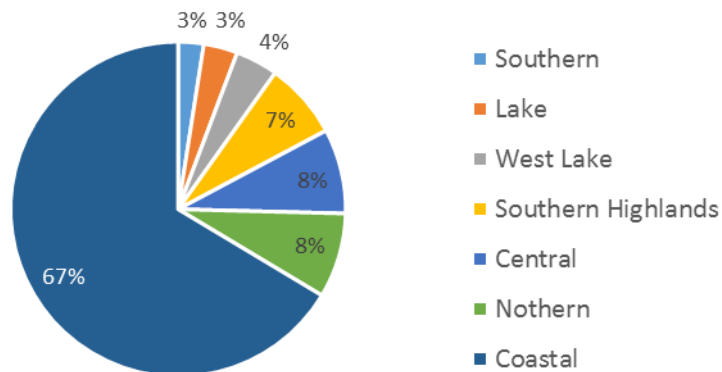
Figure 2: Pie chart showing gastric cancer patients with their seven zones of residence from Tanzania mainland

All the patients presented with features of advanced disease as depicted in the figure. Abdominal pain was the most common presentation in 92.6% of patients followed by weight loss in 86.8% and gastric outlet obstruction in 55.4% of patients. Other clinical presentations are presented in **figure 3**.
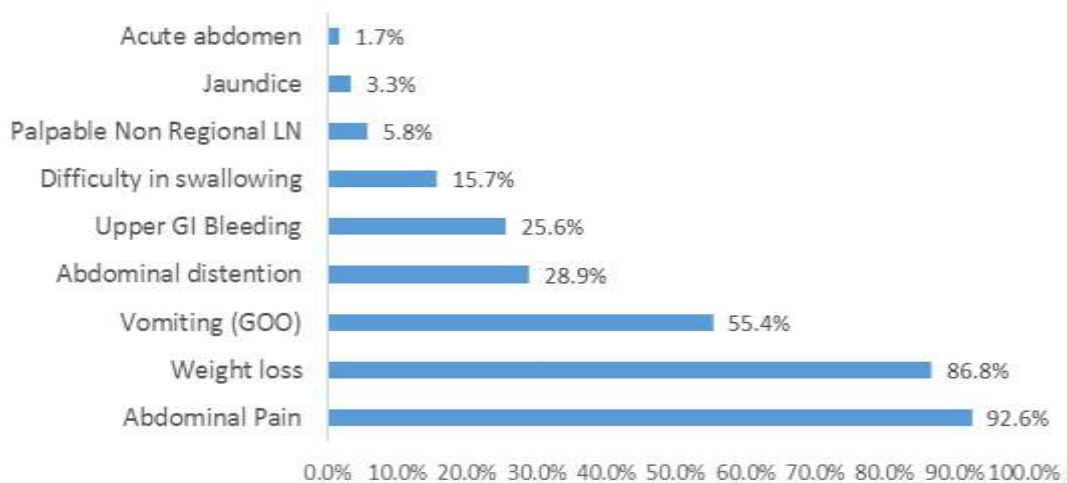
Figure 3: Presenting symptoms of Gastric Cancers treated at MNH between 2015 and 2019.

Distant metastasis was documented among 73(59.8%) patients. The commonest site of metastasis was the liver in 50 (68.5%) patients, followed by peritoneal carcinomatosis in 34 (46.6%) patients. **Figure 4** shows sites of metastasis.
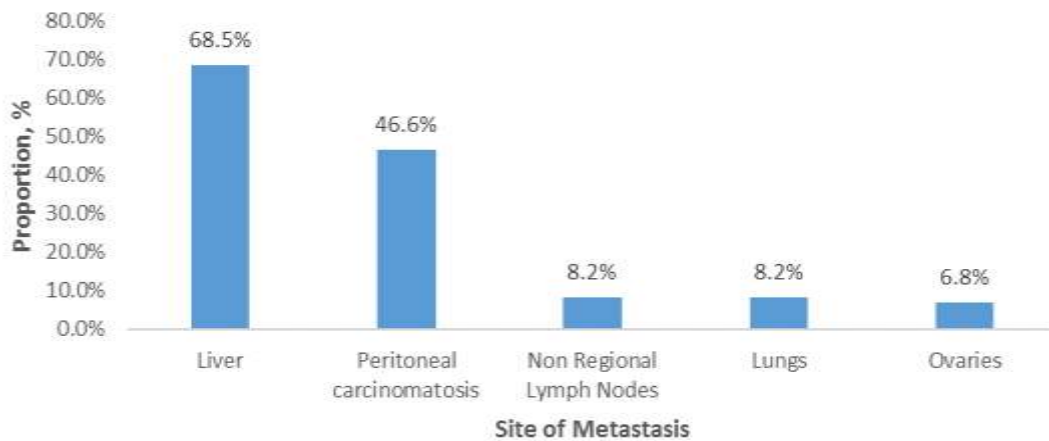
**Figure 4: Areas of metastasis in patients with gastric adenocarcinoma at MNH between 2015 and 2019**

Four modalities of investigations were used in patients with gastric cancer as displayed in **Figure 5**: All except one had an OGD done. For metastatic and staging workup, most of the patients (86%) had an abdominal CT scan. In addition, 36.3% of the patients had an abdominal ultrasound done. Lung metastases were screened by either a chest x-ray or chest CT scan in 37%.
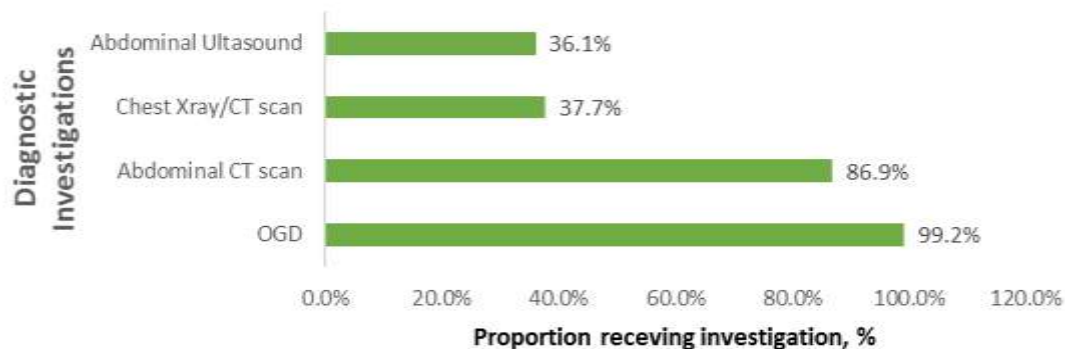
Figure 5: Imaging and Endoscopy investigations in gastric cancer patients at MNH between 2015 and 2019

In **Figure 6** we show, 67 patients (55%) had surgery done. Among the patients who had surgery, 37 (30%) patients had gastric resection and 24 (20%) patients had palliative procedures. In 6 (5%) patients, laparotomy was done for exploration and biopsy without additional procedure.
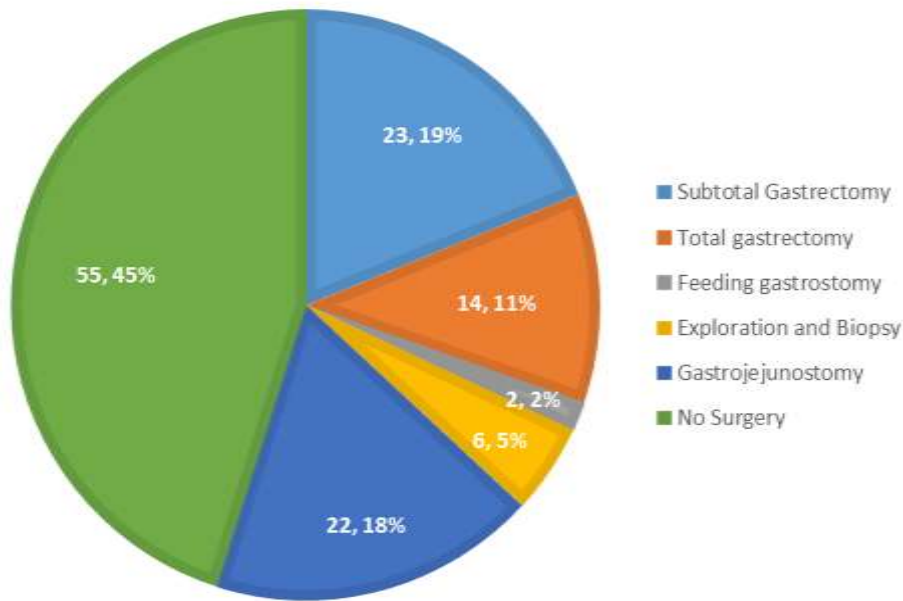
Figure 6: Types of surgeries done on patients with gastric adenocarcinoma at MNH between 2015 and 2019

Payment category, age of the patient, metastasis status, and Bormann classification had shown significant influence on resection rates. Patients who were privately paying or were on medical insurance had significantly more resection rates than their public counterparts (p=0.001). Patients between 50 and 70 years of age were more likely to undergo a resection (p=0.009). Lack of evidence of metastasis (p=0.001) and the presence of a polypoid lesion (p=0.01) was associated with significantly higher resection rates. Longer duration of symptoms had a higher resection rate but failed to reach a significant level.

Table 2: Association between demographic and clinical characteristics of gastric cancer and resection of gastric tumors

VARIABLES	Resection (%)	No resection (%)	p-Value
Sex			
Male	26 (35.1%)	48(64.9%)	0.15
Female	11 (22.9%)	37(77.1%)	
Payment Category			
Public Patient	14 (18.9%)	60 (81.1%)	0.001
Private/Insurance	23 (47.9%)	25 (52.1%)	
Age of Patient			
< 50	4(11.4%)	31(88.6%)	0.009
50 – 70	26(41.3%)	37(58.7%)	
> 70	7 (29.2%)	17 (70.8%)	
Duration of Symptoms (months)			
≤ 6	25 (29.8%)	59 (70.2%)	0.240
7 – 12	6 (23.1%)	20 (76.9%)	
≥ 12	6 (50.0%)	6 (50.0%)	
Metastasis Status			
M0	32 (65.3%)	17 (34.7%)	0.001
M1	5 (6.8%)	68 (93.2%)	
Tumor Location			
Antrum	19 (31.7%)	41 (68.3%)	0.865
Body	7 (26.9%)	19 (73.1%)	
Proximal stomach	8 (34.8%)	10 (76.9%)	
Diffuse	3 (23.1%)	15 (65.2%)	
Bormann Classification			
Polypoid	32 (42.1%)	44 (57.9%)	0.01
Ulcerative/Fungating	2 (8.3%)	22 (91.7%)	
Diffuse	3 (13.6%)	19 (86.4%)	
Lauren Classification (N=90)			
Diffuse type	9(33.3%)	18(66.7)	0.999
Intestinal type	21(33.3%)	42(66.7)	

CHAPTER FOUR

4.0 DISCUSSION

Gastric adenocarcinoma has not been extensively studied in the Tanzanian context and this is the first study from a national hospital with a long history of treating patients with GC that we are aware of. This study has dissected the clinical picture of patients with GC including its epidemiology, presentation, and histopathology, and treatment practices. The findings will help inform future research in this field to improve patient outcomes through early referral and individualized care.

Our study has demonstrated a male predominance like other studies in the region (37). But this predominance was slightly lower than that reported from the lake zone in Tanzania whereby male predominance was three-fold compared to just under twofold from this study (11). Why this difference is observed in the same country might suggest a difference in exposure of different sexes to risk factors by zoning within the country. In this current study, most patients were from the coastal region with insignificant contributions from the lake zone. Only 9 patients in this study were coming from the same catchment as patients studied in the report. There is a need to study and see the differences and similarities in risk factor occurrence between these two regions.

This study has demonstrated a relatively young age of patients with GC when compared to patients from North America and Asia(38–40). At the mean age of 59 years, this was a decade earlier than in the former counties. This young age is in full agreement with that reported from the previous study from the Tanzanian lake zone region (11). Hypothetically, younger age at presentation would demand an aggressive approach to the treatment of these patients, but this would depend on the stage at presentation. The younger age at presentation might be having a bearing on the prevailing risk factors which have not been studied locally yet. Both environmental, dietary, and genetic factors that contribute to the local GC development need to be explored in detail and urgently.

Patients under the age of 50 years were more likely to present with diffuse histology, and with metastatic disease than those older than 50 years. The aggressive nature of the disease at a young age should be of concern to the epidemiologists and surgeons alike on the possibility of a difference in the pathophysiologic pathways of gastric carcinogenesis. The aggressive nature of the disease in younger patients precluded the possibility of a curative resection among them. This grim picture of GC in the younger ones has been reported before (41,42).

Gastric carcinoma is known to present with vague symptoms hence a delay in presentation as was witnessed in our study. Most of the presenting symptoms listed in this study were those of advanced disease in almost all the patients. By being not a very prevalent disease, the lack of screening (43), only means that earlier diagnosis can only be by chance. This factor has been established by other studies where most patients are diagnosed with alarm symptoms which are markers of advanced disease (44). Good use of endoscopy can aid in the early diagnosis of GC at its fairly early stages (45), but it is not widely available out of major cities apart from being costly.

Most of the GCs were in the distal stomach which is consistent with that found in the regions with a high prevalence of *H. pylori* infections like East Asia (46). We could not establish whether *H. pylori* are also prevalent among this group of patients as it is not routinely tested for. This is contrary to findings from North America and Europe where distal GC are declining, and cardia tumors are increasing (47,48). In East Asia however, the incidence of tumors in both the cardia and antrum has remained the same (49,50). Due to lack of local trends on the same, it would be good to assume that if we can establish the role of *H. pylori* and embark on its eradication, we can experience the same trend as that of North America.

There are several classifications to GC with Lauren standing out to be of prognostic value (51,52). Only 90 of 122 had this classification, reflecting a lack of local standardized protocol in histology reporting at our facility. Patients with intestinal histology are known to have a relatively good prognosis as they were more likely to be older, absent metastasis and with a resectable tumor (53–55). Despite this fact, only a small proportion of patients with intestinal histology in our study underwent gastric resection. This suggests other factors that affect the

prognosis such as TNM status, tumor grade, and duration of symptoms at the time of presentation(56).

For optimized care, appropriate staging is needed for each patient with a histological diagnosis of GC. The majority but not all the patients had a CT scan of the abdomen for assessment of TNM status within the abdomen. CT has been shown to accurately provide staging information in patients with stage II to IV of GC. Its sensitivity decreases in evaluating stage I GC (57–59).

Abdominal CT scans are generally available in urban centers. Patients from rural areas often do not have readily available and accessible CT services but Ultrasound services are more broadly available in the country. In our study, we found a small proportion of patients who had an abdominal ultrasound done. There are studies that evaluated the role of transabdominal ultrasound screening and staging of GC. These show transabdominal ultrasound can be used in staging advanced gastric malignancies (60,61). Therefore, transabdominal ultrasound can be used in areas where CT scan is not readily available in the staging of GC patients.

Staging laparoscopy has now gained an acceptable role in the preoperative staging in GC. This can be done on the same seating with a planned gastrectomy or as a different session (62). Diagnostic laparoscopy offers details on resectability, and local peritoneal spread (macroscopic and microscopic through peritoneal fluid cytology) (63,64). While laparoscopy and the necessary competency are available at the hospital, none of our patients had a diagnostic laparoscopy done. This lack of diagnostic laparoscopy exposed many patients to unnecessary surgery with complications that could have been avoided. Diagnostic laparotomy increases hospital stay, and cost to the patients and facilities treating the patients. Moreover, diagnostic laparoscopy would select patients who would benefit from neo-adjuvant therapy.

We found that the liver and peritoneum were the two most common sites of metastasis. These sites were common in other studies that examined patterns of metastasis in GC (65). The presence of metastasis was a significant determinant of patients not to undergo gastric

resection. However, 5 patients had resection despite having metastasis. These had metastasis in the liver in 2 patients and peritoneal metastasis in 3 patients. It is known that gastrectomy in a patient with peritoneal metastasis in the adjacent peritoneum and a few scattered peritoneal metastasis results in improved survival (66,67). Cytoreductive surgery is an acceptable strategy when the primary tumor is resectable (68–70).

Of all patients who had GC, 30% had a gastric resection. This implies that most patients who were diagnosed with GC at MNH did not undergo curative treatment. Much has not changed in the past decade as a study done in 2012 showed only 24% of patients with GC had undergone resection (11). These findings are like studies conducted in other lower- and middle-income countries (14, 30, and 31). However, in developed countries like Japan and China more than 80% of GC patients presented with operable disease (13, 29).

Patients who had medical insurance and those who were able to make private payments had a statistically significant higher rate of gastric resection compared to those who were treated under public funding. This study did not investigate the factors for late presentation which could make curative treatment impossible. Hence, we cannot draw inference to the role of financial access to cancer treatment contributes to low resection rates in uninsured patients. However, there are studies have investigated this relation, they show there exists an inequality in the access to cancer treatment based on economic status, ethnicity, and region of residence (12,71).

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATIONS

5.1 Conclusions

Gastric cancer is a predominantly male disease affecting people in the 5th and 6th decades of life. Most patients presented with symptoms of advanced disease with a variable duration of symptoms ranging from 1 to 36 months. The tumors were more common in the distal stomach with the intestinal type being the most common histological type. Most of the patients are diagnosed after they have developed metastatic disease.

Only 30% of patients with gastric cancer underwent gastric resection. Having advanced disease was a major determinant for patients not to undergo gastric resection. Also, age less than 50 years is associated with lower rates of gastric resection. This is attributed to more aggressive disease presentation in young patients aged less than 50 years. Patients without medical insurance also had low resection rates. However, barriers to access to cancer treatment were outside the scope of this study.

5.2 Recommendations

i. A prospective study should be conducted to study the factors that are associated with the late presentation of patients with gastric cancer and barriers to cancer treatment.

ii. There should be operationalization of the Tanzania Cancer Treatment guidelines of 2020 for gastric cancer to ensure all patients are offered standardized care.

iii. Steps should be taken to enhance the early detection of gastric cancer at the primary health care level.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2018;68(6):394–424.

2. Globocan 2018 Africa Fact Sheet [Internet]. [cited 2020 Jul 14]. Available from: https://gco.iarc.fr/today/data/factsheets/populations/903-africa-fact-sheets.pdf

3. Globocan 2018 Tanzania Fact sheet.

4. Rawla P, Barsouk A. Epidemiology of gastric cancer: Global trends, risk factors and prevention. Przeglad Gastroenterologiczny. 2019;14(1):26–38.

5. Mukaisho KI, Nakayama T, Hagiwara T, Hattori T, Sugihara H. Two distinct etiologies of gastric cardia adenocarcinoma: Interactions among pH, Helicobacter pylori, and bile acids. Frontiers in Microbiology. 2015;6(MAY):11.

6. Shi Y, Hu Z, Wu C, Dai J, Li H, Dong J, et al. A genome-wide association study identifies new susceptibility loci for non-cardia gastric cancer at 3q13.31 and 5p13.1. Nature Genetics. 2011 Dec;43(12):1215–8.

7. Balakrishnan M, George R, Sharma A, Graham DY. Changing Trends in Stomach Cancer Throughout the World.

8. Sitarz R, Skierucha M, Mielko J, Offerhaus GJA, Maciejewski R, Polkowski WP, et al. Gastric cancer : epidemiology , prevention , classification , and treatment. Cancer Management and Research. 2018 Feb 7;10:239–48.

9. Wang J, Sun Y, Bertagnolli MM. Comparison of Gastric Cancer Survival Between Caucasian and Asian Patients Treated in the United States: Results from the Surveillance Epidemiology and End Results (SEER) Database. Annals of Surgical Oncology. 2015 Sep 12;22(9):2965–71.

10. Asombang AW, Rahman R, Ibdah JA, Asombang AW, Rahman R, Ibdah JA. Gastric cancer in Africa : Current management and outcomes. 2014;20(14):3875–9.

11. 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 Journal of Surgical Oncology. 2012;1–10.

12. Rana N, Gosain R, Lemini R, Wang C, Gabriel E, Mohammed T, et al. Socio-demographic disparities in gastric adenocarcinoma: A population-based study. Cancers. 2020;12(1):1–10.

13. Katai H, Ishikawa T, Akazawa K, Isobe Y, Miyashiro I, Oda I, et al. Five-year survival analysis of surgically resected gastric cancer cases in Japan: a retrospective analysis of more than 100,000 patients from the nationwide registry of the Japanese Gastric Cancer Association (2001–2007). Gastric Cancer. 2018;21(1):144–54.

14. A. A, A.Y. U, J.G. M, I. M, Ahmed A, Ukwenya AY, et al. Management and outcome of gastric carcinoma in Zaria, Nigeria. African Health Sciences. 2011;11(3):353–61.

15. Ibingira CBR. Management of cancer of the stomach in Mulago hospital Kampala, Uganda. East African Medical Journal. 2001;

16. Yu J, He Y, Guo Z. Age trend of the male to female sex ratio in surgical gastric cancer patients at a single institution. World Journal of Surgical Oncology. 2014 Aug 21;12(1).

17. Sun B, Ma T, Ding J, Ai S, Cao M, Zhu Z, et al. Gender differences of risk factors for early gastric cancer with lymph node metastasis. Vol. 10, Int J Clin Exp Med. 2017.

18. Roder DM. The epidemiology of gastric cancer. Vol. 5, Gastric Cancer. 2002.

19. RS S, KL H. Trends in gastric cancer sex ratio in the United States. Cancer. 1987;59(5).

20. Li X, Deng Y, Tang W, Sun Q, Chen Y, Yang C, et al. Urban-rural disparity in cancer incidence, mortality, and survivals in Shanghai, China, during 2002 and 2015. Frontiers in Oncology. 2018;8(DEC):579.

21. Nachaeva M, Grjibovski A, Izmailov T, Ruzhnikova A, Solovyova E, Dubovichenko D, et al. Anuari estadístic de Catalunya. Població 1 gener. European Journal of Public Health. 2016 Oct 1;26(6):1006–10.

22. Tjulandin SA, Tryakin AA, Besova NS, Sholokhova E, Ivanova JI, Cheng WY, et al. Real-world treatment patterns among patients with advanced gastric cancer in Russia: a chart review study. Journal of Drug Assessment. 2019 Jan 1;8(1):150–8.

23. Stock M, Otto F. Gene deregulation in gastric cancer. Gene. 2005 Oct 24;360(1):1–19.

24. Ntakiyiruta G. Gastric cancers at Kibogora Hospital. East and Central African Journal of Surgery. 2009;14(1):130–4.

25. Kendig C, Samuel J, Tyson A, Khoury A, Boschini L, Mabedi C, et al. Cancer Treatment in Malawi: A Disease of Palliation. World Journal of Oncology. 2013;4(3):142–6.

26. Eskandar H, Mohammad Hossein SS, Rahim M, Jalal H, Mehrdad A, Rajabi T. Clinical profile of gastric cancer in Khuzestan, southwest of Iran. World Journal of Gastroenterology. 2006 Aug 14;12(30):4832–5.

27. M S-M, WY J-F, A M-F, M E, MT A-A, G N, et al. Cervical cancer survival in sub-Saharan Africa by age, stage at diagnosis and Human Development Index: A population-based registry study. International journal of cancer [Internet]. 2020 Dec 1 [cited 2021 Oct 11];147(11):3037–48. Available from: https://pubmed.ncbi.nlm.nih.gov/32449157/

28. Pervaiz R, Faisal F. Cancer incidence and mortality are associated with human development index and health setups in Africa. Journal of the Egyptian National Cancer Institute. 2017 Sep 1;29(3):123–6.

29. Johnson O, Ersumo T, Ali A. Gastric carcinoma at Tikur Anbessa hospital, Addis Ababa. East African Medical Journal. 2000;77(1):27–30.

30. A. A, A.Y. U, J.G. M, I. M, Ahmed A, Ukwenya AY, et al. Management and outcome of gastric carcinoma in Zaria, Nigeria. African Health Sciences. 2011;11(3):353–61.

31. Barad AK, Mandal SK, Harsha HS, Sharma BM, Singh TS. Gastric cancer-a clinicopathological study in a tertiary care centre of North-eastern India. Journal of Gastrointestinal Oncology. 2014;5(2):142–7.

32. Qiu MZ, Cai MY, Zhang DS, Wang ZQ, Wang DS, Li YH, et al. Clinicopathological characteristics and prognostic analysis of Lauren classification in gastric adenocarcinoma in China. Journal of Translational Medicine. 2013 Mar 6;11(1).

33. Fall B, Dieng M, Mbengue M, Dangou JM. Care management of lower gastric tumors at Dakar. Preliminary study of 60 cases. Dakar médical. 2003;48(1):50–3.

34. Ayite AE, Adodo K, Dosseh E, Abita T, Ocloo A. [Management of primary gastric cancer at university hospitals in Lome. Report of 63 cases]. La Tunisie medicale. 2004 Aug;82(8):747–52.

35. H S, J F, RL S, M L, I S, A J, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: a cancer journal for clinicians [Internet]. 2021 May [cited 2021 Oct 6];71(3):209–49. Available from: https://pubmed.ncbi.nlm.nih.gov/33538338/

36. Jeffrey J. Walline. Designing Clinical Research: an Epidemiologic Approach, 2nd Ed. In: Optometry and Vision Science. 2001. p. 75.

37. Obayo S, Lukwago L, Orem J, Faulx AL, Probert CS. Gastrointestinal malignancies at five regional referral hospitals in Uganda. African Health Sciences. 2017;17(4):1051–8.

38. Ledonyo H, Rogena E SiS. Gastric Cancer in Kenya. African Journal of Health Sciences. 2018;31(1):51–9.

39. Braga-Neto MB, Carneiro JG, de Castro Barbosa AM, Silva IS, Maia DC, Maciel FS, et al. Clinical characteristics of distal gastric cancer in young adults from Northeastern Brazil. BMC Cancer. 2018 Feb;18(1):131.

40. Al-Refaie WB, Hu CY, Pisters PWT, Chang GJ. Gastric adenocarcinoma in young patients: A population-based appraisal. Annals of Surgical Oncology. 2011 Oct;18(10):2800–7.

41. Santoro R, Carboni F, Lepiane P, Ettorre GM, Santoro E. Clinicopathological features and prognosis of gastric cancer in young European adults. British Journal of Surgery. 2007 Jun;94(6):737–42.

42. Wang Z, Xu J, Shi Z, Shen X, Luo T, Bi J, et al. Clinicopathologic characteristics and prognostic of gastric cancer in young patients. Scandinavian Journal of Gastroenterology. 2016 Sep;51(9):1043–9.

43. Axon A. Symptoms and diagnosis of gastric cancer at early curable stage. Best Practice and Research: Clinical Gastroenterology. 2006;20(4):697–708.

44. Maconi G, Manes G, Porro GB. Role of symptoms in diagnosis and outcome of gastric cancer. Vol. 14, World Journal of Gastroenterology. Baishideng Publishing Group Inc; 2008. p. 1149–55.

45. Zhu L, Qin J, Wang J, Guo T, Wang Z, Yang J. Early Gastric Cancer: Current Advances of Endoscopic Diagnosis and Treatment. Vol. 2016, Gastroenterology Research and Practice. Hindawi Limited; 2016.

46. Smith S, Fowora M, Pellicano R. Infections with Helicobacter pylori and challenges encountered in Africa. Vol. 25, World Journal of Gastroenterology. Baishideng Publishing Group Co., Limited; 2019. p. 3183–95.

47. Holster IL, Aarts MJ, Tjwa ETTL, Lemmens VEPP, Kuipers EJ. Trend breaks in incidence of non-cardia gastric cancer in the Netherlands. Cancer Epidemiology. 2014 Feb;38(1):9–15.

48. Anderson WF, Rabkin CS, Turner N, Fraumeni JF, Rosenberg PS, Camargo MC. The Changing Face of Noncardia Gastric Cancer Incidence Among US Non-Hispanic Whites. JNCI: Journal of the National Cancer Institute. 2018 Jun;110(6):608–15.

49. Kaneko S, Yoshimura T, by histological types J. Time trend analysis of gastric cancer incidence in Japan by histological types, 1975•1989. 2001;

50. Eom BW, Jung KW, Won YJ, Yang H, Kim YW. Trends in gastric cancer incidence according to the clinicopathological characteristics in Korea, 1999-2014. Cancer Research and Treatment. 2018 Oct;50(4):1343–50.

51. Yu C-W, Levison D, Dunn J, Ward L, Demonakou M, Allum W, et al. Pathological prognostic factors in the second British Stomach Cancer Group trial of adjuvant therapy in resectable gastric cancer. British Journal of Cancer. 1995 May;71(5):1106–10.

52. Garnier P, Vielh P, Asselain B, Durand JC, Girodet J, Pilleron JP, et al. [Prognostic value of the Lauren and Ming classifications in gastric adenocarcinoma. Multidimensional analysis]. Gastroenterologie clinique et biologique. 12(6–7):553–8.

53. Ma J, Shen H, Kapesa L, Zeng S. Lauren classification and individualized chemotherapyin gastric cancer (Review). Oncology Letters Spandidos Publications; May 1, 2016 p. 2959–64.

54. Chen YC, Fang WL, Wang RF, Liu CA, Yang MH, Lo SS, et al. Clinicopathological Variation of Lauren Classification in Gastric Cancer. Pathology and Oncology Research. 2016 Jan 1;22(1):197–202.

55. Asombang AW, Kayamba V, Banda L, Colditz G, Mudenda V, Zulu R, et al. Gastric Malignancy Survival in Zambia, Southern Africa: A two year follow up study. Medical Journal of Zambia. 2014;41(1):13-18–18.

56. Alshehri A, Alanezi H, Kim BS. Prognosis factors of advanced gastric cancer according to sex and age. World Journal of Clinical Cases. 2020 May;8(9):1608–19.

57. Zytoon AA, El-Atfey SIB, Hassanein SAH. Diagnosis of gastric cancer by MDCT gastrography: diagnostic characteristics and management potential. Egyptian Journal of Radiology and Nuclear Medicine. 2020 Dec 1;51(1):1–7.

58. Sharara SM, Nagi MA, Soliman SS. Multidetector computed tomography in the evaluation of gastric malignancy; A multicenteric study. Egyptian Journal of Radiology and Nuclear Medicine. 2018 Jun 1;49(2):304–9.

59. Almeida MFA, Verza L, Bitencourt AGV, Boaventura CS, Barbosa PNVP, Chojniak R. Computed tomography with a stomach protocol and virtual gastroscopy in the staging of gastric cancer: An initial experience. Radiologia Brasileira. 2018 Jul 1;51(4):211–7.

60. Tomizawa M, Shinozaki F, Fugo K, Hasegawa R, Shirai Y, Motoyoshi Y, et al. Detection of gastric cancer using transabdominal ultrasonography is associated with tumor diameter and depth of invasion. Experimental and Therapeutic Medicine. 2015 Nov 1;10(5):1835–9.

61. Yu XZ, Yang YN, Li JG. Application of ultrasound in the diagnosis of gastrointestinal tumors. European Journal of Inflammation. 2020 Oct 19;18.

62. Machairas N, Charalampoudis P, Molmenti EP, Kykalos S, Tsaparas P, Stamopoulos P, et al. The value of staging laparoscopy in gastric cancer. Vol. 30, Annals of Gastroenterology. Hellenic Society of Gastroenterology; 2017. p. 287–94.

63. Oida T, Kano H, Mimatsu K, Kawasaki A, Kuboi Y, Fukino N, et al. Technical considerations in laparoscopic staging for advanced gastric cancer. Hepato-Gastroenterology. 2012 Jan;59(113):164–7.

64. Fukagawa T. Role of staging laparoscopy for gastric cancer patients. Vol. 3, Annals of Gastroenterological Surgery. Wiley-Blackwell Publishing Ltd; 2019. p. 496–505.

65. Riihimäki M, Hemminki A, Sundquist K, Sundquist J, Hemminki K. Metastatic spread in patients with gastric cancer. Oncotarget. 2016 Aug;7(32):52307–16.

66. Hioki M, Gotohda N, Konishi M, Nakagohri T, Takahashi S, Kinoshita T. Predictive factors improving survival after gastrectomy in gastric cancer patients with peritoneal carcinomatosis. World Journal of Surgery. 2010 Mar;34(3):555–62.

67. Ellison LM, Man Y, Stojadinovic A, Xin H, Avital I. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in treatment of gastric cancer with peritoneal carcinomatosis. Vol. 29, Chinese Journal of Cancer Research. AME Publishing Company; 2017. p. 86–92.

68. Bonnot PE, Piessen G, Kepenekian V, Decullier E, Pocard M, Meunier B, et al. Cytoreductive Surgery with or without Hyperthermic Intraperitoneal Chemotherapy for Gastric Cancer with Peritoneal Metastases (CYTO-CHIP study): A propensity score analysis. In: Journal of Clinical Oncology. American Society of Clinical Oncology; 2019. p. 2028–40.

69. Manzanedo I, Pereira F, Rihuete Caro C, Pérez-Viejo E, Serrano Á, Gutiérrez Calvo A, et al. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Gastric Cancer with Peritoneal Carcinomatosis: Multicenter Study of Spanish Group of Peritoneal Oncologic Surgery (GECOP). Annals of Surgical Oncology. 2019 Aug 15;26(8):2615–21.

70. van der Kaaij RT, Wassenaar ECE, Koemans WJ, Sikorska K, Grootscholten C, Los M, et al. Treatment of PERItoneal disease in Stomach Cancer with cytOreductive surgery and hyperthermic intraPEritoneal chemotherapy: PERISCOPE I initial results. British Journal of Surgery. 2020 Oct 1;107(11):1520–8.

71. Foerster M, Anderson BO, McKenzie F, Galukande M, Anele A, Adisa C, et al. Inequities in breast cancer treatment in sub-Saharan Africa: Findings from a prospective multi-country observational study. Breast Cancer Research. 2019 Aug 13;21(1):93.

APPENDICES

Appendix I: Data Collection Checklist

1. Serial Number ………………
2. MRN …………………………….
3. Sex of patient
    i. Male
    ii. Female
4. Age of Patient ……………. years

Clinical Presentation

5. Presenting Signs and Symptoms
    i. ………………………………………….
    ii. ………………………………………….
    iii. ………………………………………….
    iv. …………………………………………..
    v. …………………………………………

6. Duration of symptoms ………………………

7. Diagnostic Investigations Done
    i. …………………………………………………………………………………………
    ii. …………………………………………………………………………………………
    iii. …………………………………………………………………………………………
    iv. …………………………………………………………………………………………....
    v. …………………………………………………………………………………………

8. H. pylori Serology
    i. Positive
    ii. Negative
    iii. Not Documented

9. OGD Results if Done

    i.   Tumor location …………………………………………………….

    ii.   Borrmann Classification …………………………………………

10. Histological Type …….………………………………………………………..

11. Histological grade …………………………………………………………………...

12. TNM Staging

    i.   T …………………

    ii.   N …………………

    iii.   M ………………..

    iv.   STAGE ………….

13. Treatment path

    i.   Surgery + Adjuvant therapy

    ii.   Neo-Adjuvant therapy + Surgery

    iii.   Treatment of systemic disease without resection

14. Type of Surgery Performed

    i.   Partial distal gastrectomy

    ii.   Total gastrectomy

    iii.   Gastro-jejunostomy

    iv.   Exploration + Biopsy

15. Extent of LN dissection (for resection)

    i.   D0

    ii.   D1

    iii.   D2

    iv.   Not Documented

16. Post-Operative Complications ……………………………………….

17. Duration of Hospital Stay ……………………………………………….

18. Outcome of Admission
    i.   Discharged
    ii.   Died