HISTOPATHOLOGIC PATTERNS OF PRIMARY BONE TUMORS AND TUMOR LIKE LESIONS IN JIMMA UNIVERSITY MEDICAL CENTER, JIMMA, SOUTH WEST ETHIOPIA: A FIVE YEAR CROSS SECTIONAL RETROSPECTIVE STUDY.

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A RESEARCH PAPER TO BE SUBMITTED TO JIMMA UNIVERSITY DEPARTMENT OF PATHOLOGY FOR PARTIAL FULFILLMENT OF SPECIALITY IN HUMAN ANATOMIC PATHOLOGY

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JIMMA, ETHIOPIA

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ADVISORS: DR. GEBI NEMO (MD, ASSISTANT PROFESSOR OF PATHOLOGY)

DR. MULUSEW GERBABA (BSC, MPH, PhD)

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Abstract

Background: *Great morphologic diversity and clinical behaviors were exhibited by primary bone tumors—from benign to aggressively malignant. Overall, matrix-producing and fibrous tumors are the foremost common, and among the benign tumors, osteochondroma and fibrous cortical defect occur most often. Osteosarcoma is that the commonest primary bone cancer, followed by chondrosarcoma and Ewing sarcoma. Benign tumors greatly outnumber their malignant counterparts, particularly before the age of 40 years; bone tumors in elderly persons are far more likely to be malignant. Most bone tumors develop during the primary several decades of life and have a propensity to originate within the long bones of the extremities.*

Methods: *A cross sectional retrospective descriptive study design was applied for patients seen at JUMC pathology department services with primary bone tumors and tumor like lesions from September 2014 to August 2019. Data was collected using structured check lists from the patient's biopsy report record in pathology department manually by histopathology technicians working in the department. Data was entered into Epi data v.3.1. , cleared and exported to SPSS V.26 for analysis. Descriptive statistics such as frequency, percentage, mean and cross tabulation were used for analysis.* Before the study begins ethical clearanc*e was obtained from the Institutional Review Board (IRB) of JUMC.*

Result *A total of 121 cases of primary bone lesions were diagnosed between August 2014 and September 2019 at pathology department, JUMC South West Ethiopia. Seventy five (61.79%) were males and 46(38.21%) were females patients with male to female ratio of 1.63:1 with mean age of 22.57±15.17 years and age range of 1-85 years. Sixty-four cases (53.71%) were benign, 21(16.53%) were tumor like lesions, and 36(29.75%) were malignant. Osteochondroma is the most common of all tumors, 34 cases (28.10%) and the most common benign tumor representing 53.71%. Osteosarcoma is the most common malignant tumor, 30 cases (24.79%) of all lesions and 83.33% of malignant tumors.*

Conclusion: *The result of this study showed that the distribution of primary bone lesions varies with age, sex and anatomic site. Cartilage forming tumors are the most common primary tumors of bone. The most common benign tumor is osteochondroma followed by chondroma and the most common malignant tumor is osteosarcoma followed by chondrosarcoma.*

Key words: histopathologic patterns, primary bone tumors, tumor like lesions, JUMC

ABBREVATION AND ACRONYMS

ABC--------------------------Aneurysmal bone cyst

JUMC--------------------------Jimma University Medical Centre

WHO--------------------------world health organization

SPSS--------------------------Statistical Package for the Social Science

EPI info--------------------------Epidemiological information

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Chapter one: Introduction

Bone consists of cartilaginous, osteoid, fibrous tissue, and bone marrow elements. Each tissue can give rise to benign or malignant tumors. Bone tumors are classified on the idea of cell type and recognized products of proliferating cells. Bone tumors may be primary which originate in the bone or secondary (1).

Primary bone tumors are comparatively uncommon among the wide array of human neoplasms. This has contributed to a paucity of meaningful data concerning the relative frequency and incidence rates of the various subtypes of bone tumors, as well as only a rudimentary understanding of risk factors (2).

Bone tumors are categorized into three major subtypes: benign, locally aggressive, and malignant. Benign tumors are defined as having a limited growth potential. Examples of tumors in this category include osteoid osteoma and chondroblastoma. Intermediate, locally aggressive tumors are subdivided into two groups. The first are those tumors that often recur in an infiltrative, locally destructive manner but do not have any evident potential to metastasize. The exemplary lesion in this category is grade 1 chondrosarcoma. The second group of intermediate tumors, in addition to having locally aggressive recurrence, has the capacity for distant metastasis although the risk for such metastasis is minimal, typically less than 5%. The prototypic tumor of this category is a conventional giant cell tumor of bone, which may occasionally metastasize, typically to the lung. Malignant tumors are defined by their ability to grow locally in a destructive pattern, as well as to have a high propensity for both local recurrence and distant metastasis. Many of the tumors in this category have a risk for distant metastasis exceeding 20%; in some of them the metastasis develops in virtually every instance without therapeutic intervention. The recommended grouping of bone tumors into these three categories does not correspond to histologic grading. Specifically, it is important to mention that the intermediate category in this grouping does not correspond to the histologic intermediate grade (3).

Tumor-like lesions of bone are lesions having appearance and cytogenetic characteristics of neoplasm but their clinical behavior supports a non-neoplastic nature and currently categorized tumors of undefined neoplastic nature. Significance of the tumor-like bony lesions is that, they

are very common and their radiological appearance mimics that of true bone tumors including malignant lesions (4).

Great morphologic diversity and clinical behaviors were exhibited by primary bone tumors—from benign to aggressively malignant. Overall, matrix-producing and fibrous tumors are the foremost common, and among the benign tumors, osteochondroma and fibrous cortical defect occur most often. Osteosarcoma is that the commonest primary bone cancer, followed by chondrosarcoma and Ewing sarcoma. Benign tumors greatly outnumber their malignant counterparts, particularly before the age of 40 years; bone tumors in elderly persons are far more likely to be malignant. Most bone tumors develop during the primary several decades of life and have a propensity to originate within the long bones of the extremities. Nevertheless, specific tumor types target certain age groups and anatomic sites; these associations are often helpful in arriving at the right diagnosis. For instance, most osteosarcomas occur during adolescence, with half arising round the knee, either within the distal femur or proximal tibia. By contrast, chondrosarcomas tend to develop during mid- to late adulthood and involve the trunk, limb girdles, and proximal long bones (5).

A proper histopathological diagnosis is beneficial in confirming the diagnosis and helps in staging the tumor and aid the surgeon in planning limb salvage surgery for early malignant and benign bone lesion (3).

Histopathological assessment of a bone tumor needs to take into account the clinical background and features of the lesion, its radiological appearances and the results of relevant laboratory investigations. Relevant clinical information should be provided on the pathology request form and its content should be recorded in the final pathology report. The age of the patient is crucial for bone tumor diagnosis as a number of bone tumors, both benign and malignant, tend to develop most commonly within a given age range. Some tumors and tumor-like lesions have a predilection to arise in certain bones. Most bone tumors present with bone pain and swelling. Rapid growth is characteristic of some malignant tumors but is also seen in some benign tumors and tumor-like lesions. Radiological information is essential for bone tumor diagnosis (6).

1.1. Statement of the problem

The precise incidence of primary bone tumors and tumor-like lesions is not known because many benign bone lesions are not biopsied for histopathological analysis (7). Primary bone sarcomas are rare representing 0.2% of all human neoplasms (2). The overall annual incidence rate for bone sarcomas in North America and Europe is 0.8 per 100000 populations. Somewhat higher incidence rates were reported in Argentina and Brazil (1.5-2) and Israel (1.4) per 100000 populations (8).

Bone tumors and tumor-like lesions are found to occur mainly between the primary and fourth decades of life. It is therefore clear that these tumors have a potentially devastating effect on the most productive segment of the population (9).

Histopathological study enables us to understand the spectrum of bone lesions and gives an idea of different bone tumors and tumor-like lesions in population among different age group and sex. Bone lesions often pose diagnostic challenges to surgical pathologists. Therefore, an integrated approach involving radiographic, histologic, and clinical data are necessary to form an accurate diagnosis and to determine the degree of activity and malignancy of each lesion (10).

Literature on bone tumors in Africa is scarce. bone tumors represented 0.53% of all cancers seen in a hospital-based registry in Nigeria and 2.3% of the childhood cancers, with the most affected group being between ages 10 and 14 years In a study from Uganda analyzing data from the 1960s, osteosarcoma was found to be the most common primary malignant bone tumor with a peak age of 10 to 19 years (11).

1.2. Significance of the study

Conducting research on histopathologic patterns of primary bone tumors and tumor like lesions in South west Ethiopia, JUMC may provide baseline information on the topic which is scarce in the region. May help health professionals on gaining knowledge on histopathologic patterns of primary bone tumors and plan treatment. The final result will serve as baseline information for individuals who are willing to do further research on the area.

Chapter two: Literature review
2.1. Common bone tumors along with age, sex, anatomic site distribution

Study done in Texas, USA shows, bone tumors have a remarkably consistent predilection for certain skeletal sites and even for precise localization in specific bones, thus, anatomic localization can provide important clues to diagnosis. For example, osteosarcoma mostly occurs around knee joint (12) and one study done in Italy shows, proximal end of humerus is the most common location for chondroblastoma (13). Bone tumor incidence and mortality is higher in males than in females at all age groups, with a peak ranging from 15- 20 years, then a low level in young adult life and a steady increase after 40 years of age (14). Although as a group, bone tumors affect all ages and can arise in virtually every bone, specific types of bone tumors target certain age groups and anatomic sites. Benign tumors have their greatest frequency within the first three decades of life, whereas in elderly, a bone tumor is likely to be malignant. For instance, most osteosarcomas occur during adolescence and about half arise around knee. In contrast, chondrosarcomas tend to develop in mid to late adult life and involve trunk, limb girdles and proximal long bones. Malignant fibrous histiocytoma (including fibrosarcoma) and chordoma occur but rarely and show a gradual increase in incidence with age and occur most frequently in patients older than 50 years of age (2).

Study done in England showed different morphologic patterns of bone sarcomas. Osteosarcoma accounts for 34.2%; chondrosarcoma, 27.2%; Ewing sarcoma, 19.3%; other, 19.4%. The distribution varied by age. Ewing sarcoma was most common in 0-9-year old, osteosarcoma in 10-29-year old and chondrosarcoma in 30-84-year-old. Twenty-nine point two (29.2%) of all tumors occurred in 0-24-year-old. Highest incidence of osteosarcoma and Ewing sarcoma in females was in 10-14-year olds. In males, peak incidence occurred at 15-19 years and exceeded that in females. Chondrosarcoma incidence steadily increased with age. The proportions of Ewing sarcomas occurring in respective bones were consistent with those of the adult skeleton by weight. In osteosarcoma tumours of long bones of lower limb were markedly over-represented in the adolescent peak, being six times more than at any other site. Variation in incidence patterns with age and site suggests pubertal bone growth to be a key factor in osteosarcoma while different biological pathways could be relevant for Ewing sarcoma (1).

In Sweden, in 10 years from a group of 832 cases of malignant primary bone tumors; osteosarcoma is 28.8%, chondrosarcoma is 22.9% and Ewing's sarcoma is 8.8%. All three tumors showed a predilection for males (15).

Study shows that in North America and Europe, the incidence rate for bone sarcomas in males is approximately 0.8 new cases/100,000 populations. The incidence rate is higher on males in Argentina and Brazil (1.5-2/1=M/F) and Israel (1.4/1=M/F). From histological point of view osteosarcoma is the most common primary malignant tumor of bone, accounting for approximately 35%, chondrosarcoma (25%), Ewing sarcoma (16%(16).

The distribution of histological type for primary bone cancer in Japan showed osteosarcoma accounting for approximately 40% (17). The second-most frequent malignant tumor was Chondrosarcoma accounting for approximately 25%. Ewing sarcoma accounting for approximately (10%) was the third-most frequent Malignancy. Fibrous histocytoma and giant cell tumor accounted for approximately 6 and 2%, respectively (18).

Study done in India on 62 cases shows 66.01% was benign bone lesions, 17.71% was malignant bone tumors and 16.1% was tumor-like lesions. Out of the 62 cases of neoplastic bone lesions, the most common benign and malignant tumors were osteochondroma 22 (35.42%) and osteosarcoma 7(11.27%), respectively; while the most common tumor-like lesion was fibrous dysplasia five (8.05%). Among the benign lesions, osteochondroma was seen in 53.65%; giant cell tumor in 21.95%; and osteoma, osteiodosteoma, and chondroma in 4.87% each. Osteoblastoma, chondroblastoma, chondromyxoid fibroma, and desmoplastic fibroma accounted for 2.43% each. Of the 11 (17.71%) malignant tumors, osteosarcoma was seen in 63.63%, metastatic adenocarcinoma in 18.18% and chondrosarcoma and metastatic squamous cell carcinoma in 9.09% each. Out of 10 (16.1%) tumor-like lesions, fibrous dysplasia was seen in 50%, aneurysmal bone cyst in 40% and non-ossifying fibroma in 10%.

The age range of neoplastic bone lesions was from 8 years-74 years, in which 34 (55%) were males and 28 (45%) were females with M: F ratio of 1.2:1.

 The peak incidence for most lesions was between 2nd and 3rd decade of life accounting for 47 (75.8%) cases. The most common site of occurrence of tumor was in the femur 19 (30.6%) followed by tibia 18 (29%). Osteochondroma mostly involved the tibia (45.4%) whereas

Osteosarcoma mostly involved the femur (71.4%) and fibrous dysplasia commonly involved the femur and tibia equally (40% each) (19).

Study done in Ife-Nigeria on a total of 6,464 cases of neoplastic conditions shows 38.4% was benign and 61.6% was malignant. Hundred cases (1.55% of all cases seen) were selected for this study of which 57 were males and 43 were females giving a male to female ratio of 1.3:1. The average annual incidence of primary bone tumors during this period was 7.7%.

Fifty cases (50%) were primary malignant bone tumors and the age range was 8 to 76 years with a mean age of 35.4 years and a peak incidence in the second decade of life. Osteosarcoma was the most common primary malignant bone tumor which is 42%. The mean age at a diagnosis for osteosarcomas was 21.33 years and majorities (76.2%) were seen in the second and third decades of life. Nine cases occurred in the distal third of the femur (42.86%), three in the distal tibia (14.28%), three in the proximal tibia (14.28%), two in the mandible (9.52%) and one case each in the proximal third of the femur, the maxilla, humerus and calcaneus (4.76% each). Twenty eight cases (28%) were benign and the age range was 4 to 60 years. Osteochondroma was the most common benign tumors seen and accounted for 32.1% of all benign bone tumors. The commonest site was tibia contributing 33.3% of all cases. Twenty two cases (22%) were tumor-like conditions. The age range was 9 to 65 years with a mean age of 31.5 years. The commonest site for tumor-like lesions was the maxilla representing 50% of cases and the most frequent variant was fibrous dysplasia with 36.4% (20).

In Tanzania, one study shows of 80 patients treated for primary bone tumors; the mean age at diagnosis is 12 years with male: female ratio 1.4:1. Seventy one percent was malignant. The most common diagnosis was osteosarcoma (61.2%) and chondrosarcoma (10%). Benign diagnoses included osteochondroma (11.2%), giant cell tumor, and cavernous hemangioma (3.8% each). Other less common diagnoses included chondromyxoid fibroma, enchondroma, chondroblastoma, fibrous histiocytoma, and solitary aneurysmal bone cyst. The long bones of the lower extremity were most commonly affected, with (40%) in the femur and (8.8%) in the tibia. Other locations included the humerus (7.5%), phalanges (4 tumors, 5%), scapula (3 tumors, 4%), and clavicle (3 tumors, 4%). The vertebral column, calcaneus, and talus were affected in one patient each (21).

Study done in Ethiopia at Black Lion Hospital shows 89% of the biopsied bone lesions were neoplastic whereas (11%) of the lesions were non neoplastic conditions. Primary tumors accounted for 94.5% of the neoplastic lesions. Metastasis was diagnosed in 5.5% of the neoplasms.

Benign lesions accounted for 57% and malignant lesions for 43 % of the primary neoplasms. The histological diagnosis shows 36.1% of the tumors are malignant:(22%)osteosarcoma, 5.36 % Ewing's sarcoma, 0.5% leiomyosarcoma, 2.0% lymphoma, 1% malignant fibrous histiocytoma and 0.5% spindle cell neoplasm. The median age at diagnosis is 19 years with male to female ratio 1.08:1 (22).

Other study done in Black lion Hospital on six hundred and eighty-nine patients; shows 400 (58%) had benign tumors and 289(42%) were malignant. Forty two percent of patients had malignant tumours giving a benign to malignant ratio of 1.4:1. Osteochondroma was the most common benign bone tumor with 36.5% followed by chondroma (20.5%), Giant cell tumor (13.75%), Osteoma (11.5%), and others (17.75%). Osteosarcoma constitutes 35.1% of all primary malignant bone neoplasms, followed by chondrosarcoma (27.1%), Ewing's Sarcoma (11.1%), Multiple myeloma and fibrosarcoma (8.9% each), and others (8.9%). Metastatic neoplasms are much more common than are primary malignant tumours of bone in Western English literatures. In this material metastatic neoplasms (64 cases) were preceded by osteosarcoma (79 cases). In this study, 74% of benign and 47% of malignant bone and articular cartilage tumours occurred in the age group between 10 and 29 years of age with males out numbering females in most cases (23).

2.2. Conceptual framework
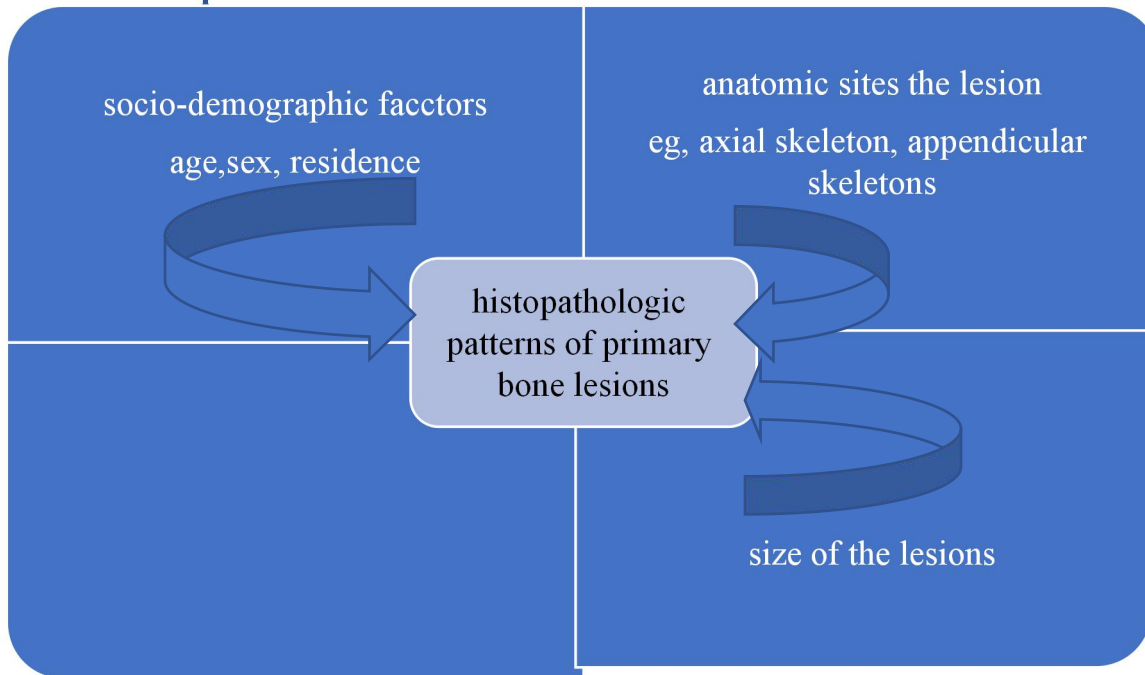
Chapter three: Objective
3.1. General objectives

To describe the histopathologic patterns of primary bone tumors and tumor like lesions in Jimma University Medical center from September 2014-August 2019.

3.2. Specific objectives

To assess the distribution of histopathologic patterns of primary bone tumors and tumor like lesions among age groups.

To describe the site of occurrence of histopathologic patterns of primary bone tumor and tumor like lesions.

To describe the distribution of histopathologic patterns of primary bone tumors and tumor like lesions among gender.

Chapter 4: Methods

4.1. Study Area and period

Study was conducted in Jimma University Medical Center, pathology department, located in Jimma town, south western part of Ethiopia, from September 2014 to August 2019. Jimma Zone has a total population of 120,960, of whom 60,824 are men and 60,136 women. With an area of 50.52 square kilometers, Jimma city has a population density of 2,394.30 all are urban inhabitants. A total of 32,191 households were counted in this Zone, which results in an average of 3.76 persons to a household, and 30,016 housing units (24). JUMC serves a total population of around 15 million populations annually. The pathology department of JUMC has four pathology seniors, 14 residents, and two histopathology technician and seven assistant technicians. Services given by the pathology department of JUMC include histopathology with average number of biopsies above 1600, FNAC above 5000 and Hematopathology and fluid 200-300 cases annually. The study will be conducted from May to August 2020.
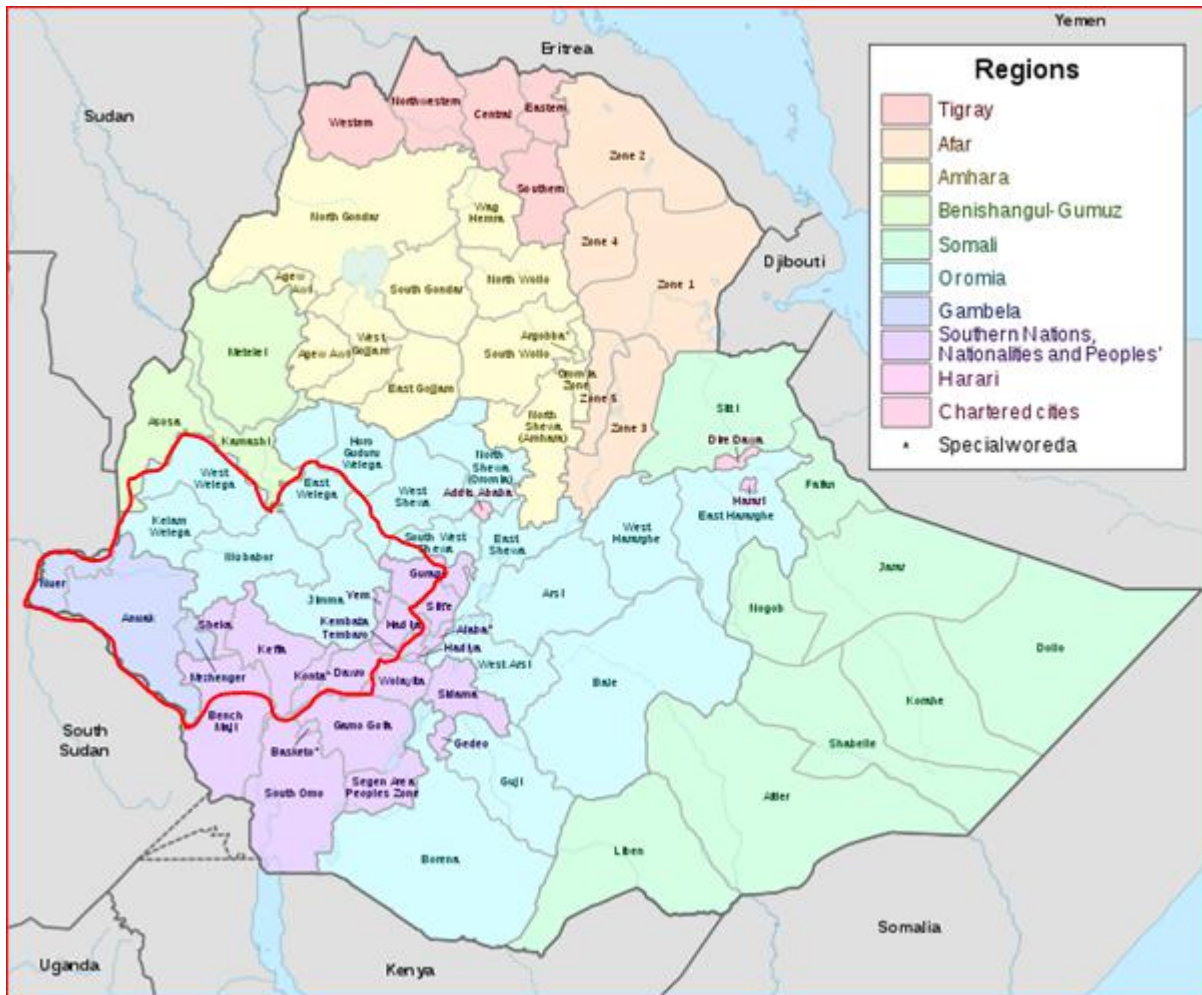
Figure 1: study area map.

4.2. Study Design

Facility based descriptive cross sectional retrospective study design was applied.

4.3. Population

4.3.1 Target population

The population of South West Ethiopia.

4.3.2. Source population

All patients for whom biopsy is requested and histopathologic diagnoses were made between September 2014 and August 2019.

4.3.3. Study population

All patients with bone lesions for whom biopsy was done; from September 2014 to August 2019 fulfilling inclusion and exclusion criteria.

4.4. Inclusion and Exclusion criteria

4.4.1. Inclusion criteria

All biopsy report records on bone lesions having; Age, Sex, address, site and diagnosis.

4.4.2. Exclusion criteria

1) Records which missed at least two or more of the variables: - age, sex, site.

2) Bone lesions with a diagnosis of inflammatory conditions and

3) Secondary bone tumors are also excluded from the study.

4.5. Sampling technique

Conveniently, all biopsy records with bone lesions on biopsy request form from September 2014 to August, 2019 were identified. Case fulfilling the inclusion criteria and exclusion criteria were reviewed.

4.6. Data collection procedures

Data was collected using structured check lists from the patient's biopsy report record in pathology department manually by technicians working in the department. Socio-demographics of the patients, location of the lesion and diagnosis were collected from patients' biopsy report records. One supervisor from junior pathology residents and three data collectors from histopathology technician were enrolled. Training was given for data collectors and supervisor on objective of the study, data collection tools and procedures. The principal investigator supervised data collection daily.

4.7. Study variables

Age

Sex

Address

Site

Histopathologic diagnosis

4.8. Data processing and Analysis

Data was entered into Epi data v.3.1., cleared and exported to SPSS V.26 for analysis and descriptive statistics such as frequency, percentage, mean and median was used for analysis. Cross-tabulation was done to measure degree of association between variables. Result was presented using narration, tables and figures.

4.9. Data quality management
Data was collected by trained histopathology technicians and completeness, accuracy and clarity of collected data was checked carefully by the principal investigator and supervisor on daily basis.

4.10. Ethical consideration
Before the study begins ethical clearance was obtained from the Institutional Review Board (IRB) of JUMC. Before conduct of the study permission was also obtained from pathology department. Name of patient was excluded on all information obtained from patients and confidentiality was ensured.

4.11. Operational definition
Tumor like lesions- bone lesions with undefined neoplastic behavior

Chapter 5: Results

The total number of biopsy seen at JUMC Pathology department in these five years is 7925 cases. A total of 121 bone lesions fulfilling inclusion and exclusion criteria were included in this study which were seen between August 2014 and September 2019 which accounts for 1.53% of total biopsies. Eighteen (19) cases in 2014/15, 17 cases in 2015/16, 20 cases in 2016/17, 35 cases in 2017/18 and 31 cases in 218/19 are seen.
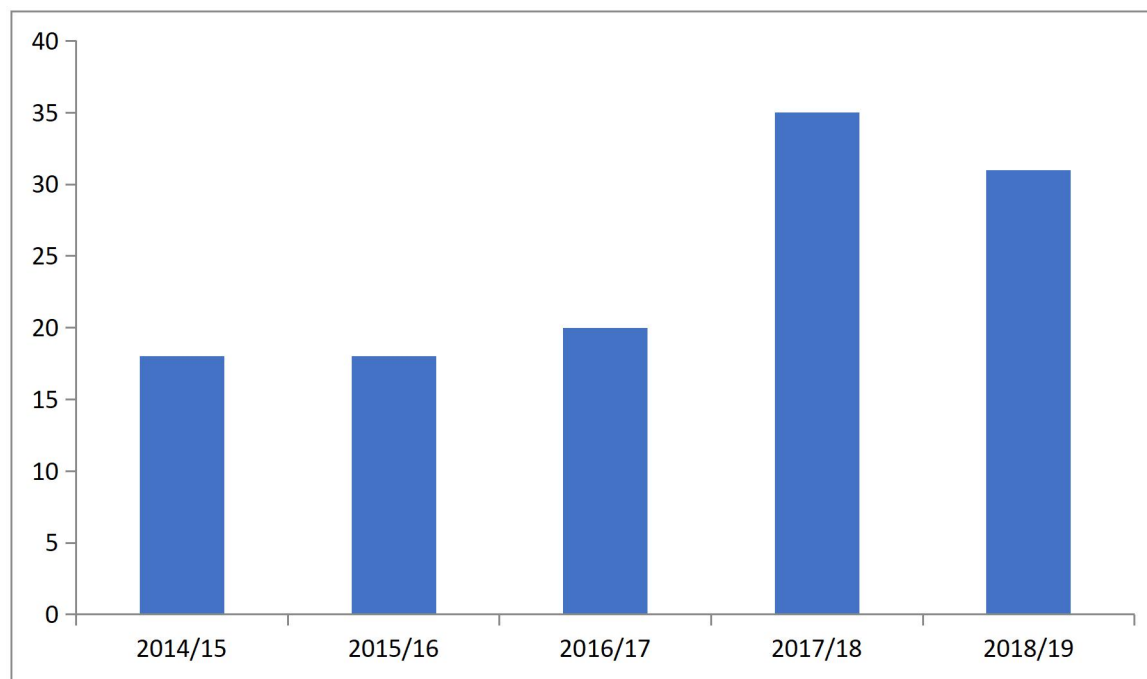
 Figure 2: Number of cases per year biopsy at JUMC, South West Ethiopia, from September 2014-August 2019, n=121.

 Seventy five (61.98%) were male and 46(38.01%) were female patients with male to female ratio of 1.63:1 and mean age of 22.57±15.17years and age range of 1-85 years. Of 121 cases, 69.42% were from rural area, 27.27% were from urban area and 3.30% of patients` residence was not documented.   Of 121 cases, 64 (52.89%) were benign, 21(17.35%) were tumor like lesions, and 36(29.75%) were malignant. Osteochondroma is the most common of all tumors, 34 cases (28.01%) and the most common benign tumor representing 53.71% followed by chondroma 10(15.38%), osteoid osteoma 6(9.23%), giant cell tumor 5(6.69%), osteoma 5(6.69%), enchondroma 2(3.08%), chondroblastoma and osteoblastoma 1(1.54%) each of benign tumors. Osteosarcoma is the most common malignant tumor 30 cases (83.33%) of malignant tumors followed by chondrosarcoma 3(8.33%), Ewing sarcoma 2(5.56%) and malignant giant cell tumor 1(2.78%) of malignant tumors.
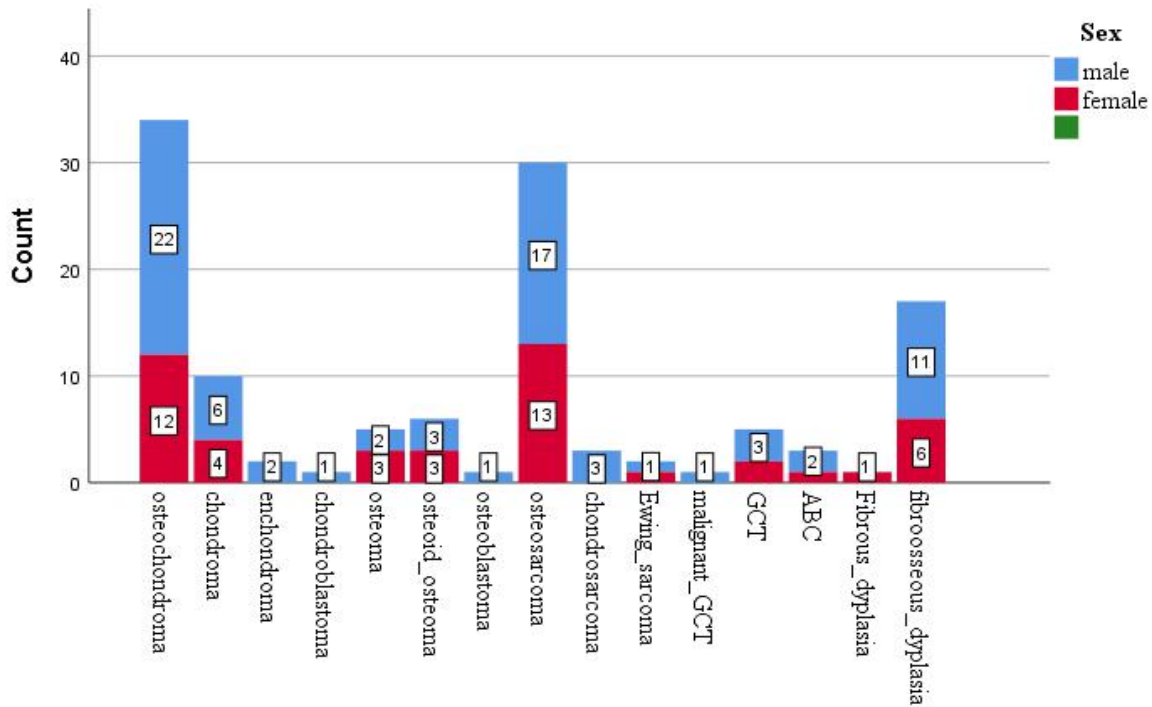
Figure 3: distribution of bone lesions along with sex .JUMC South West Ethiopia, September 2014-august 2019, (n=121).

5.1. Cartilage forming tumors

Cartilage forming tumors are the most common tumors in this study, 50 cases (41.12%) of 121 patients and 34 males and 16 females with average age of 22.22± 15.57years. Osteochondroma is 34(68%), chondroma 10(20%), enchondroma 2(4%), chondroblastoma 1(2%) and chondrosarcoma 3(6%) of cartilage forming tumors.

Osteochondroma is the most common cartilage forming tumor with male to female ratio of 1.83:1 and average age of 19.32±14.62 years.
Femur is the most common bone involved followed by tibia and 9 cases are not specified by specific bone involved.

Figure 4: distribution of osteochondroma among major bones at JUMC, South West Ethiopia, from September 2014-August 2019, n=121

Chondroma is the second most common cartilage forming tumor with average age of 29.4 ±20.49years and the most common site is bone of the hand which is 6 out of 10 cases. Three cases of chondrosarcoma are identified and all are males. Two cases affected lower extremities bones (femur and fibula) and one case upper extremity (humerus).
Cartilage forming tumors generally affect the bones of extremities and rare in other sites

Table 1: Distribution of cartilage forming tumors by anatomic sites at JUMC South West Ethiopia, September 2014-August 2019, n=121.

Cartilage forming tumors	Pelvic bone	Bone of extremities	Spine	Rib	Not specified	Total
Osteochondroma	1	30	1	1	1	34
Chondroma	0	10	0	0	0	10
Enchondroma	0	2	0	0	0	2
Chondroblastoma	1	0	0	0	0	1
Chondrosarcoma	0	3	0	0	0	3
Total	2	45	1	1	1	50

The most common affected age groups by cartilage forming tumors is 11-20 years followed by age group of 21-30 years which is almost similar to age groups affected by bone forming tumors.
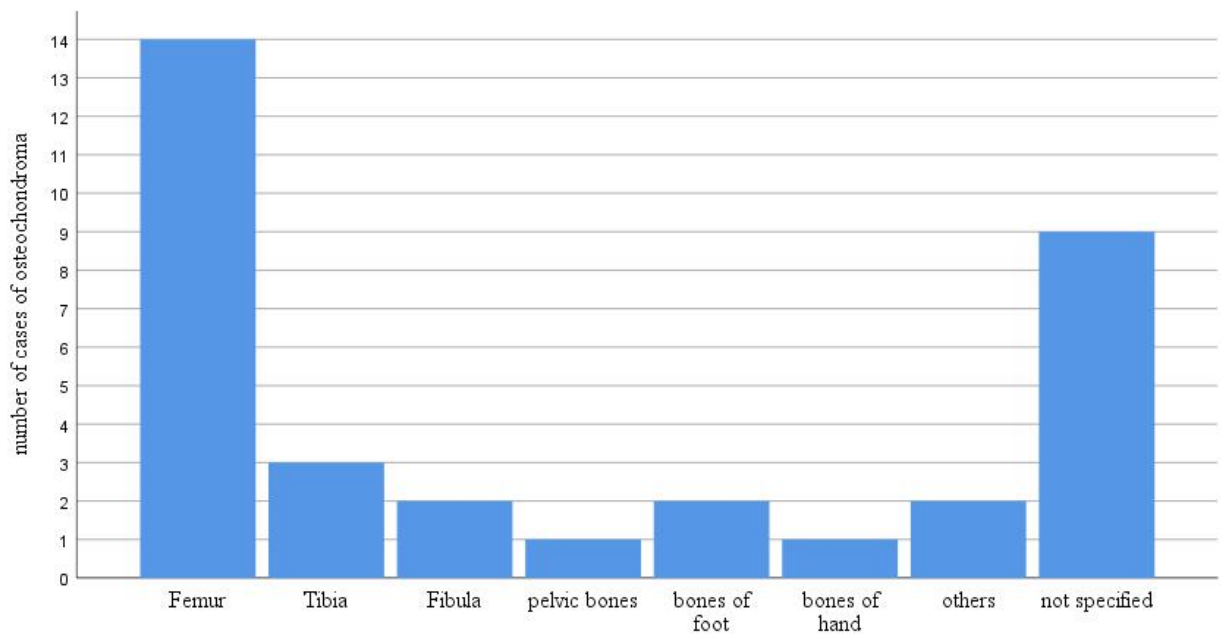
Table 2: Distribution of osteochondroma among major bones at JUMC, South West Ethiopia, September 214-August 2019 n=121

Age groups	Cartilage forming tumors					Total
	Osteochondroma	Chondroma	enchondroma	Chondroblastoma	Chondrosracoma	
1-10	5	1	0	0	0	6
11-20	21	3	0	1	2	27
21-30	5	3	1	0	1	10
31-40	1	0	1	0	0	2
41-50	0	2	0	0	0	2
51-60	1	0	0	0	0	1
>60	1	1	0	0	0	2
Total	34	10	2	1	3	50

5.2. Bone forming tumors

These are the second the most common tumors next to cartilage forming tumors and osteosarcoma is the most common accounting for 71.42%, osteoid osteoma 14.28%, osteoma 11.90% and osteoblastoma is 2.38%.

From 42 cases, 23 patients are males and 19 patients are females with male to female ratio of 1.21:1 and average age at diagnosis is 24.76±16.25years. The age groups between 11-20 and 21-30 are most affected.
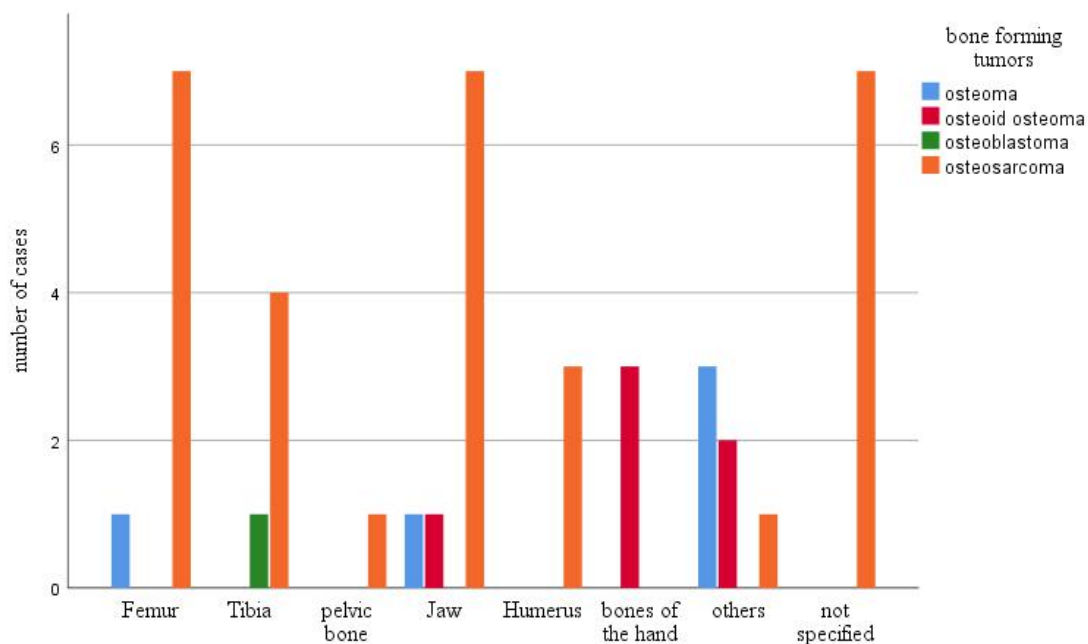
Figure 5: distribution of bone forming tumors among major bones at JUMC, South West Ethiopia, September 2014-August 2019, n=121.

Osteosarcoma

Osteosarcoma is the most common malignant bone tumor with average age at diagnosis of 23.57±17.03 years and with age range of 1-75 years. From 30 cases of osteosarcoma 17 patients are males and 13 patients are females with male to female ratio of 1.31:1. The age group of 11-20 year is the most common affected followed by age group of 1-10 years.

Table 3: Distribution of osteosarcoma in the age groups at JUMC, South West Ethiopia, September 2014-August 2019, n=121

SN	Age groups	Number of cases
1.	1-10	6
2	11-20	12
3.	21-30	4
4.	31-40	4
5.	41-50	1
6.	51-60	2
7	>60	1
Total		30

Generally, bones of the extremity are the most common site (21 cases) followed by craniofacial bones (7 cases). About 36.67% (11) occurred around knee joint area.
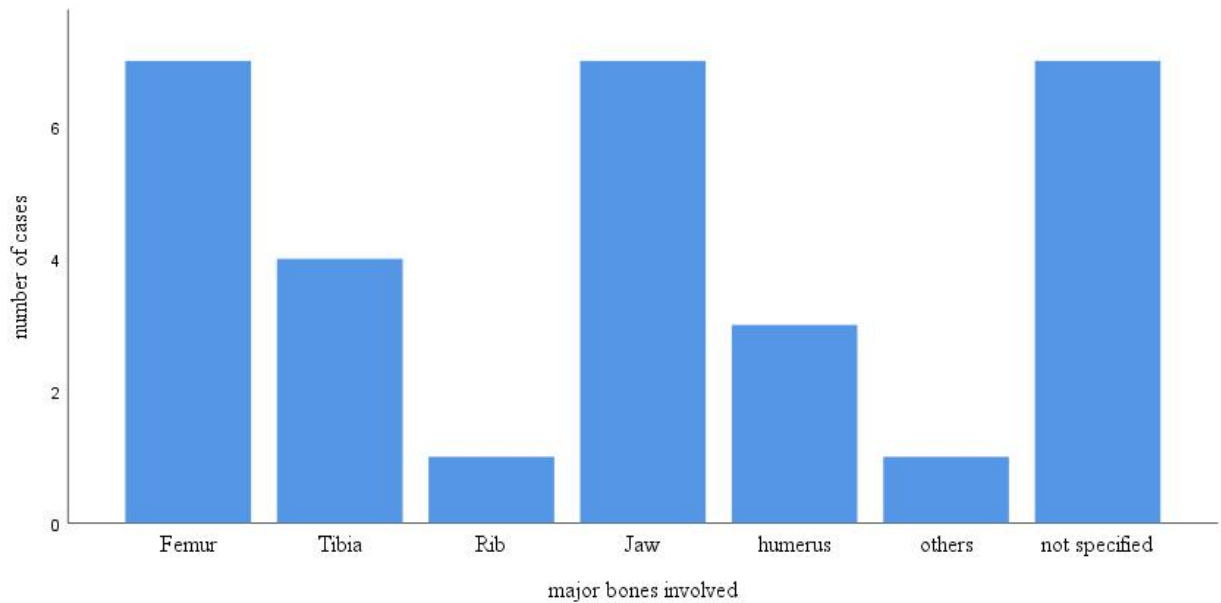
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Figure 6: distribution of osteosarcoma in major bones at JUMC, South West Ethiopia, from September 2014-August 2019, n=121.

The histologic features of the reported conventional osteosarcoma is reported only in 8 cases, 4 is osteoblastic and 4 is chondroblastic conventional osteosarcoma and 4 cases are graded, 2cases as low grade and 2 cases as high grade osteosarcoma.

Ewing sarcoma is the third common malignant bone tumor next to chondrosarcoma.

Two cases identified, a 6 years old female, and 12 years old male patients both affecting femur bone.

Giant cell tumor of the bone

Six cases of giant cell tumor of the bone have been identified and one malignant GCT in femur of a 20 years old male patient and 5 cases of benign GCT, 3 patients are males and 2 patients are females affecting almost all age groups. Two of 5 cases occurred in jaw and 1 bone of the foot, 1 bone of the hand and the other one case, site is not specified.

Tumor like-lesions

A total of 21 tumor like-lesions were diagnosed and the most common is fibro-osseous dysplasia, 17 cases (73.91%) and 1 fibrous dysplasia, 3 Aneurysmal bone cysts (ABC). The average age for fibro-osseous dysplasia is 18.05 years and male to female ratio is 1.83:1. The most common site for fibro-osseous dysplasia is jaw which is 47.05%.

Table 4: Distribution of tumor like-lesions by anatomic sites at JUMC, south west Ethiopia, September 2014-August 2019, n=121

Major bone involved	Tumor like lesions			
	ABC	Fibrous dysplasia	fibro-osseous dysplasia	Total
Tibia			3	3
Rib			1	1
Jaw	2		8	10
Bones of the foot			1	1
Bones of the hand		1	1	2
Others			1	1
Not specified	1		2	3
Total	3	1	17	21

5.3. Discussion

Of 121 cases of bone lesion biopsy seen 64(52.89%) were benign, 36(29.75%) were malignant and 21(17.35%) were tumor like lesions. The average age at diagnosis for all bone lesions was 22.57±15.17 years. The age range was between 1-85 years and the most common age group affected was 11-20 years which accounts for 46.34% of all cases. No significant relationship is seen between the age and residence of the patient and histopathologic patterns. Benign to malignant ratio is 1.72:1 and Seventy five (61.98%) were male and 46 (38.01%) were female patients with male to female ratio of 1.62:1 and has shown a male predilection. This figure is comparable with study done in Ethiopia, Black lion Hospital on 689 patients showing 58% had benign tumors and 42% had malignant tumors with benign to malignant ratio of 1.41:1 and male to female ratio of 2:1 and study done in Ife-Nigeria, on 100 patients has also shown male female ratio of 1.31:1 (20,25).

The peak age for benign primary bone tumors is 2nd and 3rd decade of life. For malignant tumors, it`s 1st and 2nd decades of life. This finding is in agreement with that of Oyemade (Ibadan), Omololu et al (Ibadan), Odetayo (Lagos) and Solomon (South Africa) and Aina et al (Nigeria).

The peak age for tumor like lesions is 2nd decade of life which is similar with study done by Solomon in South Africa. However, study done by Umar at Zaria, who reported that 70 cases (36.6%) out of 191 cases were tumor like lesions and were seen in the third decade of life (20,26–28).

The most common benign and malignant tumors were osteochondroma 34(28.01%) and osteosarcoma 30(24.79%) respectively while the most common tumor like lesion is fibro-osseous dysplasia 17(14.05%).

Among the benign tumors osteochondroma represented 53.13% and osteosarcoma was 83.33% of malignant tumors. This finding is similar with study done in India showing the most common benign tumor was osteochondroma which was 53.65% of benign tumors (29) .

Osteochondroma was also the most common cartilage forming tumor 34(68%) with male to female ratio of 1.83:1 and average age of 19.32 years.

Femur is the most common bone involved followed by tibia and 9 cases are not specified by specific bone involved. This finding is similar with study done in Ethiopia, at Black lion Hospital, osteochondroma was the most common cartilage forming tumor(70.9%) with male to female ratio of 2.1:1 and affecting majorly the long bones lower limb(23). Gert et al reported similar figure for osteosarcoma and osteochondroma (21).

Osteosarcoma is the most common malignant tumor 30 cases (83.33%) followed by chondrosarcoma 3(8.33%), Ewing sarcoma 2(5.56%) and malignant giant cell tumor 1(2.78%) of malignant tumors. This finding is similar with study done in South Africa on 117 patients with malignant primary bone tumors which showed that the most common malignant bone tumor is osteosarcoma (72.6%), chondrosarcoma (11.1%), Ewing sarcoma (9.4%), malignant GCT (1.7%) and others 10.3% and other study done in Nigeria showed the most common malignant tumor was osteosarcoma (80.1%) (30,31).

The average age at diagnosis for osteosarcoma is 23.57±17.03 years and age range of 1-75 years. The commonest age group affected was 11-20 year and lacks bimodal distribution which is common for osteosarcoma in other studies. The male to female ratio was 1.31:1. Pillay et al reported similar peak age groups, male to female ratio and which lacks bimodal distribution.

Study done in Sweden also indicated similar age group affected and male to female ratio of 1.40:1 (31,32).

In many studies frequency, distribution and male to female ratio of osteosarcoma is comparable.

Table 5: Comparison of frequency, common age groups and male to female ratio of osteosarcoma in various studies at JUMC , South West Ethiopia, September 2014-August 2019,n=121

Study group	Frequency of osteosarcoma in malignant bone tumors (%)	Common age group	Male to female ratio(M/F)
Index study	83.33%	11-20	1.31:1
Pillay et al.South Africa 2016	72%	10-19	1.1:1
Lasebikan et al. Nigeria 2014	80.10%	11-20	1.13:1
Gemechu.T Ethiopia.	35%	20-29	1.82:1
Aina,O.J, et al Nigeria 2018	42%	11-20 & 21-30	1.33:1

 The common sites for osteosarcoma was bones of the extremity, about 36.67% especially femur (7/30) and tibia 4(13.33%) humerus 3(10%) and the other common site is jaw 7(23.33%). This is almost similar with study done in Nigeria on 100 cases of primary bones tumors where 9/21(47.61%) cases of osteosarcoma occurred in femur, 6(28.57%) in the tibia, three in the jaw (14.29%) and one case each in humerus and calcaneus (4.76% each) (20).

A total of 21 tumor like-lesions were diagnosed and the most common is fibro-osseous dysplasia 17 cases (80.95%) and 1 fibrous dysplasia, 3 cases of ABC. The average age for fibro-osseous dysplasia is 18.05 years and male to female ratio is 1.83:1. The most common site for fibro-osseous dysplasia is jaw which is 47.05%.

This result is similar study done in Nigeria which showed that twenty two cases (22%) were tumor-like conditions. The age range was 9 to 65 years with a mean age of 31.5 years. Peak incidence was in the 2nd and 3rd decades of life (72.7%). The commonest site for tumor-like lesions was the maxilla as seen in 11 cases (50%) and the most frequent variant was fibrous dysplasia with 8 cases (36.4%) (20).

5.4. Conclusion

The result of this study showed that the distribution of primary bone lesions vary with age, sex and anatomic site. Cartilage forming tumors are the most common tumors of bone lesions.

The most common benign tumor is osteochondroma followed by chondroma and the most common malignant tumor is osteosarcoma followed by chondrosarcoma.

Generally, all primary bone tumors have predilection for males and the most common age group affected by osteosarcoma is 11-20 years and long of the limbs are the most common site followed by craniofacial bones. The most common tumor like-lesion is fibro-osseous dysplasia and common site being craniofacial bones.

5.5. Limitations of the study

Since the study was done on secondary data some information was not be complete and the size of the tumor was not properly documented as well as incisional and excisional biopsy was not identified by the requesting physician so that it was not possible to do correlation between the size and behavior of the tumor.

5.6. Dissemination plan

The results of this study will be disseminated or communicated to the Jimma University and other concerned bodies. Publication on an appropriate journal will also be done.

5.8. Recommendation

- As articles on bone tumors and tumor like lesion are scare our country as well as worldwide. We recommend others interested researcher to further conduct research on this area.
- Most of the samples seen in this study are incisional biopsies, we recommend the physicians to send whole sample after surgery so that the size of the tumor can be assessed and further research can be done to correlate the size with the tumor behavior.
- In addition, most of the tumors affect young ages, so that we recommend the ministry of health create awareness and early intervention can be done.

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Annexes

No	Variables		Choice
1.	Biopsy no		
2.	Year of biopsy	A) 2015/14 B)201615 C)2017/16 D)2018/17 E)2019/18	
3.	Age in years		
4.	Sex	Male(M) Female(F)	
5.	Residence	Urban Rural	
6.	Anatomic site by WHO	Pelvic bones Bones of the limb Craniofacial bones Scapula Rib Spine Others Not specified	
7	Major bone involved	Femur Tibia Fibula Humerus Bones of the foot Bones of the hand Jaw others not specified	
8	Histopathologic	Osteochondroma	

	pattern	Chondroma	
		Enchondroma	
		Chondroblastoma	
		Chondrosarcoma	
		Osteoma	
		Osteoid osteoma	
		Osteoblastoma	
		Osteosarcoma	
		Ewing sarcoma	
		Malignant GCT	
		Benign GCT	
		ABC	
		Callus	
		fibrous dysplasia	
		Fibro-osseous dysplasia	
9	Size of the lesion (cm)		

DECLARATION
ASSURANCE OF PRINCIPAL INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the college of public and medical science in effect at the time of grant is forwarded as a result of the application.

Name of the principal investigator   Signature   Date

Dr. Jebessa Gemechu (MD)   ---------------   ---------------

APPROVAL OF THE ADVISORS

This thesis has been submitted with my approval as university advisor

Name of the advisors   Signature   Date

Dr. Gebi Nemo   -------------   ---------

Dr. Mulusew Gerbaba   ---------------   -----------