CLINICO-MORPHOLOGICAL PATTERN OF MUSCULOSKELETAL TUMOURS AMONG PATIENTS SEEN AT MUHIMBILI ORTHOPAEDIC INSTITUTE, FROM JANUARY 2013 TO DECEMBER 2014

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MMed (Orthopaedics and Traumatology) Dissertation
Muhimbili University of Health and Allied Science
October, 2016

CLINICO-MORPHOLOGICAL PATTERN OF MUSCULOSKELETAL TUMOURS AMONG PATIENTS SEEN AT MUHIMBILI ORTHOPAEDIC INSTITUTE, FROM JANUARY 2013 TO DECEMBER 2014

By

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A Dissertation submitted in (Partial) Fulfilment of the Requirement for the Degree of Master of Medicine (Orthopaedics and Traumatology) of Muhimbili University of Health and Allied Sciences

Muhimbili University of Health and Allied Science
October, 2016

CERTIFICATION

The undersigned certifies that, he has read and hereby recommends for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation titled; ***Clinico-morphological pattern of musculoskeletal tumours among patients seen at Muhimbili Orthopaedic Institute, from January 2013 to December 2014,*** in (partial) fulfilment of the requirements for the Degree of Master of Medicine (Orthopaedics and Trauma) of the Muhimbili University of Health and Allied Sciences.

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Supervisor

_____

Date

DECLARATION AND COPYRIGHT

I, **Salome Mduma** declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for similar or any other degree award.

Signature …….....…… Date.....

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ACKNOWLEDGEMENTS

I would like to express my sincere appreciation to my supervisor Dr, R. I. Mhina for accepting to supervise this study. His relentless sacrifice, keen interest, moral support, advice, analytical criticism and constant encouragement have made this study successful.

I would also like to express my gratitude to Muhimbili Orthopaedic Institute administration through the Executive Director Dr. Othman Kiloloma and Medical Director, Dr. C. N. Mcharo for their permission to conduct the study at MOI and their subsequent recommendations.

I wish to acknowledge the continued assistance from Dr. Billy Haonga and, the technical support from Dr. Respicious Boniface.

I recognize equally the role played by and contributions firstly from: (i) all teaching, theatre and registry staff from Department of Orthopaedic and Traumatology but also all Central Pathology Laboratory staff including : Dr. Mosha, Sr. Grace, Mr. Erick for assistance in the data collection process.

Last but not least I'm grateful to the Tanzania Peoples' Defences Forces for sponsoring my course.

I thank the Almighty God for the good health I enjoyed throughout my study and for enabling to complete this task.

DEDICATION

Every challenging work needs self-effort as well as guidance of elders especially those who are close to our hearts.

My humble effort, I dedicate to my family, whose affection, love, encouragement and prayers of day and night enabled to get such success and honour,

And to all hardworking and respected lecturers.

ABSTRACT

Musculoskeletal tumours are relatively rare, with low incidence compared to other tumours. Their geographic distribution varies greatly around the world, in Asia; the annual distribution of musculoskeletal tumour was 624 against 8,805 cases of colorectal cancer and 6532 cases of lung cancer in 2008 – 2012. In USA, the annual distribution of bone was 0.2% and soft tissue tumours was 0.7% against 18.3% of digestive system cancers, 14.5% of breast cancer, 13.9% of respiratory system cancers and 7.9% of urinary system in 2006 – 2010

Objective: The aim of this study is to determine the clinico-morphological pattern of musculoskeletal tumours, seen at Muhimbili Orthopaedic Institute, from January 2013 to December 2014.

Study design: A retrospective hospital based descriptive study of patients with musculoskeletal tumors seen at MOI from January 2013 to December 2014.

Materials and methods: Data was collected retrospectively from musculoskeletal registry of MOI, notes from patients' files and histopathology reports of biopsies from patients clinically diagnosed with musculoskeletal lesions from January 2013 to December 2014.The histopathology results of specimen sent to CPL were correlated with clinical findings for diagnosis of patients. Musculoskeletal tumours were diagnosed by, incisional, excisional or tru-cut biopsy. The malignant and metastatic tumours in additional were diagnosed radiological. Data was collected on age, sex, anatomical site, and histo-pathologic type from 210 patients.

On the basis of histopathology reports, the tumours were classified as benign bone tumours, primary malignant bone tumours, secondary bone tumours (metastasis), benign and malignant soft tissue tumours (STT) and tumour like lesions.

Description statistics were performed using SPSS software version 20.0 for windows (SPSS Inc., Chicago, IL, USA). Frequency and percentage of the mentioned variables were calculated.

Results: Data of a total from 210 patients with musculoskeletal tumours was collected and 181 analysed. The total number of male was 99 with an age range from 8 – 85 years and median age of 25 years. The total number of female was 82 with an age range from 3 – 75 years and median age 28.5 years.

Primary malignant bone tumours, (osteosarcoma, chondrosarcomaand Ewing's sarcoma) were seen in 54 (29.8%) of cases, demonstrated higher predilections for male 31 (57. 4%).

Generally, benign tumours, demonstrated slightly higher predilections for male 25 (53.2%). Whereas osteochondroma and chondroma among the benign bone tumours, demonstrated higher predilection for male, giant cell tumour 21 (44.6%) the most common benign bone tumour showed higher predilection for female 12 (57.1%)

Secondary malignant bone tumours 32 (17.6%), the carcinoma from breast, prostate, lung and thyroid demonstrated higher predilections for female 13 (68.4%). Secondary malignant tumours and are seen mainly in elderly patients > 50yrs of age.

Both Benign and malignant soft tissue tumours 48 (26.5%), demonstrated higher predilections for male 28 (58.3%).

From the study, the most common site of the musculoskeletal tumours is the femur 39 (21.5%)**,** followed by the tibia 28 (15.5%) and humerus 26

Conclusion: Among 181 musculoskeletal tumours analysed, 99 cases were male with an age range from 8 – 85 years and median age of 25 years and 82 cases were female with an age range from 3 – 75 years and median age 28.5 years. From this study, musculoskeletal tumour have shown slightly male predilection at a M;F ratio of 1.2:1

The most affected age was the 11 – 20year age group.

The frequent histological types were osteosarcoma 47 (21.6%), Metastases 32 (17.7%), Giant cell tumours 21 (11.6%), osteochondroma 10 (5.5%) and Synovial sarcoma 10 (5.5%).
The commonest sites for musculoskeletal tumours are femur, tibia and humerus, the bones sites with highest growth rate.

Recommendation: This study throws some light on the existing musculoskeletal tumour burden at MOI. A long period and multicentre study is needed to throw more light on the burden of disease nationwide.

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LIST OF ABBREVIATIONS

A BC	Aneurysm Bone Cyst
AJCC	American Joint Committee on Cancer
CT-SCAN	Computer Tomography SCAN
EMD	Emergency Medicine Department
GCT	Giant Cell Tumour
IARC	International Agency for Research on Cancer
KCMC	Kilimanjaro Christian Medical College
MFH	Malignant Fibrous Histiocytoma
MoHSW	Ministry Of Health and Social Welfare
MOI	Muhimbili Orthopaedic Institute
MRI	Magnetic Resonance Imaging
MSTS	Musculoskeletal Tumour Society
MUHAS	Muhimbili University of Health and Allied Sciences
NCR	National Cancer Registry
OTA	Orthopaedic and Trauma Association
SPSS	Statistical Program for the Social Sciences
STT	Soft Tissue Tumour
WHO	World Health Organization
X-RAY	Röntgen Radiation

CHAPTER ONE

1.0 INTRODUCTION

The study is presenting the clinico-morpholpgical pattern of MST, but this chapter will give thorough information on musculoskeletal tumours background, aetiopathogenesis, clinical manifestations, tumour classification and staging and management as per existing knowledge.

1.1 BACKGROUND

Benign musculoskeletal tumours are not common and make up approximately 1% of primary tumours of the body[1]. Primary malignant bone tumours constitute approximately 0.2% and 5% of malignant tumours in adults and children respectively[2]. Secondary or metastatic tumours to bone from primary tumours (usually carcinomas from prostate, breast, lungs, kidney and thyroid) are much more common in the elderly, and perhaps 50% of these patients, at time of presentation, will have tumour that has spread to bone [1].Distribution of musculoskeletal tumours is variable, in different parts of the world, where the highest rates are seen in Europe and the USA, and lower incidence and prevalence is seen in Asian countries[2]. According to the international agency of research on cancer, only few African countries have reliable statistics of bone cancer. Among them, Mali has the highest standardized rate among males while Algeria exhibits the highest rate among females[2].There hasn't been recent documented data on musculoskeletal tumours in Tanzania.

In Tanzania, the diagnosis of musculoskeletal tumours remains to be a major source of concern is due to delay in presentation and diagnosis (either due to non-specificity of clinical manifestation, limited diagnostic and therapeutic resources or limited financial support) and lack of statistics.

AETIOPATHOGENESIS

Bone tumours may occur in settings of inherited syndromes, but they have similar histopathology as those that arise sporadically[3].Although the majority of primary bone malignancies arise sporadically there is increasing evidence that some can be a result of genetic cancer syndrome predisposition as in patients with retinoblastoma, Werner syndrome,

Rothmund-Thompson syndrome and Li-Fraumeni syndrome[3]. Some are associated with and develop from non-neoplastic precursors (radiation therapy, Paget's disease and cartilaginous dysplasia).[2]In most tumours however; no specific aetiology can be identified. Development risk of malignant transformations varies in primary malignant tumour of bone[4]. High risk malignant transformations are seen in Ollier's disease, Maffucci syndrome, familial retinoblastoma syndrome and Rothmund Thompson syndrome[4]. Moderate risk for malignant transformation is associated with multiple osteochondromas, Paget's disease and radiation osteitis[4]. Low risk precursors are seen in fibrous dysplasia, bone infarct, chronic osteomyelitis, prosthetic implants, osteogenesis imperfecta, giant cell tumour, osteoblastoma and chondroblastoma[4].

CLINICAL MANIFESTATION

The clinical manifestations of benign and some malignant musculoskeletal tumours are non-specific. This causes delays in the diagnosis. Patients with bone tumour occasionally present with pain at rest or at night, soft tissue or bone swelling, decrease in range of motion, and approximately 5 -10% present with fracture after trivial or minor trauma[2].

CLASSIFICATION OF MUSCULOSKELETAL TUMOURS

WHO Classification has been adopted widely, and the revised and expanded classification (WHO classification 1993)[5], has similar concept and framework to the original version to allow comparisons between data collected in the past and one that will be collected in future. It has promoted uniformity in diagnosis and provided the basis for a number of clinical, pathologic, and epidemiologic studies.

The WHO classification is based on histological criteria and malignancy clinical criteria[4],

(1) Bone forming tumours.
    Benign: Osteoma, Osteidosteoma, Benign Osteioblastoma
    Malignant: Osteosarcoma
(2) Cartilage forming tumours.
    Benign: Chondroma, Osteochondroma, and Chondroblastoma
    Malignant: Chondrosarcoma

(3) Bone Marrow tumours

Round cell tumours: Ewing's sarcoma, malignant bone lymphomas, Myelomas

(4) Giant cell tumours

Giant cell tumour was classified in the benign bone tumour despite its radiographic characteristics of indistinct borders, which resulted from permeation into host bone. Giant cell tumour is locally aggressive with increasing incidence of recurrence but it rarely metastasizes[4].

(5) Vascular tumours

Hemangioma, Angisoarcoma

(6) Other connective tissue tumours.

Benign: Lipoma

Malignant: Malignant Fibrous Histiocytoma, Liposarcoma, and Fibrosarcoma

ENNEKING STAGING SYSTEM

The Enneking system is the most widely used staging system and has been adopted by the Musculoskeletal Tumour Society Staging System[6]. The system aids in assessing prognosis & planning management. The system is reserved for staging mesenchyme lesions, thus is not applicable to tumours originating in either the marrow or reticulo-endothelial system (lesions of Ewing sarcoma, lymphoma, and myeloma), since they differ in their biologic behaviour. The surgical staging of bone and soft-tissue tumours is based on grade (G), site (T), and metastasis (M) and uses histological, radiological, and clinical criteria.

Table1: Enneking System for the Surgical Staging of Malignant Bone and Soft-Tissue Tumours.

Stage	Grade	Site	Metastasis
IA	Low (G1)	Intracompartmental (T1)	No metastasis (M0)
IB	Low (G1)	Extracompartmental (T2)	No metastasis (M0)
IIA	High (G2)	Intracompartmental (T1)	No metastasis (M0)
IIB	High (G2)	Extracompartmental (T2)	No metastasis (M0)
III	Any (G)	Any (T)	Regional or distant metastasis (M1)

(Adapted from Enneking system for the surgical staging of musculoskeletal society[5])

Table2: Enneking System for Surgical Staging of Benign Bone and Soft-Tissue Tumours.

Stage	Description	Grade	Site	Metastasis
1	Latent	G0	T0	M0
2	Active	G0	T0	M0
3	Aggressive	G0	T1 or T2	M0 or M1

(Adapted from Enneking system for surgical staging for Musculoskeletal Tumour Society[5])

- **G0** - Benign lesion
- **G1** - Low-grade malignant lesion
- **G2** - High-grade malignant lesion
- **T0** - A benign tumour confined within a true capsule and its anatomic compartment of origin (i.e., an intracapsular, intracompartmental lesion)

- **T1**- An aggressive benign or malignant tumour confined within its anatomic compartment (i.e., an intracompartmental lesion)
- **T2** - A lesion that has spread beyond its anatomic compartment of origin (i.e., an extra compartmental lesion)

- **M0** - No regional or distant metastasis
- **M1** - Regional or distant metastasis

MANAGEMENT

The aim of treatment is to control pain, improve function and to treat pathological or impending pathological fractures. It is multidisciplinary involving surgeon oncologist, radiation oncologist, pathologist psychologists, nurses, counsellors, palliative care teams, rehabilitation specialist and physical therapist. The choice of treatment generally depends on the type, the size and location of the primary cancer; number of metastatic tumours; the patient's age and general health, and the types of treatment the patient has had in the past.

Quite large numbers of benign tumour do not require treatment but a follow up for its regression or progression.

For malignant tumours; the confined tumours, primary tumours or tumours spread only to regional lymph node are managed by local excision, radical excision or enbloc resection.

Advanced, inaccessible, metastatic and re-current tumours are managed by systemic therapy (chemotherapy, biological therapy, targeted therapy and hormonal therapy), or local therapy such as surgery and radiotherapy, or a combination of these treatments. Radiotherapy and chemotherapy can be used as neo-adjuvant or as adjuvant.

Correlation of Tumour Staging and Management

Benign tumours

- Stage 1 tumours - Intracapsular excision (or curettage) is adequate.
- Stage 2 tumours - Extracapsular excision passing through the reactive zone is needed.
- Stage 3 tumours - Wide margins of resection are required in stage 3 lesions (aggressive benign tumours). In areas that are not amenable to wide excision, marginal excision together with adjuvant treatment (e.g. radiation therapy) may be acceptable.

Malignant tumours

- Stage IA - Treated with wide excision and are usually amenable to limb salvage procedures.
- Stage IB - Treated with wide excision, with amputation or limb salvage depends on the estimated amount of residual tumour left behind after a limb salvage procedure.
- Stage II (high grade, are usually extra compartmental, and have a significant risk for skip metastases) - Amenable to limb salvage operations and require radical amputation or disarticulation in most patients. However, bone tumours responsive to chemotherapy may be treated successfully using wide excision and adjuvant therapy.
- Stage III – Tumours responsive to chemotherapy may be treated with aggressive resection. Tumours non responsive to adjuvant therapy are treated with palliative resection.

1.2 LITERATURE REVIEW

1.2.1EPIDEMIOLOGY

The incidence of primary malignant bone tumours 0.2% in adults [2], is lesser than that of benign bone tumours 1%[1], though it's likely that benign lesions are under estimated because they often are asymptomatic and not clinically recognized. Primary bone tumours are outnumbered by metastatic lesions[2]. The majority of benign bone tumours and tumour like lesions occur in the 1st two decades, while primary malignant bone tumours typically show a bimodal distribution with the 1st peak occurring in the 1st decade and the 2nd peak in patients older than 60years of age[2]. In a study done in Italy, the age specific incidence rates of bone sarcomas demonstrated a bimodal distribution, with the first peak occurring in the second decade, and a second peak occurring in patients older than sixty[3].

In patients aged less than 45years primary bone tumours account for 60% of cases with a peak incidence in 15 -19 years age group.

Secondary or metastatic tumours of bone from primary tumours such as carcinomas from prostate, breast, lungs, kidney and thyroid are much more common in elderly. At the time of presentation about 50% of these malignant tumours will have spread to bone [1].

Age distribution of Musculoskeletal Tumours

The patient's age and clinical presentation are very helpful in predicting the clinical diagnosis in musculoskeletal tumours and greatly aid in the interpretation of the imaging studies.

In a study done in Ethiopia, between Dec 2003 and Mar 2008, has shown that the most affected age group was 15 – 29 years, among 215 biopsies done[7].

One other study has shown different age distribution of main histological subtype, where Ewing's sarcoma and osteosarcoma are most frequent in 1st and 2nd decades, chondrosarcoma, chondroma and osteosarcoma show increase incidence after 4th decade [2]. An overview on epidemiology of bone cancer has shown principle malignant tumours being Osteosarcoma seen in children and young adults, Chondrosarcoma that usually affects people > 40years of age & Ewing's sarcoma that impacts mainly children & teenagers [8]. According to U.S. Surveillance, Epidemiology and End Results Program, the incidence of osteosarcoma appears

to be more frequent in two periods of life, during adolescence and old age[9].In Britain, over recent years the number of cancer registered has been relatively stable, with Osteosarcoma showing a bimodal distribution, 1st peak in adolescence around 17years and 2nd peak later in life around 80 years. Chondrosarcoma which is rare in childhood and rates rises with advancing age, peaking 70 and 80 years of age. And Ewing's sarcoma with similar distribution to osteosarcoma for early years but is rare in over 35years of age[10].

Sex distribution of musculoskeletal Tumour

Sex distribution of the commonest bone tumours by number of cases from National Cancer Registry, has shown that, for the benign tumours: osteochondroma 325females and 547 males, chondroblastoma 47 females and 72 males while for malignant tumours: chondrosarcoma 393 females and 502 males, Ewing's sarcoma 209 females and 303 males and giant cell tumours were 319 females and 249 males[11]. In a retrospective in Mexico, between 2000 and 2005, of the 566 bone tumours, 53.7% were of men and 46.3% were of females [12]. In a study done in Ethiopia, of 215 biopsies done between Dec 2003 and Mar 2008, 51.3% were of males and 48.1% were of females [7].In a study done in Al-Sabah Hospital, Kuwait, between 1995 and 2004, among 142 malignant bone tumours, 76 primary bone tumours showed a male predilection with 42% [8].

1.2.2. HISTOLOGICAL TYPES

Characteristic distribution of musculoskeletal tumours occurrence varies in different parts of world. In Ethiopia, of 215 histopathology biopsies of all bone tumours studied between Dec 2003 and Mar 2008, 38% of biopsies were malignant, and the most common primary malignant tumour from biopsy was osteosarcoma at 28% [7].

.In Kuwait, of 142 malignant bone tumours, the commonest bone tumours were Ewing's sarcoma, multiple myeloma, osteosarcoma, chondrosarcoma and non-Hodgkin's lymphoma[8]. In a study done in Iran from 1997 to 2008, the most frequent musculoskeletal tumours diagnosed were Metastasis 32.6%, Soft tissue tumours 20.9%, Osteochondroma11.6%, and Osteosarcoma10.5%. The commonest malignant bone tumours were osteosarcoma (50.6%), metastasis (17.0%), Ewing's sarcoma (15.9%), and chondrosarcoma (8.0%), and the most

frequent benign bone tumours were osteochondroma (63.9%), enchondroma (10.8%), giant cell tumour (9.9%), and osteoid osteoma (6.6%) [13]. In study done in Basrah medical college in Iraq between 1980 1nd 1999, the most common primary malignant bone tumours are osteosarcoma (39%), Ewing's sarcoma (30%), chondrosarcoma (25%), fibrosarcoma (16%) and giant cell tumours (13%) [14].

Bone cancer is not a common cancer, 0.2%[11] as compared to other cancer disease. According to the U.S. Surveillance, Epidemiology and End Results Program, Osteosarcomas contribute 36% of all type of bone cancer, followed by Chondrosarcoma 30% and Ewing's sarcoma with around 16%[9].

In another study done in the USA, malignant bone tumours represent a small percentage of cancers nationwide and are much less common than malignant soft-tissue tumours[15]. The most common primary malignant bone tumours are osteosarcoma and Ewing's sarcoma, which occur in childhood. Chondrosarcoma occurs more frequently in older adults[15].

From a study done in Mexico City between 2000 and 2005, of 566 bone tumours the commonest malignant bone tumours were osteosarcoma (46.6%) and chondrosarcoma (8.7%), while the most common benign bone tumour was osteochondroma (43.7%) followed by giant cell tumour of bone (14.6%) and chondroma (10.1%) [12].

A study from the University of Florence Medical School in Italy showed that primary bone tumours are rare overall, with bone sarcomas accounting for 0.2% of all malignancies[3].

A study done in Britain has shown that ,over recent years the number of cancer registered has been relatively stable. The main three types of bone cancer were Osteosarcoma, followed by Chondrosarcoma and lastly, Ewing's sarcoma[10].

Another study has shown that from a total of 3,623 primary malignant bone tumours that were registered (1980 to 1991), the commonest histological diagnosis were, Osteosarcoma (44.1%), chondrosarcoma (16.1%), multiple myeloma (13.0%), malignant fibrous histiocytoma (7.7%), Ewing's sarcoma (6.7%), and chondroma (3.8%) [16].

1.2.3 SKELETAL DISTRIBUTION OF MUSCULOSKELETAL TUMOURS

In overview of epidemiology of bone cancer in USA, osteosarcoma occurs mostly in the femur and tibia while chondrosarcoma, a slow growing tumour, starts in the pelvis. Ewing's sarcoma, a fast growing tumour, infiltrates large bones such as the femur, humerus, tibia and pelvis[15]. In Kuwait between 1995 and 2004, femur was the most common site for secondary bone tumours [8]. In Iran from a study reviewed in Shiraz University Orthopaedic Hospitals between 1997 and 2008, of the 426 cases, common involved sites in musculoskeletal tumours were femur, tibia and humerus[13]. A retrospective analysis study done in Mexico has shown that of 566 benign and malignant bone tumours, femur was the most common location of the tumours (39.9%), followed by the tibia (17.7%) and humerus (11.8%) [12].

1.3 PROBLEM STATEMENT

Distribution of musculoskeletal tumours is variable in different parts of the world. The highest rate is seen in Europe and the USA and a lower incidence and prevalence seen in Asian countries. A few countries in Africa have reliable statistics on bone cancer. The diagnosis of musculoskeletal tumours remains to be a major source of concern is due to delay in presentation and diagnosis (either due to non-specificity of clinical manifestation, limited diagnostic and therapeutic resources or limited financial support) and lack of statistics.

There's no recent documented data of musculoskeletal tumours in our setting.

1.4 RATIONALE OF STUDY

The non-specificity of clinical manifestation, limited diagnostic and therapeutic resources or limited financial support makes it imperative that orthopaedic surgeons are able to recognize clinically the symptoms that suggest possibly musculoskeletal tumours and be able to do proper clinical and radiographic evaluation for proper diagnosis and prompt management.

The study results will give baseline data on epidemiology, histology and anatomical site for specific tumours of which can be used as protocol to establish a diagnosis for early intervention.

1.5OBJECTIVES OF THE STUDY

1.5.1 Broad objective

To determine, clinico-morphological pattern of musculoskeletal tumours, seen at MOI, from January 2013 to December 2014.

1.5.2 Specific objectives

1. To determine demographic distribution of patients with musculoskeletal tumours seen at MOI, from Jan 2013 to Dec 2014.
2. To determine histological types of musculoskeletal tumours of patients seen at MOI, from Jan 2013 to Dec 2014.
3. To determine anatomical site distribution of musculoskeletal tumours.

CHAPTER TWO

2.0 METHODOLOGY

2.1 INTRODUCTION

This chapter will highlight on materials and methodology: study design, study setting, study population, study size, study variables data collection and method of data analysis. Also, inclusion criteria and ethical consideration will be highlighted.

2.2 STUDY DESIGN

A retrospective hospital based descriptive study of patients with musculoskeletal tumours seen at MOI from January 2013 to December 2014.

2.3 STUDY SETTING

MOI is among other 2 centres (KCMC and BUGANDO) that treat musculoskeletal tumours in Tanzania. It is a tertiary and teaching hospital specialized in orthopaedics, traumatology and neurosurgical care, receiving patients from all over the country and neighbouring countries. It attends approximately a total of 7050 patients with approximately 100 musculoskeletal tumour patients attended annually. It has capacity of 185 beds capacity with few number of musculoskeletal tumour patients occupying beds annually. Management decision for musculoskeletal tumour is done is done in 2 stages, first by orthopaedic surgeons in clinical meetings and secondly by a tumour board comprising of general/vascular surgeon, pathologist, radiologist, rehabilitative and palliative care team.

2.4 STUDY POPULATION

Records of data of all patients, diagnosed with musculoskeletal tumour from Jan 2013 to Dec 2014, evaluated retrospectively. The diagnosis of tumour was done through clinical, radiological and / or biopsy.

2.5 SAMPLE SIZE

All registered patients diagnosed with musculoskeletal tumours, from Jan 2013 to Dec 2014 will be evaluated

2.5.1 Inclusion Criteria

All registered patients clinical, radiological and histological diagnosed with musculoskeletal tumour from Jan 2013 to Dec 2014

2.5.2Exclusion Criteria

1. All patients with missing or incomplete information will be excluded from study.

2.6 DATA COLLECTIONAND MANAGEMENT

Retrospective study data was collected by the principal investigator, from MOI admission register, clinical and operative notes from patient's hospital records and the histopathology biopsy result from central pathology registry. Then data filled in structured questionnaire. From structured questionnaire, the data entered into SPSS software version 20.0 for windows for cleaning and coding**.**

2.7 STUDY VARIABLES

Independent variables

1. Age
2. Sex
3. Site of the tumour

Dependent variables

1. Benign bone tumours
2. Primary malignant bone tumours
3. Secondary malignant tumours
4. Soft tissue tumours

2.8 DATA ANALYSIS

Description statistics were performed using SPSS software version 20.0 for windows (SPSS Inc., Chicago, IL, USA). Frequency and percentage of the mentioned variables were calculated. Median and standard deviation used for continuous variables.

2.9 ETHICAL CONSIDERATION

Data kept anonymous by the use of file number, to ensure confidentiality instead of patient's name. Patient's information carefully handled with utmost confidentiality. The data for the study collected from MOI admission registry, clinical and operative notes from patient files from records and the histopathology biopsy studies from central pathology registry.

Since its retrospective study, proposal requested exemption for consent from patients at Director of Research and Publications (DRP's) office.

CHAPTER THREE

3.0 RESULTS

3.1 INTRODUCTION

Between January 2014 and Dec 2015 there were a total of 210 cases attended at MOI for MS tumours. 29cases were excluded from study and 181 cases were analysed. Among 29 cases, 9cases were excluded due to missing information, 10 cases due to inadequate biopsy and 10 cases due to tumour like lesions (chronic inflammation and osteomyelitis).

3.2 DEMOGRAPHIC DISTRIBUTION OF PATIENTS WITH MUSCULOSKELETAL TUMOURS

From the retrospective analysis study of 181 musculoskeletal tumours cases, 99 (54.7%) of cases were of men and 82 (45.3%**)** of cases were of females (Table3).This gives a male to female ratio of 1.2:1. The median age at presentation was 27 years with age range from 3 -85 years. The commonest affected age group was 11-20 years (Table3).

Table 3: Demographic distribution of patients with musculoskeletal tumours seen at MOI (N = 181)

Variable	n	Percentage
SEX		
Male	99	54.7
Female	82	45.3
AGE GROUP (years)		
1 – 10	11	6.1
11 – 20	53	29.3
21 – 30	33	18.2
31 – 40	24	13.3
41 – 50	23	12.7
>50	37	20.4

Age distribution of histological types of musculoskeletal tumours

Among patients diagnosed with musculoskeletal tumours, the peak incidence for benign and primary malignant tumours was seen at 11 – 20 years age group. The benign and primary malignant accounted for 40 (75.4 %) among 53 patients seen in adolescent age. Secondary or metastatic tumours are much more common in elderly, >50yrs accounting for 32 (17.7%). Soft tissue tumour was seen frequently at adolescent age and accounted for 11 (22.9%). They were mainly contributed by rhabdomyosarcoma 3(27.3%), hemangioma (vascular tumour) and myxoid fibroma (benign soft tissue tumour) within 11 – 20years age group.

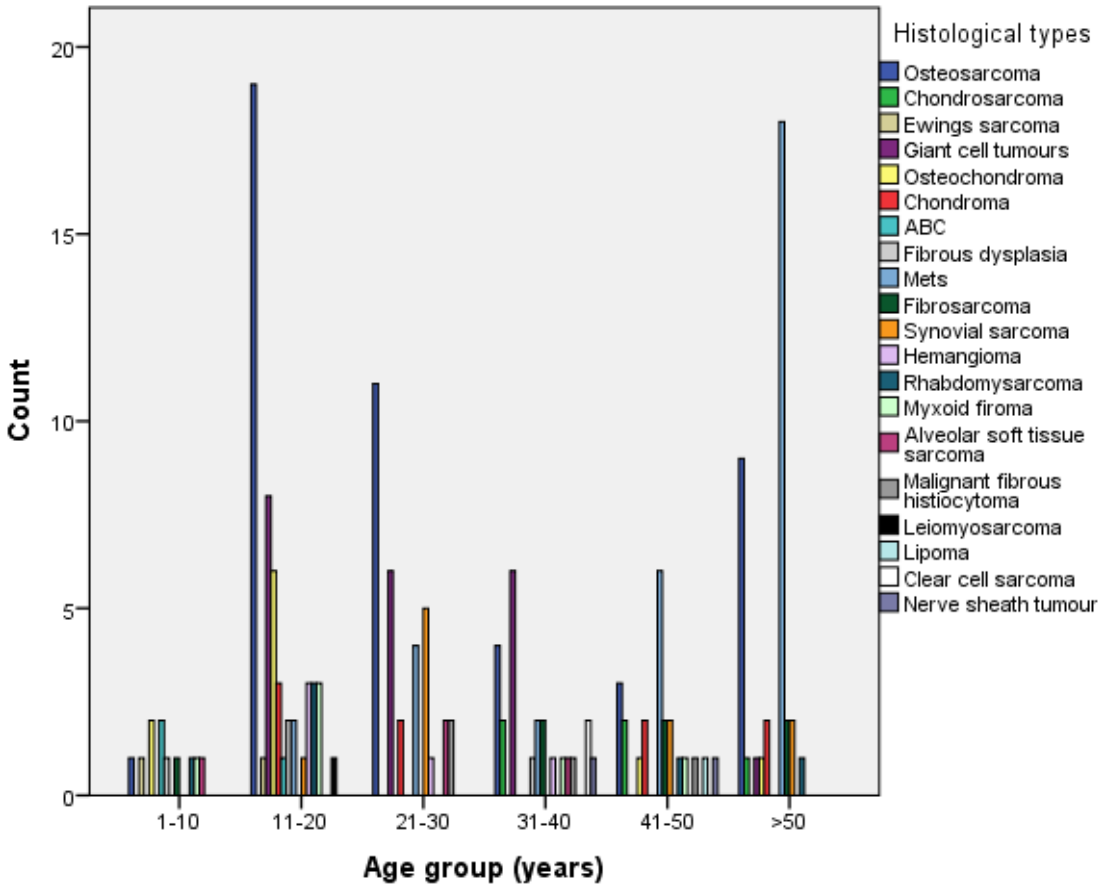


Figure 1: Histological types of patients of musculoskeletal tumours by Age group

Sex distribution of histological types of musculoskeletal tumours

Generally, the primary malignant tumours 54, Benign bone tumours 47 and Soft tissue tumours48, showed male preponderance with 31 (57.4%), 25 (53.2%) and 29 (60.4%) respectively, while the Secondary malignant tumours 32, showed female predilection, 18 (56.3%) against 14 (43.7%) males.

Among benign tumours, osteochondroma and chondroma demonstrated higher predilection for male, and giant cell tumour 21 (44.6%) the most common benign bone tumour showed higher predilection for female 12 (57.1%)

Among primary malignant bone tumours, osteosarcoma and chondrosarcoma demonstrated higher predilections for male 31 (57. 4%) and all Ewing's sarcoma were female 2(100%)
Among secondary malignant bone tumours, the carcinoma from breast, prostate, lung and thyroid demonstrated higher predilections for female 13 (68.4%) while myelomas and
The benign and malignant soft tissue tumours, had demonstrated higher predilections for male 28 (58.3%).

Table 4: Histological types of musculoskeletal tumours of patients by Sex

Musculoskeletal Tumour	**Female n (%)**	**Male n (%)**	**Total n (%)**
Benign bone tumours	22 (46.8)	25 (53.2)	47 (100)
Primary malignant bone tumours	23 (42.6)	31 (57.4)	54 (100)
Secondary malignant bone tumours	18 (58.1)	14 (41.9)	32 (100)
Soft tissue tumours	19 (38.8)	29 (61.2)	48 (100)
TOTAL	**82 (45.3)**	**99 (54.7)**	**181(100)**
Benign bone tumour			
Osteochondroma	3 (30.0)	7 (70.0)	10 (100)
Giant Cell Tumour	12 (57.1)	9 (42.9)	21 (100)
Chondroma	3 (33.3)	6 (66.7)	9 (100)
Fibrous dysplasia	3 (100)	0 (0.0)	3 (100)
ABC	1 (25.0)	3 (75.0)	4 (100)
TOTAL	**22 (46.8)**	**25 (53.2)**	**47 (100)**
Primary malignant bone tumours			
Osteosarcoma	19 (40.4)	28 (59.6)	47 (100)
chondrosarcoma	2 (40.0)	3 (60.0)	5 (100)
Ewing sarcoma	2 (100)	0 (0.0)	2 (100)
TOTAL	**23 (42.6)**	**31(57.4)**	**54 (100)**
Secondary malignant tumours			
Carcinoma	13 (68.4)	6 (31.6)	19 (100)
Lymphoma	2 (50.0)	2 (50.0)	4 (100)
Myeloma	3 (42.9)	4 (57.1)	7 (100)
Skin cancer	0 (0.0)	2 (100)	2 (100)
TOTAL	**18 (58.1)**	**14 (41.9)**	**32 (100)**
Soft tissue tumours			
Rhabdomyosarcoma	2 (33.3)	4 (67.7)	6 (100)
Alveolar soft tissue sarcoma	3 (75.0)	1 (25.0)	4 (100)
Synovial sarcoma	5 (50.0)	5 (50.0)	10 (100)
Malignant Fibrous Histiocytoma	0 (0.0)	4 (100.0)	4 (100)
Myxoid Fibroma	1 (16.7)	5 (83.3)	6 (100)
Fibrosarcoma	4 (57.1)	3 (42.9)	7 (100)
Leiomyosarcoma	1 (100)	0 (0.0)	1 (100)
Hemangioma	2 (40.0)	3 (60.0)	5 (100)
Lipoma	0 (0.0)	1 (100)	1 (100)
Nerve sheath tumours	1 (50.0)	1 (50.0)	2 (100)
Clear cell sarcoma	1 (50.0)	1 (50.0)	2 (100)
TOTAL	**20 (38.8)**	**28 (61.2)**	**48 (100)**

3.3HISTOLOGY TYPE

Histology distribution of musculoskeletal tumours

Of the 181 tumours included in the study, frequently seen histological types were Osteosarcoma 47(26.0%), Metastases 32 (17.7%), Giant cell tumour 21 (11.6%), Osteochondroma 10 (5.5%) and Synovial sarcoma 10 (5.5%).

The musculoskeletal tumours comprise of 54 (29.8%) primary malignant bone tumours, 47 (26.0%) benign bone tumours, 48 (26.5%) soft tissue tumours and 32 (17.7%) metastatic lesions.

The leading causes of metastases were carcinomas contributing 19 (59.4%) out of the 32 metastatic lesions followed by myeloma 7 (21.9%) and lymphomas 4 (12.5%).

The soft tissue tumours comprised skeletal muscle (rhabdomyosarcoma 6 (12.5%)) smooth muscle (leiomyosarcoma 1 (2.0%)), vascular tumours (hemangioma 5 (10.4%)), tumour of uncertain differentiation (alveolar soft tissue sarcoma 4 (8.3%), myxoid fibroma 6 (12.5%) and synovial sarcoma 10 (20.8%)), Lipid (lipoma 1 (2.0%)), and Fibrous (fibrosarcoma7 (14.6%) and MFH 4 (8.3%)**)**.

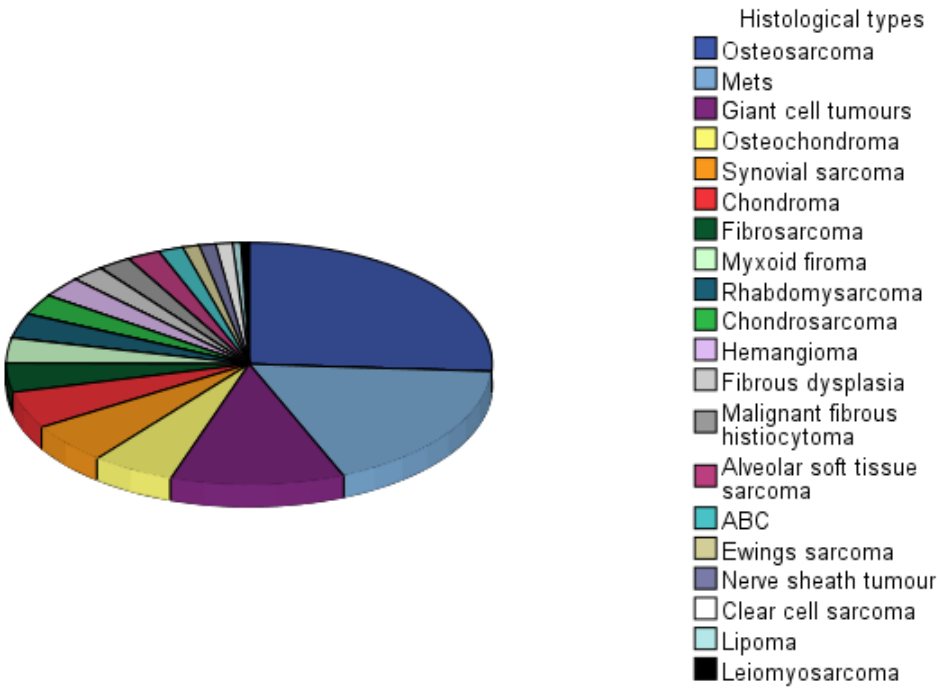


Figure 2: Histology of musculoskeletal tumours at MOI (N=181)

3.4SKELETAL DISTRIBUTION OF TUMOURS

From the study, the most common site of the musculoskeletal tumours is the femur 39 (21.5%)**,** followed by the tibia 28 (15.5%) and humerus 26 (14.4%) (Fig 3)

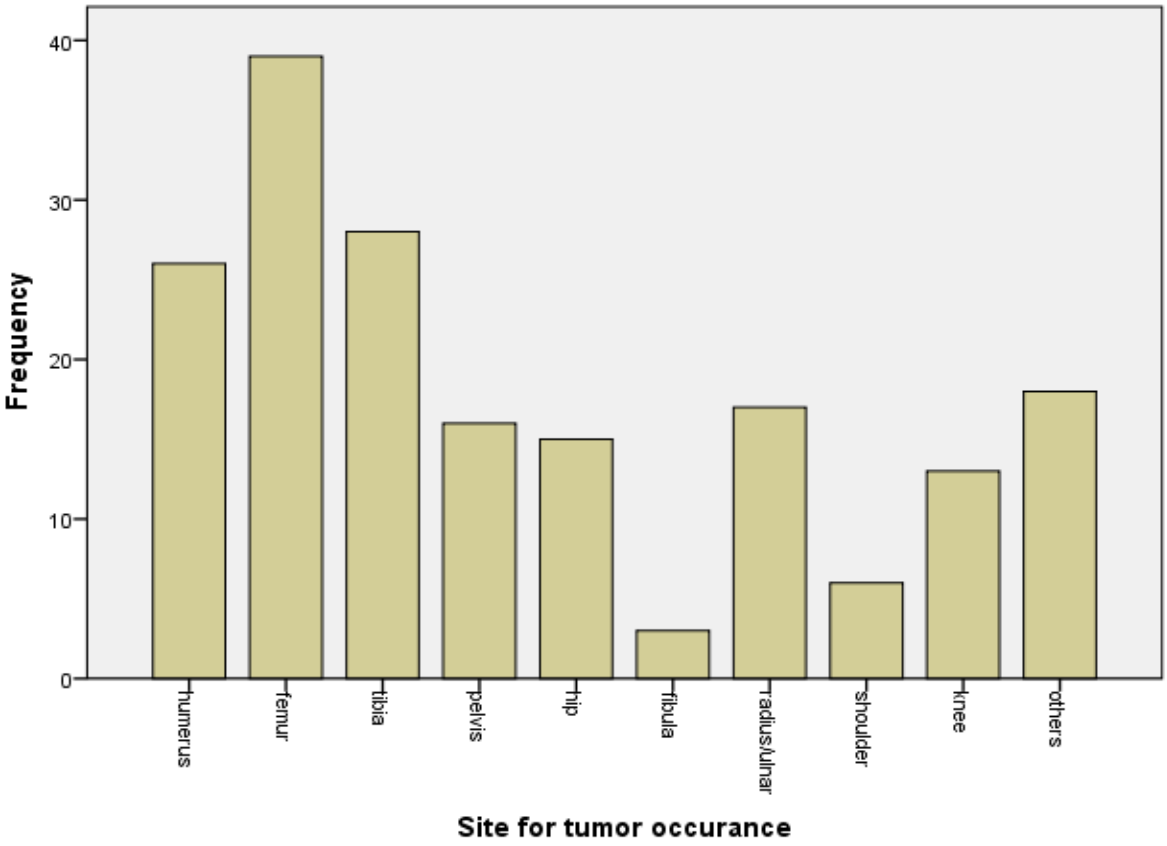


Figure 3: Anatomical frequency distribution of musculoskeletal tumours

For benign bone tumours, the commonest site is the tibia 13(7.2%), followed by the humerus 8 (4.4%) and femur 5 (2.4%) Primary malignant bone tumours are more common in the femur accounting for 19 (10.5%) while, secondary malignant tumours were frequent seen in femur7 (21.9%), followed by hip.6 (18.8%) and pelvis 5 (15.5%). Among 48 cases of soft tissue tumours, frequent sites were femur 10 (20.8%), radius and ulnar 8(16.7%) and knee that accounted 6 (12.5%)

CHAPTER FOUR

4.0 DISCUSSION

4.0.1 AGE DISTRIBUTION OF MUSCULOSKELETAL TUMOURS

From the study the age at presentation of musculoskeletal tumours ranged between 3 -85 years, with a median age of 27 years. The commonest affected age group was 11-20 years. Another study done in South India, by Jain, revealed that, among 117 patients (aged 5 to 82 years) the peak age group for primary bone tumours was the 11-20 years age group[17]**.** This peak incidence finding is consistent with the fact that the majority of primary bone tumours develop in late adolescent or early adulthood, coinciding with growth spurt and time of maximum constructive activity of bone [18, 19].

From the study the peak incidence for primary malignant tumours, was 20 (37.7%), during 2nd decade, among 53 patients. Different findings were seen in a study done in Kuwait, by Katchy, which has shown 42% of primary bone tumours occurred below age of 20 years[8]. The distribution in primary malignant tumour from this study is attributed to the high occurrence of osteosarcoma with prevalence of 19 (40.4%) in 2nddecade**.**

From the study, soft tissue tumours 11 (22.9%) were frequently seen in patients of 11 -20 age groups. The finding is contributed by rhabdomyosarcomas and hemangioma accounting 3(27.3%) each, among 11-20years.A study in Nigeria by Mandong et al has also shown that rhabdomyosarcoma occurred more in paediatric and adolescent age groups[20].

The age group for soft tissue tumours depends on their morphology where, soft tissue sarcoma are seen in elderly, similar to carcinomas, and benign soft tissue tumours were seen in children and adolescents.

From this study, secondary malignant tumours are frequently seen in elderly patients, above 50 years of age. Finding from this study is different from a study by Katchy et al, which has showed that most (50 out of 66) of metastatic bone tumours occurred after the age of 40 years[8].

4.0.2 SEX DISTRIBUTION OF MUSCULOSKELETAL TUMOURS

From 181analysed musculoskeletal tumour cases, 99 (54.7%) were men and 82 (45.3%) were females. The findings of male predominance at presentation are comparable to those of Bayush et al, where out of 215 bone tumour biopsies studied, 51.3% were of males and 48.1% were of females[7]. Baena-Ocampo et al. also had 53.7% and 46.3% as males and females respectively[12]. Other similar study done by Jain in South India has shown male preponderance with 76 (64.9%) among 117 patients.[17].

In the benign tumour group, this study revealed that, Giant Cell Tumours had female preponderance at 57.1% and Osteochondroma had male preponderance at 70%. Records from the National Cancer Registry from USA, revealed that, males dominated the osteochondroma cases and females the giant cell tumours cases [11].

From the study, frequent primary malignant tumour, Osteosarcoma and chondrosarcoma showed male predominance with 59.6%, and 60% respectively, and Ewing's sarcoma had all female patients. Different finding had been shown in records from National Cancer Registry, where all tumours, osteosarcoma, chondrosarcoma and Ewing's sarcoma showed male preponderance[11].

From the study, soft tissue tumours showed male preponderance 29 (60.4%) against female with 19 (39.6%). A study done in Nigeria by Mandong et al has also shown male preponderance 183 against 83 in females, with male, female ratio of 2:1. Among 266 analysed soft tissue tumours[20].

4.0.3 HISTOLOGICAL TYPES.

In this study primary malignant bone tumours were 54 (29.8%), benign bone tumours 47 (26.0%), soft tissue tumours 48 (26.5%) and Metastasis 32 (17.7%). The higher frequency of primary malignant tumour is contributed by preponderance of osteosarcoma 47 (87.0%) seen.

The frequency of primary malignant tumours observed in this study differs from other studies[12, 21, and 22] where benign bone tumours outnumbered the primary malignant tumours. This was also seen in a study done by Davies et al in the UK, which showed, primary malignant being rare and constitute only 0.2% of all malignancies[2]. The high frequency of primary malignant tumour in this study is note worth, the probable cause could be due to

either benign looking lesion are far from sent to hospital for complaint or the difference is due to a reflection of selection bias; as more sinister looking lesions are more likely to biopsied than obviously benign looking lesions which tend to be diagnosed clinico-radiologically.

From this study, Osteosarcoma was found to be the most frequent primary malignant bone tumour (87.0%), followed by chondrosarcoma (9.3%) and Ewing's sarcoma (3.7%). Generally many researchers had similar findings [8, 10, 13, 14, 15, 17]. Different findings were seen in a study by Fuqua, which has shown, osteosarcoma (44.1%) being the frequent primary malignant tumors, followed by chondrosarcoma (16.6%), multiple myeloma (13.0%), MFH (7.7%) and Ewing's sarcoma (3.8%)[16]. In a study done in UK, where, the second most common primary malignant tumour was Ewing sarcoma after Osteosarcoma. The difference in the ranking of Ewing sarcoma in later study can be explained by the different ethnic groups studied since as noted in studies by Scully, Ewing sarcoma is 9 times more common in Caucasians than black Americans[23]. Okpokowuruk et al, believe that Ewing sarcoma is rare in Africa[24].

Giant cell tumours were most frequent in this study (44.7%) among benign bone tumours, followed by osteochondroma (21.3%) and chondroma (19.9%). A study done by Settakorn et al from 2000 to 2004 had similar findings[25]. Different finding were seen in study by Jain, with osteochondroma being the most frequent 26, followed by Giant Cell Tumout 24 among 67 benign bone tumours[17].

Secondary or metastatic tumours accounted for 32 (17.7%) of all musculoskeletal tumours in the study, with carcinomas having higher frequency 19 (59.6%). In study done by Katchy et al has shown carcinoma as frequent malignant tumour to metastasize to bone[8]. The most common carcinomas that metastases to bone arebreast in females and prostate in males, followed next by thyroid and lung[1].

From the study, frequently seen soft tissue tumours were synovial sarcoma 10 (20.8%), fibrosarcoma 7 (14.6%), rhabdomyosarcoma 6 (12.5%) and malignant fibrous histiocytoma 6 (12.5%). It has been pointed out that, in Africa, incidence rates could not generally be calculated, but there were substantial numbers of registrations for rhabdomyosarcoma and fibrosarcoma[27]. Different finding are seen in study done in Nigeria by Mandong et alwhich has shown that, among 266 (11.3%) of STT, Kaposi sarcoma 69 (25.9%) Rhabdomyosarcoma 63

(23.7%), Malignant Fibrous Histiocytoma 56 (21.1%), and Fibrosarcoma 49 (18.4%) were the commonest histological subtypes[20]. The difference from study could be that, Kaposi sarcoma cases as HIV/AIDS associated cancer are attended by physicians.

4.0.4SKELETAL DISTRIBUTION OF TUMOUR

Out of the 181 patients with tumours 39 (21.5%) had tumours on the femur, 28 (15.5%) located on the tibia and 26 (14.4%) the humerus. Similar findings were seen in a study of 426 cases by Solookiet al[8]and in a review of 566 bone tumours by Baena-Ocampo et al[12]. The later reports 39.9% to be located at the femur, 17.7% the tibia and 11.8% the humerus. Both benign and primary malignant tumours had predilection to these anatomical sites. This could be explained by the fact that, primary bone tumours frequently affect long bones and tend to occur at the end of long bones where there is maximum growth[19].

Of the 32 cases of secondary malignant tumours found in this study, the most frequent site for secondary malignant tumours were seen in femur 7 (21.9%), hip.6 (18.8%) and pelvis 5 (15.5%). Different findings were seen in studies done by Katchy et al, the femur was the most common followed by vertebra and pelvis[8] and in study by Jain et al with femur being most frequent site for secondary tumours followed by hip joint and then spine[17]. The most common site for metastatic disease is vertebral spine, followed next by the pelvis, femur, ribs, humerus and skull**.**

The predilection of axial skeleton (vertebra spinal, pelvis, femur, humerus and skull) by secondary tumours can be explained by evidence of the presence of vertebral venous plexus of vessels of axial skeleton through which venous blood from breast and pelvis flows and drain into[26].This can also be explained by the persistence of red bone marrow (in vertebrae, pelvis, femur and tibia), presumably reflecting increasing blood flow[28]**.**

Synovial sarcoma was the most frequent soft tissue tumour in this study and the knee the commonest site. Some STT extends to bone eg; synovial sarcoma usually occurs in juxta articular structures, and only 10% will be found inside major joints (synovial tissue origin) [29]. An explanation for the finding from this study remains to be determined. Synovial sarcoma is commonly seen about knee, shoulder, elbow and wrist areas[29]. The joint involvement by synovial sarcoma could be due to direct tumour extension through articular cartilage

(following a pathological fracture with seeding of joint cavity), periarticular extension, joint structure acts as conduit of tumour growth or trans capsular skip nodules (demonstrated in 1% of Osteosarcomas)[30].

CHAPTER FIVE

5.0 CONCLUSION

From the study, among 210 musculoskeletal tumour cases, 181 cases were analysed and 29 cases were excluded due to missing information (9cases), inadequate biopsy (10cases) and tumour like lesions: chronic inflammation and osteomyelitis (10cases).

Among 181 musculoskeletal tumours analysed, 99 cases were male with an age range from 8 – 85 years and median age of 25 years and 82 cases were female with an age range from 3 – 75 years and median age 28.5 years. From this study, musculoskeletal tumour have shown slightly male predilection at a M; F ratio of 1.2:1. The most affected age was the 11 – 20 year age group.

The frequent histological types were osteosarcoma 47 (21.6%), Metastases 32 (17.7%), Giant cell tumours 21 (11.6%), osteochondroma 10 (5.5%) and Synovial sarcoma 10 (5.5%).

The musculoskeletal tumours comprises of 54 (29.8%) primary malignant bone tumours 47 (26.0%) benign bone tumours, 48 (26.5%) soft tissue tumours and 32 (17.7%) metastatic lesions

Secondary tumours (metastases) are seen mainly in elderly patients > 50yrs of age. The most frequent metastases were from carcinomas contributing 19 (59.4%) cases. The carcinoma were from breast 8 (42.2%), prostate 5 (26.3%), lung 2 (10.5%), thyroid 1 (5.3%), and others 3 (15.8%).

The most frequent anatomical sites for musculoskeletal tumours were femur, tibia and humerus, the bones sites with highest growth rate.

5.1 RECOMMENDATION

From a long study period, a large number of cases (sample size) will be collected hence give an actual burden of musculoskeletal tumours. A multicentre study is needed to throw more light and do comparison on the burden of disease with other countries in Africa and worldwide. Further nationwide studies are needed to improve strategies in musculoskeletal tumour diagnosis and treatment

5.2 LIMITATION OF THE STUDY

Total of 29 musculoskeletal tumour cases were excluded from study due to missing information (9cases), inadequate biopsy (10cases) and tumour like lesions: chronic inflammation and osteomyelitis (10cases), hence reducing size of study..

The results from use of hospital data gives only a representative picture of musculoskeletal tumours but not the actual burden of patients, due to small sample size and disproportional contribution of number of cases.

REFERENCE

1. Schajowicz F, Tumour and Tumour like lesions of bone: Pathology, Radiology and Treatment. New York, Springer verlag 1994. 24 (2) 26-38
2. Sundaram M, Davies AM, James SJ., Bone tumours Epidemiology, Classification Pathology in Imaging of bone tumours and tumour like lesions: Techniques and Application. Spring Verlag. 2009 (1), 2-5
3. Franchi, A. Epidemiology and classification of bone tumours. *Clinical Cases in Mineral and Bone Metabolism*, 2012. 9 (2), 92-95
4. https://www.iarc.fr/en/publications/pdfs-online/pat-gen/bb5/BB5.pdf
5. Jawad JM, SkullySP,Enneking classification: benign and malignant tumors of the musculoskeletal system.ClinOrthopRelat Res. 2010 July; 468(7): 2000–2002
6. Enneking WF. A system of staging musculoskeletal neoplasms. *ClinOrthopRelat Res*. 1986. (204):9-24.
7. Bayush E. N, Daniel A, Biruk L. W and Mihiret W. T, Bone tumours: Agreement between radiological and histo-pathological diagnoses, International Journal of Medicine and Medical Science, 2009. 4, 119-125
8. Katchy KC, Ziad F, Alexander S, Gad H, Abdel Mota AM, Malignant bone tumors in Kuwait: A 10-year clinico-pathological study. *International Orthopaedics*, 2005. *29*, 406–411.
9. Parviz G, Kazem, et al. Epidemiology of Bone Cancer - An Overview. An American Academy of Neurological and Orthopaedic Surgeons, 2014
10. Brown T, Young C, Rushton L, Occupational cancer in Britain, British Journal of Cancer, 2012. 107, 85-91
11. Feuer EJ, Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, et al. National Cancer Institute SEER Cancer Statistics Review. National Cancer Institute. 2015; 103 (7) 1975 -2012.

12. Baena-Ocampo LC, Ramirez-Perez E, Linares-Gonzalez LM, & Delgado-Chavez R, Epidemiology of bone tumours in Mexico City: *Ann of DiagnPathol*, 2009.*13*, 16–21
13. Solooki S, Vosoughi AR, Masoomi V, Epidemiology of musculoskeletal tumours in Shiraz, south of Iran, Indian J Med PaediatrOncol. 2011; 32(4): 187–191.
14. Thamir AH, pattern of malignant bone tumours,SICOT online report, 2004 news.sicot.org/resources/File/IO_reports/02-2004/E055.pdf
15. Weber K, Damron TA, Frassica F J, &Sim FH. Malignant bone tumours. Instructional Course Lectures, 2008. 57, 673–688.
16. Fukuma H, Bone tumour registration. Gann Monographs on cancer Research, 1995; 43, 129 - 146
17. Jain, K, SunilaRavishankar, R, Mruthyunjaya, Rupakumar, CS, Gadiyar, HB, Manjunath, GV. Bone tumors in a tertiary care hospital of south India: A review 117 cases. Indian J Med PaediatrOncol. 2011; 32 (2) 82 – 85.
18. Arora, R S., Alston, R D., Eden, T O B., Geraci, M., Birch, J M.The contrasting age-incidence patterns of bone tumours in teenagers and young adults: Implications for aetiology. International J of Cancer. 2012. 131 (7) 1678 - 1685
19. Ghalazi H. Samira Z. Mahush H. et al, Clinico-morphological pattern of bone lesions in children. Biomedica 2009; 25, 59 – 62.
20. Mandong BM, Kidmas AT, Manasseh AN et al, Epidemiology of soft tissue sarcomas in Jos, North Central Nigeria. Niger J Med. 2007 16 (3) 246 – 9.
21. Ramdass M J. et al An 8-YEAR analysis of bone tumours in a Caribbean island, Annals of Med and Surg. 2015; 4, 414-416
22. AbdulkareemF B., Eyesan S. U., Akinde O. R., Ezembakwe M. E., Nnodu O. E., Pathological study of bone tumours at the National Orthopaedic Hospital, Lagos, Nigeria. West African Journal of Medicine 2007; 26 (4) 306 – 311.
23. Scully S.P., Jawad M.U., Cheung M.C., Min E.S., Schneiderbauer M.M.,Koniaris L.G.Ewing sarcoma demonstrates racial disparities in incidence-related and sex-related differences in outcome. Cancer. 2009 Aug 1;115(15):3526-36.

24. Okpokowuruk F, Oleyede I, Congenital Ewing's Sarcoma in a neonate in Uyo - A case report. Pan African Medical Journal 2013; 15
25. Settakorn J, Lekawanivivjit, Arpomchayon et al. Spectrum of bone tumours Chiang Mai University Hospital, Thailand. According WHO classification 2002. A study of 1001 cases. J med Assoc Thai 2006;89:780-7
26. Batson O, The Function of the Vertebral Veins and Their Rôle in the Spread of Metastases Annals of surgery.1940; 112 (1) 138 – 149
27. Stiller CA, Parkin DM,International variations in the incidence of childhood soft-tissue sarcomas. Br, J Cancer 1990; 62 (6) 1026 - 30
28. Choudhry M, Cockshott S, Secondary malignant tumours of bone. Surgery journal 2009; 27 (2) 86 – 89.
29. James OJ, An atlas of musculoskeletal oncology 2003; 11 (3) 2 – 5
30. http://www.sarcoma.org/public/mcs/chl.pdf

APPENDIXES

Appendix I: WHO Classification of Musculoskeletal Tumors

I. BONE FORMING TUMORS

A. BENIGN

1. Osteoma 2. OsteoidOsteoma and Osteoblastoma

B. INTERMEDIATE

1. Aggressive (malignancy)

C. MALIGNANCY

1. Osteosarcoma a. Central (medullary) b. Peripheral (surface)

II. CARTILAGE FORMING TUMORS

A. BENIGN

1. Chondroma a. Endochondroma b. Periosteal
2. Osteochondroma a. Solitary b. Multiple hereditary
3. Chondroblastoma
4. Chondromyxoid fibroma

B. MALIGNANCY

1. Chondrosarcoma 3.Differentiated chondrosarcoma
2. Periosteal 4. Clear cell Chondrosarcoma

III. **BONE MARROW TUMORS** (Round cell tumours)

1. Ewing sarcoma of bone 3. Malignant lymphoma of bone
2. Neuro-ectodermal tumour of bone 4. MultipleMyeloma (Plasmacytoma)

IV. GIANT CELL TUMORS

1. Osteoclastoma

V. VASCULAR TUMORS

1. Hemangioma and Lymphangioma 2. Angiosarcoma

VI. OTHER CONNECTIVE TISSUE TUMOURS

A. BENIGN: Benign Fibrous Histiocytoma 2. Lipoma

B. MALIGNANCY: 1.Malignant Fibrous Histiocytoma 2. Liposarcoma 3. Fibrosarcoma

Appendix II: WHO Classification of Soft Tissue Tumours

I.ADIPOCYTIC TUMOURS

1. Lipoma 3. Lipomatosis
2. Lipoblastoma 4. Liposarcoma

II. FIBROBLASTIC / MYOFIBROBLASTIC TUMOURS

1. Fibroma 4 Fibromatosis
2. Fibroblastoma 5. Myofibroblastic tumours /sarcomas
3. Fibrosarcomas

III. FIBROHISTIOCYTIC TUMOURS LIKE

1. Giant cell tumour: - of tendon sheath - of soft tissue
   - diffuse type - deep benign
2. Malignant fibrous histiocytoma
   - Giant cell - Pleomorphic - Inflammatory

IV. SMOOTH MUSCLE TUMOURS

1. Leiomyoma 2. leiomyosarcoma

V. SKELETAL MUSCLE TUMOURS

1. Rhabdomyoma
2. Rhabdomyosarcoma

-Embryonal- Pleomorphic - Alveolar

VI. VASCULAR TUMOURS

1. Hemangioma 3. Lymphangioma
2. Endothelioma 4. Angiosarcoma

VII.TUMOURS OF UNCERTAIN DIFFERENTIATION

1. Synovial sarcoma 3. Alveolar soft part sarcoma
2. Clear cell sarcoma 4. Epitheloid sarcoma

Appendix III: Enneking and Musculoskeletal Tumour Society Staging System

It based on surgical grading, local extent and presence or absence of metastasis

Stage	**Grade**	**Site**	**Metastasis**
IA	Low (G1)	Intracompartmental (T1)	No metastasis (M0)
IB	Low (G1)	Extracompartmental (T2)	No metastasis (M0)
IIA	High (G2)	Intracompartmental (T1)	No metastasis (M0)
IIB	High (G2)	Extracompartmental (T2)	No metastasis (M0)
III	Any (G)	Any (T)	Regional or distant metastasis (M1)

Appendix IV: Research Questionnaire

TITLE: CLINICO-MORPHOLOGICAL PATTERN OF MUSCULOSKELETAL TUMORS SEEN AT MOI FROM JAN 2013 TO DEC 2014

1. Formnumber: ……
2. Registration NO: …….
3. Age: (a) <10 years (b) 10-20 years (c) 21-30 years (d) 31-40years (e) 41-50 (f)>50 years
4. Sex: a) Male b) Female
5. Contact: ……
6. Residence ……..
7. Level of education: …….

   a) Never been to school (NIL)

   b) Primary education

   c) Secondary education

   d) Tertiary education (UNIVERSITY)
8. Patient signs and symptoms at 1st visit
   a) Pain
   b) Swelling
   c) Pathological fractures
   d) Reduced range of movements
   e) Others (Mention: ……..)

9. Site of tumour……

    a) Humerus
    b) Femur
    c) Tibia
    d) Pelvis
    e) Fibula
    f) Radius/Ulnar
    g) Others …….

10. History-pathology results were

    a) Osteosarcoma
    b) Chondrosarcoma
    c) Ewing's sarcoma
    d) Giant cell tumour
    e) Osteochondroma
    f) Chondroma
    g) Bone cysts
    h) Fibrous dysplasia
    i) Metastatic tumours (Prostate, Breast, Lungs, Kidneys, Thyroid)
    j) Others (mention: Haemangioma…)

Appendix V: Dodoso

AINA ZA MAUMBILE NDANI NA NJE YA UVIMBE KWENYE MISULI NA MIFUPA KWA WAGONJWA WANAOTIBIWA MOI, KUTOKA JAN 2013 MPAKA DEC 2014

1. Namba ya fomu: ……
2. Namba ya utambuzi …….
3. Umri: a) miaka 3-10 b) miaka11-20 c) miaka 21-30 d) miaka 30-50 e) zaidiyamiaka 50
4. Jinsia: a) Mme b) Mke
5. Anuani yako: ……
6. Mahali unapoishi:
7. Kiwango cha Elimu:

   a) Sijahudhuriashule

   b) Shule ya msingi

   c) Shule ya sekondari

   d) Elimu ya juuya Chuo

8. Malalamiko yaliomleta mgonjwa hospitali kwa mara ya kwanza

   a) Maumivu
   b) Uvimbe
   c) Mvunjiko wa mfupa sababu yapathologia ya uvimbe
   d) Kupungua kwa movement ya joint
   e) Mengineyo (Taja: ……..)

9. Eneoambapo kuna maumivu au uvimbe……
    a) Mfupa wa mkono
    b) Mfupa wa paja
    c) Mfupa wa mguu
    d) Nyonga
    e) Sehemu nyingine (Taja……)

10. Majibuyahisto-pathologia ya uvimbe :
    a) Osteosarcoma
    b) Chondrosarcoma
    c) Ewing's sarcoma
    d) Giant cell tumour
    e) Osteochondroma
    f) Chondroma
    g) Bone cysts
    h) Fibrous dysplasia
    i) Metastatic tumours (Prostate, Breast, Lungs, Kidneys, Thyroid)
    j) Mengineyo (Taja:
       Hemangioma……..)

Appendix VI: Letter to Request Exemption for Consent from Client

Muhimbili Orthopedics Institute,
P. O BOX 65474,
Dar es Salaam.
29th June 2015.

Director of Research and Publications,
MUHAS,
P.O BOX 65001,
Dar es Salaam.

UFS: Supervisor,
Dr. Robert Mhina
Department of Orthopaedics and Traumatology,
MUHAS.

Dear Sir/Madam,

REF: REQUEST FOR EXEMPTION FOR CONSENT FROM CLIENTS

Please, refer to the heading above.

I am a postgraduate student with registration number **HD/MUH/T.194/2013**pursuingMMed in Orthopaedics and Traumatology at MUHAS.

I submit a retrospective study titled "Clinico-morphological pattern of musculoskeletal tumours among patient seen at Muhimbili Orthopaedic Institute, January 2013 – December 2014" for exemption for consent from clients. The data for the study will be collected from MOI admission registry, operative notes from patient files from records and the histopathology biopsy studies from central pathology registry.

Data will be kept anonymous by the use of file number and Patient's information will be handled with utmost confidentiality.

Yours faithfully,

Dr. Salome Mduma