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Review Article

MRI evaluation of suspected malignant bone tumors with their histopathological correlation

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Abstract

Background: Bone tumors and other lesions like tumors need to be diagnosed in early stage, they require more than one imaging modality, which incorporates conventional radiography, bone scintigraphy, CT, MRI and PET.
Aim: (1) To determine the imaging characteristics of different malignant bone tumors
(2) To evaluate the role of MRI in suspected malignant bone tumors with their histopathology correlation.
Methodology: This was a hospital based cross sectional study enrolling 58 participants over the duration of November 2019 to September 2021. All patients with suspected malignant bone tumor were included in the study. Information on basic details and investigations were noted. Data collection and analysis was done.
Results: Mean age of study participants was 39.56±20.31 years. 63.7% were male, 44.8% cases reported vertebra as site of lesion involvement. MRI observed epiphyseal involvement (81.1%), cortical involvement (89.7%), joint involvement (15.5%) and neurovascular involvement (13.7%) at the site of lesion. Sensitivity of MRI was maximum for osteosarcoma (91.67%) followed by chondrosarcoma, metastasis, Ewing's sarcoma, and Multiple myeloma. The diagnostic accuracy was above 90% for osteosarcoma, chondrosarcoma, wings sarcoma and multiple myeloma.
Conclusion: MRI is one the important investigations should be done if we are clinically suspecting a malignancy. Adequate knowledge of all these findings will aid in orthopaedist's level of confidence which further helps in therapy planning.

Keywords: Bone tumors, cross sectional study, sensitivity, diagnostic accuracy.

1. Introduction

Malignant bone tumors account for a smaller fraction of all cancers and are far less prevalent than malignant soft-tissue. Most common symptom of a patient with a malignant bone tumor is pain, which mainly observed at rest or even at night [1]. Physical examination leads to characteristic findings such including decreased joint range of motion and swelling [1]. The common primary malignant bone tumors are osteosarcoma and Ewing's sarcoma, occur in childhood [2] while in adults, Multiple myeloma, which is a monoclonal gammopathy, is the most common primary malignant bone neoplasm [3]. Other tumor common in older adults is Chondrosarcoma [4]. Occasional tumors such as chordoma and adamantinoma have anatomic predilections for the sacrum and tibia [1].

Bone tumors and other lesions like tumors need to be diagnosed in early stage, they require more than one imaging modality, which incorporates conventional radiography, bone scintigraphy, CT, MRI and PET. Conventional radiography is the fundamental step in the diagnostic process. For evaluating changes in bone marrow MRI is most sensitive and accurate method because it also narrows down the differential diagnosis [5]. As a result, MRI has changed the diagnostic approach for bone and other bone tumor like lesions [5]. Histology obtained from percutaneous or surgical biopsy serves as the reference standard for the conclusion of diagnosis of soft tissue malignancy and its tumor grade [6]. Thus, the research was conducted to find out the characteristics of different malignant bone tumors through imaging and to evaluate the role of MRI with their histopathology correlation.

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2. Materials and methodology

Study design: Current study was cross sectional Hospital based study.
Study duration: duration of the study was from November 2019 to September 2021
Sample population: Total no of participants in this study including male and female was 58.
Methodology: Institutional ethical committee clearance was obtained for the current study.
The study was conducted on patients of suspected malignant bone tumors who were referred to Department of Radiodiagnosis for MRI evaluation. All the patients first underwent MRI. Contrast study was performed as and when required. All participants were informed about the study and then information in prescribed format were obtained.

The questionnaire included socio-demographic variables such as age, gender etc. All patients underwent MRI scan with 1.5 Tesla machine. Various region of interest was scanned with T1w, T2w, STIR, PD, T2 GRE, DWI, pre contrast T1 fs, Post contrast T1 fs sequences in Sagittal, coronal, and axial planes with 3-4 mm slice thickness. A matrix size of 358 x 448 used with a 24-30 cm sized Field of Vision for coronal and sagittal scans and 14- 16 cm for axial scans. Further changes were made according to the patient requirement.
Histological examination of lesions was performed at Department of Pathology in the same centre.

The MRI findings were compared with the histopathology examinations to judge relative efficacy of MRI in diagnosing malignant bone tumous.

The results thus obtained were recorded and analysed.
Inclusion criteria:

- All patients who are referred to the hospital for MRI evaluation of suspected malignant bone tumors within the course of research.
- Cases of all age groups irrespective of sex.

Exclusion criteria:

- Likely benign bone lesions.
- Patients with history of metallic implant, foreign body, pacemaker, aneurysm clip, cochlear implant, any electric stimulator recently implanted prosthetic valve.
- Patients too unstable to undergo MRI scan who are on ventilator support.

Investigation:

- MRI: 1.5 T
- Histopathology examination of the lesion

Statistical analysis: After collecting all required data into MS excel sheet further analysis was carried out with the help of Epi info Version 7.2.2.2. Frequency and percentages were calculated. Categorical data was expressed as percentage. Diagnostic accuracy, sensitivity, specificity, NPV and PPV for MRI were calculated and expressed as percentage. P value <0.05 was considered significant.

3. Results

Mean age of study participants was 39.56±20.31 years. Age ranged from three to 79 years. Table one shows baseline characteristics of study participants. 37 out of 58 (63.7%) patients were male while 36.3% were females. 44.8% of patients reported vertebra as site of lesion involvement. This was followed by involvement of tibia/ femur constituting 25.8%. Majority (51.7%) of patients reported symptoms within 6 months of duration. Based on clinical presentation and MRI characteristics figure one outlines distribution of study participants was done. On clinical presentation, 52/58 (89.7%) of participants complained of pain at the site of lesion, 29 (50%) presented with swelling at the lesion site, 13 out of 58 (22.4%) participants were found to have fracture at the site of involvement, 17.24% of participants reported numbness and around 55.2% of the patients presented with deformity/ disability at the site of lesion. Only 4/58 (6.9%) of participants reported any discharge at and around the site of lesion.

MRI characteristics shows that 50/58 (86.2%) of participants displayed soft tissue involvement. In 81% of participants epiphyseal/ apophyseal involvement was observed. Metaphyseal involvement was observed in 24.1% of patients. Diaphyseal involvement was observed in 12% of patients. 52/58 (89.7%) of participants displayed cortical involvement. In 15.5% of participants joint involvement was observed. In 13.7% of participants neurovascular bundle involvement was observed. Expansion along medullary cavity was observed in 51.7% participants. Around 87.9% of patients reported soft tissue oedema on MRI. Skip metastasis was observed only in 1 (1.7%) participant.

Table two depicts distribution of study participants on the basis of various parameter of MRI Images. Majority (67.2%) of participants reported hypointense images followed by isointense (19%) images. Around 48.3% of participants reported heterogenous images followed by hyperintense (44.8%) images. 72.4% of participants were found to have heterogenous post contrast enhancement while only 27.6% had homogenous enhancement. Out of 58 participants, GRE blooming was observed in 43 (74.1%) of cases. Presence of fluid levels was found in one out of 58 participants (1.7%). No periosteal reaction was found in 68.9% of participants. 24.1%, 3.4% and 3.4% of participants presented with sunburst, lamellar and disorganized periosteal reactions respectively. Out of 14 sunburst periosteal reactions, 12 showed Codman's triangle.

Table three outlines distribution of study participants based on diagnosis on MRI and histopathology. On MRI around 32.7% of participants had metastatic lesions. 20.6% of participants reported osteosarcoma followed by chondrosarcoma (17.2%) and Ewing's sarcoma (15.5%).

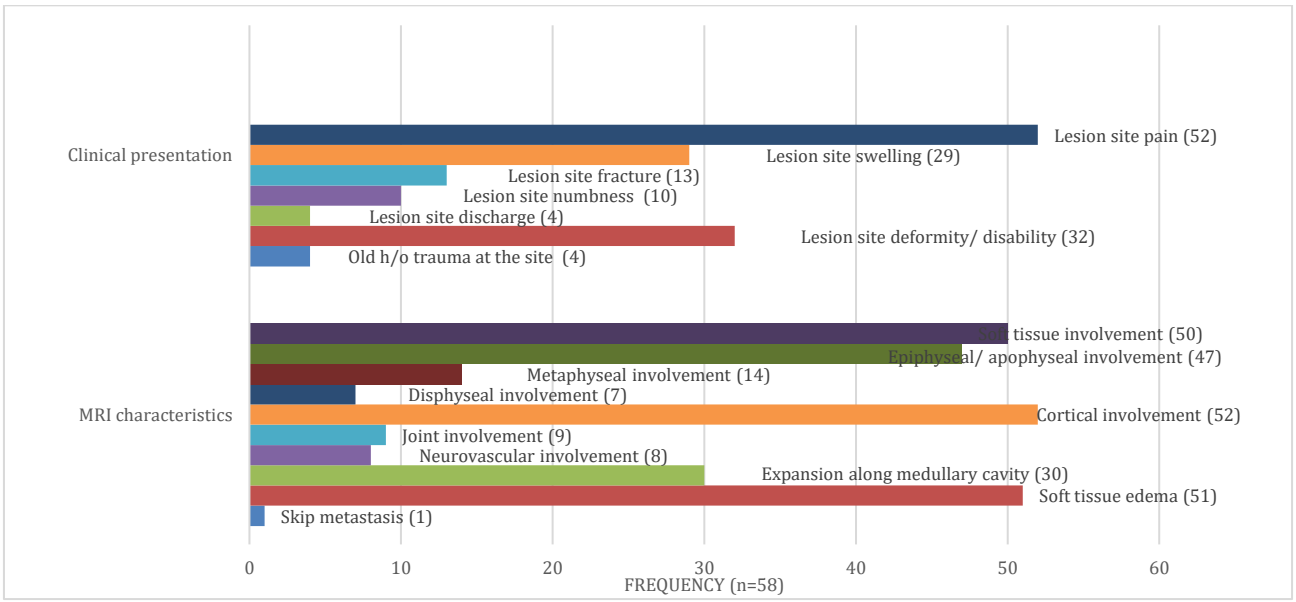

Figure 1: Distribution of study participants on the basis of clinical and MRI characteristics

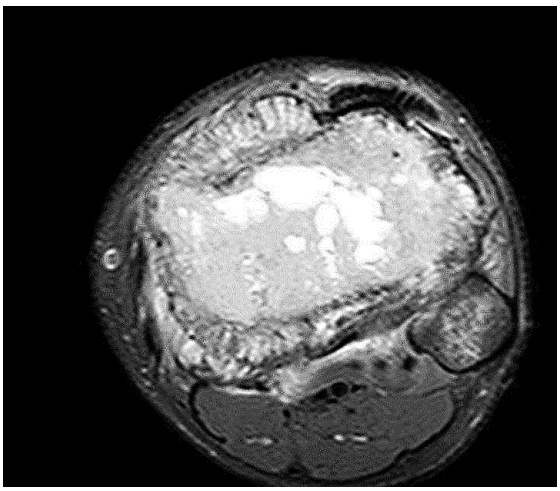

Figure 2: T2 Axial images of proximal tibia showing heterogenous lesion with sunburst periosteal reaction in case of osteosarcoma.

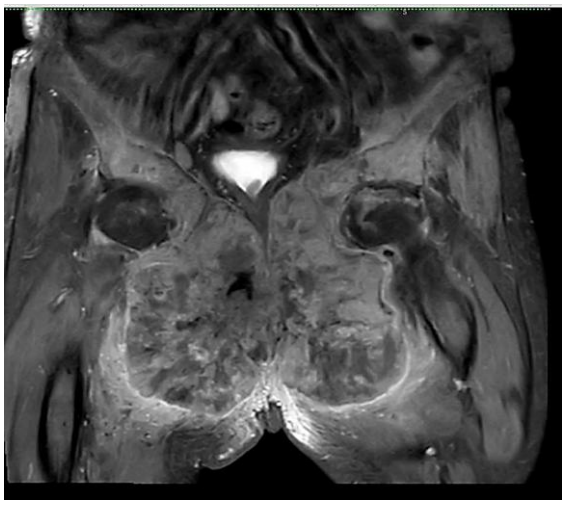

Figure 3: Chondrosarcoma pelvis showing heterogenous contrast uptake on T1coronal fat sat post contrast image.

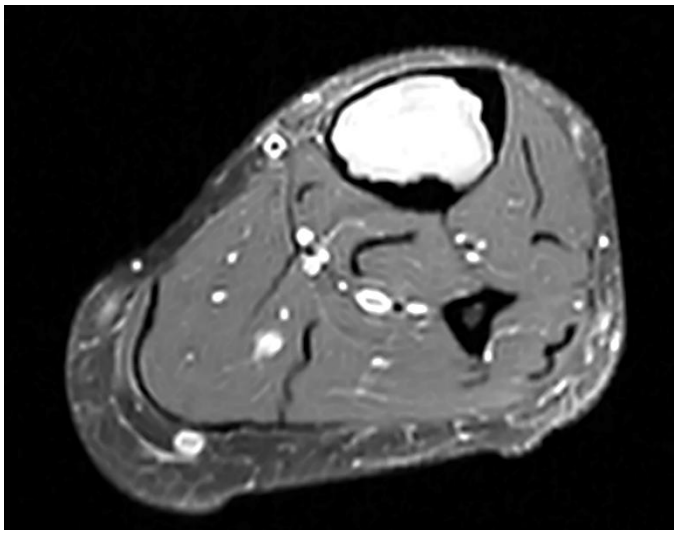

Figure 4: T2 GRE post contrast image of tibia showing intraosseous diaphyseal involvement of adamantinoma showing lobulated hyperintense signal.

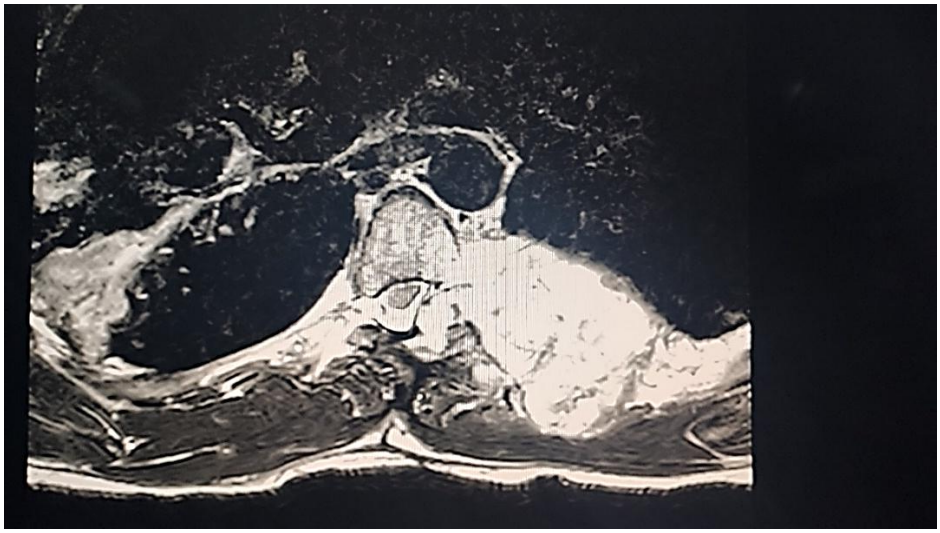

Figure 5: Ewings sarcoma vertebral and rib involvement: T2WI of dorsal spine showing hyperintense mass lesion involving second rib and adjacent D2 vertebra with soft tissue component.

Table 1: Baseline characteristics of patients with bone tumors

Sl. No.	Variable	Category	Frequency (n=58)	Percentage (%)
1	Gender	Female	21	36.3
		Male	37	63.7
2	Site	Clavicle	1	1.7
		Scapula	1	1.7
		Humerus /Radius	5	5.1
		Vertebra	26	44.8
		Rib	2	6.8
		Rib + Vertebra	2	3.4
		Ilium/ Ischium/pubis	4	6.8
		Tibia/ Femur	15	25.8
		Fibula	1	1.7
		Mandible	1	1.7
3	Duration of symptoms (in months)	0 To 6	30	51.7
		7 To 12	15	25.9
		13 To 18	6	10.3
		19 To 24	6	10.3
		More Than 24	1	1.7

Table 2: Distribution of study participants based on MRI characteristics

Sl. No.	Variable	Category	Frequency (n=58)	Percentage (%)
1	T1WI	Heterogenous	6	10.3
		Hyperintense	2	3.4
		Hypointense	39	67.2
		Isointense	11	19.0
2	T2WI	Heterogenous	28	48.3
		Hyperintense	26	44.8
		Hypointense	3	5.2
		Isointense	1	1.7
3	Contrast enhancement	Heterogenous	42	72.4
		Homogenous	16	27.6
4	GRE blooming (Present)		43	74.1
5	Presence of Fluid levels (Present)		1	1.7
7	Periosteal reaction	Absent	40	68.9
		Sunburst	14	24.1
		Lamellar	2	3.4
		Disorganized	2	3.4

Table 3: Distribution of study participants based on diagnosis on MRI

Sl. No.	Bone tumor type	Diagnosis on MRI		Diagnosis on Histopathology	
		N=58	Percentage	N=58	Percentage
1	Osteosarcoma	12	20.6	12	20.6
2	Ewing's sarcoma	10	17.2	11	18.9
3	Chondrosarcoma	9	15.5	7	12.0
4	Adamantinoma	2	3.4	2	3.4
5	Chordoma	2	3.4	0	0.0
6	Multiple myeloma	4	6.8	5	8.6
7	Metastasis	19	32.7	18	31.0
8	Others	0	0.0	3	5.1

Table 4: Diagnostic performance of MRI in diagnosing various carcinomas in comparison to histological diagnosis

	Statistic	Sensitivity	Specificity	PPV	NPV	Kappa(sig.)
Osteo-Sarcoma	Value	91.67%	97.83%	91.67%	97.83%	0.847 (<0.001)
	95% CI	61.52% to 99.79%	88.47% to 99.94%	61.11% to 98.72%	87.32% to 99.66%	
Chondro-Sarcoma	Value	85.71%	94.00%	66.67%	97.92%	0.710 (<0.001)
	95% CI	42.13% to 99.64%	83.45% to 98.75%	39.06% to 86.19%	88.43% to 99.66%	
Ewing's sarcoma	Value	72.73%	95.74%	80.00%	93.75%	0.709 (<0.001)
	95% CI	39.03% to 93.98%	85.46% to 99.48%	49.57% to 94.21%	85.08% to 97.53%	
Multiple Myeloma	Value	60.00%	98.11%	75.00%	96.30%	0.639 (<0.001)
	95% CI	14.66% to 94.73%	89.93% to 99.95%	27.48% to 95.96%	89.88% to 98.70%	
Metastasis	Value	83.33%	90.00%	78.95%	92.31%	0.722 (<0.001)
	95% CI	58.58% to 96.42%	76.34% to 97.21%	59.13% to 90.67%	80.95% to 97.13%	

While on histopathology around 31% of participants had metastatic lesions. 20.6% of participants reported osteosarcoma followed by Ewing's sarcoma (18.9%) and chondrosarcoma (12.0%). Others included osteochondroma and dedifferentiated liposarcoma.

Diagnostic performance of MRI in diagnosing various carcinomas in comparison to histological diagnosis has been displayed in table four. For osteosarcoma, out of the total 58 patients 45 malignant tumors were correctly excluded as "no osteosarcoma" one malignant tumor had a wrong false positive diagnosis on MRI and one was classified as false negative, with a diagnostic accuracy of 96.55%. Sensitivity, Specificity, Positive predictive value, and Negative predictive value in differentiating MRI from histopathological findings was found to be 91.67% 97.83%,91.67% and 97.83% respectively. Kappa value for the study is 0.847.

Diagnostic performance was calculated on the comparison of histological diagnosis with MRI in diagnosing chondrosarcoma. Of the 58 patients, 48

malignant tumors were correctly excluded as "no chondrosarcoma", three were classified as false positive and only one of the malignant tumors had a false negative diagnosis on MRI and, with a diagnostic accuracy of 92.98%. Sensitivity, Specificity, Positive predictive value and Negative predictive value in differentiating MRI from histopathological findings was found to be 85.71%, 94.00%, 66.67% and 97.92%respectively. Kappa value for the study is 0.710 and p-value of < 0.001.

Diagnostic performance was calculated on the comparison of histological diagnosis with MRI in diagnosing Ewing's sarcoma. Of the total 58 patients,45 malignant tumors were correctly excluded as "no Ewing's sarcoma", two malignant tumors had a wrong false positive diagnosis on MRI and three were classified as false negative, with a diagnostic accuracy of 91.38%. Sensitivity, Specificity, Positive predictive value and Negative predictive value in differentiating MRI from histopathological findings was found to be 72.73%, 95.74%, 80.00% and 93.75% respectively. Kappa value for the study is 0.709 with p-value is < 0.001.

Diagnostic performance was calculated on the comparison of histological diagnosis with MRI in diagnosing Multiple myeloma. Of the 58 patients, ,52 malignant tumors were correctly excluded as "no multiple myeloma", one of the tumors had a wrong false positive diagnosis on MRI and two were classified as false negative, with a diagnostic accuracy of 94.83%. Sensitivity, Specificity, Positive predictive value and Negative predictive value in differentiating MRI from histopathological findings was found to be 60%, 98.11%,75% and 96.30% respectively with a kappa value of 0.6390. The *p*-value is <0.001.

Diagnostic performance was calculated on the comparison of histological diagnosis with MRI in

diagnosing metastasis. Of the 58 patients, 36 malignancies were correctly excluded as "no metastasis", two malignant tumors had a wrong false positive diagnosis on MRI and four was classified as false negative, with a diagnostic accuracy of 87.93%. Sensitivity, Specificity, Positive predictive value and Negative predictive value in differentiating MRI from histopathological findings was found to be 83.33%, 90.00%, 78.95% and 92.31% respectively. Kappa value for the study is 0. 722. The p-value is < 0.001.

4. Discussion

As malignant bone tumors are rare so a small number of participants (n=58) could be enrolled. This was similar to findings of studies by Ambreen *et al* (2021) [5], Salazar C *et al* (2020) [7], Murad Asiltürk *et al* (2020) [8], Ashish Gulia *et al* (2019) [9], Yingwei Sun *et al* (2017) [10] and Nitish Kumar *et al* (2016) [11] with enrolment of 50, 64, 96, 100, 34 and 40 cases of bone tumour respectively.

Current study shows that mean age of study participants was 39.56±20.31 years. Age ranged from three to 79 years. Age ranged from three to 79 years. Around 25.8% of study participants were in the age group of 51 to 60 years. 20% of participants were aged less than 20 years and only 5.1% aged more than 70 years. Similar observations were reported by Ambreen *et al* (2021) [5], Salazar C *et al* (2020) [7], Murad Asiltürk *et al* (2020) [8], Pustthay Kumar *et al* (2016) [12], and Nitish Kumar *et al* (2016) [11], with mean age of 54.5 ± 14.3 years, 33.5 ± 27 years, 49.3 ± 22.7 years, 45 years and 40 years respectively. Alex Daniel *et al* [13] conducted a study in AMU Aligarh in 2009. The age-range of patients included in this study was from 11 to 80. These studies were in accordance with our study results. As per our study 37 out of 58 (63.7%) patients were males while 36.3% were females. Similar results were also reported by various studies [5, 7, 8, 11, 13] with male predominance.

4.1 Clinical profile of patients with bone tumors

Recent study shows that 44.8% of patients reported vertebra as site of lesion with predominant metastatic involvement. This was followed by involvement of tibia/ femur constituting 25.8% which include predominantly primary malignancies. Similar results were found in a study by Ashish Gulia *et al* [9] in 2019 where proximal tibia and distal femur were the most common sites involved. Also, in 2017 the study conducted by Yingwei Sun *et al* [10], most primary malignant bone tumors were all located in the long bones. In this study majority (51.7%) of patients reported symptoms within 6 months of duration. Contrary to this Murad Asiltürk *et al* (2020) [8], conducted a study where the mean duration of preoperative symptoms was 3.4 ± 7.8 (0.1–15) years.

Our study showed that 52/58 (89.7%) of participants complained of pain at the site of lesion. Out of 58 participants, 29 (50%) presented with swelling at the lesion site. 13 out of 58 (22.4%) participants were found to have fracture at the site of involvement. 17.24% of participants reported numbness at the site involved. Only 6.9% of participants reported any discharge at and around the site of lesion. Around 55.2% of the patients presented with deformity/ disability at the site of lesion. The findings were like study by Murad Asiltürk *et al* (2020) [8] where the most common symptom was radicular pain (upper/lower extremity pain) (88.5%), followed by motor deficit (87.5%) and loss of sensation (75.0%). Also, in another study Nitish kumar (2016) [11], the common clinical symptoms were pain in the region of tumor and swelling lasting for 2-3 months on average.

In current study, 6.9% participants reported old history of trauma at site involved. This was somewhat similar to study by Nitish kumar (2016) [11], where 7.5% participants reported similar history.

4.2 MRI characteristics of patients with bone tumors

In our study on T1WI imaging, it was observed that, majority (67.2%) of participants reported hypointense. In 2017 a study conducted by Yingwei Sun *et al* [10], it was observed that the tumors were shown to have mixed low signal on T1-weighted images (T1WI) and high signal on T2-weighted images (T2WI). As per current study, in 81.1% of the participants epiphyseal/ apophyseal involvement was observed on MRI. In 2017 Yingwei Sun *et al* [10], found that 2/5 cases showed a laminar periosteal reaction. The tumor appeared with mixed MRI signals and with involvement of the epiphysis and epiphyseal plates.

Recent study outlines that 52/58 (89.7%) of participants displayed cortical involvement, 15.5% of participants displayed joint involvement and 13.7% of participants had neurovascular bundle involvement on MRI. This was like the results by Nitish Kumar (2016) [11], and Pustthay Kumar *et al* [12], where 82.5% and 86% cases demonstrated cortical break on MRI respectively. 32.5% [11], and 13% [12], cases demonstrated involvement of joint on MRI respectively. 10% cases demonstrated involvement of neurovascular bundle [11, 12]. This was in accordance to the findings of our study.

4.3 Diagnostic performance of MRI in diagnosing malignant tumors

As per recent study the Sensitivity, Specificity, Positive predictive value and Negative predictive value in differentiating MRI of Osteosarcoma from histopathological findings was found to be 91.67% 97.83%,91.67% and 97.83% respectively with diagnostic accuracy of 96.55%. The sensitivity, Specificity, Positive predictive value, and Negative predictive value in differentiating MRI of chondrosarcoma from histopathological findings was found to be 85.71%, 94.00%, 66.67% and 97.92% respectively with diagnostic accuracy of 92.98%. The Sensitivity, Specificity, Positive predictive value, and Negative predictive value in differentiating MRI of Ewing's sarcoma from histopathological findings was found to be 72.73%, 95.74%, 80.00% and 93.75% respectively with diagnostic accuracy of 91.38%. The Sensitivity, Specificity, Positive predictive value, and Negative predictive value in differentiating MRI of multiple myeloma from histopathological findings was found to be 60%, 98.11%,75% and 96.30% respectively with a diagnostic accuracy of 94.83%.

In a study by Salazar C *et al* (2020) [7], on comparison of histological versus MRI diagnosis was done, the Cohen's kappa value for the correlation was 0.9, with a diagnostic accuracy of 95.1%. Murad Asiltürk *et al* (2020) [8], reported that MRIs had a high accurate rate to diagnose the most common spinal neoplasms (69.8%). Study by Nitish Kumar (2016) [11], reported sensitivity, specificity, positive predictive value and negative predictive value of MRI in detecting cortical involvement were 96.2%, 100%, 100% and 80% respectively. It also showed the sensitivity of 100%, specificity 90.4%, positive predictive value 83.3% and negative predictive value 100% in detection of joint involvement by MRI. The sensitivity was 100%, specificity 96.2%, positive predictive value 100 % and negative predictive value was 96.2% for detection of neurovascular bundle involvement.

Pustthay Kumar *et al* (2016) [12], the sensitivity for detecting joint involvement was 100%, specificity 90.4%, positive predictive value 83.3% and negative predictive value 100%. For the detection of NV bundle involvement, the sensitivity was 100%, specificity 96.2%, positive predictive value 100% and negative predictive value was 96.2%. Alex Daniel *et al* (2009) [13], observed that the sensitivity for a MRI diagnosis of malignant tumor was 85% and specificity was 84%.

Conclusion

Based upon the findings of our study, it is concluded that MRI is one the important investigations should be done if we are clinically suspecting a malignancy. Present study revealed males are most affected, mainly elder age group. However primary malignant bone tumor such as Osteosarcoma and Ewing sarcoma were seen in children and young adults with elderly involvement in chondrosarcoma and multiple myeloma. Sensitivity of MRI was maximum for osteosarcoma (91.67%) followed by chondrosarcoma, metastasis, Ewing's sarcoma, and Multiple myeloma. The diagnostic accuracy was above 90% for osteosarcoma, chondrosarcoma, wings sarcoma and multiple myeloma.

MRI also very clearly delineated the extend of cortical involvement, soft tissue involvement, neurovascular bundle involvement, skip metastasis and expansion along medullary cavity which helps for staging of the disease. Adequate knowledge of all these findings will aid in orthopedist's level of confidence which further helps in therapy planning.

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