

# Pattern of Distant Metastasis and Their Frequency in Metastatic Breast Cancer Patients Presented in a Tertiary Care Hospital

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## ABSTRACT

**Introduction:** Commonest reason of death from breast cancer (BC) is metastasis. The most common sites of metastasis are lung, liver, and bone as a solitary focus or may be in combination with tumor metastasis in more than one site. Detection of rare site of metastasis is now becoming possible due to advancement in imaging and prolongation of life with the new improved treatments. Purpose of the study is to see the various sites of metastasis and its frequency in our setup.

**Material and Methods:** It was a retrospective review of patients' data attending breast clinic of Liaquat National hospital from 1999 to 2018. Total 1495 patients of stage IV were reviewed.

**Results:** Most frequent solitary metastatic site of BC metastasis was bone 491(32.84%) followed by lung 356(23.81%), liver 242(16.19%) and brain 56(3.75%). Whereas, 331(22.14%) patients had more than one metastatic site involved (combination). Most frequent combination was bone and lung metastasis together 95(6.35%) then lung and liver combination 68(4.55%). Rare metastatic sites were witnessed in 19(1.27%) cases only.

**Conclusion:** Stage IV breast cancer is a poor prognostic factor which impacts on overall survival of patients. Knowledge about most common as well as rare anatomical site is helpful for clinician for early detection and decision making about treatment modalities to improve survival.

**Keywords:** *Distant metastasis, Solitary metastasis, Combined metastasis.*

## INTRODUCTION

Incidence of breast cancer is on the rise with approximately 1.7 million new cases worldwide yearly [1]. Early diagnosis and multidisciplinary treatment have reduced morbidity and mortality over the recent years [2]. Advancement in imaging modalities and effective screening programs has led to early diagnosis. However, 2.4-6% of the cases are still diagnosed at the Stage IV in initial presentation [3]. In the 3<sup>rd</sup> world delayed presentation of patients has more incidence of metastatic breast cancer. Distant metastasis leads to poor prognosis and high mortality. Bones, lungs, liver and brain are the commonest sites of metastasis from breast cancer[4]. Furthermore, the site of metastasis also influence the overall survival of the patient. Patients with bone and lung metastasis have relatively better survival as oppose to brain and liver involvement [5, 6].

Early imaging and targeted therapies have helped in improving the overall survival of the patients. However, it has been observed that metastasis to unusual sites is also on the rise. Knowledge of unusual metastasis sites is of paramount importance as it would help to detect new onset of symptoms in patients and also better staging of the patients.

More and more sites of breast cancer metastasis have been reported in literature. The definition of "unusual metastasis" is not universally accepted; however, it defines a systemic failure with a frequency of  $\leq 1\%$  at each site and according to this unusual metastasis involves the central nervous system, secretory/endocrine organs and glands, internal organs and structures, and gynecological organs [7]. The objective of the study is to know the various sites of distant metastasis both in common and rare unusual sites *i.e.* peritoneum, gastrointestinal tract, spleen, adrenal and spinal *etc.* and its frequency in our population and to compare it with international data.

## MATERIAL AND METHODS

From 1999 to 2018, patients who were initially diagnosed as stage-IV breast cancer according TNM classification were identified retrospectively from patients' electronic record and hospital data of breast clinic, Department of General Surgery, Liaquat National Hospital, Karachi.

All patients primarily diagnosed with breast cancer along with solitary or multiple distant metastatic sites including common and rare locations were included in the study. Recurrent breast cancer and previously treated breast cancer were excluded from the study. Most frequent solitary and multiple metastatic sites, combination (more than 1 distant site) were determined.

Data was entered into SPSS version 21 for data analysis. Metastatic sites were summarized in terms of frequency with percentage.

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## RESULTS

Records for total 1495 patients were reviewed. Most frequent metastatic site was bone 491(32.84%) followed by lung 356(23.81%), liver 242(16.19%) and brain 56(3.75%). 331(22.14%) patients had more than one site involved (combination). 19(1.27%) patients had metastasis to rare sites namely esophagus, colorectal, spleen, adrenal, skin and peritoneum (**Fig. 1**). Among combined metastatic sites, the most frequent combination was bone and lung 95(6.35%) and then liver with lungs 68(4.55%).

Out of 19 rare sites, adrenal metastasis was highest in frequency 6(31.58%) followed by peritoneal 3(15.79%), splenic 3(15.79%) colonic 2(10.53%). Skin, heart, renal, esophageal, and spinal cord metastasis were seen only in 1(5.26%) (**Fig. 2**).

## DISCUSSION

Breast cancer (BC) is a heterogeneous disease. Clinical presentation and treatment response are variables. Distant metastasis is a challenge in the war against breast cancer, as it is unpredictable in the beginning and it does have a significant direct clinical impact to the patient. The pathophysiology of tumor spread is still debatable.

Research has shown that breast cancer preferentially spreads to some organs and rarely in the other remote sites. Our focus of discussion is to see breast cancer distant metastatic pattern and frequency for both common and in rare sites and its comparison to international data. This will help physicians in detecting early symptoms corresponding to the metastatic site.

Early detection of metastatic sites with the appropriate treatment has an impact on the overall survival of the patient. Hence acquiring new knowledge of rare sites may benefit patients at large with stage IV disease.

Rao M-Y *et al.* showed in his study that different biological sub-types have pattern of metastasis. Bone metastasis has been reported as the most common metastatic site followed by lung, liver, and brain [8, 9] which was similar to our study. Previous studies have found brain and liver metastatic sites, found to be independent, unfavorable prognostic factors in breast cancer patients [10].

For rare sites breast cancer is one of the most common tumors to metastasize to the head and neck. It constitutes 15-20% of all metastases to this region and has been reported in almost every head and neck anatomical area [11]. Although, there were no such reported cases in our setting.

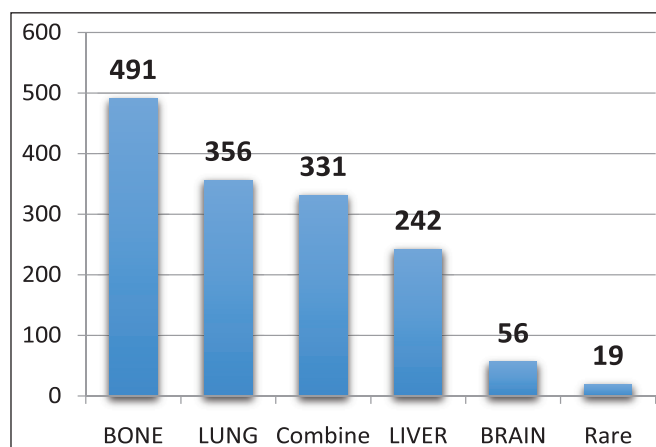
The prevalence of symptomatic central nervous system metastases among patients with breast cancer ranges from 5% to 16% [12], although autopsy studies have reported prevalence rates of up to 30%. The prevalence of spinal metastasis in our data was found as 5.26% which is comparable to the international data.

Gastrointestinal (GI) tract metastases from breast cancer are also considered rare. Their incidence in autopsy series varies from 8% to 35% [13]. It can involve any area of GI tract from oral cavity to anus [14]. Most common sites are stomach and colon. Lobular carcinoma has great tendency to spread to GI tract and peritoneum [15]. This finding is also consistent with our study which showed 21.05% of GI tumor in rare sites. Ovarian metastasis from breast cancer has an incidence of 13-47% with most likely cause of spread *via* lymphatics rather trans-coelomic [16]. Although we didn't find any ovarian metastasis, the incidence of peritoneal metastasis was 15.79%.

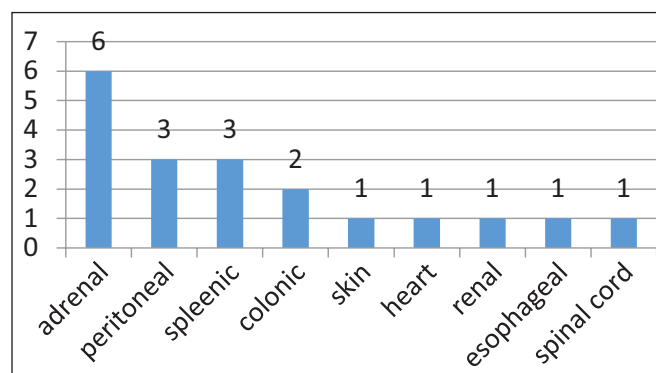
In our study, rare sites of metastasis included esophagus, stomach, pancreas, colon, adrenals, skin, spleen and heart. Interestingly none of the rare sites occurred in isolation but were in combination with the major sites.

## CONCLUSION

Early diagnosis of rare sites of metastatic breast cancer is a challenge. Better understating of the disease may help to improve the overall life expectancy of the patients.



**Fig. (1):** Frequency of metastatic sites among stage IV breast cancer patients.



**Fig. (2):** Break-up of rare metastatic sites.

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None.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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