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### STUDY OF CLINICAL, RADIOLOGICAL, AND HISTOPATHOLOGICAL FEATURES OF BONE LESIONS- A TWO YEAR STUDY

**Dr Vivek Kharolkar<sup>1</sup>, Dr Naveen Chawla,<sup>2</sup> Dr Pratik Chide<sup>3</sup>, Dr Megha Kinake<sup>4</sup>**

1. Assistant Professor, Department of Pathology, Grant Government Medical College, Mumbai, Maharashtra, India.

2. Professor, Department of Pathology, Indian Naval Hospital Ship Asvini, Mumbai, Maharashtra, India.

3. Assistant Professor, Department of Pathology, Grant Government Medical College, Mumbai, Maharashtra, India.

4. Assistant Professor, Department of Pathology, Grant Government Medical College, Mumbai, Maharashtra, India.

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#### ABSTRACT

**Background:** A pathological bone lesion can present in any form of inflammatory to neoplastic conditions and they pose a definite diagnostic challenge. The aim of the present research was to study the incidence, age of presentation, and site of bone lesions, overview the clinical, imaging, and pathologic findings, and also compare radiological and histological findings. **Methods:** This study was conducted in 30 cases of bone lesions, who presented to a tertiary care hospital from May 2010 to September 2012. Clinical examination was done initially, followed by radiological imaging (X-ray, CT & MRI). Based on imaging, the decision of biopsy was taken for final diagnosis. Histopathological examination was done on Hematoxylin and Eosin stained slides. **Results:** Out of 30 cases, 14(46.66%) cases were benign, 14(46.66%) were malignant tumors and 2(6.66%) were non-neoplastic lesions. Osteochondroma (35.71%) was the most common benign bone tumor and multiple myeloma (28.57%) was the commonest malignant tumor while non-neoplastic lesions were avascular necrosis of hip & chronic osteomyelitis. The primary bone tumors occurred mostly in 0-50 years, while half cases of multiple myeloma and metastatic tumors were seen 1-2 decades higher. 85.71% of benign tumors occurred in males while malignant tumors showed equal sex incidence. All non-neoplastic cases occurred in males. The femur was most commonly involved long bone while the pelvis was the most commonly involved flat bone. Radiological diagnosis was consistent with histopathological diagnosis in 80% of cases. **Conclusion:** Age, sex, and site are important clinical parameters. Radiology and imaging investigation is an essential

#### ORIGINAL RESEARCH ARTICLE

**Corresponding author**  
**Dr. Naveen Chawla \***

step in the diagnosis, prior to histopathological study. Clinical, imaging and histopathology thus remains the key for diagnosing bone lesions; especially so in bone tumors.

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## INTRODUCTION

A bone lesion is any abnormality found on or in a bone that is caused by disease or injury. It ranges from inflammatory to 'tumor-like to neoplastic. Bone tumors are the oldest form of neoplasia documented in paleopathology; they existed on earth long before human life appeared. In bones, neoplasms occur in all races and all countries. Among the wide array of human neoplasms, primary bone tumors are relatively uncommon constituting only 0.5% of the total world cancer incidence [1-3]. Studies in India have shown that bone tumors comprise 0.9% of total lesions seen [4].

However, the benign and non-neoplastic bony lesions are more common than malignant lesions. The more common benign lesions are frequently asymptomatic and are detected as incidental findings. Many tumors produce pain or are noticed as a slow-growing mass. In some circumstances, the first hint of a tumor's presence is a sudden pathologic fracture. The broad spectrum of bony lesions makes the definitive diagnosis difficult. Clinical presentation can be misleading as in Ewing sarcoma – Fever and raised ESR suggestive of Osteomyelitis [5, 6]. The relevant data on age, gender, bone involved, specific area within the bone (location of the lesion- epiphysis, metaphysis, or diaphysis; cortex, medulla or periosteum), radiographic appearance are the basic parameters and key pieces of information necessary for the establishment of diagnosis [7]. The roentgenogram helps to define the exact location of the lesion and its aggressiveness; it reflects the gross manifestation of the lesion [5, 8]. To establish an accurate diagnosis, an integrated approach toward these lesions is

necessary for the form of clinical data, radiograph, and histopathology.

In recent years, tremendous advances have been made in the field of skeletal pathology. These are histochemical studies, autoradiography, tissue culture in vitro, genetic studies, fluorescent and electron microscopy, radioisotopes and study of undecalcified sections which are of help in the diagnosis of bone tumors. In the current study, all the primary bone tumors and other lesions of this series have been analyzed critically for their clinical, pathological and radiological features. In all the cases, a definitive diagnosis was made by histological examination of surgically resected specimens or open biopsy/ image guided needle core biopsy material.

## MATERIALS AND METHODS

It was an observational study of all bone lesions done for 2 years from May 2010 to September 2012 in the Department of Pathology at tertiary care hospital. The institutional ethical committee consent and informed consent was obtained from all the patients before start the of the study. A total of around 30 patients presented with complaints of pain/ swelling/ pathological fracture and patients with incidentally detected lesion diagnosed on radiological imaging were included in study irrespective of age and sex. All representative & adequate specimen was included in the study and all inadequate samples were excluded from the study.

The case history, clinical details were taken from patients' interview case sheets. Imaging details were taken from the Department of Radio-diagnosis and Imaging. Radiographic studies were done with GE Wipro 500mA and Neutrolex 300mA x-ray machines. Imaging studies were carried out by the Department of Radiology using Siemens

Somatome 4AR CT scan machine and 1.5 T Siemens MRI machine. After a detailed history, clinical and radiological examination; a biopsy was carried out. The specimen received by different methods such as CT guided core biopsy and excision biopsy; were fixed in Bouin's fixative & decalcified in 5% nitric acid. Tissues were processed and stained with Hematoxylin and Eosin stain and examined under the microscope for histopathological evaluation. The final diagnosis was made into inflammatory, benign, and malignant lesions accordingly. Data were tabulated and analyzed using SPSS (statistical package for social sciences) and

Cohen's kappa test was applied to determine the level of agreement between radiological and histopathological diagnosis [9].

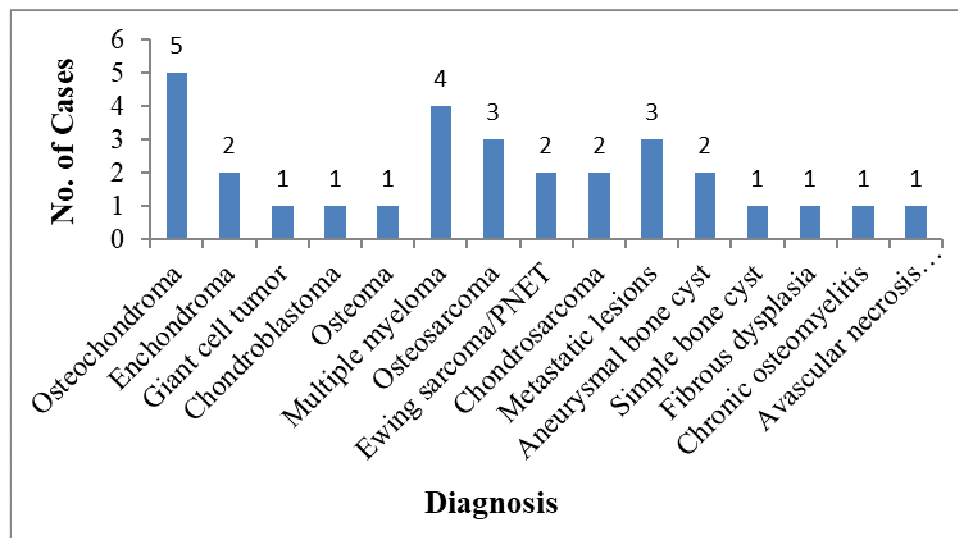
## RESULTS

Total 30 cases of bone lesions were studied, of these, 28 were bone tumors (93.33%) and 2 (6.66%) were non-neoplastic lesions. In the 28 cases of bone tumors, 14 (50%) cases were benign bone tumors and 14 cases (50%) were of malignant bone tumors. In the non-neoplastic lesions & malignant lesion, the pain was the most common presentation while in benign lesions pain & swelling was the common presentation as shown in table 1.

**Table 1:** Clinical presentation of bone lesions

Symptoms	Benign	Malignant	Non-neoplastic
Pain	7	10	2
Fever	-	-	-
Swelling	8	7	1
Pathological fracture	1	4	
Hearing loss	1	-	
Asymptomatic	1	-	-

The distribution of individual lesions is shown in figure 1, Osteochondroma was the most common diagnosis in 5 cases (16.67%) followed by Multiple myeloma 4 cases (13.33%).



**Figure 1:** Distribution of individual lesions

Among benign bone tumor, the most common was Osteochondroma (35.71%) while in malignant bone tumors most common was

multiple myeloma (28.57%) as shown in table 2.

**Table 2:** Distribution of bone tumors (Benign and Malignant) and incidence of other bone lesions

Benign Tumors (14 cases)		Malignant Tumors(14 cases)				Other bone Lesions (2 cases)	
Tumors	No	Primary (n=11)	No	Metastatic (n=3)	No	Lesions	No
Osteochondroma	5	Multiple myeloma	4	Upper end humerus	1	Avascular necrosis of hip	1
Enchondroma	2	Osteosarcoma	3	Upper end of femur	2	Chronic osteomyelitis	1
Chondroblastoma	1	Ewing sarcoma/PNET	2	-	-		
Giant cell tumor	1	Chondrosarcoma	2	-	-		
Aneurysmal bone cyst	2	-	-	-	-	-	-
Simple bone cyst	1	-	-	-	-	-	-
Fibrous dysplasia	1	-	-	-	-	-	-
Osteoma	1	-	-	-	-	-	-

Lesions like osteochondroma, multiple myeloma, and osteosarcoma showed characteristic age distribution patterns. Cases of osteochondroma were seen in two distinct age groups i.e. 11-20 (3 cases) and 31-40 years

(2 cases). Osteosarcoma showed a bimodal distribution, with the first in 11-30 years and the second 51-60 years. Multiple myeloma cases were also seen in two peaks; one in 31-40 and the other in 61-70 years, (Table 3).

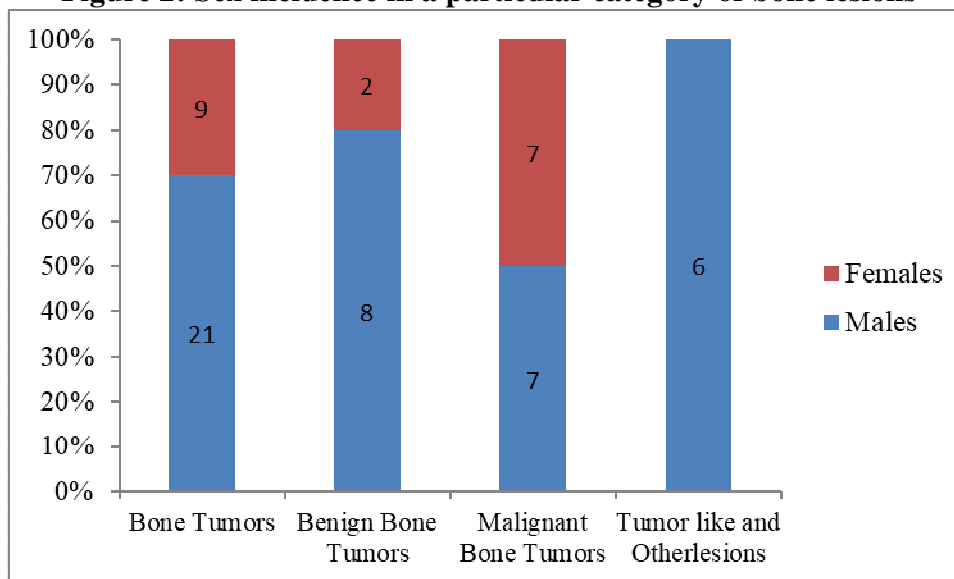
**Table 3:** Age range and histological types (lesions)

Lesion	Age in years						
	0-10	11-20	21-30	31-40	41-50	51-60	61-70
Osteochondroma	-	3	-	2	-	-	-
Enchondroma	-	-	1	1	-	-	-
Giant cell tumor	-	-	-	-	-	-	-
Chondroblastoma	-	-	-	1	1	-	-
Osteoma	-	-	1	-	-	-	-
Multiple myeloma	-	-	-	2	-	-	2
Osteosarcoma	-	1	1	-	-	1	-
Ewing sarcoma/PNET	1	1	-	-	-	-	-
Chondrosarcoma	-	-	1	1	-	-	-
Metastatic lesions	-	-	-	1	1	-	1
Aneurysmal bone cyst	1	-	1	-	-	-	-
Simple bone cyst	-	1	-	-	-	-	-
Fibrous dysplasia	-	-	1	-	-	-	-
Chronic osteomyelitis	-	-	-	-	-	-	1
Avascular necrosis of hip	-	-	-	-	-	1	-
Total	2	6	6	8	2	2	4

Of the 30 cases studied, 21 (70%) were male patients while 9 (30%) were females, so male: female ratio was 2.3:1. In terms of sex incidence, 85.71% of benign bone tumors

occurred in males while malignant bone tumors showed equal sex incidence. All non-neoplastic cases occurred in males as shown in figure 2.

**Figure 2: Sex incidence in a particular category of bone lesions**



Out of 30 lesions, 29 lesions primarily arise in the bone while one case of peripheral osteoma arising in the mandibular region. Among 29 lesions, 23(79.31%) involved long bones, and 6 lesions (20.69%) involved flat bones. Overall, the femur was the most involved site 7 cases (23.33%) of all bone lesions, followed by tibia 5 cases (16.67%). Pelvic bones, phalanx and metacarpals were

the most commonly involved flat bone. Other flat bones involved were rib and skull bones (Table 4). In all the lesions studied, arising from long and short bones, metaphysis was the frequently involved one (14 lesions out of 23, 60.87%). 6 lesions (26.08%) involved diaphysis. 3 cases involving epiphysis were noted (13.05%).

**Table 4:** Distribution of bone lesions as per site and most common lesions and their sites involved

Distribution of bone lesions		Most common lesions and their sites involved			
Site	Incidence	Lesion	Most common sites involved	No. of cases	Total
Tibia	5 (16.67%)	Osteochondroma	Tibia	3	5
Fibula	3 (10.00%)		Fibula	1	
Femur	7 (23.33%)		3rd left metacarpal	1	
Radius	0 (0.0%)	Enchondroma	Femur	1	2
			Proximal phalanx little finger	1	
Ulna	1 (3.33%)	Osteosarcoma	Fibula	1	3
			Humerus	1	
			Femur	1	

Humerus	4 (13.33%)	Multiple myeloma	Pelvic bones	2	4
			Clavicle	1	
			Humerus	1	
Rib	1 (3.33%)	Chondrosarcoma	Pelvic bone	1	2
Clavicle	1 (3.33%)		Rib	1	
Pelvic bones	3 (10.00%)	Ewing sarcoma	Tibia	1	2
Phalanx and metacarpal	3 (10.00%)		Humerus	1	
Skull bones	1 (3.33%)	Aneurysmal bone cyst	Femur	1	2
Mandibular region	1 (3.33%)		Fibula	1	

In 24 cases (80.00%) radiological diagnosis together with the differential diagnosis offered was consistent with histopathological diagnosis. Cohen's kappa value (0.78) was calculated online and it showed good agreement between radiological and histological diagnoses of all bone lesions. In 6

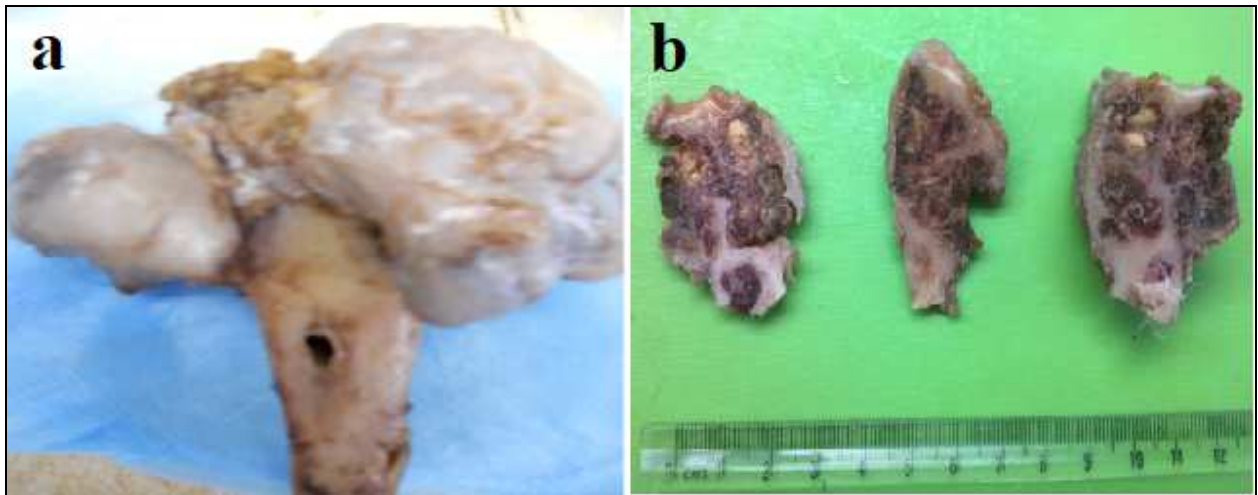
cases, the radiological opinion was inconsistent (20.00%), these include two cases of multiple myeloma, two cases of osteosarcoma, and one case each of chondroblastoma and simple bone cyst (Table 5).

**Table 5:** Comparison between Radiological and Histopathological Diagnosis

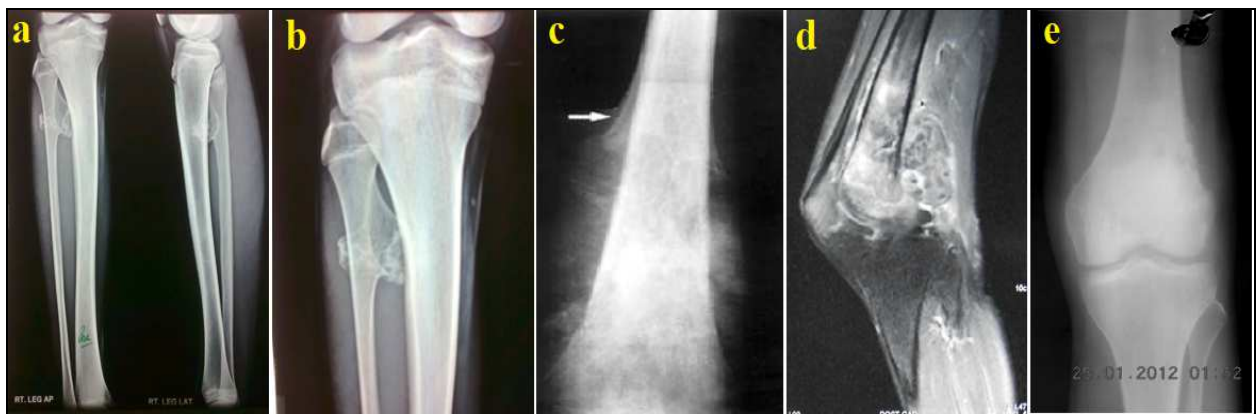
Histopathological Diagnosis	Diagnosed cases	Radiological diagnosis matching with histopathological diagnosis	Radiological diagnosis matching with histopathological diagnosis
Osteochondroma	5	5	0
Enchondroma	2	2	0
Giant Cell Tumour	1	1	0
Chondroblastoma	1	0	1
Osteoma	1	1	0
Multiple Myleoma	4	2	2
Osteosarcoma	3	1	2
Ewing sarcoma/PNET	2	2	0
Chondrosarcoma	2	2	0
Metastatic lesions	3	2	0
Aneurysmal bone cyst	2	2	0
Simple bone cyst	1	0	1
Fibrous dysplasia	1	1	0
Chronic osteomyelitis	1	1	0
Avascular Necrosis	1	1	0
<b>Total</b>	<b>30</b>	<b>24</b>	<b>6</b>

A cases of Fibular exostosis and Giant cell tumor showed classical gross features (Figure 3a & 3b). Radiological features of Osteochondroma (Figure 4a & 4b) and Osteosarcoma (Fig 4c, 4d & 4e). Fibrous dysplasia (Figure 5a) and Chondrosarcoma (Figure 5b and 5c)

Classical histopathological features were seen in the various patient. Osteochondroma (Figure 6a), Giant cell tumor (Figure 6b), Aneurysmal bone cyst (Figure 6c), Osteosarcoma (Figure 6d), low-grade chondrosarcoma (Figure 6e), and metastatic squamous cell carcinoma (Figure 6f).



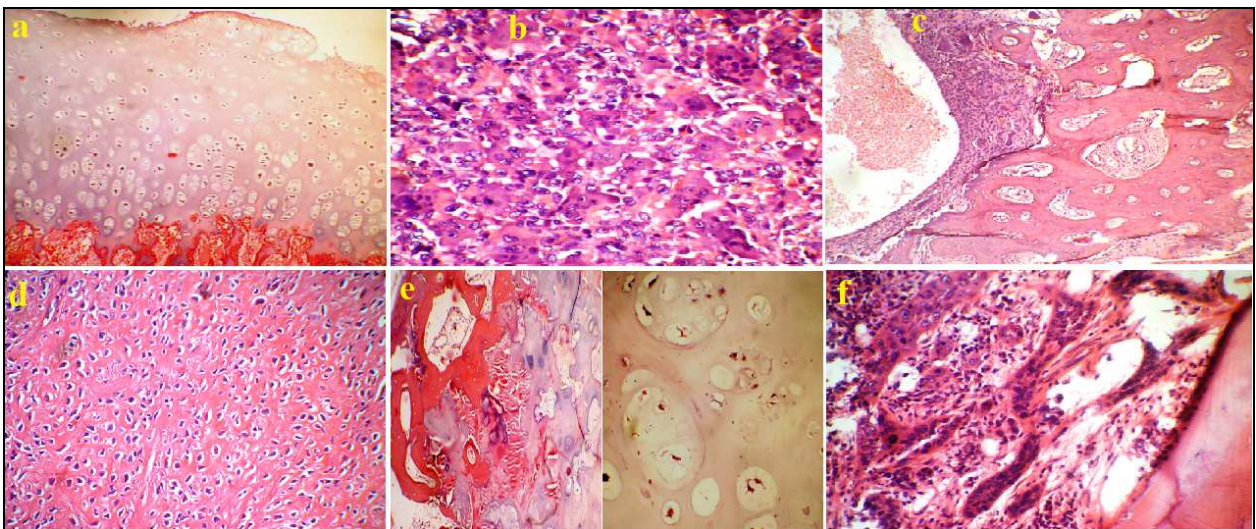
**Figure 3:** Gross pictures - a) A case of Fibular Exostosis- Large, mushroom-like growth with bluish, lobulated cartilaginous cap measuring 9x4x5 cm; b) Giant Cell Tumor- The growth on the cut surface is expansile with brownish-red discoloration



**Figure 4: Radiograph shows:** - a & b) Radiograph right leg showing a well-defined smoothly margined lesion involving the proximal fibula. It shows a trabecular pattern continuous with the bone. Diagnosis- Osteochondroma; c, d & e) Radiograph shows well-defined lucent bone lesion involving distal metaphysis of the femur along its lateral cortex. The lesion has a wide zone of transition and shows Codman triangle and Sunburst type of periosteal reaction. The MRI shows heterogeneously enhancing mass lesion with soft tissue component. Diagnosis- Osteosarcoma.



**Figure 5: CT Scan:** a) CT scan of base of the skull shows expansile lesion involving the right petrous and squamous temporal bone with cortical thinning, ground glass matrix, and bone deformity. Diagnosis- Fibrous dysplasia; b & c) 20: CT Axial section and coronal reformatted images show a well-defined, lucent lesion with calcified matrix involving the right side of sacrum extending into the sacroiliac joint. Diagnosis: Chondrosarcoma



**Figure 6: Histopathology:** a) Osteochondroma. Cartilage cap covered by fibrous periosteum maturing by enchondral ossification. An orderly arrangement of cartilage cells at the base of cartilage cap (H&E Stain 100 X); b) Giant cell tumor. Evenly dispersed giant cells with nuclei similar to mononuclear cells (H&E Stain 400X); c) Aneurysmal bone cyst. Blood-filled cystic space with its wall, Wall shows fibroblast and osteoclast-like giant cells (H&E Stain 100 X); d) Osteosarcoma. High-grade spindle cell neoplasm-producing osteoid matrix (H&E Stain 400 X); e) Low-Grade Chondrosarcoma. Photomicrograph to left shows permeation of preexisting trabecular bone (H&E Stain 40X). Photomicrograph to right shows doubly nucleated cells and moderate atypia. (H&E Stain 400 X); f) Metastatic Squamous cell Carcinoma to bone in a case of Carcinoma cervix. (H&E Stain 400 X)

## DISCUSSION

This present study emphasizes the importance of three-pronged approaches i.e. clinical, radiological, and pathological

findings in the diagnosis of the spectrum of a bone lesion. This study demonstrated the increasing incidence of imaging-guided core biopsies for the diagnosis of bone tumors.



The present study found an equal incidence of malignant bone tumors & benign bone tumors which is variable with the study done by Mohammad and Isa [10]. A commonest benign tumor in the current study was osteochondroma which is comparable with the study conducted by Kumavat et al and Bamanikar et al followed by multiple myeloma which is in concordance with the study by Jain et al [11-13]. The lesions ranged from 8-64 years with a mean age of 33.17 years. In these primary bone, tumors occurred mostly in 0-50 years, while half cases of multiple myeloma and metastatic tumors were seen one to two decades higher. The non-neoplastic lesions, avascular necrosis of the hip, and chronic osteomyelitis occurred in the geriatric age group. These results are similar to the study done by Baena Ocampo et al which showed a mean age of 25 years, primary bone tumors in 0-50 years, while in the higher age group malignant and metastatic tumors predominated [14]. The male predominance (2.3:1) was observed in the present study which is similar to the study done by Kokode and Deoghare et al (1.35:1) [15, 16]. It is partly because of the small sample size and partly because this institute is a service hospital, male patients come to attention more frequently because of mandatory regular health checkups.

The femur (23.33%) was the most commonly affected site followed by the tibia (16.67%). 20.69% of cases affected flat bones and pelvic bones were the most commonly involved. These findings correlated well with the previous studies done by Bamnikar SA et al, Jain K et al, Baena Ocampo LC et al [12-14]. Pain and swelling (9 cases, 30.00%) was the most common overall clinical presentation as similar to Kumavat et al and Kokode [11,15]. In this further 50% of benign bone, tumors had pain and swelling while 21.43% of malignant tumors had pain and swelling. In non-neoplastic lesions and malignant bone tumors, the pain was the most common

presentation. Similar findings are reported in the literature (WHO classification of tumors of soft tissue and bone -2002 ) which states that malignant tumors present with worsening pain [17].

Enchondroma accounted for 6.67 % of bone lesions and 7.14 % of bone tumors. Both were males; involved both long bone and classical site of short bone of hand and presented in the third and fourth decade. One case presented with symptoms while the other was asymptomatic. Radiological features were either diagnostic of enchondroma or suggestive of a cartilaginous tumor. These results are comparable with other studies [10,13]. A single case of Giant cell tumor was studied. The patient was 36 yrs male with pain and swelling involving femoral lower end metaphysis. Radiology and histopathology showed classical features of Giant cell tumors as described in the literature [18].

A single case of chondroblastoma in a diaphyseal location in 49 years males in the left index finger was studied. The location was unusual as chondroblastoma is an epiphyseal lesion and rarely in diaphysis as in this case [19]. Radiologically GCT and enchondroma are its mimickers [19]. In this case, radiologically, the differentials were 1) Enchondroma with possible malignant transformation, 2) Giant cell tumor. Histologically, classical features of Chondroblastoma were seen. A classic case of peripheral osteoma in 36years female in the mandibular region was studied as reported in a study by Kaplan et al [20].

In the malignant bone tumors, plasma cell myelomas (Multiple myeloma) were the most common primary malignant bone tumor and second most common bone lesion (13.33% of the bone lesion). Sites with hematopoietic marrow – clavicle, humerus, and pelvic bones were involved. The presentation was varied ranging from pain to pathological fracture. 50% of cases occurred in the 4th decade and 50% in the 7th decade with

a median age of 50 yrs. Two cases (50%) on radiology were diagnosed as multiple myeloma but two differed. One case in sacrum was reported as tuberculosis while the other in pubic ramus was reported as a giant cell tumor. Three cases of osteosarcoma, all males with a bimodal age distribution, metaphyseal involvement, and varied presentation were studied. Long bones of the lower and upper limb were involved. Radiologically one case showed classical features of osteosarcoma while in two radiological diagnoses together with differential diagnosis differed. They were reported as malignant transformation in osteochondroma (Chondrosarcoma) in one case and differentials of lymphoma and Ewing sarcoma in other case. Ewing sarcoma and chondrosarcoma are mimickers of osteosarcoma on imaging as described in literature [21]. Metastatic bone tumors occurred in 4th, 5th & 7th decades. Cervix, Lung and bladder were the primary sites. Femur and humerus were the involved bones and presented with pain, pathological fracture. Ewing sarcoma followed next to osteosarcoma in this study. However, the small sample size of our study limits its extrapolation to the entire region. Further present study showed a female sex predilection and presentation in first and second decade with involvement of long bones. One occurred in meta-diaphysis while other unusually in epiphysis. These findings matched with Jain *et al* [13]. Chondrosarcoma accounted for 6.67% of bone lesions and was the third most common malignant tumor along with Ewing sarcoma. Rib and pelvis were the sites involved; pain, swelling and pathological fracture were the symptoms and involved both male and female in 3rd & 4th decade. Both the cases were radiologically and histopathologically in coherence. These findings are correlated with the previous studies [22,23].

Aneurysmal bone cyst accounted for 6.67% of bone lesions; in children and young adult involving metaphysis of long bones of

lower limb. Radiology and histopathology showed classical features. These findings are as described in the literature and the study by Baena- Ocampo *et al* [22,14]. A single case of the simple bone cyst, fibrous dysplasia, avascular necrosis of hip, and chronic osteomyelitis were studied which showed features as described in the literature [24]. In the case of a simple bone cyst, there was no radiological correlation but there was clinical concordance.

Overall, the radiological diagnosis and final histopathological diagnosis were in agreement in 80.00% of cases with Cohen's kappa value of 0.78 and this value is a good level of agreement between radiological and histological diagnoses of all bone tumors which is comparable with the study done by Negash *et al* [25]. However, we found a comparatively lower level of agreement because of the presentation of tumors at unusual site and mimickers of lesion on radiology due to their unusual sites. Further the disagreement in 20% of cases meant; histopathological confirmation was mandatory.

#### **LIMITATIONS**

Sample size was small. Although many lesions were seen; a further larger spectrum of lesions would have been better. Small sample size limits extrapolation to larger region.

#### **CONCLUSION**

To conclude, bone lesions have varied presentation. Age, sex and site are important clinical parameters. Radiology and imaging investigation is an essential step in diagnosis, prior to histopathological study. Radiology helps in further planning of Management. In 80 percent cases, Radiological diagnosis matched with Histopathology. But in 20 percent; Radiological diagnosis differed with histopathology for giving final diagnosis. Benign & malignant bone lesions found equal incidence with male preponderance. Osteochondroma, enchondroma, aneurysmal bone cyst & Multiple myeloma were the most

common benign & malignant bone lesions, respectively. Avascular necrosis and Chronic osteomyelitis were the non-neoplastic lesions seen. Clinical, imaging and histopathology thus remains the key for diagnosing bone lesions; especially so in bone tumors.

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