DIAGNOSES OF SPECIMENS COLLECTED THROUGH FLEXIBLE BRONCHOSCOPY FROM PATIENTS AT MUHIMBILI NATIONAL HOSPITAL JANUARY 2013 TO NOVEMBER 2017

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Department of Internal Medicine

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By

Deusdedit J. Ndilanha

A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Internal Medicine) of

Muhimbili University of Health and Allied Sciences
October, 2018

CERTIFICATION

The undersigned certify that, she has read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: **"Diagnoses of specimens collected through flexible bronchoscopy patients at Muhimbili National Hospital January 2013 to November 2017"**, in (partial) fulfillment of the requirement for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences.

_____

Dr. Grace Shayo

(Supervisor)

_____

Date

DECLARATION AND COPYRIGHT

I, **Dr. Deusdedit Javan Ndilanha**, 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:** ……

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My sincere gratitude should extend to my employer Ministry of Defense for partly funding this study.

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I would like to thank all the staff members of the Muhimbili National Hospital for their support and contribution in the fulfillment of this dissertation.

DEDICATION

To Rosemary Bilikundi my wife and our children Joyce, Nicole and Sasha

To my parents Mr. and Mrs. J. Ndilanha and my Guardian George B. Nyamugali

To Dr. Grace Shayo, my supervisor

ABSTRACT

Background: Flexible bronchoscopy is the technique of visualizing the respiratory airway mucosa from the oropharynx to third generation branching. It is useful in the diagnosis of lung malignancies, lung infections, inflammatory conditions and interstitial lung diseases. It is more than a decade since flexible bronchoscopy was first used at Muhimbili National Hospital in routine diagnosis of pulmonary conditions. Despite its use for several years the diagnoses made have not been structurally organized and studied

Objective: The study aimed at describing diagnoses of all specimens collected from patients who underwent bronchoscopy at MNH in the past five years from January 2013 to November 2017.

Methodology: A retrospective hospital based cross sectional study was conducted among 451 patients and 360 patents had sample collected for analysis. Data collected included demographic and clinical variables. Descriptive statistics were used to summarize the study findings

Results: The number of flexible bronchoscopy increased from 57 cases in 2013 to 180 cases in 2017, a more than threefold increase. Bronchoscopic samples studied included lung biopsies which accounted to 48.3% (174/360) and fluid samples (bronchioalveolar lavage and bronchial washings) which accounted to 80.8% (291/360). Adenocarcinoma was the most common lung cancer among all lung histological subtypes accounting to 33.9% (59/174). Generally, 64.3% (112/174) of all lung biopsies were malignant. Of 76 fluid sample sent for bacterial culture and sensitivity, 11/76 (11.8%) were culture positive, 49/76 (64.5%) did not grow any bacteria, 18/76 (23.7%) isolated normal flora. A total of 6 (10.7%) out of 56 samples which were sent for *M.tuberculosis* screening through GeneXpert MTB/RIF technology tested positive for *M.tuberculosis.*

Conclusion: Lung tumor was the leading indication for bronchoscopy. Adenocarcinoma was the most common malignancy among others. Bacterial infections were among the reported findings in cytological samples.

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LIST OF ABBREVIATIONS

AFB	Acid Fast Bacilli
CRF	Clinical record form
GHSP	Global Health Service Partnership
HIV	Human Immunodeficiency Virus
HR CT	High resolution computer tomography
ICU	Intensive care unit
ILD	Interstitial Lung Diseases
MAMC	MUHAS Academic Medical Center
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
PI	Principle Investigator
PJP	Pneumocystic Jirovecii Pneumonia
PTB	Pulmonary Tuberculosis

CHAPTER ONE

1.0 BACKGROUND

1.1 Bronchoscopy

Bronchoscopy is an endoscopic procedure that utilizes the technique for visualizing the respiratory tree mucosa all the way from the oropharynx to the third generation of branching. Bronchoscopy can be employed for either diagnostic or therapeutic purposes of lung conditions. The bronchoscopy procedure is usually performed in a specialized procedure room such as; bronchoscopy room, in theater, at emergency department or on bedside for patients admitted in Intensive Care Unit (ICU). Whether the patient have to undergo rigid or flexible bronchoscopy depends much on the indication for the procedure. In the bronchoscopy room a patient is either put on conscious sedation if he/she is to undergo flexible bronchoscopy or put on general anesthesia if a patient will undergo rigid bronchoscopy. A successful bronchoscopy needs the availability of the following equipment namely; bronchoscope, light source, biopsy forceps, cytology brushes, needle aspiration catheters, supplemental oxygen, suction apparatus, pulse oximetry, sphygmomanometer and resuscitation kit. The bronchoscopy team consists of a endoscopist, registered nurse who is trained in bronchoscopy, respiratory therapist and other supporting staff who are familiar with procedure and handling of the specimens(1,2).

1.2. Types of Bronchoscopes

1.2.1 Flexible Bronchoscope

Flexible bronchoscope is the smallest type of bronchoscope. It has the ability to access the respiratory mucosa from proximal to the distal airways such as the third order bronchi. Flexible bronchoscope consists of a flexible sheath that contains cables that allow the tip of the bronchoscope to be flexed and extended. It also has fiber optic wires for transmitting endobronchial images, a light source, and a working channel(3).

The flexible bronchoscope can be used for both diagnostic and therapeutic purposes. The diagnostic uses include; bronchoalveolar lavage (BAL) sampling, transbronchial biopsy,

bronchial washing or brushing, transbronchial needle aspiration and endobronchial ultrasound, whereas the therapeutic uses include balloon dilatation, endobronchial laser ablation, electrocautery, photodynamic therapy and at times used for stent placement(4).

1.2.2 Bronchoscopy Procedure

Patients are required to fast for about four hours before the procedure is done. Upon arrival into the bronchoscopy room, an intravenous access is established first. The patient is then placed into examination bed either in a semi-recumbent or supine position. Topical anesthetic agents are applied to the pharynx and nasal passage. Shortly after the topical anesthetic effect has taken place the scope is introduced either through the nose or mouth. When the scope arrives at the vocal cord the patient is given another topical anesthesia to allow smooth passage through the cord. Having passed through the vocal cord then the rest of the respiratory airway can be examined(5).

1.2.3. Indications for Flexible Bronchoscopy

The indications for flexible bronchoscopy are numerous. The choice of a particular indication depends much on the present chest symptoms or abnormal radiographic findings that warrant investigation. The indications for flexible bronchoscopy can be categorized into diagnostic or therapeutic. Common diagnostic indications include; patient with suspected pneumonia who cannot produce sputum, patients with hemoptysis, and sampling lung nodules or lymph nodes that are within or adjacent to the airways. Common therapeutic indications include; the removal of excess mucus or foreign bodies, the treatment of endobronchial abnormalities, and endobronchial stents placement(1,3).

1.2.4. Contraindications to Flexible Bronchoscopy

Flexible bronchoscopy is a procedure that has notable risks for causing the following complications; bronchospasm, hypoxemia, pneumothorax, seizure, bleeding and cardiac arrhythmias. Based on these possible complications, the following have been stated to be the major contraindications for the procedure namely, uncontrolled heart failure, recent myocardial ischemia, notable hypotension or hypertension, exacerbation of chronic obstructive pulmonary diseases or asthma, life-threatening cardiac arrhythmia. Apart from these absolute

contraindications, other relative contraindications includes; history of recent anticoagulant usage, low platelets count, bleeding tendencies and renal failure(1,6).

In conjunction to the above indications and contraindications, flexible bronchoscopy is reported to have a number of advantages. These advantages include; the ability to access distal airways, easily tolerated by most patients and it doesn't require general anesthesia. Flexible bronchoscope is, however not suitably applied for large and deeper biopsies(1,3,7).

1.3 Rigid Bronchoscope

This is another type of bronchoscope which can be used for both therapeutic and diagnostic purposes. In recent years its use has significant lost popularity following the advent of flexible bronchoscope. Rigid bronchoscopy is however reported to be the best choice for interventional procedures such as removal of foreign bodies and removal of large biopsies. Compared to flexible bronchoscope, rigid bronchoscope is relatively large, more rigid and thus can best be used to access proximal part of the respiratory tract from the oropharynx to the tracheobronchial junction. In some special circumstances, rigid bronchoscope can be combined with flexible bronchoscope to access distal respiratory airway(5,8). For rigid bronchoscopy to be done successful a minimum of the following equipment are required, these equipment include; different sized ventilating bronchoscopes, light sources, telescopes which are to be placed at 0, 30 and 90 degrees down the rigid barrel, biopsy forceps, graspers and suction devices, normal saline and lubricant jelly(8).

1.3.1. The Rigid Bronchoscopy Procedure

A pre-procedure fasting of about eight hours is required. While the patient is on examination bed, the patient lies in a supine position and head placed onto a pillow on the examination table. The examination table is of the type which can be flexed or extended accordingly. The patient is then given general anesthesia plus sedation and muscle relaxants. The bronchoscope is then introduced, in the process, the epiglottis is gently lifted with the end of the bronchoscope henceforth the larynx and vocal cord can be seen. Upon visualization of the vocal cords, the bronchoscope is turned 90 degrees vertically in order to pass through it. Once

the vocal cord is passed the bronchoscope is turned back to its normal neutral position. At this point of the procedure, the ventilation is initiated through the side ports of the bronchoscope. The bronchoscope is further gently advanced towards the carina and systematically inserted into each main bronchus(5,8).

1.3.2. Indication for Rigid Bronchoscopy

Rigid bronchoscopy has been of useful importance in the management of massive hemoptysis, intrabronchial bleeding, large volume deeper biopsy, extraction of foreign bodies, tracheal or bronchial stenosis dilatation, endobronchial obstruction by tumors, stent placement and mechanical tumor ablations and tracheobronchial laser therapy(8).

1.3.3. Contraindications for Rigid Bronchoscopy

Rigid bronchoscopy would not be suitably performed in the following situations; Patients in acute respiratory distress, patients with unstable cervical spine, obstructive diseases of the oral or larynx and severe maxillofacial trauma. Despite these notable contraindications, rigid bronchoscopy is as well not free of the possible complications that can occur. Major complications that have frequently been reported includes; trauma to teeth and gums, tracheobronchial tear and severe bleeding. Despite the just mentioned complications, rigid bronchoscopy has been reported to have the following advantages; used for deeper and large bronchial biopsies, has the ability to accommodate other accessory tools during the procedure, has larger suction ability, it allows direct airway control during the procedure and is good for prolonged bronchoscopy. However, it requires general anesthesia which is the greatest disadvantage(3,5).

1.4 Bronchoalveolar Lavage (BAL)

This is a medical procedure of taking samples from the respiratory tree during a bronchoscopy. Usually, a small amount (about 20mls) of sterile saline is instilled endoscopically into the respiratory tree and then aspirated. The collected sample is then sent for laboratory analysis. The sampled fluid is useful in the diagnosis of a number of lung diseases such as lung cancer and lung infections. Of particular importance, endoscopic sampling of fluids for cytological

and microbiological analysis is the best alternative especially in patients admitted in ICU. Other techniques along with BAL are bronchial brushing and bronchial washing. The later procedures, when employed in combination with other bronchoscopic sampling techniques have been reported to have complementary yield in the diagnosis of lung pathologies (9).\

1.5. Bronchoscopy in Lung Infections

The use of bronchoscopy to obtain respiratory samples can be used in the diagnosis of both upper and lower respiratory infections but often its use is mostly employed in lower respiratory infections. A bronchoscopic sampling in search for a particular infection is reported to have gained new vigor after HIV/AIDS infections became pandemic. It is reported that the HIV/AIDS infections have changed most of the classical presentation of wide range of diseases making the diagnosis difficult with the use of none invasive procedure (conventional methods). The growing population of immunosuppressed patients has also caused the occurrence of wide range of opportunistic lung infections notably in Sub-Saharan Africa where HIV is more prevalent. The common opportunistic infections among others which often times will require the use of bronchoscopy to obtain samples for respiratory tree for microbiological diagnosis includes; *Mycobacterium tuberculosis* especially in smear-negative individuals and *Pneumocystis jirovecii* pneumonia (PJP). Bronchoscopic sampling also is useful in patients admitted in Intensive Care Unit (ICU) who acquire chest infections while on a ventilator(1,10–12).

1.6 Bronchoscopy in Interstitial Lung Diseases (ILD)

Bronchoscopy has also been of valuable importance in the diagnosis of interstitial lung diseases notably in combination with radiological findings. Except for idiopathic pulmonary fibrosis which requires no histopathological diagnosis due to its classical pattern on High-Resolution Computed Tomography (HR-CT Scan), other diseases that are included in this spectrum of diseases that make ILD require lung biopsy to make a histological confirmation of the diagnosis. Bronchoscopic biopsy is currently the most advocated option compared to open lung biopsy due to its safety and fewer mortality rates that have been reported(13–15).

1.7 Bronchoscopy in Lung Neoplasms

Patients who present with symptoms, signs and radiological features which are suggestive of a lung neoplasm have usually required bronchoscopic examinations to confirm or refute the diagnosis. In recent years bronchoscopy has almost surpassed open lung biopsy which was previously the diagnostic procedure of choice in lung nodules sampling. Except in some few situations where open lung biopsy is mandated, the choice of bronchoscopy to open lung biopsy is based on recently published data which are in favor of bronchoscopy. Bronchoscopy is employed for both central and peripheral lung lesions. Either a rigid or flexible bronchoscopy can be used in sampling of lung neoplasm depending on the lesion size, location in the lung parenchyma.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.0.1 Bronchoscopy in Lung infections

A retrospective cross-sectional study carried out at Mulago Hospital in Uganda assessed the cause of lower respiratory infection among HIV-infected adults with sputum AFB smear-negative. Among the bronchioalveolar lavage samples assessed during the study, it was revealed that 38.6% had carinii pneumonia, 24% had Mycobacterium tuberculosis and 11% had pulmonary Kaposi's sarcoma and pyogenic infection was found in 8% (10, 11).

Whereas a cross-sectional study in Thailand which recruited patients who were suspected to have mycobacterium tuberculosis and had minimal infiltrated on chest x- ray plus smear negative for AFB. It was revealed that bronchoscopy facilitated the diagnosis of M. tuberculosis in 47.5% of all studied patients (16)

A prospective cohort study was conducted in Lilongwe Malawi among smear negative TB suspects due to start anti TB. The patients were to undergo bronchoscopy and their bronchioalveolar lavage analyzed. It was found that 39% were confirmed to have Mycobacterium *tuberculosis*, 37% no diagnosis confirmed, 14% had other non-TB infections, Kaposi's sarcoma 3%, other diagnosis 6% (12).

2.0.2 Bronchoscopy in lung Neoplasm

The yield of bronchoscopy for neoplastic lesions is reported to range between 64-82%. Moreover, the yield has been shown to increase to as high as 93% when bronchoscopy is coupled with other bronchoscopic techniques such as BAL and brush cytology(17–19)**.** A cohort study carried out in Japan between 1984 and 2000 looked at the various cytological examinations of samples obtained by bronchoscopy in the diagnosis of peripheral lung lesions. The study revealed that 88.3% of patients who underwent bronchoscopy were diagnosed to have lung cancer from the results of their first bronchoscopic examination, 82.1% from the second, third and subsequent examinations. Accordingly, the overall diagnostic rate by bronchoscopy was 93.4% (19).

An observational study in India looked at the role of fiber optic bronchoscopy in the histopathological analysis of lung lesions. The study revealed that 55% of all bronchoscoped subjects had malignant lesions. Histologically, the most common malignant lesion was squamous cell carcinoma, followed by adenocarcinoma and lastly small cell carcinoma(17). Whereas another retrospective 2 years study in India which looked at the role of flexible fiber optic bronchoscopy in the diagnosis of pulmonary diseases. The study found that malignancy was diagnosed in 68% of all suspected cases (20)

In Houston Texas, a four years retrospective analysis study was carried out in a tertiary Hospital. The study analyzed the histopathological diagnosis of all the bronchoscopies performed among patients with pulmonary nodules. The results found that about 85% of the studied lesions were malignant lesions. Further analysis of the diagnosis made indicated that 53% were adenocarcinoma, 38% were squamous cell carcinoma and the rest were undifferentiated lesions(18).

2.0.3 Bronchoscopy in Interstitial lung diseases

Studies have also reported utility of bronchoscopy in the diagnosis and management of patients with interstitial lung diseases.

A prospective non-randomized study was carried out in India among patients with radiological features of diffuse parenchyma lung diseases. The histological diagnosis of interstitial lung disease was made in 85.7% of patients studied. Among the diagnoses made, the histological variants were 22.4% nonspecific interstitial lung pneumonia, 18.4% tuberculosis and granulomatous inflammatory diseases like sarcoidosis which accounted to 16.3%.The remaining percent was accounted by other rare pathologies that constitute ILD(13).

A prospective randomized controlled trial was carried out in New York. The study compared the efficacy and effectiveness of Cup versus Alligator biopsy in patients with suspected sarcoidosis. Sarcoidosis was similar in both groups 64.4% for cup forceps biopsy and 60.6% for alligator forceps(14).

Whereas a pragmatic systematic review of all unique citation related to BAL in patients with ILD that were published between 1970 and 2006, it was concluded that when used in conjunction with comprehensive clinical information and adequate thoracic imaging such as high resolution CT chest, The BAL cell pattern and other characteristics frequently provided useful information for the diagnosis evaluation of patents with suspected of ILD (21)

2.1 Problem Statement

The use of flexible bronchoscopy has made the diagnosis of different lung diseases much easier. The range of lung pathologies that can be diagnosed with the aid of bronchoscope includes chest infections (bacterial, fungal and parasitic), interstitial lung diseases as well as malignancies.

In some of the East and Central Africa countries the use of bronchoscopy made it possible the diagnosis of tuberculosis and other chest infections in patients whose diagnosis were not possible with the use of other means (12,22). Moreover, Lung cancer has been recently reported to be the overall most common cancer among other cancers in both male and females. It is projected that by 2025 the number of patients with lung cancer will double in the low and middle income countries where the burden is on the increase (23)

Unfortunately, there is paucity of organized data on the diagnosis made from the specimens that were collected endoscopically among patients who underwent bronchoscopy at MNH. There is therefore a diagnosis gap in that regard that needs to be addressed.

2.2 Rationale

It is more than a decade since flexible bronchoscopy was first used at Muhimbili National Hospital in routine diagnosis of pulmonary conditions. Despite its use for several years the diagnoses made have not been structurally organized and studied. This study was specifically conducted to describe the various diagnosis made among specimens from patients who underwent flexible bronchoscopy in the largest tertiary hospital in the country, The Muhimbili National Hospital.

Being the first study, which has organized the diagnoses from bronchoscopy specimens, its findings can be used as a benchmark for other similar researches in the hospital and the country as a whole**.**

2.3 Objectives

2.3.1 Broad Objective

To describe the diagnoses of specimens collected through flexible bronchoscopy at Muhimbili National Hospital from January 2013 to November 2017.

2.3.2 Specific Objectives

1. To describe the indications for bronchoscopy in patients who underwent flexible bronchoscopy at MNH from January 2013 to November 2017
2. To describe the histopathological diagnoses of all patients who underwent flexible bronchoscopy lung biopsies at MNH from January 2013 to November 2017.
3. To describe the cytological diagnoses of lung fluid specimens from all patients who underwent flexible bronchoscopy at MNH from January 2013 to November 2017
4. To describe the bacteriological diagnoses of lung fluid specimens of all patients who underwent flexible bronchoscopy and had endoscopic lesion suspicious for infections at MNH from January 2013 to November 2017

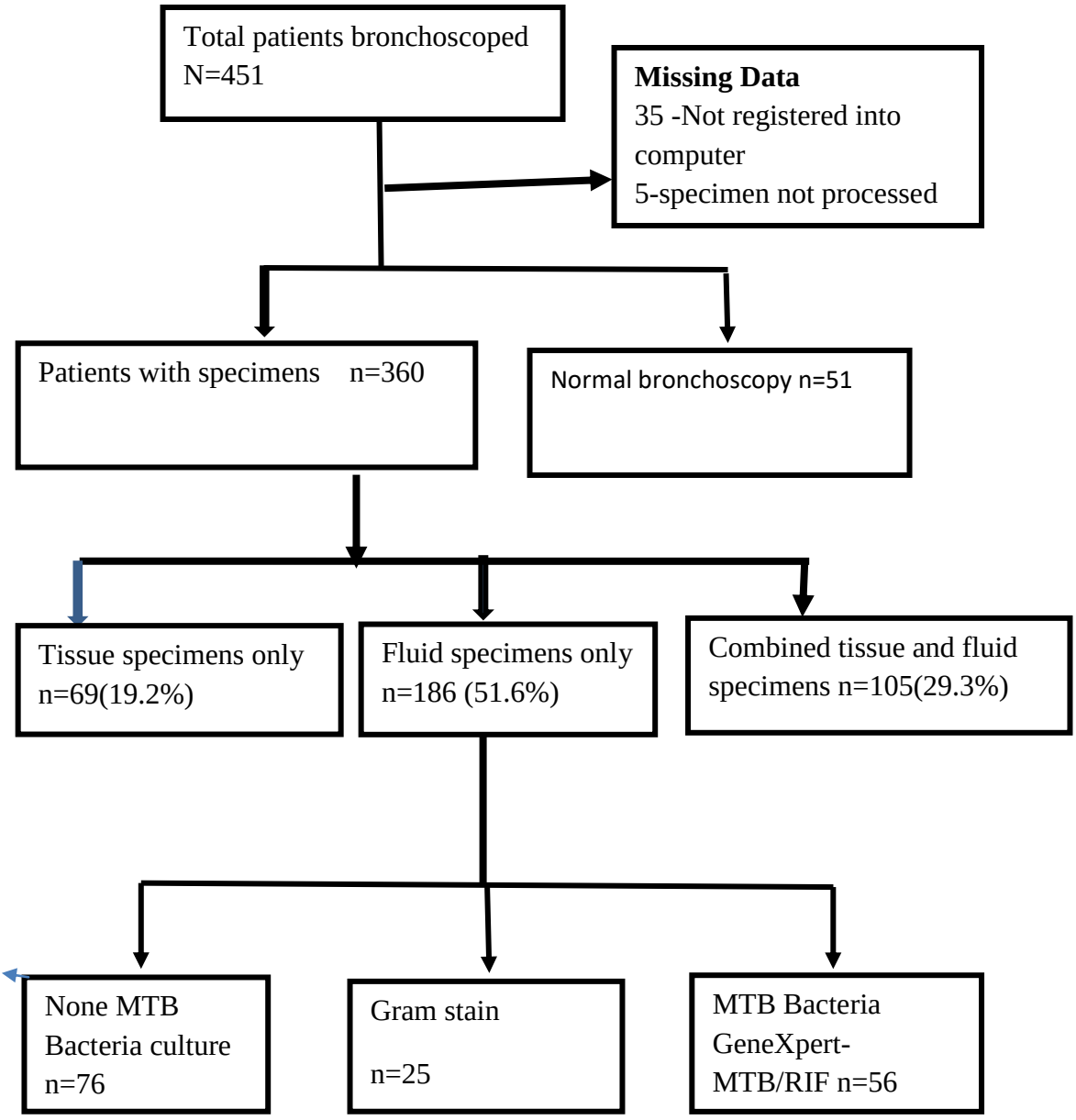


Figure 1: Flow chart showing the various specimens collected from patients

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

This was a hospital based descriptive cross-sectional study intended to use retrospective electronic/physical achieved data of all patients who underwent bronchoscopy from January 2013 to November 2017.

3.2 Study site

The study was done at Muhimbili National Hospital in Dar es Salaam. It covered a period of five years from January 2013 to November 2017. Muhimbili National Hospital is one of the four tertiary hospitals in the country. It is located in the Eastern Coast city of Dar es Salaam which is also the commercial capital city of Tanzania. MNH serves as a University teaching hospital for Muhimbili University of Health and Allied Sciences (MUHAS). MNH has pulmonary units in both medical and surgical departments. The units serve patients who are admitted in the hospital and those patients who come on outpatient basis. The bronchoscopy unit has a total of four trained bronchoscopist assisted by four medical/surgical specialists. The endoscopies are done every Monday on a weekly bases by the bronchoscopist in conjunction with the other bronchoscopy team. Bronchoscopy unit has a capacity of performing bronchoscopy in four to six patients per week.

3.3 Study population

The study utilized archived data of all patients who underwent bronchoscopy from January 2013 to November 2017 at MNH in Dar es Salaam. The unit has a standard operating procedure that requires all patients to be reviewed pre-bronchoscopy through history and physical examination. laboratory and radiological tests, i.e (sputum for AFB, chest x-ray and chest computer tomography) .Furthermore it is the standard of the unit that all patients with endobronchial tumorous lesions underwent biopsy whereas those without were subjected to bronchial lavage

The archived culture results are those who were read after 48 hours of incubation period and therefore didn't include culture results for M.*tuberculosis* which are not routinely done and requires a minimum incubation period of 6 weeks. Patients who underwent bronchoscopy either came from medical pulmonology clinic, chest surgery clinic, and medical and chest surgery wards for admitted patients or from other hospitals in/and outside Dar es Salaam.

3.3.1 Inclusion Criteria

Patients with the following characteristics were included

- Patients aged 18 years and above who underwent bronchoscopy from January 2013 to November 2017.

3.3.2 Exclusion criteria

None

3.4 Study period

The study covered a period of five years from January 2013 to November 2017.

3.5 Study duration

Data collection was done for six months from July to December 2017. It involved data from previous specimen collected and new specimen which were collected and had to be reported during the study period. Apart from the electronic data which were accessed patient files were also reviewed in search for patient data.

3.6 Sample size

Archived data of all patients who underwent bronchoscopy from January 2013 to November 2017 were studied.

3.7 Data Management

3.7.1 Data Collection Procedure

Having obtained the permission to conduct the study from the responsible authorities, bronchoscopy record books were accessed. Records of patients who underwent the procedure from January 2013 to November 2017 were obtained. This included patient's name and hospital registration number, age, sex and indications for bronchoscopy. Hospital registration number was used to trace patient's file which were used to extract information pertaining to clinical characteristics and risk factors for the occurrence of most of the lung pathologies. These files were also used for ascertainment of clinical respiratory conditions which made them to undergo bronchoscopy. Using the Hospital registration number and patient's name, the MNH Jeeva database was searched for patients' clinical records and laboratory histopathological, cytological and bacteriological results. The data collection was done by the principle investigator and Research assistant who is medical personnel. The obtained results were entered into clinical record forms (CRF).

3.7.2 Data Management and Analysis

Data were captured into the computer using EPI Info software version 3.0. Then the recorded data were transferred into SPSS version 20 for analysis. Descriptive statistics such as frequencies and their corresponding percentages were used to summarize categorical variables while continuous variables were summarized using mean and standard deviation.

3.8 Ethical Clearance

Ethical clearance was obtained from the MUHAS institution review board (IRB) and the permission to conduct the study was obtained from MNH administration. Confidentiality was maintained throughout the study by coding of patient's identifiers and therefore patient's identifiers did not appear in any place throughout the data set, data collected were confidentially stored into a computer such that unauthorized person could not access the information.

3.9 Sponsor

The study was sponsored by the Ministry of Defense of Tanzania, the later was not involved in any way during data collection and analysis.

CHAPTER FOUR

4.0 RESULTS

4.1 Socio-demographic Characteristics of Study Patients

A total of 451 patients underwent flexible bronchoscopy. Majority were male 269(59.6%). The mean (SD) age of the study participants was 54.06 (15.7) years. The age range was between 18 years and 91 years. A total of 283/451 (62.7%) patients were aged 50 years or older. Majority of the Patients were married 138(70.4%) and sixty eighty (45.9%) had attained primary education level. Majority were residing in Dar es Salaam 154/270(57%) (Table 1).

Table 1: Socio-demographic Characteristics of Study Patients (N=451)

Characteristics		Number	Percentage
Sex	Male	269	59.6
	Female	182	40.4
Age			
	18-29	34	7.5
	30-39	50	11.1
	40-49	84	18.6
	50-59	102	22.6
	60+	181	40.1
Marital Status n=196*			
	Single	30	15.3
	Married	138	70.4
	Widowed	18	9.2
	Widower	10	5.1
Education Level n=148*			
	Primary School	68	45.9
	Secondary School	38	25.7
	College or above	25	16.9
	No Formal Education	17	11.5
Residence n=270*			
	Dar es Salaam	154	57.0
	Outside Dar	116	43.0

*Participants with marital status, residency and/or Education level

4.2 Trend of Bronchoscopy at Muhimbili National Hospital.

From 2013 to 2017 a total of 451 bronchoscopy were done at MNH. During this period there were gradual increase in number of bronchoscopy year after year except for the year 2014 where there was a slight drop compared to yesteryear. Between 2016 and 2017, the procedures appeared to rise significantly compared to the preceding years. Comparatively there were 57 patients who underwent bronchoscopy in 2013 whereas there were 180 patients who underwent bronchoscopy from January to November 2017, a more than threefold increase from the 2013 annual number. (Figure 2)

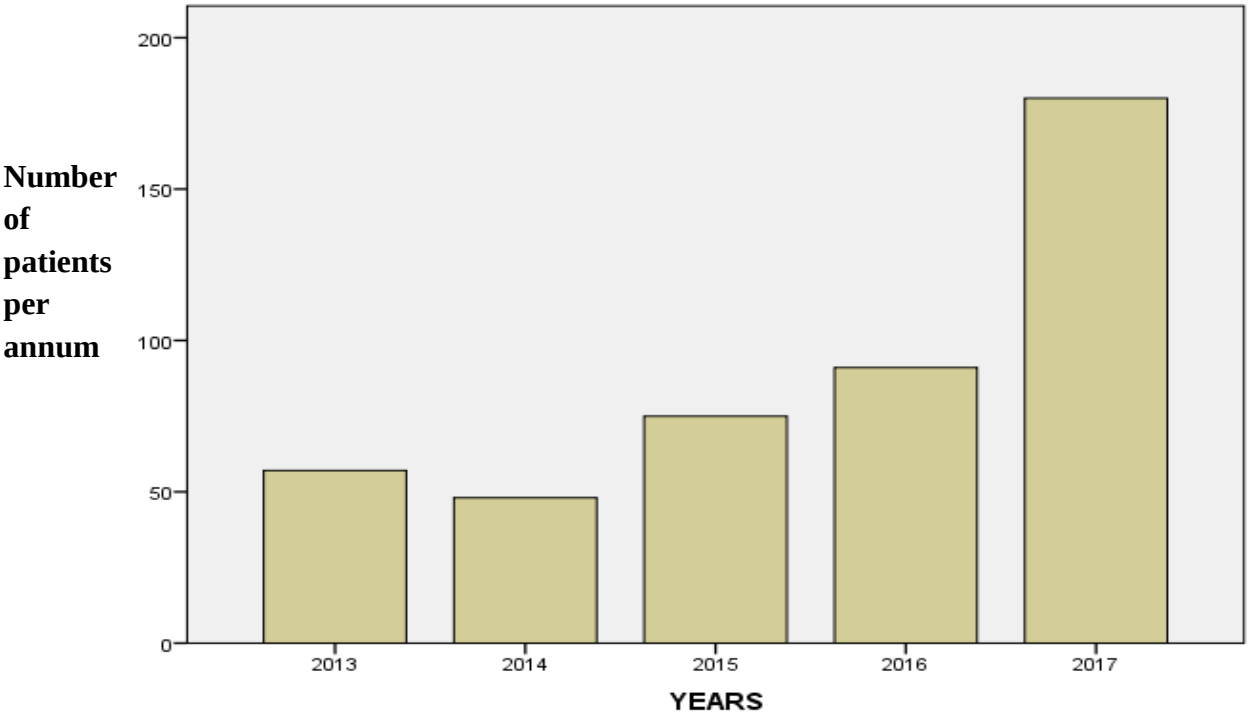


Figure 2: Bronchoscopy trend at Muhimbili National Hospital over a period of 5 years from 2013 to 2017

4.3 Indications for Bronchoscopy for all patients who underwent Bronchoscopy at Muhimbili National Hospital from 2013 to 2017

Bronchoscopy indications were lung tumors 305/451(67.6 %), bronchiectasis 24 /451(5.3%), hemoptysis-unexplained 21/451(4.7%), mediastinal mass 16/451(3.5%), cavitary lung diseases 16/451(3.5%), malignant-effusion 15/451(3.3%), aspergillosis 15/451(3.3%), pneumoconiosis 14/451(3.1%), lung collapse 10/451(2.2%), empyema locules 7/451(1.6%), atypical pneumonia 5/451(1.1%) and exploratory bronchoscopy 3(.7%) (Table 2).

Table 2: Indications for Bronchoscopy for all patients who underwent bronchoscopy at Muhimbili National Hospital from 2013 to 2017

Indication	Number	Percentage
Lung tumor	305	67.6
Bronchiectasis	24	5.3
Hemoptysis-unexplained	21	4.7
Mediastinal Mass	16	3.5
Cavitary lung diseases	16	3.5
Malignant Effusion	15	3.3
Aspergillosis	15	3.3
Pneumoconiosis	14	3.1
Lung collapse	10	2.2
Empyema Locules	7	1.6
Atypical pneumonia	5	1.1
Exploratory bronchoscopy	3	.7
Total	451	100.0

4.4 Histological findings for all patients who underwent lung biopsy through flexible bronchoscopy at Muhimbili National Hospital from January 2013 to November 2017.

Table 3 summarizes histological findings of 174/451 patients who underwent lung tissue biopsy. Of the 174 biopsies done majority were Adenocarcinoma 59/174(33.9%). Nonspecific acute/chronic inflammation was seen in 37/174(21.3%), squamous cell carcinoma 26/174(14.9), carcinoma not otherwise specified 16/174(9.2%) and small cell carcinoma 10/174 (5.7%). A total of 13/174(7.5%) samples were deemed inadequate and thus did not yields any results. Sarcoidosis, Aspergillosis and M.t*uberculosis* were the least found histological findings accounting to 1.7%, 1.1% and 1.1% respectively. One case of Kaposi's sarcoma was reported 0.6%. (Table 3)

Table 3: Histological findings of specimens collected among patients who underwent flexible bronchoscopic lung biopsy at Muhimbili National Hospital from 2013 to 2017, n=174

Histopathological findings	Subtypes	Number	Percentage
Malignancy	Adenocarcinoma	59	33.9
	Squamous cell carcinoma	26	14.9
	Carcinoma not otherwise classified	16	9.2
	Small cell lung carcinoma	10	5.7
	Kaposi's sarcoma	1	.6
Infection/inflammation	Nonspecific Acute/Chronic Inflammation	37	21.3
	Tuberculosis	2	1.7
	Aspergilloma	2	1.1
Interstitial lung disease	Sarcoidosis	3	1.7
Others	Inadequate sample	13	7.5
	Normal respiratory tissue	5	3.0
	Total	**174**	**100.0**

4.5 Cytological findings for all fluid specimens of patients who underwent Bronchoalveolar lavage or bronchial washing from 2013 to 2017.

A total of 291 patients out of 451underwent fluid sampling for cytological analysis, the later sample were either collected through bronchoalveolar lavage or bronchial washing. Majority of the findings were nonspecific acute/chronic inflammation samples 199/291(68.4%). There were 45/291(15.5%) cytological samples which were found to be inadequate for reporting. Malignancy was found in 28/291(9.6. Normal respiratory cells were reported in 11/291(3.8%). M.*tuberculosis* 3(1.0%) and fungal infection 5(1.7%) were the least findings of all fluid samples reported. (Table 4)

Table 4: Cytological findings for all patient with Bronchoalveolar lavage and/or bronchial washing from 2013 to 2017 (n=291)

Cytological finding	**Number**	**Percentage**
None Specific Acute/Chronic Inflammation	199	68.4
Acellular smear	45	15.5
Malignant Smear	28	9.6
Normal respiratory cells	11	3.8
Fungal infection*	5	1.7
Tuberculosis	3	1.0
Total	291	100.0

*candida species, aspergillosis

4.6 Bacteriological findings among patients who underwent bronchoalveolar lavage and/or bronchial washing (n=157)

A total of 157 samples were taken for bacteriological analysis out of 291 fluid specimens. A total of 25/157(15.9%) underwent gram staining. There was a predominance of gram positive cocci 15/25(60%) while gram negative cocci and bacilli each had 16% each. Among the cytological samples sent for bacteriological analysis,76 samples were sent for culture analysis, no growth was reported in 49/76(64.5%), normal flora was reported in 18/76 (23.7%). *Pseudomonas aeruginosa* was reported in 4/76 (5.3%), *Streptococcus pneumoniae* was reported in 3/76 (3.9%) while Escherichia *coli* was found in 2(2.6%).

A total of 56 samples were sent for mycobacterium tuberculosis processing through GeneXpert MTB/RIF molecular technique. Of these, 50/56(89.3%) did not detect any *Mycobacterium tuberculosis* whereas 6(10.7%) samples detected *Mycobacterium tuberculosis*. (Table 5)

Table 5: Bacteriological findings among patients who underwent bronchoalveolar lavage and/or bronchial washing (n=157)

Laboratory findings		**Frequency(n)**	**Percent (%)**
Gram stain(n=25)			
Gram +ve	Bacilli	2	8
	Cocci	15	60
Gram -ve	Bacilli	4	16
	Cocci	4	16
None MTB Bacterial Culture (n=76)			
Culture	No Growth	49	64.5
	Normal Flora	18	23.7
	Strep pneumonia	3	3.9
	P.aeruginosa	4	5.3
	E.coli	2	2.6
M.*Tuberculosis* (n=56)			
GeneXpert	No *M. tuberculosis*	50	89.3
MTB/RIF	*M. tuberculosis* detected	6	10.7

CHAPTER FIVE

5.0 DISCUSSION

5.1 Indication for Bronchoscopy at Muhimbili National Hospital

Worldwide indication for bronchoscopy varies from one locality to another. It has been found that in this study lung tumor was the predominant indication for bronchoscopy. This finding tallies with other study findings carried in other studies. In a retrospective study conducted in India for a period of 34 years, it was found that suspicious malignant lesion was the most common indication (24). Whereas a seven years study in Egypt also showed suspected malignant lesion to be common indication among other indications(25). Other common indications found in the study which have also been reported in other studies included hemoptysis-unexplained, and pneumonia (23,24,25).

5.2 Histological diagnosis among specimens from patient who underwent bronchoscopy

Tissue biopsies results in this study has shown Adenocarcinoma to be the common lung cancer followed by squamous cell carcinoma, carcinoma not otherwise classified, and small cell carcinoma. The predominance of adenocarcinoma in this study is similar to other recent study findings carried in United States, Norway and Japan where the commonest malignancy was found to be adenocarcinoma , followed by squamous cell carcinoma and undifferentiated malignancy (18)(29)(30).The study findings also tallies with recent European countries cohort studies which found an increase in the proportion of patients with adenocarcinoma among all histological subtypes(28,29,30).

There are number of theories that have been put forward to explain the changes from squamous cell carcinoma as the previous predominant lung malignancy up until 80’s and the rise of adenocarcinoma as the recent predominant lung malignancy in the recent years in studies held in developed countries.

One of the hypotheses is change in smoking behaviour where smokers now use low tar filter cigarettes, the filters are supposedly less effective in filtering small particles, the small particles that escape the filtration penetrate deeper into the peripheral lungs, the later are carcinogenic and hence are implicated in the occurrence of adenocarcinoma which anatomically occurs in the peripheral lung fields. In conjunction to this theory it is also hypothesized that the use of filtered cigarettes which contain low nicotine concentration necessitate smokers to use large puffs to attain a satisfactory desire which ultimately retains large amount of smoke and nicotine particles, the later practice leads to deposition of large amount of nicotine in the peripheral lung fields and hence the development of adenocarcinoma(30,(34).

The second hypothesis that has been put forward is the presence of large amount of nitrates concentration in filter cigarettes, nitrates are thought to be carcinogenic, the evidence for this theory is drawn from animal studies where large amount of nitrates has been found in nitrate induced adenocarcinoma(27,30,31).

The third hypothesis is related to air pollution especially of oxides of nitrogen in urban high-income countries, worldwide it is estimated that 3% of lung cancers are due to air pollution. The rapid growing urbanisation in developing countries Tanzania being one of them partly explains the observed study findings. Last but not least is the evidence from study which show that the risk of adenocarcinoma is high in none smokers and those who quit smoking while the risk of squamous carcinoma and small cell carcinoma is directly related to smoking and the risk decreases with smoking cessation, this means that, it is possible that the predominance of adenocarcinoma is an aftermath of smoking exposure and /or cessation contributed by worldwide anti-smoking campaign(30,31,27).

Generally, about 2/3 (64.3%) of tissue specimens had a diagnosis of lung malignancy. This finding concurs with findings from another study in Houston in United Sate that found lung malignancies in a range of 64-82% from patients who underwent bronchoscopic lung biopsy (18).

4.3 Cytological diagnosis among specimens from patients who underwent Bronchoscopy

Majority of the specimen of bronchoalveolar lavage and bronchial washings revealed inflammatory process in 68.4% of all the specimen, a finding similar to studies in India and Greece (25,18).This finding is probably due to lung tumour as a primary cause bearing the fact that it has appeared to be most common indication, however other pulmonary conditions which necessitated bronchoscopy could also lender a person to inflammatory process.

Among the fluid specimens collected for cytological analysis, malignancy was picked in about 9.6% of all the fluid specimens. This is similar to other study in India which also picked malignancy in about 17% in fluid specimens send for cytological analysis (25). This low percent of these cellular results in this study might be because of limitation of the technique used namely bronchioalveolar lavage and washing in obtaining fluid sample in lesions that are peripherally located (20). Further to later reason is inability of the current bronchoscopy setting not favouring a technique called bronchial brushing which has relatively good yield. In this study it has been found that 15.5% of fluid specimens were acellular, this is similar to another study in India which found 11.8% of the specimens were inadequate/inconclusive for reporting (35)

Other specific diagnosis like fungi and M.*tuberculosis* infections were also picked in low percentages by the cytological samples. The later low percentage for M.*tuberculosis* could be partly because patients sent for bronchoscopy needed to be tuberculosis infection free, thus were actively screened to rule out tuberculosis before the procedure is done. Another reason for this is the mere fact that not all cytological samples were sent for microbiological tests but only from those patients with suspected infections(19)**.**

4.4 Bacteriological diagnosis among patients who underwent bronchoscopy

About two thirds (64.5%) of fluid specimen were sent for none tuberculous bacteriological analysis. Off these, 23.7% grew normal flora bacteria, twelve percent of these specimen had positive bacteriological results for *P. aeruginosa*, *S. pneumoniae* and *E.coli.* The presence of *E. coli* which is an organism found in the lower gastrointestinal tract could have been a contaminant. Nevertheless, the later findings suggest that these patients needed antibiotic treatment before consideration for bronchoscopy.

Mycobacterium tuberculosis was detected in 10.7% of samples which were sent for molecular detection of Mycobacteria Tuberculosis DNA through a technique called GeneXpert MTB/RIF. In the ground that all patient who were sent for bronchoscopes were almost excluded from having tuberculosis through sputum and radiological tests, 10.7% of detected mycobacterium mean some of the tuberculosis cases are missed through the use of conventional methods of sputum staining. There was no documentation whether those who had scanty/unable to produce sputum underwent sputum induction pre-bronchoscopy as a way to maximise the methods of excluding tuberculosis

The study finding has similarities with other studies which detected M.tuberculosis in various percent as shown in brackets, Malawi (39%), Uganda (24%),Egypt (58.5%)and Thailand (32.5%).The difference in percentage between this study and the later studies is probably attributed by differences in study population (for example for studies in Malawi, Uganda and Egypt, the study population involved HIV positive smear negative patients), social demographical differences and Epidemiological differences in Tuberculosis prevalence among these countries (11,10,12,22,32). Accuracy of GeneXpert –MTB/RIF in detection of M.*tuberculosis* in bronchoalveolar lavage samples has also been reported to be fairly good in other studies in Tanzania and South Africa among patients with smear negative or scanty sputum collected through none invasive procedure.(33,34). Of the 6 patients detected with M.*tuberculosis*, two of them (33.3%) were HIV positive and the rest were HIV negative.

CHAPTER FIVE

5.0 STUDY STRENGTH, LIMITATIONS AND MITIGATION.

5.1 Strength

This is the first study which looked at the various lung diagnosis made through the use of bronchoscopy. The study has also shown the usefulness of bronchoscopy techniques in the diagnosis of various lung pathologies.

5.2 Limitation

1. This was a retrospective study which solely depends on secondary data.
2. There were also significant missing data/spacemen in the files and MNH database
3. There were significant number of specimens which turned to be inadequate samples or did not grow any microbe.

5.3 Mitigation

Patients with complete and incomplete data were both summarized differently

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATION

6.1 Conclusion

Lung tumor was the leading indication for bronchoscopy. Adenocarcinoma was the most common malignancy sub-type among others. Both bacterial and mycobacterial infections were among the reported findings in cytological samples. It was possible to diagnose tuberculosis despite the fact that TB used to be excluded before consideration for bronchoscopy

6.2 Recommendation

All patient suspected of lung malignancy should be sent for bronchoscopy and lug biopsy should be preferred whenever necessary. Bronchial brushing should be employed so as to maximise the yield in fluid spacemen. Sputum for GeneXpert and sputum induction should be preferred as part of screening methods before patients are sent for bronchoscopy

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APPENDIXES

Appendix I: Questionnaire – English Version

Diagnoses of specimens collected through flexible bronchoscopy from patients at Muhimbili National Hospital January 2013 to November 2017

A. Social demographic characteristics

1. Patient code …….

2. Age (years)……...3.Gender……□ Female ……□ Male……..

Resident…….

6. Level of education

1. No Education
2. Primary School
3. Secondary School
4. College or above
5. No formal education

B. Clinical and laboratory measurements

1. Anthropometric measurement

   Weigh (kg)…….. Height (cm)……..

2. Vital signs

   BP……Pulse rate…….Respiratory rate……..Temperature.....

3. Full blood picture

   1. Total wbc……predominant differential…….
   2. Rbc……..
   3. Hb level…….
   4. Platelet counts…….

C; Occupations history-current /past

1. Farm work **Y**es [ ] No [ ]
2. Automotive mechanic **Y**es [ ] No [ ]
3. Painter **Y**es [ ] No [ ]
4. Welder **Y**es [ ] No [ ]
5. Laboratory worker **Y**es [ ] No [ ]

6. Sand blaster **Y**es [ ] No [ ]
7. Insulator **Y**es [ ] No [ ]
8. Longshoreman **Y**es [ ] No [ ]
9. Pipe fitter **Y**es [ ] No [ ]
10. Carpenter **Y**es [ ] No [ ]
11. Mine **Y**es [ ] No [ ]
12. Railroad **Y**es [ ] No [ ]
13. Paper mill **Y**es [ ] No [ ]
14. Bakery **Y**es [ ] No [ ]
15. Smelting **Y**es [ ] No [ ]
16. Plastic factory **Y**es [ ] No [ ]
17. Tunnel construction **Y**es [ ] No [ ]

D. Patient Clinical presentation

1. Cough Yes [ ] No [ ]
2. Chest pain Yes [ ] No [ ]
3. Hemoptysis Yes [ ] No [ ]
4. Shortness of breath Yes [ ] No [ ]
5. Wheezing Yes [ ] No [ ]
6. Fever Yes [ ] No [ ]
7. Weight loss Yes [ ] No [ ]
8. **Others……**

E. Medical History

1. Documented histories of the following medical conditions

1. Tuberculosis (TB) **Y**es [ ] No [ ]
2. Asthma **Y**es [ ] No [ ]
3. COPD **Y**es [ ] No [ ]
4. Chronic bronchitis **Y**es [ ] No [ ]
5. Emphysema **Y**es [ ] No [ ]

2. HIV status

1. Positive **Y**es [ ] No [ ]
2. Negative **Y**es [ ] No [ ]

3. Unknown **Y**es [ ] No [ ]

3. Smoking history Y**es [ ] No [ ]**

F. Indication for bronchoscopy……..

G. Diagnosis made

1. Histological findings
    1. Small cell lung carcinoma Yes [ ] No [ ]
    2. Squamous cell carcinoma Yes [ ] No [ ]
    3. Adenocarcinoma Yes [ ] No [ ]
    4. Large cell carcinoma Yes [ ] No [ ]
    5. Kaposi's sarcoma Yes [ ] No [ ]
    6. Acute/Chronic inflammation Yes [ ] No [ ]
    7. Other Histological Diagnosis (specify)……..

2. Cytological findings (BAL)……..
    1. Types of cells observed
        1. White blood cells Yes [ ] No [ ]
        i. Lymphocyte Yes [ ] No [
        ii. Neutrophils Yes [ ] No [
        iii. Eosinophils Yes [ ] No [
        2. Red blood cells Yes [ ] No [ ]
        3. malignant cells Yes [ ] No [ ]

3. Bacteriological diagnosis
    1. Gram stain…….
    2. Culture……
    3. Gene xpert…….

4. Predominant Affected Lung site

    Right Yes [ ] No [ ]

    Left Yes [ ] No [ ]

    4. Other findings…….