



Research Article

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Frequency Distribution of Bone metastasis in Breast cancer: A retrospective study in Khartoum Oncology Hospital 2019

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Abstract

Background: Breast cancer (BC) is a common cancer in women worldwide and leading cause of bone metastasis (BM). This study reveals the incidence of bone metastases and the most frequent BM sites secondary to BC in Khartoum Oncology Hospital.

Materials and method: Retrospective study in Khartoum oncology hospital of medical record from January 2019 to September 2019. Demographic and clinical information extracted from the medical records of eligible patients in the last 5 years 2015-2019 included age, sex, social habits, duration of breast cancer, duration of treatment and location of bone metastasis. Statistical analyses were performed using SPSS, Version 22.0. (IBM, USA).

Results: From all patients diagnosed with BC, 3.03% had developed BM out of whom 50% of patients developed bone metastases in 2-5 years of diagnosis of BC and 39.7% in less than 2 year of diagnosis. The median age was 54 years (range 28-78). The most common site is lumbar vertebrae (48.8%), followed by thoracic vertebrae (32.9%), pelvis 34 (32.9%), sternum (27.1%), ribs (25.7%), femur (15.7%), skull (15.7%), clavicle (14.3%), sacral vertebrae (14.3%), cervical vertebrae (12.8%), hummers (11.4%), and tibia (4.3%). Right side BC contribute to 57.1% of BM whereas left side BC to 40%. The duration of BC significantly correlates to number of distant bone metastases (P=0.006).

Conclusion: The most common site of BM in BC patients is lumbar vertebrae, the duration of BC affects development of BM, Exploring the knowledge of patient populations prone to develop bone metastasis helps in further intervention and management.

Keywords: Breast cancer, Bone metastasis, Distribution pattern, Lumbar vertebra.

Introduction

Breast cancer (BC) is the most common malignancy affecting women and a leading cause of women's death over the world [1, 2]. It has always been a global concern since More than one million women were diagnosed with breast cancer worldwide in 2008 [3]. Moreover, BC is the most prevalent malignancy in Europe, significantly associated with disease morbidity and mortality in Africa it constitutes about 19% of all cancers

representing the second most cancer affecting women [4-6]. Though it was not much discussed in Sudan; due to the heavy burden of communicable diseases, but it remains the most common cancer in women, compromising approximately 22.9% of overall malignancies with most of the patients presenting in advanced disease stage [7, 8]. This has emphasized the need for mammographic screening for early detection of disease, and the availability of treatment facilities. There are different treatment modalities used in breast cancer such as surgery, radiation therapy chemotherapy, hormonal therapy, and recently nanotechnology and gene therapy [9].

In an aggressive disease course, BC tends to metastasize to bone, lung, liver, and brain respectively which severely complicates the condition with a more stable and better outcome in patients with first bone metastases than in those with first visceral metastases [10-12]. However, bone is the commonest first site of distant spread in breast cancer patients [13]. Over the year's treatment of early-stage breast cancer is instantly improving, while bone remains the commonest site of distant metastases, it's estimated that almost half of all patients with the metastatic disease having at least one bone metastases during disease progression and its prevalent in a large population of patients with advanced disease, in which is considered as the site of most significant tumor burden [11, 14-16]. In particular, the spine is the most common site involved, followed by ribs, pelvis, and sternum [17].

Moreover, it's observed that the time at which bone metastasis diagnosis is made was at the second, third, or fourth year of cancer diagnosis in 2-7% of cases. In 14% of cases, metastatic spine disease observed in the fifth year and beyond [18]. In breast cancer metastases bone loss is a common consequence which is associated with skeletal-related events (SRE) that may present with bone pain, pathologic fractures, nerve compression syndrome, and metabolic disturbances that severely disturb the quality of life [19]. The most common sites associated with SRE occurrence were the thoracic and lumbar spine respectively [20]. Bisphosphonate therapy has an important part of the standard management of bone metastases, by reducing skeletal-related events, and improving bone pain and quality. More recently, denosumab, prevents skeletal complications [21].

During our study we found that previous data on metastatic bone disease in patients with breast cancer were limited especially regarding the contribution of BC site and duration to number of distant bone metastases and in particular the specific vertebral segments involvement. The aims of this review were to determine the size of patient's population with BM from BC, to identify and analyzes specifically the most potential sites for BM, to find out the time of diagnosis of BM after BC, the BC site specific risk to develop BM and the contribution of BC duration to number of distant bone metastases.

Material and Method

A health facility-based Retrospective record review was conducted in Khartoum oncology hospital, Khartoum, Sudan from January 2019 to September 2019. A retrospective review of patients with Breast cancer metastasizes to bone was done. We collected clinical datasets from the medical records of 2309 patients with Breast cancer at Khartoum hospital for Oncology between January 2015 and September 31, 2019. During this 5 years' period, a total of 70 Patients (3%) who had been initially diagnosed with breast cancer and then later developed the metastatic bone disease were included. The targeted patients were:

- 1. Any female patient, 18 years or older, with a diagnosis of BC.
- 2. All male patients diagnosed with BC in the above-stated time frame, given the rarity of male BC.

Patients with incomplete information regarding their metastatic bone disease presentation and patients with primary bone cancer were excluded. Demographic and clinical information extracted from the medical records of eligible patients included age, sex, social habits, duration of breast cancer, duration of treatment, and location of bony metastasis. Investigations included a plain X-ray of the affected limb, chest X-ray, and computed tomography (CT) scan of chest, abdomen, pelvis, and bone and bone scan. All investigations were performed before a biopsy was done.

The Statistical Analysis

The following Parameters: Age, sex, social habits, Site of breast cancer, duration of breast cancer, and duration of treatment were analyzed for validity as prognostic factors.

Statistical significance was defined as P < 0.05. Analyses were performed using SPSS, Version 20.0. (IBM, USA).

Results

A total of 2309 patients had breast cancer were identified via the medical records database search method, of whom 95.5 % (2205) were female and 3.03% (70 patients, 69 females, 1male) with bone metastases secondary to breast cancer (BC). The median age was 54 years (range 28-78), Right and left BC with secondary bones metastasis comprised 57.1%, 40% respectively (Figure 1). 50% of patients developed bone metastases in 2-5 years of diagnosis of BC and 39.7% in less than 2 years of diagnosis. The most common site of bones metastasis secondary to BC is lumbar vertebrae (48.8%), followed by thoracic vertebrae (32.9%), pelvic (32.9%), sternum (27.1%), ribs 117 (25.7%), femur (15.7%), skull (15.7%), clavicle (14.3%), sacral vertebrae (14.3%), cervical vertebrae (12.8%), hummers (11.4%), and tibia (4.3%) (Figure 2).

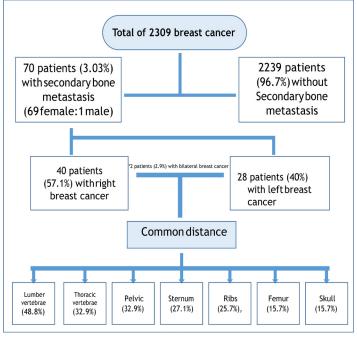


Figure 1: Show selection flow diagram with common bone sites metastasis.

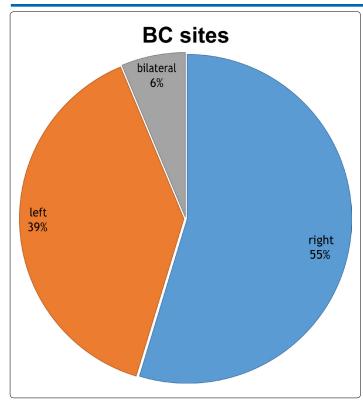


Figure 2: Pie chart show percentages of right, left and bilateral breast cancer sites. 356

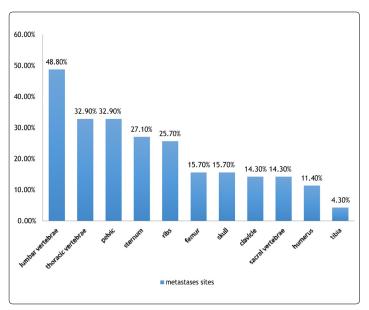


Figure 3: Bar chart show frequency percentages of different breast cancer sites with secondary bone metastasis sites.

There was no correlation between BC site and the number of distant bone metastases (P = 0.754) but the correlation was significant between the duration of BC and the number of distant bone metastases (P = 0.006). 55.8%,38.2%, and 5.8% of lumbar metastasis originate from right, left and bilateral BC respectively, the rest of sites shown in (Table 1), and (44.3%) of secondary bone metastases affect spinal vertebrae as shown in (Table 2).

Table 1: Show frequency percentages of different breast cancer sites with secondary bone metastasis sites.

Sites of secondary metastases	BC site				
	right	Left	Bilateral	<u>Total</u>	
Femur	8 (11.4%)	3 (4.3%)	0	11 (15.7%)	
Pelvic	11 (15.7%)	12 (17.1%)	0	23 (32.9%)	
Ribs	8 (11.4%)	9 (12.8%)	1 (1.4%)	18 (25.7%)	
Skull	5 (7.1%)	5 (7.1%)	1 (1.4%)	11 (15.7%)	
Cervical vertebrae	8 (11.4%)	1 (1.4%)	0	9 (12.8%)	
Thoracic vertebrae	11 (15.7%)	11 (15.7%)	1 (1.4%)	23 (32.9%)	
Lumbar vertebrae	19 (27.1%)	13 (18.6%)	1 (1.4%)	34 (48.8%)	
Sacral vertebrae	6 (8.6%)	4 (5.7%)	0	10 (14.3%)	
Sternum	9 (12.8%)	10 (14.3%)	0	19 (27.1%)	
Clavicle	5 (7.1%)	5 (7.1%)	0	10 (14.3%)	
Tibia	2 (2.9%)	1 (1.4%)	0	3 (4.3%)	
Humerus	5 (7.1%)	3 (4.3%)	0	8 (11.4%)	
Total count	40 (57.1%)	28 (40%)	2 (2.9%)	70	
Percentages are frometastases	m total 70 ca	ses of PBC w	ith secondary	bone	

Table 2: Show frequency percentages of different breast cancer sites with secondary spinal vertebrae metastasis sites.

Spinal vertebrae metastases sites	BC site				
	right	Left	Bilateral	<u>Total</u>	
C3	1 (1.4%)	0	0	1 (1.4%)	
C4	2 (2.9%)	0	0	2 (2.9%)	
C5	2 (2.9%)	0	0	2 (2.9%)	
C6	3 (4.3%)	0	0	3 (4.3%)	
C7	4 (5.7%)	0	0	4 (5.7%)	
T1	2 (2.9%)	0	0	2 (2.9%)	
T2	2 (2.9%)	0	0	2 (2.9%)	
Т3	5 (7.1%)	2(2.9%)	0	7 (10%)	
T4	2 (2.9%)	2 (2.9%)	0	4 (5.7%)	
T5	1 (1.4%)	2 (2.9%)	0	3 (4.3%)	
T6	1 (1.4%)	3 (4.3%)	0	4 (5.7%)	
T7	0	5 (7.1%)	0	5 (7.1%)	
T8	2 (2.9%)	5 (7.1%)	0	7 (10%)	
Т9	1 (1.4%)	5 (7.1%)	0	6 (8.6%)	
T10	2 (2.9%)	3 (4.3%)	0	5 (7.1%)	
T11	3 (4.3%)	4 (5.7%)	1 (1.4%)	8 (11.4%)	
T12	3 (4.3%)	3 (4.3%)	0	6 (8.6%)	
L1	1 (1.4%)	1 (1.4%)	0	2 (2.9%)	
L2	3 (4.3%)	6 (8.6%)	1 (1.4%)	10 (14.3%)	
L3	10 (14.3%)	4 (5.7%)	0	14 (20%)	
L4	8 (11.4%)	3 (4.3%)	0	11 (15.7%)	
L5	6 (8.6%)	5 (7.1%)	0	11 (15.7%)	
Total count	17 (24.3%)	13 (18.8%)	1 (1.4%)	31 (44.3%)	

Discussion

In women, the leading cause of cancer deaths is Breast Cancer, with approximately 90% of these deaths are caused by metastasis

[22, 11]. In this difficult incurable advanced breast cancer, palliative treatment is the only choice. Most studies showed that breast cancer preferentially metastases to the bone as the most common site, R.E. Coleman and R.D. Rubens conducted a study in England in early 1987s and they revealed by radiological evidence that 69% of patients dying with breast cancer in the period of 1979-1984 had skeletal metastases before death in comparison of 27% had lung metastasis and 27% had liver metastases and in other study conducted by RE [23]. Coleman in 1997 noted that from (20 up to 45 %) of first or (60 up to 80 %) of recurrent breast cancer is always metastasis to the bone as the first site [24].

This perceptive study aims to explore the common sites of bone metastases secondary to the patient have BC in Khartoum Oncology Hospital during the period of 5 years from January 2015 to September 2019 in order to better understanding the bony sites metastases and early detection of bone involvement. Spinal vertebrae are particularly the most frequent site of bone metastases in patients with breast cancer, Analogues study was approved by Ethics Committee of First Affiliated

Hospital of Nanchang University between 2005 and 2015 of 2133 patients with breast cancer, including 327 with bone metastasis found spinal vertebrae to be the most common site for bone metastases followed by ribs (57.5%), pelvis (54.1%) and sternum (44.3%), our study carries the same finding regarding the spinal vertebrae by 2/3 (67.14%) of total bony metastases, then pelvis (32.9%), sternum (27.1%) and ribs (25.7%). this difference may reflect the racial disparities, psychosocial stress, and environmental difference and need further studying [25].

Although, some studies discuss the genetic component which determines the different patterns of distance metastases, and others focused on risk factors or measured survival rate or complications of bone metastases, to our knowledge this is the first study to explore which part of spinal vertebrae mostly affected than others [26, 27].

In our study, we found (51.5%) of spinal metastases affected mainly lumbar vertebrae in comparison of (34.8%) in thoracic vertebrae and (13.6%) in cervical vertebrae. Other Studies argued that the thoracic spine is the region more involved with metastasis, while other studies showed how the lumbar spine is more involved [28-30]. The cervical spine is the least involved and rarely in the sacral spine. Generally, the route of breast cancer spreading is either locally through the lymphatic system or to the far distant site through the venous system, both lymphatic drainage and locally tumor distribution between each side of the body can be considered symmetric according to study done at the RPAH Medical Centre, Sydney, Australia 2011 [31]. Moreover, the breast venous system is more complex and shows great variations through populations but all Breast veins typically lack valves and intramammary venous anastomoses are common [32].

Venous drainage from the right and left breast collect usually in azygos vein and hemiazygos vein respectively, azygos veins formed by the union of ascending lumbar veins with right subcostal veins in comparison of hemiazygos vein which don't have a direct connection to lumber veins, this can explain why here in our study we found there is a slight difference between the frequency of right and left BC metastases to lumbar vertebrae, which show right BC tend to metastases more frequently to lumbar vertebrae than left one.

Also, not all lumbar vertebrae were affected equally, some vertebrae affected more than others, we found L3 affected in 14 cases of total 48 lumbar metastases (29.10%), each one of L2, L4 or L5 found in 10 to 11 cases (20.8-22.9%), and L1 was the least affected vertebra in only 2 cases (4.2%). Male and female breast anatomy differ from each other, and accordingly, there may be slight difference between patterns of bone metastases with breast cancer, in our study we only have one case of male breast cancer metastasized to thoracic vertebrae (T3 and T4) and pelvic bone, this thesis needs further study in a large sample through different risk and environmental factors.

This study limited by single database nature, during our study we found that previous data on metastatic bone disease in patients with breast cancer were limited especially regarding the contribution of BC site and duration to the number of distant bone metastases and in particular the specific vertebral segments involvement.

The aims of this review study were to determine the size of patient's population with BM from BC, to identify and analyzes specifically the most potential sites for BM, to find out the time of diagnosis of BM after BC, and the contribution of BC site and duration to the number of distant bone metastases

Other data like age, sex, social habits, Site of breast cancer, duration of breast cancer, and duration of treatment were also collected for validity as prognostic factors.

Conclusion

Breast cancer is a women's health issue worldwide, metastases traditionally considered incurable with 2 years of median survival time, bone metastases accounted in the majority of breast cancer deaths, clinicians should be aware of common bone metastases pattern and try to detect it early and treat it urgently. Also, the examination of bone and Spinal vertebrae should be done first after the diagnosis of breast cancer. In the future, we suggest studies should test if the different risk and environmental factors will change bone metastases pattern, AND if there is a difference in pattern between male and female.

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