BONE TUMOURS; LEVEL OF AGREEMENT BETWEEN RADIOGRAPHIC AND HISTOLOGICAL DIAGNOSIS OF BONE TUMOURS

AT KENYATTA NATIONAL HOSPITAL AND PCEA KIKUYU HOSPITAL

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DECLARATION

I hereby declare that this thesis is my original work and has not been presented as a proposal at any other university.

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DEPARTMENTAL APPROVAL

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List of Abbreviations

AACCR	Addis Ababa City Cancer Registry
AFCRN	African Cancer Registry Network
CT	Computed Tomography
ECR	Eldoret Cancer Registry
ERC	Ethics and Research Committee
GLOBOCAN	Global Cancer Observatory
GCT	Giant Cell Tumour
HBCR	Hospital Based Cancer Registry
IARC	International Agency for Research on Cancer
KCMC	Kilimanjaro Christian Medical Centre
KNH	Kenyatta National Hospital
MRI	Magnetic Resonance Imaging
NCR	Nairobi Cancer Registry
OGS	Osteogenic Sarcoma
PBCR	Population Based Cancer Registry
PCEA	Presbyterian Church of East Africa
UK	United Kingdom
UPS	Undifferentiated Pleomorphic Sarcoma
USA	United States of America
WHO	World Health Organization

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Abstract

Study Background:

Bone tumours have a relatively low incidence but carry a disproportionately high mortality globally. Most benign lesions and malignant ones affect those in the second and third decades of life, the most productive age-groups in the population.

The similar presenting symptoms and coextensive anatomic patterns pose a diagnostic challenge. The problem is worse in many developing countries where laboratory and imaging facilities are few and costly to most patients. It therefore calls for a higher clinical acumen in reaching a diagnosis especially in resource-strained setting where access to diagnostic equipment is limited to inform early treatment. Radiographs are readily available, affordable and provide a wealth of valuable information. Combining clinical information with X-ray features of bone lesions helps in reaching a diagnosis or possible differential that can be confirmed by histology, the gold standard.

Published local data comparing diagnoses made based on radiographic features of bone tumours and their histology is finite. This study seeks to find out the level of accuracy of radiographical diagnoses compared to histological diagnoses among patients with bone tumours who present at the Kenyatta National Hospital (KNH) and PCEA Kikuyu hospitals.

Study Objective:

To determine the percent agreement between radiological and histological diagnoses among patients with bone tumours at KNH and PCEA Kikuyu hospitals.

Study Site(s):

KNH and PCEA Kikuyu hospitals.

Study Design:

This is both a prospective and retrospective descriptive study.

Participants and Methods:

All patients attending at KNH and PCEA Kikuyu hospitals over a period of 12 months: October 2021 to September 2022 presumed to have a bone tumour on plain radiography and additionally had histological diagnosis were recruited in the study. Data was retrieved from patient medical records in the respective hospitals. The details included patient demographics, presenting symptoms and their duration, tumour location in bone, plain radiography features of bone

tumours, initial radiological diagnosis based on radiographs as well as the final histological diagnosis.

Data management:

The data collected using patient data sheets was analysed using the Statistical Package of Social Sciences (SPSS) version 26. Patient demographics, symptoms and tumour location was analysed descriptively and presented in graphical and tabular form. Percentage agreement between radiological and histological diagnoses as well as sensitivity and specificity of roentgenography in diagnosis of bone tumours was determined.

Utility of the study:

The study findings may be projected to a national level to identify the pertinent areas needed to improve care to patients with bone cancer through;

1. Inform on creation of tailored bone tumour diagnostic protocols.
2. Form a nucleus for generation of further research studies.

Chapter 1: INTRODUCTION

1.1 Background

Bone tumours have a low incidence compared to cancers of other tissues. (1–4, 42) However, they have a pervasive impact on the patient and carry a significant rate of mortality worldwide. (1) Bone tumours are categorized into "primary tumours" that originate in the bone, and "secondary tumours or metastases" which arise in other body organs and involve the bone. The primary tumours are further classified into benign and malignant lesions. The bulk of primary bone tumours are benign and non-symptomatic. Thus, they remain undiagnosed or are recognized incidentally at radiographic examinations for other ailments. (5) Accurate incidence of primary bone tumours remains unknown because most benign lesions are not biopsied for histopathological analysis. (6)

In 2022 it is estimated there will be 3,910 (2,160 males and 1,150 female) new cases of primary bone sarcoma in United States of America. (4) Osteosarcoma, chondrosarcoma, and Ewing's sarcoma are the commonest primary bone sarcomas accounting for 0.2% of all cancers in the UK and USA. (5) Distribution of tumours varies with age, with most benign lesions and common malignant ones being diagnosed in those between age 20 to 30 years old. (5,7,8) These age groups represent the prolific segments of the population thus posing severe repercussions (9). Metastases to bone form the most common musculoskeletal lesions and mostly found in the elderly. The sources are largely the breast, prostate, kidney, lung and the thyroid gland. (5,10)

The complexity, uncommonness, wide origin, similar symptoms and signs provide a tough problem in reaching a diagnosis to physicians. This scenario is much more difficult in developing countries due to late presentation, illiteracy, religious fanatism and institutional factors. (8) Precise diagnosis is fundamental in cancer treatment and linked directly to patients' outcome and subsequent care. (11) However, there exist divergent diagnoses among clinicians, radiologists and pathologists in most instances. (12) Many institutions still don't correlate suspicious radiological and subsequent negative pathology findings. Both findings need to be tied in to avoid false negative results and guarantee proper treatment course for the patient. A multidisplinary and multimodal approach is therefore key in diagnosing and managing bone cancer cases. Factors that determine survival rates include the type and stage of bone tumour that is found out. (4) Early accurate diagnosis and identification of bone tumours helps in improving survival and quality of life through the administration of various modalities of treatment and performing limb salvage procedures. (13,14)

In Kenya there exists a lacuna on published data with few studies done specifically assessing accuracy of plain radiography in diagnosis of bone tumours other than those in the cranium and facial bones. This scarcity of information was the drive for this study seeking to find out the level of consensus between radiological and histological diagnoses in patients with bone tumours who presented at Kenyatta National Hospital. This hospital based data is not entirely representative but forms a nucleus from which further research studies can be done.

1.2 Study Justification

Bone tumours have a high mortality rate which is worse in low and middle income countries (LMICS). Early detection results in early intervention and good outcomes. Comprehensive clinical evaluation forms the basis from which imaging and histopathological investigations rely on to reach a final diagnosis for which appropriate therapy is initiated. The clinicians' preliminary diagnosis is mainly based on the radiological findings. When accurate, this diagnosis may guide management especially in resource-poor facilities where waiting for further investigations may delay treatment. (8,15)

Although histological diagnosis of bone tumours is regarded as the gold standard, it still depends on the clinicians' findings and preliminary diagnosis. Pitfalls in clinical evaluation will translate to an indeterminate or false histological diagnosis. Overreliance on one diagnostic parameter may lead to misdiagnosis or under-diagnosis and hence mismanagement of the disease. Orthopaedic surgeons and oncologists are the primary recipients of findings reported by radiologists and pathologists. It is therefore, imperative that clinico-radiological-pathological correlation is implemented for the best timely outcomes. On conclusion of the study, the data collected will be important in the process of forming protocols for diagnosis and homogenic management of bone tumours at KNH as well as other hospitals.

1.3 Study question:

How does Radiographical diagnosis of bone tumours compare with histological diagnosis?

1.4 Broad Objective:

To determine the percent agreement between radiographical and histological diagnosis of bone tumours at KNH and PCEA Kikuyu hospitals.

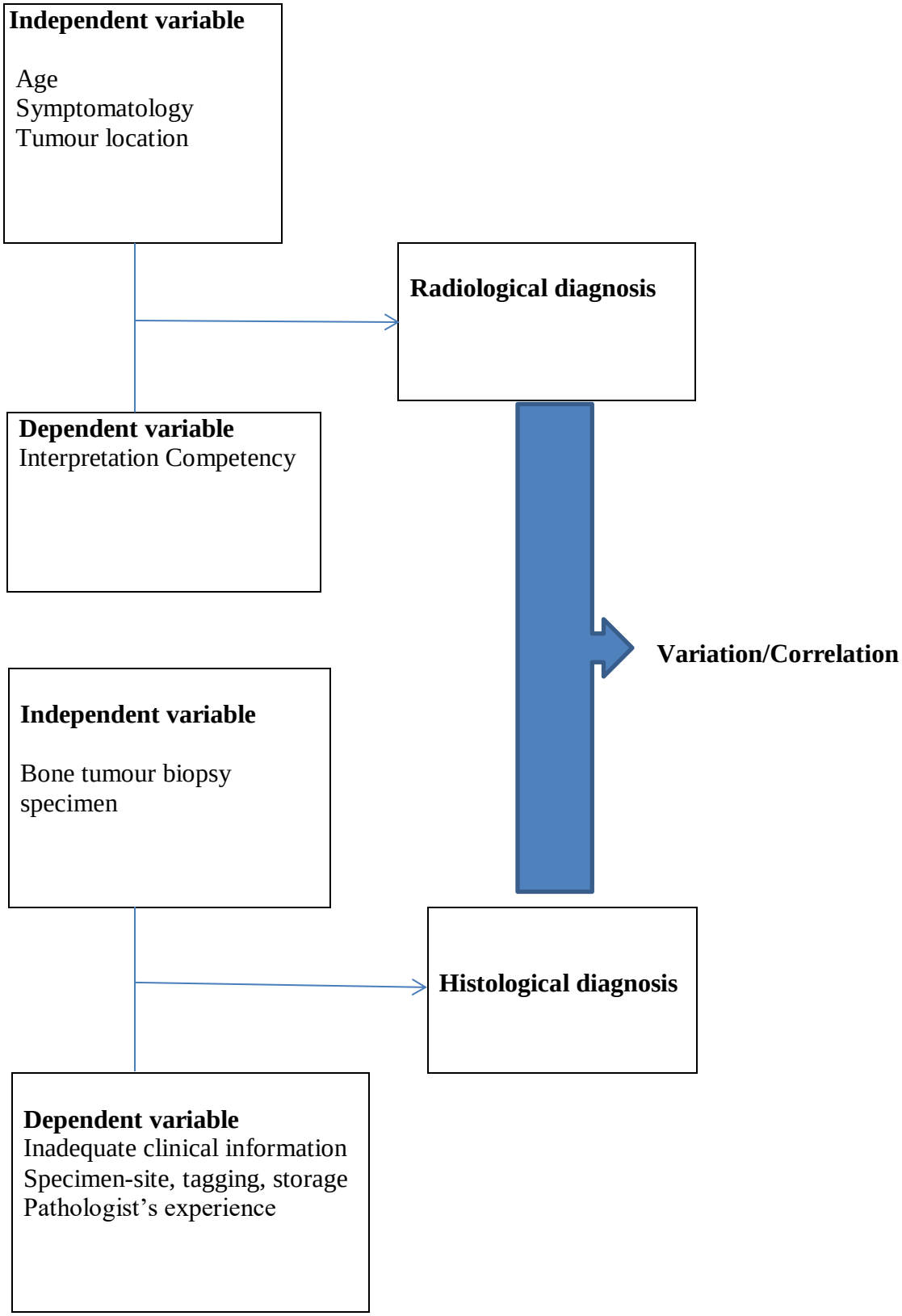
1.5 Specific Objectives:

1. To find out the plain radiographic features of primary bone tumours seen at Kenyatta National hospital and PCEA Kikuyu hospitals.

2. To determine the percent agreement between radiographic diagnosis and histological diagnosis of bone tumours.

3. To evaluate the sensitivity and specificity of plain radiography in diagnosis of bone tumours.

1.6 Conceptual Framework.



CHAPTER 2: LITERATURE REVIEW

2.1 Introduction.

Cancer is a significant public health problem and one of the chief causes of mortality worldwide. Primary Bone tumour make up less than 0.2 % of all cancers, however metastases to bones from cancer native in other tissues are significantly high. (4,16) The GLOBOCAN 2020 International Agency for Research on Cancer (IARC) repository showed that there are 1,109,209 new cancer cases (5.7% of the worldwide numbers) and 711,429 cancer deaths (7.1% of the worldwide numbers) reported in African countries in 2020 (17).Despite the overall cancer burden being dominated by breast, cervical and prostate cancers, cancer profile in Africa is diverse with bone tumours contributing significantly. (18) The global incidence for primary bone tumours varies from country to country depending on when the studies were done. The incidence patterns available are mainly from developed countries.

The American Cancer Society using data collected by the Surveillance, Epidemiology, and End Results Program; the National Program of Cancer Registries; and the North American Association of Central Cancer Registries, projects 3910 new primary bone cancer cases in 2022. It is estimated that 2,100 deaths from this disease will occur in2022. The 5-year survival rate for localized bone sarcoma varies between 60-82% but reduces to less than 40% in those with bone tumours that have metastasized to other organs (4).According to the Cancer Research UK, approximately 550 new cases of bone sarcoma are reported annually, which is more than 1 every day (2016-2018). The incidence rate has remained stable in the past decade but it was extrapolated to reduce by 5% from 2014 to 2035, due to early screening and intervention. The rate of survival five years after diagnosis for bone sarcoma is 62% in the UK (19), which is comparable to other northern and central European nations. (20–23) Contrastingly, the average 5-year survival rate was 39% in Eastern European nations. (23)

There is however, scarcity of comparable data in Africa. Information churned out from most countries is mainly from hospital based cancer registries (HBRC). Population based cancer registries (PBCR) are however the most dependable for getting incidences of cancer in any population though they require more capital than HBCR. (24) The African Cancer Registry Network (AFCRN) was formally inaugurated on 1st March, 2012. It facilitates establishing of networks of cancer registries, and coordinates international research work and disseminates results. The Addis Ababa City Cancer Registry (AACCR), a PBRC set up in 2011, reported an incidence rate of 2.3% and 1.1% for primary bone cancers in male and female respectively for the period 2014-2016. Kenya has two cancer registries, the Eldoret Cancer Registry (ECR) and Nairobi cancer registry (NCR). The ECR, established in 1999, reported an incidence rate for primary bone tumours of 2.0% and 1.0% in male and female genders respectively for the period 2012- 2016. This compared well with incidence rates at NCR that were 2.1% and 1.0% in male and female genders respectively but in a different period, 2012-2014. Corresponding incidences were reported in most of the other Sub-Saharan countries whose registries qualified as members of AFCRN. (18)

The aetiology of primary bone tumours is most often unknown though certain factors predispose an individual to having cancer. The different lineages of bone tumours have varying pathophysiology and in some cases it is poorly understood. (25) Bone tumours are heterogenic and their morphologic overlap with certain mesenchymal as well as non-mesenchymal bone lesions makes arriving at a diagnosis difficult. Categorization of these tumours is based on their histological presentation; thereby primary bone cancers are called according to their similarity to the parent tissue or type of stroma that the tumour produces [3]. Evolution in bone tumours classification continues with latest histologic, molecular, genetic, and clinical findings in uncategorized and rare bone tumours being discovered. The World Health Organization (WHO) classification of bone tumours is considered to be the gold standard reference for bone tumour diagnosis. It describes the following seven lineage groups: chondrogenic tumours, osteogenic tumours, fibrogenic tumours, vascular tumours of bone, osteoclastic giant cell-rich tumours, notochordal tumours, other mesenchymal tumours of bone, and hematopoietic neoplasms of bone. (26)

The strategy for diagnosis of bone tumours is multi-pronged involving clinical, radiological and histological evaluations to reach a definitive diagnosis. The significant morbidity and mortality call for early and accurate diagnosis and management for good outcomes. (4,27,28) Nonetheless, crucial delays in diagnosis and treatment are a reality resulting in poor outcomes in countries in the tropics. (12,29) S U Eyesan et al studied problems encountered in the diagnosis and treatment of musculoskeletal tumours in Nigeria. He found some of the problems included a high cost of diagnostic tests especially where patients had suspected malignant lesions, few orthopaedic cytologists, medical oncologists and orthopaedic oncologists. (8)

The balance of overstretched resources in LMICs is in favour of treatment intense efforts rather than backing efforts aimed at an exact diagnosis. Arriving at a correct diagnosis is cost saving compared to expenses incurred when investing in equipment for diagnosis is overlooked. (11) In 2013, an online survey was carried out across 34 institutions in Sub Saharan Africa (SSA) to assess pathology capacity. It found that 8 countries had no pathologist working in public sector. This scarcity encouraged blooming of illicit laboratories established by unqualified personnel resulting in poor services. (30,31) Where facilities are well equipped and resources permit elaborate diagnostic tests, clinicians have also been at fault. Inadequate clinical information is given in histopathology request forms, on the assumption histological evaluation is sufficient. (32) These prevailing challenges should inform clinicians including orthopaedic residents and surgeons to refine their clinical evaluation. A comprehensive clinical evaluation guides on the next course of relevant investigations resulting in reliable accurate diagnoses and best patient care.

2.2 Bone tumour diagnosis

The National guideline for cancer management in Kenya 2013 recommends triple assessment of bone tumours to come up with a diagnosis. This entails clinical examination, imaging and biopsy. Imaging can also be utilised to guide in taking the biopsy. Open incision biopsy is recommended for bone lesions. The histopathological report should give a diagnosis based on the WHO classification of bone tumours. (33) India national cancer guidelines recommend correlation of Clinical-Radiological and pathological findings. (34)

Jaffe, a pioneering authority on bone diseases, stated in a 1958 publication that a biopsy is a final procedure needed to make a diagnosis but not circumvention to diagnosis. A meticulous clinical evaluation and analysis of the imaging studies should be done before performing a biopsy. Those three parameters determine the ultimate diagnosis, if all three don't tie up it should raise an alarm. (34,35) In the event where there's discordance between clinico-radiological and pathological diagnoses, musculoskeletal radiology-pathology correlation conferences have been shown to decrease time to appropriate patient management. (36)

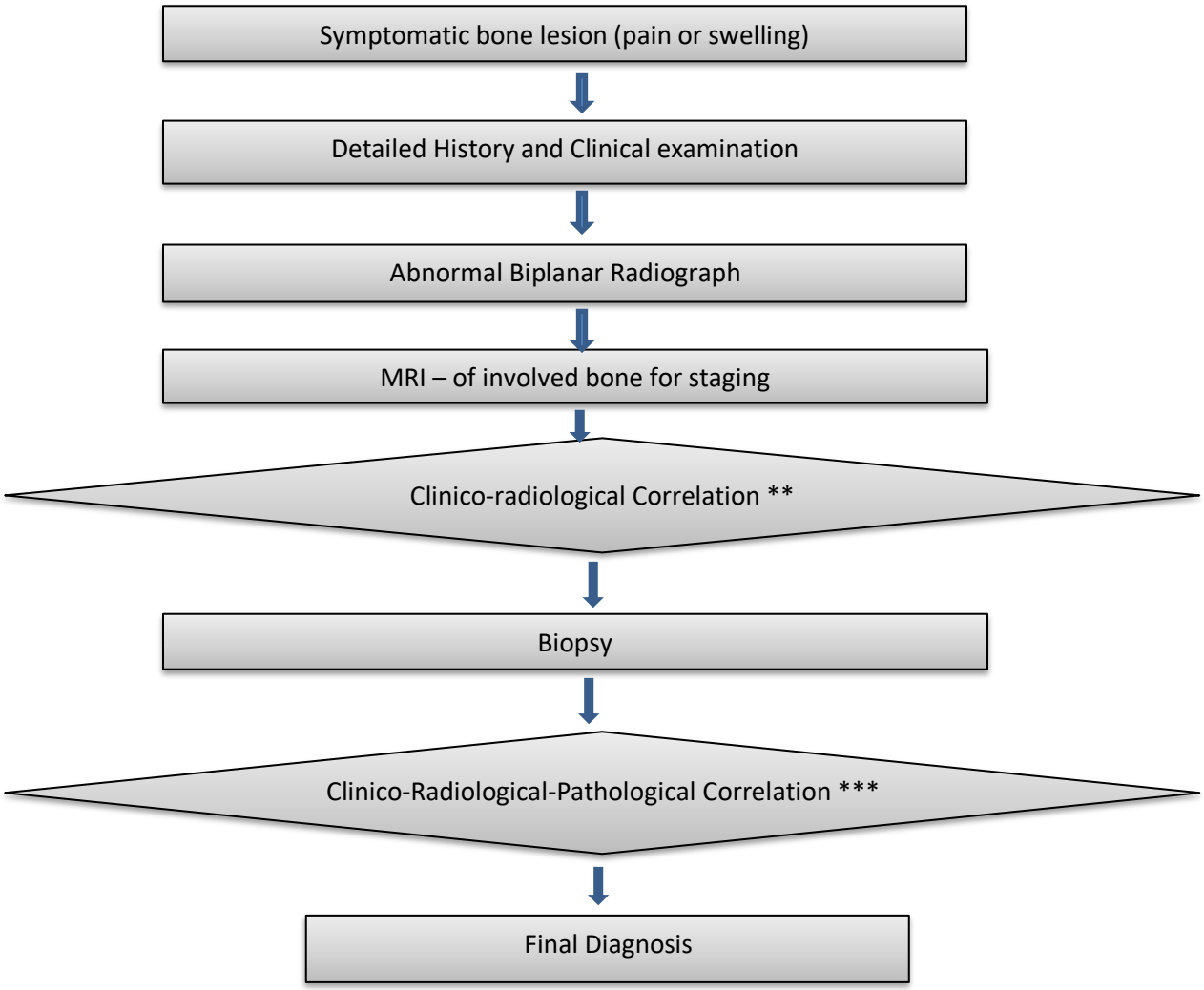


Figure 1 Bone tumour Diagnosis Algorithm. Adopted from the India National Cancer Guidelines.

2.2.1 History and Clinical evaluation

Early diagnosis of bone tumours enable clinicians to embark on initiation of timely therapeutic measures. This results in an increased chance of survival, possibility of performing a limb sparing operation in some cases and an overall better quality of life. (13,26) Orthopaedic surgeons and other clinicians may need to make a presumptive diagnosis as in some cases that may guide in the definitive treatment where limitations to access elaborate diagnostic tests exist. (8) The preliminary diagnosis is obtained by tying up information from a comprehensive patient's history, physical examination and radiography findings. Information collected during clerking includes the patient age, gender, residence, presenting symptoms including their duration, intensity and timing of complaints.

The medical history should also target on prior benign or malignant lesions, orthopaedic surgery with implanted metal prosthesis, family and occupational history as well as previous radiotherapy or chemotherapy treatments. (13,16,36,37) Precancerous conditions have a varying potential of predisposing one to a malignant bone tumour. Ollier's disease, Maffucci syndrome, familial retinoblastoma syndrome and Rothmund Thompson syndrome are high risk precursors. Multiple osteochondromas, Paget's disease and radiation osteitis have a moderate risk. A low risk for malignant transformation has been associated with fibrous dysplasia, bone infarct, chronic osteomyelitis, prosthetic implants, osteogenesis imperfecta, giant cell tumour, osteoblastoma and chondroblastoma. (38) Multiple enchondromas (autosomal dominant) and bone dysplasia in neurofibromatosis (autosomal dominant) have been noted in certain patients who have a positive family history of the same. (39)

Physical examination of possible swelling, description of the size, consistency, location, mobility and relation to the underlying bone is vital. Some cases of bone tumours may have a pulsatile mass with increased vascularity. The affected area may be warm, tender to palpation. Fever, lymphadenopathy, dyspnoea and fatigue may be found in metastatic disease. The art of clinical evaluation is supplemented with laboratory studies that help narrow down on the diagnosis among an array of possible differentials, monitoring treatment response and good prognostic indicators. Serum Alkaline phosphatase level is elevated in Paget's disease, Paget's sarcoma and is a poor prognostic sign in osteogenic sarcoma. Ewing's sarcoma and certain osteogenic sarcomas with high levels of serum lactate dehydrogenase have poor prognosis. Raised Erythrocyte sedimentation rate and C-reactive protein levels are also poor prognostic markers in Ewing's sarcoma. (36)

The understanding of the spectrum of bone tumours and how frequent they tend to occur is important. This will inform the clinician on the likelihood of a patient having a specific bone tumour. However, a large number of shortcomings in diagnosis are there as common bone tumours may have unusual clinical presentations with many rare tumours masquerading as the commonly encountered tumours. (40) Orthopaedic surgeons need to be alerts so as not to miss out on tumours that may mimic non-neoplastic or infective lesions. Additionally, with the knowledge of the large group of possible tumour diagnoses, a clinician can have several differential diagnoses based on radiological findings and make informed decisions on requisite follow up investigations and management without delay. (27,28,36) Both radiological and

histological diagnoses rely heavily on the clinical information provided by clinicians. (12,13,41,42)

2.2.2 Radiological Diagnosis

Imaging is of integral utility in determining the preliminary diagnosis and the investigations or therapeutic measures that follow in treating bone tumours. Despite the breakthroughs in computed tomography (CT) and magnetic resonance imaging (MRI), the conventional radiograph is the elementary modality in the imaging of bone lesions. A plain radiograph is quite informative since it's able to detect the hallmark morphologic features of bone lesions when standard orthogonal views are taken. (43)

Four key questions as proposed by William F Enneking need to be acknowledged to help in understanding the varying appearances of lesions on plain radiographs. (44)

- Where is the lesion? In which bone and within which anatomical region of that bone?
- What is it doing to the bone?
- How is the bone responding?
- What is in the lesion?

Where is the lesion?

The predilection of certain tumours to some bones and most often to the diaphyseal, metaphyseal or epiphyseal zone is pathognomonic. Giant cell tumours usually are found in the epiphyseal region and just below articular cartilage. Most unicameral (simple) bone cysts are found in the metaphyseal area of especially the proximal humerus and extend into the diaphysis as the skeleton matures. (43)

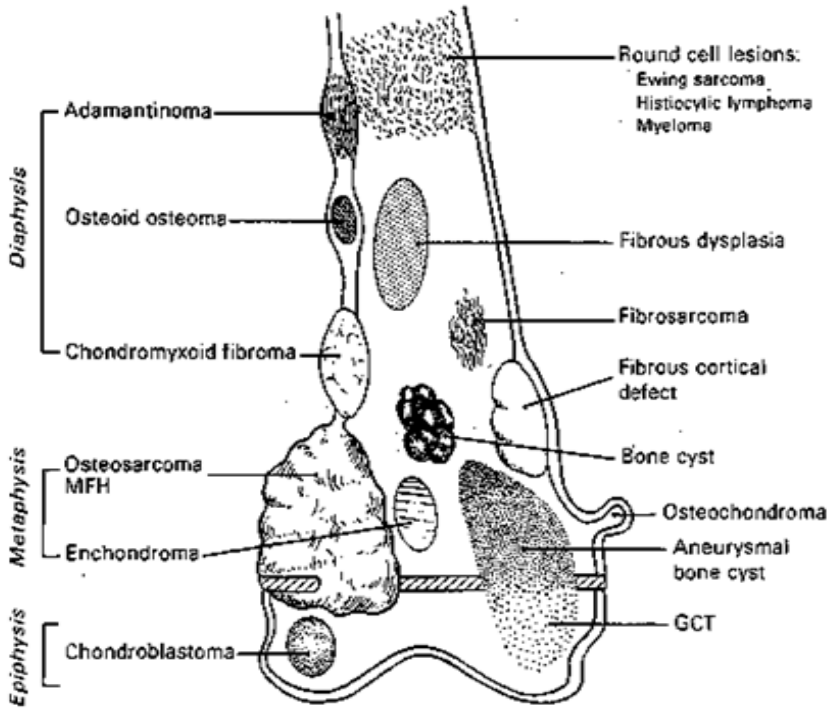


Figure 2 Illustration of tumour location in long bones

What is the lesion doing to the bone?

Osteoblastic tumours are characteristically mineralized or show a calcified deposition due to the deregulation of osteoblast activities. They are mostly bone metastases from Prostate cancer. Other possible primaries include carcinoids, lymphoma and gastric cancer. Bone metastases can be predominantly osteolytic (multiple myeloma, kidney cancer, melanoma) or mixed osteolytic and osteoblastic (breast cancer, thyroid cancer, small cell cancer). Osteolysis occurs at a cellular level by osteoclasts that are up-regulated by tumour cells via the RANK ligand pathway. At least 30% of the bone matrix has to be resorbed so as to note a lesion to be seen on an X-ray. (43)

More than half a century ago, a radiographic grading system based on margination was described by Lodwick to assess lytic bone lesions and tell their possibility of growing. This system was refined by Madewell et al to decrease complexity and better reflect risk of malignancy with increasing grade. The margins could range from well-defined (geographical) with narrow zone of transition in less aggressive lesions, moth eaten to severely ill-defined (permeative appearance) in malignant lesions. (45)

Modified Lodwick-Madewell Grading System		
Grade	Description	Comment
1A	Well-defined geographic lytic lesion with a sclerotic rim	Slow-growing or indolent lesion; typically benign
1B	Well-defined geographic lytic lesion with a sharp margin without a sclerotic rim	Most lesions are benign, although differential diagnosis may include metastatic disease and myeloma
II[a]	Geographic lytic lesion with partial or circumferential ill-defined margins	Some benign causes, but differential diagnosis should include malignancy
IIIA[b]	Focal change in margin, changing margination, or progressive endosteal scalloping on serial radiographs	Focal changes or changes over time indicate increased biologic activity and should raise suspicion for malignancy
IIIB[c]	Moth-eaten and permeative patterns of osteolysis (nongeographic osteolysis)	Scattered and confluent holes in bone giving the impression of arising from multiple foci or innumerable tiny areas of bone destruction that fade imperceptibly from completely normal bone to markedly abnormal bone
IIIC[d]	Radiographically occult	Normal or near-normal radiographic findings; lesion is seen on advanced imaging such as MRI or PET

[a]Modification: increased grade assignment from IC to II.
[b]Modification: new grade assignment for lesions showing evidence of increased biologic activity suspicious for malignancy.
[c]Modification: nongeographic osteolysis combining previous moth-eaten and permeative patterns of osteolysis.
[d]Modification: new grade system is the most aggressive pattern of growth in which tumor cells extend through bone more rapidly than host osteoclasts can produce recognizable osteolysis.

Figure 3 Modified Lodwick-Madewell Grading System

What is bone doing?

Tumour histology, grade and how rapid it grows determine how the bone responds. Benign lesions occasionally do not show a notable reaction from the osteoid forming tissues while others will result in bone becoming firm and stiff such as osteoid osteoma. Rapidly growing tumour may be overwhelmingly rapid that the periosteum forming bone cannot match, the radiological appearance that is seen can be described as onion- skinning. Codman triangles are seen where there is filling of calcified osteoid at the edges where the periosteum is elevated. Attempted vertical calcification of osteoid is produced in aggressive tumours resulting in a sunburst or hair on end appearance on roentgenograms such as in osteosarcoma.

What is in the lesion?

The appearance of the lesion matrix hints at the histological diagnosis and characterizing this appropriately is key to narrowing down on the differential diagnoses. Osteoid tissue produced by osteoblasts mineralizes in a confluent manner culminating in a radiographic density that ranges from a hazy ground glass appearance to a dense ivory-like pattern. Rapidly growing

osteosarcomas produce immature bone thereby present as ill-defined poorly structured clouds. Parosteal osteosarcoma is slow growing producing solid mature tumour bone hence well-defined heavily mineralized masses radiographically.
Fibroblastic cells that convert to functional osteoblasts via fibrous dysplasia produce woven bone that is less densely mineralized hence a hazy ground glass appearance. Chondroid matrix is produced by neoplastic cartilage. Calcification occurs in the form of stipples resulting in popcorn, floccules, arcs or ring-like appearance as in chondrosarcomas. (43)

Patients who are asymptomatic but incidentally found to have non-aggressive appearing lesions on plain radiographs, often require no further evaluation. CT, MRI or nuclear medicine may provide supplementary information where initial evaluation and X-rays information is equivocal or adequate information of anatomy is necessary. CT scan is quite useful as the first imaging test in evaluating lesions located within complex bony regions. (46) MRI is important for finding out the extent of spread into the marrow and surrounding soft tissues and spotting skip lesions. This makes MRI a useful imaging modality for staging of tumours. (47,48)

Features	Potential Diagnoses
Complete sclerotic rim	Benign lesion (95% accuracy)
Epiphyseal, solitary, lytic lesion with sclerotic border	Chondroblastoma, enchondroma, GCT
Epiphyseal, solitary, lytic lesion without sclerotic border	GCT, chondrosarcoma
"Kissing" bones (lytic lesions in contiguous epiphyses)	GCT, angiosarcoma, pigmented villonodular synovitis, infections
Cumulus cloud	Osteosarcoma, stress fracture
Ground glass	Fibrous dysplasia, osteoblastoma, grade I osteosarcoma
Ring-like to popcorn density	Enchondroma and secondary chondrosarcoma
Poorly demarcated, expansile lesion with windblown calcifications	Chondrosarcoma
Expansile, trabeculated lesion	Grade I sarcoma, GCT, myeloma
Finger-in-the-balloon	ABC
Fallen fragment sign	Simple bone cyst
Codman's triangle	Osteosarcoma, osteomyelitis, ABC
Onion-skinning	Ewing's sarcoma, osteomyelitis, osteosarcoma, eosinophilic granuloma
Bone expansion	Benign tumor (90% cases), grade I sarcoma, myeloma, metastasis
GCT = giant-cell tumor ABC = aneurysmal bone cyst	

Figure 4. Pathologic and Radiologic Features of Primary Bone Tumors. Letson et al 1999

2.2.3 Histological Diagnosis

Biopsy is usually the definitive diagnostic procedure. Pathologists study the specimen provided after requisite preparation by looking at certain histologic features that include; cellular pattern of growth and arrangement, cytological characteristics of cells, cystic changes, matrix production and the relation between the lesion and the surrounding normal bone. (41)

Although histological diagnosis is regarded as the "gold standard", it still hinges on accuracy of clinical evaluation and radiological findings. Where facilities are well equipped and patients able to access them, diagnosis requires comparison of clinical and radiological findings. A biopsy is thereby taken to grade, make clarity and validate an initial diagnosis. (43) Clinicians of all grades and specialties should ensure quality in information submitted to the pathologist for analysis of the specimens for best patient care. (49)

Members of the musculoskeletal tumours society, representing sixteen centres for bone and soft tissue tumours, produced a report on hazards associated with 329 biopsies of primary malignant musculoskeletal sarcomas in 1982. They assessed the accuracy of histological diagnoses, the incidence of complications associated with the biopsy procedure, the effects of errors in diagnosis and of complications on the patient's course, and whether these problems occurred with greater frequency when the initial biopsy was performed in a referring institution or in a treating centre. Results revealed 18.2% major errors in diagnosis and 10% technically poor biopsies. Treatment had to be altered due to biopsy related problems. The biopsy-related errors occurred more when the biopsy was performed in facilities referring patients than those testing and treating institution. Ten years later a similar study was carried out with same problems being noted. They recommended that a biopsy should be done in a treatment centre where personnel had better technical knowledge of the procedure rather than in the referring facility. (50)

Notwithstanding, an accurate diagnosis of bone sarcoma is crucial for the best patient care. To achieve this, clinical, radiologic and pathologic information is integrated together enabling the clinical team utilize optimal therapy. (6,41)

2.3 Spectrum of Bone Tumours

There are worldwide variations in pattern of bone tumours with specific tumours predominant in certain geographical regions. The American Society of Clinical Oncologists 2021 report on bone sarcomas revealed that Chondrosarcoma made up forty percent of primary bone sarcomas. Osteosarcoma 28%, Chordoma 10%, Ewing Sarcoma 8% and fibrosarcoma 4% were among the common sarcomas in adults. Other types of bone sarcoma were rare. However, in those of age less than 20 years, osteosarcoma and Ewing sarcoma are diagnosed far often than chondrosarcoma. (4)

In India, varying data based in cancer registries domiciled in tertiary care hospitals has been reported with no population based study in the near past on incidence of different types of bone tumours. A retrospective study by Rao et al on data collected over 36 years in Karnataka, revealed 523 bone tumours. Malignant tumours made 39% of these tumours. Osteogenic sarcoma and Ewing sarcoma constituted 45% and 19% of malignant tumours respectively. (51) A five year retrospective study done at a government medical college in Jammu studied a total of 110 cases of primary bone tumours. Malignant tumours were 76 cases of which OGS and Ewing sarcoma were 42 and 26 cases respectively. Among benign cases Osteochondroma were the commonest benign tumours accounting for 13.5% followed by fibrous dysplasia 5%. (52) Karun et al did an 8 year retrospective review at JSS Medical College and hospital, Mysore. He reported 117 cases of primary bone tumours. Benign tumours were 67. In this group, osteochondroma was the most common, accounting 22% followed by Giant cell tumour 20% of all cases. Osteosarcoma made up more than a third of all the primary malignant tumours. (53)

A similar picture is evident in Africa, Osteosarcoma, chondrosarcoma and Ewing's sarcoma predominate primary malignant bone tumours in most studies. However, disparate frequencies of benign bone tumours were found in most studies. (54-62) A six year retrospective descriptive study at a tertiary referral centre for Dakahlia governorate, Egypt analysed 828 cases of bone tumours. Benign cases were 523 (63.16%) and malignant cases were 305(36.83%). The most frequent benign bone tumours were Osteochondromas (30%), Aneurysmal Bone Cyst (24.2%), Giant Cell Tumours (18.35%), and Osteoid Osteoma (7.2%). (54)

Epidemiological data from Grey's Hospital Orthopaedic Oncology unit in South Africa over a period of 7.5 years was used to assess the local prevalence of primary malignant bone tumours. 117 patients with biopsy-confirmed histological diagnosis of primary malignant bone tumours were included in the retrospective study. OGS diagnosed histologically more than any other tumour (72%). This figure is more than those reported in other countries. This was followed by Chondrosarcoma (11%), Ewing's Sarcoma (9%), Spindle-cell sarcoma (4.2%) and malignant Giant Cell Tumour (1.7%). Multiple myeloma and lymphoma patients were not included. (55) Dennis Sakala et al conducted a retrospective cross-sectional study in Zambia. With inclusion of hematologic neoplasms, Multiple myeloma (27.6%) cases were frequent second to osteosarcoma and a significant number of lymphomas (1.3%). (7)

A multicentre study involving three tertiary hospitals in Lagos metropolis, Nigeria, had data over 24 years analysed retrospectively by D. C Obalum et al. Three hundred and forty two cases representing 42 % had primary malignant bone tumours while 356 (51%) were benign. Osteosarcoma constituted 62% of the primary malignant bone tumours and 30.7% of the study

population. Among the other malignant bone tumours, Chondrosarcoma accounted for 19.9%, Fibrosarcoma (7.3%), Ewing's sarcoma (6.7%) and Hemangiopericytoma (3.5%). Benign tumour cases were osteochondromas 29.5%, osteoclastoma 13.8%, aneurysmal bone cysts 12.9%, chondroma 8.7%, fibrous histiocytoma 4.5%, ossifying fibroma 4.2%, chondroblastoma 2.8%, and non-ossifying fibroma 2.8% among others. (8) Parallel findings were seen in similar studies in Nigeria and Niger. (56–58)

A 5- year retrospective analysis of congruity between radiological and histopathological diagnoses of bone tumours at Addis Ababa University, Ethiopia was done by Bayush E. Negash et al. Bone tumours enrolled in the study were 205 with majority being neoplastic cases (89%). Primary tumours accounted for 94.5% of the neoplastic lesions the rest being metastases. Among the primary tumours, malignant lesions were 43% while benign lesions were more at 57%. The three most common bone lesions were: osteosarcoma and exostosis equally first at 21.95% each, giant cell tumour 10.73% and ameloblastoma 8.29%. (59)

In northern Tanzania according to a study done by PTK Samoyo et al., [2017], 225 malignant bone tumours were recorded over a 14 year period at the Kilimanjaro Christian Medical Centre [KCMC]. However, only 75 of the total cases had adequate records for analysis. Twenty-two bone tumours (29.3%) had a histological diagnosis of osteosarcoma, followed by 18 other types of sarcomas (24%) (3 chondrosarcomas, 1 cystic sarcoma, 2 Ewing's sarcomas, 3 fibrosarcomas, 1 Kaposi's sarcoma, 1 Pleomorphic sarcoma, 2 synovial sarcomas, 1 malignant mesenchymal sarcoma, 1 rhabdomyosarcoma, 2 low-grade sarcomas, and 1 high-grade malignant sarcoma), and 9 carcinomas (12%) (3 adenocarcinomas, 2 metastatic carcinomas, 2 poorly differentiated carcinomas and 2 squamous cell carcinomas). (12) Another study in the same region but based on children and adolescents had Osteosarcoma as the most common tumour but no case of Ewing's sarcoma was recorded at the tertiary referral hospital-based database. (15)

H. O. Ong'ang'o and P. Wabomba reviewed 41 cases of thigh tumours prospectively at an orthopaedic unit in KNH over a period of 12 years. They found 6 cases (15%) of osteogenic sarcoma, 4 cases (10%) each of lipoma, inflammatory lesions and non-specific lesions, 3 cases (7.5%) of neurofibroma and 2 cases (5%) fibrosarcoma. The rest were single cases of different histological variants of tumours. (60) Notably, this study included soft tissue tumours as well.

2.4 Age of presentation.

To be able to make out the possible diagnoses of bone tumours, age is an important consideration. This is because the incidence of some bone tumours has been noted to vary in different age groups. Bickels in his study on diagnostic strategy for bone tumours linked the nature of certain bone lesions with age of a patient. Case in point, primary bone sarcomas are more frequent after age in second decade of life while patients older than 50 years are likely to have metastases unless investigations confirm a different diagnosis. (37)

Arora et al., (2011) studied age-incidence patterns for in England from 1979 through 2003 utilizing data from the national cancer registry. OGS and Ewing's sarcoma incidences climaxed at 15-19 years and 10-14 years in males and females respectively. OGS had a second but smaller incidence rise at advanced ages. After age 30 years, Chondrosarcoma numbers dominated. Pubertal bone growth is therefore an important factor in development of osteosarcoma as is evident in the incidence patterns. (61) Comparable age-incidence patterns have been found in studies carried out in other regions but in different time periods. (42,62,63)

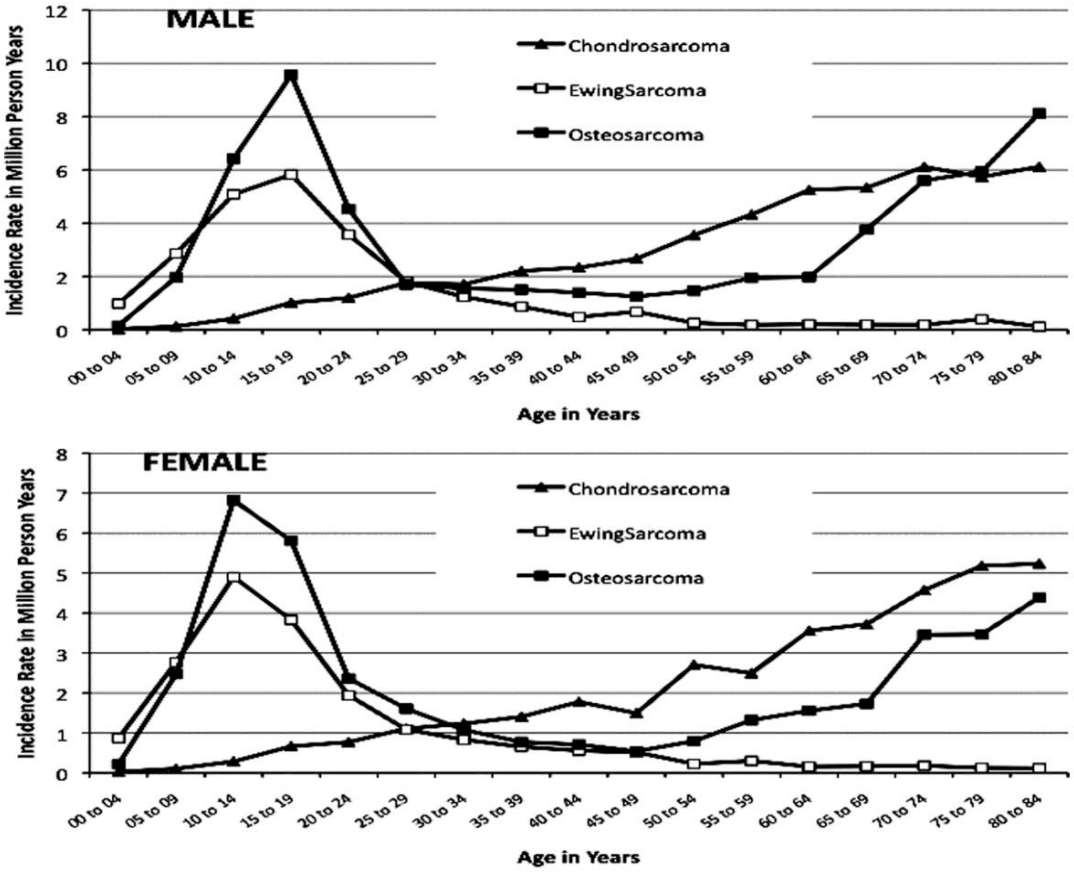


Figure 5. Age-specific incidence rate patterns of osteosarcoma, Ewing sarcoma and chondrosarcoma in males and females in England, 1979–2003

2.5 Symptomatology.

Bone tumours present generally with non-specific clinical symptoms as they may mimic common musculoskeletal injuries. Patients with latent bone lesions are usually asymptomatic with the lesions being detected incidentally when imaging is done for other purpose. The pain in some benign bone lesions may be triggered by activities or inflammation of the periosteum. Some benign lytic bone lesions show no reaction of the periosteum: fibrous dysplasia, enchondromas, non-ossifying fibroma, and simple bone cysts. In contrast, those with benign-aggressive and malignant bone tumours mostly present with a distinct pain with an insidious onset that gradually becomes progressive, and not responsive to change in position or bed rest usually due to involvement of neurovascular structures. (64) Tumours in the pelvic girdle and lower limbs produce pain that is worsened by weight bearing and ambulation.

Regional or localized pain is most frequent symptom and is usually associated with tenderness and reduced range of movement. (65,66) Less than a third of patients had either pain at night or were awoken by pain in those with osteosarcoma compared to a fifth of those with Ewing's sarcoma. (66,67)

P T K Samoyo et al., (2017) found pain in 85.6% of malignant bone tumour cases with a mean duration of 7.1months in 15 cases. Swelling was recorded in 84% of malignant tumours, this lasted an average of 20.7 months. Pallor was observed in 13.3% who had a haemoglobin level less than 7.0g/dl. Pathological fractures occurred in 18.7% of cases, where osteosarcoma, GCT, multiple myeloma, metastatic carcinomas, and high grade malignant tumours were diagnosed to be the cause. Cough, difficulty in breathing and haemoptysis were found in those with metastasis to the lungs. (12) Other common symptoms include fatigue, numbness, unexplained weight loss.

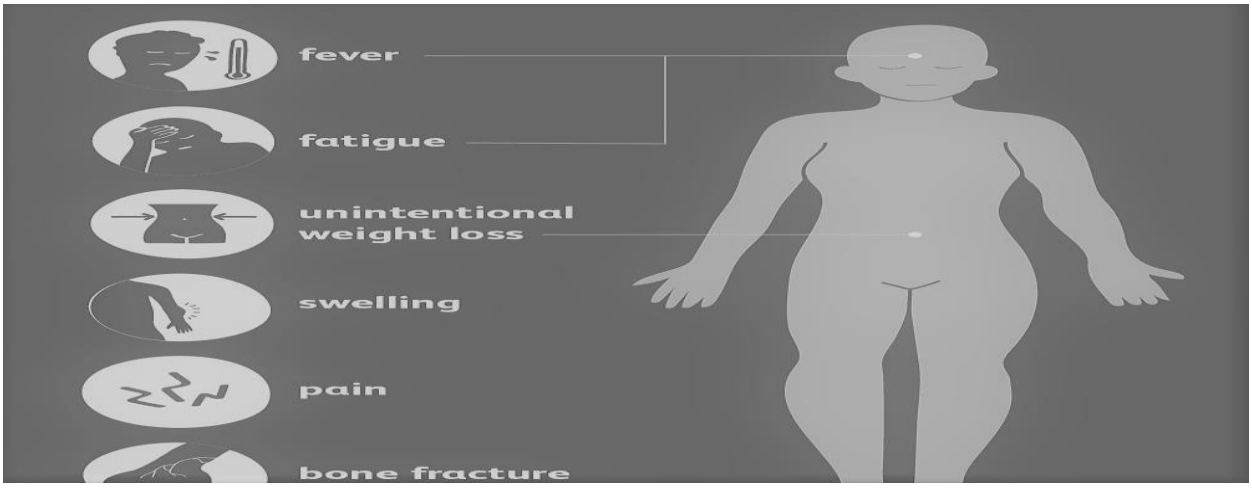


Figure 6 Common symptoms of bone tumours

2.6 Topography.

Bone tumours in most studies are notably found in long bones especially those in the lower limbs. (15,16,51–53,55–60,68) Bone tumours also show a predilection to certain zones of bone. Common epiphyseal lesions are benign and predominantly giant-cell tumour, chondroblastoma, low-grade osteogenic osteosarcoma, and clear-cell chondrosarcoma. Most often, lesions in the diaphysis will be fibrous dysplasia, enchondromas, non-ossifying fibroma, chondrosarcoma, Ewing's sarcoma, or metastasis. However, the metaphyseal region is home for most skeletal neoplasms thereby there is an extensive of possible lesions here. (69) Pillay et al., (2016) reported 88.9% of the 117 cases of primary malignant bone tumours were located in the pelvis and the lower limbs. The majority (80%) of these tumours were confined to four anatomical areas, namely distal femur, proximal tibia, proximal humerus and pelvis. (55) Elshahhat A Amr., *et al (2017)* reported distal femur and proximal tibia to have most GCT lesions. (70) Chondrosarcomas were most commonly are localized in the pelvis with the bulk in the ilium (50.5%) followed by the pubis (22.9%) and ischium (9.2%). (71)

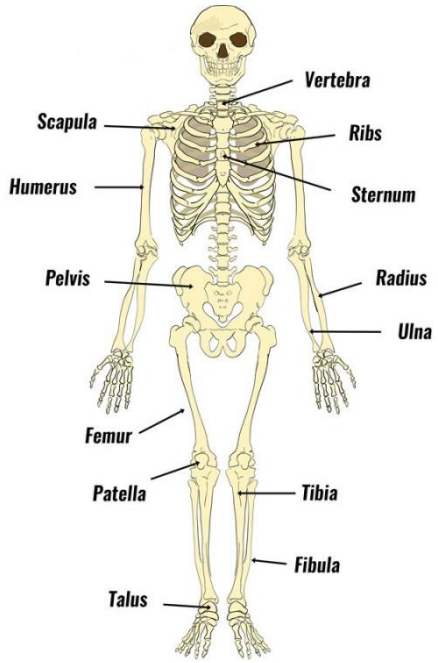


Figure 7 Long bones commonly affected.

2.7 Radio-histopathological Comparison.

2.7.1 Percent agreement

Several studies have looked at the correlation between radiological findings and the final histological diagnosis. A study done at Kenyatta National hospital by Kimari Peter found a percent agreement of 54.8% between roentgenography and histology in diagnosis of malignant bone lesions (42). Negash et al., (2009) did a study at Black lion hospital, Addis Ababa, Ethiopia. He found that 84.3% of radiological diagnoses were in keeping with the histological diagnoses. (59) A single case reported normal radiographically was diagnosed as osteoblastoma by histopathological analysis. However, major disagreement was noted in diagnosis of osteosarcoma. Histology diagnosed 15.7% of cases reported otherwise by radiology.

Similar excellent level of agreement was found in retrospective study in India by Bipul et al. Out of 90 cases of bone tumours, 73 cases with a radiological diagnosis were confirmed by histopathology. This represented 81% agreement. (39) Substantial level of agreement was noted in studies by Erhadt et al. in South Africa. Seventy out of eighty eight cases with a radiological diagnosis by plain radiography were confirmed by histopathological diagnosis representing 79.5% agreement. (72)

A prospective study (2009-2011) by Pallavi et al looked at 64 cases. The corresponding percent agreement was 74%. (73) However, a larger variation was found in a study in Northern Tanzania by P T K Samoyo et al. The overall radiological accuracy was 30% (15/50 cases) with radiologists diagnosing osteosarcoma and multiple myeloma most correctly. Other bone tumours were reported as “bone tumour” or simply “tumour” without exact recording of the likely bone tumour type. (12)

Salazar et al., did a retrospective study that had 64 cases of bone tumours. He compared different imaging modalities which were available in patients’ medical records with histopathological findings in Portugal, a developed nation. Among the 30 patients who had an X-ray used as a tool for radiological diagnosis, only 1 malignant tumour was wrongly diagnosed as benign and 2 benign tumours were reported as malignant. In the malignant category, radiography misinterpreted 2 cases of Ewing’s Sarcoma as osteosarcoma and a single case of Chondromyxoid fibroma as ABC. The percent agreement values in general for XRAY, MRI and CT were 80%, 90% and 52% respectively. (74)

Kharolkar V et al., in an observational study of bone lesions over a 2 year period, a total of 30 cases were studied. Radiology and histology diagnoses were in agreement in 24 cases (78%). Radiographical opinion was at odds with histology in 6 cases; 2 cases each of multiple myeloma and osteosarcoma as well as a single case each of chondroblastoma and simple bone cyst. Radiography is very important in diagnosis of bone tumours especially in resource-poor set up where cost and availability of advanced histopathological analysis is prohibitive. However, triple assessment of bone lesions is key for arriving at an accurate diagnosis for best outcomes. (75)

2.7.2 Sensitivity and specificity of plain radiography on bone tumour diagnosis

Sensitivity and specificity of a test are usually constant whatever the prevalence of the condition, unlike positive and negative predictive value which are affected by the prevalence of the condition under consideration. (76) Specificity is a measure of diagnostic test accuracy, complementary to sensitivity. Erhadt Gerber et al., focused on determining the accuracy of x-rays in diagnosing biopsy-proven malignant bone tumours. He reported a sensitivity and specificity of 95% and 64% respectively. The low specificity was attributed to the reason that most of the bone lesions that were said to be benign on radiography were not biopsied and in other cases the radiologists reported x-ray as inconclusive. (72) Salaria et al., found commendable figures of sensitivity [92.9%] and specificity [87.5%] in diagnosis of both benign and malignant bone tumours. (52) Comparable high accuracy percentages were noted in a study of 94 cases of bone tumours by Bipul et al. He noted a sensitivity of 91.89% and specificity of 92.45%. (39)

CHAPTER 3: METHODOLOGY

3.1 Study Design

This was both a prospective and retrospective study. Medical records for all patients with a diagnosis of bone tumour attending Kenyatta National Hospital between March 2022 and February 2023 either as inpatients or in the outpatient orthopaedics clinic were reviewed.

3.2 Study Setting

The study was conducted in two hospitals namely;

1. Kenyatta National Hospital, a level 6 national referral hospital with 1800 bed capacity. The facility has dedicated 24-hour orthopaedic surgery theatres, laboratory, diagnostic imaging centre, radiotherapy and chemotherapy facilities. The University of Nairobi radiology and pathology departments work in collaboration with KNH. The KNH and UON orthopaedic department has an oncology unit among other thematic units with dedicated consultants and orthopaedic residents. The orthopaedic-oncology clinic runs once a week and an average of 30 patients are seen in a month majority of who come for follow-up review clinic.

2. PCEA Kikuyu, a level 5 faith-based hospital with a 233 bed capacity established over a century ago. It is well resourced with a diagnostic imaging centre, operating theatres open 24 hours a day and a full-fledged semi-autonomous orthopaedic department, the PCEA Kikuyu Orthopaedic and Rehabilitation centre (KORC). KORC is fully equipped with 37 beds, provides orthopaedic, reconstructive surgery and rehabilitation for its clients. KORC was established in 1998. Annually about 5000 patients are seen in the daily orthopaedic clinics and over 800 surgical procedures performed. The department has an in-house faculty as well as outsourced specialists who also run the College of Surgeons of East, Central and Southern Africa (COSECSA) general surgery and orthopaedic surgery postgraduate training program.

3.3 Study Population

All patients, both children and adults, attending the two facilities that were suspected or had been confirmed to have a bone tumour and had consented to the study were recruited. The target population included outpatient and inpatients in the period from March 2022 to February 2023.

3.4 Eligibility Criteria

3.4.1 Inclusion criteria

- All patients with a confirmed bone tumour on histology.
- All patients referred for care with bone tumour as the diagnosis.
- Patients who consented for the study.

3.4.2 Exclusion criteria

- All non-neoplastic (fractures, degenerative diseases), infectious and odontogenic lesions.
- Patient who declined to consent to the study
- Patient who lacked either histology or radiology results.

3.5. Sample Size

The Cochran's formula is used

$n=Z^2 P(1-P)/d^2$

$n= 1.96^2 1.2(1-1.2)/ 0.05^2$

n= 368

*Whereby **n** is the sample size, **Z** [1.96] is the statistic equivalent to level of confidence, **P** [1.2] is expected prevalence (obtained from calculation based on the national average as per the AFCRN report 2016), and d [5%]is precision (corresponding to effect size)*

Current records at the two institutions reveal that each month 5 new patients are seen with a diagnosis of bone tumour. This translates to approximately 60 patients in 12 months study duration. Adjusting the sample size for small population [N=50, n=368]

$N_{(adj)} = (N*n)/(N+n)$

$N_{(adj)} = 51$

A sample size of 51 was arrived at for the study.

3.6 Sampling Techniques

3.6.1 Sampling and recruitment

This was a census study executed via consecutive sampling due to the small number of patients seen at the two facilities monthly in the past five years (2016-2021) i.e. average of 5 newly diagnosed bone tumour patients a month. Most of the patients are usually on follow up visits in the orthopaedics and oncology [cancer treatment centre]. There had been 21 admissions in the 6 months preceding the start of the study in the orthopaedic oncology unit.

This sampling method limits bias as all patients who presented at any time of the day and any day of the week at the accident and emergency department, orthopaedics, oncology clinics and wards was captured. Children were assented by their parents or guardians to participate in the study.

3.7 Data Management

3.7.1 Study procedure and Data collection

Recruitment of patients was at the orthopaedics and oncology clinics, radiology department, pathology department and the respective wards for those admitted. All patients confirmed to have a bone tumour on histological analysis were recruited in the study. Those patients referred from other facilities directly for imaging or histology in the radiology and pathology departments respectively were also recruited in the study after consenting. Patient who had already been worked up and had a diagnosis of bone tumour were also included.

Data was obtained from patients' files and image folders during the review clinics as well as from the medical records departments of both hospitals. The details obtained from the patients included age, sex, major presenting symptoms and anatomic location of the tumour after physical examination which were entered into the patient data sheet. Radiographical findings were recorded as well the final radiological diagnosis and differential diagnoses. Unreported radiograph films were read by the principal researcher and the final diagnosis confirmed by a radiologist who is also my supervisor. Where histological reports are not filed, they were obtained from the respective departments. Tumors were divided into benign and malignant according to WHO classification.

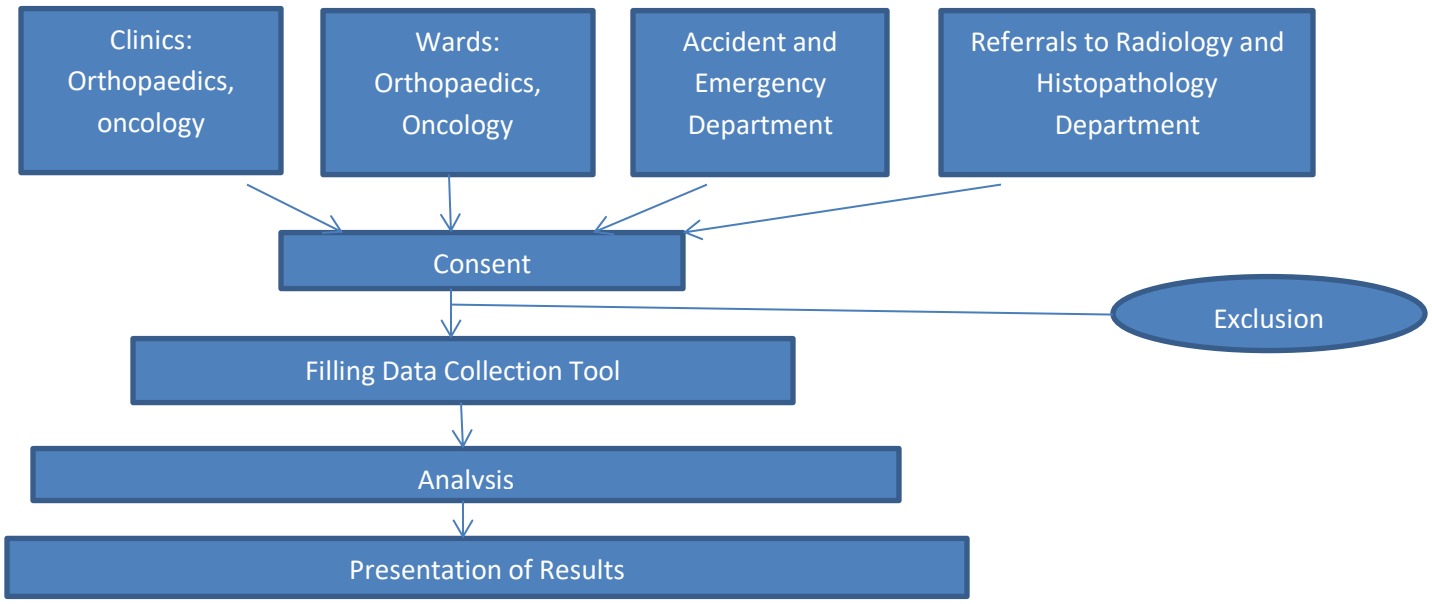


Figure 8. Recruitment schema.

3.7.2 Data Quality and Security

Printed versions of the patient data sheet (appendix 1) were filled by the principal investigator and the research assistants. These included final year medical students who were sensitized and trained on data collection by the principal researcher. The entire team strictly abided by laid down standards of data handling and security. Hard copies of the data sheets were kept under lock and key. All associated soft copies were kept in a password protected folder.

3.7.3 Data Analysis

The data was checked for errors and completion. It was coded and entered into SPSS version 26 for analysis. Analysed data was summarised in form of frequencies and percentages for categorical data and means or median for continuous data. Results were reported using frequency tables, bar charts and pie charts. Taking histopathology diagnosis as the gold standard and therefore a constant, percent agreement between radiographical and histological diagnoses of bone tumours was calculated. The plain radiography sensitivity and specificity in diagnosing primary bone tumours was also established.

3.8 Study Results Dissemination

The findings of this study were presented to the UON-Department of Orthopaedics Surgery and the UON-Library.

The results were published in a peer reviewed journal for wider audience and presented in scientific conferences.

3.9 Study limitations.

It is difficulty to study rare diseases such as bone tumours due to a limited number of cases. However, meticulous recruitment and search of records was done to ensure that the results are applicable and generalizable.

3.10 Ethical Considerations.

The approval for the study was first sought from Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UON ERC) and National Commission for Science, Technology and Innovation (NACOSTI). This was followed by administrative permission from Kenyatta National Hospital. The copies of the approvals were attached in the appendices. Data was anonymized and key patient identifiers like names, gender and age will be de-identified to maintain confidentiality. Data obtained from the study shall be disposed after one year. The research acknowledges the sources of information gathered to avoid plagiarism.

3.12 GANNT Chart

Activity	Apr 2022	May 2022	Jun 2022	Jul 2022	Aug 2022	Sep 2022	Oct 2022	Nov 2022	Dec 2022	Jan 2023	Feb 2023	Mar 2023
Proposal development												
Ethical Approval												
Data Collection												
Data Analysis and Report writing												
Reviewing and corrections by supervisors												
Submission and presentation.												

Table 1. Study Timeline

3.13 Budget

The cost of the study was met by the principal researcher.

Item	**Cost (Ksh.)**	**Budget justification**
Research Fee	2,000	Standard fee
Stationery	20,000	Cost of materials for printing, stapler, pens
Research assistant	30,000	Cost of hiring 2 assistants to cater for transport, communication and lunch.
Statistician	30,000	Standard cost
Miscellaneous	10,000	Administrative + contingencies
Total	**92,000**	

CHAPTER 4: RESULTS

4.1 Introduction

There were 65 cases seen in the orthopaedic and oncology departments with a diagnosis of bone tumours. However, 7 cases lacked histology results and were excluded from the study. Primary bone tumours were 49 and secondary (metastases) bone tumours were 9.

4.2 Demographic Information

The mean age of the patients was 28 years (SD 19), minimum age was 6 years and maximum age 76 years. Median age was 20.5 years. Peak age was between 10 to 29 years (58.6%). The number of males and females was equal, 28 cases of each (50%).

AGE	Female	Male	Grand Total
0-9	3	1	4
10-19	9	14	23
20-29	4	7	11
30-39	1	2	3
40-49	5	2	7
50-59	3	1	4
60-69	3	1	4
70-80	1	1	2
Grand Total	**29**	**29**	**58**

Table 2: Age distribution.

4.3 Clinical Presentation

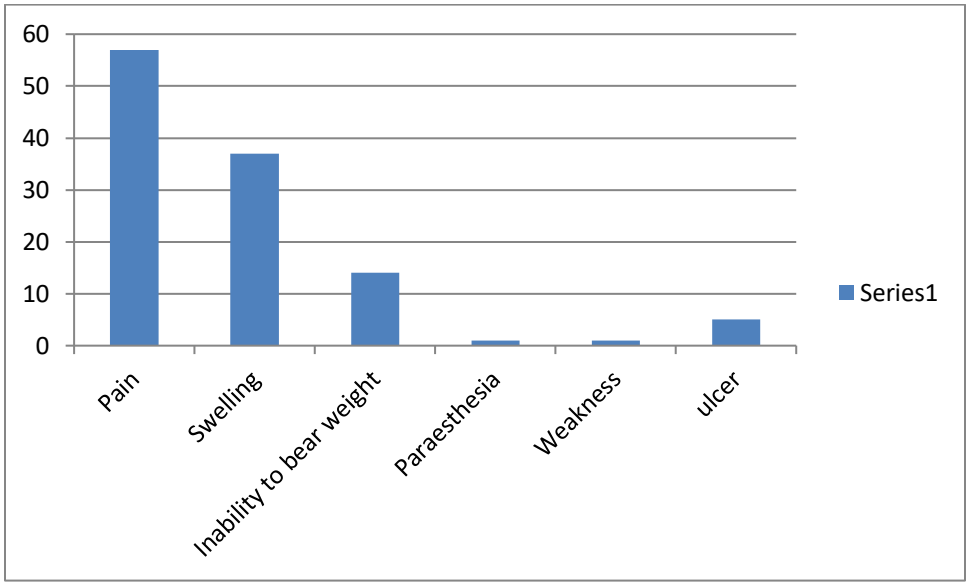


Figure 8. Signs and Symptoms

The most common presentation was pain with 57 out of the 58 patients. Swelling was noted in 65% (37/58) of the patients. Noteworthy is that all the patients who had a swelling complained that it was painful.

4.4 Clinico-radiological [Plain Radiography] Examination.

4.4.1 Bone with lesion

BONE	NUMBER	PERCENT
Cervical spine	1	2%
Thoracic spine	1	2%
Lumbar spine	3	5%
Humerus	11	17%
Clavicle	1	2%
Radius	3	5%
Ulna	2	3%
Femur	28	42%
Tibia	10	15%
Fibula	3	5%
Pelvis	3	5%
	66	

Table 3. Location of bone tumours

Most lesions were found in the bones of the lower limbs, 28 cases (42%) had lesions in the femur and 10 cases (15%) had the tibia being affected. In the upper limbs, the humerus was affected most with 11 cases (17%). The cases in lumbar spine were more than in other regions of the spine.

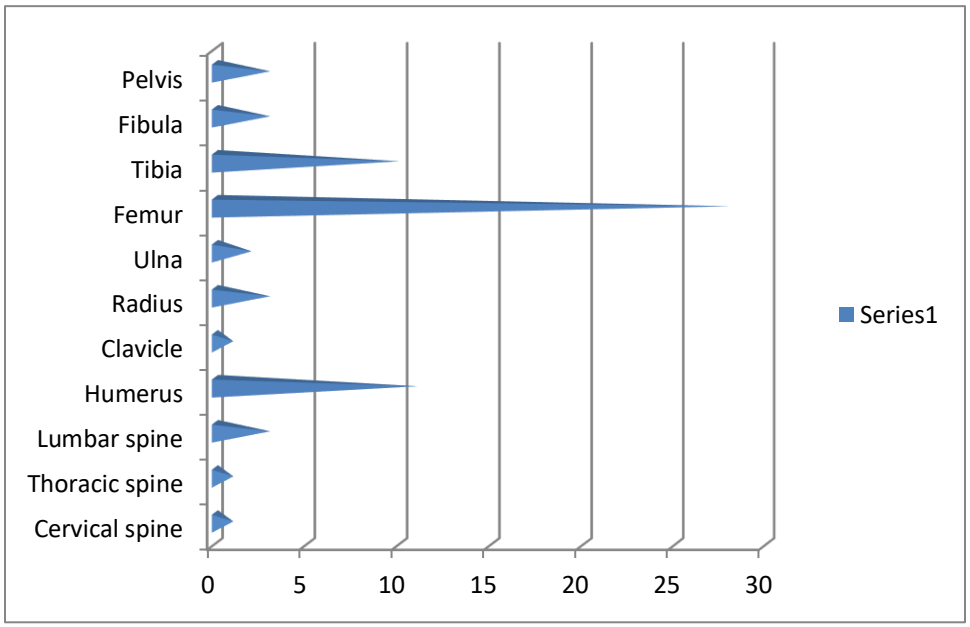


Figure 9. Graphical presentation of bone tumour location

4.4.2 Location of the lesion in bone

Bone part	Number	Percent
Epiphysis	0	
Metaphyseal-Epiphyseal	12	24%
Metaphysis	13	26%
Metaphyseal-Diaphyseal	16	32%
Diaphysis	8	16%
All Regions	1	2%

Table 4. Part of long bone affected

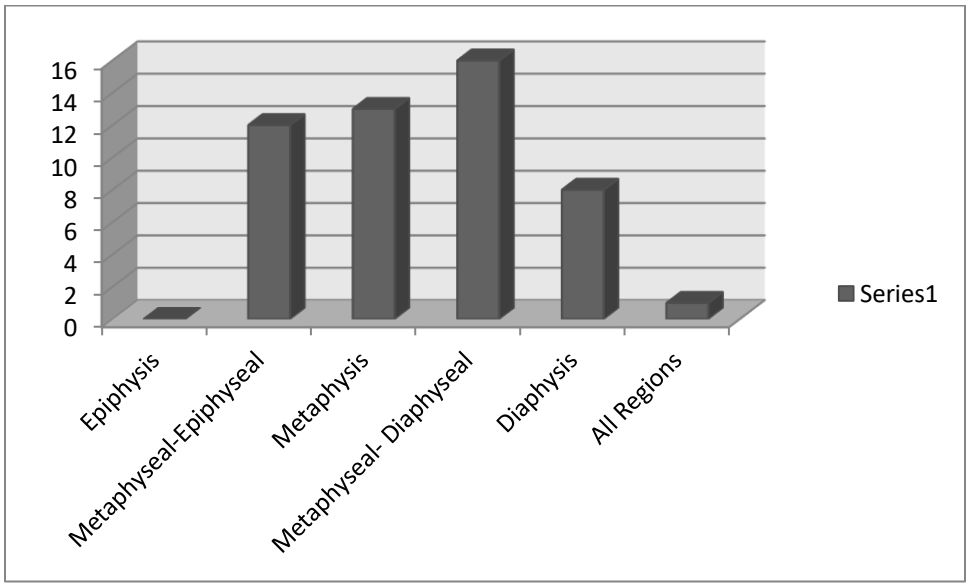


Figure 10. Graphical presentation of the regions of long bone affected.

Most 16(32%) of the cases had bone lesions spanning both the metaphysis and diaphysis (Metaphyseal-Diaphyseal region). The metaphysis and Metaphyseal-Epiphyseal regions had tumour lesions in considerable number of cases, 13 (26%) and 12 (24%) cases respectively. No cases had tumour exclusively located in the epiphysis region in our study. On transverse location, most cases (52) had tumours involving both the cortex and the medulla with only 4 just in the cortex.

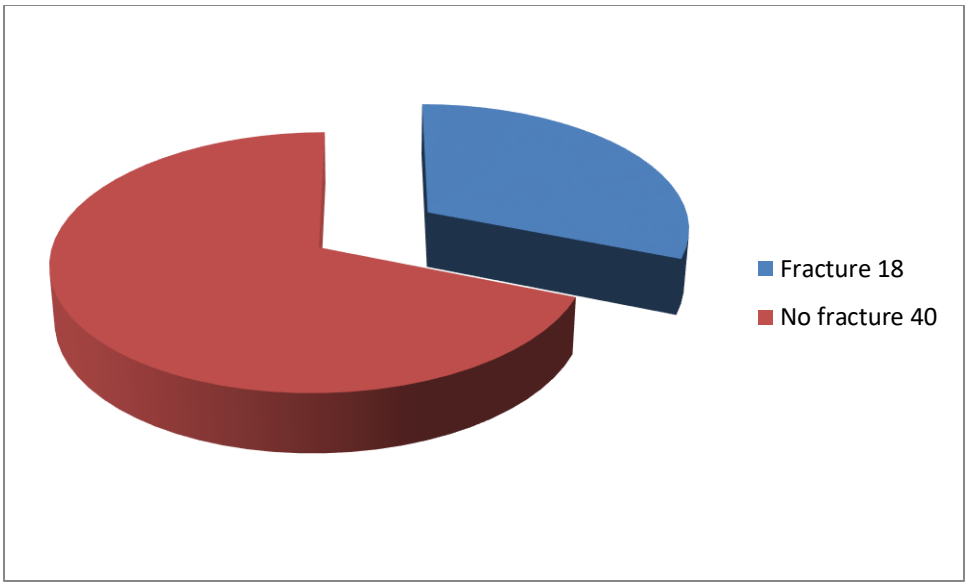


Figure 11. Number of Cases with and without fractures.

A total of 18 patients sustained Pathological fractures. Five out of the eight patients who had metastases were found to have pathological fracture. These fractures were also noted in 5 patients who were diagnosed with osteogenic sarcoma. Overall, 13 of the 18 patients had a malignant bone tumour.

4.4.3 Radiological features of Bone Tumours.

Variable	Categories	Frequency	Percent
Bone destruction	Geographic	19	32.8%
	Moth eaten	14	24.1%
	Permeative	17	29.3%
	Mixed	4	6.9%
	None	4	6.9%
Periosteal Reaction	Thin Solid	11	19.0%
	Thick Solid	4	6.9%
	Hair on end/ Sun burst	1	1.7%
	Complex[septated, disorganized, irregular]	22	37.9%
	Codman Triangle	3	5.2%
	None	17	29.3%
Zone of Transition	Wide	45	77.6%
	Narrow	13	22.4%
Matrix	Chondroid	9	15.5%
	Osteoid	22	37.9%
	Fibrous	4	6.9%
	Lytic	23	39.7%

Table 5. Plain radiography features useful in bone tumour diagnosis.

Geographic type of bone destruction was classified in 32.8% of cases followed by permeative (29.3%) and moth-eaten (24.1%) patterns. Periosteal reaction category typified by most tumours was the complex [Septate, Disorganized, Irregular] pattern, 37.9%. A majority of cases had a wide zone of transition (77.6%). There was an almost equal number of cases with osteoid and lytic types of matrix , 37.9% and 39.7% respectively.

4.4.4 Clinico-Radiological diagnoses.

	AGE GROUPS								
Clinico-Radiological Diagnoses	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-80	Grand Total
Chronic Osteomyelitis			1						1
exostosis			1						1
Giant Cell Tumor		1		1					2
Metastases					1	2	3	1	7
Metastases					1				1
Non Ossifying Fibroma		2							2
Osteochondroma		1							1
Osteogenic sarcoma	4	12	8	2	3	1	1		31
Tuberculosis								1	1
Grand Total	**4**	**23**	**11**	**3**	**7**	**4**	**4**	**2**	**58**

Table 6 . Incidence of tumours in different age groups.

The commonest tumour diagnosed after tying up both clinical and Radiographical information was Osteogenic sarcoma, 31 patients most of whom were in the second decade of life.

The other common tumours diagnosed were chondrosarcoma and aneurysmal bone cyst, 5 and 4 patients respectively. Metastases were diagnosed in 8 patients who were between age 40 and 80 years. The peak incidence of tumours in general was the age group 10-19 years.

4.5 Clinico-pathological [Histological] Findings

Histological Diagnoses	0-9yrs	10-19yrs	20-29yrs	30-39yrs	40-49yrs	50-59yrs	60-69yrs	>70yrs	TOTAL
Aneurysmal Bone Cyst	0	1	1	0	0	0	0	0	2
Chondrosarcoma	0	1	0	0	0	0	0	0	1
Chondroblastoma	0	1	0	0	0	0	0	0	1
Ewings sarcoma	0	1	0	0	0	0	0	0	1
Exostosis	0	0	1	0	0	0	0	0	1
Giant Cell Tumour	0	0	2	1	1	0	0	0	4
High grade pleomorphic Sarcoma	0	0	0	0	1	0	0	0	1
High Grade Sarcoma	0	1	0	0	0	0	0	0	1
Melanocytoma	0	1	0	0	0	0	0	0	1
Metastases	0	0	0	0	3	2	3	1	9
Neuroblastoma	0	0	0	0	0	1	0	0	1
Non small cell carcinoma	0	1	0	0	0	0	0	0	1
Non Hodgkins Lymphoma	0	0	0	1	0	0	0	0	1
Non Ossifying Fibroma	0	2	0	0	0	0	0	0	2
Osteochondroma	0	2	0	0	0	0	0	0	2
Osteosarcoma	3	13	7	1	2	1	1	0	28
Osteoid Osteoma	0	0	0	0	0	0	0	1	1
TOTAL									58

Table 7. Incidence of Tumours in different age groups

The array of diagnoses was wider after histological examination compared to radiological assessment. Osteogenic sarcoma diagnosis was arrived at in a significant number of patients, 28. Bone lesions in a good number of patients (9) were assessed and confirmed to be metastases [secondaries].

The number of patients was almost equally distributed when other tumour diagnoses were determined.

4.6 Clinico-Radiological Versus Clinico-Histological diagnosis Comparison.

	Histopathological Diagnoses																
Clinico-Radiological diagnoses	**ABC**	**CS**	**CB**	**ES**	**Exo-stosis**	**GCT**	**HGPS**	**Melano-cytoma**	**Mets**	**NB**	**NSCC**	**NHL**	**NOF**	**OC**	**OS**	**OO**	**TOTAL**
ABC	**2**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**4**
COM	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**1**
Chondro-sarcoma[CS]	**0**	**0**	**0**	**1**	**0**	**0**	**1**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**0**	**5**
Exostosis	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**
GCT	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**2**
Metastases[Mets]	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**8**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**8**
NOF	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**0**	**0**	**0**	**2**
Osteogenic-sarcoma[OS]	**0**	**1**	**0**	**0**	**0**	**4**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**25**	**0**	**31**
Osteo-chondroma[OC]	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**1**
Tuberculosis	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**
No tumour	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**0**	**2**
TOTAL	**2**	**1**	**1**	**1**	**1**	**4**	**2**	**1**	**9**	**1**	**1**	**1**	**2**	**2**	**28**	**1**	**58**

Key: ABC- Aneurysmal Bone cyst, CB-Chondroblastoma, GCT- Giant Cell Tumor, HGPS- High grade pleomorphic Sarcoma, NB-Neuroblastoma, NSCC- Non Small Cell Carcinoma, NHL- Non Hogkins Lymphoma, NOF- Non Ossifying Fibroma, OO – Osteoid Osteoma.

Table 8. Correlation between Clinico-Radiological diagnoses and Histopathological diagnoses.

Among diagnoses arrived at after clinico-radiological assessment, there was agreement mainly in Aneurysmal Bone cysts (2), Metastases (8) and Osteogenic sarcoma (25).

Some of the patients (4) who were diagnosed to have osteogenic sarcoma were found to actually have Giant cell Tumours.

Two patients who had been ruled out as having a tumour were diagnosed with Osteogenic sarcoma and Non-Small Cell Carcinoma.

Infections that were diagnosed on plain radiography as chronic osteomyelitis and Tuberculosis of the spine were determined to be osteogenic sarcoma and osteoid osteoma respectively.

4.6.1 Percentage agreement for specific radiological and histology diagnosis

Radiological diagnoses	Total Cases	Cases Correctly Diagnosed	Agreement %
Aneurysmal Bone Cyst	4	2	50%
Exostosis	1	1	100%
Metastases	8	8	100%
Non Ossifying Fibroma	2	2	100%
Osteosarcoma	31	25	81%
Osteochondroma	1	1	100%
Chondrosarcoma	5	0	0%
Chronic Osteomyelitis	1	0	0%
Giant Cell Tumour	2	0	0%
Spine Tuberculosis	1	0	0%
No Tumour/Normal	2	0	0%

Table 9: Number of cases correctly diagnosed by plain radiography

Taking histological diagnosis as the gold standard, Clinical and Radiographical assessment was able to diagnose accurately (100%) cases of Exostoses, Metastases, Non-Ossifying Fibrosis and Osteochondromas. Radiological assessment was also significantly in agreement with histological diagnosis of Osteogenic Sarcomas (81%).

4.6.2 Overall percentage agreement for radiological and histology diagnoses

Type of Tumour as per plain radiography	**Total cases**	**Number in Agreement**	**Percentage with Agreement**
Benign	12	8	66.67%
Malignant	46	44	95.65%
TOTAL	58	52	89.65%

Table 10 : Percentage agreement when cases are generally classified as either benign or malignant.

The overall percent agreement on diagnosing a bone tumour as either benign or malignant by plain radiography compared to histological diagnosis was 89.65%.

Malignant tumours were more likely to be diagnosed correctly (95.65%) compared to benign tumours (66.67%) on plain radiography. There was no statistically significant association between radiological

diagnoses [benign/malignant] and the percentage agreement between radiology finding and histological diagnosis [χ^2=0.519, p=0.4714].

4.6.3 The overall plain radiographic Sensitivity and specificity in diagnosis of Primary bone tumours.

Radiological Diagnosis	Histology Diagnosis [Gold standard]		Sensitivity	Specificity
	Malignant	Benign		
Malignant	44[TP]	2[FP]		
Benign	4[FN]	8[TN]	95.70%	80.00%
Total	48	10		

Table 11: Comparison of histological versus Radiological diagnosis of bone tumour.

The general plain radiography sensitivity for diagnosis of bone tumours was 95.70% and a specificity of 80%.

Sensitivity	95.70%
Specificity	80.00%
Positive Predictive Value (PPV)	95.65%
Negative Predictive Value (NPV)	66.67%
Diagnostic Accuracy	89.66%

Table 12: Sensitivity, specificity, PPV, NPV and Diagnostic Accuracy of Plain radiography in bone tumour diagnosis.

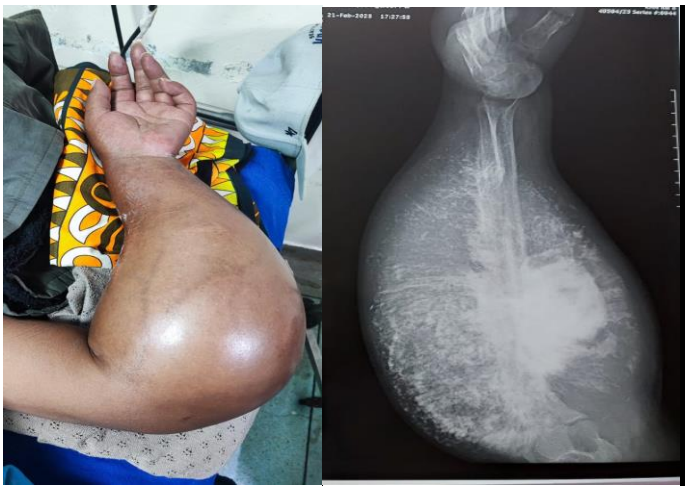


Figure 12. A 57 year old male with a painful swelling of the left forearm and elbow. The left image is a plain radiograph showing a speculated [hair-on end appearance] aggressive bone lesion involving both left radius and ulna.

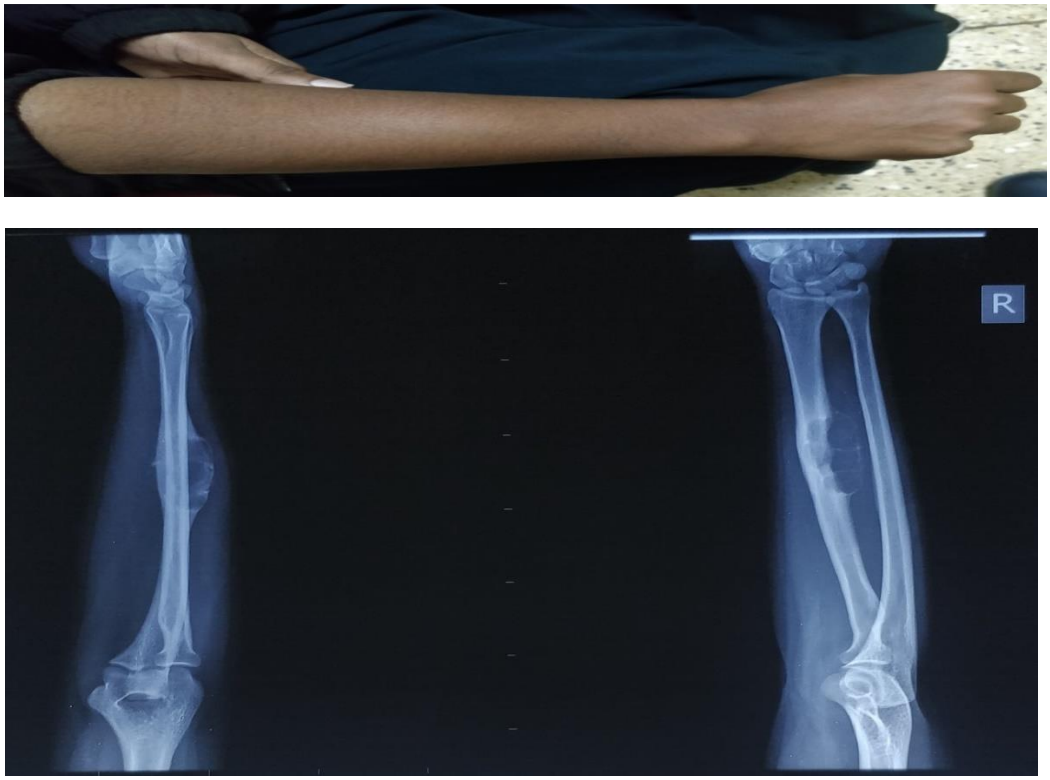


Figure 13. A 11 year old female with a tender right forearm swelling. The images below are the Anteroposterior and lateral views of her right radius and ulna including the elbow, wrist joints and part of the hand. The radius has an eccentric, expansile solitary lucent bone lesion, with thin-walled cavities

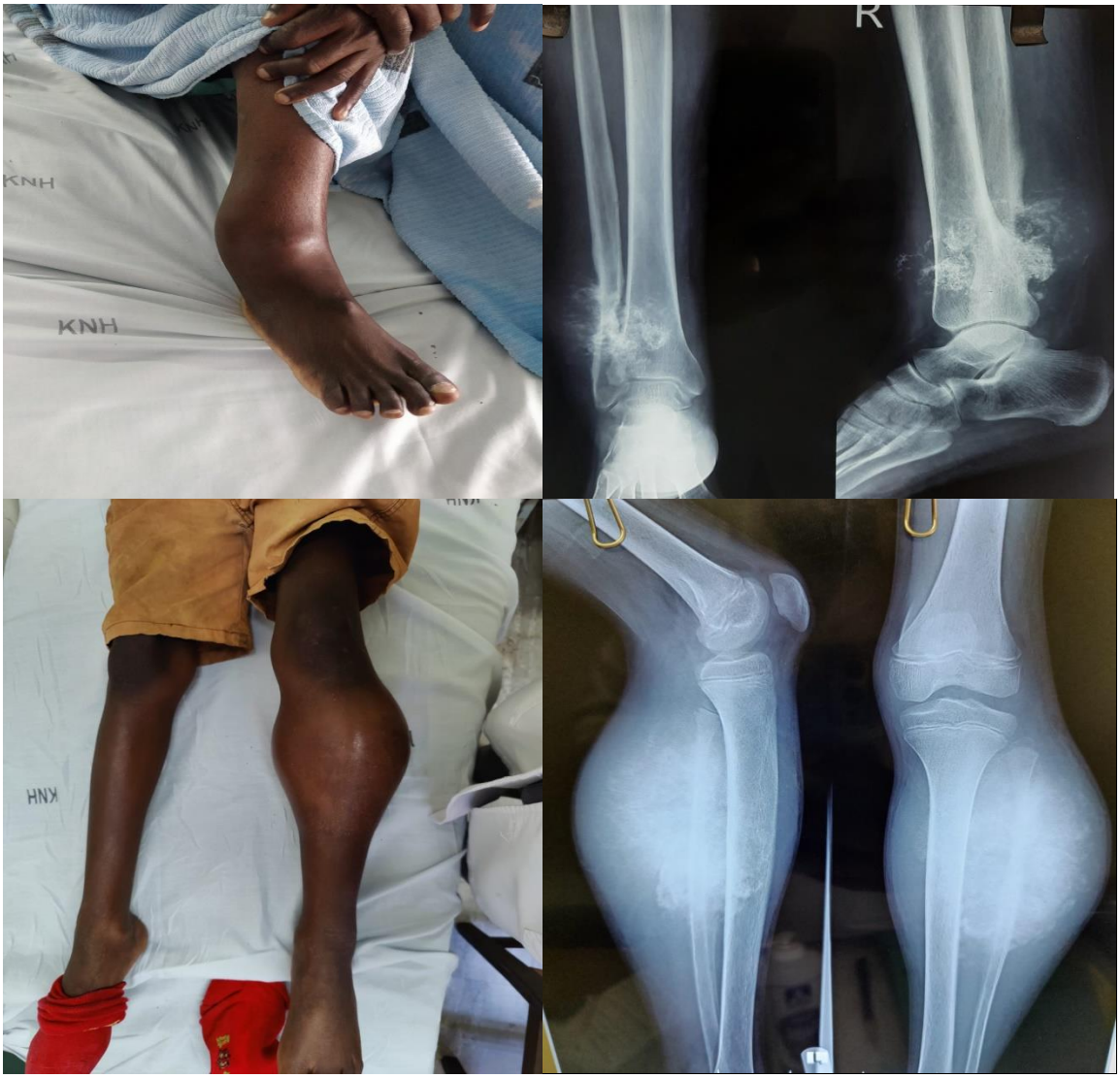


Figure 14. ***Top*****: A 39 year old male patient with painful swelling of the distal right leg. AP and lateral plain radiographs show a lesion involving the distal right fibula and tibia with cortical destruction and complex periosteal reaction.**

Bottom**: An 11 year old male with a left leg painful swelling that is rapidly progressing in size. The lesion on the radiograph involves the fibula mainly with a complex periosteal reaction, bone destruction and a wide zone of transition**

CHAPTER 5: DISCUSSION

5.1 Demographics.

A total of 58 out of the 65 patients, who were recruited in the past 1 year, fit in the inclusion criteria. The youngest patient was 6 years old and the oldest was 76 years old. The age group with the majority of bone tumours was the second decade of life (10-19) followed by the 20-29 years age group. These findings were consistent with those found in similar studies in Tanzania, England and India respectively. (15,61, 63). This increased frequency of occurrence in the preadolescent and adolescent age corresponds to the peak age of skeletal growth that is reported as 12 years for females and 14 years for males. (35)

The number of males and females was equal, 29 cases each. This was not consistent with most studies which found the male gender being slightly more affected by primary bone tumours. (15, 58, 70, 74)

5.2. Symptoms and Signs.

The most common presenting symptom was pain reported by almost all the patients, 57 out the 58 cases. This was comparable to findings in several studies. (12, 15) Swelling was reported by 37 (65%) patients. All patients who presented with a swelling reported that it was painful. This finding meant the combination of pain and swelling (37cases) predominated cared to other symptom combinations, similar to results gotten by Sakala et al.2012 [Zambia] and Bipul et al.2017 [India]. (7, 39)

5.3 Radiographic Assessment of primary bone tumours.

In general, primary bone tumours have a propensity to affect long bones of the extremities. (35) In this study, 84.4% of tumours were found in long bones. The femur was the most common location, 28 cases (42%) as was the case in comparable studies. (7,8,9,52,55,58) Metastatic malignancies represented 13.8% of all patients, noted mainly in patients who had breast and thyroid cancers as primaries. These metastatic bone tumours occurred in 4^{th}, 5^{th}, 6^{th} and 7^{th} decades. Comparable studies by Negash et al. in Addis Ababa, Ethiopia and Salazar et al. in Porto, Portugal found metastases comprised 5.5% and 17.2% of all tumours respectively. (59,74)

Majority of the primary bone tumours in terms of the longitudinal classification of location in long bones, were found in the metaphyseal-diaphyseal region (32%). This was mainly explained by the predilection of Osteosarcomas, which were the most diagnosed tumour in the study (43%), to originate in the metaphyseal region. There was paucity on comparable data that assessed the longitudinal plane location of tumours in long bones. Elshahhat et al (2017) and Pillay et al (2016) however, found out osteosarcoma mostly originated in the distal femur followed by proximal tibia and proximal humerus. (54, 55) The fact that most of the tumours occur close to the long bone epiphysis could be attributed to these being areas of maximum growth especially in the age where there is growth spurt. (1)

The bulk of the tumours were malignant and aggressive in nature as typified by the mode of bone destruction, periosteal reaction and zone of transition. Permeative bone destruction was seen in 29.3% while the moth eaten pattern was seen in 24.1% of patients. Malignant tumours, which comprised 85.7%

of tumours in this study, are rapidly growing thus more bone formation/destruction resulting in the poorly defined margins and a longer zone of transition between normal and abnormal bone.

Geographic pattern of bone destruction was found in 32.8% of cases. The cases that had this pattern were mainly benign type of tumours [aneurysmal bone cyst, Non- ossifying fibroma, osteoid osteoma] though a few aggressive types were noted such as the giant cell tumour and metastases. These tumours have a narrow zone of transition, with or without a sclerotic rim. (45)

The appearance of the matrix is an important hint to the histological diagnosis and narrowing down on the differential diagnoses. The commonest type of matrix mineralization was the lytic type at 39.7% followed by osteoid matrix at 37.9%. An osteolytic lesion with an ill-defined zone of transition is generally typical of malignant bone tumours (Ewing sarcoma, osteosarcoma, metastasis, leukemia) and aggressive benign lesions (giant cell tumour, infection, eosinophilic granuloma). (64) Osteosarcoma was the most diagnosed tumour in our study (25 cases) and 4 cases of giant cell tumours which explains the high percent of lytic lesions. This is in addition to the aneurysmal bone cysts which are benign tumours with lytic matrix.

The complex [sepatated, disorganized, irregular] type of periosteal reaction predominated (37.9%). The classical sun burst/ hair on end appearance and the Codman's triangle were noted in few cases, 1.7% and 5.2% of cases respectively. These aggressive types of periosteal reaction result when the periosteum has inadequate time to lay down and consolidate the bone formation. Malignant lesions like osteosarcoma typically cause an interrupted periosteal reaction and Codman's triangle. (64) This finding can be attributed to the high number of osteosarcoma cases.

Plain radiography diagnosed 79.3% of the cases as malignant and 20.7% as benign. Osteogenic sarcoma formed majority of the malignant bone tumours at 67.4%. Similar findings were noted in studies in Tanzania (15), Egypt (54), South Africa (55) and India (63).

5.4 Histological diagnoses

A wide variety of tumours were diagnosed after histological assessment of the biopsy specimens. A wide spectrum of 17 different histological types of tumours was diagnosed.

5.5 Comparison between radiological and histological findings.

Taking histology as the gold standard test, in this study radiology accurately (100%) diagnosed exostosis, Non-Ossifying Fibromas, Osteochondroma and metastases. Plain radiography was also able to diagnose 81% of Osteogenic sarcoma and 50% of Aneurysmal Bone Cysts. There was a disagreement whereby radiography diagnosed 5 cases as Chondrosarcoma which histology diagnosed as Ewings'sarcoma, High grade pleomorphic sarcoma, Osteogenic sarcoma, Osteochondroma and Neuroblastoma.

There were two cases where plain radiography was reported as normal (3.4%) and a case of chronic osteomyelitis (1.7%). However, these turned to be malignant bone tumours [osteogenic sarcoma and Non-small cell carcinoma] after histological assessment. The prevalence of chronic osteomyelitis was high in a study by Gerber et al. (16%) but Kharolkar V et al. found a reasonably lower prevalence of 3.3%. (72,75)

The percentage agreement between Clinico-radiological and Clinico-histological assessment in diagnosing bone tumours was higher for malignant bone tumours (95.65%) as compared to benign bone tumours (66.67%). Kimari, 1995 did a similar study at KNH and found slightly lower percentages. There

was 54.8% agreement for malignant lesions and 30% for benign bone lesions. This could be attributed to experience gained over time and the higher numbers of bone tumours being diagnosed currently as more patients present to hospitals.

Overall, Clinico-Radiological diagnosis and Clinico-Histological diagnosis were in agreement in 89.7% when tumours were classified as benign and malignant cases. This is excellent level of agreement and is comparable to Salazar et al who found 90% agreement (74). However, the overall percent agreement when the specific diagnosis of each bone tumour was considered was 67.2% (39 correctly diagnosed cases out of a total of 58 cases). Negash et al. considering all bone tumours together, his 5-year study indicated that radiological diagnosis was confirmed by histological diagnosis in 172/205 cases (84%) (59). The few cases in our study due to a shorter duration (1 year versus 5 years) and the inclusion of MRI as part of arriving at a radiological diagnosis by Negash et al. explains the disparities in the percent agreement. Kharolkar V et al in his study of 30 cases considered CT scan and MRI in addition to plain radiography. He found an 80% level of agreement between radiological and final histopathological diagnosis (75).

Plain radiography sensitivity , specificity, positive predictive value , negative predictive value and diagnostic accuracy in our study was 95.70%, 80%, 95.65%, 66.67% and 89.67% respectively. Salazar et al from an almost equal sample size got comparable values. The figures were sensitivity of 92.9%, specificity 87.5%, positive predictive value 86.7%, negative predictive value 93.3% and diagnostic accuracy of 90.0%. When MRI was utilized to arrive at the radiological diagnosis, excellent values were obtained. MRI sensitivity was 94.4%, specificity 95.7%, positive predictive value 94.4%, negative predictive value 95.7% and a diagnostic accuracy of 95.1% (74).

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusions.

1. Standard radiography, despite advances in imaging technology, remains important for establishing an accurate diagnosis for bone lesions as well as formulation of appropriate differential diagnoses owing to the wealth of information it offers, availability and accessibility.
2. The percentage agreement between radiology and histology was higher for primary malignant bone tumours (95.65%) than for primary benign bone tumours (66.67%). The overall percentage agreement between the two diagnoses was 89.7%.
3. The overall plain radiography sensitivity and specificity are 95.7% and 80% respectively in diagnosis of bone tumours.

6.2 Recommendations.

Clinicians should work in tandem with radiologists and pathologists when assessing bone lesions to arrive at an accurate diagnosis so that the right management can be offered to patients.

Where resources are lacking and histological services are not available, plain radiography should be used in diagnosis of primary bone tumours.

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CHAPTER 5: APPENDICES

Appendix 1: Data Collection Sheet.

<table>
<tr><td>Date of Data Collection: ……..</td><td>Name of Hospital: ……..</td></tr>
<tr><td colspan="2">Patient code/Serial number: ……. Date of Admission ……</td></tr>
<tr><td colspan="2">Age: ……..</td></tr>
<tr><td colspan="2">Gender: ……..</td></tr>
<tr><td>Chief presenting symptoms/complains:
1. …….
2. …….
3. …….
4. ……..</td><td>Bone(s) affected: ……

Part of bone affected:
a) Longitudinal axis
Diaphysis ☐
Diaphyseal-metaphyseal ☐
Metaphysis ☐
Metaphyseal-epiphyseal ☐
Epiphysis ☐

b) Transverse axis
Cortex ☐
Medulla ☐</td></tr>
<tr><td>Presence of pathological fracture:</td><td>Yes ☐ No ☐</td></tr>
</table>

Radiographical features:

- Type of Bone destruction : ……...
- Type of matrix mineralization: …….
- Type of Periosteal reaction: ……..
- Zone of transition: …….

Features suggestive of Benign Tumour ☐ Malignant Tumour ☐

Radiological diagnosis :	Histological diagnosis :
…….	……..

Agreement of diagnoses: Yes ☐ No ☐

A. ADULT PARTICIPANT INFORMATION AND CONSENT FORM FOR ENROLLMENT IN THE STUDY

This Informed Consent form is for patients who will be recruited to participate in the study. It will be administered to eligible patients. We are requesting you to participate in this research project whose title is "Level of agreement between Radiographical and Histological Diagnoses at Kenyatta National Hospital"

Principal Investigator: Dr. Gitau Isaac Mukuria

Institution: Department of Surgery, Orthopaedics Unit, Faculty of Health Sciences, University of Nairobi.

This Informed Consent Form has three parts:

I. Information Sheet (informs you in a brief overview about the research with you).

II. Certificate of Consent (for you to sign if you agree to take part).

III. Statement by the researcher/person taking consent.

A copy of the informed consent form will be provided.

PART I: Information Sheet

INTRODUCTION

My name is Dr. Gitau Isaac Mukuria. I am a qualified doctor, registered by the Kenya Medical Practitioners and Dentists Board. I am currently pursuing Masters of Medicine degree in Orthopaedics Surgery at University of Nairobi. I would like to recruit you into my research which is to study the level of agreement between radiographic and histopathological diagnoses of primary bone tumours at Kenyatta National Hospital.

PURPOSE OF THE RESEARCH:

I will provide information and invite you to be a participant in this research. There may be some words that you may not comprehend. Please ask me to explain as we go through the information and I will explain. After receiving the information concerning the study, you are encouraged to seek clarification in case of any doubt. This study will seek to compare the radiological and histopathological diagnosis of primary bone tumours seen at Kenyatta National Hospital. The results will help in improving care of patients.

TYPE OF RESEARCH INTERVENTION/ MATERIAL:

This research will involve use of questionnaires and medical records with your doctor's permission [or their representative], imaging results.

VOLUNTARY PARTICIPATION/RIGHT TO REFUSE OR WITHDRAW:

It is your decision to participate or not. Whether you choose to participate or not, all the services you receive at this hospital will continue and nothing will change. If you decide against participating, you will be offered the treatment that is routinely provided in this hospital for your condition. You have a choice to refuse or withdraw your participation in this study at any point.

CONFIDENTIALITY:

All information obtained in this study will be treated with utmost confidentiality and shall not be divulged to any unauthorized person. Your name will not be used. Any personal information will have a number on it instead of your name. We will not be sharing the identity of those participating in this research

STUDY PROCEDURE:

After agreeing and consenting to participate in the study you will be guided by the researcher to fill the questionnaire. Your radiology and histology results shall be followed up by the

researcher. A comparison between the radiographic and histopathology diagnosis will be determined.

SHARING THE RESULTS:

The knowledge obtained from this study will be shared with the policymakers in KNH and doctors through publications and conferences. Confidential information will not be shared.

BENEFITS:

The benefits of joining the study include:

- Contribution to the advancement of patient management.
- Improvement in the management of patients presenting with bone tumours
- There will be no risk involved by enlisting for this study

COST AND COMPENSATION:

There will be no extra cost incurred for participating in this study nor is their compensation offered.

This research proposal has been reviewed and approved by the Uon/KNH Ethics Committee, which is a committee whose task is to make sure that research participants are protected from harm.

Who to contact

If you wish to ask any questions later, you may contact:

PRINCIPAL RESEARCHER:

DR. GITAU ISAAC MUKURIA; DEPARTMENT OF SURGERY, ORTHOPAEDIC UNIT, Faculty of Health Sciences, Department of Orthopedic Surgery, UNIVERSITY OF NAIROBI

Phone: 0711460681

Email; igmukuria@gmail.com

OR

University of Nairobi /Kenyatta national hospital Supervisors:

1. Dr. Ezekiel Oburu, Consultant Orthopaedic Surgeon, Lecturer- Department of Orthopaedics, University of Nairobi,

2. Dr. John King'ori, Consultant Orthopaedic Surgeon, Lecturer- Department of Orthopaedics, University of Nairobi,

3. Dr. Callen Onyambu, Consultant Orthopaedic Surgeon, Senior Lecturer- Department of Diagnostic Imaging and Radiation Medicine, University of Nairobi.

OR

Kenyatta National Hospital _ University of Nairobi (KNH_UON) Ethical Review Committee

Email: uonknh_erc@uonbi.ac.ke

Website htttp://www.erc.uonbi.ac.ke

Facebook: https://www.facebook.com/uonknh.erc

Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERCs

PART II: Certificate of Consent

I have read and understood the above information/the above information has been read out to me. I have had the opportunity to ask questions and the questions that I have asked have been answered satisfactorily. I voluntarily agree and consent to participate in this research.

Print unique ID of Participant _____

Signature of Participant _____

Date _____

If Non -literate:

I have witnessed the reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I can confirm that the individual has given consent voluntarily.

Print Unique ID of witness_____ Thumb print of participant

Signature of witness _____

Date _____

PART III: Statement by the researcher

I have read out the information sheet to the participant, and made sure that the participant understands that the following will be done:

A decision to refuse to participate or withdrawal from the study will not in any way compromise the care of treatment.
All information given will be handled with confidentiality.

The results of this study might be published to facilitate research and improved clinical guidelines. I can confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the approval has been given voluntarily.

A copy of the Informed Consent Form has been provided to the participant.

Name of researcher/person taking consent _____

Signature of researcher/person taking consent_____

Date_____

B. PARENTAL CONSENT FOR CHILDREN

TITLE OF STUDY:

Level of agreement between Radiographical and Histological Diagnoses at Kenyatta National Hospital.

PRINCIPAL INVESTIGATOR \ AND INSTITUTIONAL AFFILIATION:

Dr Gitau Isaac Mukuria, Department of Orthopaedics surgery, University of Nairobi.

INTRODUCTION:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not your child should participate in the study. Feel free to ask any questions about the purpose of the research, what happens if your child participates in the study, the possible risks and benefits, the rights of your child as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide if you want your child to be in the study or not. This process is called 'informed consent'. Once you understand and agree for your child to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a medical research:

i) Your child decision to participate is entirely voluntary

ii) You child may withdraw from the study at any time without necessarily giving a reason for his/her withdrawal

iii) Refusal to participate in the research will not affect the services your child is entitled to in this health facility or other facilities.

May I continue? YES / NO

For children below 18 years of age we give information about the study to parents or guardians. We will go over this information with you and you need to give permission in order for your child to participate in this study. We will give you a copy of this form for your records.

If the child is at an age that he/she can appreciate what is being done the he/she will also be required to agree to participate in the study after being fully informed).

WHAT IS THE PURPOSE OF THE STUDY?

The researchers listed above are interviewing individuals who have a confirmed diagnosis of bone tumour. The purpose of the interview is to compare radiological and histological diagnoses among patients confirmed to have bone tumours. Participants in this research study will be asked questions about their age and symptoms.

There will be approximately 51 participants in this study randomly chosen. We are asking for your consent to consider your child to participate in this study.

WHAT WILL HAPPEN IF YOU DECIDE YOU WANT YOUR CHILD TO BE IN THIS RESEARCH STUDY?

If you agree for your child to participate in this study, the following things will happen:

You will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately 5 minutes.

You will be informed about the results.

We will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others.

ARE THERE ANY RISKS, HARMS, DISCOMFORTS ASSOCIATED WITH THIS STUDY

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify your child in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting confidentiality can be absolutely secure so it is still possible that someone could find out your child was in this study and could find out information about your child.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview. All study staff and interviewers are professionals with special training in these examinations/interviews.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

Information you provide will help us better understand the importance of collaboration of different medical disciplines in diagnosis of bone tumours. This information is a major contribution to science and general management of bone tumours.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

This study would not cost you anything.

IS THERE REIMBURSEMENT FOR PARTICIPATING IN THIS STUDY?

There is no reimbursement for participation.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about your child participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your child's rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to have your child participate in this research is voluntary. You are free to decline or withdraw participation of your child in the study at any time without injustice or loss of benefits.

Just inform the study staff and the participation of your child in the study will be stopped. You do not have to give reasons for withdrawing your child if you do not wish to do so. Withdrawal of your child from the study will not affect the services your child is otherwise entitled to in this health facility or other health facilities.

CONSENT FORM (STATEMENT OF CONSENT)

The person being considered for this study is unable to consent for him/herself because he or she is a minor (a person less than 18 years of age). You are being asked to give your permission to include your child in this study.

Parent/guardian statement:

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered by him or her in a language that I understand. The risks and benefits have been explained to me. I understand that I will be given a copy of this consent form after signing it. I understand that my participation and that of my child in this study is voluntary and that I may choose to withdraw it any time.

I understand that all efforts will be made to keep information regarding me and my child's personal identity confidential.

By signing this consent form, I have not given up my child's legal rights as a participant in this research study.

I voluntarily agree to my child's participation in this research study:

Yes No

I agree to have my child undergo _____ testing: Yes No

I agree to have (define specimen) preserved for later study: Yes No

I agree to provide contact information for follow-up: Yes No

Parent/Guardian signature /Thumb stamp: _____ Date _____

Parent/Guardian printed name: _____

RESEARCHER'S STATEMENT

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given his/her consent.

Printed Name: _____ Date: _____

Signature: _____

Role in the study: _____ [i.e. study staff who explained informed consent form.]

Witness Printed Name (If witness is necessary) _____

Signature: _____ Date; _____

C. FOMU YA IDHINI: KISWAHILI VERSION

Jina langu ni Gitau Isaac Mukuria, mwanafunzi wa shahada ya uzamili katika chuo kikuu cha Nairobi, Utaalamu wa upasuaji wa mifupa

Nafanya Utafiti huu ili kueleza uwiano kati ya matokeo ya picha(x-ray) ya mifupa kwa

walio na saratani ya mifupa ikilinganishwa na matokeo ya maabara ya sehemu

ndogo ya mfupa.

Utafiti huu hauna madhara yoyote kwako.

Matokea tukoka utafiti huu utatusaidia kuboresha matibabu ya wangonjwa wa shida kama yako kwenye hospitali yetu.

Ni muhimu kuelewa kuwa ushiriki ni wakujitolea na sio lazima kushiriki. Pia waweza kubadili nia yako kuhusu kuendelea kushiriki wakati wowote, bila kuathiri huduma zako za afya.

Nimekubali kwamba nimeelezwa kikamilifu kuhusu utafiti huu na nimekubali kushiriki.

Sahihi ya mshirika_____

Tarehe _____

Nimethibitisha ya kwamba nimetoamaelezo sahihi kwa mhusika pana ya utafiti, naye mhusika ametoa uamuzi wa kushiriki bila ya kushurutishwa.

Sahihi ya mchunguzi_____

Tarehe_____

iii) Administrative consent to conduct study

Dr Gitau Isaac Mukuria

H58/10977/2018

Department of Surgery, Orthopaedic Unit

Faculty of Health Sciences, University of Nairobi

Phone: 0711460681

Email:igmukuria@gmail.com

Date: 10/6/2022

To,

Deputy Director,

Medical Research,

Kenyatta National Hospital.

Dear sir/ma'am

Re: AUTHORIZATION TO CONDUCT RESEARCH STUDY

I am an Orthopaedic resident at the University of Nairobi undertaking Masters of Medicine Orthopaedic and Trauma surgery and equally the principal researcher in this study. This research is undertaken as a thesis for part fulfilment of my requirements for graduation. I hereby seek authorization to conduct research study entitled, "Level of agreement between Radiological and Histological Diagnoses among patients with bone tumours". The study aims to identify how the abductor muscles are injured during surgery with a goal of improving outcomes, policy and practice in our set up.

The data for this research will be collected from Orthopaedic clinics using a structured data collection tool. The study will be carried out at Kenyatta National Hospital. The principal researcher, myself, and research assistants, will be the one collecting the data.

To prevent Covid 19 transmission during data collection, hand sanitizer will be provided to the patient and research participants and masks will be won out throughout the examination process

This study was approved by the KNH-UON ERC under approval number _____ in a letter referenced, _____ dated _____ as seen in the attachments.

Yours sincerely,

Dr Gitau Isaac Mukuria,

Orthopaedics Registrar, University of Nairobi.

BONE TUMOURS: LEVEL OF AGREEMENT BETWEEN RADIOLOGICAL AND HISTOLOGICAL DIAGNOSES

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BONE TUMOURS: LEVEL OF AGREEMENT BETWEEN RADIOLOGICAL AND HISTOLOGICAL DIAGNOSES

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