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Research Paper

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Demographic clinical, radiological and histopathological analysis of various malignant neoplasms of bone and articular cartilage in a tertiary care hospital-A cross sectional study

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[doi:10.48047/AFJBS.6.14.2024.11812-11829](https://doi.org/10.48047/AFJBS.6.14.2024.11812-11829)**Abstract****Background:**

Malignant bone and cartilage neoplasms pose significant clinical challenges despite diagnostic and treatment advancements. Understanding their epidemiology, clinical characteristics, and histopathological features is crucial for accurate diagnosis and treatment. Further investigation into their incidence, distribution, and clinicopathological correlations, particularly in diverse patient populations is warranted.

Introduction:

This study aims to complete the analysis of malignant neoplasms of bone and cartilage, including a broad collection of tumours with a wide range of non-specific symptoms. An accurate and quick diagnosis is required to treat all tumours effectively and early on to reduce the disease's effects. This study is conducted to investigate the demographic, clinical, radiological and histopathological distribution of various malignant bone tumours in a tertiary care hospital.

Methodology:

This is a retrospective cross-sectional study conducted in the Department of Pathology at Sri Ramachandra Medical College and Research Institute from January 2020 to December 2023 with 106 study samples. Their sampling method involved demographic details, clinical history, histopathological data collected from archived slides and data collection for radiographic images, hospital records and the PACS system. The distribution of age, sex, and different types of various malignant neoplasms of bone and articular cartilage in different anatomical sites were obtained and statistical analysis were done.

Results:

Primary tumours accounted for 76 cases (71.6%), while secondary tumours constituted 30 cases (28.3%). In this study, the distribution of histopathological diagnosis was as follows: Osteosarcoma was observed (n=39;51.3%), Ewing's sarcoma (n=20; 26.3%), Chondrosarcoma(n=16; 21%), malignant GCT(n=1;1%) and metastasis(n=30; 30%). Osteosarcoma is observed in 39 cases, with the highest numbers in the Femur (19 cases), followed by Tibia (8 cases), Humerus (8 cases), and Radius (4 cases). Secondaries (metastasis) was observed most commonly involving vertebra in 16 cases (54%) followed by sacrum in 5 cases (17%), femur in 4 cases (13%), knee in 3 cases (10%), manubrium sternum in 2 cases (6%).

Conclusion:

This study gives a descriptive analysis of the distribution of malignant bone and cartilage tumours in a tertiary care setting in south India and also emphasises the importance of a multidisciplinary approach to arrive at an accurate diagnosis for tailored treatment.

Keywords: Malignant, bone and cartilage tumours

Introduction

Cancer causes ten million deaths approximately around the world, despite medical and surgical oncology advancements ⁽¹⁾. Among the cases, bone tumours are relatively rare and constitute a wide array of neoplasms that pose significant challenges in diagnosis. These malignancies account for only 0.2% of all types of cancer, depending upon the age and histological type ⁽²⁾.

Pain and swelling form the most common clinical presentation of patients diagnosed with malignant bone tumours. Symptoms of bone tumours are not specific hence a team of treating physicians, pathologists and radiologists of expertise must be involved in diagnosis.

Salom et al states that high-quality images on radiographs with several angles are important for the details in a comprehensive evaluation of malignant bone tumours⁽³⁾. The exact diagnosis of these tumours is further confirmed by histopathological analysis. Light microscopy and various other ancillary techniques in conjunction with clinical and radiological features of malignant neoplasms, help to differentiate between different types of bone neoplasms. The management of malignant bone tumours provides a consensus approach for diagnosing the given condition with utmost accuracy and gives better outcomes for the patients.

The current study focuses on the features of the demographic, clinical presentations, and diagnostic findings of malignant neoplasms of bone and cartilage in a tertiary care centre. This study is directed towards providing insights into the common presentations and most common malignant bone neoplasms. The study's findings will be useful to understand the common sites and various histological types of bone tumours from a tertiary care which may add value to the understanding and management of malignant bone neoplasms.

Materials and methods

Study design:

This is a retrospective cross-sectional study done at Sri Ramachandra Institute of Higher Education and Research from January 2020 to December 2023.

Study population:

The study included the quantitative and descriptive data of 106 samples of bone and articular cartilage biopsy from the archives retrieved from LIS (lab information software) at Sri

Ramachandra Institute of Higher Education and Research from January 2020 to December 2023.

Inclusion Criteria

This study includes all Chondrogenic, Osteogenic, Fibrogenic, Vascular, Mesenchymal and Hematopoietic malignant bone and cartilage tumours that were diagnosed at our institute.

Exclusion Criteria

Benign bone tumors are excluded from the study to have a specific focus on malignant diseases.

Data Collection tools

Clinical Data: Collected data included age, sex, duration of symptoms, the presence of edema and deformity, relation to previous trauma, presence or absence of systemic features.

Radiological Data collected included site of the tumor, matrix type (fibrous, osteogenic, cartilaginous), and specific variety of the tumor (vascular, mesenchymal, chondrogenic, osteogenic, fibrogenic, hematological neoplasms).

Data was retrieved from the LIS and medical records from MRD.

Histopathological Data: Resected specimens and biopsy samples were diagnosed by light microscopy and ancillary tests to make a specific diagnosis.

The microscopic studies of histopathology slides of all cases were documented using a light microscope, Cilika TF100, serial no: 2108837.

Data Analysis

The collected data was analysed by appropriate statistical methods. Descriptive statistics were used to summarize the clinical and sociodemographic characteristics of the patients.

Ethical approval and informed consent:

Institutional Ethics Committee(IEC) approval was obtained in March 2024 before the commencement of the study. IEC reference ID is given here.

(REF: CSP-MED/24/MAR/100/86)

Results:

In this study, out of total 106 patients, 69 were males and 37 were females. Primary tumours accounted for 76 cases (71.6%) of the cases, while secondary tumours constituted 30 cases (28.3%). Out of 106 cases, 73 cases were small biopsies and 33 large resected specimens were received in our institute (Figure 7)

Age and gender distribution of tumours:

The mean age of the patient was 41.51 with a standard deviation of 21.7 with their age group ranging from 11 to 88years. Among male patients, 53(76.8%) had primary tumours, while 16(23.1%) had secondary tumours (metastasis). Among female patients, 23(62%) had primary tumours, while 14(38%) had secondary tumours (Table 1 and Table 2)

Histopathological diagnosis and distribution of tumours:

The histopathological diagnosis for primary tumours in the study was as follows: Osteosarcoma accounted for 51.3% of cases, Ewing's sarcoma - 26.3%, Chondrosarcoma - 21%, and Malignant giant cell tumour - 1.2% (Table2). The histopathological diagnoses corresponding to the age and gender distributions were as follows: Osteosarcoma, with ages ranging from 27 to 69 years, had 24 cases (34.7%) in males and 15 cases (40.5%) in females. Ewing's sarcoma, in the age range of 11 to 33 years, had 16 cases (23.1%) in males and 4 cases (10.8%) in females. Chondrosarcoma, with age ranging from 13 to 67 years, had 12 cases (17.3%) in males and 4 cases (10.8%) in females. A single case (1.4%) of Malignant giant cell tumour was observed in a 48-year-old male. In the category of Metastasis (Secondary), age ranges from 18 to 88 years, there were 16 cases (23.1%) in males and 14 cases (37.8%) in females (Table 3)

Common clinical presentation of tumours:

The presentation of primary tumours in terms of symptoms was as follows: Osteosarcoma was associated with pain and swelling in 31 cases (51.6%), along with 2 cases (66.6%) exhibiting pathological fractures and 6 cases (46.1%) showing other associated symptoms like loss of weight and immobility. Ewing's sarcoma presented with pain and swelling in 17 cases (28.3%) and had 3 cases (23%) with associated symptoms. Chondrosarcoma was linked to pain and swelling in 11 cases (18.3%), with 1 case (33.3%) having a pathological fracture and 4 cases (30.7%) showing associated symptoms. Malignant giant cell tumour had 1 case (1.6%) with pain and swelling but no pathological fractures or other associated symptoms were noted (Table 4). Secondaries (metastasis) was observed in the femur in 5 cases (17%), knee in 4 cases (13.3%), manubrium sternum in 3 cases (10%), sacrum in 3 cases (10%) and vertebra in 15 cases (50%)(Figure 8)

Histopathological and Radiological diagnosis distribution across anatomical sites:

The distribution of malignant bone tumours based on their anatomical location and correlation with radiological findings was as follows Malignant giant cell tumours (GCT) were primarily

located in the epiphysis, Osteosarcoma and Chondrosarcoma were commonly found in the metaphysis, and Ewing's sarcoma typically affected the diaphysis.(Table 5, Fig 9)

The distribution of histopathological diagnoses across anatomical sites was as follows: Osteosarcoma was observed in 39 cases, with the highest numbers in the Femur (19 cases), followed by Tibia (8 cases), Humerus (8 cases), and Radius (4 cases). Ewing's sarcoma accounted for 20 cases, predominantly found in the Clavicle (11 cases), humerus (2 cases) and pelvis (4 cases). Chondrosarcoma was identified in 16 cases, primarily affecting the proximal humerus (9 cases), lower femur (4 cases), upper tibia (2 cases), and pelvis (1 case). Malignant giant cell tumour (GCT) was present in 1 case, located in the Femur.

Osteomyelitis was the radiological diagnosis observed in the 4 cases of osteosarcoma and 6 cases of chondrosarcoma were diagnosed as enchondroma. 3 cases of Ewing's sarcoma in the paediatric age group were misdiagnosed as osteomyelitis.

Out of 76 cases diagnosed by histopathology, only 62 cases showed concordance (Table 6)

Grading of tumours:

Primary malignant bone neoplasms were graded using a two-tier grading system. Grade 1 was considered a low grade and both grades 2 and 3 as high grades.

Out of 76 cases of primary malignant bone tumours, 54 cases were high grade and 19 cases were of low grade. In our study all 16 cases of chondrosarcoma and 3 cases of osteosarcoma were diagnosed as low grade and predominantly 36 cases of osteosarcoma, 17 cases of Ewing's sarcoma and 1 case of malignant case of giant cell tumour were graded as high grade (Table 7) Necrosis and chemotherapy response of tumours were graded as follows by Picci classification: 14%(n=8) of cases showed Grade I without necrosis, 30%(n=17) Grade II and 55%(n=30) Grade III.(Table 8)

Discussion:

The results of this study present detailed socio-demographic characteristics, clinical presentations and diagnostic challenges of malignant neoplasms of bone and cartilage.

In this study age distribution ranges from 11 to 88 years illustrating that bone tumours can affect all age groups but are more common in a middle-aged demographic, reflecting findings from other regional studies^(4,5). In our study, a higher prevalence of bone tumours in males

(65%) compared to females (34.9%) is observed which aligns with the literature indicating a slight male predominance in the incidence of bone cancers^(5,6,7).

Among 33 cases of resected specimens, 14 cases of femur and 9 cases of humerus amputations, 4 cases of hemipelvectomy and 6 cases of limb salvage were done. Grossing of the resected specimens was done as per the standard operating procedures. All the primary tumours are most commonly seen in long bones whereas the metastasis to the flat and short bones correlates with other studies^(4,8,9).

Osteosarcoma, the most common primary tumour observed, exhibited a notable predilection in the femur, with a significant proportion of cases occurring in this anatomical site. This finding is consistent with previous research indicating the femur is one of the most common locations for osteosarcoma, likely due to its large size and high bone turnover rate^(4,8,9,10,11).

Ewing's sarcoma, the second most frequent primary tumour was commonly seen in this study. The predilection for the clavicle, although less common, is noteworthy and underscores the importance of considering atypical anatomical sites in the diagnostic evaluation of bone tumours^(9,12).

Chondrosarcoma even though it is less prevalent compared to Osteosarcoma and Ewing's sarcoma, exhibited a distinct distribution of anatomical sites which arise in the axial and long bones⁽¹⁰⁾.

A single case of malignant giant cell tumour(GCT) in the femur is notable because GCTs usually occur in the epiphysis of long bones. This rare type of tumour emphasizes the histopathology importance especially when the tumour displays aggressive features or unusual clinical characteristics⁽¹²⁾.

In our study, all 30 cases of secondaries were diagnosed in small biopsies. The occurrence of metastasis in 30% of cases, predominantly found in the vertebrae, is indicative of the bone's propensity to serve as a site for secondary malignancy, which is supported by the literature indicating the vertebrae as common sites for metastatic deposits followed by sacrum^(5,9,13). This finding has significant clinical implications, highlighting the need for vigilant assessment of bone pain, particularly in cancer patients, to rule out metastatic disease.

Comparing our findings on the distribution of primary malignant neoplasms by anatomical site with existing studies, we find the localization of osteosarcoma in the metaphysis and Ewing's

sarcoma in the diaphysis, which correlates with established literature. Regarding chondrosarcoma, our findings align with the diverse anatomical distribution reported in the literature, reflecting the heterogeneity of this tumour type. However, our observation of malignant giant cell tumours (GCTs) primarily occurring in the epiphysis contrasts with some previous studies which suggest a more varied distribution of this rare tumour due to differences in geographical factors with other studies^(5,6,11). When the presenting symptoms were analysed it correlated with the literature studies⁽¹²⁾.

In our study, 73 cases and 33 cases of histopathological diagnoses were given by core needle biopsies and resection respectively. Radiological studies showed discordance in 4 cases of osteosarcoma, 6 cases of chondrosarcoma, and 3 cases of Ewing's sarcoma.

Grading of primary malignant bone tumour is essential for the prognosis and to determine the metastasis of tumours. Low-grade tumours including 16 cases of chondrosarcoma and 3 cases of osteosarcoma were diagnosed as Grade 1, low-grade. 36 cases of conventional osteosarcoma, 17 cases of Ewing's sarcoma and 1 case of malignant giant cell tumour were diagnosed as grade 3, high grade.

17 cases of conventional osteosarcomas and 13 cases of Ewings sarcoma were treated with neoadjuvant chemotherapy. By Picci et al, tumour necrosis was classified and Grade III constituted about 55%(n=8) of tumour necrosis, grade II necrosis constituted 30%(n=17), and 14%(n=8) of grade I tumour necrosis¹⁴. The rest of the cases were lost to follow up and 16 cases of chondrosarcoma were treated with surgical resection (Table 7).

When the radiological findings were compared with histological diagnosis, most of them were in concordance with radiological features except for 14 cases of tumours that had discordance. This may be due to the mimics of the lytic and sclerotic lesions in radiology. Hence whenever there is a discordance from a pathological perspective it is always essential to discuss the case with radiologists and clinicians before giving a final diagnosis.

By this study, we conclude imaging and histopathology are pivotal in the diagnosis and treatment of bone cancers.



Figure 1: Left humerus amputation showing a lesion of size measuring 4.2x3.4x2cm favouring osteosarcoma

B. Left distal femur amputation showing a tumour arising from the outer surface of the periosteum of size measuring 5.3x4.4x3cm favouring paraosteal osteosarcoma

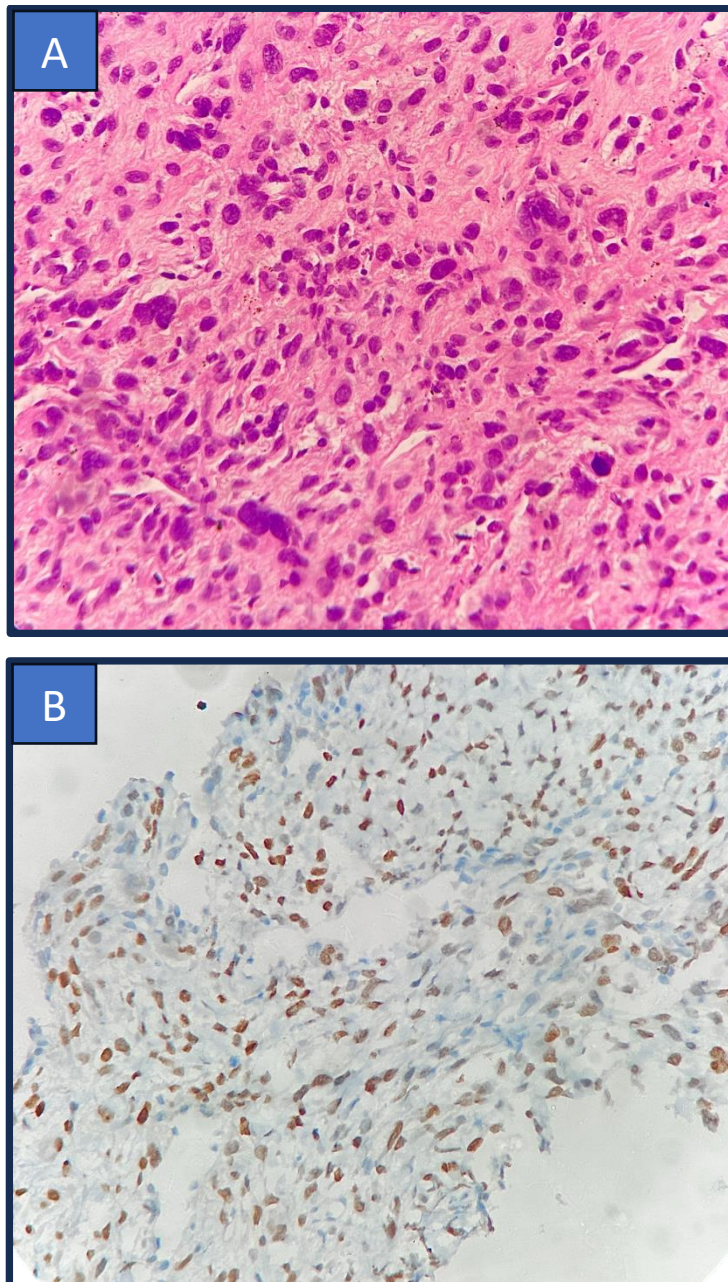


Figure 2: A.200x, cores of neoplastic tissue composed of atypical cells arranged in sheets. The individual cells are pleomorphic and spindle shaped having a moderate amount of eosinophilic cytoplasm, and large hyperchromatic nuclei.

B. Neoplastic cells are positive for Immunohistochemistry SATB2 that favours osteosarcoma.

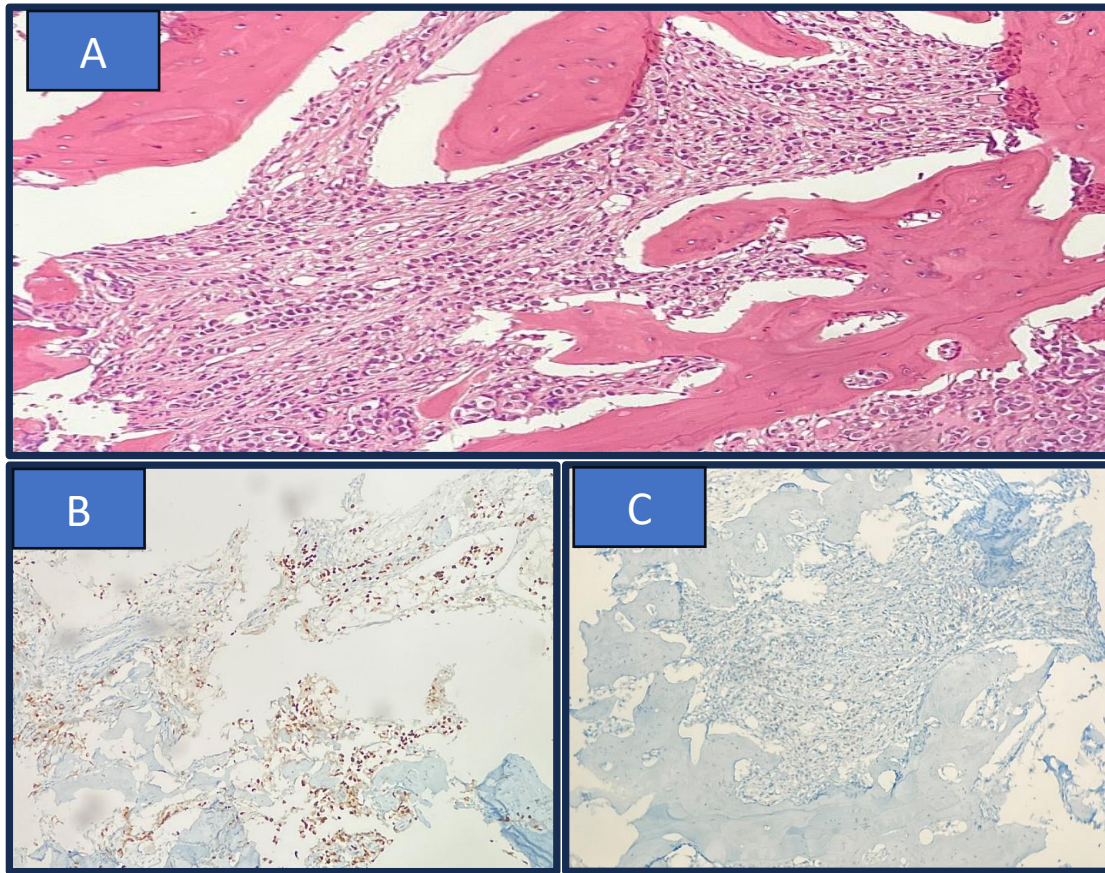


Figure 3:200x, A.Bony trabeculae with intervening marrow showing infiltration by tumour cells arranged in cords. The tumour cells show moderate nuclear pleomorphism, vesicular to hyperchromatic nuclei and prominent nucleoli

B.Immunohistochemistry for GATA3 positive in tumour cells

C.Immunohistochemistry for E-Cadherin shows a loss in tumour cells favouring lobular carcinoma for carcinoma breast.

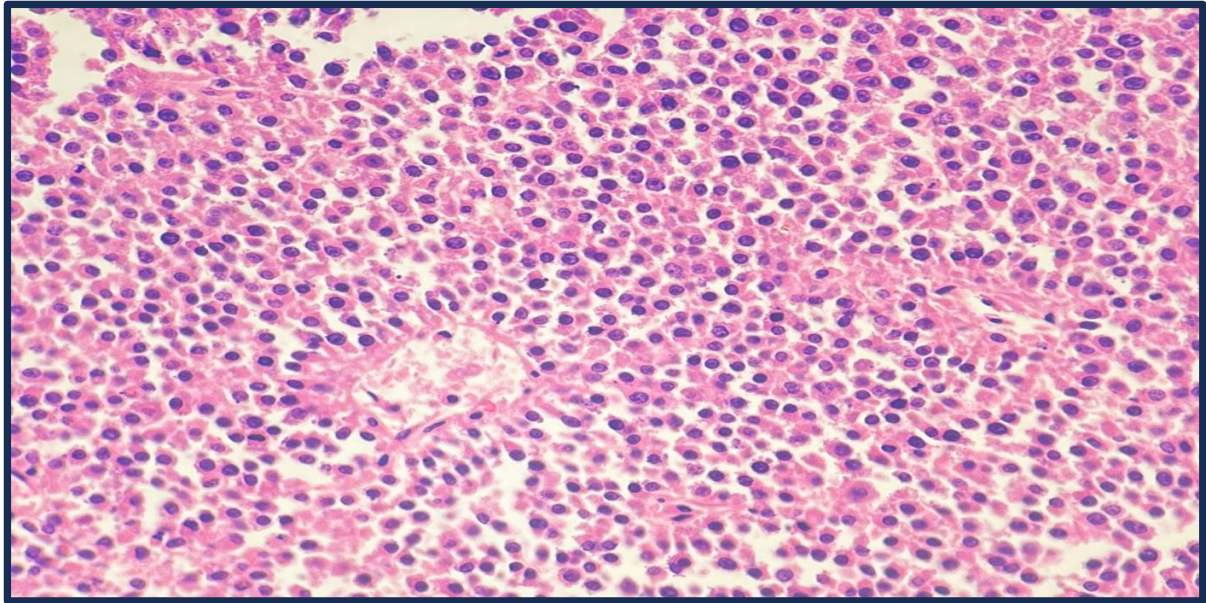


Figure 4: Ewings sarcoma, 400x Tumour cells are seen in nests and rosettes around a central lumen. Individual cells are round having moderate amphophilic cytoplasm, increased nuclear-cytoplasmic ratio, and hyperchromatic nucleoli.



Figure 5: MRI image showing a well-circumscribed eccentrically placed intramedullary lesion with peripheral sclerosis measuring 1.4x1.5x2.1 cm along the distal tibial shaft favouring the diagnosis of chondrosarcoma.

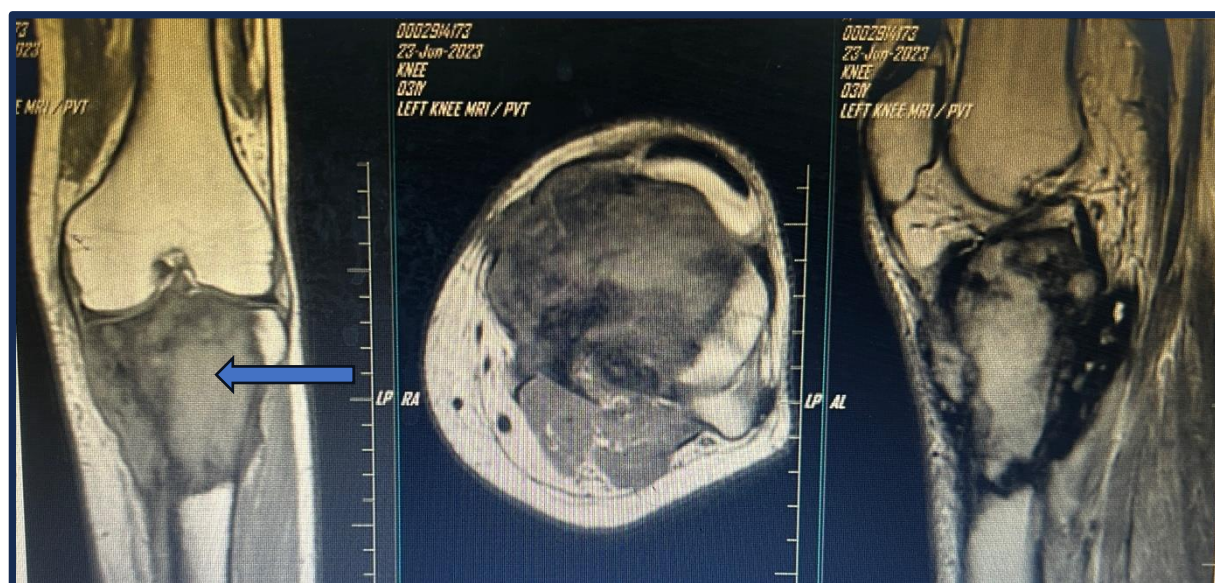


Figure 6: MRI showing eccentric lesion approximately measuring 8.2x6.6x6.5cm seen in the proximal tibia appearing hypointense on T1/T2 images favouring osteosarcoma

Tab 1. Sex distribution among primary and secondary tumours of bone and articular cartilage

Tumor types	Male (n=69)	Female (n=37)
Primary Tumor	53 (76.8%)	23 (62%)
Secondary Tumor (Secondaries)	16 (23.1%)	14 (38%)

Tab 2. Age and sex distribution of primary and secondary bone tumours:

Histopathological diagnosis	Age in years	Male (n=69)	Female (n=37)
Osteosarcoma	27-69	24(34.7%)	15 (40.5%)
Ewing's sarcoma	11-33	16(23.1%)	4 (10.8%)
Chondrosarcoma	13-67	12(17.3%)	4 (10.8%)

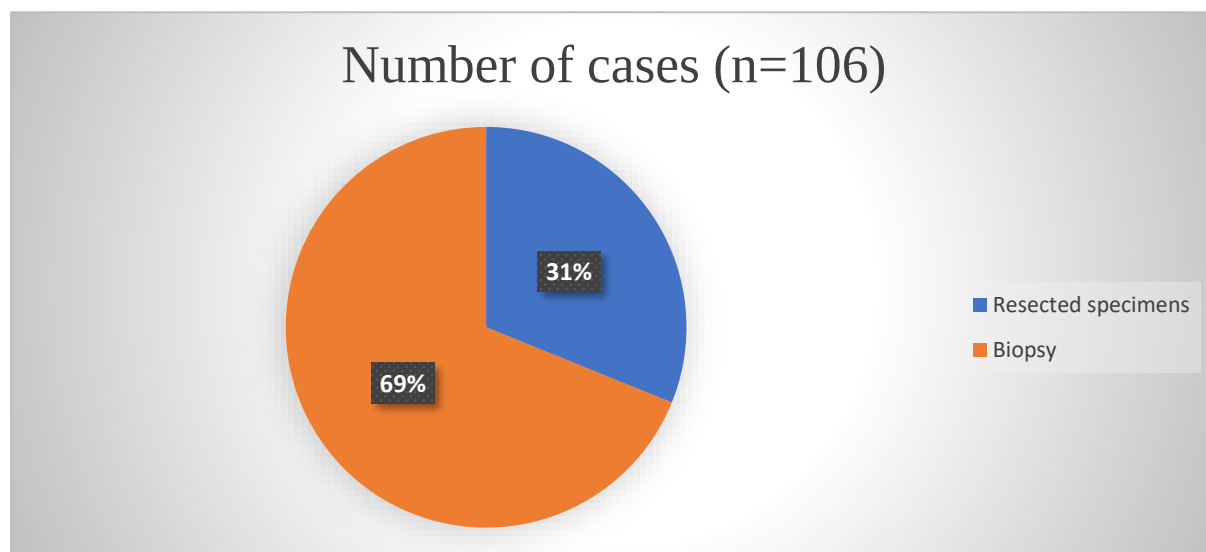
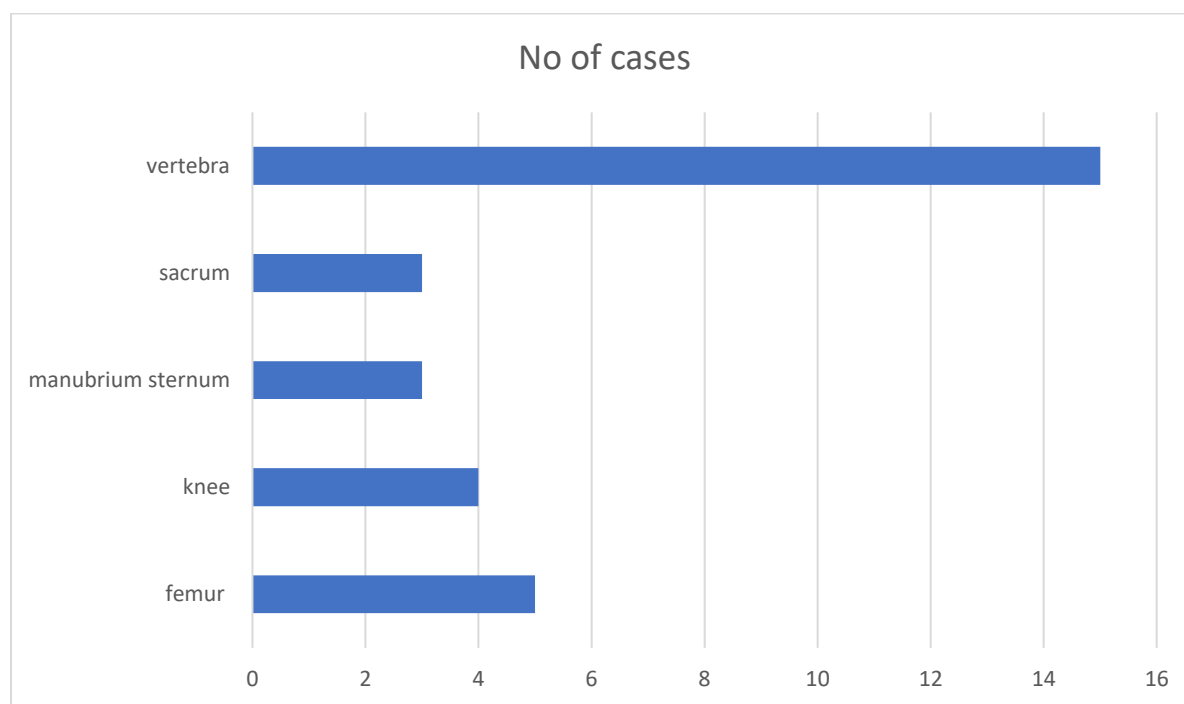
Malignant giant cell tumor	48	1(1.4%)	0
Metastasis (Secondary)	18-88	16(23.1%)	14 (37.8%)

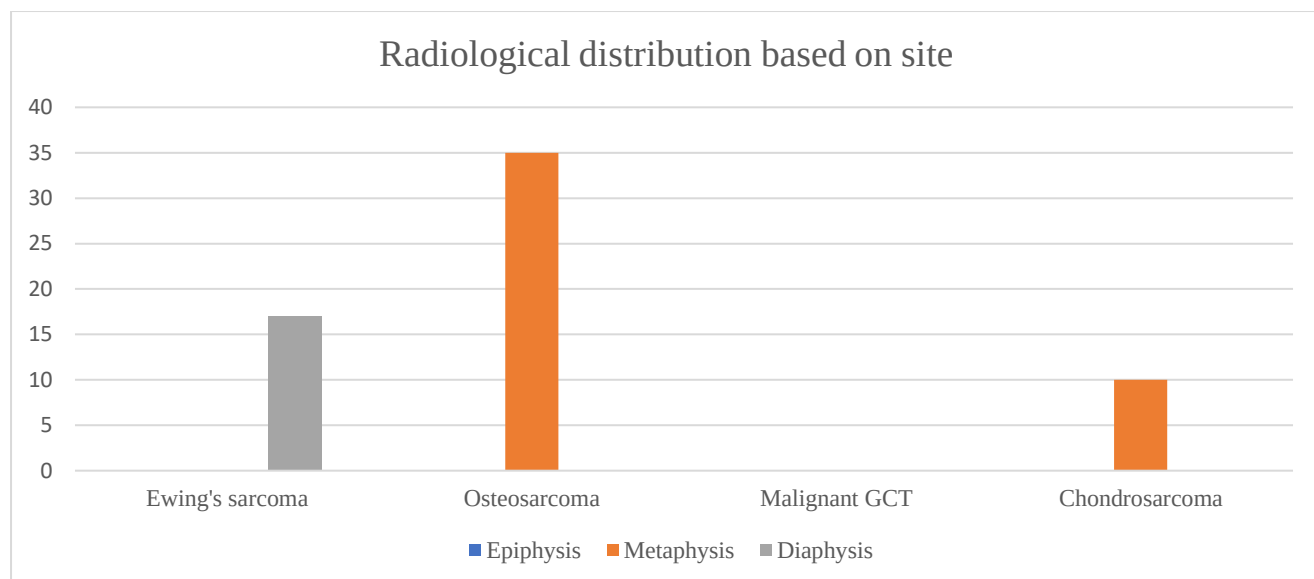
Tab 3. Different types of primary tumour based on histopathological diagnosis

Histopathological diagnosis		Number of cases (%)
Primary Tumour	Osteosarcoma	39(51.3%)
	Ewing's sarcoma	20 (26.3%)
	Chondrosarcoma	16 (21%)
	Malignant giant cell tumour	1 (1.3%)

Tab 4. Distribution of clinical signs and symptoms of primary malignant tumours:

Primary tumours	Pain and swelling (n=60)	Pathological fracture (n=3)	Associated symptoms (n=13)
Osteosarcoma	31(51.6%)	2 (66.6%)	6 (46.1%)
Ewing's sarcoma	17(28.3%)	0	3 (23%)
Chondrosarcoma	11(18.3%)	1(33.3%)	4 (30.7%)
Malignant giant cell tumour	1(1.6%)	0	0

Figure7: Distribution of tumour based on the type of specimen**Figure 8: Anatomical site of secondary bone tumours(Metastasis)****Figure:9 Radiological distribution of tumours based on site**



Tab 5. Histopathological assessment of primary malignant bone neoplasms

Histopathological diagnosis	Femur	Tibia	Humerus	Radius	Pelvis	Clavicle
Osteosarcoma	19	8	8	4	0	0
Ewing's sarcoma	0	0	2	0	4	11
Chondrosarcoma	4	2	9	0	1	0
Malignant GCT	1	0	0	0	0	0

Tab 6. Correlating diagnosis based on histopathological and radiological findings in primary bone malignant tumours

Type	Radiological diagnosis	Histopathological diagnosis	No of discordant cases
Osteosarcoma	35	39	4
Chondrosarcoma	10	16	6

Ewing's sarcoma	17	20	3
Malignant GCT	0	1	1
Total	62	76	14

Tab 7: Histopathological grading of primary malignant bone tumours based a two tier grading system

Type	Low grade	High grade
Osteosarcoma	3	36
Chondrosarcoma	16	0
Ewing's sarcoma	0	17
Malignant GCT	0	1
Total	19	54

Tab 8. Grading of necrosis after neoadjuvant chemotherapy

Grade	Number of patients (%) (n=55)
Grade I without necrosis	8(14%)
Grade II (50-89%	17(30%)
Grade III(90% ≤ necrosis <100	30(55%)
Grade IV(100% necrosis)	0

Conclusion:

In conclusion, our study not only maps the landscape of bone malignancies in a south Indian tertiary care setting but also highlights the critical need for awareness and diagnostic precision in the management of these conditions. The patterns observed in tumour type distribution and site specificity provide a crucial basis for future research and underline the importance of a

multidisciplinary approach for accurate diagnosis and effective treatment strategies in bone tumour management. Further research should focus on the molecular characterization of these tumours to better understand their pathogenesis and develop targeted therapies.

Integration with several specializations and correlating the clinical radiological and histopathological findings is essential for an accurate diagnosis and treatment.

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