Original Research Article

An Epidemiological Study of bone tumour patients with the role of needle biopsy in North Indian population

Deepak Kumar[1], Nilam Bhasker[2], Dharmendra Kumar[3*], Subham Srivastava[4], Sanjiv Kumar[5], Ashish Kumar[6], Amar Chandra Sharma[7]

[1]Associate Professor, Department of Orthopaedic Surgery, King George's Medical University, Lucknow, UP, India
[2]Specialist Pathologist, Department of Pathology, ESIC Hospital, Sarojni Nagar, Lucknow, UP, India
[3]Associate Professor, Department of Orthopaedic Surgery, King George's Medical University, Lucknow, UP, India
[4]Senior Resident, Department of Orthopaedic Surgery, King George's Medical University, Lucknow, UP, India
[5]Associate Professor, Department of Orthopaedic Surgery, King George's Medical University, Lucknow, UP, India
[6]Professor, Department of Orthopaedic Surgery, King George's Medical University, Lucknow, UP, India
[7]Post-doc fellow, Department of Orthopaedic Surgery, King George's Medical University, Lucknow, UP, India

Received: 06-06-2021 / Revised: 04-08-2021 / Accepted: 17-09-2021

Abstract

Introduction: The bone tumour is very challenging to pathologists and orthopedic surgeons due to its uncommon nature concerning other kinds of cancer. Needle biopsy of bone tumour is a simple procedure with inconsistent results. A small number of epidemiological data is available related to bone tumour. Hence, this retrospective study was performed at a tertiary healthcare center to determine the frequency, spectrum, overall burden, and importance of needle biopsy in bone tumours in Northern India. **Materials and Methods:** The present retrospective study was carried out at the tertiary healthcare center from 2017-2020. A total of 1314 patients were included in this study of which 834 were males and 480 were females. Relevant previous history, clinical data, radiological reports, needle biopsy reports, and histopathological reports are obtained from the case registers of the patients submitted at the department of orthopedic and pathology, Tertiary Healthcare Center in Northern India. **Results:** The mean age of patients was 26.65±14.84. Most males (63.47%, n=854) were affected and the common age group belongs to the second or third decade of life. The frequency of benign bone tumours (72.60%, n=954) was high in contrast to malignant tumours (27.39%, n=360). Giant cell tumour (56.6%, n=498) was the most common benign bone tumour observed in the patients and the most commonly involved bone was tibia (36.7%, n=182). In the case of malignant bone tumour, osteosarcoma (55%, n=198) was the commonest bone tumour detected in the patients and the most commonly involved bone was femur (38.3%, n=138). A needle biopsy was conclusive only in 30% (n=394). All tumour diagnosis was confirmed by histopathological examination. **Conclusion:** Benign tumour is the most prominent bone tumour. Tibia is the most common anatomical affected site in case of a benign tumour while femur is in case of a malignant bone tumour. Needle biopsy of bone tumour is not a reliable option to diagnose and confirm the diagnosis of bone tumour.

Keywords: Bone Tumour, Benign tumour, Malignant tumour, Epidemiology and Needle biopsy.

Introduction

Worldwide, cancer is the leading cause of death (23%) following cardiac failure [1]. Among the large variety of cancer, the incidence of bone tumour is relatively uncommon accounting for 0.5% of global cancer [2, 3]. Bone sarcoma mostly affects males in contrast to females and particularly emerged in the 2nd or 3rd decades of life [4]. Osteosarcoma constitutes the greatest proportion of bone tumours followed by chondrosarcoma, osteoclastoma, and Ewing's sarcoma [4]. Management of bone tumours is still a scary problem for pathologists and orthopedic surgeons and this problem is more heightened in developing countries due to unawareness, insufficient diagnostic and therapeutic facilities. Most of the patients with bone tumours report swelling and pain [5] and clinical presentation is non-specific in nature [6]. Several factors like age, affected site, microscopic and radiological appearance contribute to the final diagnosis of a bone tumour; hence a multi-model approach is required. Needle biopsy is a procedure for the diagnosis of the bone tumour while the false-negative rate was found to be high with needle biopsy, besides this, the diagnostic accuracy was variables reported by several studies [7, 8, 9, 10 11]. The relatively uncommon nature of bone tumours led to a scarcity of epidemiological data especially in the geographical region of India. Hence, we conducted a retrospective observational study at a tertiary care center to evaluate the frequency, spectrum, and overall burden of bone tumours in Northern India. Despite this, we also assessed the reliability of the needle biopsy associated with the diagnosis of bone tumour.

Materials and Methods

The present retrospective study was carried out at the tertiary center from March 2017- Dec 2020. All the patients were observed in our

*Correspondence
Dr. Dharmendra Kumar
Associate Professor, Department of Orthopaedic Surgery, King George's Medical University, Lucknow, Uttar Pradesh, India.
E-mail: dharmendra00715@gmail.com

patient department including new registration and referrals. Ethical clearance was approved by the institutional ethical review board. All patients were enrolled in this study after obtaining their consent. Data were extracted from the histopathology/cytology case registers and case sheets that were maintained at the department of orthopedic, tertiary healthcare center, northern India. The complete history of the patients was recorded including sex, age, and affected site. A routine biochemical investigation like complete blood count, blood urea nitrogen, liver function test, and serum electrolytes calcium, sodium and potassium, alkaline phosphatase (AP) were recorded in all patients. X-ray of involved extremity was done -AP and lateral views and the plain radiograph of the chest were recorded and evaluated. MRI of the involved site was done before the invasive procedure and results were recorded. Biopsy samples were collected by the percutaneous (closed technique) needle biopsy followed by surgical incisional or excisional biopsy and they were decalcified first by using a chelating agent or acid. After decalcification, specimens were analyzed for the cytological and morphological features of the tumours like degree of pleomorphism, presence of tumour necrosis, and mitotic count, and obtained data were recorded. A total of 1314 OPD patients were taken for this study with Inclusion criteria were confirmed cases of bone tumour on histopathological analysis. Exclusion criteria were patients with non-healing fractures, infectious lesions and non-neoplastic tumours. They were followed up to the beginning of the treatment. Histological classification of bone tumours was done according to the World Health Organization (WHO) [2]. An advanced form of the disease at the local site was described as a tumour that involves extremity and its components or neurovascular bundle, an adjacent structure organs such as vertebra or the chest wall[12]. All the details were filled in by the attending clinician. This information was regularly updated from case files and electronic medical records (EMR) was maintained on Microsoft Excel software.

Statistical Analysis

All statistical analyses were performed by using 21.0 version of SPSS software (SPSS Inc., Chicago, IL, USA). Descriptive statistics are expressed as mean, frequency, and percentage.

Results

From a total of 1314 patients, there were 834 males and 480 females with an average mean age of 26.65±14.84 years. The peak age of patients for these bone tumours was 26.65±14.84 corresponds to the third decade of life (Figure-1).

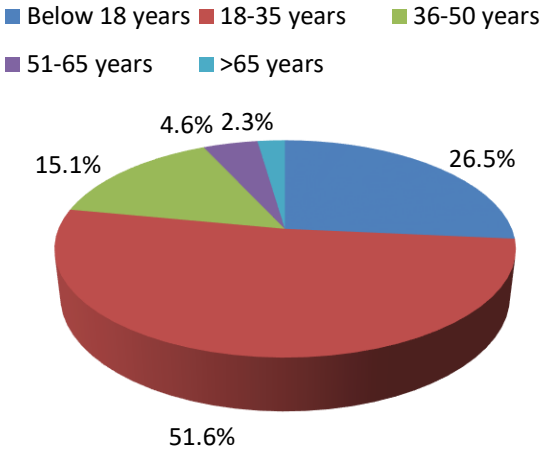

Fig 1: Association of age interval with frequency of bone tumour

Out of 1314, 954 patients (72.6 %) had a benign tumour of bone while 360 patients (27.4 %) had a malignant tumour (**Table-1**).

Table 1: Type of Tumour

	Malignancy	Frequency	%
	Benign	954	72.6
	Malignant	360	27.4
	Total	1314	100.0

The majority of the cases were from the province of Uttar Pradesh, Northern India. We have observed 13 different sites of bone involvement (**Table-2**)

Table 2: Frequency of anatomical Distribution

	Site	Frequency	%
	HUMERUS	150	11.4
	RADIUS	144	11.0
	ULNA	24	1.8
	METACARPALS	18	1.4
	FEMUR	354	26.9
	TIBIA	432	32.9
	VERTEBRAL BODY	36	2.7
	POSTERIOR ELEMENTS OF VERTEBRAL BODY	18	1.4
	FIBULA	30	2.3
	TALUS	18	1.4
	MERATARSALS	24	1.8
	PELVIS	24	1.8
	DISTAL TIBIA	42	3.2

	Total	1314	100.0

and a spectrum of 17 different kinds of bone tumours based on their histology (**Table-3**) and In the case of benign tumour, the most common age group was 18-35 years comprising 57.9% case (n=552) (**Table-3**)

Table 3: Age distribution of bone tumours

		Age intervals									
	Diagnosis	Below 18 years		18-35 years		36-50 years		51-65 years		>65 years	
		N	%	N	%	N	%	N	%	N	%
	OSTEOCHONDROMA	36	10.3%	12	1.8%	0	.0%	6	10.0%	0	.0%
	GIANT CELL TUMOUR	12	3.4%	366	54.0%	132	66.7%	24	40.0%	6	20.0%
	OSTEOID OSTEOMA	24	6.9%	24	3.5%	18	9.1%	0	.0%	6	20.0%
	EWINGS SARCOMA	66	19.0%	30	4.4%	0	.0%	0	.0%	0	.0%
	OSTEOSARCOMA	102	29.3%	90	13.3%	6	3.0%	0	.0%	6	20.0%
	ANEURYSMAL BONE CYST (ABC)	66	19.0%	60	8.8%	18	9.1%	0	.0%	0	.0%
	CNOHDROLIPOMA	0	.0%	6	.9%	0	.0%	0	.0%	0	.0%
	FIBROUS DYSPLASIA	6	1.7%	30	4.4%	0	.0%	0	.0%	0	.0%
	OSTEOCHONDROMA	0	.0%	0	.0%	0	.0%	0	.0%	0	.0%
	SIMPLE BONE CYST (SBC)	24	6.9%	18	2.7%	0	.0%	0	.0%	0	.0%
	ENCHONDROMA	0	.0%	0	.0%	6	3.0%	0	.0%	0	.0%
	FIBROSARCOMA	0	.0%	6	.9%	0	.0%	0	.0%	0	.0%
	SECONDRIES WITH UNKNOWN PRIMARY	0	.0%	6	.9%	12	6.1%	18	30.0%	6	20.0%
	CHONDROBLASTOMA	12	3.4%	24	3.5%	0	.0%	0	.0%	0	.0%
	SYNOVIAL CHONDROMA	0	.0%	0	.0%	0	.0%	0	.0%	6	20.0%
	OSTEOBLASTOMA	0	.0%	6	.9%	0	.0%	0	.0%	0	.0%
	CHONDROSARCOMA	0	.0%	0	.0%	6	3.0%	12	20.0%	0	.0%

and more frequently occurs in males (71.2%, n=630) (**Table-4).**

Table 4: Gender Distribution of bone tumours

		Gender			
	Diagnosis	Male		Female	
		N	%	N	%
	OSTEOCHONDROMA	42	5.0%	12	2.5%
	GIANT CELL TUMOUR	354	42.4 %	186	38.8%
	OSTEOID OSTEOMA	48	5.8%	24	5.0%
	EWINGS SARCOMA	54	6.5%	42	8.8%
	OSTEOSARCOMA	144	17.3 %	60	12.5%
	ANEURYSMAL BONE CYST (ABC)	96	11.5 %	48	10.0%
	CNOHDROLIPOMA	0	.0%	6	1.2%
	FIBROUS DYSPLASIA	18	2.2%	18	3.8%
	OSTEOCHONDROMA	0	.0%	0	.0%
	SIMPLE BONE CYST (SBC)	30	3.6%	12	2.5%
	ENCHONDROMA	0	.0%	6	1.2%
	FIBROSARCOMA	0	.0%	6	1.2%
	SECONDRIES WITH UNKNOWN PRIMARY	12	1.4%	30	6.2%
	CHONDROBLASTOMA	24	2.9%	12	2.5%
	SYNOVIAL CHONDROMA	6	.7%	0	.0%
	OSTEOBLASTOMA	6	.7%	0	.0%
	CHONDROSARCOMA	0	.0%	18	3.8%

Most prevalent affected bone with benign tumour was tibia (35.8%, n=342) followed by femur (22.6%, n=216) and radius (13.8%, n=132) (**Table-5**).

Table 5: Distribution of site and type of tumour

	Site	**Benign**		**Malignant**	
		N	**%**	**N**	**%**
	HUMERUS	108	11.3%	42	11.7%
	RADIUS	132	13.8%	12	3.3%
	ULNA	18	1.9%	6	1.7%
	METACARPALS	18	1.9%	0	.0%
	FEMUR	216	22.6%	138	38.3%
	TIBIA	342	35.8%	90	25.0%
	VERTEBRAL BODY	0	.0%	36	10.0%
	POSTERIOR ELEMENTS OF VERTEBRAL	18	1.9%	0	.0%

	BODY				
	FIBULA	12	1.3%	18	5.0%
	TALUS	18	1.9%	0	.0%
	CALCANEUM	0	.0%	0	.0%
	MERATARSALS	24	2.5%	0	.0%
	PELVIS	6	.6%	18	5.0%
	DISTAL TIBIA	42	4.4%	0	.0%

Based on the histological diagnosis, giant cell tumour (GCT) was the most common benign tumour (56.6 %) followed by aneurysmal bone cyst (15.1 %) and osteoid osteoma (7.5%) (**Table-6**).

Table 6: Frequency of bone tumours

	Diagnosis	Benign		Malignant	
		N	%	N	%
	OSTEOCHONDROMA	54	5.7%	0	.0%
	GIANT CELL TUMOUR	540	56.6%	0	.0%
	OSTEOID OSTEOMA	72	7.5%	0	.0%
	EWINGS SARCOMA	0	.0%	96	26.7 %
	OSTEOSARCOMA	6	.6%	198	55.0 %
	ANEURYSMAL BONE CYST (ABC)	144	15.1%	0	.0%
	CNOHDROLIPOMA	6	.6%	0	.0%
	FIBROUS DYSPLASIA	36	3.8%	0	.0%
	OSTEOCHONDROMA	0	.0%	0	.0%
	SIMPLE BONE CYST (SBC)	42	4.4%	0	.0%
	ENCHONDROMA	6	.6%	0	.0%
	FIBROSARCOMA	0	.0%	6	1.7%
	SECONDRIES WITH UNKNOWN PRIMARY	0	.0%	42	11.7 %
	CHONDROBLASTOMA	36	3.8%	0	.0%
	SYNOVIAL CHONDROMA	6	.6%	0	.0%
	OSTEOBLASTOMA	6	.6%	0	.0%
	CHONDROSARCOMA	0	.0%	18	5.0%

In the case of GCT, the most common occurs in the adolescent age group (18-35years-67.88%, n=366) followed by the older age group (36-50 years-24.4%, n=132) (**Table-3**). The most prevalent affected bone with GCT was the tibia (36.7%) followed by radius (22.2%) and femur (20%). Aneurysmal bone cyst (ABC) predominantly occurs in males (66.7%, n=96) in contrast to females (33.3%, n=48) (**Table-4**) and most prevalent affected bone with ABC was tibia (41.2%, n=60) followed by femur (29.2%, n=42). Osteoid osteoma benign tumour most frequently occurs in males (66.7%, n=48) with respect to females (33.3%, n=24) **(Table-4**) and most common involved bone was tibia (66.7%, n=48) followed by femur (16.7%, n=12). From the 360 malignant bone tumour cases, the incidence of malignant bone tumours was found to be highest in the second decade (42%) of life, and males were found to be more affected (67%) concerning females. The most prevalent site of metastasis was the lung (92%) followed by the skeleton (8%). Based on the histological diagnosis, the most common malignant tumour was osteogenic sarcoma (55%, n=198) followed by primitive neuro-ectodermal tumour (PNET)/Ewing's sarcoma (26%, n=96) and secondaries (11.7%, n=42). The most common bone involved with Ewing's sarcoma was the femur (38.3%, n=138) followed by the tibia (25%, n=90). In the case of osteosarcoma, the most common age group was 0-18 years (50%, n=102) (**Table**-3) and most commonly observed in males (70.58%, n=144) (**Table-4**). The most common bone involved with osteosarcoma was the femur (50%, n=102) followed by tibia (32.4%, n=66) and humerus (5.9%, n=12). Osteogenic sarcoma was more commonly recognized in males (72.2%) (**Table-3**). About 29.2% of Osteogenic sarcoma cases belonged to the first decade of life. The femur was the prevalent affected site (67.1%) followed by the tibia (21.7%), humerus (11%). PNET/Ewing's sarcoma was the second most prevalent malignant bone sarcoma that largely affects males (56.2%, n=54) and the most common involved bone was femur (30.2%) followed by the humerus (24%) and tibia (18%). The third most common malignant tumour was secondaries and most commonly observed during the 6th decade of life and predominantly observed in females (71.4%) (**Table-3**). In the case of secondaries, the most commonly involved bone was vertebrae (66.5%) followed by the femur (16.5%). A needle biopsy was conclusive only in 30% (n=394) of cases while the remaining 70% (n=920) cases were non-conclusive as all the patients were subjected to either incisional or excisional biopsy for confirmation of diagnosis.

Discussion

Bone tumours are relatively uncommon concerning a wide array of cancers. A bone tumour is a challenging problem for both orthopedic surgeons and pathologists, especially in developing countries due to unawareness, limited diagnosis, and facilities. The present epidemiological data on bone tumours, especially age distribution and sites of presentation, was found to be similar to published literature [13] Needle biopsy is helpful in the histopathological diagnosis of the bone tumour. Several lines of evidence demonstrated the histopathological appearance of variants of benign and malignant tumours on FNAC [14, 15, 16]. In the present study, we observed cellular smear with small clusters in the case of chondrosarcoma while cellular smear made up of pleomorphic tumour cells having round and spindle-shaped structures with mitotic bodies and malignant osteoid in case of osteosarcoma. A recent study observed similar findings regarding the histopathological appearance of chondrosarcoma and osteosarcoma on FNAC. A study led by Jeyaraman et al., [17] showed that the ABC appeared like scanty cells with the hemorrhagic background while GCT appeared like giant cells with specifically featured nuclei on FNAC. The current study also reported a similar appearance of GCT and ABC on FNAC. Kasraeian et al., [17] showed that the core needle biopsy was conclusive in 45.6% of cases. A study led by Bamanikar et al., [18] reported that FNAC was conclusive only in 31.71% of cases. In the present study, a needle biopsy was conclusive in only 30% of cases. The histopathological study is necessary to determine the spectrum of bone tumours and to correlate with demographic facets like sex, age,

and localized site of tumours. Numerous previous studies showed the geographic pattern of bone destruction related to the bone tumour [19, 20, 21]. The current study reported that the typical one or > 1 cavities of 1 cm diameter with defined border (or transition to intact bone indicating a slow rate of growth) corresponds to multiple 2 to 5 mm cavities with intermediate growth rate tending to coalesce corresponds to chondrosarcoma lymphoma, fibro-sarcoma, and myeloma, while multiple cavities of <1 mm diameter with a high rate of growth corresponds to Ewing's sarcoma, osteosarcoma, and metastasis. One of the previous studies reported a similar finding regarding the geographic pattern of bone destruction related to the bone tumour. A study performed by Costelloe et al., [21] showed that the induction of bone marrow permeation and trapping of lamellar spicules by bone-forming tumours is considered osteosarcoma while it is considered chondrosarcoma when this process is induced by hyaline cartilage tumours. The current study also reported a similar observation related to osteosarcoma and chondrosarcoma. Most of the studies reported the neoplastic lesion in the case of bone tumor in contrast to the non-neoplastic lesion [22, 23, 24, 25]. Complete reactive bone sclerosis (complete sclerotic rim) indicates the benign lesion in 95% of cases while lack of rim indicates the malignancy; hence, osteoblastic rimming is the characteristic histological feature of the benign lesion. Several reports address that incidence of benign bone tumours was high among the population with musculoskeletal cancer in contrast to malignant bone tumours [22, 23, 24, 25]. Baena-Ocampo et al., [26] reported that the incidence of benign bone tumours was high among the skeletal cancer population in Mexico City. Based on the histopathological diagnosis, we also reported a higher number of neoplastic lesions, among them; the incidence of the benign bone tumour was high in contrast to malignant bone tumour cases. Several lines of evidence reported that the peak age for a benign or malignant bone tumour is the second or third decade of life [27, 28, 29, 30]. One of the studies conducted in Central India reported that the peak age for the emergence of these bone tumours was 24.44 years [6]. In the present study, the reported peak age for these bone tumours was 26.65±14.84 corresponds to the third decade of life. Our finding was similar to other region-specific epidemiological reports on bone tumours in India as well as western populations [6, 23, 30]. Several lines of evidence showed that the males were predominantly affected with benign and malignant bone tumour [25, 27, 31]. A few studies carried out in different regions of India reported that the males were more prominently affected with benign and malignant bone tumours [6, 23, 25, 27, 31]. We also observed that the males (63.47%) were more affected with benign and malignant bone tumours in contrast to females (36.52%). Mostly long bones are more affected by bone tumours. We found in this study that the femur was the most commonly affected bone in the case of the malignant tumour while the tibia was the most common bone involved in the benign bone tumour which conforms with the results of previous studies [6, 23, 25, 31]. A benign bone tumour is the most common tumour reported in various epidemiological data which resonates with our findings except in some studies which might be due to a small sample size [32]. Several regions specific epidemiological reports showed that the most common benign bone tumour was GCT [6, 23, 33] and most of the cases of GCT belong to 20-50 years with preponderance in males and the most common bone involved was the tibia. These data were similar to our findings. We also observed that the ABC was the second most benign bone tumour with preponderance in males and the most common bone involved was the tibia and these findings were similar to earlier studies [6, 27]. Regional studies on bone tumours in India showed that osteoid osteoma was the third most common benign bone tumour with preponderance in males and the most common bone involved was the tibia [6, 27]. We also reported a similar finding in this study. Some of the epidemiological reports showed that the most common malignant bone tumour was osteosarcoma [6, 23, 33] and most of the cases of osteosarcoma belong to the second decade of life with preponderance in males and the most common bone involved was femur [6, 23, 33]. These data were similar to our findings. We observed that the PNET/Ewing sarcoma was the second most malignant bone tumour with preponderance in males and the most common bone involved was the femur and these findings were similar to earlier studies [6, 23, 27]. Regional studies on bone tumours in India showed that chondrosarcoma was the third most common malignant bone tumour with preponderance in males and the most common bone involved was the pelvis [6, 23, 27]. We also reported a similar finding in this present study.The present study has its limitations and it is a hospital-based audit, not a population-based registry, thus has an inherent selection bias. The proportion of patients with individual histopathological diagnoses is not an absolute reflection of the actual numbers in the population. This is a reflection of cases observed in a tertiary referral healthcare center which may include more malignant or aggressive cases in comparison to benign ones. The finding of this study is correlated with other available region-specific studies on epidemiological data in Asia and western countries. The same trend has been noticed in other tertiary referral centers across the globe [26, 30].

Conclusion

The tibia is the most common localized site in the case of a benign tumour while the femur is the case of a malignant bone tumour. The most common benign tumour was osteoclastoma and osteosarcoma was the most common malignant tumour. Needle biopsy of bone tumour is not a reliable option to diagnose and confirm the diagnosis of bone tumour. Further, more region-specific and large multi-centric epidemiological studies in different regions of India are required to validate these findings.

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Conflict of Interest: Nil Source of support: Nil