

### Pathological Study of Bone Tumours at the National Orthopaedic Hospital, Lagos, Nigeria

*Etude pathologique tumeurs des os à la National Orthopaedic Hospital, Lagos, Nigeria*

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#### ABSTRACT

**BACKGROUND:** Although primary bone tumours are relatively uncommon, they constitute the most important tumours in patients under 20 years.

**OBJECTIVE:** To update the literature on the relative frequency and clinico-pathologic characteristics of bone tumours in this environment.

**MATERIALS AND METHODS:** The clinical and histopathological records of patients presenting with diagnosis of bone tumours between 1999 and 2004 and managed at the National Orthopaedic Hospital, Igbobi, (NOHI) Lagos, Nigeria were review and where necessary, new ones were prepared from the paraffin blocks and stained with routine haematoxylin and eosin stain. The clinical data such as the age, sex, presenting signs and symptoms, site distribution of lesions, radiological finding as well as the record of other investigation and management were extracted from the clinical case notes of patients.

**RESULTS:** Seventy-seven cases were recorded; 61 (79.2%) benign and 16 (15.6%) malignant. The male: female ratio for all tumours was 2:1. The commonest benign bone tumours were osteochondroma and giant cell tumour accounting for 52 (67%) of all cases with >60% in males. The most common primary malignant bone tumour was osteosarcoma, all in males. The peak incidence was in the second and third decades and commonest sites were the distal femur and proximal tibia. Four (5.2%) cases of metastatic bone tumours located commonly in the proximal femur and humerus were also recorded.

**CONCLUSION:** Osteochondroma and giant cell tumours are the commonest benign tumours while osteosarcoma is the most common primary bone tumour all occurring in the first two decades of life. The age and sex distribution and morphology are similar to those already established in the African and international literature. *WAJM* 2007; 26(4): 306–311.

**Keywords:** Bone tumours, osteochondroma, osteosarcoma, Nigeria.

#### RESUME

**CONTEXTE:** Bien que les tumeurs osseuses primaires sont relativement rares, elles constituent la plus importante des tumeurs chez les patients de moins de 20 ans.

**OBJECTIF:** mettre à jour la littérature sur la fréquence et les caractéristiques clinico-pathologiques des tumeurs osseuses dans cet environnement.

**MÉTHODES:** Les dossiers cliniques et histopathologiques des patients présentant le diagnostic des tumeurs osseuses entre 1999 et 2004 et gérés à la National Orthopaedic Hospital, Igbobi, (NOHI) Lagos, Nigeria étaient réexaminés et, si nécessaire, de nouveaux produits ont été préparés à partir de la paraffine Blocs et colorés à la routine et à l'hématoxyline éosine tache. Les données cliniques telles que l'âge, le sexe, présentant des signes et des symptômes, le site de distribution des lésions radiologiques ainsi que de trouver le dossier de l'enquête et de la gestion d'autres ont été extraites de la note de cas cliniques de patients.

**RÉSULTATS:** Soixante-sept cas ont été enregistrés, 61 (79,2%) bénignes et 16 (15,6%) maligne. Les sexes pour toutes les tumeurs a 2:1. La plus fréquente des tumeurs osseuses bénignes ont été ostéochondrome et géantocellulaire tumorale comptant pour 52 (67%) de tous les cas de > 60% chez les mâles. Les plus fréquentes des tumeurs osseuses malignes primaires a été l'ostéosarcome, tous chez les mâles. Le pic d'incidence se trouvait dans la deuxième et troisième décennies et fréquente les sites ont été distale du fémur et la partie proximale du tibia. Quatre (5,2%) des cas de tumeurs osseuses métastatiques trouve communément dans la partie proximale de l'humérus, le fémur et ont également été enregistrées.

**CONCLUSION:** Osteochondroma et des tumeurs à cellules géantes sont les plus fréquentes des tumeurs bénignes alors que l'ostéosarcome est la plus fréquente des tumeurs osseuses primaires se produisent tous dans les deux premières décennies de la vie. La répartition par âge et par sexe et la morphologie sont similaires à ceux déjà établis dans la littérature africaine et internationale. *WAJM* 2007; 26(4): 306–311.

**Mots Cles:** tumeurs osseuses, ostéochondrome, ostéosarcome, le Nigeria.

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Abbreviations: NOHI, National Orthopaedic Hospital, Igbobi; GCT, Giant Cell Tumours; LOH, Loss of heterozygosity.

## INTRODUCTION

The most important challenge in orthopedics pathology is dealing with tumours. The incidence of primary bone tumours does not compare with cancer of the breast, cervix, lungs and stomach, yet excluding leukaemia and lymphomas, the primary bone tumours constitute the most important single group of tumours in patients under the age of 20 years. The frequency distribution data for primary bone sarcomas has long been used to provide clues to the diagnosis of bone cancers after their identification on radiographs. For this purpose, several demographic data have since been carried out on bone tumours.

Odetayo<sup>1</sup> reported the pattern of bone tumours from our center, the National Orthopaedic Hospital, Lagos, Nigeria over a six-year period: only 36 cases were seen with 19 males and 17 females. There were 24 benign and 12 malignant cases with osteochondroma and giant cell tumour representing over 70% of all benign tumours and osteosarcoma accounted for over 60% of all malignant tumors. Also in the South Western part of Nigeria, Omololu et al<sup>2</sup> recorded 144 cases of primary malignant bone tumours over a 24-year period at the University College Hospital, Ibadan which represented 0.53% of all the 21,390 cancers recorded over the period with male: female ratio of 1.4:1. About 45% of the tumours occurred under 20 years of age and osteosarcoma was the most common primary malignant bone tumour<sup>2</sup>.

Of the 672 cases reported from South Africa, osteocartilagenous exostosis was the commonest (35–47%) benign lesions, whilst osteogenic sarcoma was commonest malignant tumour (43.8%) followed by chondrosarcoma (12.34%) and multiple myeloma (11.11%)<sup>3</sup>. Osteosarcoma occurred throughout to the 8<sup>th</sup> decade – albeit with reduced frequency after the age of 30 years although did not show significant difference either in tumour characteristic or incidences, between Caucasians and Negroid patients.<sup>3</sup>

Shah et al in Karachi, Pakistan reviewed 169 malignant bone tumours over a period of 3 years and reported that the commonest malignant neoplasm diagnosed in osseous biopsies was

metastatic tumours (28.4%) whilst osteosarcoma was the most frequent primary bone tumour (27.2%).<sup>4</sup> This is similar to the report from Saudi Arabia which showed that secondary malignant bone lesions (from breast and lungs) are more prevalent than primary malignant bone tumours and that lymphoma and Ewing's sarcoma formed 50% of the primary tumours.<sup>5</sup>

Ewing's sarcoma was the most common primary bone tumour in India while in Thailand osteosarcoma (39.9%) was the commonest primary malignant bone tumours. The latter is similar to the finding of Dorfman and Czerniak in New York and Valdespino – Gomez et al in Mexico who reported osteosarcoma as the most frequently diagnosed sarcoma of bone in patients under 20 years.<sup>8,9</sup>

Guo et al did a comparative analysis by race, age, sex and skeletal distribution of 38,959, 20,272 and 11,087 cases of histologically confirmed bone sarcomas from the bone tumour registries of China, Japan and United States respectively.<sup>10</sup>

This study showed that the relative frequency of osteosarcoma is higher in China and Japan than in US. Osteosarcoma occurred more frequently in flat bone in the American compared to Chinese and Japanese.<sup>10</sup> The relative frequency of chondrosarcoma was higher in the American group than in the Asian group and it occurred in younger age in the Chinese than in the Japanese and the Americans. Chondroma was higher in the Americans compared to the Asians whilst giant cell tumours of bone was higher in the Chinese and Japanese than in the Americans.<sup>10</sup> The data also confirmed the previous reports that Ewing's sarcoma is commoner in the Western people compared to Asians.<sup>10</sup>

The aim of the present communication is to update the literature on the relative frequency and clinico-pathologic characteristics of bone tumours in the South Western Nigerian environment.

## MATERIALS AND METHODS

The materials for this study consisted of the clinical and histopathological records of patients presenting with diagnosis of bone tumours between 1999 and 2004 and managed at the National Orthopaedic Hospital, Igbobi, (NOHI)

Lagos, Nigeria. The relevant histopathology slides of surgical samples received at the Pathology department from the Oncology Unit of the Hospital were retrieved from the archives and where necessary, new ones were prepared from the paraffin blocks and stained with routine haematoxylin and eosin stain. Special stains such as Von Kossa and Periodic Acid Schiff stains were employed where necessary to demonstrate osteoid in cases of osteosarcoma, mucin in metastatic adenocarcinoma respectively.

The clinical data such as the age, sex, presenting signs and symptoms, site distribution of lesions, radiological finding as well as the record of other investigation and management were extracted from the clinical case notes of patients. The initial histological diagnoses were modified as appropriate and the various lesions were classified using the standard histological characteristics into: Benign and malignant and the malignant tumours were further classified into primary and metastatic. Soft tissue invasion of bone and non-neoplastic lesions resembling bone tumours were not included in the study. The results are presented as tables and figures.

## RESULTS

During the five-year period between 1999 and 2004 at NOHI, 77 cases of bone tumours were seen.

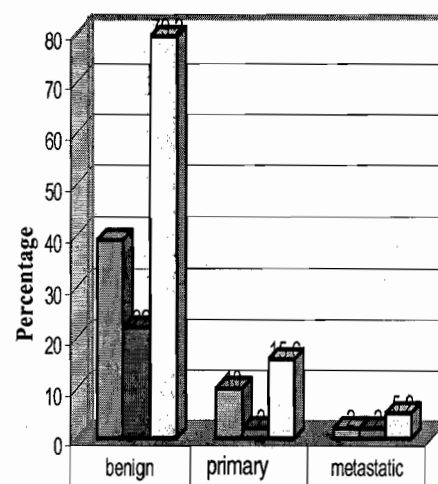


Fig. 1 Frequency of histological and Sex Distribution of Bone Tumours. Primary malign-Primary malignant tumour of bone; Metastatic-Metastatic(secondary) tumour to bone. ■ Male ■ Female □%.

Sixty-one (79.2%) cases of benign tumours and 16 (20.8%) malignant bone tumours were seen (Figure 1). The overall male: female ratio for all tumours was 2:1. The commonest benign bone tumours were osteochondroma 34 (44.1%) followed by giant cell tumours 18 (23.4%), both of

which accounted for 85% of all benign tumours. The other benign tumours encountered were fibrous dysplasia (tumour-like lesion) four (5.2%), osteoma two (2.6%) with one case each of enchondroma, adamantinoma and lymphangioma. (Table 1).

**Table 1: Histologic Classification of Bone Tumours seen Between 1999–2004 at NOH, Igbobi**

	Male	Female	Total (%)
<b>Benign Tumours</b>			
Osteochondroma	21	13	34 (44.1)
Giant cell tumour	11	7	18 (23.4)
Fibrous dysplasia	2	2	4 (5.2)
Osteoma	2	0	2 (2.6)
Enchondroma	1	0	1 (1.3)
Adamantinoma	1	0	1 (1.3)
Lymphangioma	1	0	1 (1.3)
<b>Subtotal</b>	<b>39</b>	<b>22</b>	<b>61 (79.2)</b>
<b>Malignant-Primary</b>			
Osteosarcoma	7	0	7 (9.1)
Chondrosarcoma	1	0	1 (1.3)
Synovial sarcoma	1	0	1 (1.3)
Malignant giant cell Tumour	0	1	1 (1.3)
Leiomyosarcoma	0	1	1 (1.3)
Malignant haemangioendothelioma	1	0	1 (1.3)
Secondary/metastatic tumours	2	2	4 (5.2)
<b>Subtotal</b>	<b>12</b>	<b>4</b>	<b>16 (20.8)</b>
<b>Grand Total</b>	<b>51 (66.2%)</b>	<b>26 (33.8%)</b>	<b>77 (100%)</b>

**Table 2: Distribution of patients with Osteochondroma by Age and Sex**

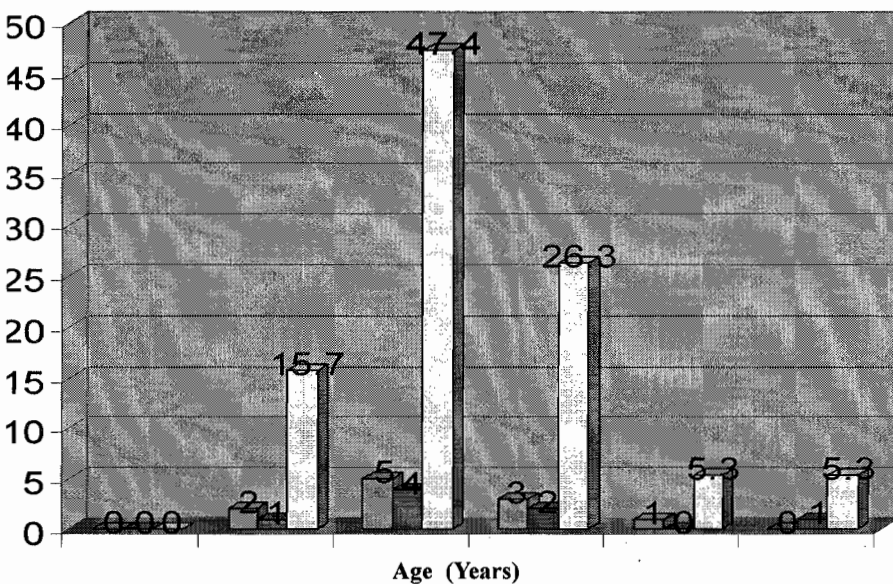
Age Group (Yr.)	Number		
	Male	Female	Total
<10	5	1	6
11-20	9	6	15
21-30	6	3	9
31-40	0	1	1
41-50	1	1	2
50-61	0	1	1
<b>Total</b>	<b>21</b>	<b>13</b>	<b>2</b>

Of the malignant tumours, metastatic tumours represented 4 (5.2%) of all tumours. The most common primary bone tumour was osteosarcoma 4 (9.1%), all occurring in males with a mean age of 22.7 years. Only one case each of chondrosarcoma, synovial sarcoma, malignant giant cell tumour, leiomyosarcoma and malignant haemangioendothelioma was recorded. (Table 1).

The peak incidence in both benign and malignant tumours occurred within the second and third decades of life coinciding with or closely following the rapid increase in the growth velocity before fusion of the most bony epiphyses. Most cases of osteochondroma occurred between the age 11 years and 20 years 15 (44.1%). However, substantial numbers of this lesion were seen between the age of 21 years and 30 years, 9 (26.5%) and among children less than 10 years 6 (17.6%). It was uncommon above the fourth decade of life. This lesion mostly affected men, 21 (61.7%). (Table 2).

Majority of giant cell tumours, 9 (47.4%), occurred between the age of 21 years and 30 years and more frequently in males 11 (57.9%) (Figure 2). Very few cases were seen at younger ages. The four cases of fibrous dysplasia seen were in their third decade of life with no sex preference. Osteosarcoma was seen mostly between ages 11 and 30 years 5 (71.4%). Above and below this age range, its incidence was each about 15%. (Figure 3). No case occurred in females.

The male: female ratio of both benign and malignant tumours was 2:1. Most of the (64%) of the benign lesions are seen



**Figure 2: Age and Sex Distribution of Giant Cell Tumours in NOH Igbobi 1999–2004**

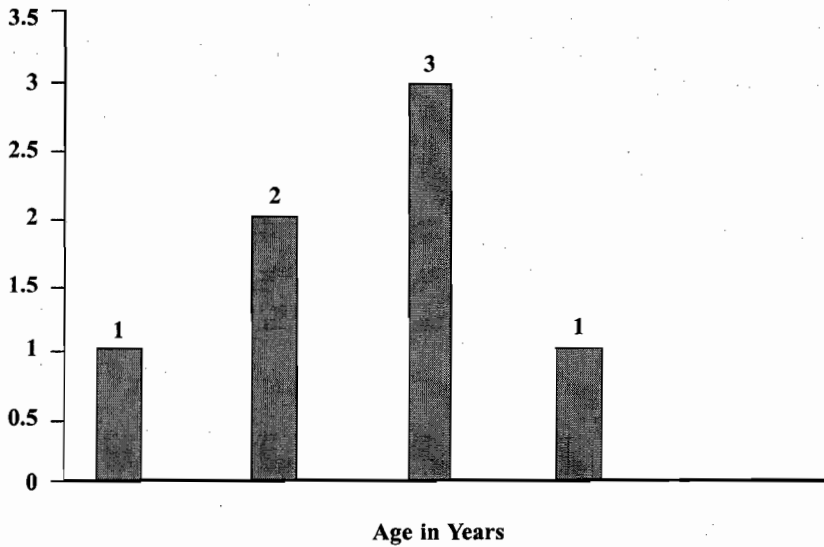


Figure 3: Age Distribution of Osteosarcoma in Males. No case occurred in females

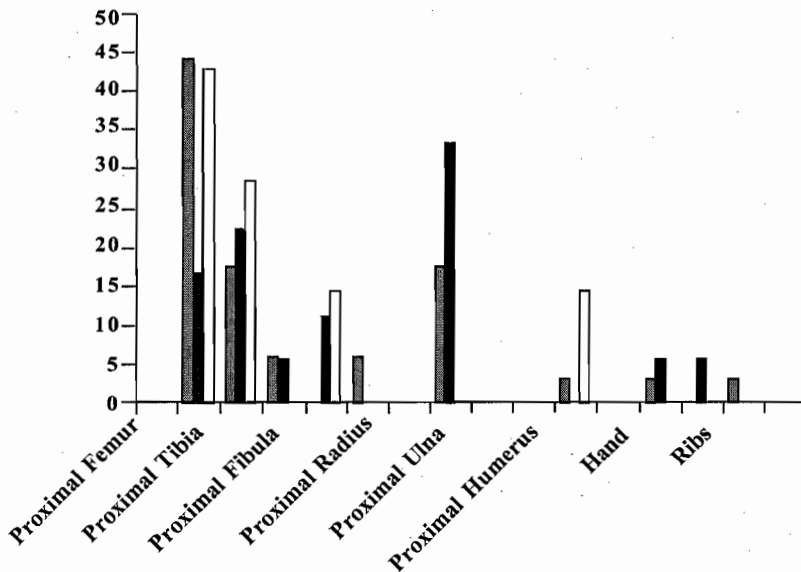


Figure 4: Showing the Site Distribution of the Three most Common Tumours (■ Osteo-chondroma, ■ Giant Cell Tumour and □ Osteo-sarcoma).

among males.(see Figure 1,and Table 1). Metastatic bone tumours had equal distribution between the sexes. The primary sites of the secondaries were not indicated. This was usually the case due to inadequate facilities

In a large number of the specimens, the site of the lesions was not specified. However, the sites most commonly

involved in both benign and malignant tumours were the distal end of the femur and the proximal end of the tibia. The commonest site for osteochondroma was around the knee (distal femur and proximal tibia) which accounted for 21 (61.6%) of the cases, followed by the wrist, (distal radius) which accounted for six (71.6%) of the cases of osteochondroma (Figure

4). One patient had osteochondromatosis involving the distal femur, proximal tibia, ribs, proximal humerus. The commonest site of giant cell tumour (GCT) was around the knee (distal femur, proximal tibia and proximal fibula) which accounted for nine (50.2%) of the cases, followed by the wrist which accounted for six (33.3%) of the cases.(Figure 4). The commonest site for osteosarcoma from this study was around the knee which accounted for six (85.7%) of the cases, followed by the proximal humerus (14.3%) while proximal femur was the commonest site for secondary metastatic tumours, followed by the proximal humerus (Figure 4). All the benign and malignant tumours presented as a mass except the fibrous dysplasias that presented variously with deformity, cova vara and genu varum, lower limb shortening and pathological fractures.

The benign tumours had a longer duration of symptoms ranging from 23 months to 468 months, with an average of 45.7 months, except for giant cell tumour whose duration of symptoms ranged from 5months to 19 months, with an average of 10.6 months. The malignant tumours had shorter duration of symptoms ranging from 0.25 to 24 months and an average of 7.5 months.

**DISCUSSION**

Bone tumours are relatively uncommon compared to other cancers. Frequencies of 0.53% and 0.9% were reported from Ibadan, Nigeria and Bombay in India respectively<sup>2,6</sup>. Odetayo recorded 36 cases over six years earlier from this center which represented average annual occurrence of six per year for bone tumours<sup>1</sup>. The yearly average in the present series was 15, which is quite high compared with the former study from the same center. This may be partly attributed to the fact that all specimens were then sent to other centers for histopathology reporting because there was no in-house histopathologist during the period reported by Odetayo and only those cases with histology reports were analyzed in the said study. Also, the Musculo-Skeletal Tumour Unit was officially established in January 2000 and many referrals now come from all over the country. Studies from other parts of the world show annual frequencies ranging

from 56 in Pakistan to 65 in Thailand and 67 in South Africa<sup>4,7,3</sup>.

Benign tumours are the commonest bone tumours and accounted for 79% of all cases in this series. This is a common finding in previous studies from Africa and other parts of the world. The M:F ratio of 2:1 in this study is however higher compared to earlier studies from Nigeria where 1.1:1 and 1.4:1 were recorded<sup>1,2</sup>. A South African study also showed equal sex ratio<sup>3</sup>. Majority of the bone tumours occurred in the 2<sup>nd</sup> and 3<sup>rd</sup> decades of life, which corroborates with most previous studies<sup>1-3, 6-10</sup>.

The two most common benign tumours in this series were osteochondroma and giant cell tumour both of which represented 67.5% of all tumours and accounted for about 85% of all benign tumours. This concurs with majority of studies from other parts of the world. In particular, osteochondroma was reported to be the commonest from most bone tumour registries from Africa, India and Saudi Arabia, Thailand and Mexico<sup>1-3,5,6,7,9</sup>.

Over 80% of osteochondroma cases in our series occurred below 30 years with the peak in the 2<sup>nd</sup> decade (15(44.1%)). Majority of them were located around the knee; distal end of the femur (44%) and proximal end of tibia (17.6%). All the cases of osteochondroma presented with non tender hard bony mass with or without deformity, only about 5% presented with associated pain. The duration of symptoms ranged from 24-468 months with the average of 85 months. The latter is long because this tumour grows slowly with no fatal clinical significance apart from cosmetic and probably pressure on surrounding structures such as nerves or blood vessels around the joint; resulting in delay of diagnosis.

Giant cell tumour (GCT) was second common benign tumour representing 23.4% of all tumours and 52% of the benign cases. The peak age incidence was a decade higher than that of osteochondroma (21-30 yrs), presenting as warm cystic/bony hard mass and predominantly located around the knee (50%) followed by the wrist (distal radius-33.3%). The duration of symptoms was 5-19 months, average 10.6 months which is lower than for osteochondroma. GCT although benign, can be locally

aggressive with recurrence rate ranging from 10-50% and 1-5% have potential to metastasize to the lungs<sup>11,12</sup>. Some studies categorize it as tumour of intermediate malignancy while others consider it as benign. The incidence of malignant transformation of as high as 10% has been reported.<sup>13, 14</sup> There was one case of malignant transformation of giant cell tumour in this series occurring in a 34 year old female and involving the upper end of humerus.

Malignant transformation though rare is said to be associated with changes in expression of certain genes such as tartrate-resistant acid phosphatase and the lysosomal H<sup>+</sup> transporting ATPase, which are also expressed by osteoclasts<sup>14</sup>. The genes found to be over-expressed in GCTs appear to reflect the genetic profile of osteoclast-lineage cells and also the genetic profile of an osteoclastogenic environment<sup>14</sup>. Skubitz et al suggested that the genes identified in the latter study may play a role in the pathogenesis of GCTs, and may indicate other possible targets to which anti-tumor therapy could be directed<sup>14</sup>. Rao et al used status of microsatellite markers located on some chromosomes to determine loss of heterozygosity (LOH) in primary giant cell tumors (GCT) of bone in 12 patients and thus categorized them into primary, locally recurrent, and metastatic GCT<sup>15</sup>. Both primary GCTs and local recurrences and lung metastases displayed LOH of three or more markers, and intratumoral heterogeneity was frequent<sup>15</sup>.

Malignancy in a giant cell tumor is controversial and often a diagnostic dilemma when a frank sarcomatous stroma component is absent. Lachat suggested the presence of cytologic atypias and flame-like tufts of infiltration of soft tissue as important clues<sup>16</sup>. Others believe that rather than the histopathological appearance, local recurrence and metastatic potential of GCT depend on its aggressiveness and are better assessed by clinical and radiological parameters<sup>17</sup>.

Osteosarcoma was the commonest malignant tumour accounting for 9.1% of all tumours, which represented 44% of all malignant tumours and 58% of primary malignant bone tumours. Except for data from Saudi Arabia and Karachi in Middle

East, Bombay in India and Papua New Guinea, where Ewing's sarcoma is reportedly higher, majority of the studies from other parts of the world showed the predominance of osteosarcoma as the commonest primary malignant bone tumour<sup>4-6,18</sup>. This is in contrast to studies from the middle East, where metastatic tumours were reportedly the most common malignant bone neoplasm and osteosarcoma being the most common primary bone tumour<sup>4</sup>. Osteosarcoma and Ewing's were commoner under 20 years and chondrosarcoma was found above 50 years<sup>8</sup>. It thus appears that the major difference is rarity of Ewing's sarcoma in Africa and Asia confirming previous studies that Ewing's sarcoma is commonly seen in the Western Countries compared to Asia and Africa<sup>10</sup>.

All the cases of osteosarcoma in this study were seen in males with the mean age of 22.7 years. Most studies from other centers showed that it is commonly seen in the 1<sup>st</sup> and 2<sup>nd</sup> decade with a relative male predominance contrasting the finding in South Africa where osteosarcoma occurred throughout the entire age range up to the 8<sup>th</sup> decade but with reduced frequency after the age of 30 years<sup>3</sup>. This observation is important for one is apt to believe that it is an exclusive disorder of young people and hence reluctance to make this diagnosis in patient over 40 years unless they have obvious Paget's disease.

As regards the site of affectation, similar to previous studies, the present series showed the bones around the knee as the most common site for osteosarcoma. These are the sites of greatest skeleton growth activity. This is however in contrast to the finding of Omololu et al in Ibadan who reported the mandible as the commonest site and that by Guo et al who reported osteosarcoma in Americans occurred in flat bones than in the Japanese and Chinese<sup>3,10</sup>.

In this environment, the clinical outcome of malignant bone tumours is dismal. Even though limb sparing surgery following chemotherapy and radiotherapy is common practice now in most developed world, amputation is still frequently the treatment of choice because of late presentation. In a study on lower limb amputation in Jos, Northern

Nigeria, malignant bone condition of the limb was one of the common causes of lower limb amputation and in Ilorin, in Nigeria, bone tumours was the 3<sup>rd</sup> common indication for amputation after trauma and diabetes<sup>19,20</sup>.

Metastatic bone tumours appear to be uncommon in this study (5%) in contrast to studies from Pakistan and Saudi Arabia where metastatic tumour was commonest representing 28.4% in Pakistan<sup>4,5</sup>. Tumours of the breast and lungs were the commonest sources of secondaries in the Saudi Arabian study<sup>5</sup>. Eighty percent of the metastatic tumours in this study were located in the proximal femur followed by the proximal humerus (20%).

Although, the cause of most bone tumors is unknown genetic alterations similar to those that occur in other tumors clearly play a role. For instance bone sarcomas occur in the Li-fraumeni and hereditary retinoblastoma cancer syndrome, which are linked to mutation in chromosome P53 and Rb. Scotlandi et al studied the prognostic and therapeutic relevance of HER 2 expression in osteosarcoma and Ewing's sarcoma and reported that over expression of HER 2 was present in 32% of osteosarcoma and 16% of Ewing's sarcoma<sup>21</sup>. The latter was significantly associated with the increase expression of P-glycoprotein, a surface molecule responsible for multi-drug resistance.

Clinically, bone tumors present in various ways. The more common benign lesions are frequently asymptomatic and are detected as incidental findings. All tumors (benign or malignant) presented with a mass except the fibrous dysplasia that presented with different form of deformity. Many malignant tumors however are painful or are noticed as slow growing mass. In some circumstances, the first hint of tumor's presence is a sudden pathological fracture. This study showed that pain is not a common presenting feature of benign bone tumors except for giant cell tumor (61% presented with pain). Due to the rapidity of growth, pains and systemic effects, malignant lesions present earlier than benign lesions.

Radiographic analysis form one of the triad of diagnosis, the others being clinical and histology. Radiological assessment

in addition to localization of site, determination of the extent can give clues to the aggressiveness of the tumor while histological assessment of biopsies are required for classification and grading of the tumor and provision of prognostic feature of malignant bone tumors for appropriate management..

Management of bone tumours poses a great challenge in this environment due to late presentation, ignorance, cultural belief and financial limitation. Half of those offered amputation rejected with more than one third of patients dying within 3months. In the benign group, about 65% had limb sparing surgeries while the remaining had amputation. Majority of them were lost to follow up.

This study provides a demographic data on bone tumors showing neither significant deviation from those obtained previously from this center or from other parts of the world. The diversity of bone tumours in gross and histological characteristics as well as biologic behaviour underscores the importance of correct diagnosis in order to give appropriate treatment. This requires complimentary information from the clinical assessment, radiological study and histological examination of the biopsied lesion, which will not only improve survival but will also reduce the incidence of un-necessary amputation.

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