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Benign bone tumors in North East Indian population – A hospital-based study

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ABSTRACT

Background: Primary bone tumors are relatively uncommon and constitute only 0.2–0.5% of all tumors in all ages in most series reported worldwide. Benign bone tumors are more common than the malignant bone tumors. Not many studies on benign bone tumors in the North Eastern Indian population are published in the available literature. **Aims and Objectives:** The current study was done with the aim to find out the epidemiological data on benign bone tumors in patients of the North-East Indian population who were admitted to the orthopedic department of a teaching institute. **Materials and Methods:** A hospital-based retrospective study with prospective effect was conducted on benign bone tumors in patients admitted to the Department of Orthopedics at our teaching institute from 2016 to 2020. Patients of all ages and both sexes with suspicion of bone tumors based on history and clinical examination were subjected to roentgenographic evaluation, including computed tomography (CT) scan and/or magnetic resonance imaging. Pre-operative core needle biopsy under C-arm/CT guidance or incisional biopsy was done for histological diagnosis, followed by appropriate intervention. Soft-tissue tumors and malignant bone tumors were excluded. Patients were followed up for recurrence, complications, and functional recovery. **Results:** Forty patients of bone tumors were treated out of 2288 patients admitted to the department (incidence of 1.75%). 29 were benign bone tumors with an incidence of 1.27%. Of 10–20 years age group was most commonly affected. Male preponderance with M: F = 6.25:1. Femur (n = 16) was the most commonly affected bone. Presenting features were swelling (n = 18), pain (n = 11), and pathological fracture (n = 5). osteochondroma (n = 15) was most common followed by giant cell tumor of bone (n = 6). Treatment ranged from intralesional steroid to wide marginal excision based on histopathological diagnosis, the extent of tumor, anatomical location, and presenting symptoms. All patients were rehabilitated to activities of daily living at the final follow-up. No recurrence or any long-term complications were reported. **Conclusion:** This study gives epidemiological data on benign bone tumors, which can be used for setting up or upgrading dedicated oncological or oncosurgery institutes. A multicentric study on a large population in the future is suggested to obtain a larger data bank.

Key words: Bone tumor; Benign, Diagnosis

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INTRODUCTION

Primary bone tumors are relatively uncommon and constitute only 0.2–0.5% of all tumors in all ages in most series reported worldwide.[1,2] Benign bone tumors are more common than malignant bone tumors, while malignant tumors are associated with a higher rate of morbidity and mortality.[3,4] Bone tumors pose a challenge to orthopedic surgeons, radiologists, and pathologists worldwide. The challenge becomes higher in developing countries because of the paucity of diagnostic and therapeutic facilities and the ignorance of the population.[3] Therefore, we need an integrated approach involving clinical data, radiographic, and histologic features to make an accurate diagnosis and

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to find out the degree of activity and malignancy associated with each lesion.[5]

Not many studies on benign bone tumors in the North Eastern Indian population are published in the available literature. Therefore, this study was conducted to find out epidemiological data on benign bone tumours in patients admitted in Orthopaedic Department of a tertiary care teaching institute located in North East India.

Aims and objectives

To find out the epidemiological data on benign bone tumors in North East Indian population amongst patients admitted in Orthopaedics Department of a tertiary care teaching institute.

MATERIALS AND METHODS

This hospital-based retrospective study with prospective effect was conducted in a teaching institute from January 2016 to June 2020. The study was on patients of the North-East Indian population who were admitted to the Department of Orthopedics. All confirmed benign bone tumor patients of different ages and both sexes were included in this study. Soft-tissue tumors, malignant bone tumors, and incomplete follow-up patients were excluded. Patients who were suspected of having bone tumors on history and clinical examination were subjected to roentgenographic evaluation at our Institution's Department of Radiology. This was followed by computed tomography (CT) scan and/or magnetic resonance imaging of the involved anatomical part. All the patients underwent pre-operative core needle biopsy under C-arm or CT guidance usually under regional anesthesia. Whenever the core needle biopsy failed to obtain an adequate amount of tissue for histopathological diagnosis or the histopathological diagnosis was inconclusive, the incisional biopsy was done. The biopsy specimen was collected and transported in 10% formaldehyde solution to our Institution's Department of Pathology for histopathological diagnosis. After correlating clinical features, radiological evaluation, and histopathological diagnosis, the patients were considered for treatment by appropriate invasive procedures or surgical intervention. The treatment modalities were based on histological diagnosis, anatomical location, extent of bone tumors, and presenting symptoms. The patients were followed up to look for recurrence, any complications, and functional recovery.

RESULTS

Forty patients of bone tumors out of 2288 admitted patients were managed at our unit (incidence of 1.75%). Out of 40 bone tumor patients, 29 were benign with an incidence of 1.27%. The youngest patient was a 4-year-old male child with a pathological fracture of the neck femur through a simple bone cyst and the oldest patient was a 54-year-old female with biopsy-proven giant cell tumor (GCT). The average age was 20.34 years. The most commonly affected age group was 10–20 years (n=11, 37.93%). More than ¾th of the patients (n=23, 79.31%) were <30 years of age (Table 1).

The femur was the most commonly affected bone (n=16, 55.17%), followed by the radius (n=3, 10.34%), tibia, and humerus (n=2, 6.9%) each. The most commonly involved side was the left (n=18, 62.07%) (Table 2).

The most common predominant complaint was swelling (n=18, 52.94%) followed by pain (n=11, 32.35%) and pathological fracture (n=5, 14.71%). Some of the patients presented with overlapping symptoms also. Osteochondroma was the most common benign bone tumor (n=15, 51.72%) and 13 of these were located in the femur. Eight of these cases with osteochondromas were aged between 10 and 20 years. The second most common tumor was GCT (n=6, 20.7%) and three of these were located in the distal radius (Table 3).

Of 25 patients were male and only four were female (male: female = 6.25:1). 13 (86.67%) out of 15 osteochondroma patients and 5 (83.33%) out of 6 GCT patients affected the males (Table 4).

Various methods of treatment were offered to the patients in our study. These were based on histopathological diagnosis, the extent of the tumor, anatomical location, and presenting symptoms, as shown in (Table 5).

The patient who underwent subtotal scapulectomy for chondromyxoid fibroma of scapula developed intraoperative hemorrhage leading to intra-operative hypotension and post-operative anemia and she was managed by intra-operative and post-operative blood transfusion. Another patient with GCT in the proximal tibia treated with the sandwich technique developed a superficial wound infection. It was controlled by regular dressing of the wound and with appropriate antibiotics

Table 1: Age (in years) distribution

Age group (years)	No of patients (%)
0–10	7 (24.14)
10–20	11 (39.93)
20–30	5 (17.24)
30–40	3 (10.34)
40–50	2 (6.90)
50–60	1 (3.45)

Figure 1: Pre-operative and post-operative X-rays and clinical photographs of giant cell tumor-distal radius

Table 2: Distribution of anatomical location

Site	Scapula	Humerus	Radius	Metacarpal	Phalanx	Pelvis	Femur	Tibia	Fibula	Metatarsal
Cases (n)	1	2	3	1	1	1	16	2	1	1

Table 3: Histological types with anatomical locations

Histological types	Frequency (%)	Bones involved
Osteochondroma	15 (51.72)	Femur (13), Tibia (1), Humerus (1)
Giant cell tumor	6 (20.70)	Radius (3), Tibia (1), Pelvis (1), Metatarsal (1)
Simple bone cyst	3 (10.34)	Femur (2), Humerus (1)
Aneurysmal bone cyst	2 (6.9)	Femur (1), Fibula (1)
Chondroma	2 (6.9)	Metacarpal (1), Phalanx (1)
Chondromyxoid fibroma	1 (3.45)	Scapula (1)

Table 4: Histological type and sex distribution

Histological type	Male	Female
Osteochondroma	13	2
Giant cell tumor	5	1
Simple bone cyst	3	0
Aneurysmal bone cyst	2	0
Chondroma	2	0
Chondromyxoid fibroma	0	1

after wound swab culture and sensitivity report. He required no surgical intervention. No patient reported with recurrence or any other long-term complications. All patients were rehabilitated to activities of daily living at the final follow-up.

DISCUSSION

Etiologically, bone tumors are multi-factorial. They most commonly arise from *de novo* somatic mutation,[6] but the other predisposing factors also include irradiation,[7] foreign bodies,[8] pre-existing bone lesions,[9,10] and less commonly trauma,[11] chemotherapy[12], and viruses.[13] Males are more commonly affected than females.[14-17] They can occur in all age groups, but more commonly affect the first and second decades of life.[3,14]

The geographic distribution of these tumors varies greatly in different parts of the world. Asian countries have lower incidence and prevalence compared to Europe and the USA.[18-20] Clinical symptoms of bone tumors are

Figure 2: Pre- and post-operative X-rays and clinical photographs of unicameral bone cyst-proximal femur

Table 5: Tumor with different treatment modalities

Treatments offered	Bone tumor	Number (n)
Intra-lesional steroid	Simple bone cyst-proximal humerus (Figure 3)	1
Excision in toto	Osteochondroma	15
Curettage and autogenous bone graft	Chondroma (2) +GCT-pelvis (1)	3
Curettage and sandwich technique	GCT-proximal tibia	1
Curettage and reconstruction arthroplasty (autogenous fibula and cancellous bone graft from iliac crest)	GCT-distal radius	1
Curettage and reconstruction arthrodesis (autogenous fibula and cancellous bone graft from iliac crest)	GCT-distal radius	1
Excision+fibular struts+K-wire fixation	GCT-metatarsal	1
Curettage and nailing	Aneurysmal bone cyst	1
Curettage, fibular struts, and fixation with K-wires	Simple bone cyst with femur neck fracture	1
Curettage, fibular struts, and fixation with plate (Figure 1)	Simple bone cyst with subtrochanteric fracture (1) + (Figure 2) aneurysmal bone cyst with subtrochanteric fracture (1)	2
Wide marginal resection (subtotal scapulectomy)	Chondromyxoid fibroma	1
Wide marginal resection and reconstruction with proximal fibula	GCT-distal radius	1

GCT: Giant cell tumor

often non-specific. They may present with pain, swelling, and sometimes with pathological fractures without supporting a specific diagnosis.[1] Characteristic clinical symptoms can be found only in a few bone tumors. Imaging studies act as an important tool for the diagnosis of bone tumors.

Our study facilitates a basis for the comparison of demographics and histology of bone tumors in the North-East Indian population with those of other population (Table 6).

Osteochondroma was found to be the most common benign bone tumor in our study with 51.72% followed by GCT (20.7%). These findings are consistent with the results of studies by Obalum et al., Baena-Ocampo et al., Jain et al., Rhutso et al., and Salawu et al.,[3,21-24] respectively. Although in most studies, GCT was the second most common benign bone tumor, Solooki et al.,[25] and Bergovec et al.,[26] found enchondroma and simple bone cyst as 2nd most common benign lesion, respectively. Interestingly, Gulia et al.,[27] and Settakom et al.,[28] reported GCT as the most common benign tumor in their studies. This difference in their study could be because of the fact that the peak age in their study

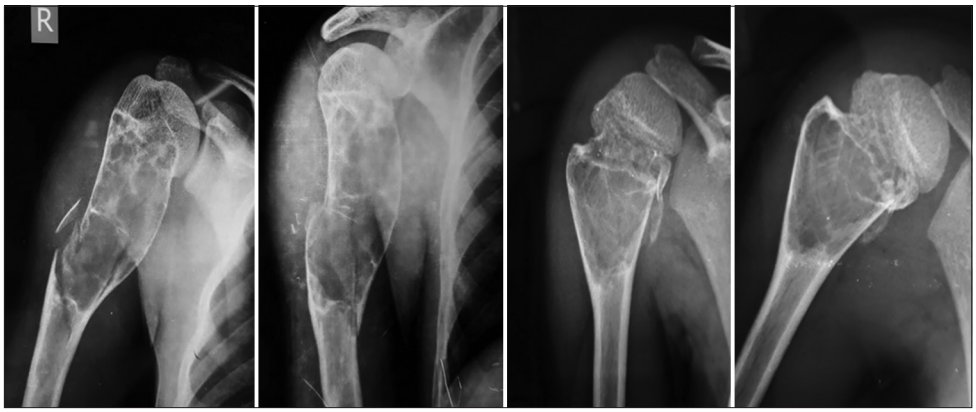

Figure 3: Pre- and post-X-rays of unicameral bone cyst-proximal humerus treated with intra-lesional steroid

Table 6: Comparison of demographics and histology of bone tumors in our environment with those of other population

Year of publication	Authors with country	Study period (years)	No of benign cases/total	Most common tumor (%)	M: F	Peak age in years (%)	Most common site (%)
2009	Baena-Ocampo et al. (Maxico)	5	405/566	OC (43.7) GCT (14.6) EC (10.1)	1.2:1	11–20 (48.9%)	Femur (37) Tibia (20) Humerus (12.3)
2009	Obalum et al. (Nigeria)	25	130/240	OC (36, 27.7) GCT (21.6) ABC (13.9)	1.6:1	22°C <20 years GCT-3rd and 4th decade	NA
2011	Jain et al. (South India)	8	67/117	OC (22.22) GCT (20.51) EC (6.84) OO (4.27)	1.48:1	11–20 (41.79)	Femur (41.79) Tibia-fibula (20.9) Radius-Ulna (8.96)
2011	Solooki et al. (Iran)	12	213/389	OC (63.9) EC (10.8) GCT (9.9)	NA	15–24 (45)	Femur Tibia Humerus
2013	Rhutso et al. (Manipur, India)	2	41/62	OC (22,53.65) GCT (21.95) Osteoma (4.87) OO (4.87) Chondroma (4.87) Chondromxoid fibroma (2.43)	1.16:1	11–20 (47.06)	Tibia (43.9) Femur (34.15)
2015	Bergovec et al. (Croatia)	30	2761/3482	OC SBC Chondroma OO GCT	1:1.08	11–20	Femur Tibia
2016	Gulia et al. (Mumbai, India)	1	181/1203	GCT (55.8) ABC (9.9)	1.41:1	21-30	Tibia (24.86) Femur (23.2)
2018	Salawu et al. (Nigeria)	2	40/72	OC (30.6) GCT (8.3)	NA	11–20 (47.5)	Femur (35) Tibia (25)
2020	Our study	4.5	29/2,288	OC (51.72) GCT (20.7)	6.25:1	11–20 (37.93)	Femur (55.17) Radius (10.34)

OC: Osteochondroma, GCT: Giant cell tumor, EC: Enchondroma, ABC: Aneurysmal bone cyst, OO: Osteoid osteoma, SBC: Simple bone cyst

population was the 21–30 years age group in which GCT is known to be common.

We found the peak age of incidence between 10 and 20 years. This finding was comparable with studies by Baena-Ocampo et al., Jain et al., Solooki et al., Rhutso et al., Bergovec et al., and Salawu et al.,[21-26] who also reported second decade of life to be the commonly affected age.

There was male preponderance in our study. Male preponderance was also similar to the results of studies by Obalum et al., Baena-Ocampo et al., Jain et al., Rhutso et al., Bergovec et al., Gulia et al., and Salawu et al.[3,21-24,26,27] However, the male-to-female ratio in our study was 6.25:1 which was much higher when compared with similar epidemiological studies. The explanation for such predominant male preponderance could not be found in

our present study and this could be a scoop for future research. Another striking finding in our study was that five out of six patients of GCT were males while studies by Mohammed and Isa[14] and Rehman et al.[29] found GCTs predominantly in females.

The most commonly affected bone in our study was femur (55.17%) which was in concordance with studies by Baena-Ocampo et al., Jain et al., Solooki et al., Bergovec et al., and Salawu et al.[21,22,24-26] However, Rhutso et al.,[23] and Gulia et al.,[27] reported tibia was the most common site of occurrence followed by femur. Radius was found to be the second most commonly affected bone in our study as against tibia in studies by Baena-Ocampo et al.,[21] Jain et al.,[22] Solooki et al.,[25] Bergovec et al.,[26] Salawu et al.[24]

The trips and tricks of various surgical exposures and procedures done to treat benign bone tumors seemed to be successful from the facts that all the patients recovered to the functional status of daily living, there were no long-term complications and there was no recurrence at final follow-up.

Limitations of the study

The limitations of our study were that this was done in a single center with a relatively small sample size.

CONCLUSION

This study gives epidemiological data on benign bone tumors. This data can be used for setting up or upgrading dedicated oncological or oncosurgery institutes. A multicentric study on a bigger population sample size is suggested in the future to obtain a larger data bank.

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REFERENCES

1. Katchy KC, Ziad F, Alexander S, Gad H and Abdel Mota'al M. Malignant bone tumors in Kuwait: A 10-year clinicopathological study. Int Orthop. 2005;29(6):406-411.
   https://doi.org/10.1007/s00264-005-0014-6
2. Dorfman HD and Czerniak B. Bone Cancers. Cancer. 1995;75(1 Suppl):203-210.
3. Obalum DC, Giwa SO, Banjo AF and Akinsulire AT. Primary bone tumours in a tertiary hospital in Nigeria: 25 year review. Niger J Clin Pract. 2009;12(2):169-172.
4. Ode MB, Misauno MA, Nwadiaro HC, Onche II, Shitta AH and Amupitan I. Pattern and distribution of primary bone tumours in Jos Nigeria. J Dent Med Sci. 2014;13(12):9-12.
5. Negash BE, Admasie D, Wamisho BL and Tinsay MW. Bone tumors at Addis Ababa University, Ethopia: Agreement between radiological and histopathological diagnosis-a 5-year analysis at Black-Lion Teaching Hospital. Malawi Med J. 2009;1:62-65.
6. Iavarone A, Mathhay KK, Stein Kirchner TM and Israel MA. Germline and somatic p53 gene mutations in multifocal osteogenic sarcoma. Proc Natl Acad Sci USA. 1992;89(9):4207-4209.
   https://doi.org/10.1073/pnas.89.9.4207
7. Huvos AG, Woodard HQ, Cahan WG, Higinbotham NL, Steart FW, Butler A, et al. Postradiation osteogenic sarcoma of bone and soft tissue. A clinicopathologic study of 66 patients. Cancer. 1985;55(6):1244-1255.
   https://doi.org/10.1002/1097-0142(19850315)55:6<1244::aid-cncr2820550617>3.0.co;2-1
8. Sindelar WF, Costa J and Ketcham AS. Osteosarcoma in associated thorotrast administration: Report of two cases and literature review. Cancer. 1978;42(6):2604-2609.
   https://doi.org/10.1002/1097-0142(197812)42::6<2604:aid-cncr2820420615>3.0.co;2-o
9. Smith GD, Chalmers J and McQueen MM. Osteosarcoma arising in relation to an enchondroma. A report of three cases. J Bone Joint Surg Br. 1986;68(2):315-319.
   https://doi.org/10.1302/0301-620X.68B2.3457012
10. Rosai J. Rosai and Ackerman's Surgical Pathology. 10th ed. Vol. 2. UK: Elsevier Inc.; 2011. p. 2013-2014.
11. Penman HG and Ring PA. Osteosarcoma in association with total hip replacement. J Bone Joint Surg Br. 1984;66(5):632-634.
   https://doi.org/10.1302/0301-620X.66B5.6594340
12. Tucker MA, D'Angio GJ, Boice JD Jr., Strong LC, Li FP, Stovall M, et al. Bone sarcomas linked to radiotherapy and chemotherapy in children. N Engl J Med. 1987;317(10):588-593.
   https://doi.org/10.1056/NEJM198709033171002
13. Cope JU. A viral etiology for Ewing's sarcoma. Med-Hypotheses. 2000;55(5):369-372.
   https://doi.org/10.1054/mehy.2000.1069
14. Mohammed A and Isa HA. Pattern of primary tumours and tumour-like lesions of bone in Zaria, Northern Nigeria: A review of 127 cases. West Afr J Med. 2007;26(1):37-41.
   https://doi.org/10.4314/wajm.v26i1.28301
15. Odetayo OO. Pattern of bone tumours at the national orthopaedic hospital, Lagos, Nigeria. West Afr J Med. 2001;20(2):161-164.
16. Omololu AB, Ogunbiyi JO, Ogunlade SO, Alonge TO, Adebisi A and Akang EE. Primary malignant bone tumour in a tropical African University teaching hospital. West Afr J Med. 2002;21(4):291-293.
   https://doi.org/10.4314/wajm.v21i4.28001
17. Eyesan SU, Obalum DC, Nnodu OE, Abdulkareem FB and Ladejobi AO. Challenges in the diagnosis and management of musculoskeletal tumours in Nigeria. Int Orthop. 2007;33(1):211-213.
   https://doi.org/10.1007/s00264-007- 0475-X
18. Stiller CA, Bielack SS, Jundt G and Steliarova-Foucher E. Bone tumours in European children and adolescents, 1978-1997. Report from the automated childhood cancer information system project. Eur J Cancer. 2006;42(13):2124-2135.
   https://doi.org/10.1016/j.ejca.2006.05.015
19. Parkin DM, Stiller CA and Nectoux J. International variations in the incidence of childhood bone tumours. Int J Cancer. 1993;53(3):371-376.
   https://doi.org/10.1002/ijc.2910530305

20. Eyre R, Feltbower RG, Mubwandarikwa E, Eden TO and McNally RJ. Epidemiology of bone tumours in children and young adults. Pediatr Blood Cancer. 2009;53(6):941-952.
https://doi.org/10.1002/pbc.22194
21. Baena-Ocampo LD, Ramirez-Perez E, Linares-Gonzalez LM and Delgado-Chavez R. Epidemiology of bone tumors in Mexico City: Retrospective clinicopathologic study of 566 patients at a referral institution. Ann Diagn Pathol. 2009;13(1):16-21.
https://doi.org/10.1016/j.anndiagpath.2008.07.005
22. Jain K, Sunila, Ravishankar R, Mruthyunjaya, Rupakumar CS, GadiyarHB, et al. Bone tumors in a tertiary care hospital of south India: A review 117 cases. Indian J Med Paediatr Oncol. 2011;32(2):82-85.
https://doi.org/10.4103/0971-5851.89778
23. Rhutso Y, Laishram RS, Sharma LD and Debnath K. Histopathological evaluation of bone tumors in a tertiary care hospital in Manipur, India. J Med Soc. 2013;27(2):135-139.
24. Salawu ON, Babalola OM, Ibraheem GH, Nwosu C, Suleiman AK, Kadir DM, et al. Musculoskeletal tumors of the extremities: Challenges and outcome of management in a Nigeria Tertiary Hospital. Afr J Med Health Sci. 2018;17(1):20-25.
https://doi.org/10.4103/ajmhs.ajmhs_64_17
25. Solooki S, Vosoughi AR and Masoomi V. Epidemiology of musculoskeletal tumors in Shiraz, South of Iran. Indian J Med Paediatr Oncol. 2011;32(4):187-191.
https://doi.org/10.4103/0971-5851.95138
26. Bergovec M, Kubat O, Smerdelj M, Seiwerth S, Bonevski A and Orlic D. Epidemiology of musculoskeletal tumors in a national referral orthopedic department. A study of 3482 cases. Cancer Epidemiol. 2015;39(3):298-302.
https://doi.org/10.1016/j.canep.2015.01.015
27. Gulia A, Puri A, Chorge S and Panda PK. Epidemiological data and case load spectrum of patients presenting to bone and soft tissue disease management group at a tertiary cancer center. Indian J Cancer. 2016;53(2):333-338.
https://doi.org/10.4103/0019-509X.197734
28. Settakom J, Lekawanvijit S, Arpornchayanon O, Rangdaeng S, Vanitanakom P, Kongkarnka S, et al. Spectrum of bone tumors in Chiang Mai University Hospital, Thailand according to WHO classification 2002: A study of 1,001 cases. J Med Assoc Thai. 2006;89(6):780-787.
29. Rehman A, Qureshi H, Ullah S. Bone tumors and tumor-like lesions: 10 years retrospective analysis of biopsy results. J Postgrad Med. 2004;18:40-45.

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