Chapter 4

Findings of the study

4.1 Overview

This section presents the findings of the study. The main objective of the study was to establish the pattern of primary malignant bone tumours.

The specific objectives of the study were as follows:

1. To outline the socio-demographic characteristics of patients presenting with primary malignant bone tumours with respect to age, gender and geographic origin.
2. To determine frequency of primary malignant bone tumours at UTH
3. To determine the hospital prevalence of primary malignant bone tumours including their histological distribution
4. To determine the clinical presentation of primary malignant bone tumours

4.2 Socio-demographic characteristics of the patients

There were a hundred and fifty-three (153) patients. Sixty six (43%) were females while 87 (57%) were males. The youngest patient was 3 years while the oldest patient was 78 years old. The average age of the patients was 31.6 years. Table 3 below, shows that 9.9 % of the patients were aged 10 years and below, 35.1% were aged 11-20 years, 12.6% were aged 21-30 years, 11.3% were aged 31-40 years, 7.3% were aged 41-50 years, 10.6% were aged 51-60 years, 9.9% were aged 61-70 years, and 3.3% were aged 71-80 years. Therefore the findings indicate that almost 69% of the patients were aged 40 years and below.

Table 3: Bone tumour frequency by age of patients

Age range (in decades)	Frequency	Percent	Valid Percent	Cumulative Percent
10 years and below	15	9.8	9.9	9.9
11-20 years	53	34.6	35.1	45.0
21-30 years	19	12.4	12.6	57.6
31-40 years	17	11.1	11.3	68.9
41-50 years	11	7.2	7.3	76.2
51-60 years	16	10.5	10.6	86.8
61-70 years	15	9.8	9.9	96.7
71-80 years	5	3.3	3.3	100.0
Total	151	98.7	100.0	
Not stated	2	1.3		
Total 153	100.0			

4.3 Sex stratified age distribution of patients with primary bone cancers

It was noted in the study, as is demonstrated in **figure 1** below, that there was more male patients than females. A Chi Square test was conducted to establish whether there was any association between gender and the occurrence of bone tumours at a significance level of 0.05. The results were; Chi Square = 2.882; df=1; p=0.09. Since p>0.05; there was no association.

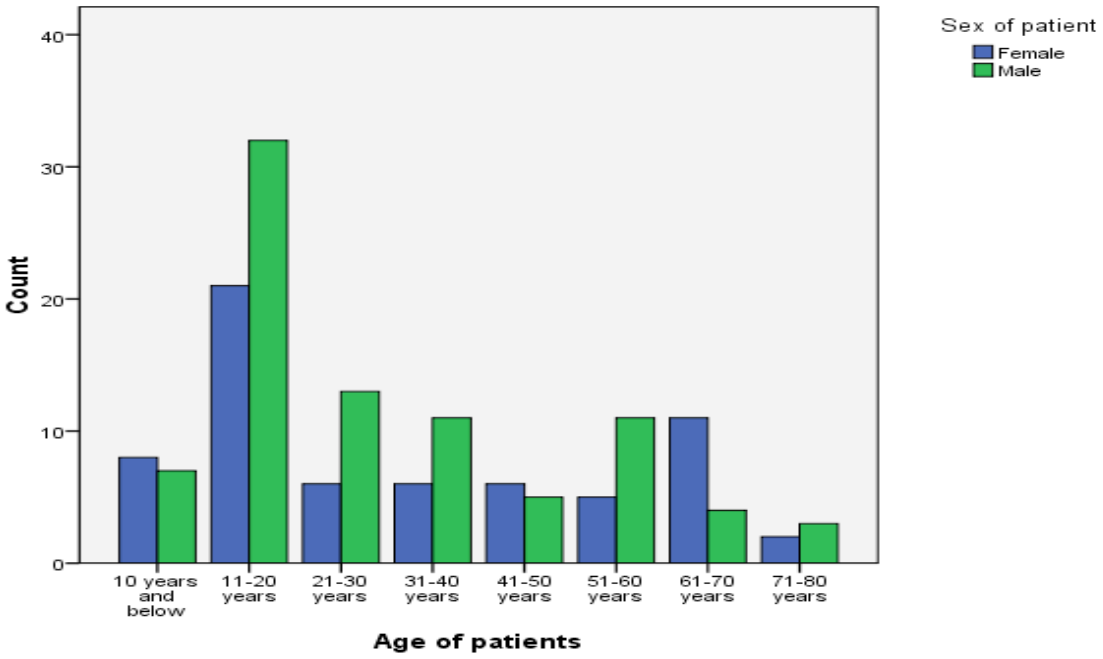

Figure 1: Sex stratified Age Distribution of patients

4.4 Geographic distribution

Table 4 below shows the domicile of the patients. The majority (35%) of the patients came from Lusaka Province, 17.5% from Southern Province, 12.4% from Copperbelt Province, 10.2% from Eastern Province, 7.3% from Northern Province, 5.1% from Luapula Province. The remaining 9.5% of the patients came from Central Province (4.4%), Western Province (2.9%), and North Western Province (2.0%).

Table 4: Patience's domicile

Geographic origin of patient (domicile)	Frequency	Percent	Cumulative Percent
Lusaka	54	35.3	35.3
Southern	26	17.0	52.3
Copperbelt	19	12.4	64.7
Eastern	16	10.5	75.2
Northern	12	7.8	83.0
Luapula	9	5.9	88.9
Central	7	4.6	93.5
North Western	5	3.3	96.7
Western	5	3.3	100.0
Total	**153**	**100.0**	

4.5 The frequency of primary malignant bone tumours by year of presentation

Figure 2 below shows the distribution of the patients by year of attendance. Twenty-seven (18.8%) of the patients attended treatment at the University Teaching Hospital (UTH) in 2008; 31 (21.5%) in 2009; 27 (18.8%) in 2010; 20 (13.9%) in 2011, and 39 (25.5%) in 2012.

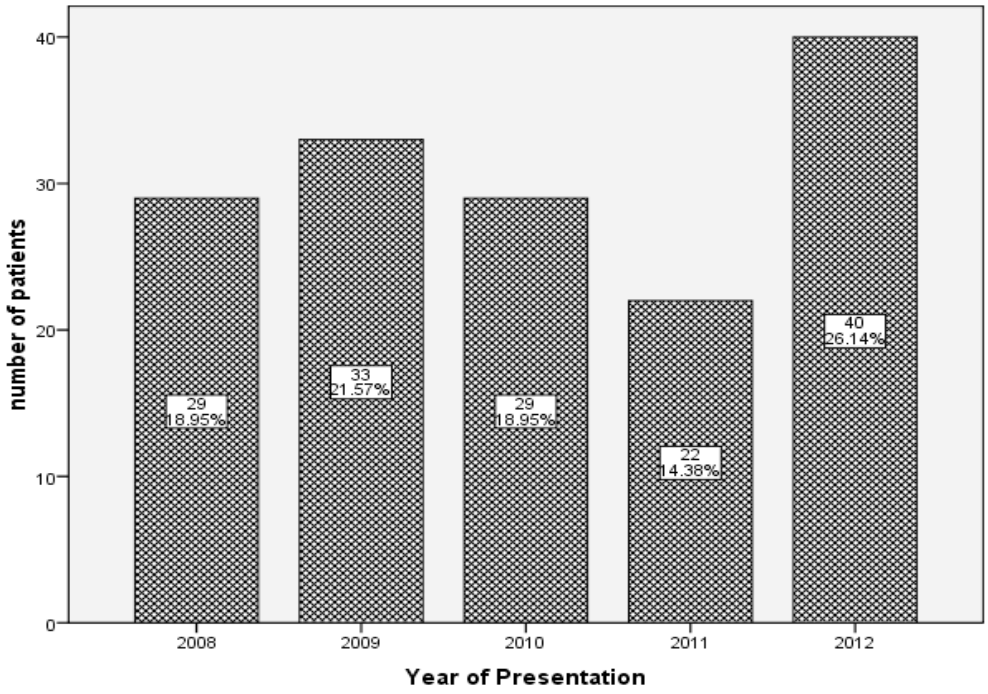

Figure 2: Year of attendance

4.6 Tumour frequency as an annualized relative proportion of the total cancer burden at UTH

Table 5 below shows the total number of cancer patients recorded at the University Teaching Hospital Cancer registry from 2008 to 2011. The overall proportion of patients with primary malignant bone tumours compared to all the other cancers ranged between 1.7 to 2.8%.

Table 5: Total number of cancer patients seen annually from 2008 to 2011 at UTH

YEAR	TOTAL NUMBER OF PRIMARY BONE CANCER PATIENTS SEEN AT UTH	TOTAL NUMBER OF CANCER PATIENTS SEEN AT UTH	PROPORTION	%
2008	29	1034	0.028	2.8
2009	33	1548	0.021	2.1
2010	29	1736	0.017	1.7
2011	22	1108	0.020	2.0
2012	40	-	-	-[1]

[1] At the time of data collection the statistics for 2012 had not been compiled yet by the National Cancer Register.

4.7 Relative frequencies of different types of primary bone cancers

Table 6 below shows the common types of primary malignant bone tumours recorded at UTH during the period under review. Eighty four (55.3%) of the patients had osteosarcoma, 42 (27.6%) had multiple myeloma, 11 (7.2%) had chondrosarcoma, 8 (5.3%) had Ewing's sarcoma, 3 (2.0%) were fibrosarcoma, 2 (1.3) were lymphoma. The rest (2) had osteoclastoma and sarcoma, accounting for 0.7% each. These findings indicate that the most common primary malignant tumours recorded during the period under review were osteosarcoma and multiple myeloma. These two accounted for 82.9% of the cases.

Table 6: Distribution by histological diagnosis

Histological type of tumour	Frequency	Percent	Cumulative Percent
Osteosarcoma	84	54.9	54.9
Multiple Myeloma	42	27.5	82.4
Chondrosarcoma	11	7.2	89.5
Ewing's sarcoma	8	5.2	94.8
Fibrosarcoma	3	2.0	96.7
Lymphoma	2	1.3	98.0
Malignant Giant Cell Tumour	1	.7	98.7
Osteoclastoma	1	.7	99.3
Sarcoma	1	.7	100.0
Total	**153**	100.0	

4.8 Clinical presentation of the primary malignant tumours

The findings show that the majority of patients (35.5%) experienced pain and swelling only. 27% reported pain alone and 17% reported swelling. Pathological fractures were reported in 19.8% of the patients. Pain was a common finding in 75% of the patients who either reported pain, swelling, pathological fracture or a combination of the symptoms with pain as their presenting symptoms. Table 7 below shows the commonly reported presenting symptoms of many of the bone tumour patients seen at UTH.

Table 7: Clinical presentation

Clinical presentation	Frequency	Percent	Valid Percent	Cumulative Percent
Pain & Swelling	54	35.3	35.5	35.5
Pain	41	26.8	27.0	62.5
Swelling	27	17.6	17.8	80.3
Pain & Pathological Fracture	12	7.8	7.9	88.2
Pathological Fracture	8	5.2	5.3	93.4
Pain, Swelling & Pathological Fracture	7	4.6	4.6	98.0
Swelling & Pathological Fracture	3	2.0	2.0	100.0
Total	152	99.3	100.0	
Not stated	1	.7		
Total	153	100.0		

4.9 Anatomic site of involvement of primary malignant bone tumours

The single and most commonly reported anatomic site was from multiple myeloma with systemic involvement (27%); the second most commonly involved site was the femur with 23.7% cases of femoral involvement reported, the third site was the tibia with 17.1% cases reported, 12.5% were limb bones Not otherwise specified (NOS), and 7.5% were located on the humerus (**Table 8**). This gives a total of 88.2%. The rest of the tumours (9.8%) were located on the radius (3.9%), fibula (2.0%), pelvis (2.0%), spine (1.3%), calcaneum (0.7). Long bone of the lower limb was (0.7%), ribs (0.7%), and scapula (0.7%).

Table 8: Table of primary malignant bone tumour distribution by anatomic site

Anatomic site involved	Frequency	Percent	Valid Percent	Cumulative Percent
Systemic	41	26.8	27.0	27.0
Femur	36	23.5	23.7	50.7
Tibia	26	17.0	17.1	67.8
Limb bone NOS	19	12.4	12.5	80.3
Humerus	12	7.8	7.9	88.2
Radius	6	3.9	3.9	92.1
Fibula	3	2.0	2.0	94.1
Pelvis	3	2.0	2.0	96.1
Spine	2	1.3	1.3	97.4
Calcaneum	1	.7	.7	98.0
Long bone of lower limb	1	.7	.7	98.7
Ribs	1	.7	.7	99.3
Scapula	1	.7	.7	100.0

Anatomic site involved		Frequency	Percent	Valid Percent	Cumulative Percent
Total		152	99.3	100.0	
System		1	.7		
153	100.0				

The commonest site was systemic involvement as a result of multiple myeloma. Multiple myeloma by nature has a generalized skeletal involvement. On the other hand, the majority of osteosarcoma (74) were located on the femur (29), tibia (19), limb bone NOS (16), and humerus (10).

Chapter 5

Discussion

5.1 Socio-demographic characteristics of primary bone cancer patients

A higher average age (31.6years) was observed in patients who presented to The University Teaching Hospital; this is in contrast to that reported by Baena-Ocampo and colleagues in 2009, (25years). The observed higher average age at presentation may be due to selection bias in the patient population due to the fact that patients may not have had equal access to UTH and the sample size was relatively small. In general the age distribution was observed to be bimodal in agreement with what has been observed in literature (Fletcher & Unni 2002). The majority of patients were observed in the second decade of life between the ages of 10 and 20years, similar to observations in literature with a gentle second peak occurring in the sixth decade of life (Baena-Ocampo et al. 2009).

5.2 Sex distribution of primary malignant bone tumours

Primary malignant bone tumours have also been seen to have minor gender variations with a slight male preponderance (Katchy et al. 2005; Baena-Ocampo et al. 2009), the same was observed to have been true at UTH as shown in **figure 1**. A Chi Square test conducted in chapter 5 to establish whether there was any association between gender and the occurrence of bone tumours at a significance level of 0.05, demonstrated the absence of an association.

5.3 Geographic distribution of primary malignant bone tumours

The frequency of primary malignant bone tumours with respect to the geographic origin of the patients by province demonstrated a higher number of patients from Lusaka, Table 4. Southern and the Copperbelt provinces recorded the second and third largest number of patients accessing treatment from UTH. It would be expected that the larger number of patients would come from Lusaka largely due to the fact that local patients would access treatment from UTH with ease compared to those from outside Lusaka province. Patients with greater proximity to UTH would have relative ease to accessing health care from UTH than those from other provinces. Notably, the provinces outside the line of rail including the Eastern, Northern, Luapula, Central, North Western and Western recorded relatively fewer numbers of patients a finding that may be due to ease of access to UTH.

Further, the observed geographic variations in the numbers of patients originating from different provinces can be explained by a number of factors including the fact that there may be real geographic variations in the incidence of primary bone cancer. It is also possible that primary malignant bone tumours are under-diagnosed in other provinces partly due to the rarity of the condition (Bramer & Somford 2010). Another possibility is that Lusaka was reported as the domicile for most patients given the fact that many patients originating from other provinces would lodge with Lusaka based relatives and therefore Lusaka would be reported as the patients' domicile when in fact not.

5.4 The frequency of primary malignant bone tumours at UTH.

Figure 2 demonstrated the distribution of the patients by year of attendance. The largest number of patients with primary malignant bone tumours was recorded in 2012 where 40 (26.14%) were seen, whereas the lowest was observed in 2011 22 (14.38%). The observed increase in the total number of bone tumour patients in 2012 could have been as a result of factors such as: better record keeping; a true increase in the number of patients presenting to the University Teaching Hospital; an active referral system or a real increase in the incidence of the disease.

Table 5 in chapter 4, showed the total number of all the cancer patients recorded at the University Teaching Hospital Cancer registry from 2008 to 2011. Despite the fact that the overall proportion of patients with primary malignant bone tumours compared to all the other cancers ranged between 1.7 to 2.8%, with the years 2009 and 2010 having had the highest number of cancer patients recorded. This finding could have been because of a higher incidence in cancers; better referral system, or better record keeping. Notwithstanding the number of patients on record at the National cancer register, there are some patients who are never recorded due to low capacity by the Zambia National Cancer Register to comprehensively record all cancer patients.

As shown in Table 6 of chapter 4, osteogenic sarcoma was the commonest malignancy reported during the period under study. Osteosarcoma alone accounted for 54.9% of all the primary malignant bone tumours treated at UTH. Meanwhile Literature demonstrates that histologically stratified cancer registry data, shows that osteosarcoma occurs at the rate of

35% (Fletcher & Unni 2002); a percent lower than the study findings. The general distribution in terms of tumour type and frequency was consistent with that reported in literature. Multiple myeloma was the next common tumour observed in the study. These findings are replicated in other studies also (Larsson & Lorentzon 2010), and may imply that the overall relative distribution of primary malignant bone tumours is variable and geographic factors may have very little to do with the relative distribution of primary malignant bone tumours.

5.5 The clinical presentation of primary malignant bone tumours

5.5.1 Clinical presentation

According to Table 7 in chapter 4 most patients (35.5%) reported pain and swelling. Pain was common to most (75%) the patients including those who had reported a combination of symptoms including swelling and pathological fractures. Pain is a usual finding in patients with malignant bone tumours (Middlemiss et al. 2011). Swelling was reported in 59.9% of all the patients. Pathological fractures were reported in 19.8% of the patients. The finding of a pathological fracture in a patient is used as a surrogate to determining the local tumour. This finding indicates that approximately one in five patients with primary malignant bone tumours had extra-compartmental spread of the tumour. Therefore in order of frequency; pain was the commonest cause for hospital presentation by the patients; this was followed by swelling and pathological fractures. The above clinical findings, however, cannot be said to be fully reliable because the information was historical and certain clinical findings may have been under-reported by the patient or the attending physician at the time of attendance. The pain-specific findings were similar to those reported in Ibadan, Nigeria (Oyemade & Edinburgh 1982).

5.5.2 Anatomic site involvement

The commonest anatomic site(s) involved was mostly due to multiple myeloma, a multisystemic tumour which virtually affects all the bones. The femur was the commonest monostotic site, followed by the tibia, humerus and radius, in order of declining frequency. 12.5% of all the tumours were located on long bones of unspecified location. The findings were similar to those cited in literature (Omololu et al. 2002; Jain et al. 2011).

Chapter 6

Conclusion, Limitations and Recommendations

6.1 Conclusion

Primary malignant bone tumours are rare globally. The aetiology remains poorly characterized but the observed pattern of occurrence has been replicated at the University Teaching Hospital with respect to all the parameters investigated. The socio-demographic characteristics with respect to age and gender observed for patients with primary malignant bone tumours were similar to those reported in literature also showing a bimodal pattern of distribution.

As a proportion of the overall cancer disease burden bone tumours were found to be relatively low in number. The proportion of primary malignant bone tumours in comparison to the over number of cancer patients treated at UTH has been below 3% from January 2008 to 2011.

Pain and swelling were common presenting complaints in most of the bone tumour patients. Excluding multiple myeloma, the most commonly involved anatomic site due to other tumours, was the femur. The commonly observed tumours were mostly osteogenic sarcoma, multiple myeloma and chondrosarcoma. Multiple myeloma was the commonest cause for diffuse skeletal involvement

6.2 Study limitations

The results presented in this study by and large are limited to describing the pattern of primary malignant bone tumours, within the parameters set, at the University Teaching Hospital alone and cannot be said to be representative of the pattern of distribution of bone tumour in society at large.

While this study did attempt to characterize the pattern of bone cancers seen at UTH. The number of bone tumour patients captured by the study is likely to be lower than the true number of patients who presented to UTH from 1st January 2008 to 31st December 2012 due to the fact that some records were most likely missing and others were inadvertently excluded from the study due to the stringent inclusion and exclusion criteria. Therefore the study only

goes as far as describing the pattern of primary malignant bone tumours among patients who had traceable histological records.

Some of the critical pieces of information were missing from the patients' records, including the actual hospital records in some cases. This may have been due to incomprehensive history taking by clinicians whereas in other instances it was due to the fact that some patients may have left with their hospital records. Some of the patients' records may have been held up within the hospital file courier system at the time of the study.

The reported geographic origin of the patients cannot be confirmed as the true patients' domicile and may tend to skew the results showing higher patient numbers from Lusaka or places around Lusaka because patients from outside Lusaka may have reported their temporal domiciles with their Lusaka based relatives as their geographic area of origin.

There is need to further conduct dedicated prospective studies specifically aimed at describing the socio-demographic characteristics of patients with primary malignant bone tumours, their clinical presentations, and relationships between histological tumour types and clinical presentations.

Tumour-type specific frequencies per year where not presented in this study, therefore it was not possible to characterize tumour frequency with respect to the annual occurrence.

6.3 Recommendations

In view of the study findings pertaining to the high frequency of Multiple Myeloma and osteosarcoma it is imperative that the University Teaching Hospital conducts a needs assessment of its bone tumour diagnostic and therapy capacity including acquisition of appropriate but missing resources.

It is important also that the Cancer Diseases Hospital streamlines its therapy modalities and capacity to reflect the disease spectrum as is highlighted by the study findings.

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APPENDIX 1

DATA COLLECTION FORM FOR UTH MAIN RECORDS AND CDH

NAME	DATE	HOSPITAL NUMBER	HOSPITAL CDH / UTH	AGE (YRS)	SEX	YEAR OF PRESENTATION TO UTH	PROVINCE OF ORIGIN (domicile NOT ethnicity)	TUMOUR SITE	HISTOLOGY	CINICAL PRESENTATION
Cut name column out										

Key:

Clinical data can either be

Pathological fracture (1)

Pain (2)

Swelling (3)

Incidental finding (4)

Other (Specify)

Note: Cut the name column out after the form is full

APPENDIX 2

HISTOPATHOLOGY LABORATORY DATA COLLECTION FORM

PATIENT'S NAME	DATE	STUDY No	FILE No	LABORATORY No	SEX	AGE	CLINICAL DATA	HISTOLOGY DIAGNOSIS	ANATOMIC SITE	WARD	CLINIC
Cut name column out											

Key:

Clinical data can either be

pathological fracture (1)

pain (2)

Swelling (3)

Incidental finding (4)

Other (Specify)

Note: Cut the "patient's name" column out after the form is full

APPENDIX 3

THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
E-mail: unzarec@unza.zm
Assurance No. FWA00000338
IRB00001131 of IORG0000774

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

22nd January, 2013.

Your Ref: 002-01-13.

Dr. Dennis Sakala
School of Medicine,
Department of Surgery
PO Box 50110
Lusaka

Dear Dr. Sakala,

RE: SUBMITTED RESEARCH PROPOSAL: **"A REVIEW OF THE PATTERN OF PRIMARY MALIGNANT BONE TUMOURS SEEN AT THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA"**

Your application for a waiver of ethics review for the protocol **"A Review of the Pattern of Primary Malignant Bone Tumours Seen at the University Teaching Hospital in Lusaka, Zambia"** was reviewed. The waiver is hereby granted in accordance with the University of Zambia Biomedical Research Ethics Committee procedure on granting waiver of ethics review.

CONDITIONS:

- The waiver is based strictly on your submitted proposal. Should there be need for you to modify or make changes to the proposal you will need to seek clearance from the University of Zambia Biomedical Research Ethics Committee.
- This waiver does not release you from any other applicable obligations in ensuring confidentiality.
- If you need any clarifications please consult this office.
- **Ensure that a final copy of the results is submitted to this Committee.**

Yours sincerely,

Dr. J.C Munthali
CHAIRPERSON

Date of approval: 22 January, 2013 **Date of expiry**: 21 January, 2014