Bone Secondaries at Basra Oncology Center

By

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Abstract

Background: Bone metastasis is a relatively frequent complication of cancer, often occurring as cancers progress, particularly in prostate and breast cancer. The bone is the most common and favored site for cancer to spread. During the advanced stages of cancer, bone metastases frequently develop. **Aims of the study:** The study aims to determine the prevalence of secondary bone tumors and bone-related symptoms among various primary cancer sources in Basra city Oncology center. **Patients and methods:** The study included (124) cancer patients aged (18 to 80) years with bone metastases. The patients were treated at the Oncology Centre in Basrah city between April 2022 and July 2023. Voluntarily participants were enrolled and provided with written informed consents. The study was approved by the Ethical Committee of the University of Basrah, College of Medicine. Patients completed a questionnaire covering socio-demographic information and pain history. PET scan and X-ray results were evaluated by a single observer to determine metastasis sites and bone lesion appearance on X-rays. Primary tumor information was extracted from patient's medical records.**Results:** The study cases had an average age of (67.0±9.2) years. Males constituted 79(56.5%) of the cases, while females constituted 54(43.5%). The distribution of primary malignancies significantly differed by gender ($p<0.001$). Prostate cancer exclusively affected males (85.7%), while breast cancer was exclusive to females (81.5%). Lung and unknown primary sources of cancer had lower prevalence in both groups. Regarding secondary bone tumors, spinal involvement was the most common in both females (72.2%) and males (68.6%), without a significant gender difference ($p=0.11$). Pain site exhibited a significant gender disparity ($p=0.002$), with localized pain was more common in females (74.1%), and generalized pain was more prevalent in males (54.3%). X-ray findings were also significantly correlated with gender ($p<0.001$), with blastic lesions mainly seen in males (94.3%) and lytic lesions were more prevalent in females (88.9%). Mixed lesions were rare and only found in males (7.4%). The distribution of secondary sites varied significantly among cancer types ($p<0.001$), with the spine being the most affected site across

all groups. Pain site and severity also highly significantly differed among cancer types ($p<0.001$). X-ray findings demonstrated highly significant differences ($p<0.001$), with prostate cancer showing a predominance of blastic lesions (100.0%), breast cancer predominantly displaying lytic lesions, and lung cancer having an equal distribution of blastic and lytic lesions among cases.**Conclusion**: The spine was identified as the primary site for metastatic involvement. Pain intensity showed variability, with moderate pain affected (41.9%) of patients, severe pain affected (29.8%), and mild pain was reported in (28.2%) of the cases. Prostate cancer was strongly associated with blastic lesions (100%) of cases, while breast cancer was significantly linked to lytic lesions on X-rays (90.9%) of cases.

Keywords: Bone metastasis, Bone pain, Bone changes, Cancer

Introduction

Bone metastasis is a relatively prevalent occurrence in cancer, often emerging as the disease advances, particularly in cases of prostate and breast cancer. The presence of bone metastasis can significantly impact the daily lives and overall quality of life for patients due to intense pain and related significant complications. During the later stages of cancer progression, advanced cases frequently result in the spread of cancer to the bones [1].

The development of bony metastasis is a catastrophic complication for most patients with cancer and indicates that the malignant process is incurable and only palliation is available. Metastatic destruction of bone reduces its load bearing capabilities, trabecular destruction resulting and in microfracture and subsequently in loss of bony integrity. Bone metastasis thus causes considerable morbidity, including pain, impaired mobility, Correspondence to hypercalcaemia, compression of spinal cord or nerve roots, and particularly with osteolytic lesion, pathological fracture [2].

The primary tumor can release substances that guide the migration of hematopoietic progenitor cells from the bone marrow, causing them to gather in specific locations, including the bone. This creates an environment suitable for future metastatic growth, termed the premetastatic niche [3]. The initiation of metastatic spread is now increasingly seen as an early event occurring before the primary tumor becomes clinically detectable, rather than being tied to a high tumor burden [4]. Once situated within the bone marrow niche(s), disseminated tumor cells could remain dormant for many years, influenced by the surrounding bone microenvironment [5].

Patients and methods

The current study involved patients affected with bone metastases. These patients were observed at the Oncology Centre in Basra city between April 2022 and July 2023. All patients provided with written informed consents, and the study received approval from the Ethical Committee of the University of Basra, College of Medicine.

Each patient completed a questionnaire regarding socio-demographic details and pain history. A single observer assessed PET scan and X-ray outcomes to identify metastasis locations and bone lesion appearances, respectively. Information about the primary tumor was extracted from the patient's medical record at the oncology center.

Statistical analysis

Continuous variables were expressed as means and standard deviations. Categorical variables were expressed as frequency and percentages. The Welch's t-test (for two independent variables) and One-way ANOVA (for three or more independent variables) were performed. The difference between categorical variables was investigated using either the $\chi 2$ test with yates' correction or Fisher's exact test, depending on the context. A P-value less than 0.05 was considered statistically significant.

Results

In this cross-sectional analytic study, a total of (124) cases were analyzed to investigate the characteristics of the population under consideration. The cohort exhibited an average age of (67.0±9.2) years. Among the cases, 70(56.5%) were males, while 45(43.5%) were females.

The primary sources of cancer were predominantly prostate (48.4%) and breast (35.5%), with lung (12.9%) and unknown (3.2%) sources accounting for the remaining cases. Among cases with bone secondaries, the most common sites were the spine (70.2%), followed by multiple sites (17.7%), pelvis (9.7%), and femur (2.4%). Pain distribution was reported as local in 58.1% of cases and generalized in 41.9% of cases. Regarding pain severity, moderate pain was experienced by 41.9% of patients, severe pain by 29.8%, and mild pain by 28.2%. On X-ray findings, blastic lesions were identified in 54.8% of cases, lytic lesions in 41.9%, and a mixed pattern in 3.2% of cases, as shown in table (1).

Table (1): Distribution of study cases according to age, sex, primary source of cancer, bone secondaries, pain site, pain severity and X-ray findings

Characteristics	Cases, N = 124
Age, years	67.0 ± 9.2
Sex	
Males	70 (56.5%)
Females	54 (43.5%)
Primary source of cancer	
Prostate	60 (48.4%)
Breast	44 (35.5%)
Lung	16 (12.9%)
Unknown	4 (3.2%)
Bone secondaries	
Spine	87 (70.2%)
Multiple	22 (17.7%)
Pelvis	12 (9.7%)
Femur	3 (2.4%)
Pain site	
Local	72 (58.1%)
Generalized	52 (41.9%)
Pain severity	
Moderate	52 (41.9%)
Severe	37 (29.8%)
Mild	35 (28.2%)
X-ray finding	
Blastic lesion	68 (54.8%)
Lytic lesion	52 (41.9%)
Mixed	4 (3.2%)

Results in table (2) showed that the mean age of females was (64.5±11.7) years, which was significantly lower than that of males (68.9±6.1) years (p=0.016). The primary source of malignancy differed significantly between the genders (p<0.001). Lung and unknown sources

of cancer showed comparatively lower prevalence in both groups. Regarding bone secondaries, spinal involvement was the most common in both females (72.2%) and males (68.6%), with no significant gender difference (p=0.11). Pain site demonstrated a significant gender disparity (p=0.002), with localized pain being more prevalent in females (74.1%) and generalized pain more frequent in males (54.3%). Pain severity did not significantly vary between genders (p=0.3), with moderate pain being the most common. Notably, X-ray findings showed a significant association with gender (p<0.001), with blastic lesions were predominant in males (94.3%), and lytic lesions were more prevalent in females (88.9%). Mixed lesions were rare and found exclusively in males (7.4%).

Table (2): Description of study characteristics by sex

Characteristic	Female, N = 54[1]	Male, N = 70[1]	P-value[2]
	64.5 ± 11.7	68.9 ± 6.1	**0.016**
Primary source			**<0.001**
Prostate	0 (0.0%)	60 (85.7%)	
Breast	44 (81.5%)	0 (0.0%)	
Lung	7 (13.0%)	9 (12.9%)	
Unknown	3 (5.6%)	1 (1.4%)	
Bone secondaries			0.11
Spine	39 (72.2%)	48 (68.6%)	
Multiple	7 (13.0%)	15 (21.4%)	
Pelvis	8 (14.8%)	4 (5.7%)	
Femur	0 (0.0%)	3 (4.3%)	
Pain site			**0.002**
Local	40 (74.1%)	32 (45.7%)	
Generalized	14 (25.9%)	38 (54.3%)	
Pain severity			0.3
Moderate	27 (50.0%)	25 (35.7%)	
Severe	13 (24.1%)	24 (34.3%)	
Mild	14 (25.9%)	21 (30.0%)	
X-ray finding			**<0.001**
Blastic	2 (3.7%)	66 (94.3%)	

Lytic	48 (88.9%)	4 (5.7%)	
Mixed	4 (7.4%)	0 (0.0%)	

[1]Mean ± SD; n (%)
[2]Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test

The mean age of patients did not differ significantly across the groups (p=0.2), with the prostate cancer group exhibiting the highest average age (68.7 ± 6.0) years, and the unknown group being the youngest (63.3±9.5) years. Sex distribution showed significant variation (p<0.001), with the prostate cancer group exclusively comprising males (100.0%) and the breast cancer group being entirely females (100.0%). Notably, the distribution of secondaries differed significantly among the cancer types (p<0.001), with the spine being the most affected site in all groups. Pain site and pain severity also displayed significant variations among the cancer types (p<0.001).

X-ray findings exhibited significant differences (p<0.001), with the prostate cancer group showing a predominance of blastic lesions (100.0%), while the breast cancer group showed mostly lytic lesions; lung cancer had both blastic and lytic lesions distributed equally among cases, as illustrated in table (3).

Table (3): Description of study characteristics among different types of cancers

Characteristic	Breast, N = 44[1]	Lung, N = 16[1]	Prostate, N = 60[1]	Unknown, N = 4[1]	P-value[2]
Age, years	64.8 ± 12.0	67.2 ± 9.9	68.7 ± 6.0	63.3 ± 9.5	0.2
Sex					**<0.001**
Male	0 (0.0%)	9 (56.3%)	60 (100.0%)	1 (25.0%)	
Female	44 (100.0%)	7 (43.8%)	0 (0.0%)	3 (75.0%)	
Secondaries					**<0.001**
Spine	33 (75.0%)	5 (31.3%)	45 (75.0%)	4 (100.0%)	
Multiple	4 (9.1%)	6 (37.5%)	12 (20.0%)	0 (0.0%)	
Pelvis	7 (15.9%)	5 (31.3%)	0 (0.0%)	0 (0.0%)	
Femur	0 (0.0%)	0 (0.0%)	3 (5.0%)	0 (0.0%)	
Pain site					**<0.001**
Local	32 (72.7%)	12 (75.0%)	24 (40.0%)	4 (100.0%)	
Generalized	12 (27.3%)	4 (25.0%)	36 (60.0%)	0 (0.0%)	
Pain severity					**<0.001**

Moderate	24 (54.5%)	0 (0.0%)	24 (40.0%)	4 (100.0%)	
Severe	12 (27.3%)	1 (6.3%)	24 (40.0%)	0 (0.0%)	
Mild	8 (18.2%)	15 (93.8%)	12 (20.0%)	0 (0.0%)	
X-ray finding					**<0.001**
Blastic	0 (0.0%)	8 (50.0%)	60 (100.0%)	0 (0.0%)	
Lytic	40 (90.9%)	8 (50.0%)	0 (0.0%)	4 (100.0%)	
Mixed	4 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

[1]Mean ± SD; n (%)
[2]One-way ANOVA; Fisher's exact test

The mean age distribution demonstrated (66.1±9.3) for spine, (68.3±10.0) for Pelvis, (62.3±4.2) for Femur, and (70.2±8.7) for Multiple sites, with significant differences (p=0.2). Gender distribution indicated variations, with a trend across the groups (p=0.11). The primary source of cancer exhibited significant differences (p<0.001), with varying proportions for Prostate, Breast, Lung, and Unknown sources. Pain site distribution showed differences as well (p=0.10), with localized and generalized pain reported. Pain severity differed significantly (p<0.001), ranging from moderate to severe and mild. X-ray findings showed some distinctions (p=0.3) among Blastic, Lytic, and Mixed categories, as shown in table (4).

Table (4): Description of study characteristics among different types of bone secondaries.

Characteristic	Spine, N = 87[1]	Pelvis, N = 12[1]	Femur, N = 3[1]	Multiple, N = 22[1]	p-value[2]
Age, years	66.1 ± 9.3	68.3 ± 10.0	62.3 ± 4.2	70.2 ± 8.7	0.2
Sex					0.11
Male	48 (55.2%)	4 (33.3%)	3 (100.0%)	15 (68.2%)	
Female	39 (44.8%)	8 (66.7%)	0 (0.0%)	7 (31.8%)	
Primary source					**<0.001**
Prostate	45 (51.7%)	0 (0.0%)	3 (100.0%)	12 (54.5%)	
Breast	33 (37.9%)	7 (58.3%)	0 (0.0%)	4 (18.2%)	
Lung	5 (5.7%)	5 (41.7%)	0 (0.0%)	6 (27.3%)	
Unknown	4 (4.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Pain site					0.10

Local	52 (59.8%)	9 (75.0%)	0 (0.0%)	11 (50.0%)	
Generalized	35 (40.2%)	3 (25.0%)	3 (100.0%)	11 (50.0%)	
Pain severity					**<0.001**
Moderate	46 (52.9%)	0 (0.0%)	0 (0.0%)	6 (27.3%)	
Severe	23 (26.4%)	7 (58.3%)	0 (0.0%)	7 (31.8%)	
Mild	18 (20.7%)	5 (41.7%)	3 (100.0%)	9 (40.9%)	
X-ray finding					0.3
Blastic	45 (51.7%)	5 (41.7%)	3 (100.0%)	15 (68.2%)	
Lytic	39 (44.8%)	7 (58.3%)	0 (0.0%)	6 (27.3%)	
Mixed	3 (3.4%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	

[1]Mean ± SD; n (%)
[2]One-way ANOVA; Fisher's exact test

Discussion

In cancer research, the development of incurable metastasis is a major contributor to cancer-related deaths [6]. Among the organs prone to metastasis, the bone is frequently targeted by solid tumors [7].

Notably, metastases to bones are most common in certain cancers, such as multiple myeloma, breast, and prostate cancers, while being less prevalent in others like lung, kidney, and thyroid cancers [8]. The process of solid tumor metastasis is complex and involves several stages, including the formation of a niche for metastasis, the spread of tumor cells through circulation, their attraction to the target site, and interactions with the new microenvironment [9]. In cases like prostate cancer metastasis to bone, this involves a series of steps: colonization, dormancy, reactivation, and reconstruction [10].

Bone metastases significantly impact patients' prognosis and quality of life, especially in cases like multiple myeloma, breast, and prostate cancers, where survival after bone metastasis diagnosis is limited [11].

The proximal ends of long bones, such as the femur and humerus, are variably impacted. This bone marrow compartment exhibits a robust vascular network and distinctive cellular composition, fostering the attraction of circulating tumor cells and facilitating the establishment of secondary deposits within the bone. As a result, metastases predominantly

manifest within the axial skeleton. Coleman et al. [11] found that over 80% of cases involved metastasis to the spine. Within this context, the thoracic spine is most frequently affected (70%), followed by the lumbosacral region (20%) and cervical vertebrae (10%). Moreover, metastases involving the pelvic bones, ribs, and skull occur in 63%, 77%, and 35% of cases, respectively. Notably, the proximal long bones, including the humeri and femur, exhibit a higher frequency of involvement (53%) compared to the distal appendicular skeleton (1%) in Coleman et al. [11] study.

In the present study, the predominant cancer origins within this cohort encompassed prostate (48.4%), breast (35.5%), lung (12.9%), and cases of undisclosed origin (3.2%). The spatial prevalence of bone metastases predominantly manifested in the spinal region (70.2%), succeeded by multiple sites (17.7%), pelvis (9.7%), and femur (2.4%).

When comparing our study's findings to those of Itokazu et al. [12] conducted in 2022 in Japan, notable variations arise in the primary cancer types. Their study identified a prevalence of lung and esophageal cancers, followed by breast cancer, hepatocellular carcinoma, and gastric cancer. In contrast, our study predominantly observed prostate, breast, lung, and cases with unknown primary tumors as the sources of cancer within our cohort. Furthermore, the spatial distribution of bone metastases demonstrated similarities and disparities. While both studies noted spine involvement as a primary site, Itokazu et al. [12] reported a higher proportion (73.9%) compared to our study (70.2%). Pelvic metastases were also prominent in their study (47.8%), and limb metastases were observed (15.2%), diverging from our findings.

Hong et al.'s [13] investigation in 2020 in Korea showcased a distinct cancer profile, with lung cancer as the most prevalent (53.4%), followed by liver (50.9%), prostate (45.9%), breast (43.6%), and colorectal (40.2%) cancers. In contrast, our study revealed a higher prevalence of breast and prostate cancers (35.5% and 48.4% respectively), with lung cancer comprising 12.9% of cases. The observation of spine metastases as the primary site of bone metastasis aligned with our findings, although differences in cancer distribution necessitate careful consideration when comparing these outcomes.

Additionally, Huang et al.'s [14] work in 2020 in China emphasized varied incidences of bone metastases among different cancer types. Notably, the incidence was highest in prostate cancer (88.74%), followed by breast cancer (53.71%), and renal cancer (38.65%). While our study's focus did not extend to comparing incidence rates across specific cancer types, this comparison highlights the distinct dynamics of bone metastases occurrence in various malignancies.

In terms of pain localization in the current study, localized discomfort was encountered by 58.1% of patients, whereas 41.9% reported pain that extended more broadly. The intensity of pain exhibited diversity, with 41.9% experiencing moderate pain, 29.8% facing severe pain, and 28.2% describing their pain as mild.

In accordance with Smith et al. [15] systematic review encompassing 122 studies on cancer pain across various disease subtypes, the prevalence of cancer-related pain among cancer patients is notably substantial. Specifically, 66.4% of individuals with advanced, metastatic, or terminal cancer encountered pain linked to their cancer condition. Deeper analysis demonstrated that within this subset, 51.9% of patients faced moderate to severe cancer pain. The etiology of cancer-related pain is multifaceted, with bone metastases emerging as the most prevalent cause in advanced stages of the disease [16]. It is noteworthy that while bone metastases are relatively infrequent during initial cancer diagnosis, their frequency increases as cancer metastasizes. For most solid tumors, the incidence of bone metastases at the point of initial diagnosis is relatively low, ranging from single digits. Moreover, the majority of patients who develop bone metastases also experience pain, with around 80% of patients across all cancer subtypes reporting moderate to severe bone pain. Consequently, the regular assessment of pain intensity in patients remains pivotal for the efficacious management of pain associated with cancer and bone metastases [17].

In comparison to prior studies, the present research demonstrates a lower prevalence of pathological fractures at 4.8%. Saad et al. [18] reported higher fracture incidences across various cancer types, with the highest in multiple myeloma (43%), followed by breast (35%), prostate (19%), and lung cancer (17%). Similarly, Oliveira et al. [19] noted a higher prevalence of bone metastases (28.2%) and pathological fractures (19.1%) specifically among lung cancer patients.

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