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Original Research Article

CLINICOPATHOLOGICAL PROFILE OF BENIGN AND MALIGNANT LESIONS OF BONE - A RETROSPECTIVE STUDY AT A TERTIARY CARE CENTRE

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Abstract

Background: Primary neoplasms of the bone are not much common amongst the huge array of human neoplasms which is considered as a reason for lesser amount of information regarding the incidence of these tumors. **Materials and Methods:** This study was conducted in the Department of Pathology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar Jammu & Kashmir and included all primary bone tumor specimen including excision biopsies, Computed Tomography (CT) guided biopsies and amputations received over a period of ten years from May 2006 to June 2016. **Result:** A total of 123 bone tumour biopsies and specimen were received during the period of 10 years. Benign tumors were more common than malignant tumors. Out of 123 cases received, 76 were benign and 47 were malignant. Males were more affected than females. The most common benign tumor in our study was Osteochondroma. Among malignant tumors Osteosarcoma followed Ewing's sarcoma, and chondrosarcoma were more common. Bones around knee joint were most commonly affected. **Conclusion:** The management of bone tumors requires a meticulous study involving clinical, radiological, morphological, immunohistochemical, cytogenetic and molecular aspects. A proper utilization of such techniques can aid clinicians as well as pathologists in optimal treatment and diagnosis of these unusual tumors.

INTRODUCTION

Bone tumours have never been considered common lesions and are not seen frequently clinically as well. Most commonly patients present with symptoms of pain, mass or sense of fullness, loss of function, deformities and pathologic fracture. Benign lesions are often well circumscribed while malignant tumours are poorly circumscribed and infiltrate the adjoining tissues.Age of the patient and site of the lesion have importance because many bone lesions have been shown to have preference for some specific sites within the bone like for epiphysis, metaphysis or diaphysis. Some bone tumours are known to produce a periosteal reaction e.g. Langerhans cell histiocytosis produces a periosteal new bone while as Ewing's sarcoma lesions usually form multiple layers of periosteal bone. Some lesions lesions show additional features like calcification, cortical damage, periosteal reaction and soft tissue extension. Many tumors known to forma pseudocapsule. Most lesions arise de novo but some may have association with particular syndromes e.g Li Fraumeni syndrome or may occur in pre-existing bone lesions like Paget's disease.

The grading of bone tumors is equally important and requires a meticulous assessment of cellularity, nuclear features and degree of cytologicatypia. Staging is popularly done according to two main staging systems which include the TNM system and the Enneking system. The TNM system is mostly useful in staging epithelial tumors because bone neoplasms rarely metastasize to lymph nodes. The other system which was first proposed by Enneking and colleagues in 1980 and is being more widely used for staging sarcomas.1This staging system is based on two main characteristics of the neoplasm which include the anatomic location and the grade of the tumor.

Specimens of bony lesions could be obtained by a variety of methods, the most commonly used methods being the fine needle aspiration cytology (FNAC), CT or USG guided core needle biopsy or

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by an incisional open biopsy. Incisional biopsies are better because they provide a relatively larger amount of tissue and less artifacts.

MATERIALS AND METHODS

Our study was conducted in the Department of Pathology at the Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jammu & Kashmir and included retrospective data analysis for 8 years and a prospective study over a period of 2 years. All the cases of bone tumors received in the Department during the ten years of study period were included in our study. The study included True cut biopsies, CT guided biopsies, amputation specimen and blocks for review. The specimen/biopsies for bone tumors received were subjected to gross and detailed histopathological examination In case of bone biopsies, whole tissue was submitted for processing. The specimen/biopsies were fixed in 10% buffered formalin. In case of amputation specimen a minimum of four sections were taken from the tumor and sections were taken attached soft tissue, resection margins, lymph nodes (if present). Bone specimen were initially kept for decalcification and then the tissue was sent for tissue processing. 4 to 5 micron sections were cut on the rotary microtome and stained with haematoxylin and eosin stain and special stains like PAS was done wherever required. The findings were compiled and then analyzed. Microphotographs of tumors were taken respectively. All metastatic bone tumors were excluded in the study.

RESULTS

Out of 56,000 biopsies/specimen received during the 10 years period at our centre, a total of 123(0.21%) cases of bone tumors were analyzed in our study.Out of the 54 cases (41.1%) were bone biopsies followed by CT- guided biopsies which were 25 in number (20.32%). Excised bone specimens comprised of 23 cases (18.6%). 11 blocks were received for review. Amputations were least common specimens received i.e. 10 cases (8.9%). We found out that 75 were males and 48 were females and benign tumors (76) were more common than malignant tumors (47). Out of 76 cases of benign tumors, osteochondroma (16 cases)was the most common followed byGiant cell tumor (12 cases), 7 cases of osteoid osteoma and fibrous dysplasia and 6 cases eachof Exostosis,Non ossifying fibroma. Other tumors seen were Cavernous haemangioma, Aneurysmal bone cyst, osteoma, Chondroma, Odontogenic cyst and a single case of osteoblastoma. Distribution of benign cases according to histological type are shown in Table1. In our study we found that Osteochondroma, Giant cell tumor, Osteoid osteoma, NOF were common in males and Fibrous dysplasia, Aneurysmal bone cyst were common in females. Osteoma, Chondroma, odontogenic cyst showed equal distribution among both sexes. The maximum number of cases were seen in age group 20–29 years and 30–39 years age group. The common site involved by osteoid osteoma was tibia showing maximum number of cases followed by femur bone. The common site of involvement by osteochondroma was proximal tibia followed by distal femur and scapula. Cases of non-ossifying fibromawere common in femur followed by tibia. In fibrous dysplasia mandible was involved mostly followed by maxilla, tibia and rib bone.

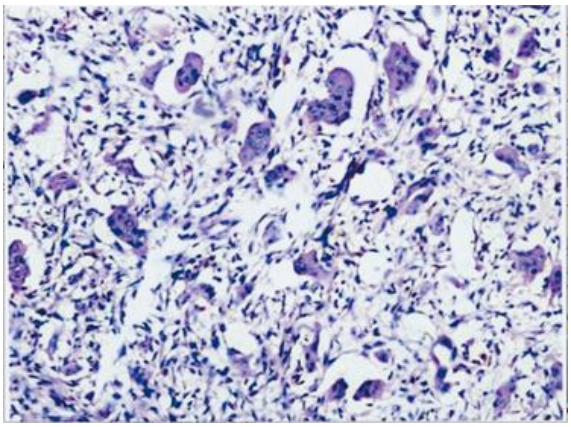

Figure 1: Giant cell tumor of bone showing both stromal cells and giant cells with multiple nuclei (H&E)

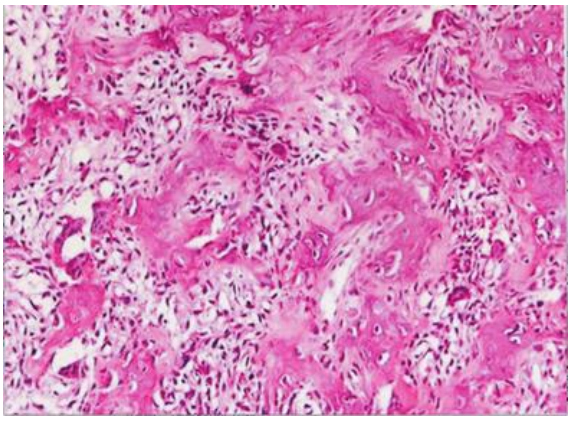

Figure 2: Osteoid osteoma showing a new osteoid and bone formation by plump osteoblasts (H&E)

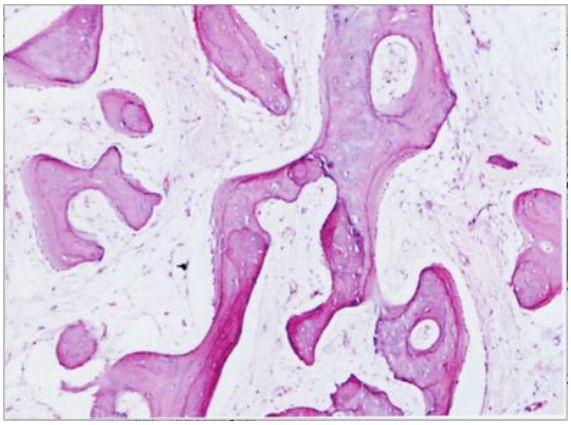

Figure 3: Fibrous dysplasia showing curved bony trabeculae interspersed with fibrous tissue (H&E)

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The commonest site involved by cavernous hemangioma was cervical vertebra, lumber vertebra, humerus and femur bones. Aneurysmal bone cyst cases were seen most commonly in femur followed by humerus and cervical vertebra.

Pain and swelling were the most common clinical features in benign tumors followed by tenderness and difficulty in movement. Fever and pathological fracture were seen in two cases of GCT and aneurysmal bone cyst in any case.Gender wise distribution of malignant cases is shown in [Table 2].

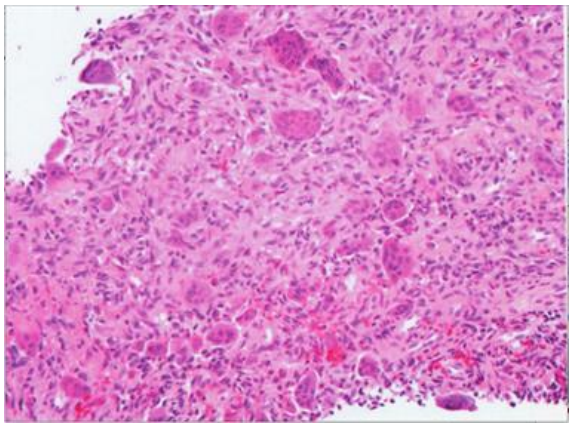

Figure 4: Aneurysmal bone cyst showing interconnecting vascular spaces filled with blood without endothelial lining with many osteoclast like giant cells

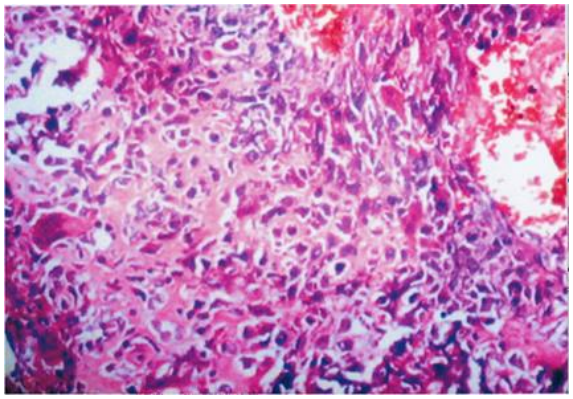

Figure 5: Osteosarcoma showing malignant bone formation by tumor cells without interposition of cartilage(H&E)

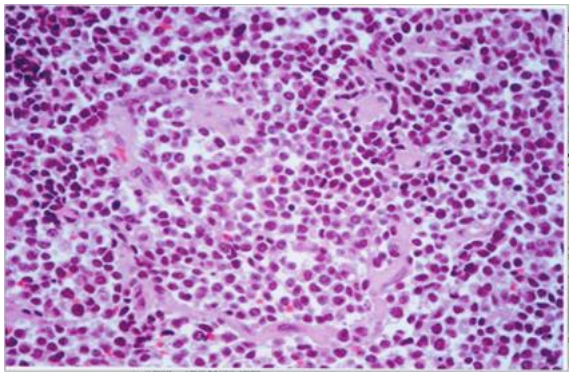

Figure 6:Ewing's sarcoma showing uniform small cells with scant cytoplasm (H&E 10x)

Malignant Bone Tumors: Osteosarcoma was the most common malignant tumor seen in 18 cases (38.29%) followed byEwing's sarcoma 11 cases (23.24%) and 9 cases (19.14%) were chondrosarcoma, 6 cases were Chordoma (12.76%) and angiosarcoma were 3 cases (6%).All tumors were common in males while Chordoma was seen to be equally distributed in both sexes. Maximum number of cases were in age 10-19 years (16 cases). Osteosarcoma and Ewing's sarcoma were more common in the age group 10 to 19 years and 20 to 29 years, however osteosarcoma showed bimodal distribution. Most cases of chondrosarcoma were seen in 4th and 5th decades of life while chordoma was seen commonly in fourth and fifth decades.

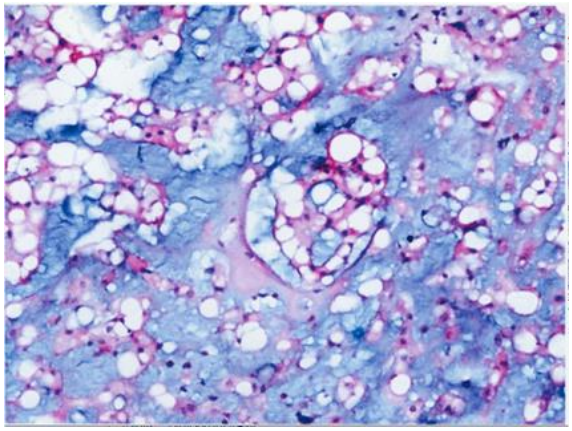

Figure 7: Chordoma showing tumor cells arranged in cords and lobules with abundant vacoulated cytoplasm in a myxoid stroma

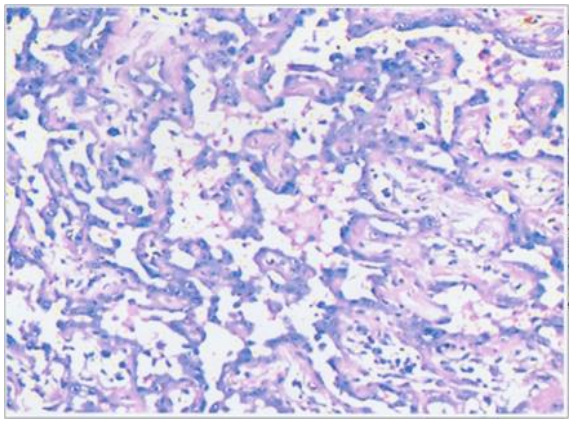

Figure 8: Angiosarcoma of bone showing anastmosing vascular channels lined by highly atypical endothelial cells (H&E).

Femur was the commonestsite involvedby Osteosarcoma followed by tibia and humerus iliac bone. Out of 18 patients, 12 patients had stage 1A disease, 3 patients had stage IIB, one stage hadIVA and one had Stage IVB disease according to the WHO guidelines.

The commonest site involvedby Ewing Sarcoma was femur followed by tibia, metatarsal and calcaneum.

Pain and swelling was leading clinical features in all malignant tumors followed by localized tenderness

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and difficulty in movements. Pathological fractures were seen in 2 cases of osteosarcoma and one case of angiosarcoma. Neurological deficit was seen in 3 cases of Chordoma.

Table 1: Distribution of benign cases according to histological type

S.No.	Histological type	Number of cases
1	Osteochondroma	16
2	Giant cell tumor	12
3	Osteoid osteoma	7
4	Osteoma	4
5	Aggressive osteoblastoma	1
6	Exostosis	6
7	Odontogenic cyst	2
8	Aneurysmal bone cyst	5
9	Cavernous hemangioma	6
10	Fibrous dysplasia	7
11	Non ossifying fibroma	6
12	Chondroma	4

Table 2: Distribution of malignant cases according to gender

Histological type	Male	Female	Total
Angiosarcoma	2(66.66%)	1(33.33%)	3
Osteosarcoma	10(55.5%)	8(44.44%)	18
Ewing's sarcoma	6(54.54%)	5(45.45%)	11
Chondrosarcoma	5(55.5%)	4(44.5%)	9
Chordoma	3(50%)	3(50%)	6

DISCUSSION

The present study was a clinicopathological study focused upon the analysis of the pattern of primary benign and malignant lesions of bone which was carried out in the Department of Pathology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar over a period of ten years. It was a retrospective study extending over a period of 8 years from June 2006 to May 2014 & the prospective study over a period of two years from June 2014 to May 2016. Out of a total of 56000 samples received during the ten-year period, bone tumors constituted only 123 cases which is 0.21% of all cases. Males were more affected then females 75 (60.9%) and females with 48 cases (39.02%). Benign tumors outnumbered the malignant counterparts representing 76 cases (62.7%) and malignant counterpart representing 47 cases (38.21%). Thus the bone cancers in our study represented only a small proportion of all malignancies which is comparable with the results from other studies.Dahlin et al, Shah et al and Price et al reported similar results.[1-5]

We found in our study that out of 76 benign cases, maximum number of cases were osteochondroma 16 cases followed by Giant cell tumor 12 cases [Figure 1] and 7 cases of osteoid osteoma[Figure 2] and fibrous dysplasia [Figure 3] and 6 cases eachof Exostosis, Non ossifying fibroma, Cavernous haemangioma. Aneurysmal bone cyst [Figure 4] were diagnosed in 5 cases.

Osteochondroma was the most common benign tumor in our study outnumbering other benign tumors representing 16 cases received during our study period. Jain et al, in their study of 117 patients, studied over a period of 8 years from 2002-2009 found that 67 cases were benign tumors and Osteochondroma was the most common accounting for 26 cases followed by giant cell tumor 24 cases.6 Sarma et al 1994 recorded total number 165 bone tumors in a ten years. In their series 125 cases were benign and 40 cases were malignant.[7] Similar pattern was observed by Rao et al,[8]Negash et al,[9]Dimpal et al.[10] The results reported by these authors was coherent with our study.

The most common site involved in our study was tibia in 31% cases followed by femur 25% caseswhich was similar to findings reported by Rao et al with tibia and femur being the most common sites followed by scapula and radius.[8] In our study osteochondroma was seen more commonly in males (62.5%) than in females (37.5%) thus making a ratio 1.6:1. Our observations were in correlation with other studies.[6,8]The most common age group affected by osteochondroma in our study was 2nd and 3rd decade of life which also correlates with the observations made by Rao et aland Jain et al.[6,8]

Giant cell tumor (osteoclastoma) was 2nd most common benign tumor seen in our study 12(15.7%) cases out of 76 cases. Jain et al in their study found out that osteochondroma was the most common benign tumor accounting for 26 cases (22.2%) followed by giant cell tumor 24 cases (20.51%). Rao et al recorded 91 cases out of 317 benign bone tumors making (28.8%) and only benign variant of giant cell tumor (osteoclastoma) was observed in their study.8,6In our study in cases of giant cell tumor males and females were equally affected and male to female ratio was 1:1. The observation made by authors Christenson et al, Sung et al, Rao et al,Sharma et alreported male to female ratio of 1:1.1,1.2:1,1:1.3,1:1.2 respectively.[8,11-13] which was similar to our results. The age range affected by GCT in our study was from 12 -45 years and the common ages being the 2nd,3rd and 4th decade (25%each).The above results correspond well with other studies.[8,11-13]In our study bones of lower extremity was the most common site involved.

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Femur was involved in 41% and tibia in 33% cases followed by scapula 25% our results correspond well with other authors.[8,11-13]

Osteoid osteoma along with fibrous dysplasiawas the 3rdmost common benign tumor in our study consisting 7 cases (9.21%). In our study 4 patients were male and 3 were femaleand male to female ratio was1.5:1which was incorrelation with a study by Freiberger et al.[14] The most commonly affected age group was 4thdecade which was similar to studies by Freibergeret al, Rao et al, Sunita et al.[8,14,15]In our study tibia was involved in 5 cases and femur in 2 cases which corresponds with other authors.[14,15]

Fibrous dysplasia was the 4th most common benign tumor in our study 7 cases out of 76(9.21%). Females were more affected than males and most of cases were seen in 3rd and 4th decade of life. In fibrous dysplasia mandible involved in 3 cases followed by maxilla in 2 cases, tibia and rib in one case each.Our results correspond well with the study done by other authors.[13,15,16]In our study females were slightly affected more than males. In other studies male were affected more. The reason may be because we had less number of patients in our study.

We had 6 patients of non-ossifying fibroma with 4 being males and two females. Commonest age group was 3rd and 4th decade and the most frequent site involved was tibia and femur. Our results were similar to a study byGeorg HW et al.[17]

Aneurysmal bone cyst was seen in 5 patients and 2 were male and 3 female. The most frequent age group affected was the 2ndecade and the common site involved was femur followed by humerus. Our results were coherent with a study by Cottalorda et al who in their study found that the mean age of diagnosis was 10.2 years and tibia and femur was frequent site involved.[18]

Osteoma was seen in 4 cases out of which 3 were males and one female. 3 patients were in 4th decade and one in 5th decade and the frequent site involved was facial bone which was similar to a study bySharma et aland Wani et al.[13,19]

Chondroma was seen in four cases one male and 3 female and most patients were in 2ndecade. Common sites involved werephalanges and metacarpal bone. Our results were similar to Rao et al, Sharma et al.[8,13]

Malignant tumors: Osteosarcoma [Figure 5] was the leading malignant tumor seen in 18 cases followed by Ewing's sarcoma [Figure 6] 11 cases and 9 cases were chondrosarcoma, 6 cases were Chordoma[Figure 7] and Angiosarcoma[Figure 8] were 3 cases.

Osteosarcoma was most common primary malignant tumor of bone in our study comprising 18 cases (38.29%) out of 47 cases. Dorfman et al,[22]in their studyreported the incidence of 35.1% and Jain et al reported the incidence of osteosarcoma as 35%.6 Sharma et al,[13] in their study found 12(38.7%) cases of osteosarcoma out of 31 which was in accordance with our study. Males were more often involved thanfemales and male to female ratio was 1.3:1.In our study 9 (50%) patients belonged to the age group of 10-19 years. 2nd decade of life was the most common age group affected in other studies.[2,6,8,11,13,20]

Ewing's sarcoma was 2nd most common primary malignant tumor in our study comprising 11cases (23.4%).The higher percentage of these tumors in our study compared to studies done by Larson et al,[21]Dorfman et al,[22] and Jain et al6may be due to the fact that the present study comprised of less number of cases compared to other studies.Another reason could be that our institute is a primarycancer institute in Kashmir and hence a higher number of cases of Ewing's sarcoma come for treatment there. However our results correspond with similar study by Wani et al.[19]Males were more affected than females and male to female ratio was 1.1:1, however the male female ratio in other series varies as 2.1:1 in Christenson et al,[11] 2:1 in Bhansali et al,[23] 2.3:1 in Rao et al,[8] and 1.2:1 in Sharma et al.[13]In our study most of the cases were recorded in 2nd and 3rd decade of life and 50% cases were in 2nd decade of life. These findings were correlating well with results from other series where 2nd decade was commonly affected.[11,13,23] In the present study femur and tibia was involved 5 and 4 cases respectively and our results correspond with that of Christenson et al, Bhansali et al, Sharma et al.[11,13,23]

Chondrosarcoma was the 3rd common primary malignant tumor in our study constituting 9 cases (19.1%) with five male patients and 4 female patients.The percentage is slightly lower than that observed by other authors like Larson et al (23%), Dorfman et al(25%) but slightly higher than the studies done by Rao et al (17%), Sharma et al(16%). The reason for this little variation could be explained by the fact that we had less number of patients than taken by other authors in their respective studies.[8,13,21,22]Out of 9 patients 5 were males and 4 were females which corresponds with other authorsRao et al and Henderson et al.[3,8,24]The common site for chondrosarcoma in our study were tibia and femur followed by illeum and humerus. Results in our study correspond with other authors.[3,8,24]

Chordoma was seen in 6 cases in our study and both sexes were equally affected. The common site of involvement was the sacrococcygeal region. Our findings were in coherent with Sunita et alwho also found Chordoma as the 4thcommon primary malignant tumor.[15]

Other rare tumor in our study was Angiosarcoma which was seen in three patients and most commonly involved femur in 2 cases and humerus in one case. Two were males and one female, most patients were in 5th decade.Palmerini E et al in their study found similar results.[25]

Metastatic bone tumors were not included in our study.

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CONCLUSION

The study was focussed on primarytumors of bone. A recent increase in such cases is contributed to the advancement in technology and increasing knowledge regarding such tumours. A slightly higher percentage of malignant tumors in our study is due to fact that our institute is a primary and regional cancer centre so we are getting more number of cancer patients. The main conclusions of our study are as follows:

Benign tumors were more common than malignant tumors. Males were more affected than females. The most common benign tumors noticed were Osteochondroma followed by Giant cell tumor, and Osteoid osteoma. The most common age group affected by benign tumors was 2nd & 3rd decade of life.Long tubular bone were commonest sites involved especially tibia, femur (around knee joint) and humerus.Other common benign tumors were Aneurysmal bone cyst, Fibrous dysplasia, non-ossifying fibroma. Most common clinical features were pain at the affected site, swelling and difficulty in movements. Among the malignant tumors osteosarcoma followed by Ewing's sarcoma and chondrosarcoma were more common. Other tumors like Chordoma and Angiosarcoma were also seen. The most common age group affected by malignant tumors was 2nd, 3rd and 4th decade of life. Among malignant tumors osteosarcoma showed bimodal age involvement. Bones around knee joint were commonly affected. Most of affected patients presented with pain,swelling, tenderness, pathological fracture and other constitutional symptoms like fever. However radiographic imaging has proved to be a very valuable modality for diagnosis and computed tomography(CT) and magnetic resonance imaging(MRI) have importance in staging the tumors.

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