

**PRESENTATION, MANAGEMENT AND SHORT-TERM OUTCOMES
OF EXTRADURAL SPINAL TUMOURS AT THE UNIVERSITY
TEACHING HOSPITAL IN LUSAKA, ZAMBIA**

BY

HILGARD MUTEMBO

MBChB (UNZA), BScHB (UNZA)

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DECLARATION

I hereby declare that this dissertation herein presented for the degree of Master of Medicine in Orthopaedic and Trauma Surgery represents my own work and has not been previously submitted nor is it being currently submitted wholly or in part for any other degree at this or any other University.

Signed by: **Dr Hilgard Mutembo** (Candidate) _____

(Comp No. 2017016401)

Approved by: **Dr Brian Sonkwe** (Supervisor) _____

Approved by: **Dr James Munthali** (Co-Supervisor) _____

APPROVAL

This dissertation by Dr Hilgard Mutembo is approved as fulfilling part of the requirements for the award of the degree of Master of Medicine in Orthopaedic and Trauma Surgery by the University of Zambia, subject to the examiner's report.

Examiner 1: _____ Signature: _____ Date: _____

Examiner 2: _____ Signature: _____ Date: _____

Examiner 3: _____ Signature: _____ Date: _____

Chairperson: _____ Signature: _____ Date: _____
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Supervisor: _____ Signature: _____ Date: _____

ABSTRACT

Following an observation of lack of statistics locally, a retrospective study to determine the presentation, management and short-term outcomes of extradural spinal tumours from 2013 to 2016 at the University Teaching Hospital was conducted after approval from the University of Zambia Biomedical Research Ethics Committee. The objectives were to investigate the clinical presentation of patients with extradural spinal tumours at the University Teaching Hospital establish the factors that determine the treatment they receive and the outcomes of that treatment. A questionnaire was used to obtain data from patients' records. This data was analysed using the Statistical Package for Social Sciences software. Of the 62 patients in the study, 34 were female and 28 male. The age range from 14 to 87 years had a mean of 55.03 years. Backache (93.8%), Limb weakness (91.9%), loss of sensation (50%), urine and stool incontinence (43.5% and 41.9% respectively), back deformity (11.3%), night pain (85.5%), weight loss (67.7%), poor appetite (61.3%), fever (35.5%) and night sweats (29%) were common symptoms. 68% of patients were bedridden. Visual Analogue Scale scores were more than 5 in 84% of patients. A muscle power grade of 3 or less (n=48), impaired muscle tone (n=38), abnormal reflexes (n=52), presence of a sensory level (n=37) and back deformity (n=17) were common signs. Plain radiography, Computed Tomography Scans, Magnetic Resonance Scans and Technetium Bone scans were done in 60, 35, 17 and 2 patients respectively. The commonest surgical host category was A (64%). Secondary Extradural Spinal Tumours comprised 82% (51 patients) while 18% (11 patients) were primary. Surgery was done in fourteen (14) patients with one (1) failing to afford implants. The rest (48) received nonsurgical treatment. Eleven percent of patients reported improvement in pain scores but the rest of the symptoms remained the same or worsened after treatment. Complications included decubitus ulcers, Urinary Tract Infection, Deep Venous Thrombosis, pneumonia, sepsis and joint stiffness. Fourty (40) patients died and eighteen (18) patients were lost to follow-up. The ages of patients followed normal distribution with female to male ratio of 1.2 to 1. Most patients presented with symptoms of late or advanced disease, a finding similar to studies done elsewhere. The physical signs at presentation are supportive of this. The type of extradural spinal tumour, stage of disease, completeness of diagnostic workup, availability of implants, need for tissue diagnosis, type of surgical host and availability of nonsurgical treatment modality determined the choice of treatment. Poor outcomes in terms of quantity and quality of life are a reflection of the late presentation, delayed diagnosis, lack of resources and difficulty of treating these tumours. The relocation of the main hospital registry led to loss of documentation and this negatively affected the sample size. Extradural spinal tumours are relatively uncommon but cause significant morbidity and mortality in those affected.

Keywords: spinal tumour, extradural, clinical presentation, treatment outcome

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TABLE OF CONTENTS

COPYRIGHT	ii
DECLARATION	iii
APPROVAL	iv
ABSTRACT	v
ACKNOWLEDGEMENTS	vi
TABLE OF CONTENTS.....	vii
LIST OF TABLES	x
LIST OF FIGURES	xi
LIST OF APPENDICES	xiii
ABBREVIATIONS	xiv
CHAPTER ONE: INTRODUCTION	1
1.1 Background of the Study	1
1.2 Statement of the Problem	4
1.3 Research Questions	5
1.4 Objectives of the Study	5
1.4.1 General Objective	5
1.4.2 Specific Objectives	6
1.5 Study Justification	6
1.6 Organisation Of Dissertation	7
CHAPTER TWO: LITERATURE REVIEW	8
2.1 Introduction	8
2.2 Background Literature	8
2.3 Clinical Presentation	10

2.4 Diagnosis and Imaging	13
2.5 Oncological Staging	17
2.6 Treatment and Outcomes	17
 CHAPTER THREE: METHODOLOGY	30
3.1 Study Design	30
3.2 Sources of Data and Data-Collection Tools	30
3.2.1 Secondary Data	30
3.2.2 Primary Data	30
3.3 Study Population, Case Definition, Inclusion Criteria And Exclusion Criteria	30
3.3.1 Study Population	30
3.3.2 Case Definition	30
3.3.3 Inclusion Criteria	31
3.3.4 Exclusion Criteria	31
3.4 Sampling Method And Sample Size	31
3.4.1 Sampling Method	31
3.4.2 Sample Size	31
3.5 Research Instruments, Data Collection Method And Study Variables	32
3.5.1 Questionnaire Development	32
3.5.2 Data Collection Method	32
3.5.3 Study Variables	32
3.5.4 Pilot Study	33
3.6 Data Analysis Tools And Procedure	33
3.7 Ethical Considerations	33

3.8 Study Limitations	34
 CHAPTER FOUR: RESULTS	 36
4.1 Background Characteristics	36
4.2 Symptomatology	38
4.3 Examination Findings	41
4.4 Imaging and Diagnosis	45
4.5 Treatment and Outcomes	53
 CHAPTER FIVE: DISCUSSION	 63
5.1 Background Characteristics	63
5.2 Clinical Presentation	64
5.3 Determinants of Treatment	65
5.4 Treatment and Outcomes	66
 CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS	 71
6.1 Conclusion	71
6.2 Recommendations	72
 REFERENCES	 76
 APPENDICES	 83

LIST OF TABLES

Table 1: Frequency of Symptoms	39
Table 2: Frequency of Constitutional Symptoms	40
Table 3: Other Symptoms	40
Table 4: Muscle Tone	42
Table 5: Muscle Power Grade	43
Table 6: Sensory Level and Back Deformity	44
Table 7: Profile of EDSTs in Patients Aged 40 years or Younger	49
Table 8: Type of Tumour and Spinal Involvement	50
Table 9: Age and Sex Distribution of Primary EDSTs	52
Table 10: Indication for Surgery in 14 patients.....	53
Table 11: Reasons for Nonsurgical Treatment:	53
Table 12: Follow-up Periods	56
Table 13: Correlation of VAS, Post-Treatment VAS and Backache	67
Table 14: Correlation of Age, Sex and Death:	68
Table 15: Correlation of Death, Backache and Treatment plan	69
Table 16: Correlation of Death, Treatment Plan and Final Diagnosis	70

LIST OF FIGURES

Figure 1: Sex Distribution of Patients	36
Figure 2: Age Distribution of Patients	36
Figure 3: Employment Status of patients	37
Figure 4: Marital Status of patients	37
Figure 5: Patients' Domicile	38
Figure 6: Frequency of Symptoms	39
Figure 7: Mobility at Presentation	41
Figure 8: VAS Scores for Backache	42
Figure 9: Reflexes at Presentation	43
Figure 10: DRE Findings	44
Figure 11: Radiological Investigation	45
Figure 12: Reasons for Not Doing Radiological Investigation.....	46
Figure 13: Co-morbidities	47
Figure 14: Surgical Host Category	47
Figure 15: Type of EDSTs	48
Figure 16: Source of Secondary EDSTs	51
Figure 17: Aetiology of Primary EDSTs	51
Figure 18: Reasons for Not Giving Neoadjuvant Therapy	54
Figure 19: Reasons for Not Giving Adjuvant Therapy	55
Figure 20: Response to Treatment	57
Figure 21: Surgical Wound Status	58
Figure 22: Complications	59
Figure 23: Cause of Death	60

Figure 24: Weeks to Death	61
Figure 25: Deaths Per Week in First 4 Weeks	62

LIST OF APPENDICES

Appendix i : Application for Ethical Approval.....	83
Appendix ii : Application for Waiver of need for Consent.....	84
Appendix iii : Corrections To UNZABREC	85
Appendix iv : Graduate Proposal Presentation Forum Permission Letter	86
Appendix v : Request for permission to conduct research at UTH	87
Appendix vi: Response from UNZABREC	88
Appendix vii: Study Questionnaire	89
Appendix viii: Waiver for the Protocol from UNZABREC	106

ABBREVIATIONS

ABC:	Aneurysmal Bone Cyst
AIDS:	Acquired Immunodeficiency Syndrome
CD4:	Cluster of Differentiation type 4
CNB:	Core-Needle Biopsy
CRP:	C- Reactive Protein.
CT:	Computed Tomography
DRE:	Digital Rectal Examination
DVT:	Deep Vein Thrombosis
ECHO:	Echocardiogram
ES:	Ewing's Sarcoma
ESR:	Erythrocyte Sedimentation Rate
FNAB:	Fine-Needle Aspiration Biopsy
GCT:	Giant Cell Tumour
HB:	Haemoglobin
HIV:	Human Immunodeficiency Virus
LUTS:	Lower Urinary Tract Symptoms
MESCC:	Metastatic Epidural Spinal Cord Compression
MM:	Multiple Myeloma
MRI:	Magnetic Resonance Imaging
NSAID:	Nonsteroidal Anti-inflammatory Drugs
OS:	Osteogenic Sarcoma (Osteosarcoma)
PET:	Positron Emission Tomography
SBRT:	Stereotactic Body Radiation Therapy
SPSS:	Statistical Package for the Social Sciences
Tc:	Technetium 99
UNZA:	The University of Zambia
UNZABREC:	University of Zambia Biomedical Research Ethics Committee
U/S:	Ultrasonography
USA:	United States of America
UTH:	University Teaching Hospital
UTI:	Urinary Tract Infection
VAS:	Visual Analogue Scale

CHAPTER ONE: INTRODUCTION

1.1 Background of the Study

The spinal cord is surrounded by a tough fibrous tissue called the dura mater. The cord and the dura around it are located within a bony canal created by the vertebral column. The vertebral column is composed of irregularly shaped but well aligned bones from the base of the occiput to the coccyx. There are also blood vessels, lymphatics and fat around and within these structures. Spinal tumours or neoplasms are abnormal new growths arising from any of these tissues. They may also be secondary deposits (metastases) to these tissues from tumours elsewhere in the body. Depending on their location in relation to the dura mater, spinal tumours are classified anatomically as:

Extradural: when they are located outside the dura mater. These are the commonest at 60%. The majority of extradural spinal tumours involve the vertebrae (Heller, 1997)

Intradural: when they are located within the confines of the dura mater. These are further sub-classified as either extramedullary when they do not involve the parenchyma of the spinal cord or intramedullary when they do (Wilne and Walker, 2010).

A small number of spinal tumours may have both intramedullary and extramedullary components as some intradural tumours may extend through the nerve root sleeve into the extradural compartment (Vasudeva and Groff, 2017). Extradural spinal tumours are most commonly metastatic. They arise from tumours elsewhere in the body, mainly the breast, lung, prostate, kidney and thyroid. Primary extradural tumours are rare, accounting for less than 5% of all neoplasms (Heller, 1997). They may be benign or malignant. The benign tumours include aneurysmal bone cyst, chondroma/enchondroma, haemangioma, osteoid osteoma, osteoblastoma, eosinophilic granuloma and fibrous dysplasia. The malignant primary tumours include chondrosarcoma, osteosarcoma, Ewing's sarcoma and multiple myeloma/plasmacytoma (Ropper *et al.*, 2012).

Primary intradural spinal tumours are uncommon but constitute an important consideration in the differential diagnosis of a patient with back pain, radicular pain, sensorimotor deficits or sphincter dysfunction (Traul, Shaffrey and Schiff, 2007). Primary intradural-extramedullary tumours mostly encountered are meningiomas, neurofibromas and schwannomas while intradural-intramedullary tumours commonly

seen are ependymomas and astrocytomas (Chamberlain and Tredway, 2011). Extradural spinal tumours present in unfamiliar ways with symptoms that can easily be disregarded or trivialized by an inexperienced or unsuspecting clinician. Back or neck pain is the most common symptom at presentation (Bach, 1996). This is usually at the level of the tumour and is typically worse at night. The patient may present with a deformity localized to the affected area. Clarke *et al.* (2014) argued that some of the symptoms at presentation are due to spinal cord or nerve compression and weakening of the vertebral column.

Furthermore, symptoms attributable to spinal cord compression include weakness, rapid onset paralysis or sensory loss and numbness in the upper and lower limbs. There may be bowel and urinary bladder dysfunction. Incontinence and decreased sensation in the saddle area are generally considered warning signs of cauda equina compression by the tumour. The symptoms may be of short duration or longstanding and getting worse with time. The patient may have constitutional symptoms of poor appetite, weight loss, night sweats and fever or chills [(Okeke *et al.*, 2006); (Schiff, 2016); (Karuna, Shekdar and Schwartz, 2014) and (Wilne and Walker, 2010)]. The diagnosis of primary spinal cord tumours is difficult mainly due to their symptoms, which, in the early stages, mimic more common and benign conditions such as infective spondylitis or degenerative spinal disorders.

Magnetic Resonance Imaging (MRI) and bone scanning are useful diagnostic tools and have made it relatively easy to diagnose tumours of the spine early, especially with the use of contrast such as gadolinium. With these it is possible to assess not only the location of the tumour but also its relationship to the spinal cord, and presence or risk of cord compression as well as tumour spread into surrounding soft tissue compartments (Segal *et al.*, 2012). Lesions may be biopsied using imaging-guided techniques or by open means and specimens examined grossly and histologically to provide a tissue diagnosis and help direct therapy. Histochemical analysis, where applicable, may also be done on the biopsy tissue so obtained (Garg *et al.*, 2016). Bone marrow biopsy and immune-electrophoresis may be done as well (Clarke *et al.*, 2014).

Unlike metastatic spine tumours, primary tumours localized to a single location have the potential for true cure. However this potential may be eliminated by late recognition and/or improper workup. Many of these lesions respond poorly to chemotherapeutic agents and radiation therapy, and so missteps in diagnostic workup can have devastating effect on outcome (Clarke *et al.*, 2014). The management of patients with spinal tumours, like that of those with other musculoskeletal tumours, requires a multidisciplinary approach involving orthopaedic spine surgeon, radiologist, pathologist, radiation oncologist, medical oncologist and physiotherapist/occupational therapist. Other specialties that may have a role to play are vascular, thoracic, plastic and neuro-surgeons (Toy and Heck Jr, 2013). Steroids may be administered if there is evidence of cord compression as a form of medical decompression. These do not affect the tumour mass itself but tend to reduce the inflammatory reaction around it and thus decrease the overall volume of the mass impinging on the spinal cord (Ribas and Schiff, 2012).

Chemotherapy may be administered for chemosensitive tumours. Radiation is usually delivered to the involved segment as well as segments above and below it. Radiotherapy proves successful in fighting somatic pain but fails in patients with mechanical pain caused by fractures or spinal instability. It does not prevent nervous structures' compression and neurological complications in these patients (Ribas and Schiff, 2012). Surgery is sometimes possible, the goals of which include histopathological tissue diagnosis, local tumor control or oncological cure, pain relief, spinal cord decompression and restoration of neurological function, restoration of spinal stability and deformity rectification (Ribas and Schiff, 2012). The combination of minimally invasive surgery and radiotherapy or chemotherapy is a new technique for treating some spinal tumors (Hamamoto *et al.*, 2009).

Given the above description, this research study seeks to look at the presentation, management and short-term outcome of extradural spinal tumours at the University Teaching Hospital (UTH), a third-level and highest referral hospital located in Lusaka, Zambia. The University Teaching Hospital can be said to have a catchment area of approximately 15 million people. Currently, there is no data on the disease burden that extradural spinal tumours pose and local treatment guidelines and data on outcomes of the treatment that these patients receive are lacking.

1.2 Statement of the Problem

The commonest tumours in the spine are metastatic in origin, arising from a primary tumour in the breast, lung, prostate and kidney and less commonly thyroid and skin. Spinal metastases occur in nearly 30% of patients with malignant tumours. The spine is the commonest site for skeletal metastatic disease, accounting for 60% of all skeletal metastases. Primary vertebral tumours are rare, making up less than 5% of all tumours in the spine. This makes them 40 times less common compared to metastases (Clarke *et al.*, 2014). Unlike spinal metastases which represent a systemic disease process, primary tumours localized to a single location in the spine have potential for true cure. However this possibility may be eliminated by late recognition or improper workup. Many of these lesions respond poorly to chemotherapy and/or radiotherapy and so missteps in diagnosis may have devastating effect on outcome. The disease burden from spinal tumours in general and extradural spinal tumours in particular in terms of incidence and prevalence, morbidity, treatment and outcomes is not well known or documented for our institution and country.

This study has focused on bringing out these core issues to the fore. Anecdotal observation and opinion indicate that there is a general difficulty in distinguishing tumours of the spine from the more common infective processes or degenerative conditions in the spine in our setup. This contributes to late or incorrect diagnosis and therefore late institution of treatment or institution of incorrect treatment and therefore poor outcomes in patients with tumours of the spine. This observation applies to both referring hospitals and surgical units admitting the patients to the University Teaching Hospital. This is especially true considering the fact that nonspecialised personnel are the ones who first come into contact with these patients first and are responsible with determining where the patient will eventually end-up as they refer them. The other observation worth noting is that patients tend to present late on in the disease process, when the disease is well advanced or when they have developed complications as a result of advanced disease. This may be attributed to lack of information or knowledge about spinal tumours as the patients tend to trivialise some of the early symptoms of a serious condition. The health-seeking behaviour of our population may be regarded as one of the poorest in the world. Again where there are no locally available statistics, it is not possible to educate the population to improve their health-seeking behaviour on a condition they may consider to be uncommon or non-existent among them.

Thirdly poverty or lack of resources is a major contributing factor in terms of presentation, diagnosis and treatment of spinal tumours. A patient who stays very far from a health care facility and has no or little means of getting there will only be compelled to seek medical help when the condition has gotten worse or is out of control. A health facility that does not have enough resources in terms of qualified personnel and diagnostic tools will not be able to recognise a serious condition such as spinal tumour in a peasant farmer, for example, who presents with backache. Even in centres where the expertise is available, it may be difficult to diagnose these tumours when advanced diagnostic imaging such as computed tomographic scanning, magnetic resonance imaging and bone scanning is not available or the patient cannot afford these from private hospitals that are able to offer the service but at an economical fee.

1.3 Research Questions

In developing the objectives for this study we asked the following research questions:

- i. What are the clinical features of patients presenting with extradural spinal tumours (EDSTs) at the University Teaching Hospital (UTH)?
- ii. What factors determine the treatment the patients with extradural spinal tumours receive at UTH?
- iii. What are the outcomes of treatment for patients with extradural spinal tumours presenting at UTH?

1.4 Objectives of the Study

1.4.1 General Objective

The General Objective of the study was:

To investigate the clinical presentation of patients with extradural spinal tumours at UTH and establish the factors that determine the treatment they receive and the outcomes of that treatment.

1.4.2 Specific Objectives

The specific objectives were:

- i. To determine the symptomatology and examination findings in patients presenting to the University Teaching Hospital with extradural spinal tumours.
- ii. To document the determinants of surgical and nonsurgical treatment given to patients with extradural spinal tumours at UTH.
- iii. To outline the outcomes of surgical and nonsurgical treatment of patients with extradural spinal tumours at UTH.

1.5 Study Justification

In so far as the presentation, management and outcomes of spinal tumours at the University Teaching Hospital are concerned, and from the literature so far reviewed, there has been no study that has been carried out locally. The closest local study looking at primary malignant bone tumours at the University Teaching Hospital over a four –year period from January 2008 to December 2012 found that, save for multiple myeloma which had a generalised skeletal distribution, there were only 2 out of 152 (1.3%) patients with primary malignant tumours affecting the spine (Sakala, 2015). Although this finding is consistent with other estimates it is far much less than expected and may be indicative of diagnostic challenges prevalent in our setting. Boriani and Fisher (2015) estimated primary spine tumours to account for 10% or less of bone tumours in the United States of America (USA).

Our retrospective study was a deliberate attempt to bring out that data in order to have a starting point for future studies in relation to extradural spinal tumours at local level. In bringing such information to the fore, the results of this study will give both planners and clinicians enough leverage and a basis to forge ways of improving the presentation, management and outcomes of patients with spinal tumours in general and extradural spinal tumours in particular. With statistics in hand, it will be easier for public health practitioners and clinicians to come up with awareness campaigns aimed at educating the general population and encourage them to seek medical attention early once they have symptoms that are suggestive of tumour of the spine. These tumours are associated with very high morbidity and mortality, hence it is critically important that they are diagnosed early and management instituted expeditiously. It is desirable and important to standardise and increase awareness on management

especially that there are few specialised orthopaedic spine and neurosurgeons and so there is high reliance on non-specialised personnel in the initial care of these patients.

When this data is readily available it will be more convincing to advocate for appropriate resource allocation in terms of personnel training and allocation, appropriate instrumentation and equipment acquisition and expansion of services to other centres. Although the majority of extradural spinal tumours are benign, malignant types do arise. These tumours are associated with great morbidity and mortality despite aggressive multimodal treatment strategies. Unfortunately, because of the rarity of these tumours, few prospective studies exist to guide treatment and much of the current knowledge is derived from small retrospective case series and reports. The data from this study will be suitable for benchmarking the status locally for the period under review and describing prevailing patterns of the disease and the care thereof. It will be useful in generating additional and/or other hypotheses in relation to spinal or indeed other musculoskeletal tumours for future studies.

1.6 Organisation of Dissertation

This report is arranged in chapters as follows:

Chapter 1 describes the background of the study, statement of the problem, research questions, objectives of the study and study justification.

Chapter 2 deals with the literature review and includes studies done locally, regionally and internationally in relation to the presentation, management and outcome of treatment of extradural spinal tumours

Chapter 3 describes the methodology used in the study in detail. It also notes the ethical issues that were considered and takes into account the study limitations and challenges.

Chapter 4 gives, in narrative, graphical and tabular form, the results of the study.

Chapter 5 discusses the results in light of the literature that was reviewed

Chapter 6 is comprised of the conclusions drawn from the study results in light of the specific objectives and proposes recommendations based on those conclusions.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter has focused on reviewing literature relevant to the study to identify what others have done in developing and developed countries. The reviewed literature helped to identify gaps in our setup and formed, in part, a basis for the statement of the problem.

2.2 Background Literature

Tumours of the spine may arise directly from tissues in the spine as primary spinal tumours or may come about as a result of secondary spread to tissues in the spine from cancer elsewhere in the body.

Primary bone tumours of the spine are very rare, comprising only 10% or less of all bone tumours. In the United States about 7,500 new cases are estimated per year. The overall world occurrence can be expected to be 2.5 to 8.5 per one million inhabitants per year. Compared with primary spinal tumours, metastatic tumours are much more common. The spine is the most common skeletal region for secondary tumours (Boriani and Fisher, 2015). As many as 30 to 70% of cancer patients are found to have spinal metastases at autopsy (Li *et al.*, 2015). This piece of information is true for western countries. The prevalence in our local setup is not truly known. This study provides a window into which of these tumours are commonly seen at UTH and tried to formulate the reason for any disparity with data from elsewhere.

Primary bone tumours are more common in the thoracic and lumbosacral regions than in the cervical spine (Beer and Menezes, 1997). These tumours occur according to a typical anatomical distribution within the vertebra. In general, malignant tumours occur more frequently in the anterior elements and benign tumours in the posterior elements of the vertebrae. (Sansur *et al.*, 2007).

Sharma *et al.* (2016) indicate that about 55% of spinal tumours are extradural, arising from vertebral bodies, epidural and surrounding neural and soft tissues. More than 90% of extradural spinal tumours are metastatic lesions. In their retrospective study of 36 patients who were operated for extradural spinal tumours between May 1999

and December 2012, there were 20 male and 16 female patients and ages ranged from 10 to 80 years. Common pathologies were neurofibromas (16), Ewing's sarcoma (7), granulomas (3), metastatic lesions (2), angiolipomas (2), chondroma (2), aneurysmal bone cyst (1), plasmacytoma (1), rhabdomyosarcoma (1) and neuroblastoma (1).

However, in a retrospective study spanning 10 years from January 1985 to December 1994 looking at spinal tumours causing cord compression at Kenyatta National Hospital, a teaching and referral hospital in Nairobi, Kenya, Mwang'ombe and Ouma (2000) found that primary spinal tumours (65.8%) were more common than secondary tumours (34.2%). They attributed the high frequency of metastatic spinal cord tumours in developed countries to the long life expectancy rates seen in those countries which are associated with development of more malignant tumours in their population. They argue that life expectancy rates are still low in the developing world and people may not be living long enough to develop excessive metastatic tumours. Their study highlighted two observations which are commonly seen in patients undergoing treatment for neurological illness in the developing world. These are late presentation into hospital and a significant delay while in hospital before definitive surgery. The late presentation is usually associated with the fact that patients commonly go for traditional forms of treatment before seeking conventional treatment. The delay while in hospital is associated with shortage of specialists and hospital resources. This situation will only improve following campaigns to increase public awareness on the relevance of seeking early medical treatment and after improvement of primary health care facilities and the referral system. They argue that although the number of specialists within their country is now higher than it was before, greater emphasis will need to be put on ways and means of utilising these specialists more efficiently through provision of necessary auxiliary resources.

According to Clarke *et al.* (2014), clinical and radiological features that will distinguish primary from metastatic spinal tumours include younger age at onset. Also, lesions in primary spinal tumours may be localized to vertebral bodies or posterior elements whereas metastases are localized to vertebral bodies in 80% of cases and to posterior elements in 20% of cases (Nater and Fehlings, 2017). Primary tumours tend to have a longer duration of symptoms at the time of initial presentation.

This study endeavoured to establish whether patients with extradural spinal tumours present in similar fashion in the various sections of the spine and also highlighted the frequency of the various extradural spinal tumour types at UTH.

2.3 Clinical Presentation

Patients with spinal tumours may present in a variety of ways. The symptoms that will make the patient seek medical attention may have been present for a varied length of time, depending on the age of the patient, the causative lesion and its behaviour or aggressiveness.

Back pain or neck pain related to activity are very frequent symptoms and mostly are due to disc prolapse, degenerative changes, and myofascial strains caused by the tumour. Conversely a spinal tumour should be suspected in a patient with history of cancer (current, recent or past) who complains of back or neck pain which is particularly progressive, unrelenting, not closely related to activity and increasing during the night. Tumour growth may cause expansion of the bony cortex of the vertebral body resulting in pathological fracture and invasion of paravertebral structures. Acute or chronic compression of neurologic tissues results in radiculopathy or myelopathy. Some spinal tumours may present as incidental findings or following a workup for nonspecific symptoms without neck or back pain. Latent lesions such as haemangiomas, fibrous dysplasia and exostosis are asymptomatic by definition. Some slow growing malignant tumors such as chordomas may also be discovered incidentally and may be quite big masses at diagnosis (Boriani and Fisher, 2015).

Mwang'ombe and Ouma (2000) found that the commonest presentation in their study was sensory loss (89%), followed by limb weakness (63%) paraesthesia (42%), back pain (39%) and, incontinence (23%). Thirty-one out of 38 of their patients were unable to walk at presentation.

For tumours that originate in the vertebral body, symptoms are usually due to periosteal stretching with growth and localized bony destruction. Thus unremitting pain that worsens at night or in the supine position is common. Mechanical pain due to instability may be reported (Clarke *et al.*, 2014; Bach 1996). The patient may present with a back deformity that may be of recent onset or longstanding and worsening or

has recently become painful. Painful scoliosis in an adolescent is strongly suggestive of osteoid osteoma or osteoblastoma affecting the spine at that level.

Karuna, Shekdar and Schwartz (2014) state that symptoms of spinal tumours in children may be vague and misleading. This explains the significant delay in diagnosis and institution of appropriate treatment. Children may present with back or neck pain, mild motor weakness, progressive scoliosis and gait disturbance. These tumours may tend to exhibit remissions and exacerbations due to varying degrees of peritumoral cord oedema, further contributing to patients' delay in seeking medical assistance.

The widely recognised features of spinal pathology occur late in children in the natural history of the disease. The clinical features of early cord disease are not well defined in this category of patients. The early symptoms may fluctuate in intensity and neurological examination in a child may be normal in the setting of a spine or spinal cord tumour. (Rautenbach and Stone, 2011)

According to Wilne and Walker (2010), tumours of the spine and spinal cord are rare in children, making up 2% of all childhood malignancies. Frequently the child has had symptoms for months before a diagnosis is made, by which time the child may have developed permanent and disabling neurological deficits. They present in a variety of ways but generally the more rapidly dividing the tumour, the faster the clinical progression and vice versa. The commonest symptoms are back pain at 67% and spinal deformity at 31%. The child may exhibit clumsiness, abnormal gait and incoordination. Other symptoms are headache, vomiting, voice change, head tilt (torticollis), upper limb weakness, quadriplegia, paraplegia or focal motor weakness. Sphincteric disturbance and developmental delay may also occur.

Adult patients might present with symptomatology related to involvement of neural tissue. Clarke *et al.* (2014), indicate that radicular and myelopathic symptoms are rare in the early stages. A new or progressive deformity, especially in younger patients, may be the only feature at presentation. For these patients, or patients with persistent symptoms, appropriate imaging studies should be requested to help in diagnosis.

For metastatic tumours the patients' clinical presentation is a key consideration in their management. Neurological dysfunction in the form of sensorimotor dysfunction, autonomic dysfunction as well as long tract signs are common. Approximately 5 to 10% of patients with metastatic spine tumours develop metastatic epidural spinal cord compression (MESCC). Pain is also common, occurring in approximately 83 to 95 % of patients and usually precedes the development of neurological symptoms. The pain is of different types and its nature may impact on its management. It may be local, radicular or mechanical in origin. Local pain is due to periosteal stretching, elevation of endosteal pressure or inflammation caused by tumour growth. This pain can be localized, is constant and presents in the evenings or mornings. It is described as deep "gnawing" or "aching" pain at the site of the disease. It does not worsen with movement and may improve with activity. This type of pain responds to anti-inflammatory or corticosteroid medication, and radiation therapy can improve it by shrinking the tumour and decreasing production of inflammatory mediators (Li *et al.*, 2015; Hamamoto *et al.*, 2009).

Radicular pain is caused by nerve root impingement which may occur when the spinal metastasis compresses exiting nerve root within the spinal canal, neuroforamen or outside the neuroforamen. It follows a dermatomal distribution and is described as sharp, shooting or stabbing in nature. It is constant and may or may not be relieved with change of posture. Radicular pain may respond to therapies that can reduce the effective size of the tumour, including radiotherapy, chemotherapy and corticosteroids. Mechanical pain is severe and movement related. It worsens with loading of the spine as patient changes posture from lying down to sitting or standing. Bending would make the pain worse and recumbency relieves it. It is typically associated with vertebral collapse, as the weakened vertebra is no longer able to support the mechanical load. This type of pain is often refractory to anti-inflammatory medication, chemotherapy or radiotherapy. It requires cement augmentation of the affected vertebra or spine stabilisation. Often patients with mechanical pain have neoplastic spinal instability, defined as the loss of spinal integrity as a result of a neoplastic process that is associated with movement-related pain, symptomatic or progressive deformity and/or neural compromise under normal physiological loads. (Li *et al.*, 2015; Hamamoto *et al.*, 2009).

The patients might present with constitutional symptoms of poor appetite, malaise, weight loss, night sweats and fever or chills [(Okeke *et al.*, 2006); (Schiff, 2016); (Karuna, Shekdar & Schwartz, 2014); (Wilne and Walker, 2010)].

According to Laubscher, Held and Dunn (2015), from their literature review the most common presenting complaint of patients with primary spinal tumours is pain, with roughly 60% complaining of axial pain and 25% of radicular symptoms, which was confirmed in their series. The presence of a neurological deficit carries a worse prognosis. Pain at rest or night pain are red flag symptoms that warrant further investigation. Spinal deformity is obvious when present, but occurs in less than 10% of patients. The most common cause of a painful scoliosis in adolescents is an osteoid osteoma. A delay in diagnosis was common and their finding was confirmed in other series. They attributed this to the presenting symptoms often being vague, pain often being the only symptom, and the initial radiographs often only showing subtle or no abnormalities leading to the symptoms not being properly investigated. Most patients report a slow, gradual onset of pain in the involved area. In benign tumours of the spine an average of 26 weeks of symptoms before presentation are reported. This was confirmed in their series where the average delay in presentation was 7 months.

This massive wealth of information has been lacking in our setup and this study endeavoured to establish the symptomatology and examination findings in patients with primary and secondary extradural spinal tumours (EDST). What we had previously concerning presentation of spinal tumours in general and EDST in particular are undocumented and anecdotal data gathered from the experience of the clinicians. Was it true, for example that the majority of our patients would present with back pain? This study answers this question.

2.4 Diagnosis and Imaging

Spinal tumours cause significant morbidity in terms of limb dysfunction. In the differential diagnosis of a spinal lesion, location is one of the most important features. Others are clinical presentation, age and gender of the patient. Magnetic resonance imaging plays a key role, allowing easy classification of the tumour as being extradural, intradural-extramedullary or intradural-intramedullary, which is very useful for tumour characterisation. For the osseous spine, in addition, computed

tomography (CT) scanning is important. Extradural tumours are more common with the metastatic group being more prevalent than the primary types (Van Goethem *et al.*, 2004).

Imaging studies remain very important diagnostic modalities in the workup of a patient with suspected spinal tumour. Initially, plain radiographs are performed, but a negative radiograph does not rule out the diagnosis of a spinal tumour. Computed tomography (CT) scanning provides superior information on cortical bone and tumour calcification than plain radiographs. Magnetic Resonance Imaging (MRI) is excellent at delineating soft tissue, paraspinal lesions, neural encroachment, bone marrow infiltration and epidural extension (Clarke *et al.*, 2014).

Depending on the differential diagnoses suggested by the imaging studies, it is reasonable to start staging the tumour, particularly in cases in which distant metastases are likely and may provide easier access at biopsy than the spinal lesion, although these may not give a clue to which of the lesion is primary and which one is secondary. A technetium bone scan or positron emission tomography (PET) may be done to look for metabolic activity related to the tumour in remote skeletal sites. (Clarke *et al.*, 2014). MRI and CT scans can generate a working diagnosis, as some patterns are characteristic. Examples abound: giant cell tumour (GCT) and Ewing's sarcoma are lytic lesions, and most osteosarcomas are characterised by extensive aggressive bone formation with ill-defined borders. A multicameral balloon-like pattern with a double density content is typical of aneurysmal bone cysts. Infiltrating erosions inside cancellous bone of a vertebral body arising from the posterior wall is suggestive of a chordoma. Soft tissue masses arising from the posterior elements with rounded calcifications are typical of peripheral chondrosarcomas. (Boriani and Fisher, 2015)

Positron emission tomography (PET) scan is becoming more relevant, particularly in its ability to differentiate tumours from infectious disease processes, which are quite common in our setting. Technetium isotope bone scan is able not only to localise one but multiple lesions, including skip and metastatic lesions (Boriani and Fisher, 2015). Angiography shows the tumour's vascularity, and its role in enabling selective arterial embolisation has become an indispensable tool to reduce intraoperative bleeding from the tumour at resection (Boriani and Fisher, 2015).

Biopsy of the lesion is often the most important step toward diagnosis, but may also be a stumbling block to the treatment paradigm. Technical mistakes at biopsy, leading to tumour spread may preclude complete resection in a potentially curable patient. Thus a multidisciplinary approach that combines an experienced interventionalist in direct consultation with the spine surgeon responsible for potential resection is appropriate to avoid errors at this stage. Consideration for biopsy should be given to lesions that do not have a diagnostic appearance and harbour malignant characteristics such as bony destruction. More benign lesions, particularly those in posterior elements and in younger patients should be watched for signs of activity. There are four main biopsy techniques: Fine Needle Aspiration Biopsy, Core Needle Biopsy, Incisional Biopsy and Excisional Biopsy. In patients in whom imaging studies suggest a differential diagnosis that includes only benign lesions, excisional biopsy will be appropriate for both diagnosis and treatment. Otherwise, Fine Needle Aspiration and Core Needle Biopsy are recommended for suspected malignant lesions. For core needle biopsy, sealing the biopsy hole or site with bone wax or using the coaxial technique is recommended to obviate possibility of spreading the tumorous cells. CT guided Fine Needle Aspiration is the most commonly used procedure, yielding a tissue diagnosis in 70 to 80% of procedures. It has a low complication rate and a lower likelihood of an extra-lesional spread of the tumour cells. Open biopsy is to be avoided as much as possible due to increased risks of local tumour recurrence. Early referral to a tertiary centre capable of treating the patient and with appropriate surgical expertise is beneficial prior to biopsy despite diagnostic uncertainty (Clarke *et al.*, 2014).

Garg *et al.*, (2016) in a study confirmed the higher sensitivity (87.9%) and diagnostic yield (84.6%) of imaging-guided percutaneous needle biopsy for vertebral neoplasms, increasing the sensitivity to 100% with the use of a novel needle biopsy technique performed coreaxially through a core biopsy track compared to 61.1% for blind fine needle aspiration biopsy (FNAB).

Histological diagnosis should always be achieved by biopsy, but clinical, laboratory and imaging studies are important before doing the biopsy to orientate diagnosis and to select biopsy technique. At biopsy, tissue cultures should be taken to rule out infection. (Boriani and Fisher, 2015).

The pathological diagnosis must involve a thorough review. If necessary repeat the Fine needle aspiration to ensure adequate diagnostic tissue is obtained. The diagnosis impacts treatment planning and prognosis, therefore it is important not to hesitate to seek a second pathological opinion. As these primary tumours are rare it is important to send specimens to a recognised expert to confirm the diagnosis. An example would be in a case of atypical or typical haemangiomas, where it is not uncommon for biopsy to be reported as normal bone marrow (Clarke *et al.*, 2014).

Pathological diagnosis together with results of a thorough metastatic workup in malignant disease dictates the treatment plan. Metastatic disease at presentation alters the extent and type of surgery to be done. For example a solitary lesion may undergo local treatment while a metastatic lesion necessitates a systemic approach to treatment. Evidence of metastasis also affects surgical decision making. If there is no evidence of metastasis, en block resection of a malignant lesion poorly responsive to adjuvant therapy may offer opportunity of cure. Such a possibility is eliminated with evidence of metastatic lesion, with preference for less aggressive surgery or no surgery at all depending on the intended purpose of such surgery. The type of metastatic workup is dictated by the pathological diagnosis as specific pathologies have specific metastatic predilections. Positron emission tomographic (PET) scanning is an excellent option. Computed tomographic (CT) scan of the chest, abdomen and pelvis is appropriate. Isotope bone scan, though not specific, would show other skeletal metastasis or skip lesions. Other tests include skeletal survey for multiple myeloma. Bone marrow biopsy and immunoelectrophoresis may be done as well (Clarke *et al.*, 2014).

In their retrospective study of 36 cases of extradural spinal tumours, Sharma *et al.* (2016) found that after gross total excision of masses 36 were neurofibromas, 7 were Ewing's Sarcomas, 3 were granulomas, 2 were metastatic tumours, 2 were angiolipomas, 2 were chordomas, one was aneurysmal bone cyst, one was plasmacytoma, one was Rhabdomyosarcoma and one was neurofibromatosis. However this list of tumours is not exhaustive as there are other tumours which may affect the spine not represented here.

With all these investigative tools available in the developed world, it is worthwhile to look at the situation in our resource limited setup. Which tools do we have and are they readily available to the patient? Is their unavailability a constraint to providing a certain level of care and treatment to patients with EDST?

2.5 Oncological Staging

Once imaging and biopsy results are available the tumour can then be staged according to the Enneking system. This system is based on clinical, imaging and histological findings and divides tumours into benign and malignant types. Benign tumours are staged from I to III depending on whether they are latent, inactive and asymptomatic (stage I), or slow growing and mildly symptomatic (stage II) or aggressive and fast growing (stage III). Malignant tumours are staged into six stages as IA and IB, IIA and IIB, IIIA and IIIB and IVA and IVB. Type A lesions are intracompartmental whereas type B lesions are extracompartmental. Stage I lesions are low grade, stage II are high grade and stage III are any grade with metastasis. Each stage is related to overall prognosis and by necessity, directly linked to categories of surgical procedures based on the concept of “margin” (Boriani and Fisher, 2015).

Guzilik (2016) in a study has indicated that imaging examinations, magnetic resonance in particular, are crucial for the proper planning of spinal surgery in consequence of metastatic lesions. Magnetic resonance clearly visualises the morphology of metastasis, yet does not allow for clear-cut differentiation of the aetiology of bone destruction, Clinical instability in the thoracic spine is significantly less common than its MRI features. MRI is not sufficient for clear-cut differentiation between the actual infiltration of the tumour into soft tissues, particularly into the dura mater, and its adherence and modelling.

2.6 Treatment and Outcomes

Hsu et al (2009) state that primary spinal neoplasms are rare tumours that can lead to significant morbidity secondary to local bone destruction and invasion into adjacent neurological, vascular and other structures. The approach to treating benign or malignant primary tumours of the spine may be dictated by the stage. For metastatic spinal tumours the primary goal of treatment may be palliation to improve the quality of life. Metastatic tumours of the spine may cause a significant impact on quality of

life. In select cases with spinal instability, pain and neurological deficit, surgical management is indicated. Tumours of the spine represent a clinical challenge to even the most experienced physician and require a multidisciplinary approach to ensure optimal patient outcomes

Spacca *et al.*, (2015), in a retrospective study looking at paediatric tumour location, histology and outcomes indicate that although spinal tumours in childhood are rare and heterogeneous, their treatment is very demanding. It is necessary to both manage the disease and preserve the spinal stability so that the spine can grow normally. As a consequence, results in terms of both mortality and morbidity are often suboptimal. In their series, clinical and radiological outcomes were evaluated to assess mortality, morbidity, and surgical outcomes. A special interest was directed toward morbidity related to spinal deformity and neurological deficits. One hundred and seventeen patients were surgically treated, with a total of 138 surgical procedures. A posterior approach was chosen in 111 cases, with osteoplastic laminotomy in 80 patients. Radiotherapy was administered to 22 patients and chemotherapy to 26. At the last follow-up, 16 patients (11.9%) had died. A good control of the tumour with clinical improvement was reported in 100 patients (74.6%). Five patients developed spinal instability (3.7%). They concluded that the goals of surgery should be histology, spine and nerve root decompression, and preservation of spinal stability. In their experience, osteoplastic laminotomy was a good surgical approach to perform the resection of the tumour as it had a low risk of secondary spinal instability.

The first stage of benign tumours (latent, inactive) includes asymptomatic lesions bordered by a true capsule, which is usually seen as a sclerotic rim on plain radiographs. These tumours do not grow, or grow very slowly, and no treatment is required unless surgery is needed for decompression or stabilisation. Benign stage II tumours grow slowly, causing mild symptoms. The tumour is bordered by a thin capsule and a layer of reactive tissue sometimes visible on plain radiographs as an enlargement of the tumour outline. For these, intralesional excision can be performed with the risk of a low recurrence rate (based on very low quality evidence). The incidence of recurrence can be lowered further by local adjuvants such as cryotherapy, embolisation, and radiation therapy. Benign stage III tumours are aggressive and grow rapidly, with a capsule that is very thin, discontinuous or absent. The tumour invades

local compartments and a wide reactive hypervascularised tissue (pseudocapsule) is often present. For these, the ideal surgical treatment is en-bloc excision with marginal or wide margins (Boriani and Fisher, 2015).

For low grade (stages IA and IB) malignant tumours there is no true capsule but a pseudocapsule of reactive tissue permeated by small microscopic islands of tumour in it. A marginal resection performed along the pseudocapsule will leave residual foci of active tumour, therefore stereotactic radiation or proton beam therapy can be added to reduce the risk of recurrence. Treatment of choice, if feasible is a wide en-bloc resection, and careful marginal dissection if neural tissues are involved. In high grade malignancies (Stages IIA and IIB), the neoplastic growth is so rapid that there is no time for the host bone to form a continuous reactive zone tissue. There is continuous seeding with neoplastic nodules (satellites). More over these tumours tend to have neoplastic nodules at some distance from the main tumour mass (skip metastases). For these tumours, the margin of resection must be wide as it is not possible to achieve radical margin in the spine. A course of radiotherapy and chemotherapy, according to the tumour type, must be considered for the local control and the avoidance of distant spread. In areas of anatomical constraints, marginal margins or planned intralesional transgressions must be accepted, or consideration given to the sacrifice of neurological structures. Stage IIIA and IIIB are described the same lesions as IIA and IIB but are associated with distant metastasis, and in the majority of cases would be considered incurable. (Boriani and Fisher, 2014)

Surgical planning must be based on what the procedure will achieve in relation to the margin of resection. The final pathological margin achieved through the surgical technique is directly related to prognosis. By retrospectively reviewing his large case series, Boriani was able to establish significant relationship between margin and outcome specific to the spine (Boriani and Fisher, 2014).

Quraishi *et al.*, (2016) indicate that most patients in their series underwent a piecemeal resection with intralesional margins. They note that this remains safe with a low local recurrence rate and that en bloc excision may provide more chance of complete excision of the nidus but is not mandatory. The importance of complete excision of the nidus cannot be over-emphasized. This was in a multicentre ambispective cross-

sectional observational cohort study of osteoid osteoma looking at results of surgical resection and analysis of local recurrence. Spinal osteoid osteomas are benign primary tumours arising predominantly from the posterior column of the spine. These 'osteoblastic' lesions have traditionally been treated with intralesional excision.

In a systematic clinically based review of literature on the treatment of benign tumours of the spine, Charet-Morin *et al.*, (2016), a multidisciplinary panel of spine surgeons, radiation oncologists, and medical oncologists, elaborated specific focused questions regarding aneurysmal bone cyst, giant cell tumour, and osteoid osteoma. Denosumab, bisphosphonate, interferon, bone marrow aspirate, doxycycline, thermal ablation, and selective arterial embolisation were identified as areas of interest for the article. A systematic review was performed through MEDLINE and EMBASE. Recommendations based on the literature review and clinical expertise were issued using the GRADE system. Their results showed that the overall quality of the literature was very low with few multicentre prospective studies. For giant cell tumour, combination with Denosumab identified 14 pertinent articles with four multicentre prospective studies. Nine studies were found on bisphosphonates and six for selective arterial embolisation. The search on aneurysmal bone cyst and selective arterial embolisation revealed 12 articles. Combination with Denosumab, Doxycycline, and bone marrow aspirate identified four, two, and three relevant articles respectively. Eleven focused articles were selected on the role of thermal ablation in osteoid osteoma. They concluded that alternative and adjuvant therapy for primary benign bone tumours have emerged. Their ability to complement or replace surgery is now being scrutinised and they may impact significantly the algorithm of treatment of these tumours. They indicated that most of the data are still emerging and further research would be desirable. Close collaboration between the different specialists managing these pathologies is crucial.

As earlier stated, palliative surgical procedures may be performed solely for functional purposes, for example to decompress neurologic structures or stabilise the spine, and are usually performed for metastatic spine disease (Boriani and Fisher, 2015).

Tomita *et al.*, (2001) designed a new surgical strategy for treatment of patients with spinal metastases. Their scoring system was designed for deciding between excisional or palliative surgical procedures. They noted that recently, aggressive surgery, such as total en bloc spondylectomy for spinal metastases, had been advocated for selected patients. They further stated that surgical strategies should include various treatments ranging from wide or marginal excision to palliative treatment with hospice care. Sixty-seven patients with spinal metastases who had been treated from 1987–1991 were reviewed, and prognostic factors were evaluated retrospectively (phase 1). A new scoring system for spinal metastases that was designed based on these data consists of three prognostic factors: grade of malignancy (slow growth 1 point; moderate growth, 2 points; rapid growth, 4 points), visceral metastases (no metastasis, 0 points; treatable, 2 points; untreatable, 4 points), and bone metastases (solitary or isolated, 1 point; multiple, 2 points). The scores from these three factors were added to give a prognostic score between 2 and 10. The treatment goal for each patient was set according to this prognostic score. The strategy for each patient was decided along with the treatment goal: a prognostic score of 2 to 3 points suggested a wide or marginal excision for long-term local control; a score of 4 to 5 points indicated marginal or intralesional excision for middle-term local control; a score of 6 to 7 points justified palliative surgery for short-term palliation; and a score of 8 to 10 points indicated non-operative supportive care.

Sixty-one patients were treated prospectively according to this surgical strategy between 1993 and 1996 (phase 2). The extent of the spinal metastases was stratified using the surgical classification of spinal tumours, and technically appropriate and feasible surgery was performed, such as en bloc spondylectomy, piece-meal thorough excision, curettage, or palliative surgery. Their results indicated mean survival time of the 28 patients treated with wide or marginal excision of 38.2 months (26 had successful local control). The mean survival time of the 13 patients treated with intralesional excision was 21.5 months (nine had successful local control). The mean survival time of the 11 patients treated with palliative surgery and stabilization was 10.1 months (eight had successful local control). The mean survival time of the patients with terminal care was 5.3 months. They proposed a new surgical strategy for treatment of spinal metastases based on the prognostic scoring system. This strategy provides appropriate guidelines for treatment in all patients with spinal metastases.

The aim of this study was to analyse and discuss the results of extradural spinal tumours after surgical treatment and relevant literature was reviewed.

Another scoring system is the revised Tokuhashi scoring system, which is different from the Tomita system in that it considers performance status, types and locations of metastatic lesions, and paralysis with use of the Frankel classification to assign a score.

These scoring systems indicate an assessment on prognosis. In the Tokuhashi system, high scores indicate good prognosis while in the Tomita system, lower scores indicate good prognosis.

In an instructional course lecture of the American Academy of Orthopaedic Surgeons (AAOS), Kim *et al.*, (2012) indicated that the surgical management of metastatic disease of the spine continues to evolve. For most of the recent three decades, radiation therapy provided the main stay of treatment for patients with symptomatic metastatic disease of the spine. Surgical treatment during this era often involved dorsal spinal cord decompression with no or limited spinal instrumentation. These procedures generally provided only an indirect decompression of the spinal cord and often increased spinal instability. However, with advances in the understanding of metastatic processes in the spine and evolution of surgical techniques and instrumentation, surgical treatment plays a prominent role in the care of patients with metastatic epidural spinal cord compression (MESCC). Studies have now yielded level-I evidence on the efficacy of surgery for metastatic disease of the spine for improving quality of life and outcomes in patients with spinal metastasis. Concurrently, advances in radiation oncology now allow high precision targeting of tumours and increased efficacy when treating radio-resistant lesions. Kim *et al.*, (2012) further state that in considering treatment methods, it is essential to account for factors such as tumour type and/or biology, extent of disease, neurological status, an individual patient's expectations, quality of life, and life expectancy.

Surgical management of spinal metastases is considered for four primary indications: compression of the neural elements; spinal instability, including pathological fracture; unrelenting pain, and, rarely, when a histologic diagnosis must be established. Patients

with metastatic spinal disease requiring surgical intervention may be treated with either an en bloc spondylectomy (considered in the rare patient with a solitary metastasis and favourable prognosis) or more commonly with an intralesional decompression and stabilization. Traditionally, anterior approaches were used because they aided in achieving disease-free margins in en bloc spondylectomies but an all posterior approach is more desirable as it adds little to morbidity compared to an anterior one. At times clear margins and true en bloc spondylectomies cannot be performed because of the local extent of the tumour as is the case in patients in whom the metastatic lesion has spread to the posterior elements through the lamina or vice versa from the lamina through the pedicle into the anterior vertebral body. In such situations, the most feasible approach is to achieve a marginal resection since a laminectomy and violation of the posterior elements is necessary to remove the anterior elements en bloc without injury to the spinal cord. In this respect, the majority of vertebral en bloc resections are, at best, contaminated marginal resections. In such cases, postoperative radiation may aid in minimizing local recurrence of disease.

Improved survival in patients undergoing en bloc resection compared with those who have marginal resection for metastatic disease of the spine has not been documented; in addition, these procedures are technically demanding and are associated with a high rate of morbidity. It is therefore reasonable to reserve these aggressive procedures for patients with a solitary metastasis following a long disease-free interval. Most patients with metastatic spinal disease requiring surgical intervention are treated with an intralesional resection. The goals of surgery are to adequately decompress the neural elements, stabilize the spine, and achieve a gross total resection of the tumour. The offending tumour is most commonly located in the vertebral body; however, the surgical approach need not be anterior in all patients. In patients with multilevel disease or (nearly) circumferential dural compression, anterior approaches may not be suitable for decompression. Posterolateral transpedicular or costotransversectomy approaches have been increasingly utilized to provide safe and effective neural decompression and spinal stabilization while avoiding the morbidity (particularly pulmonary) associated with anterior approaches and providing the flexibility to extend the surgery over multiple symptomatic levels. Regardless of the approach utilised, adequate spinal fixation or instrumentation is necessary to provide immediate stability and to avoid the use of spinal orthoses postoperatively. Usually, subsequent radiation

therapy is employed to minimize the risk of local tumour recurrence. Anterior procedures will require structural support to replace the resected volume of bone in the form of metallic cages, cortical structural allografts or methyl-methacrylate bone cement. Spinal stability will have to be maintained or restored with plate and screws for anterior procedures or pedicle screw systems for posterior procedures. Less invasive options of kyphoplasty and vertebroplasty may be employed for patients with poor prognostic indicators for the relief of pain. These may be complimented with chemotherapy and/or radiotherapy (Dolan *et al.*, 2016)

Ejima, Matsuo and Sasaki (2015) in their review article wrote that radiotherapy is typically the mainstay of treatment for spinal bone metastases. They indicated that a number of studies have shown that palliative radiotherapy can be effective for painful bone metastases, while relatively little is known about the management of spinal bone metastases, especially metastatic epidural spinal cord compression(MESCC). The management of MESCC requires a consideration of motor function and spinal instability as well as pain and local control. Stereotactic body radiotherapy (SBRT) can safely administer a higher dose to the target, and can potentially provide lasting local control. SBRT is a promising method, however, epidural recurrence after SBRT and SBRT-induced vertebral compression fractures continue to be problematic, and require the appropriate application of combination SBRT and surgery. An evaluation of functional outcomes following spinal SBRT and the identification of indicators for surgery are needed to establish an optimal treatment strategy for spinal metastases.

Goodwin *et al.*, (2016) reviewed literature on molecular markers and targeted therapeutics in metastatic tumours of the spine with the aim to discuss the evolution of molecular signatures and the history and development of targeted therapeutics in metastatic tumour types affecting the spinal column. They concluded that for the providers who will ultimately counsel patients diagnosed with metastases to the spinal column, molecular advancements will radically alter the management/surgical paradigms utilised. Ultimately, the translation of these molecular advancements into routine clinical care will greatly improve the quality and quantity of life for patients diagnosed with spinal malignancies and provide better overall outcomes and counselling for treating physicians.

Sharma *et al.*, (2016) in a retrospective study of 36 patients who were operated for spinal extradural tumours between May 1999 and December 2012 assessed functional neurological outcome by McCormick's grading. Out of 14 patients who harboured malignant pathology 12 patients received radio and chemotherapy. Post-operative wound infection occurred in 5 patients. Regarding post-operative neurological status, 18 patients showed improvement, 6 patients remained same and 12 patients had deteriorated neurologically. Tumour recurrence occurred in 15 patients; 12 patients with malignant and 3 patients with benign lesions on follow up period. There was no surgery related mortality, however, 11 patients died during 3 years follow up period due to adverse pathology they were having. They concluded that total excision should be the aim of all extradural spinal tumours whether they are benign or malignant. They also concluded that benign extradural tumours show excellent results after total surgical excision and that malignant lesions, whether primary or metastatic, have poor prognosis despite all modalities of treatment.

In a study of features and outcome of surgical management of spinal tumours in a cohort of Nigerian patients, Adeolu *et al.*, (2015) concluded that metastases are the commonest histological finding and are commonly located in extradural space. Surgical outcome was satisfactory in most cases with neurologic function remaining the same (52%) or improving (45%) after surgery. Only 2.5 % deteriorated neurologically.

Amendola *et al.*, (2014), in a retrospective study of en bloc resection of spinal tumours concluded that statistical analysis of the long-term results referred to 103 patients affected by aggressive benign and malignant primary spine tumours indicated that an en bloc resection is associated with a high rate of complications. Nevertheless, it decreases the risk of local tumour recurrence and tumour-related mortality and that en bloc tumour resection is a highly demanding procedure but can be performed to an acceptable degree of safety.

Boriani *et al.*, (2016) indicated that en bloc spinal tumour resections aim at surgically removing a tumour in a single, intact piece. The approach must be planned for the complete removal of the tumour without violation of its margins. The shared knowledge of the morbidity, mortality, and risk assessment for local disease

recurrence, complications and death, related to spine tumours excised en bloc could improve the treating physician's apprehension of the diseases and decision making process before, during and after surgical treatment. The purpose of their study was to review and report the experience gained in one of the world's biggest spine oncological centres of over 25 years. They concluded that treatment of spinal aggressive benign and malignant bone tumours through en bloc resections is beneficial, in terms of better local control and prognosis, although it is a highly demanding and risky procedure. Margins are the key point of this procedure, thus, a careful preoperative oncological and surgical staging is necessary to define the optimal surgical approach. The adverse event profile of these surgeries is high; therefore, they recommended that it should be performed by experienced and multidisciplinary teams in specialised high volume centres.

Arutyunyan and Clarke (2015) indicated that management of spinal tumours depends not only on clinical presentation but also on histology, stage and grade of the tumour. Primary benign lesions are a focal problem, however they may be locally aggressive. Primary malignant lesions are always considered aggressive and are managed in a multidisciplinary fashion. Surgical treatment often requires aggressive en bloc resection to maximise potential for cure.

Fuchs *et al.*, (2005) conducted a retrospective study of en bloc resection of sacrococcygeal chordomas. They indicate that this tumour presents a difficult diagnostic and therapeutic problem, with a high rate of local recurrence. Fifty-two patients underwent surgical treatment for sacrococcygeal chordoma between 1980 and 2001. Their series included 18 female patients and 34 male patients, with an average age of 56 years (a range of thirteen to seventy-six years) at the time of diagnosis. The surgical approach depended on the level and extent of the lesion, with a posterior approach performed in twenty-two patients and a combined anteroposterior approach used in thirty. A wide surgical margin was achieved in twenty-one patients. At an average of 7.8 years (range, 2.1 to 23 years) postoperatively, 23 patients were alive with no evidence of disease. Twenty-three patients (44%) had local recurrence. The rate of recurrence-free survival was 59% at five years and 46% at ten years. The overall survival rates were 74%, 52%, and 47% at 5-, 10- and 15- years respectively. All patients with a wide margin survived, and this survival rate was significantly

different from that for patients who had had either marginal or intralesional excision ($p = 0.0001$). Of the 21 patients with a wide margin, 17 (81%) had undergone a combined anteroposterior approach and only 4 had been treated with a posterior approach. They conclude that a wide surgical margin is the most important predictor of survival and of local recurrence in patients with sacrococcygeal chordoma and that use of a combined anteroposterior approach increases the likelihood of obtaining a wide margin of resection.

Nasser *et al.*, (2016) highlight the use of intraoperative stereotactic navigation which they say has become more available in spine surgery. These authors undertook a multicentre retrospective study to assess the utility of intraoperative CT navigation in the localisation of spinal lesions and as an intraoperative tool to guide resection in patients with spinal lesions. They say O-arm 3D imaging with stereotactic navigation may be used to localize lesions intraoperatively with real-time dynamic feedback of tumour resection. Stereotactic guidance may augment resection or biopsy of primary and metastatic spinal tumours. It offers reduced radiation exposure to operating room personnel and the ability to use minimally invasive approaches that limit tissue injury. In addition, acquisition of intraoperative CT scans with real-time tracking allows for precise targeting of spinal lesions with minimal dissection. They further state that more work may need to be done to assess the utility of stereotactic guidance in oncological tumour resection, particularly with respect to surgical outcomes for patients.

Kadhim *et al.*, (2016) write that intraoperative radiographic guidance has traditionally been utilized in orthopaedic surgery through 2-D navigation with the C-arm and recently with 3-D navigation with the O-arm. Their study aimed at describing the outcome of surgical treatment of spinal osteoblastoma and osteoid osteoma with the utilisation of the O-arm and conventional C-arm guidance. This was a retrospective cohort study of patients with spinal osteoid osteoma and/or osteoblastoma who were treated at their institution between 2002 and 2011. Seventeen patients were examined in this study including seven with spinal osteoblastoma and 10 with spinal osteoid osteoma. The O-arm was used in seven patients and the C-arm in 10 patients. The C-arm failed to identify the tumour in one case and they needed to perform a computed tomographic-scan. The length of surgery was shorter when the O-arm was used,

especially in the osteoblastoma group. Thirteen patients were pain free at the last follow-up visit and two patients developed recurrence. Radiographs at the last follow-up did not show signs of vertebral instability following tumour resection. Safe and effective localization of spine tumours and confirmation of tumour removal during surgery was achieved by intraoperative radiographic guidance specifically with the O-arm 3-D navigation system.

In a retrospective study of incidence, histopathology and surgical outcome of spine tumours at Sher-i-Kashmir Institute of Medical Sciences, Bhat *et al.*, (2016) concluded that surgical outcome in terms of recovery and spinal stability of benign tumours is comparatively better than malignant ones.

For osteogenic sarcoma and Ewing's sarcoma of the spine, age of the patient, extent of disease and surgical resection are key survival determinants. Radiotherapy may be associated with worse outcomes in Osteogenic Sarcoma while it is of potential benefit in Ewing's sarcoma of the spine. This is according to Arshi *et al.*, (2016).

Sanjay *et al.*, (1993) indicated that giant cell tumours of the spine are a surgical challenge and treatment remains controversial. Tumour recurrence is common. Wide resection can only be advised at the expense or risk of neurological deficit and spinal instability. They suggest complete removal, but because of their location, this usually means excision with an intralesional margin. Because of the risk of sarcomatous transformation, radiation therapy is reserved for patients with incomplete excision and for those with local recurrence.

Luzzati *et al.*, (2016) indicate that despite the mainstay of treatment for primary malignant bone tumours being wide surgery in the spine as well, most cases undergo the first approach in a non-specialized centre. This often means adopting the inappropriate approach with contamination which consistently decreases the effectiveness of a second surgery. The aim of their study was to evaluate recurrence and survival rates after en-bloc resection. Their patients underwent wide resection by the senior author from January 1997 to December 2013 after the first inappropriate approaches were reviewed. Fifty-six patients were included in the evaluation. Epidemiological and clinical characteristics, surgeries, early and late complications

and survival rate were reported. The margin obtained was wide, marginal and intralesional in 9, 28 and 19 cases, respectively. The complication rate was 55.4% and 44.6% for early and late complications, respectively. 73.2% of patients had complications. The survival rate was 82.1% at one year, then decreased 10% each year until 42.1% at 5 years from surgeries. No statistically significant correlation was found between margin and local recurrence and survival. They conclude that in their series, the first inappropriate approach had already compromised patient prognosis, so in case of suspicious primary spine tumour the patient had to be referred to a specialized centre. The margin obtained during salvage surgery did not appear to influence recurrence and survival, probably because it was already compromised by the first surgery. They recommended that more prospective studies are necessary to confirm their findings and to verify the impact of the margin obtained during salvage surgery on patients' survival.

Resection of tumours leaves large bony defects and is associated with high morbidity with complications up to 35% being described in some series (Fisher *et al.*, 2009). Both sepsis and mechanical failure are prevalent. Previous papers report a deep sepsis rate of greater than 5%, mechanical failure in 7% and mortality related to the surgery in 2% of cases of en bloc resections in the spine. Combined anterior and posterior approaches and number of levels resected are predictors of increased complications (Laubscher, Held and Dunn).

This study will aim to bring out the surgical approaches employed and the outcomes of surgical and non-surgical treatment of EDST in our institution. It will compare our treatment outcomes with the outcomes from other setups. It will attempt to answer the questions whether our outcomes are favourable or not and whether there are areas needing improvement or not.

CHAPTER THREE: METHODOLOGY

3.1 Study Design

This was a retrospective study of the presentation, management and short-term outcomes of extradural spinal tumours at the University Teaching Hospital, a third level referral (tertiary) and teaching hospital in Lusaka, Zambia. It involved the reviewing of patients' files and hospital records between 1st January, 2013 and 31st December, 2016.

3.2 Sources of Data and Data Collection Tool

3.2.1 Secondary Data

The secondary source of data was the literature review of published research findings related to extradural spinal tumours as shown in chapter two. This was important in order to show what other researchers have done and found or shown with regard to extradural spinal tumours and their findings' applicability in our setup.

3.2.2 Primary Data

Primary data was collected from the patients' files and hospital records using a predetermined questionnaire that had both closed and open-ended questions and statements. This data was both quantitative and qualitative. Quantitative data was used to give statistical value to the study.

3.3 Study Population, Case Definition, Inclusion Criteria and Exclusion Criteria

3.3.1 Study Population

This comprised male and female patients of all ages and races diagnosed with primary or secondary extradural spinal tumours and treated for such at the University Teaching Hospital during the study period.

3.3.2 Case Definition

A patient diagnosed with an extradural spinal tumour of any tissue origin, primary or secondary was considered a case for study.

3.3.3 Inclusion Criteria

Any patient with an extradural spinal tumour that may be primary or secondary who:

- was of any age, sex and race
- Had a histopathological or tissue diagnosis
- Was treated or presented between 1st January 2013 and 31st December 2016

3.3.4 Exclusion Criteria:

- Any patients who was diagnosed with or treated for an intradural spinal tumour
- Presence of symptomatic concurrent injury, infection or degenerative condition of the spine or vertebral column.

3.4 Sampling Method and Sample Size

3.4.1 Sampling Method

The study used non-probability sampling technique in form of convenience and purposive sampling. We used convenient sampling of all patients with spinal tumours who presented during the study period to identify those with extradural spinal tumours who were then included in the study. This was because the prevalence and incidence of these tumours are low and the rates are currently unknown in our set up.

3.4.2 Sample Size:

Sample size was 66, and was derived from the formula

$$N = \frac{(t^2) X p(1 - p)}{m^2},$$

Where N was the sample size, t was the confidence level at 95% (1.96), p was the estimated prevalence at 45% (0.45) and m was the allowable margin of error at 12% (0.12).

3.5 Research Instruments, Data Collection Method and Study Variables

3.5.1. Questionnaire Development

A full structured questionnaire was developed for use to answer the questions in the study objectives. The questionnaire included both closed questions with defined responses and open-ended questions. The closed questions were included to give the statistics, whilst the open-ended questions enabled collection of qualitative data.

3.5.2. Data Collection Method

Data was collected from patients' hospital records using a predetermined data collection questionnaire as a guide. Participants' hospital case notes, admission records and theatre and histopathology registers were reviewed and requisite data extracted. The radiology data base was utilised as a source of data as well. Two Research Assistants were engaged and trained to help collect all the hospital records required for data search.

3.5.3 Study Variables

Independent variables included age, sex, marital status, employment status and residence. Dependent variables included all possible symptoms as described in the literature review and included backache, back deformity, loss of power in limbs, sensory loss, loss of bladder and bowel control, abnormal gait, incoordination, clumsiness, poor appetite,, weight loss, night pain, fever, cough, neck mass, abdominal pain, breast lumps and lower urinary tract symptoms. Dependent variables related to signs included pain scores based on the visual analogue scale, patients' mobility status, muscle tone, muscle power, deep tendon reflexes, sensory level, and Frankel grade. Others were presence of back deformity and digital rectal examination findings. In addition the type of radiological investigations (plain X-rays, CT scan, MRI scan, Tc Bone Scans and others) done were indicated and the reasons for not doing any radiological investigation were determined. All laboratory tests done were recorded, including special or specific tests and their findings. Presence of co-morbidities and host type, provisional diagnosis and treatment plan and the indications

for that were also included. Outcome measures included indication whether there was improvement, stagnation or worsening of initial symptomatology and examination findings. Other outcome measures were presence and type of complication as well as mortality.

3.5.4 Pilot Study

A pilot study was conducted to answer the question of availability of patients' files for data retrieval and whether the files would contain data needed for this study. The study was able to establish that it is possible to retrieve the files (four patients' files who were seen in the study period were retrieved in one day from main registry and ward record stores) and that all but one were well documented with necessary data that this study seeks to bring out (according to the questionnaire).

3.6 Data Analysis Tools and Procedure

After the data was collected, the questions and responses were coded to ensure that all values and variables under study are correctly defined and captured in the data sheet. The data collected from the questionnaire were checked for uniformity, consistency and accuracy. The quantitative data in the questionnaires were coded and entered into computer software. Analysis and interpretation of data was done using computer software and statistical tools such as Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 25. The SPSS has enough space for a long range of numbers (especially responses for open ended questions in questionnaire) and it also allows mathematical manipulations because of its in-built functions. To aid our interpretation of data, frequency tables and percentages were used. The qualitative data was analysed manually using themes. This involved transcribing and indexing the data into various themes.

3.7 Ethical Consideration

This research study was conducted after ethical approval from The University of Zambia Biomedical Research Ethics Committee (UNZABREC). Permission was

sought and obtained from UNZABREC for exemption (in form of a waiver) from obtaining patients' written informed consent and assent, considering the fact that this was a retrospective study and there was no contact or interaction with the patients. A numbering system was used to identify each participant. The patients' anonymity was honoured and no patient's names were indicated in the study or subsequent reports. No disclosure of the findings was made to any third parties except for the intended purpose of the study as required under UNZABREC and the University of Zambia Senate guidelines for medical research.

3.8 Study Limitations

Although all attempts have been made to capture as many patients as may have presented with EDSTs during the study period, it is still possible that some have been missed as their details were missing from the registers or their files were not available from the records department. Further, the records department was relocated to another building within the hospital at the time of data collection. This contributed to some files and registers going missing, being misfiled or misplaced and as such being untraceable.

Some patients with cancer who later complained of symptomatology likely to be related to metastasis to the spine were not fully investigated by their attending surgeons, particularly Urologists and General Surgeons. These were not included in the study as they did not meet the criteria. Some of the patients' details in some files were inadequate or scanty making data retrieval difficult.

There was a transition period when patients referred to the Cancer Diseases Hospital from peripheral hospitals had to be seen and admitted by general and orthopaedic surgical units at the University Teaching Hospital who commenced investigations and symptomatic treatment prior to referral to the Cancer Diseases Hospital. Most often, these patients have had to re-start basic and advanced investigations once they were finally seen at CDH, causing delays in diagnosis and commencement of treatment as well as increasing cost to the patient and to the government. It is good to note that this is no longer the case.

Although the results of this study have given us a glimpse into what is going on regarding extradural spinal tumours in terms of diagnosis, management and outcomes at the University Teaching Hospital, its retrospective nature as well as the small sample size make the generalisability of the results herein contained statistically difficult.

CHAPTER FOUR: RESULTS

4.1 Background Characteristics

A total of 62 patient files met the inclusion criteria and data was extracted from these and analysed. Out of these, 34 were for female patients and 28 for male patients as displayed in Figure 1.

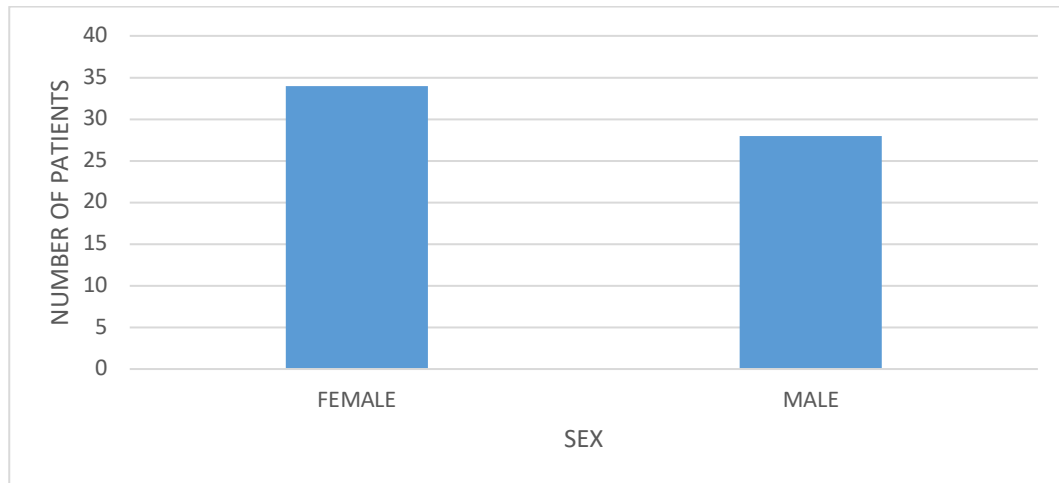


Figure 1: Sex Distribution of Patients

The age ranged from 14 to 87 years, with a median of 55.55 years and a mean of 55.03 years. This followed a normal distribution curve as shown if Figure 2.

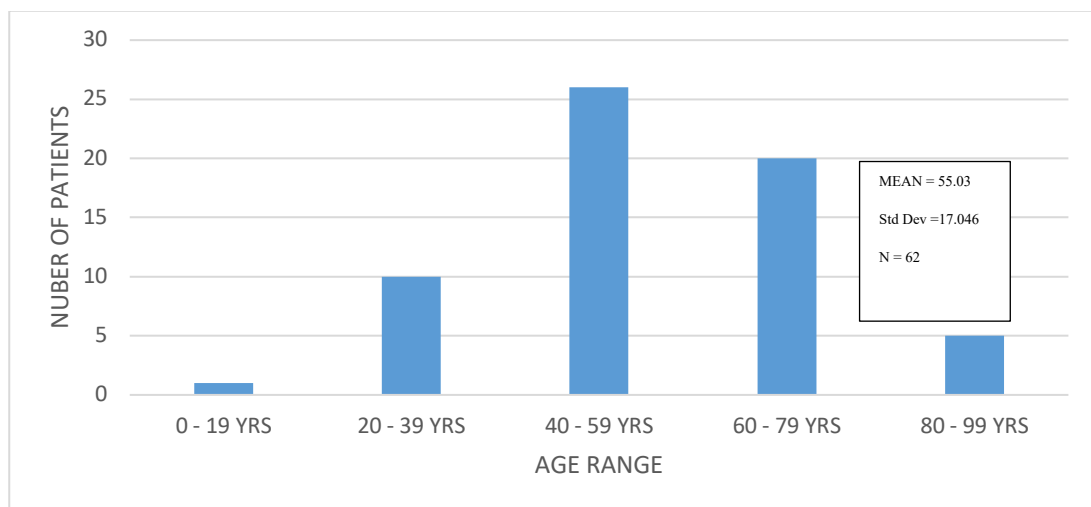


Figure 2: Age Distribution of Patients

Only 15 patients (24.2%) were in some form of employment, with 47 (75.8%) being unemployed. Figure 3 highlights this.

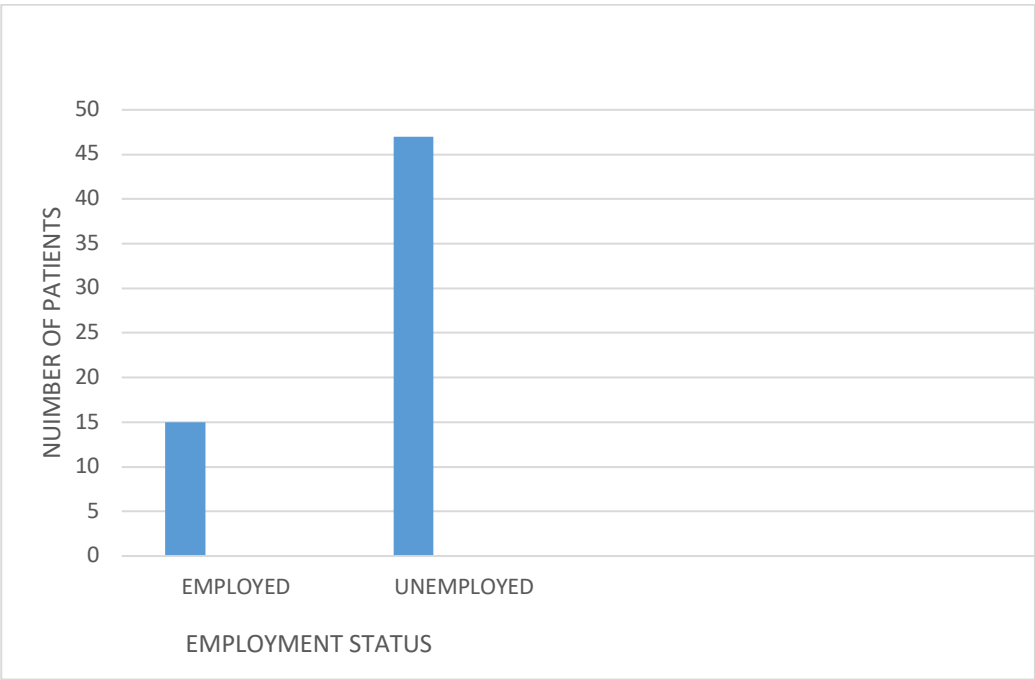


Figure 3: Employment Status of Patients

Forty-seven patients were married, 8 were widowed, 6 were single and 1 was divorced at the time of being seen in Hospital as depicted in Figure 4.

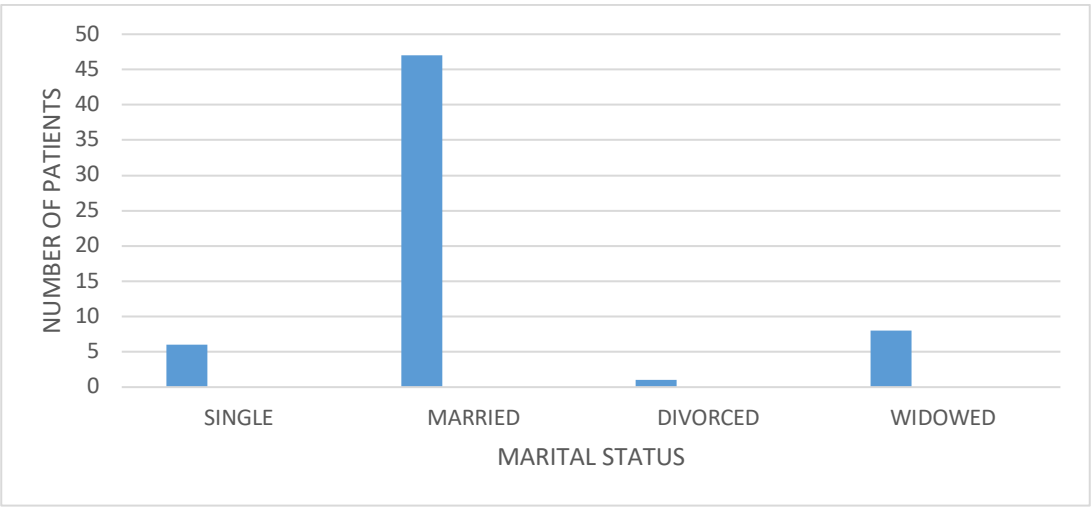


Figure 4: Marital Status of Patients

Thirty-three patients (53.4%) came from urban areas while 29 (46.8%) came from rural areas as shown in Figure 5.

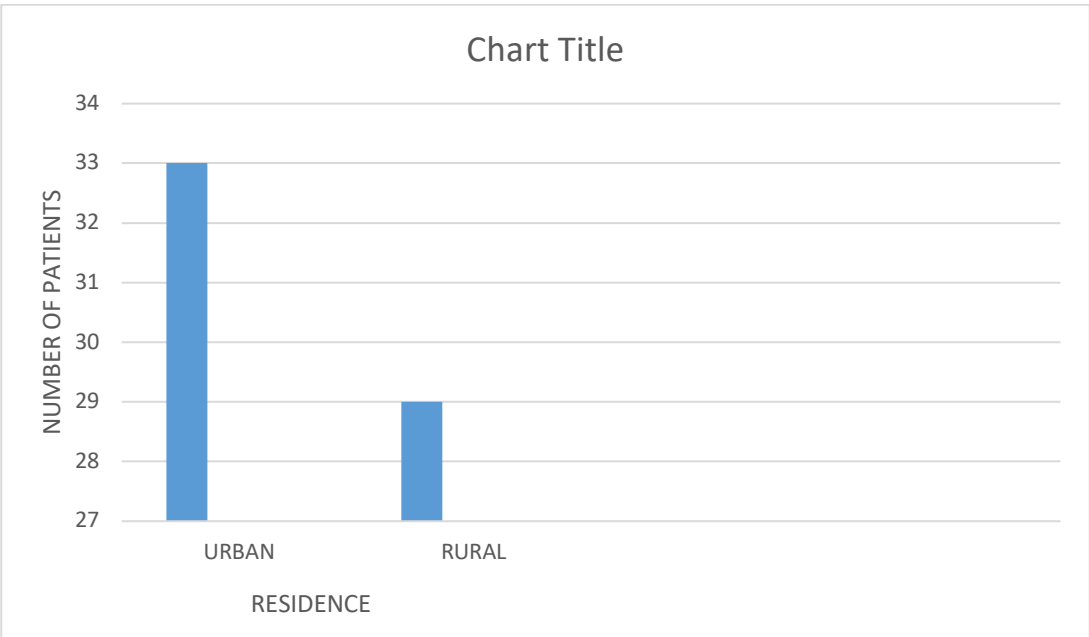


Figure 5: Patients’ Domicile

4.2 Symptomatology

The patients with extradural spinal tumours (EDSTs) presented with a combination of symptoms related to the location of the disease or its effects on the spinal cord or nerve roots. These symptoms included backache present in 93.5% of patients, weakness in limbs (91.9%), sensory loss (50%), loss urine (43.5%) and stool (41.9%) control, back deformity (11.3%), and abnormal gait 8.1%). These symptoms are shown in Figure 6 and in Table 1. None presented with incoordination or clumsiness.

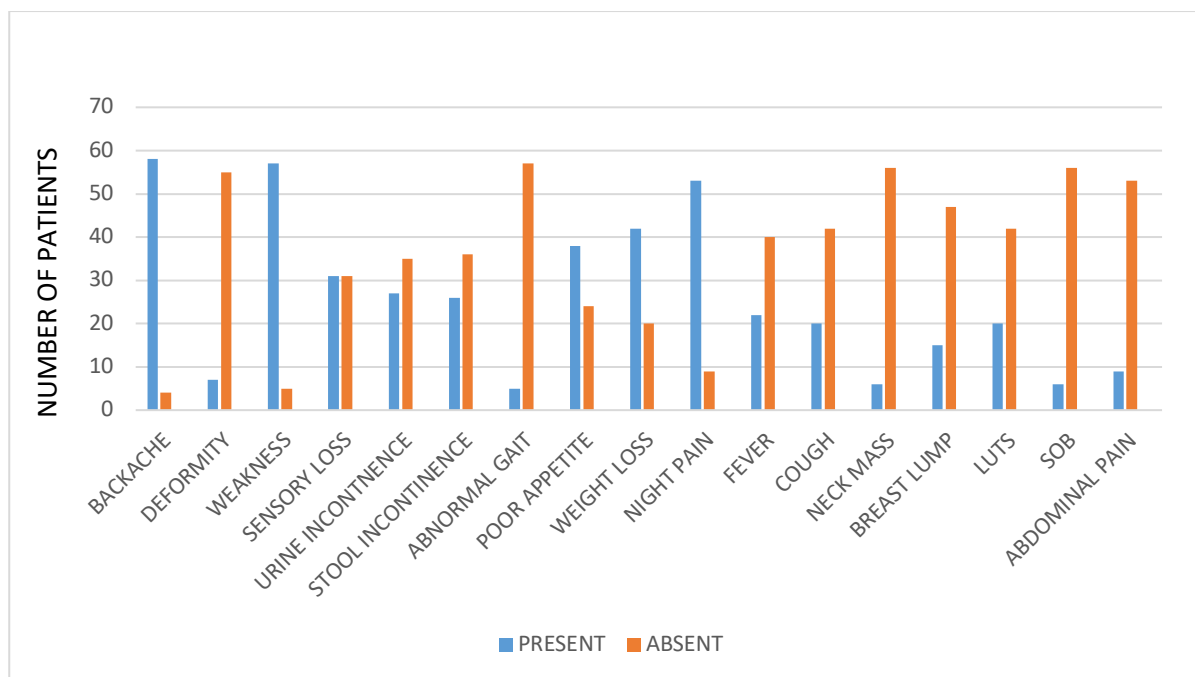


Figure 6: Frequency of Symptoms

Table 1. Frequency of Symptoms

SYMPTOM	NUMBER OF PATIENTS	PERCENTAGE
Backache	58/62	93.5%
Back Deformity	7/62	11.3%
Weakness in Limbs	57/62	91.9%
Sensory Loss	31/62	50%
Loss of Urine Control	27/62	43.5%
Loss of Stool Control	26/62	41.9%
Abnormal Gait	5/62	8.1%

In those patients who presented with constitutional symptoms, poor appetite accounted for 61.3%, weight loss 67.7%, night pain 85.5%, night sweats 29% and fever 35.5% of all patients as shown in Table 2.

Table 2. Frequency of Constitutional Symptoms

SYMPTOM	NUMBER OF PATIENTS	PERCENTAGE OF ALL PATIENTS
Poor Appetite	38/62	61.3%
Weight Loss	42/62	67.7%
Night Pain	53/62	85.5%
Night Sweats	18/62	29%
Fever	22/62	35.5%

In addition, patients with metastases to the spine presented with complaints related to the location of the primary tumour such as breast, prostate or thyroid. These included lower urinary tract symptoms (LUTS) in 32.3%, breast lump in 24.2% and mass in the neck in 9.8% of all patients. Other symptoms were related to the extent of spread of the disease to other organ systems, particularly in those with secondary spread (metastatic disease). In this regard 32.3% presented with cough, 9.7% had shortness of breath and 14.7% had abdominal mass. These symptoms are displayed in Table 3.

Table 3: Other Symptoms

SYMPTOM	NUMBER OF PATIENTS	PERCENTAGE
Cough	20	32.3%
ABD Mass	9	14.5%
SOB	6	9.7%
LUTS	20	32.3%
Breast Lump	15	24.3%
Neck Mass	6	9.7%

4.3 Examination findings

Forty-two patients, representing 67.7% of the study population, were bedridden at the time of presentation to hospital. This was because of either paralysis, pain or both. Only 17 patients (27.4%) were able to ambulate normally while 3 (4.8%) required use of a wheel chair (Figure 7).

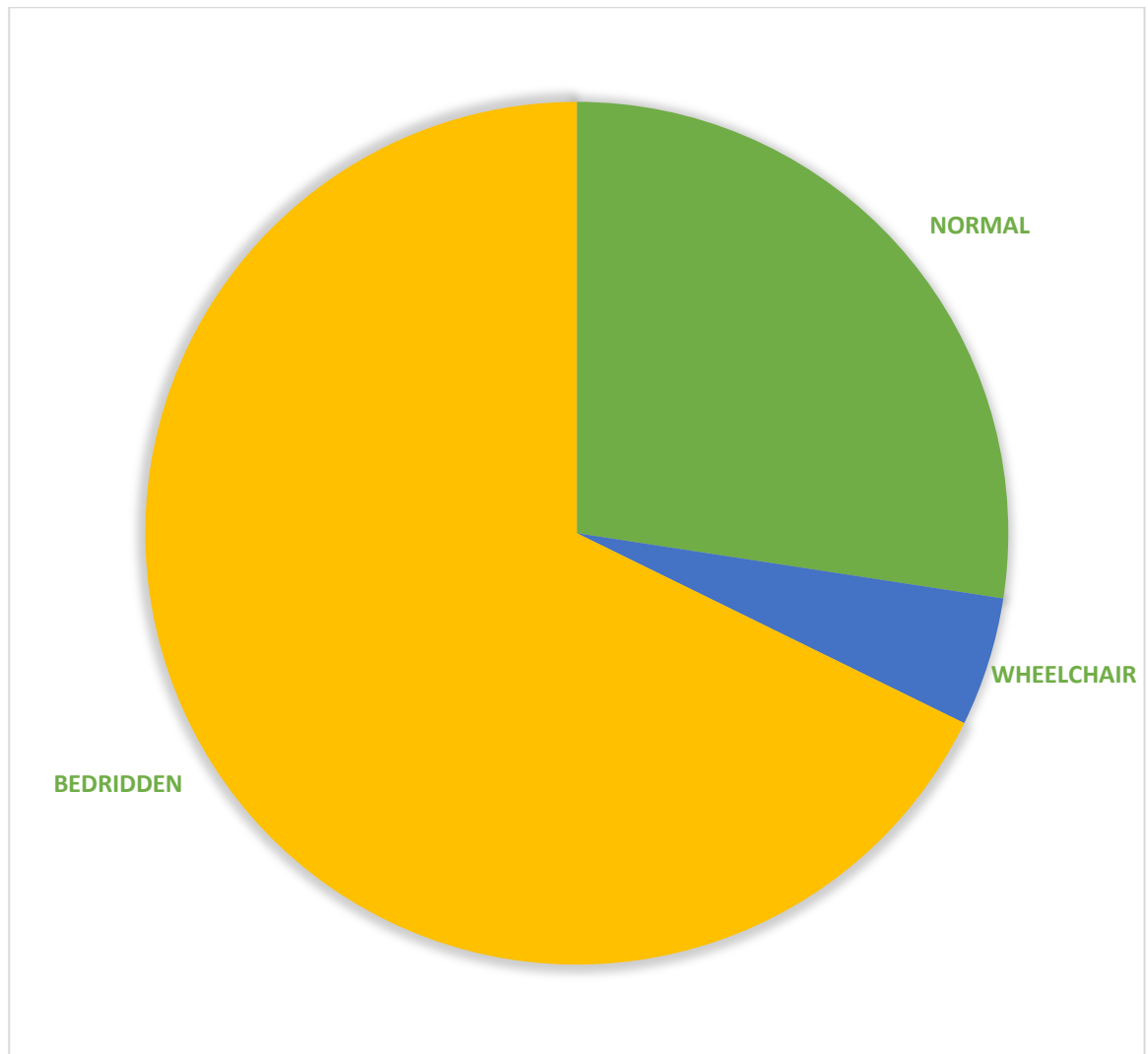


Figure 7: Mobility at Presentation

In terms of scoring their pain using the Visual Analogue Scale (VAS), 57 out of 62 patients reported scores of more than 5, three patients scored 5 and only two patients scored less than 5 at the time of first initial presentation to UTH as shown in Figure 8.

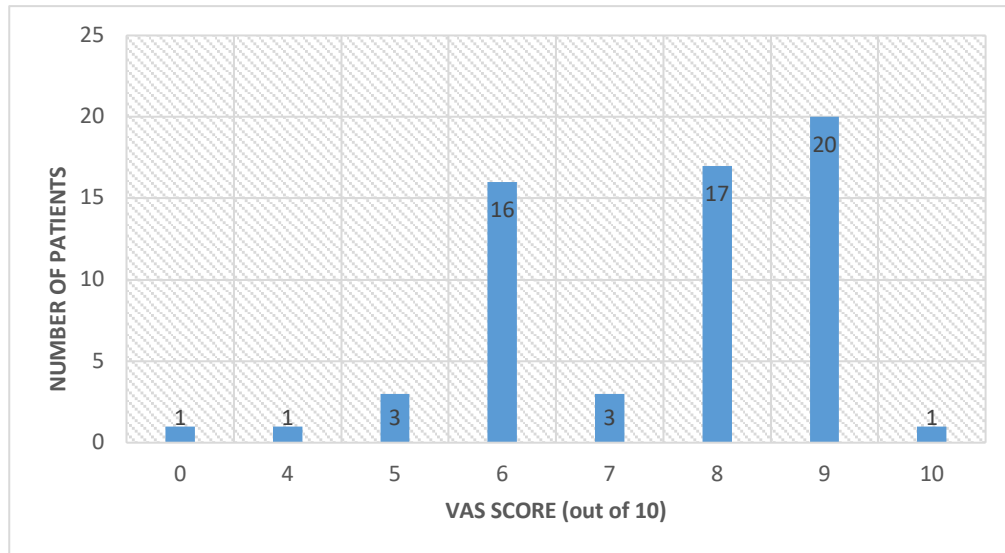


Figure 8: VAS Scores for Backache

Muscle tone was reduced in 38 patients, normal in 6 patients and increased in the rest as displayed in Table 4.

Table 4: Muscle Tone

MUSCLE TONE	NUMBER OF PATIENTS	PERCENTAGE
Normal	6	9.7%
Reduced	38	61.3%
Increased	18	29%

Muscle power was graded 0 in twenty-four patients, 2 in two patients, 3 in seventeen patients, 4 in thirteen patients and 5 in six patients respectively (Table 5).

Table 5: Muscle Power Grade

MUSCLE POWER GRADE	NUMBER OF PATIENTS	PERCENTAGE
0	24	38.7%
2	2	3.2%
3	17	27.4%
4	13	21.0%
5	6	9.7%

Deep tendon reflexes in the ankles and knees were absent in 10 patients, reduced in 26 patients, normal in 8 patients and increased in 18 patients as displayed in figure 9.

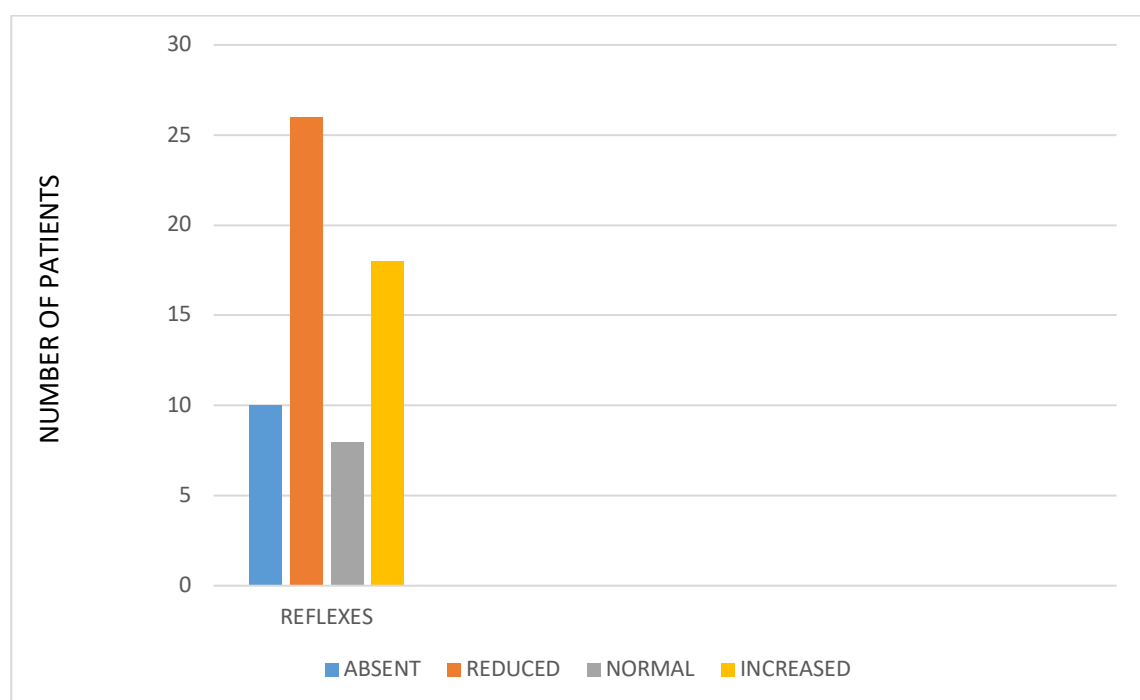


Figure 9: Reflexes At Presentation

A sensory level on examination was present in 37 patients but only 17 patients had an objectively determinable back deformity as shown in Table 6.

Table 6 Sensory Level and Back Deformity

FINDING	PRESENT	ABSENT	TOTAL
Sensory Level	37	25	62
Back Deformity	17	45	62

Digital rectal examination revealed findings as shown in Figure 10.

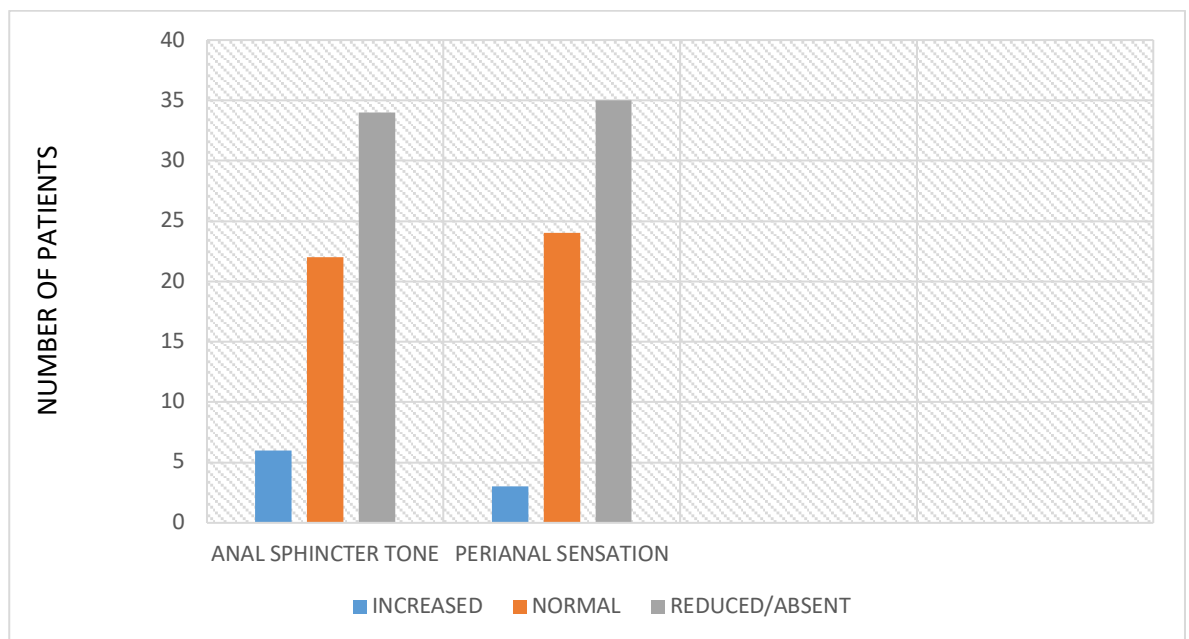


Figure 10: DRE Findings

4.4 Imaging and Diagnosis

Several radiological studies were available for investigating patients who presented with suspected extradural spinal tumours. Plain radiographs of the affected part were routinely done whereas CT scan, MRI scan and Technetium Bone Scan were done to help elucidate the diagnosis and plan treatment. Ultrasound scan, ECG and Echocardiography were only done, where indicated, as supportive studies to further assess the patients. The findings are highlighted in Figure 11.

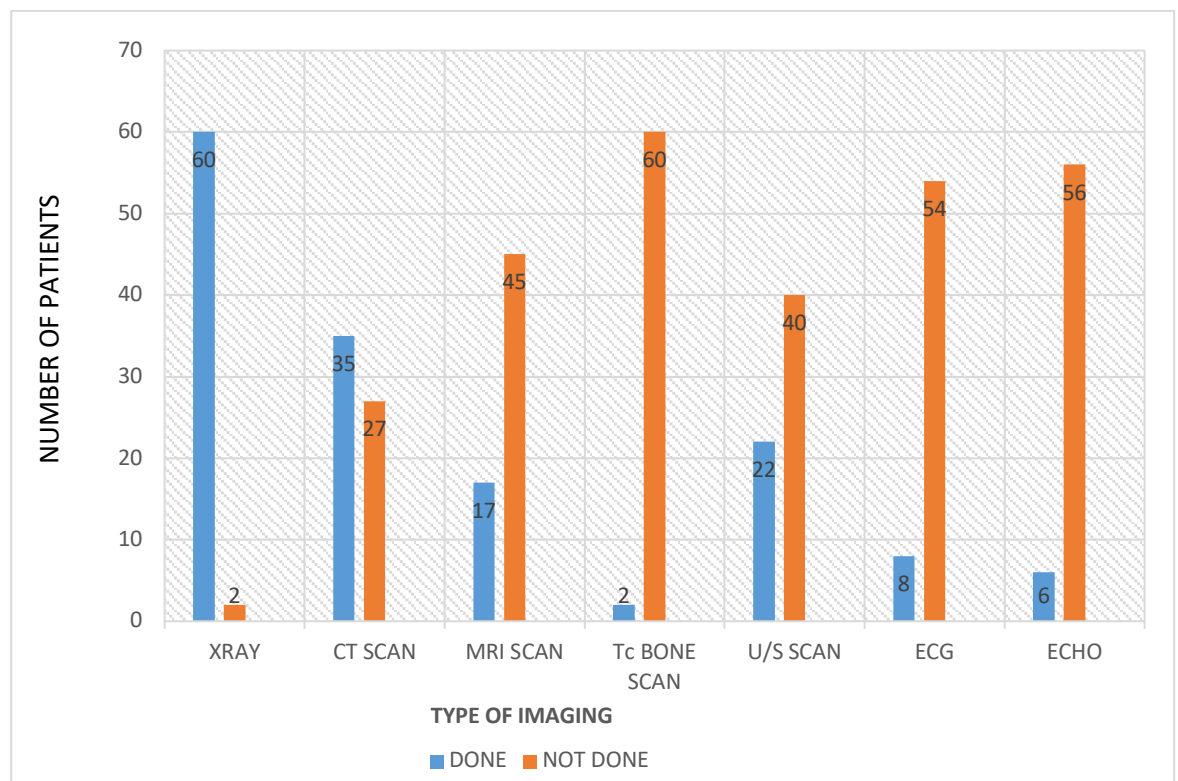


Figure 11: Radiological Investigations

Figure 12 highlights the various factors that were identified as being the reason for not doing particular radiological investigations in some patients.

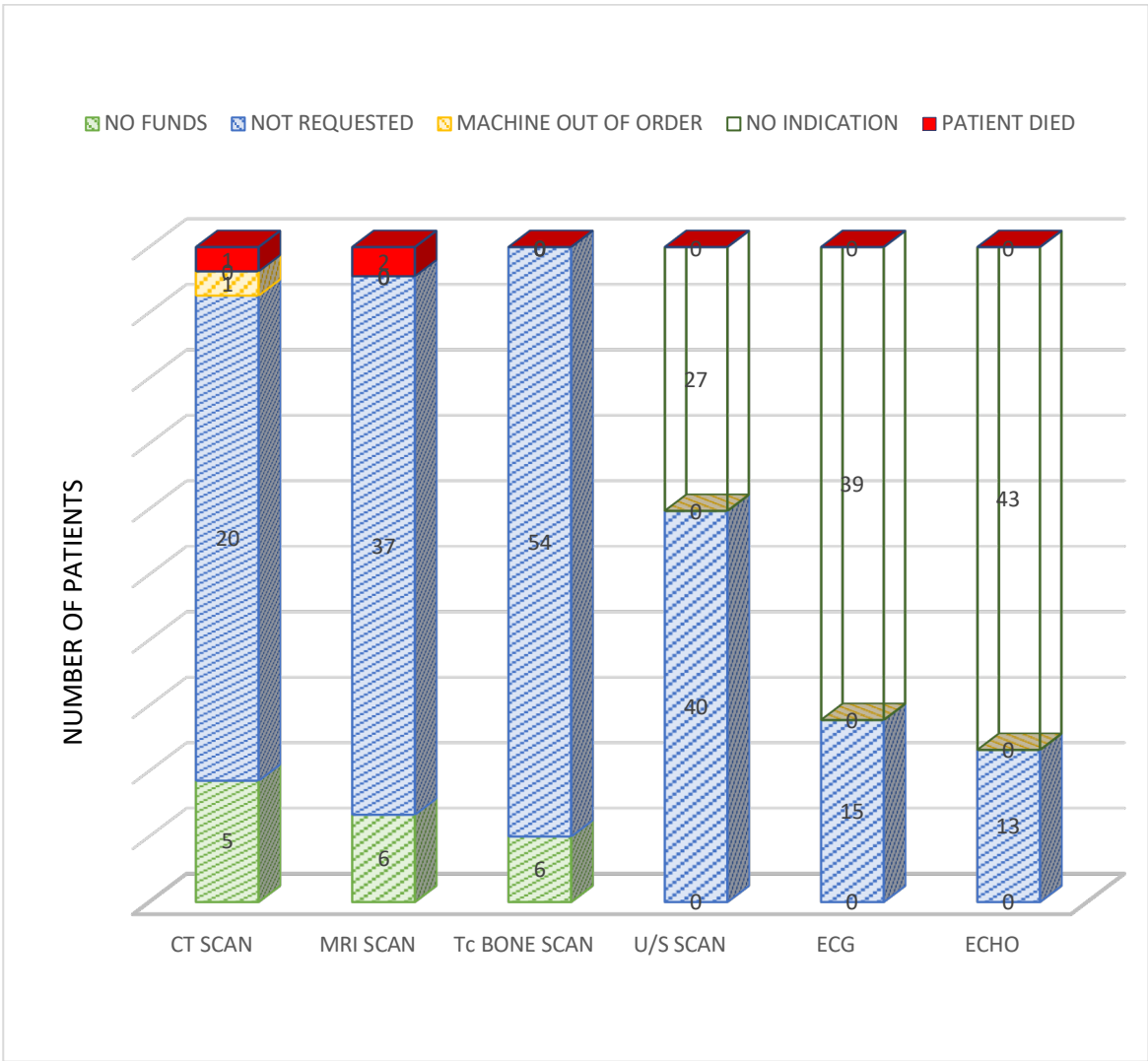


Fig. 12: Reasons for not Doing Radiological Investigations

The type of surgical host takes into account the general physiological health status of a patient, the presence of co-morbidities and how well controlled these co-morbidities are. The co-morbidities present were as shown in Figure 13.

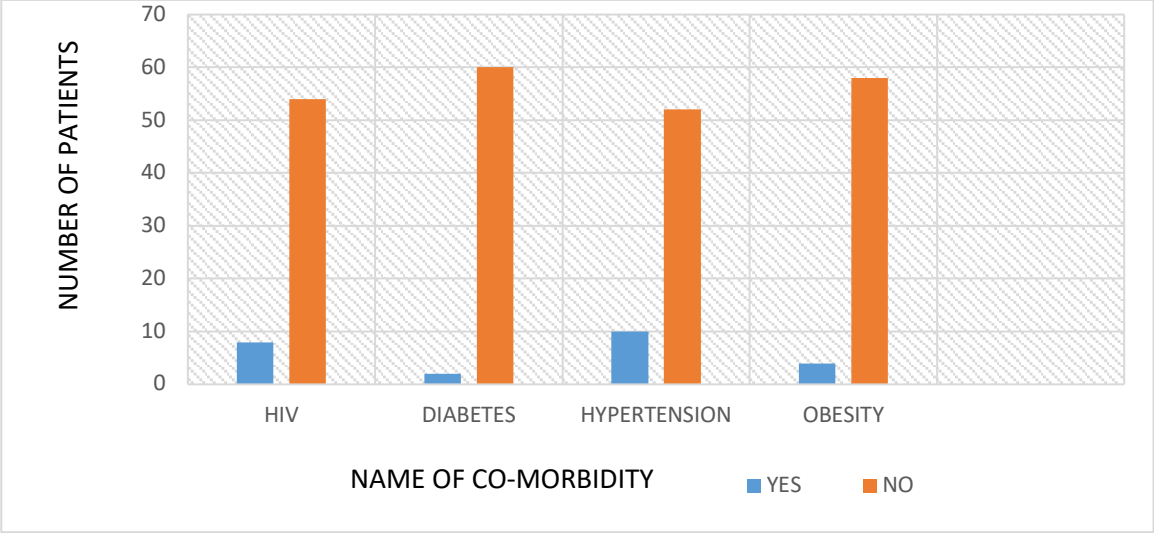


Figure 13: Co-morbidities

In terms of type of host, most patients were healthy and generally fit for surgery when indicated. The categories in which patients could be classified are shown in Figure 14.

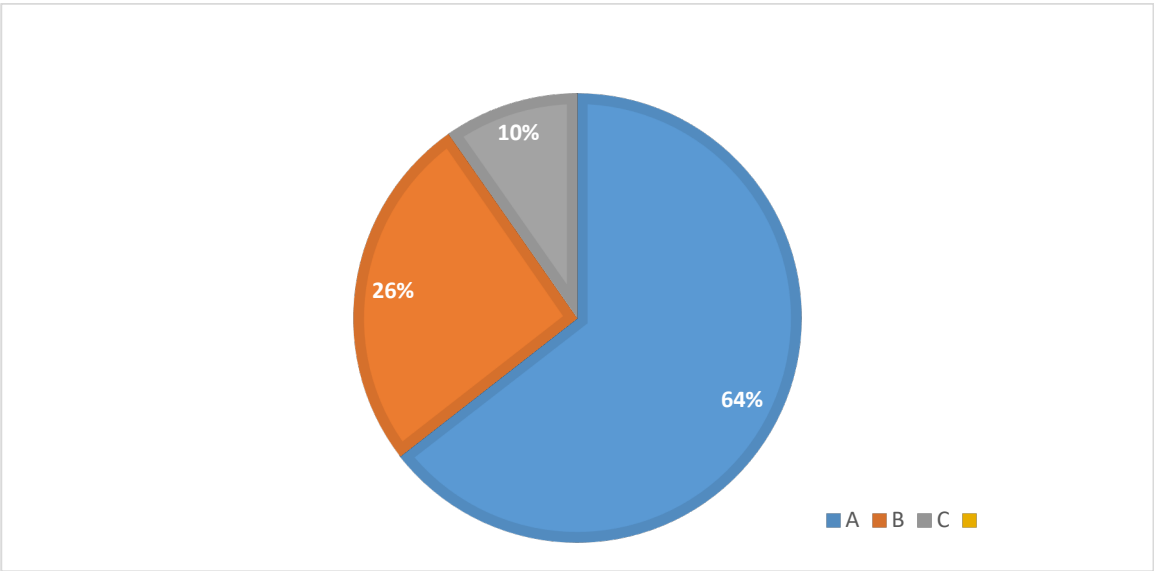


Figure 14: Surgical Host Category

There were more secondary EDSTs than primary EDSTs as shown in Figure 15.

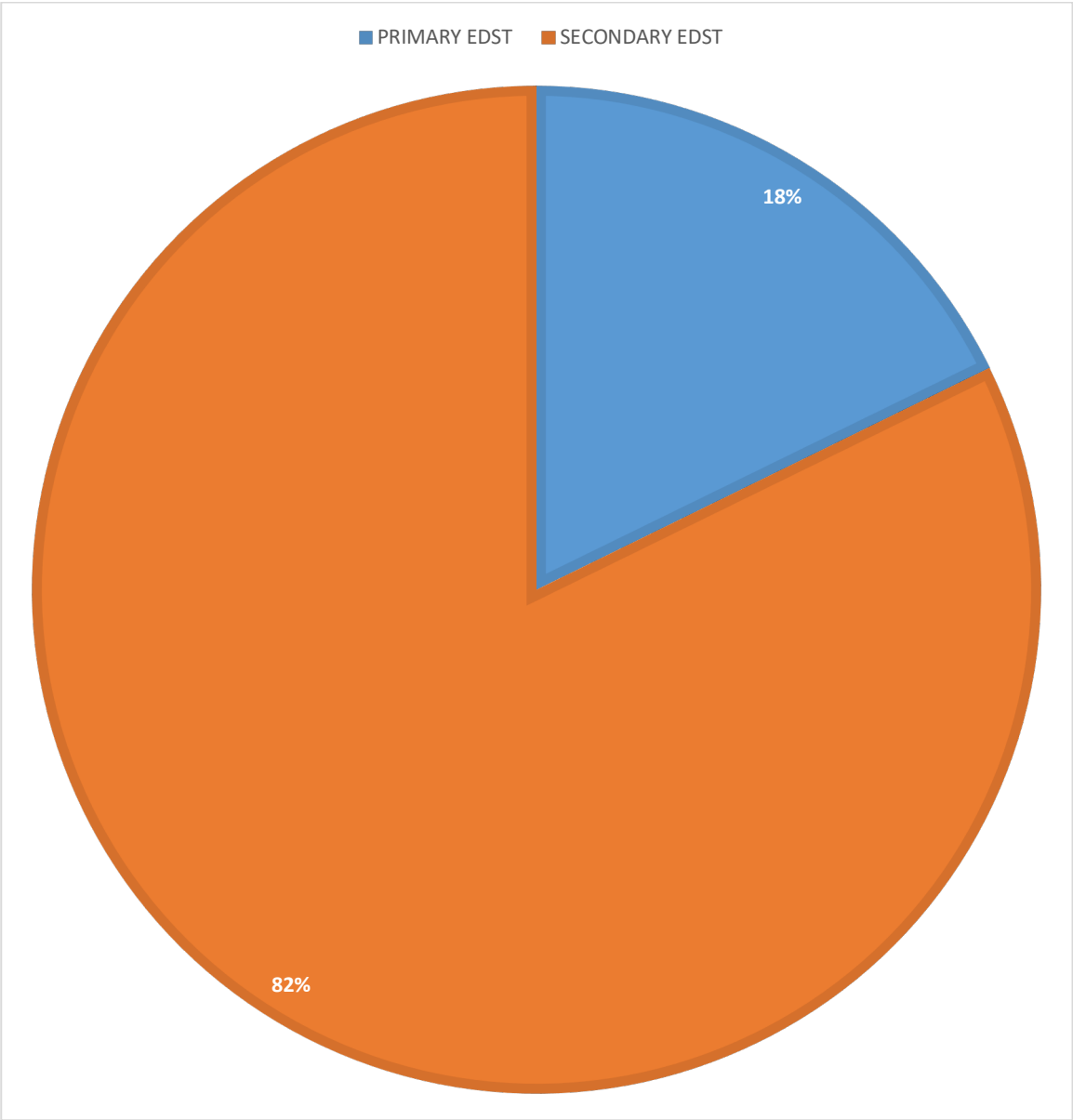


Figure 15: Type Of EDSTs

Two out of 11 patients who were aged 40 years or below had primary extradural spinal tumours while the rest (n=9) had secondary extradural spinal tumours as shown in Table 7.

Table 7: Profile of EDSTs in Patients 40 years or Younger

NUMBER	AGE (YEARS)	SEX	TISSUE DIAGNOSIS	TYPE OF SPINAL INVOLVEMENT
1	26	F	Breast Ca	Secondary
2	26	M	Lymphoma	Secondary
3	14	F	Inconclusive	Primary
4	33	F	Breast Ca	Secondary
5	32	F	Breast Ca	Secondary
6	29	F	Thyroid Ca	Secondary
7	32	F	Breast Ca	Secondary
8	36	F	Breast Ca	Secondary
9	27	F	Breast Ca	Secondary
10	38	F	Breast Ca	Secondary
11	26	M	Lymphoma	Primary

The frequency of tumours and type of spinal involvement they caused are shown in Table 8.

Table 8: Type of Tumour and Spinal Involvement

TUMOUR	SPINAL INVOLVEMENT	FREQUENCY	PERCENTAGE
Breast	Secondary	18	29%
Kaposi's Sarcoma	Primary	1	1.6%
Undifferentiated Lymph Node Sarcoma	Secondary	1	1.6%
Lymphoma	Primary	3	4.8%
Multiple Myeloma	Primary	2	3.2%
Peripheral Nerve Sheath Tumour	Primary	1	1.6%
Plasmacytoma	Primary	1	1.6%
Prostate	Secondary	18	29%
No Tissue Diagnosis	Mixed	15	24.2%
Thyroid	Secondary	2	3.2%
TOTAL	Combined	62	100%

Breast and prostatic carcinomas were the commonest causes of secondary spread to the spine. Patients with no tissue diagnosis of their tumours included renal and pulmonary tumours with clinical metastases to the spine that were not biopsied as well as biopsied tumours from the spine, lymph node, breast and prostate whose results were not available to help in making a histopathological diagnosis. Figure 16 highlights the specific sources of secondary extradural spinal tumour. There were no skin malignancies with evident spread to the spine.

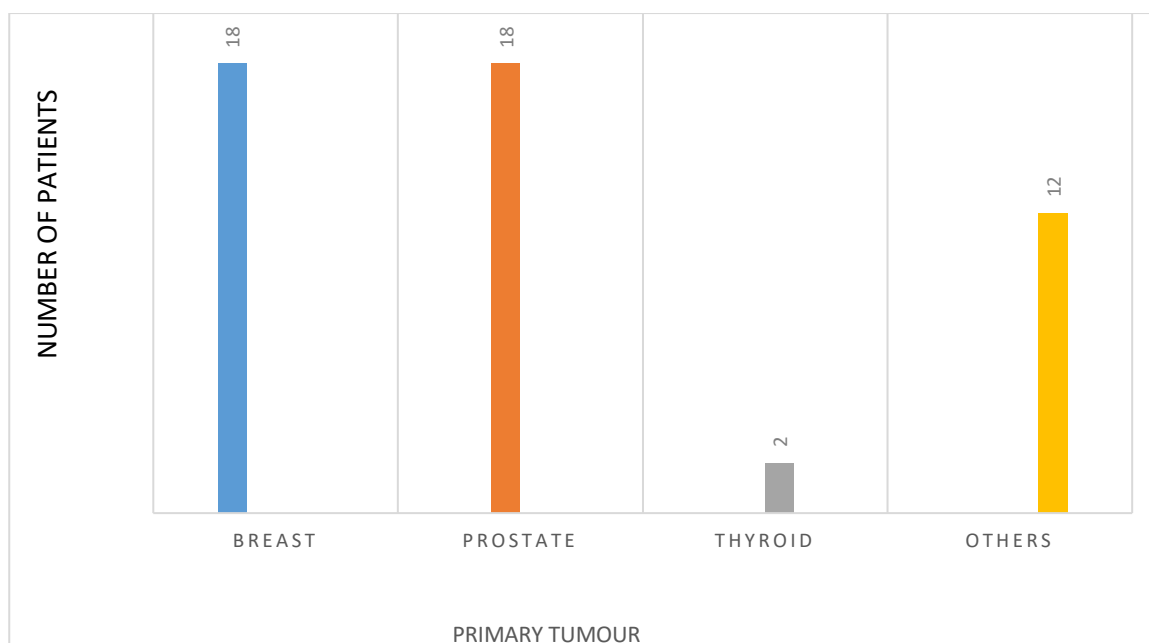


Figure 16: Sources of Secondary EDSTs

Only 8 of the 11 primary Extradural Spinal Tumours had histopathology reports while one had an inconclusive report and the other two did not have their biopsy specimens worked on by the pathologists. The results are shown in Figure 17.

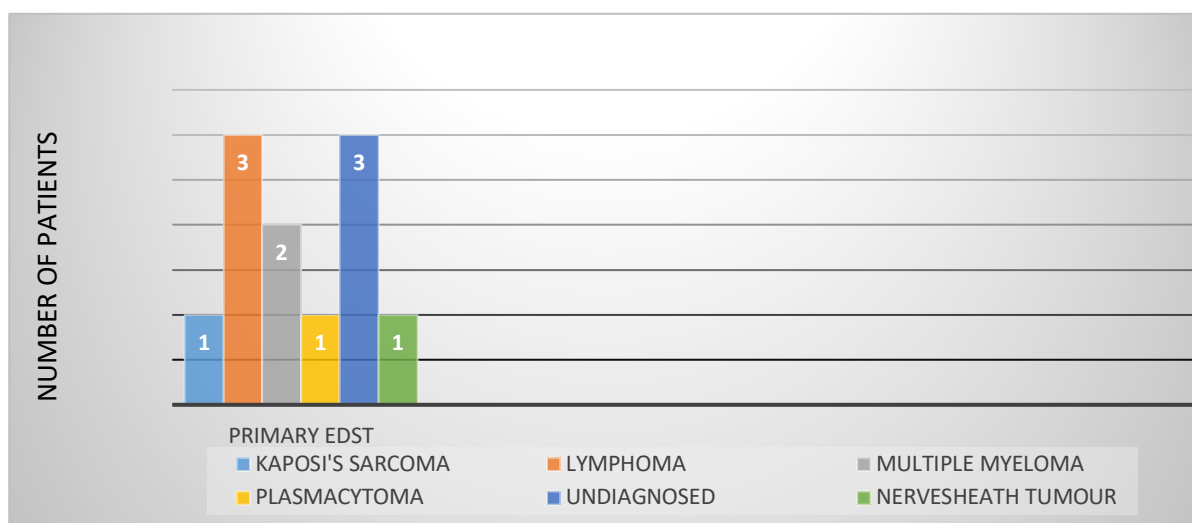


Figure 17: Aetiology of Primary EDSTs

The age and sex distribution for primary extradural spinal tumours is shown in Table 9.

Table 9: Age and Sex Distribution of Primary EDSTs

SERIAL NUMBER	AGE (YEARS)	SEX	TISSUE DIAGNOSIS
1	48	Male	Multiple Myeloma
2	47	Male	Kaposi's Sarcoma
3	70	Female	Plasmacytoma
4	26	Male	Lymphoma
5	57	Male	Multiple Myeloma
6	62	Female	Lymphoma
7	14	Female	Undiagnosed
8	52	Female	1° Nerve Sheath Tumour
9	48	Male	Undiagnosed
10	49	Female	Lymphoma
11	52	Female	Undiagnosed

4.4 Treatment Outcomes

Surgical treatment was planned and carried out in 14 patients while 48 patients received nonsurgical treatment. Indications for surgery are as highlighted in Table 10 and the reasons for nonsurgical treatment are indicated in Table 11.

Table 10: Indication for surgery in 14 patients

INDICATION	NUMBER OF PATIENTS	PERCENTAGE OF SURGICAL PATIENTS	PERCENTAGE OF ALL PATIENTS
Biopsy	3	21.4%	4.8%
Biopsy And Decompression	2	14.3%	3.2%
Biopsy, Decompression And Stabilisation	9	64.3%	14.5%
Total	14	100%	22.5%

Table 11: Reasons for Nonsurgical Treatment

REASON	NUMBER OF PATIENTS	PERCENTAGE OF NONSURGICAL PATIENTS	PERCENTAGE OF ALL PATIENTS
Advanced Disease	43	89.6	69.4
Nonsurgical Treatment Available	5	10.4	8.1
Total	48	100	77.5

Regarding implants for spinal surgery, of the 14 patients who had to undergo surgical intervention, 12 patients required implants and had to buy these as the

hospital did not have readily available implants. One patient was unable to afford the implants and 2 patients did not require implants.

Neoadjuvant chemotherapy or radiotherapy was given to 18 patients with secondary extradural spinal tumours. All patients with primary extradural spinal tumours did not receive any neoadjuvant therapy.

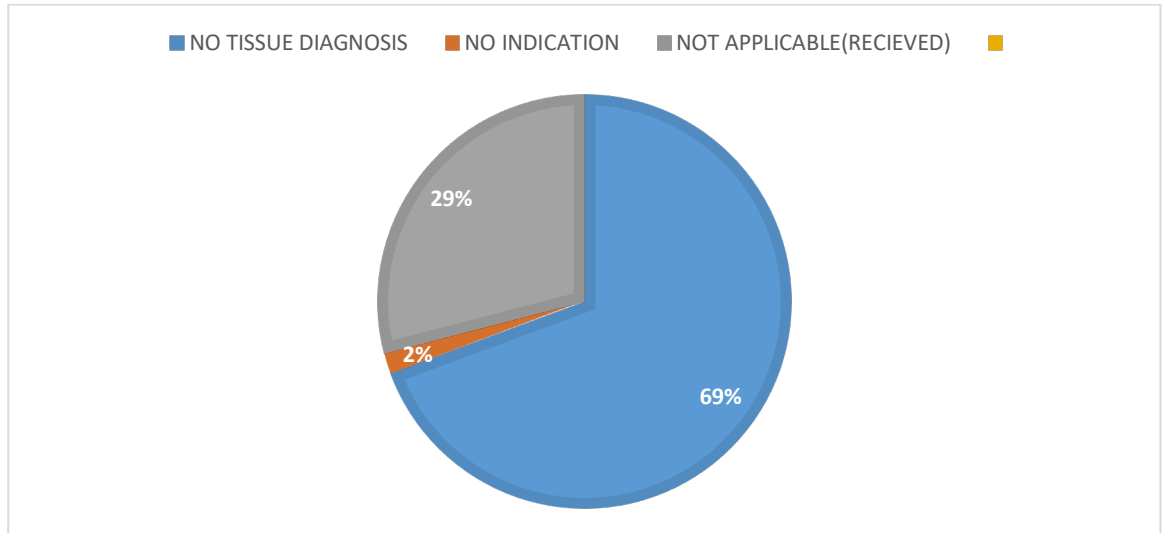


Figure 18: Reasons for not giving Neoadjuvant Therapy

Adjuvant chemotherapy and/or radiotherapy was intended for patients with indications for that. It was given in 25 patients out of the 62 patients. The reasons for patients not receiving adjuvant therapy were varied and included delayed tissue diagnosis (9 patients whose histopathology results came out after the patients had died), no tissue diagnosis (13 patients who either had inconclusive tissue diagnosis or no results at all), death of patient before therapy could be commenced (5 patients diagnosed and booked for adjuvant therapy but died before booking day), patients lost to follow-up (5 patients), patients unable to afford further tests at the Cancer Diseases Hospital as work-up before adjuvant therapy could be instituted (3 patients), patients unfit to undergo adjuvant therapy (2 patients) and patients not referred for adjuvant therapy (1 patient). Figure 19 demonstrates these findings.

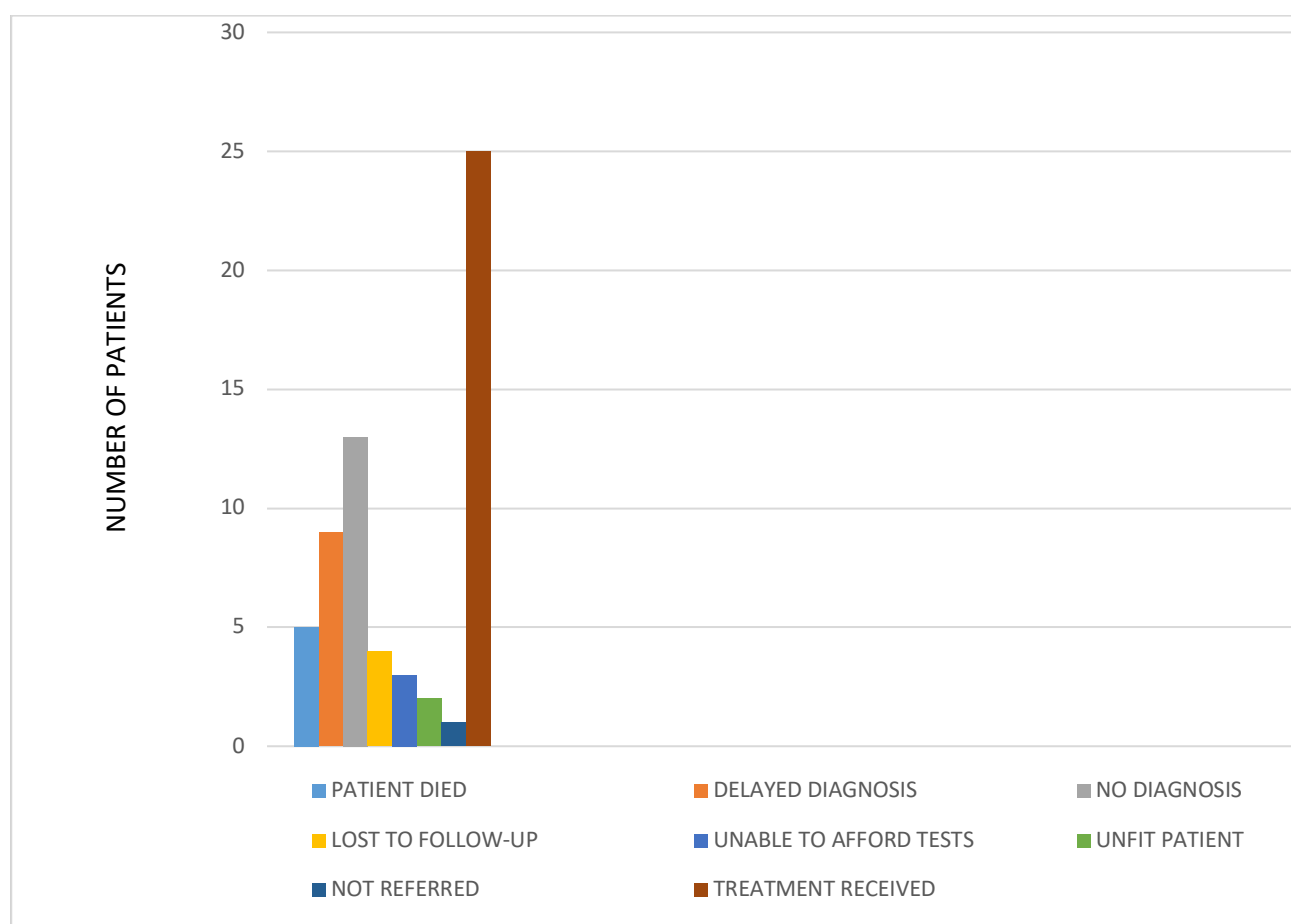


Figure 19: Reason for not giving Adjuvant Therapy

Records indicated varying periods of patient follow-up prior to death, leaving hospital, absconding, loss to follow-up or discharge. These periods represented the number of weeks the individual patient was followed up before the endpoint which was either death, absconding, leaving hospital against medical advice or discharge from hospital with failure to return for a scheduled review. These periods are depicted in Table 12 and were determined from the final doctors' notes in the patients' hospital file.

Table 12: Follow-up Periods

PERIOD	NUMBER OF PATIENTS	PERCENTAGE OF ALL PATIENTS
0 to 4 Weeks	26	41.9%
5 to 8 Weeks	9	14.5%
9 to 12 Weeks	7	11.3%
13 to 16 Weeks	4	6.5%
17 to 20 Weeks	4	6.5%
21 to 24 Weeks	4	6.5%
More than 24 Weeks	8	12.9%
Total	62	100%

Post treatment responses varied among patients depending on the parameter being looked at and the stage of disease at presentation. In terms of symptomatology, there was generally either no improvement or deterioration to the extent that some patients opted to leave hospital against medical advice (LHAMA, 7 patients) or abscond altogether (1 in-patient). Figure 20 shows the observable symptomatic responses to treatment.

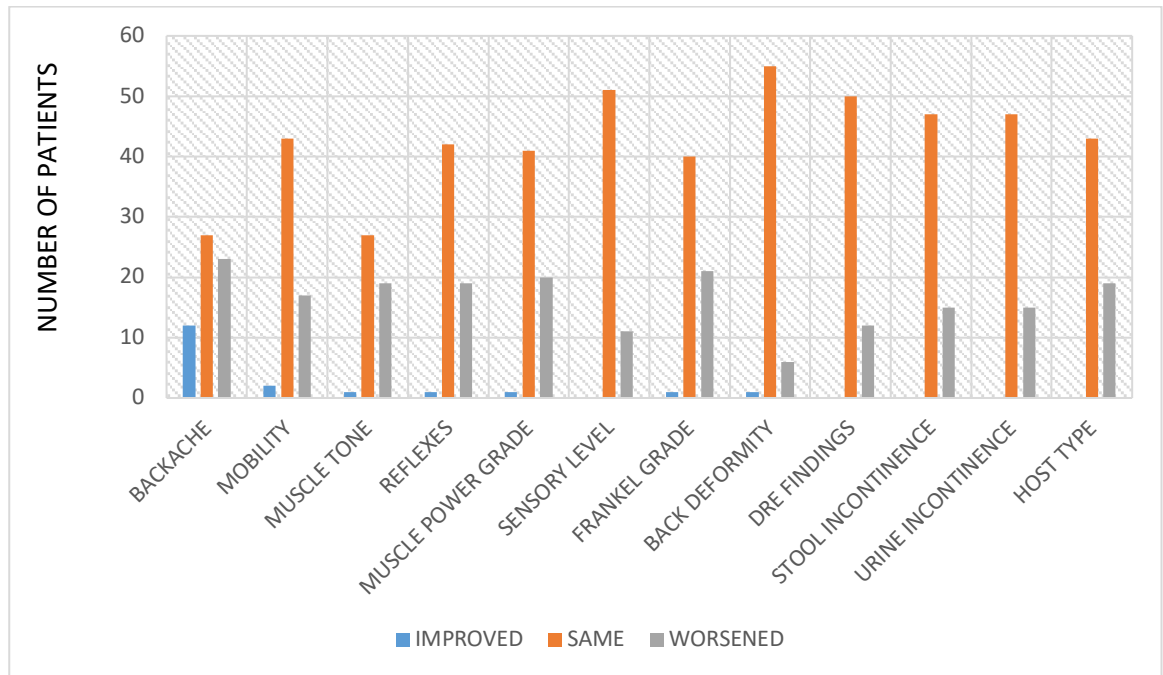


Figure 20: Symptomatic Response To Treatment

For patients who underwent surgery (n=14), issues related to surgical wound healing were noted. Twelve patients had incident free wound healing while two had superficial wound infection as shown in Figure 21.

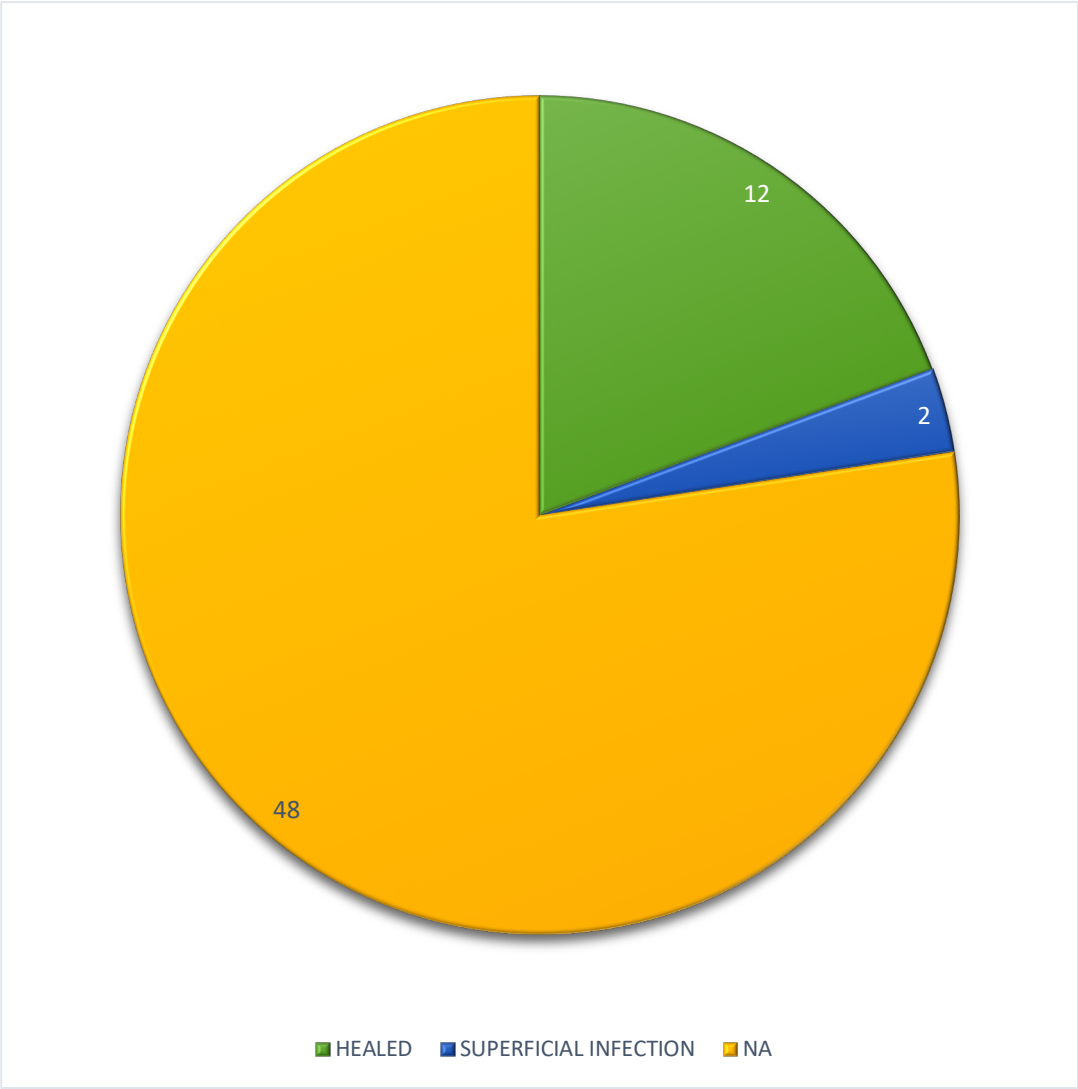


Figure 21: Surgical Wound Status

In terms of complications arising from disease or its treatment, the following were noted: presence of decubitus ulcers, deep veinous thrombosis, pneumonia, urinary tract infection, sepsis and joint stiffness. Figure 22 displays the number of patients with and without these complications.

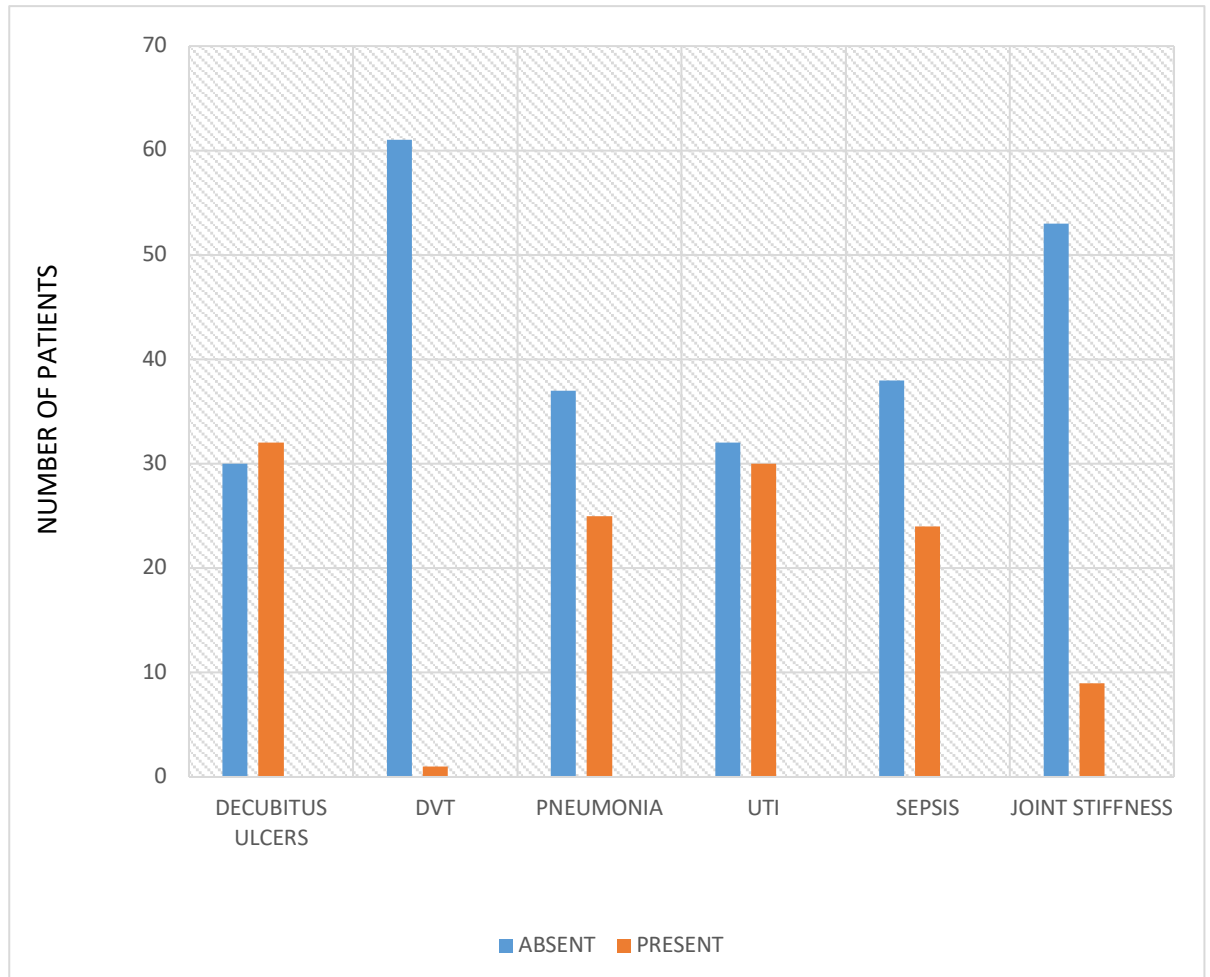


Figure 22: Complications

Records showed that 40 patients out of the 62 died, 4 patients were alive and the rest (18 patients) were lost to follow-up. The Death-to-Case ratio was high at 64.5 and the Cause-Specific Death Rate was 0.3 per 100,000 population. The causes of death are shown in figure 23.

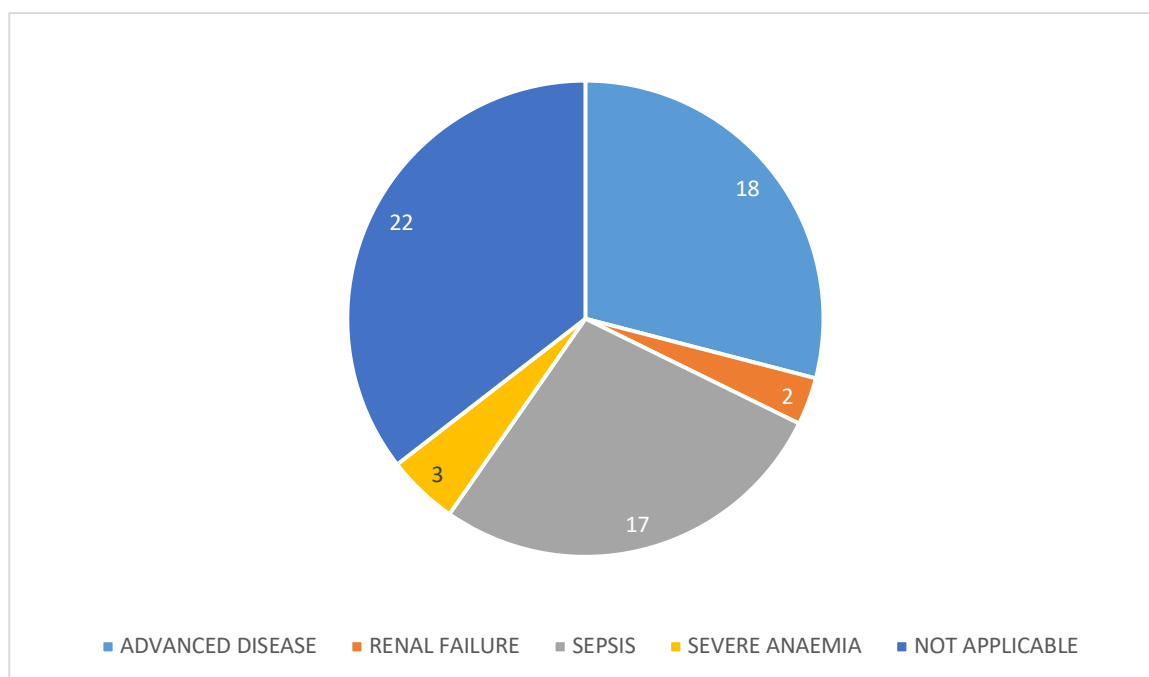


Figure 23: Causes Of Death

The number of weeks from the date of presentation at hospital to the date of death varied, but the majority (45%) of deaths occurred in the first four weeks of admission.

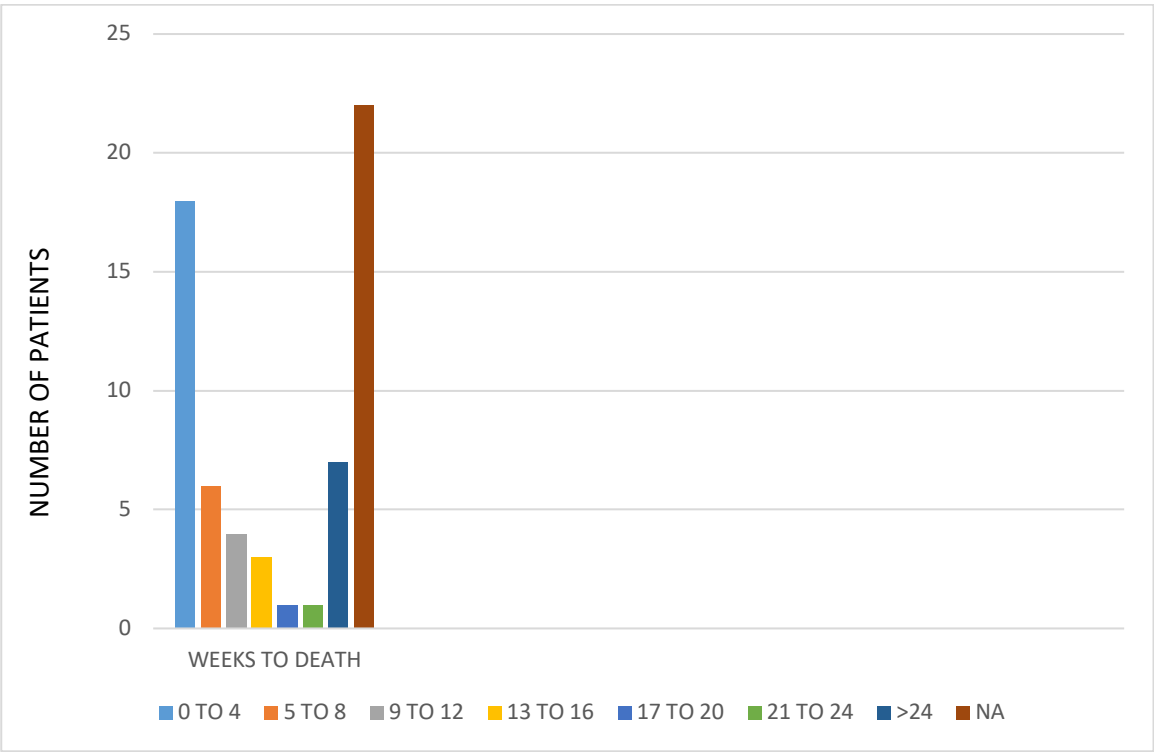


Figure 24: Weeks To Death

Most of those who died in the first four weeks died within two weeks ($n = 10$ or 56%) of admission, a period which is one week short of the average turn-around time for histopathology/biopsy results. Deaths in the first four weeks were distributed as shown in Figure 25.

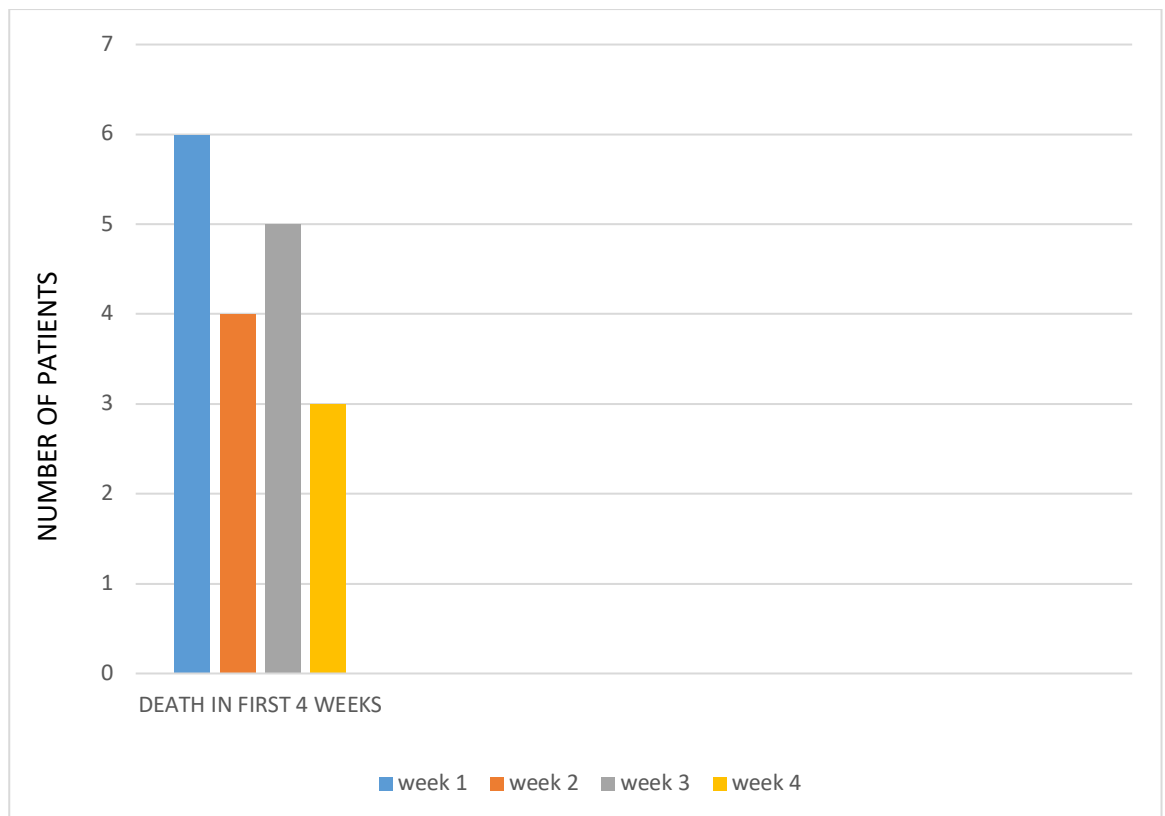


Figure 25: Deaths Per Week In First Four Weeks

CHAPTER FIVE: DISCUSSION

5.1 Background Characteristics

The occurrence of extradural spinal tumours tended to follow a normal distribution with regard to age at presentation. Out of 62 patients, 28 (45%) were male, while 34 (55%) were female. Interestingly, the findings have revealed that the minimum age was 14 years and the maximum age was 87 years. The range was 73 years and the standard deviation was 17.046. The mean age of 55.03 years meant that each of the participants was expected to be 55.03 years. The standard deviation of 17.046 years meant that each of the participants was expected to be 17.046 years below or above the mean age of 55.03 years. The mode was 42 years, meaning that the majority of the participants were 42 years old. The Median was 56 years meaning that half of the participants were below 56 years and the other half were above 56 years old. The research findings have further revealed that 1 (1.6%), 47 (75.8%), 6 (9.7%), and 8 (12.9%) patients were divorced, married, single and widowed respectively.

The results indicate that with a female to male ratio of 1.2 to 1, the occurrence of extradural spinal tumours in females is slightly higher than in males. But this was not a statistically significant difference (p-value of 0.523).

Extradural Spinal Tumours tended to occur mostly at a significantly much higher age range in males than in females.

By far more married people (n=47) presented to hospital than those without spouses (n=15), reflecting the importance of family support in the health-seeking behaviour of the population under study. This is especially so when it is noted that the majority of patients were bedridden (n=42) or wheel-chair bound (n=3) at the time of presentation and therefore needed family support to get to the hospital.

There were over 3 times more unemployed people (n = 47) than employed people (n = 15) who presented for treatment. This was reflected in the inability of some patients to afford certain special tests, radiological studies and surgical implants for the investigation and treatment of extradural spinal tumours.

5.2 Clinical Presentation

The most common symptoms at presentation were backache (93.5%) and weakness in lower limbs (91.9%) which had been present for weeks before the patients sought medical help. This is in agreement with Bach (1996) and Clarke *et al.*, (2014). Patients tended to present to hospital much earlier mainly when they started having difficulties with control of urine and stool and were unable to walk than when they developed backache alone. The former are late symptoms of a serious surgical condition that has truly advanced.

Night pain was the most common of the constitutional symptoms, with poor appetite and weight loss in second. Night sweats and fever were not as common. The presence of these symptoms are in agreement with various studies (Okeke *et al.*, 2006; Wilne & Walker, 2010; Karuna, Shekdar & Schwartz, 2014 and Schiff 2016) on the subject. With 42 out of 62 patients being bedridden at presentation, this study is in agreement with Mwang'ombe and Ouma (2000) whose series showed 83% of their patients were unable to walk at presentation. Unless the tumour is rapidly expanding, the inability to walk is indicative of long standing illness and reflects a delay in seeking medical help.

Patients with backache (57 out of 62 patients) mostly had pain scores of 6 or more according to the Visual Analogue Scale (VAS). There was significant correlation between VAS scores at presentation and VAS scores at last follow-up, indicating adequate pain management of these patients once they presented at the hospital.

In terms of physical examination findings, muscle power was 3 out of 5 (that is 3/5) in a significant number of patients (n=43). Muscle tone and deep tendon reflexes were abnormal in 56 and 54 patients respectively. A sensory level and a back deformity was present in 37 and 17 patients respectively. On digital rectal examination anal sphincter tone was reduced in 34 patients, increased in 6 and normal in 22 patients whereas sensation was normal in 23 patients and abnormal or absent in 39 patients. There was no study in the literature review that looked at these parameters to compare with but these physical examination findings are indicative of advanced disease processes in the majority of patients at presentation.

5.3 Determinants of Treatment

The type of extradural spinal tumour (that is primary or secondary) was taken into consideration when deciding the treatment approach as evidenced by the significant correlation between provisional diagnosis and treatment plan. For secondary EDSTs, the stage of disease was a key factor in deciding the type and timing of treatment.

Surgery was mainly done to obtain tissue biopsy for diagnostic purposes, decompress neural elements, stabilise the spine or for a combination of these and this is in agreement with Spacca *et al.*, (2015).

Initial clinical diagnosis and the completeness of a diagnostic work-up were key consideration in progressing to either surgical or nonsurgical treatment. Van Goethem *et al* (2004) and Clarke *et al.*, (2014) agree that MRI scans are key in the clinical evaluation of these patients. It is therefore surprising to note that in only 17 of the 62 patients was MRI done (particularly those who underwent surgery) and none was done in those deemed to have terminal stage cancer with secondary spread to the spine. The major reason for not requesting MRI scans in such patients was that the result was not going to change the course of management as patients were terminally ill or had stage four disease. Knowingly or unknowingly the clinicians, particularly those attending to patients with secondary EDSTs from the other surgical units, were using some prognostic tool to determine the investigations and subsequent treatment a particular patient would receive as guided by Tomita *et al.*, (2001). However, Guziklik (2016) in a study has indicated that imaging examinations, magnetic resonance scanning in particular, are crucial for the proper planning of spinal surgery in consequence of metastatic lesions. Further, Kim *et al.*, (2012) indicated that the surgical management of metastatic disease of the spine continues to evolve and that studies have now yielded level-I evidence on the efficacy of surgery for metastatic disease of the spine for improving quality of life and outcomes in patients with spinal metastases.

It was generally difficult to offer treatment or make treatment decision based on an indeterminate clinical diagnosis or incomplete radiological and laboratory workup. Although Kim *et al.*, (2012) state that surgery for metastatic spine disease showed level 1 evidence that it improved quality of life and outcomes, they support the

consideration that tumour type and biology, extent of disease, neurological status, patient's expectations, quality of life and life expectancy were key determinants of what treatment a patient would receive.

Tissue diagnosis was a critical factor in deciding whether a patient would benefit from neoadjuvant or adjuvant chemotherapy and radiotherapy. The majority of patients did not receive this therapy for various reasons as pointed out in the results section.

The type of surgical host a patient conformed to was an equally important determinant to surgical treatment, although most patients were generally fit for surgical treatment, and none received treatment based solely on the host category they fell in as evidenced by the lack of significant correlation between these two variables.

The availability of implants for surgical stabilisation was also key in determining the type of treatment and also the type and extent of surgery to be done on a particular patient. Those who did not need implants with the initial workup were mainly patients who underwent open transpedicular needle biopsy.

The availability of a nonsurgical treatment option as standard treatment or treatment of choice for a particular condition determined which treatment option to offer the patient. Again this was largely dependent on the tissue diagnosis either from a biopsy of affected tissue (bone marrow, breast, thyroid, lymph node, skin and prostate) or the spine itself.

Optimisation requirements and adequacy of optimisation was another consideration particularly for those patients who underwent surgery. Patients with co-morbidities needed physiological optimisation prior to being subjected to the stresses of anaesthesia and surgery and were boosted accordingly. This did not stand in the way of surgery because the few that were significantly compromised were not suitable surgical candidates to start with.

5.4 Treatment Outcomes

These were related to the effects of doctor-patient interaction and decisions made in terms of treatment on the quality and quantity of life for the patient. Symptomatic relief and mortality were key outcome measures. These outcomes were determined at

the end of the doctor-patient interaction by comparing their presence and severity then to what they were at initial presentation. The end of the doctor-patient interaction was marked by the last notes taken by the attending doctor in each individual patient's hospital file and was indicative of death, absconding, leaving hospital against medical advice and failure to return for a scheduled review.

Most patients either remained the same or deteriorated symptomatically at the end of doctor-patient interaction. Improvement was seen in terms of relief of backache in 19% of patients, indicating the significance that clinicians attached to pain relief as a component of care, particularly in terminally ill patients, at the University Teaching Hospital. The significant correlation between VAS scores at initial presentation and those at last follow-up is testament to this.

Table 13: Correlation of VAS, Post Treatment VAS and Backache

		VAS	POST TREATMENT VAS	BACKACHE
VAS	Pearson Correlation	1	-.486**	.123
	Sig. (2-tailed)		.000	.340
	N	62	61	62
POST TREATMENT VAS	Pearson Correlation	-.486**	1	-.080
	Sig. (2-tailed)	.000		.539
	N	61	61	61
BACKACHE	Pearson Correlation	.123	-.080	1
	Sig. (2-tailed)	.340	.539	
	N	62	61	62

**. Correlation is significant at the 0.01 level (2-tailed).

Pearson Correlation coefficients were -0.39, 0.186, 0.59, 0.194 and -0.157 between Frankel grade (neurology) at presentation and each of DVT, pneumonia, UTI, sepsis, joint stiffness and death respectively indicating no significant correlation at the two-tailed 0.01 or 0.05 level between Frankel grade and the indicated complications. However, there was significant correlation at the two-tailed 0.01 level between

decubitus ulcers and sepsis, UTI and sepsis and pneumonia and sepsis, indicating a vicious circle for each of these complications. There was also significant correlation at the two-tailed 0.05 level between death and sepsis, death and pneumonia, decubitus ulcers and UTI, decubitus ulcers and joint stiffness and decubitus ulcers and pneumonia.

Mortality was high with a death-to case ratio of 64.5, with advanced disease and sepsis or a combination of these two accounting for more than 56% of deaths. The cause-specific death rate was 0.3 per 100,000 population. These rates could be higher if it is to be assumed that those patients who left hospital against medical advice, absconded from hospital or did not return for their scheduled reviews may have died at home. This seems to be a fairly reasonable assumption considering that most of those who left or absconded did so at the request of relatives when they noticed that the patients were deteriorating or not improving at all. There was no significant correlation between death and age, death and sex, death and treatment plan or death and final diagnosis as indicated in Tables 14, 15 and 16. The common denominator to all those who died was a constellation of factors including type and biology of tumour, late presentation, delay in diagnosis, delay in institution of treatment as well as difficulties with treatment. This agrees with the findings of Mwang'ombe and Ouma (2000).

Table 14: Correlation of Age, Sex and Death

		AGE	SEX	DEATH
AGE	Pearson Correlation	1	-.451**	.038
	Sig. (2-tailed)		.000	.770
	N	62	62	62
SEX	Pearson Correlation	-.451**	1	.110
	Sig. (2-tailed)	.000		.393
	N	62	62	62
DEATH	Pearson Correlation	.038	.110	1
	Sig. (2-tailed)	.770	.393	
	N	62	62	62

** . Correlation is significant at the 0.01 level (2-tailed)

Table 15: Correlation of Death, Backache and Treatment Plan

		DEATH	BACKACHE	TREATMENT PLAN
DEATH	Pearson Correlation	1	.177	.028
	Sig. (2-tailed)		.170	.827
	N	62	62	62
BACKACHE	Pearson Correlation	.177	1	.148
	Sig. (2-tailed)	.170		.250
	N	62	62	62
TREATMENT PLAN	Pearson Correlation	.028	.148	1
	Sig. (2-tailed)	.827	.250	
	N	62	62	62

Table 16: Correlations of Death, Treatment Plan and Final Diagnosis

		DEATH	TREATMENT PLAN	FINAL DIAGNOSIS
DEATH	Pearson Correlation	1	.028	.239
	Sig. (2-tailed)		.827	.061
	N	62	62	62
TREATMENT PLAN	Pearson Correlation	.028	1	.428**
	Sig. (2-tailed)	.827		.001
	N	62	62	62
FINAL DIAGNOSIS	Pearson Correlation	.239	.428**	1
	Sig. (2-tailed)	.061	.001	
	N	62	62	62

** . Correlation is significant at the 0.01 level (2-tailed)

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

This study has been able to outline the presentation, management and short-term outcomes of extradural spinal tumours at the University Teaching Hospital for the period 1st January 2013 to 31st December 2016.

6.1 Conclusions

- i. With regards to the clinical presentation, patients present with backache, weakness/paralysis, sensory loss, incontinence of urine and incontinence of stool which are symptoms of late or advanced disease. This is especially true for those with secondary extradural spinal tumours. Other symptoms, which are constitutional, are also common: night pain, weight loss, poor appetite, night sweats and fever. Physical findings at presentation are consistent with the symptomatology and commonly include inability to walk, increased Visual Analogue Pain scores, reduced muscle tone, reduced muscle power grade, abnormal reflexes, presence of a sensory level, presence of back deformity and abnormal digital rectal examination findings. These are signs of late and advanced disease.
- ii. The type of extradural spinal tumour (primary or secondary) dictates the treatment to be instituted. The stage of disease for secondary extradural spinal tumours is a key factor as it has implications for the quantity (life expectancy) and quality (morbidity) of life for the patient. Other determinants of treatment include: need for tissue diagnosis, decompression or spinal stabilisation; completeness of diagnostic workup and availability of a nonsurgical treatment modality as standard treatment of choice. The type of surgical host and optimisation needs are considered but do not dictate the need for surgical or nonsurgical treatment. The availability of implants is key for those patients needing spinal decompression and stabilisation but not for those needing biopsy only. Resource constraints in terms of diagnostic/therapeutic equipment and their affordability as well as availability of skilled personnel to run or operate these are a major contributor to the outcomes noted in this study.

- iii. In terms of quality and quantity of life, most improvement is seen in pain scores following treatment. Other symptoms and signs either remain the same or deteriorate. The rates of complications are high with decubitus ulcers, pneumonia, UTI and sepsis being the commonest. Mortality is high in these patients because of late presentation or presentation at the time when the disease has advanced.

6.2 Recommendations

The results of this study highlight a number of areas in the presentation, management and outcomes of patients with extradural spinal tumours that need to be strengthened or improved upon. We believe that the high morbidity and mortality highlighted in the results could be reduced if some or all of the following recommendations are done or initiated by relevant authorities as it were. With this in mind, we make the following recommendations:

1. Patient Education and Counselling

A lack of an adequate and functioning patient education and counselling service contributes to patients' lack of understanding of their condition and contributes to noncompliance to treatment and unreasonable expectations that when not met can contribute to increased rates of leaving hospital against medical advice, absconding or not returning for scheduled reviews. Although part of this responsibility can be borne by the attending surgical unit, it is imperative that the bulk of the counselling be done by a dedicated patient education and counselling unit run by qualified personnel employed by the Ministry of Health at the University Teaching Hospital.

2. Public Awareness Campaign

There is need to address the issue of late presentation of patients with extradural spinal (or indeed other) tumours. In this regard focus may be given to programs aimed at public awareness on cancers in general and extradural spinal tumours in particular with emphasis on seeking medical help at the earliest indication of cancer-related ill-health and symptomatology. This is a role that can be carried out by relevant district health offices in collaboration with other partners across the country.

3. Continuing Medical Education and Training of Primary Health-Care Providers

This will improve awareness and increase the index of suspicion for extradural spinal tumours in this important cadre of health-care providers to enable early diagnosis and referral of patients suspected to have these tumours. These are the ‘frontline or foot soldiers’ to whom most patients go to seek medical attention first. This is can be actioned by the relevant primary health care units (District) across the country

4. Radiology Department improvements

A well-equipped and functioning radiology department in terms of personnel numbers and skills as well as equipment is of paramount importance. The radiology department should be able to do advanced radiological investigations and interventions such as CT and MRI angiography. This will make it possible for patients with highly vascular tumours to undergo CT guided angiographic embolisation of the tumours to assure the possibility of biopsy and tumour resection for diagnosis and/or treatment (Boriani and Fisher, 2015). Radiological reports should be able to reach the requesting clinicians in good time to help make patient-specific treatment decisions timely. The Orthopaedic Spine operating theatre needs to be equipped with appropriate technology suitable for conducting comprehensive and technically-advanced surgical procedures on patients with spinal tumours. This would include acquisition of O-arm radiology equipment which has been shown to offer better use with reduced length of surgery and better localisation of spinal lesions (Kadhim et al, 2016). An intraoperative CT Navigation System which offers real-time tracking to localise spinal lesions and guide resection less traumatically with little radiation exposure to theatre staff (Nasser et al, 2016) would be a great asset. This would help improve the accuracy of biopsy, for example, and enable the conduction of technically advanced surgical procedures in the shortest possible time with less surgical trauma to the patient. The University Teaching Hospital, through the Ministry of Health should invest in these pieces of equipment and train staff to operate and maintain them

5. Pathology Laboratory improvements

The pathology laboratory needs to improve in terms of turn-around time for laboratory results. Histopathology results have tended to take quite long and often are a cause of

delay or lack of commencement of treatment. As a specialist and tertiary institution, there is need for the University Teaching Hospital's Pathology Laboratory to be able to do frozen specimens collected at time of surgery to give the surgeon an impression regarding a possible diagnosis and also the adequacy of tumour excision margins at the time of surgery. These factors have important implications on the treatment process as they would reduce on the rates of "repeat biopsy" histopathology reports (a result of missed pathological tissue at biopsy or no pathology) and the need for further surgery that would expose patients to stresses of anaesthesia and surgical trauma again. There were cases in which histopathology results were at variance with clinical and radiological assessment of patients. Indeed pathology specimens of two patients in this study had not been processed at the time of study conclusion, more than two years after the index biopsies were done.

6. Inter-Disciplinary Collaboration

There is need to strengthen the inter-disciplinary approach to the management of patients with EDSTs. This should involve General Surgeons, Orthopaedic and Spine Surgeons, Radiologists, Pathologists, Radio-oncologists, Physiotherapists and Medical Counsellors. Other disciplines may be involved as and when need arises. In terms of administration of inter-disciplinary consultations, which service is currently available but rudimentary, we recommend that consultations be made at Consultant level and be enhanced with physical and electronic follow-ups to ensure patients are attended to in good time. The re-introduction of (multidisciplinary) grand rounds on particular cases would greatly enhance this interaction for the benefit of the patient. Another area that should be explored and put to great use is telemedicine for online interactions with other specialists international experts

7. Full-fledged Orthopaedic Spine Unit

There is need to make the spine unit a full-fledged surgical unit with specific wards allocated to the unit. The unit should have a full complement members of staff including porters, ward attendants, nurses, junior/senior medical officers, registrars and senior registrars trained in the care and management of spine patients, a team led by consultant. In a well-equipped ward set-up, the care for and treatment of these patients will be ably stream-lined and focussed to the particular needs of the individual patient. This, we believe, will ultimately lead to reduction in the frequency of

complications, which are more or less related to the nursing care given to patients. It will be easier to collaborate with other units and departments in terms of patient care and management. It will also be possible for the orthopaedic spine unit to increase the scope of operations that they will be able to offer this category of patients, especially if the other recommendations are also met.

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APPENDICES

Appendix i: Application for Ethical Approval

9/8/2017

Hilgard Mutembo
[Type the sender company name]
The University of Zambia
School of Medicine
Department of Surgery
LUSAKA

The Chairperson
University of Zambia Biomedical Research and Ethics Committee
Ridgeway
LUSAKA

Dear Sir,

REF: APPLICATION FOR ETHICAL APPROVAL

I am a postgraduate student at the University of Zambia, School of Medicine, intending to conduct a study entitled "Presentation, Management and Short-term Outcome of Extradural Spinal Tumours at the University Teaching Hospital in Lusaka, Zambia", in partial fulfilment of the requirements for the degree of Master of Medicine in Orthopaedic and Trauma Surgery.

This will be a retrospective study covering the period 1st January, 2013 to 31st December, 2016. It will involve collecting data from patients' hospital records using a predetermined data collection questionnaire.

The study aims to investigate the clinical presentation of patients with extradural spinal tumours at UTH and establish the factors that determine the treatment they receive and outline the outcomes of that treatment.

I am here by writing to request permission to carry out this research.

Your favourable consideration of this request will be highly regarded.

Yours faithfully,


Hilgard Mutembo

Appendix ii: Application for Waiver of Need for Consent

2nd August, 2017.

Hilgard Mutembo
The University of Zambia
School of Medicine
Department of Surgery
LUSAKA

The Chairperson
University of Zambia Biomedical Research and Ethics Committee
Ridgeway
LUSAKA

Dear Sir,

RE: WAIVER OF THE NEED TO OBTAIN CONSENT

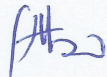
I am a postgraduate student at the University of Zambia, School of Medicine, intending to conduct a study entitled "Presentation, Management and Short-term Outcome of Extradural Spinal Tumours at the University Teaching Hospital in Lusaka, Zambia", in partial fulfilment of the requirements for the degree of Master of Medicine in Orthopaedic and Trauma Surgery.

This will be a retrospective study covering the period 1st January, 2013 to 31st December, 2016. It will involve collecting data from patients' hospital records using a predetermined data collection questionnaire.

The study aims to investigate the clinical presentation of patients with extradural spinal tumours at UTH and establish the factors that determine the treatment they receive and outline the outcomes of that treatment.

I am here by writing to request permission from your office to conduct the said study in the absence of written informed consent and/or assent from the participants as there will be no contact with them.

Yours faithfully,



Hilgard Mutembo

Appendix iii: Corrections to UNZABREC

18th September, 2017

Hilgard Mutembo.
The University of Zambia,
School of Medicine,
Department of Surgery,
LUSAKA.

The Chairperson,
University of Zambia Biomedical Research Ethics Committee,
Ridgeway,
LUSAKA.

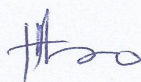
Dear Sir,

**RE:CORRECTIONS TO THE PROTOCOL: “PRESENTATION ,
MANAGEMENT AND SHORT-TERM OUTCOME OF EXTRADURAL
SPINAL TUMOURS AT THE UNIVERSITY TEACHING HOSPITAL IN
LUSAKA, ZAMBIA” (REF. NO.012-08-17)**

Thank you for your letter dated 12th September, 2017 with respect to the above subject.

I have made the recommended additions and they are to be found at pages 33 and 34 of the copy of the revised research proposal submitted with this letter.

Yours faithfully,



Dr. Hilgard Mutembo

Appendix iv: Graduate Proposal Presentation Forum Permission Letter



UNIVERSITY OF ZAMBIA

SCHOOL OF MEDICINE

Telephone : +260211252641

Telegram: UNZA, Lusaka

Telex: UNZALU ZA 44370

Email: assistantdeanpgmedicine@unza.zm

P.O Box 50110
Lusaka, Zambia

17 July 2017

Dr. Hilgard Mutembo
Department of Surgery
University of Zambia
LUSAKA

Dear Dr. Mutembo,

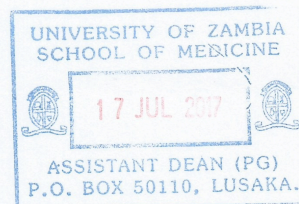
RE: GRADUATE PROPOSAL PRESENTATION FORUM

Following the presentation of your proposal entitled **“Presentation, Management and Outcome of Extradural Spinal Tumours at the University Teaching Hospital in Lusaka”** your supervisor has confirmed that the necessary corrections to your research proposal have been done.

You can proceed and present to the Research Ethics.

Yours faithfully

Dr. L. Prashar
Assistant Dean, Postgraduate
SCHOOL OF MEDICINE



cc: HOD – Surgery

Appendix v: Request for Permission to Conduct Research at UTH

2nd August, 2017.

Hilgard Mutembo
The University of Zambia
School of Medicine
Department of Surgery
LUSAKA

The Head-Clinical Care
University Teaching Hospitals-Adult Hospital
P/B RW1
LUSAKA

Dear Sir,

RE: REQUEST FOR PERMISSION TO CONDUCT ACADEMIC RESEARCH

I am a postgraduate student at the University of Zambia, School of Medicine, intending to conduct a study entitled "Presentation, Management and Short-term Outcome of Extradural Spinal Tumours at the University Teaching Hospital in Lusaka, Zambia", in partial fulfilment of the requirements for the degree of Master of Medicine in Orthopaedic and Trauma Surgery.

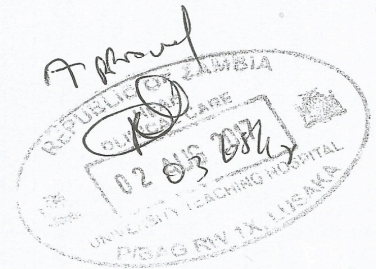
This will be a retrospective study covering the period 1st January, 2013 to 31st December, 2016. It will involve collecting data from patients' hospital records using a predetermined data collection questionnaire.

The study aims to investigate the clinical presentation of patients with extradural spinal tumours at UTH and establish the factors that determine the treatment they receive and outline the outcomes of that treatment.

I am here by writing to request permission from your office for me to conduct the said study.

Yours faithfully,


Hilgard Mutembo



Appendix vi: Response from UNZABREC



THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
E-mail: unzarec@unza.zm
Assurance No. FWA00000338
IRB00001131 of IORG0000774

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

12th September, 2017.

Your Ref: 012-08-17

Hilgard Mutembo,
The University of Zambia,
School of Medicine,
Department of Surgery,
Lusaka.

Dear Sir/Madam,

**RE: "PRESENTATION, MANAGEMENT AND SHORT-TERM OUTCOME OF
EXTRADURAL SPINAL TUMOURS AT THE UNIVERSITY TEACHING
HOSPITAL IN LUSAKA, ZAMBIA" (REF. NO. 012-08-17)**

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee meeting on 30th August, 2017 and the following concerns were raised.

CORRECTIONS:

- (i) The study seeks a waiver from obtaining written informed consent since it is only analysing patient records retrospectively. This can be granted.
- (ii) Under data analysis there is need for more information on what variables will be analysed.

Approval will only be granted after the raised concerns are addressed. Please resubmit one copy of the revised proposal, with highlighted changes and one copy of a cover letter of the responses regarding the comments with cited page numbers of each response of the concerns. This should be done within two weeks period.

Yours sincerely,

Dr. S. H Nzala
VICE-CHAIRPERSON

Appendix vii: Study Questionnaire

THE UNIVERSITY OF ZAMBIA

SCHOOL OF MEDICINE

DEPARTMENT OF SURGERY

Research Proposal on the Presentation, Management and Short-term Outcomes of Extradural Spinal Tumours at the University Teaching Hospital in Lusaka, Zambia.

PART 1: DEMOGRAPHICS

1. Date of Birth: _____
2. Sex: Male _____ Female _____
3. Age at presentation (Yrs) _____
4. Date of presentation: _____
5. Marital Status: Married _____ Single _____ Divorced _____
Widowed _____ Separation _____
6. Occupation _____
7. Residence Urban _____ Rural _____
8. Social Habits:
 - a. Sports: YES (specify) _____ NO _____
 - b. Alcohol consumption YES _____ NO _____
 - c. Cigarette Smoking YES _____ NO _____

PART 2: SYMPTOMATOLOGY

1. BACK PAIN:

- YES _____ NO _____
- Duration: Less than 6mo _____; 6 – 12 Mo _____ 12 -18 Mo _____
18-24 Mo _____; More than 24 Mo _____
- ONSET: Sudden _____ Insidious _____
- Remissions: YES _____ NO _____
- Persistent: YES _____ NO _____
- Getting Worse: YES _____ NO _____
- Related to Change in Posture: YES _____ NO _____

Relief from Pain-killers: YES _____ NO _____

Worse at night YES _____ NO _____

VAS Score (out of 10): _____

2. BACK DEFORMITY: YES _____ NO _____

_____ Duration: Less than 6 Mo _____ ; 6-12 Mo _____
12-18 Mo _____ 18-24 Mo _____ ; More than 24 Mo _____

ONSET: Sudden _____ Insidious _____

3. LOSS OF POWER IN:

a. upper limbs YES _____ NO _____

b. Lower limbs: YES _____ NO _____

ONSET: Sudden _____ Insidious _____

Duration of loss: Less than 6 Mo _____ ; 6-12 Mo _____ ;

12-18 Mo _____ 18 – 24 Mo _____ ; More than 24 Mo _____

Type of loss:

Partial: YES _____ ; NO _____

Complete: YES _____ ; NO _____

Effect of loss:

Able to use affected limbs: YES _____ NO _____

Cannot use affected limbs: YES _____ NO _____

4. SENSORY LOSS:

YES _____ NO _____

If YES, specify type of loss:

a. Only altered sensation: YES _____ NO _____

Level (specify) _____

b. Complete loss: YES _____ NO _____

Level (specify) _____

c. ONSET: Sudden _____ Insidious _____

d. Duration of loss: Less than 6 Mo. _____ ; 6-12 Mo _____

12-18 Mo _____ 18-24 Mo _____ ; More than 24 Mo _____

5. LOSS OF BLADDER CONTROL:

YES _____ NO _____

ONSET: Sudden _____ Insidious _____

DURATION: Less than 6Mo _____; 6-12 Mo _____ 12-18 Mo _____

18-24 Mo _____; More than 24 Mo _____

6. LOSS OF BOWEL CONTROL:

YES _____ NO _____

ONSET: Sudden _____ Insidious _____

DURATION: Less than 6Mo _____; 6-12 Mo _____

12-18 Mo _____ 18-24 Mo _____ More than 24 Mo _____

7. ABNORMAL GAIT:

YES _____ NO _____

ONSET: Sudden _____ Insidious _____

DURATION: Less than 6Mo _____; 6-12 Mo _____; 12-18 Mo _____

18-24 Mo _____ More than 24 Mo _____

8. INCOORDINATION:

YES _____ NO _____

DURATION: Less than 6 Mo _____; 6 -12 Mo _____; 12-18 Mo _____;

18-24 Mo _____; More than 24 Mo _____

9. CLUMSINESS:

YES _____ NO _____

DURATION: Less than 6 Mo _____; 6 -12 Mo _____; 12-18 Mo _____;

18-24 Mo _____; More than 24 Mo _____

10. OTHER SYMPTOMS (SPECIFY)

SYMPTOM	ONSET	DURATION

PART 3: PHYSICAL EXAMINATION FINDINGS

1. **BACKACHE GRADING BY VISUAL ANALOGUE SCALE :** _____

2. MOBILITY:

a. Ambulant (Normal) YES _____ NO _____

b. Using aids:

i. Cane YES _____ NO _____

ii. Crutches: YES _____ NO _____

iii. Frame: YES _____ NO _____

iv. Wheel chair: YES _____ NO _____

c. Bedridden YES _____ NO _____

3. CRANIAL NERVES:

a. Normal: YES _____ NO _____

b. Abnormality (specify):

4. MUSCLE TONE

a. Normal: YES _____ NO _____

b. Abnormality (specify)

5. REFLEXES:

a. Normal: YES _____ NO _____

b. Abnormality (specify):

6. SENSORY LEVEL:

YES _____ LEVEL _____

NO _____

7. FRANKEL GRADING (Specify A, B, C, D or E)

8. BACK DEFORMITY

TYPE OF DEFORMITY	LEVEL(S) AFFECTED	EFFECT OF DEFORMITY

9. DIGITAL RECTAL EXAMINATION

a. Sensation : Present _____ Absent

b. Sphincter tone: Normal _____ Increased _____ absent

c. Contents: Soft stool _____ hard stool/pellets _____ empty _____

d. Other findings (specify) _____

PART 4: IMAGING AND FINDINGS

1. PLAIN RADIOGRAPHY:

- a. Lytic lesion:
 - i. YES _____ Location (specify) _____
 - ii. NO _____
- b. Blastic lesion
 - i. YES _____ Location (specify) _____
 - ii. NO _____
- c. Pathological Fracture
 - i. YES _____ Location (specify) _____
 - ii. NO _____
- d. Other findings (specify finding and location) _____

2. COMPUTED TOMOGRAPHY SCAN:

- a. DONE YES _____ NO _____
- b. REASON/S FOR NOT DOING CT SCAN:
 - i. Machine out of order: YES _____ NO _____
 - ii. Not requested by doctor : YES _____ NO _____
 - iii. Patient not able to afford : YES _____ NO _____
 - iv. Other reasons (specify)

- c. Findings if done (Specify)

3. MAGNETIC RESONANCE IMAGING

- a. DONE: YES _____ NO _____
- b. REASON/S FOR NOT DOING:
- i. Machine out of order YES _____ NO _____
 - ii. Not requested by doctor YES _____ NO _____
 - iii. Patient not able to afford :YES _____ NO _____
- c. Other reason/s (specify) _____
- d. Findings if done (specify) _____
- _____
- _____

4. TECHNETIUM BONE SCAN:

- a. DONE: YES _____ NO _____
- b. REASON/S FOR NOT DOING:
- i. Machine out of order: YES _____ NO _____
 - ii. Not requested by doctor: YES _____ NO _____
 - iii. Patient not able to afford: YES _____ NO _____
- c. Other reason (specify) _____
- d. FINDINGS IF DONE(Specify)
- _____
- _____

5. OTHER IMAGING STUDIES PERFORMED

MODALITY	FINDINGS

PART 5: LABORATORY INVESTIGATIONS AND FINDINGS

1. FULL BLOOD COUNT:

a. DONE

FINDINGS: Haemoglobin: _____ Haematocrit _____

WBC: _____ Platelets: _____

Other findings (specify):

b. NOT DONE: Reasons (specify): _____

2. DIFFERENTIAL COUNT:

a. DONE

FINDINGS:

Neutrophils: _____ RBCs _____

Lymphocytes: _____ Monocytes: _____

Eosinophils: _____ Basophils _____

Other findings (specify):

b. NOT DONE Reasons (specify)

3. LIVER FUNCTION TESTS:

a. DONE

Findings: Albumin _____ Total Protein _____

Bilirubin _____

Other findings (specify)

b. NOT DONE: Reason (specify) _____

4. RENAL FUNCTION TESTS

a. DONE:

FINDINGS: Urea _____ Creatinine _____

Potassium _____ Sodium _____

Bicarbonate _____ Chloride _____

5. HISTOPATHOLOGY

a. DONE: _____ Date: _____

Report _____

b. NOT DONE: Reason

6. OTHER LABORATORY TESTS AND FINDINGS

LABORATORY TEST	RESULT

PART 6: COMORBIDITIES PRESENT

1. HUMAN IMMUNODEFICIENCY VIRUS INFECTION STATUS:

A. Negative _____ Date _____

B. Positive _____ Date _____

i. Duration

ii. On Treatment:

YES _____ Date Started Treatment _____

NAMES OF DRUGS (specify)

NO _____ REASON/S (specify)

iii. Latest CD4 Count _____ Dated: _____

iv. Latest Viral Load: _____ Dated: _____

C. Unknown _____

2. DIABETES MELLITUS:

A. YES: _____

i. Type : _____ Duration _____

ii. Treatment (specify drugs and dosages) _____

iii. Fasting Blood Sugar _____ Date _____

iv. Glycosylated RBCs _____ Date _____

3. HYPERTENSION

A. YES

i. On treatment: YES _____ NO _____

If Yes specify drugs and dosages

ii. Not on treatment (specify reasons)

4. CIGARRETTE SMOKING

A. YES: _____ Duration _____ Number of sticks per day _____

B. NO _____

5. OTHER MEDICAL CONDITION/S SUFFERED (specify Condition, Duration and Treatment)

6. TYPE OF HOST:

A. TYPE A _____ REASON _____

B. TYPE B _____ REASON _____

C. TYPE C _____ REASON _____

D. INDETERMINATE:

REASONS _____

PART 7: DIAGNOSIS AND TREATMENT

1. PROVISIONAL DIAGNOSIS:

2. PROVISIONAL TUMOUR STAGING:

3. TREATMENT PLAN:

- a. Neoadjuvant Therapy Indicated: YES (Specify Type and date given)_____

NO (Specify Reason/s)_____

- b. SURGICAL- INDICATIONS (Specify)_____

- c. NONSURGICAL – REASONS (Specify)_____

4. SURGICAL TREATMENT:

- a. Preoperative optimisation requirements (specify):

- i. _____
- ii. _____
- iii. _____
- iv. _____
- v. _____

- b. Instrumentation/implants required:

- i. YES _____ NO _____

- ii. If YES Specify type

- iii. If YES state if instrumentation/implants available at surgery:

iv. If not implants not available at surgery state reasons:

v. Surgical technique

1. Anaesthesia

2. Patient position _____

3. Intraoperative Imaging: YES: ____ NO _____

Type: _____

4. Surgical approach

a. Anterior: _____

b. Posterior _____

c. Combined: _____

i. Single sitting _____

ii. Two or more sittings _____

Interval: _____

vi. Intraoperative findings (specify)

vii. What was done (intraoperative treatment procedure):

1. En bloc resection

2. Piecemeal resection and curettage:

3. Other (specify)

4. Method of Intra-Operative Spine Stabilisation

YES (specify): _____

NO (specify Reason): _____

5. Vacuum drain used: YES ____ NO _____

Reasons for not using drain (Specify):

6. Wound closure:

5. IF SURGERY INDICATED BUT NOT DONE SPECIFY REASONS:

a. Patient not fit for major surgery:

b. Instrumentation/Implants not available

c. Nonsurgical treatment option available for condition (specify treatment)

d. Other reason/s (specify):

6. ADJUVANT THERAPY INDICATED:

YES (Specify type/s and date/s given)

NO (Specify Reasons):

PART 8: OUTCOMES

1. MOBILITY

MEASURE	PERIOD	0 Mo.	6 Mo	12 Mo.	18 Mo.	24 Mo.	36 Mo.
NORMAL							
CRUTCHES							
FRAME							
BEDRIDDEN							

2. PAIN (VAS)

MEASURE	PERIOD	0 Mo	6 Mo	12 Mo.	18 Mo.	24 Mo.	36 Mo.
SAME							
IMPROVED							
WORSENER							

3. DEFORMITY ; Specify type _____

MEASURE	PERIOD	0 Mo.	6 Mo.	12 Mo	18 Mo	24 MO.	36 Mo.
SAME							
IMPROVED							
WORSENER							

4. STOOL INCONTINENCE

MEASURE	PERIOD	0 Mo.	6 Mo.	12 Mo.	18 Mo.	24 Mo.	36 Mo.
SAME							
IMPROVED							
WORSENER							

5. URINE INCONTINENCE

MEASURE	PERIOD	0 Mo.	6 Mo.	12 Mo.	18 Mo.	24 Mo.	36 Mo.
SAME							
IMPROVED							
WORSENER							

6. HOST TYPE (Specify A, B or C)

MEASURE	PERIOD	0 Mo.	6 Mo.	12 Mo.	18 Mo.	24 Mo.	36 Mo.
SAME							
IMPROVED							
WORSENER							

7. FRANKEL GRADING

MEASURE	PERIOD	0 Mo.	6 Mo.	12 Mo.	18 Mo.	24 Mo.	36 Mo.
SAME							
IMPROVED							
WORSENER							

8. SURGICAL WOUND INFECTION

TYPE	PERIOD	0 Mo.	6 Mo.	12 Mo.	18 Mo.	24 Mo.	36 Mo.
SUPERFICIAL							
DEEP							

9. DEATH (Specify cause of death)

CAUSE	PERIOD	0 Mo.	6 Mo.	12 Mo.	18 Mo.	24 Mo.	36 Mo.

CONFIRMED BY POST MORTEM:

1. YES _____
2. NO _____ Reason/s for no post mortem _____

10. COMPLICATIONS

TYPE	PRESENT(YES/NO)
DECUBITUS ULCERS	
DEEP VEINOUS THROMBOSIS	
PNEUMONIA	
URINARY TRACT INFECTION	
SEPSIS	
JOINT STUIFFNESS	

Appendix viii: Waiver for the Protocol from UNZABREC



THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
E-mail: unzarec@unza.zm

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

Assurance No. FWA00000338
IRB00001131 of IORG0000774

13th September, 2017.

Your Ref: 012-08-17.

Dr. Hilgard Mutembo,
University of Zambia,
School of Medicine,
Department of Surgery,
P.O Box 50110,
Lusaka.

Dear Dr. Mutembo,

RE: WAIVER FOR THE PROTOCOL: "PRESENTATION, MANAGEMENT AND SHORT-TERM OUTCOME OF EXTRADURAL SPINAL TUMOURS AT THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA" (REF. NO. 012-08-17)

Your application for waiver of ethics for the aforementioned proposal was reviewed. However, it was noted that this is a waiver of written informed consent. The waiver is hereby granted. The approval was conducted in line with the University of Zambia Biomedical Research Ethics Committee guidelines on granting waiver of Ethics review.

CONDITIONS:

- The waiver is based strictly on your submitted proposal. Should there be need for you to modify or make changes to the proposal; you will need to seek clearance from the Biomedical Research Ethics Committee.
- This waiver does not release you from the obligation of ensuring confidentiality.
- If you need any clarifications please consult this office.
- **Ensure that a final copy of the results is submitted to this Committee.**

Yours sincerely,

Dr. S. H Nzala
VICE-CHAIRPERSON

Date of approval: 13th September, 2017.

Date of expiry: 12th September, 2018.