A Clinico-Pathological Overview of Bone Metastasis of Solid Tumor at National Institute of Cancer Research & Hospital, Mohakhali, Dhaka

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Abstract

Background: The dynamic bony skeleton is the third most common site for the metastasis from the adult solid tumors. The most osteotropic solid malignancies are breast cancer, prostate cancer, lung, renal, thyroid cancer and melanoma and vary in their predilection to various site of the bone. The aim of the study was to assess the clinico-pathological pattern of bone metastasis (BM) among the solid tumor patients at National Institute of Cancer Research and Hospita(NICHR)l, Mohakhali, Dhaka.

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Methods: *It was a cross-sectional observational study conducted at the department of medical oncology of NICRH. Seventy seven clinically diagnosed cases of bone metastasis of solid tumor were included in the study.*

Results: *The mean age of the patients was 48.99 ±13.01 years. Leading age group was 51-60 years. BM was found among the patients without any gender predilection. Pain was the leading complaint made by more than half of the patients. Breast was the leading primary organ of bone metastasis among female. In male prostate and lung were the two leading primary organs of metastasis. Ductal cell carcinoma was the leading histological type of the solid tumors studied followed by adenocarcinoma. In patients age less than 50 years ductal carcinoma was predominant type (71%) and patients aged ≥60 years, adenocarcinoma was prevalent type. Bisphosphonates was mostly used in the treatment of metastasis as monotherapy or in combination with other treatment modalities like radiotherapy.*

Conclusion: *Risk of developing Skeletal-Related Events (SRE) in metastatic cancer patients is very high. SRE is directly related to quality of life of the each cancer patient. Each and every patient should be screened for these conditions and proper measures should be instituted timely.*

Key words: Bone metastasis, Solid tumor, Cancer patient

Introduction:

Cancers of breast, lung and prostate constitute 45% of all sites, and they are especially prone to metastasis to bone (Costa *et al.* 2008). A post mortem analysis of bone metastases revealed an incidence of 73 % in breast, 68% in prostate and 36 % in Lung cancers (Galasko 1981, Rubens 1998, Scarantino *et al.* 2001), also admit these findings. Other carcinomas like thyroid, kidney, and bladder also tend to metastasize to bone in the range of 30-40 %. Due to the improved facilities of cancer treatment hence the patients are living longer, which puts increased burden of metastasis disease (American cancer society 2005,

American Academy of orthopedic surgeons 2016, Hortobagyi *et al*. 1998).

Already having a malignant disease, patient is compromised in every aspect, moreover a weakening of the bone's structural integrity, leading to increased risk of Skeletal Related Events (SRE) such as severe bone pain, pathological fractures, Humoral Hypercalcaemia of Malignancy (HHM), Spinal Cord Compression (SCC), bone marrow suppression etc (Bagi 2005, Janjan 2001). This in turn causes considerable morbidity and adversely affects the patient's quality of life. At the same time, elimination of SREs improves the quality of life (Theriault 1991). Bone metastases are classified under 3 headings: 1) Osteolytic 2) Osteoblastic and 3) Mixed. Most of the breast cancer patients have lytic lesions although 15-20% has blastic lesions (Roodman 2004). Secondaries from prostate are often blastic and can have both type of lesions simultaneously. Only multiple myeloma gives exclusive lytic lesions (Coleman 2001). The metastases formation includes complex mechanisms which progress through a series of steps, which begins with the affinity of cancer cells to bone. This bone tropism moves through the homing, adhesion, proliferation and survival and a give and take type interaction starts within the matrix (Knerr 2004). A variety of factors like bone micro environment, adolescent growth spurt, disease states, hormones, medications, age, nutritional status influences the skeletal turn over. Metastasis can occur in any bone in the body but is most often found in bones near the center of the body. The spine is the most common site of bone metastasis (Knerr 2004, Abelof *et al*. 2008). It is estimated that over the 10% of patients with cancer will develop a symptomatic spinal metastasis (Harrington 1997). It was suggested that the initial anatomic location of metastases within vertebrae is in the posterior portion of the body. Analysis of CT scans shows that the body is involved before the pedicles, although destruction of the pedicles is the most common finding on plain films. Destruction of the pedicles occurs only in combination with the involvement of the vertebral body (Lipton 2005). Other common sites are the hip bone (pelvis), upper leg bone (femur), upper arm bone (humerus), ribs, and the skull (Harrington 1997). Studies showed that the thoracic spine is the region more involved with metastasis (Lipton 2005), while others

studies highlighted how the lumbar spine is more involved (Delea T., Langer C & McKiernan J 2004, Hillner 2001). The cervical spine is the least involved (10%) (Sundaresan *et al.*1991). More than 50% of patients with spinal metastasis have multiple levels involved, and 10 to 38% of patients have multiple, noncontiguous segments involved. Prognosis of metastatic bone cancer is influenced by primary tumor site, presence of extraosseous disease, and the extent and tempo of the bone disease. Disease progression is best estimated by a combination of imaging tests and measurement of bone-specific markers. Recent studies have shown a strong correlation between the rate of bone resorption and clinical outcome, both in terms of skeletal morbidity and disease progression or death. Improvements in understanding prognostic and predictive factors are expected to contribute to the delivery of more personalized treatment for individual patients and more cost-effective use of health care resources. Each and every patient of solid tumor should be screened for these conditions and proper measures should be instituted timely.

MATERIALS AND METHODS

It was a cross-sectional observational study. The study period was one year from July 2015 to June 2016.This study was carried out at National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka. All the clinically diagnosed case of bone metastasis of solid tumor, at the age of 18 and above, admitted in the Department of Oncology of NICRH were selected as study population. The sample size was diagnosed case of solid tumor. All the patients were recruited as per inclusion and exclusion criteria who used to come to NICRH for treatment. The relevant socio-demographic characteristics, clinical findings as well as the physical examination were performed. If the patient already had a histopathology or bone scan then these were recorded. If no histopathology or bone scan then the patients were sent for histopathology and /or bone scan. The routine investigation including serum calcium level and serum alkaline phosphatase level were recorded. If not available then patient were sent for the investigations and the results were recorded accordingly. The Inclusion criteria were age more than 18 years,

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Diagnosed bone metastasis of solid tumor, Patients was included irrespective of sex. And exclusion criteria were Patients with following characteristics were excluded from the study, Patients with severe handicap or psychological condition which would make an interview impossible, Unwilling to participate in the study. Purposive sampling technique was used. Patients were selected from the department of Medical Oncology on the basis of inclusion and exclusion criteria. A pre tested semi-structured questionnaire in Bangla was used for data collection. At first an English questionnaire was developed using the selected variables according to the study objectives. The questionnaire contained questions related to: 1) socio-demographic and 2) life style characteristics and other relevant information. After necessary correction and through checking the English questionnaire was translated into Bangla. Addition and omission was done according to advice. The questionnaire was then pretested on 4 respondents with similar types of background who were not included in the study sample. Then the questionnaire was finalized after necessary corrections. After taking verbal consent from the patients following introducing and informing the study purpose and objectives, data were collected by face to face interview ensuring privacy and confidentiality by using the questionnaire. All other required data were collected from history sheet and investigation papers.

RESULTS

This cross-sectional study was done to see the clinico-pathological pattern of bone metastasis among the solid tumor patients attending National Institute of Cancer Research & Hospital.

Seventy-seven patients were enrolled in the study. The findings derived from the data analysis are presented in this section.
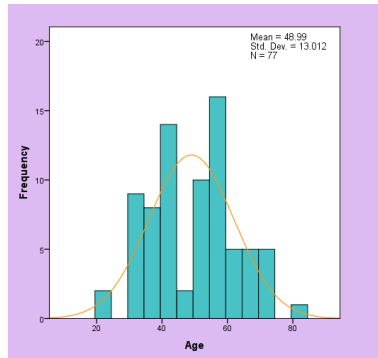
Figure 1: Age distribution of the patients

Figure 1 shows the age distribution of the patents. The mean age of the patients was 48.99 (±13.01). Leading age group was 51-60 years with 31.2% (24/77) representation. Equal numbers of patients (17) were from 31-40 years and 41-50 years age group. Around 18% (14/77) of the patients were >60 years old. Only six patients' age was 30 years or less.
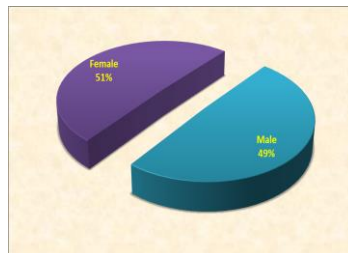

Figure 2: Distribution of the patients by gender

Figure 2 shows the sex distribution of the patents. Almost equal numbers of were from both sexes i.e. out of 77 patients 39 (51%) were female and 38 (49%) were male.

Table I: Distribution of the respondents by educational status

Level of education	Frequency	Percent
Illiterate	13	16.9
Primary	34	44.2
Secondary	24	31.2
Higher secondary	1	1.3
Graduate	5	6.5
Total	77	100.0

Table I shows the educational statuses of the two groups. About 17% (13/77) of the respondents had no education and about 44% (34/77) of the respondents had primary level education. A considerable number of patients (31.2%) had SSC level education. Only six patients had higher secondary or graduate level educational attainment.

Table II: Distribution of the respondents by occupation

Level of education	Frequency	Percent
Farmer	16	20.8
Service	13	16.9
Retired	06	7.8
Business	05	6.5
Student	02	2.6
Housewife	35	45.5
Total	77	100.0

Table II shows the occupational statuses of the patients. About one-fifth of the patients were farmers (16/77). For about 17% (13/77) patient service was the means of living. Five patients were business persons. Most of the female patients were housewives (35/39).

Table III: Distribution of the respondents by 'ABO' blood group

Blood group	Frequency	Percent
A	14	18.2
B	30	39.0
AB	4	5.2
O	29	37.7
Total	77	100.0

Table III shows the 'ABO' blood grouping of the patients. It was noted that blood group 'B' & 'O' were the most prevalent groups among the patients (39% & 37.7% respectively). Fourteen patients had blood group 'A' while only four patients had 'AB' blood grouping.
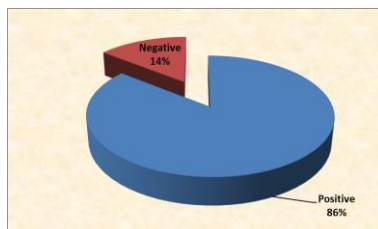

Figure 3: Distribution of the patients by Rh type

Figure 3 shows the distribution of the patents by Rh type. Most of the patients (66/77) exhibit positive Rhesus type while remaining 11 patients were Rhesus negative.

Table IV: Distribution of the respondents by chief complaint

Chief complaint	Frequency	Percent
Pain	45	58.4
Anorexia	11	14.3
Weight loss	8	10.4
Unable to walk	6	7.8
Others	7	9.1
Total	77	100.0

Table IV shows the chief complaints made by patients. Pain was the leading complaint made by more than 58% (45/77) patients. Eleven patients (14.3%) complained about anorexia while eight patients (10.4%) experienced weight loss.

Table V: Distribution of the respondents by histopathological type

Histopathological type	Frequency	Percent
Ductal cell carcinoma	31	40.3
Adenocarcinoma	25	32.5
Squamous cell carcinoma	10	13.0
Transitional cell carcinoma	11	14.3
Total	77	100.0

Table V shows the histopathological types of malignancy. Ductal cell carcinoma (31/77) was the leading histological type of the solid tumours studied. Second leading type was adenocarcinoma (25/77). Ten patients were diagnosed to have squamous cell carcinoma.
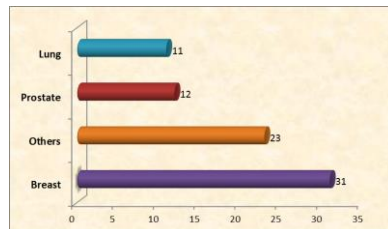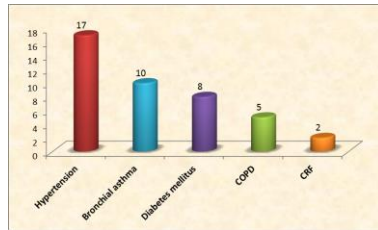

Figure 4: Distribution of the patients by organ involved

Figure 4 shows the distribution of the patents by organ involved through metastasis. Breast was the leading site of metastasis (31/39) among female. In male prostate and lung were the two leading organs for metastasis (12 & 11 respectively). In 23 patients various organs including thyroid, bones, brain etc. were involved.

COPD Chronic Obstructive Pulmonary Disease; CRF Chronic Renal Failure
Figure 5: Distribution of the patients by co-morbidity

Figure 5 shows the co-morbidity of the patients found during the data collection. Beside malignancy 17(22.1%) patients were suffering from hypertension. Ten patients (13%) had bronchial asthma and eight patients (10.4%) had diabetes mellitus. COPD and CRF were present in five and two patients respectively.

Table VI: Distribution of the respondents by type of treatment received

Treatment type	Frequency	Percent
Radiotherapy (RT)	1	1.3
Chemotherapy (CT)	12	15.6
Surgery (S)	16	20.8
RT+CT	9	11.7
CT+S	10	13.0
RT+CT +S	26	33.8
None	3	3.9
Total	77	100.0

Table VI shows the type of treatment received by the patients. Around 34% patients (26/77) received radiotherapy, chemotherapy and surgical treatment. Surgery was the single leading treatment modality (16/77) followed by chemotherapy (12/77). Ten patients received both surgery and chemotherapy. Three patients did not receive any treatment.
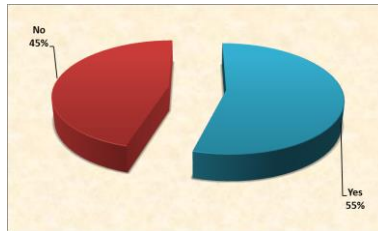
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Figure 6: Distribution of the patients by treatment status

Figure 6 depicts the treatment status of the patients. Majority of the patients (42/77) did complete their treatment of cancer while 45% (35/77) patients did not.

Table VII: Distribution of the respondents by family history of cancer

Family H/o cancer	Frequency	Percent
Father	2	15.4
Brother	5	38.5
Sister	1	7.7
Uncle	5	38.5
Total	13	100.0

Out of 77 patients 13 had family history of cancer. Eight patients (61.5%) had cancers in first degree relatives. Five patients (38.5%) had cancer in second degree relatives.

Table VIII: Distribution of the respondents by bone involvement

| Bone involved | Responses | | Percent of |
	Frequency	Percent	cases
Vertebra	66	50.8	85.7
Hip bone	25	19.2	32.5
Rib	24	18.5	31.2
Femur	4	3.1	5.2
Humerous	2	1.5	2.6
Other	9	6.9	11.7
Total	130	100.0	168.8[*]

[*] Multiple responses

Vertebra was the main bone involved with metastasis (85.7%). Hip bone was second leading site of bone metastasis (32.5%) followed by rib (31.2%). In more than 5% cases femur was the site of metastasis.
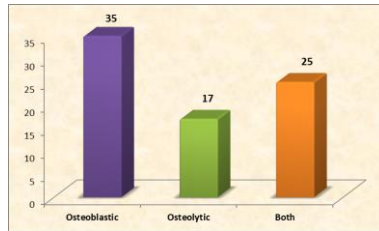
Figure 7: Distribution of the patients by type of metastatic lesion

Figure 7 shows the type of metastatic lesion. Majority of the patients (35/77) showed osteoblastic lesions. In about 22% (17/77) cases osteolytic lesion was found. However, 25 patients had both types of lesions.

Table IX: Distribution of the patients by other clinical features (n=57)

Other features	Frequency	Percent
Hypercalcaemia	40	70.2
Fracture	5	8.8
Spinal Cord compression	3	5.3
Hemiplegia	2	3.5
Others	7	12.3
Total	57	100.0

Hypercalcaemia was present in 40 (70.2%) patients which was most prevalent other features present in the solid tumour patients with metastasis. Five patients (8.8%) experienced pathological bone fractures. Life threatening spinal cord compression was found in three patients (5.3%) and hemiplegia was evident in two patients (3.5%).

Table X: Distribution of the patients by treatment of metastasis

Other features	Frequency	Percent
Bisphosphonates (B)	29	55.8
Radiotherapy (RT)	1	1.9
RT + B	18	34.6
RT+CT + B	2	3.8
RT+CT+B+S	2	3.8
Total	52	100.0

CT Chemotherapy; S Surgery

Bisphosphonates was mostly used (29/52) in the treatment of metastasis as monotherapy or in combination with other treatment modalities. In 18 patients (34.6%) bisphosphonates was used in

conjunction with radiotherapy and in two cases (3.8%) in with radiotherapy and chemotherapy. Two patients got all treatment modalities including surgery.

DISCUSSION:

This cross-sectional study was done to find the clinico-pathological pattern of bone metastasis among the solid tumor patients attending National Institute of Cancer Research &Hospital. The mean age of the patients was 48.99 ±13.01 years. Leading age group was 51-60 years with 31.2% representation. Equal numbers of patients (17) were from 31-40 years and 41-50 years age group. Around 18.0% of the patients were >60 years old. Only five patients' age was 30 years or less. There was no gender predilection for bone metastasis. Almost equal numbers of were from both sexes i.e. out of 77 patients 39 (51%) were female and 38 (49.35%) were male. It was noted that blood group 'B' & 'O' were the most prevalent groups among the patients (39% & 37.7% respectively). Fourteen patients had blood group 'A' while only four patients had 'AB' blood grouping. There was no relationship between any specific blood group or Rh factor and bone metastasis preference. Pain was the leading complaint made by more than 58.4% patients. Eleven patients (14.3%) complained about anorexia while eight patients (10.4%) experienced weight loss. Ductal cell carcinoma (31/77) was the leading histological type of the solid tumors studied. Second leading type was adenocarcinoma (25/77). Ten patients were diagnosed to have squamous cell carcinoma. In younger patients age less than 50 years DCC was predominant type (71%). In elderly patients (age ≥60 years) adenocarcinoma was prevalent type. This difference was statistically significant (Fishers Exact test=35.212; p=<0.001). Breast was the leading solid tumor for metastasis (31/39) among female. In male prostate and lung were the two leading solid tumor for metastasis (12 & 11 respectively). In 23 patients various organs including thyroid, renal, urinary bladder, melanoma etc. were involved. Out of 77 patients 13 had family history of cancer. Eight patients (61.5%) had cancers in first degree relatives. Five patients (38.5%) had cancer in second degree relatives.so, we could not rule out, is there any relationship between severity or frequency of BM and

family history of solid tumor. Vertebra was the main bone involved with metastasis (85.7%). Hip bone was second leading site of bone metastasis (32.5%) followed by rib (31.2%). In more than 5% cases femur was the site of metastasis. Majority of the patients (35/77) showed osteoblastic lesions. In about 22% cases osteolytic lesion was found.   However, 25 patients had both types of lesions. Hypercalcaemia was present in 70.2% patients which was most prevalent SRE's withother features present in the solid tumor patients with metastasis. Five patients (8.8%) experienced pathological bone fractures. Life threatening spinal cord compression was found in three patients (5.3%) and hemiplegia was evident in two patients (3.5%).

CONCLUSION:

The current study was conducted at the NICRH to assess the clinico-pathological pattern of bone metastasis (BM) among the solid tumor patients. BM was mainly found among the middle aged patients without any gender predilection. Pain was the leading complaint made by more than half of the patients. Breast was the leading type of solid tumor related to metastasis among female. In male prostate and lung were the two leading organs for metastasis. Ductal cell carcinoma was the leading histological type of the solid tumors studied followed by adenocarcinoma. . Vertebra was the main bone involved with metastasis (85.7%). Hypercalcaemia was present in 70.2% patients which was most prevalent SRE's with other features present in the solid tumor patients with metastasis.

Competing interest:
The authors declare that they have no competing interest.

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