

Original Research Article

Characteristics of metastatic lung cancer patients on osimertinib therapy in Bangladesh

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ABSTRACT

Background: Lung cancer is a major cause of mortality worldwide and metastasis plays a vital role in determining treatment and survival rate. Osimertinib showed significant success in the treatment of lung cancer, as evidenced by the literature, however, this outcome varies according to age, site of metastasis, etc. The objective of this study was to obtain demographic information on patients and assess the frequency of metastatic sites based on their age and sex.

Methods: This descriptive cross-sectional study included eighty metastatic lung cancer patients on osimertinib therapy attending a tertiary level health facility in Dhaka, Bangladesh. Data were obtained through reviewing their clinical reports.

Results: According to the findings, the patients' mean ($\pm$ SD) age was 60.95 $\pm$ 13.98 years. Patients who were between the ages of 55 and 75 had the highest rate of metastases. Under the age of 55, brain metastases (27%) were more common in both sexes (16.2%). While spinal metastasis was more frequent in female patients (8.1%), skin metastasis was more common in male patients (16.2%). Skin metastases were most frequently observed in patients aged 55 to 65 (10.8%), followed by those aged 25 to 45 (5.4%).

Conclusions: Mid-age male patients have been observed to have more cases of brain metastases and metastatic lung cancer. The findings are not conclusive due to the small sample size but suggest that the site of metastasis varied according to the patient's demographic characteristics. Further research on this topic is recommended to yield evidence for practitioners and policymakers.

Keywords: Lung cancer, Metastasis, Osimertinib, Patient characteristics

INTRODUCTION

Lung cancer was the main cause of cancer-related mortality in 2020, accounting for 1,796,144 fatalities (18%

of all cancer deaths) worldwide. Still, it was also the second most often diagnosed malignancy globally, with 2,206,771 new cases annually (11.6% of all cancer cases), according to the Global Cancer Observatory. According to

GLOBOCAN 2020, lung cancer ranks 2nd by mortality with an 8.8 age-standardized mortality rate and 9.5 age-standardized incidence rate in Bangladesh which is almost double that of India according to this report.¹ Non-small-cell lung cancer (NSCLC), which includes adenocarcinoma, squamous cell carcinoma, and large-cell lung cancer, accounts for approximately 85% of lung cancer cases. These malignancies are typically identified as locally progressed or metastatic.² Recent advancements in targeted antineoplastic drugs have changed cancer treatment and enhanced clinical results owing to a greater understanding of the pathophysiology and several oncogenic drivers associated with cancer, including non-small cell lung cancer (NSCLC).³⁻⁵ In several countries, osimertinib is approved to treat patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC that has progressed during or after EGFR TKI therapy. Osimertinib, a third-generation EGFR TKI, is an effective first-line treatment with a reasonable tolerability profile in patients with advanced NSCLC with EGFR TKI-activating mutations.⁶ In a double-blind, phase 3 trial, osimertinib demonstrated efficacy superior to that of standard EGFR-TKIs in the first-line treatment of EGFR mutation-positive advanced NSCLC with a similar safety profile and fewer incidences of major side events.⁷

Patient survival was reported to be influenced by factors such as performance status, comorbidity, and therapy responsiveness.^{8,9} In recent research, patient demographic variables such as gender and ethnicity have been connected to treatment outcomes and survival, primarily in the Western world.^{10,11} Despite substantial evidence from developed countries, data regarding characteristics of patients on osimertinib treatment is rare in resource-constrained countries such as Bangladesh.¹² Several factors, including histopathological variety, stage at diagnosis, and treatment modality, are linked with the prognosis and survival.¹³⁻¹⁵ Though osimertinib has been widely used recently in lung cancer patients, there's no baseline study regarding patient information in a documented way. Since most cancer registries do not include metastases, there is a dearth of population-based data on metastatic sites and survival in site-specific metastases for lung cancer and all cancers. This baseline study may contribute to determining the role of demographic characteristics and metastatic sites in the outcome of osimertinib therapy. Previous literature showed that age, sex, and sites of distant metastasis play significant roles in determining prognosis and treatment plans. In Bangladesh, the National Cancer Registry has not yet been established. As a result, this study may help to obtain information on patients with metastatic lung cancer, which may inform policymakers and physicians about recent lung cancer age and sex trends. Furthermore, therapeutic success with osimertinib and other EGFR TKIs is dependent on several parameters, including age and site of metastasis, and treatment outcomes vary accordingly. Other studies have shown that sex and age are associated with the place of metastasis, but there is a lack of verified evidence in this area. This study therefore determined the

demographic composition of the patients suffering from lung cancer and the frequency of metastatic sites according to age and sex of the patients.

METHODS

This descriptive cross-sectional study was carried out between July 2020 and June 2023 among 80 patients with metastatic lung cancer attended a tertiary specialized cancer hospital in Dhaka, Bangladesh. Patients, regardless of age or gender, taking osimertinib as monotherapy or in combination were purposefully enrolled in this study based on selection criteria. Data were collected through reviewing their clinical reports and then documented in a checklist. Demographic information (patient age and sex) and the sites of lung metastasis were identified, followed by the distribution of metastasis pattern based on age and sex. Privacy and confidentiality of the patients throughout the study including other ethical consideration. Descriptive analysis was performed to obtain study's objectives using SPSS statistical software.

RESULTS

Table 1 shows that the mean age of the patients was 60.95±13.98 years. Maximum of them were aged between 55 to 75 years though the frequency was maximum for 55 to 65 years (28.7%). The minimum age was found 25 years. In this study, the majority (63.7%) of patients were male according to the Table 1.

Table 1: Demographic information of the patients (n=80).

Attributes	Categories	Frequency (%)	Statistics
Age group in years	25-45	15 (18.8)	Mean age ± SD: 60.95±13.98 years Minimum age: 25 years Maximum age: 90 years
	45-55	11 (13.8)	
	55-65	23 (28.7)	
	65-75	22 (27.5)	
	75-85	7 (8.8)	
	85-95	2 (2.5)	
Sex	Male	51 (63.7)	
	Female	29 (36.3)	

Figure 1 shows a detailed age distribution pattern of the respondents on osimertinib therapy in a bar chart with a trend line. More frequencies were recorded in the 55 to 75 age range, but the highest frequencies were reported in the 65 and 70 age groups. The trend line of this bar chart shows a drop among patients over 75. Six of the responders were under 40 years old, and one was under 25. According to this data, four patients were 40 years of age.

Of the 80 respondents, 51 had no specific metastatic site mentioned in their prescriptions. Table 2 shows the results

of the analysis conducted on the remaining 37 respondents (n=37). Brain metastasis had the highest frequency (27%) followed by skin metastasis (21.6%). The submandibular lymph, left neck, supraclavicular nodes, and trachea had the lowest recorded frequencies (2.7% each).

Table 2: Distribution of the patients according to the site of metastasis of lung cancer (n=37).

Site of metastasis	Frequency (%)
Skin	8 (21.6)
Submandibular lymph nodes	1 (2.7)
Brain	10 (27.0)
Skeletal metastasis	3 (8.1)
Liver metastasis	3 (8.1)
Left neck nodes	1 (2.7)
Metastasis to spine	5 (13.5)
Metastasis to trachea	1 (2.7)
Mediastinal lymph nodes	4 (10.8)
Supraclavicular nodes	1 (2.7)

Table 3 shows that male patients had higher rates of brain (18.9%) and skin (16.2%) metastasis than other sites. Female patients had the highest frequencies of brain and spine (8.1% each), followed by skin and mediastinal lymph nodes (5.4% each). Females did not have metastases in the submandibular lymph nodes, left neck nodes, or trachea, but males had one in each of the mentioned sites.

Except for patients over 75, brain metastases were seen in nearly every age category, as seen in Table 4. The highest rate of brain metastases was observed in patients under the age of 55, with 8.1% in each group (16.2%). Patients aged 55 to 65 years had the highest rate of skin metastases (10.8%), followed by those aged 25 to 45 years (5.4%). According to the data, there were higher metastases in the trachea (2.7%), spinal (8.1%), skeletal (5.4%), submandibular (2.7%), and mediastinal lymph nodes (5.4%) among those aged 55 to 65. Further metastases were seen in the skin (5.4%), skeleton, and liver (2.7% each) in individuals aged 25 to 45. Again, the extreme age group (75-85 years) had 2.7% metastases in the skin, liver, left neck node, and spinal region.

Table 3: Distribution of metastatic sites according to the sex of the patients (n=37).

Metastatic site	Sex of the patients (%)	
	Male	Female
Skin	6 (16.2)	2 (5.4)
Submandibular lymph nodes	1 (2.7)	0 (0.0)
Brain	7 (18.9)	3 (8.1)
Skeletal metastasis	2 (5.4)	1 (2.7)
Liver metastasis	2 (5.4)	1 (2.7)
Left neck nodes	1 (2.7)	0 (0.0)
Metastasis to spine	2 (5.4)	3 (8.1)
Metastasis to trachea	1 (2.7)	0 (0.0)
Mediastinal lymph nodes	2 (5.4)	2 (5.4)
Supraclavicular nodes	1 (2.7)	0 (0.0)

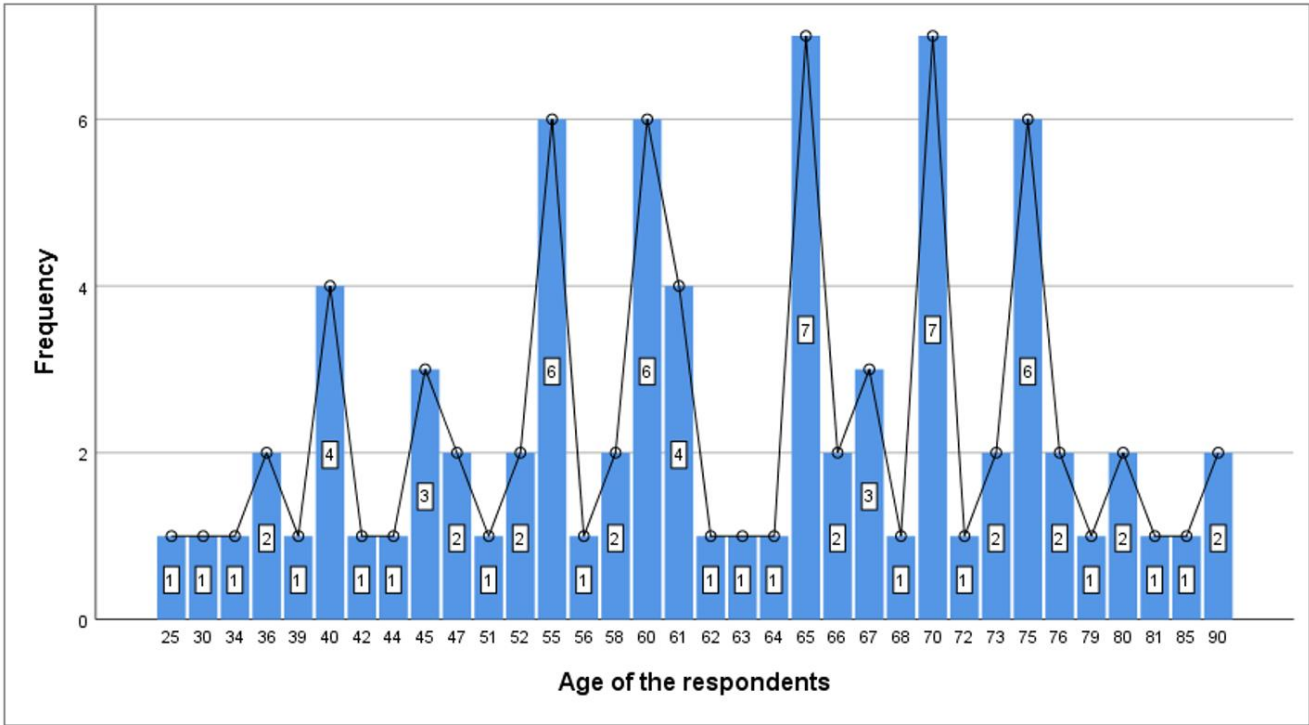


Figure 1: Age distribution pattern of the patients (n=80).

Table 4: Distribution of metastatic sites according to age groups of the patients (n=37).

Metastatic site	Age group of the patients (in years)				
	25-45	45-55	55-65	65-75	75-85
	N (%)	N (%)	N (%)	N (%)	N (%)
Skin	2 (5.4)	1 (2.7)	4 (10.8)	0 (0.0)	1 (2.7)
Submandibular lymph nodes	0 (0.0)	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)
Brain	3 (8.1)	3 (8.1)	2 (5.4)	2 (5.4)	0 (0.0)
Skeletal system	1 (2.7)	0 (0.0)	2 (5.4)	0 (0.0)	0 (0.0)
Liver	1 (2.7)	0 (0.0)	0 (0.0)	1 (2.7)	1 (2.7)
Left neck nodes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.7)
Spine	0 (0.0)	1 (2.7)	3 (8.1)	0 (0.0)	1 (2.7)
Trachea	0 (0.0)	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)
Mediastinal lymph nodes	0 (0.0)	1 (2.7)	2 (5.4)	1 (2.7)	0 (0.0)
Supraclavicular nodes	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.7)	0 (0.0)

DISCUSSION

The mean age of the respondents was 60.95 ± 13.98 years and male patients were more in number according to the findings of the current study. These findings match with a study conducted at the National Institute of Cancer Research & Hospital (NICRH), Bangladesh which found the mean age $\pm$ SD as 59.6 ± 10.9 years with significant male predominance and concluded age ≥ 70 years, having co-morbidity and receiving radiotherapy treatments only are significant predictors of poorer prognosis of lung cancer.¹⁶ Previous studies found that among single-organ metastases for lung cancer, adenocarcinoma and adenosquamous carcinoma had the highest percentages of bone metastases, while the brain was most frequent in large cell carcinoma and large cell neuroendocrine carcinoma.^{17,18} Though subtyping wasn't done in our study, however, brain metastasis was found to have the highest frequency as a site of metastasis. The site of metastasis is an important prognostic indicator for lung cancer patients' survival. Liver metastases conferred the worst prognosis followed by bone metastasis reported in a study compared with nervous system metastases.

In metastatic lung cancer, age at diagnosis and sex have an impact on survival and metastasis sites.¹⁹ A difference in the site of metastasis and the sex of the patients was observed in this study. In the following study, brain metastasis was found to be higher in both sexes however, for male patients the percentage was higher (18.9%) compared to female patients (8.1%). Again, female patients were reported to have a higher frequency of spinal metastasis in our study. According to previous literature, brain metastases occur in a third of all adult cancer cases and occur more frequently in males.²⁰ Although more research is advised, a prior study indicated that females typically experience more bone metastases.²¹ However, multiple studies concluded that lung cancer shows clear sex-related differences in disease progression.^{20,22,23} Aging is an important factor affecting the metastasis patterns.²¹ Age was found to be a key factor for distant metastasis patterns and prognosis specially in brain, lung, bone and

liver metastases of small-cell lung cancer. Bone, liver and lung metastasis were found in higher frequency in younger age groups.²⁴ The results of the current study, which show that brain metastasis was higher among patients under the age of 55 (16.2%) than in other groups, are consistent with this finding. A case of hepatic metastases was identified among the youngest age group.

In the treatment of brain metastasis in lung cancer, osimertinib is a widely practiced drug. According to a meta-analysis comprising 15 randomized controlled trials, it was shown that osimertinib appears to be the most successful and safest treatment for NSCLC patients with brain metastases containing EGFR-positive mutations, providing both the highest PFS and OS.²⁵ In another recent retrospective cohort study, the continuation of osimertinib with chemotherapy was associated with increased progression-free survival and overall survival compared to other chemotherapy approaches without osimertinib in advanced epidermal growth factor receptor (EGFR)-mutated non-small-cell lung cancer (NSCLC).²⁶ This finding was also supported by a recent double-blind, phase 3 trial that showed that osimertinib treatment efficacy was superior to that of standard EGFR-TKIs like gefitinib or erlotinib in the first-line treatment of EGFR mutation-positive advanced NSCLC.²⁷ Patients with CNS metastases benefit after osimertinib, however their PFS is lower.

This study has few limitations. Due to limitation of sample size, findings of the study can't be representable. It was a single centre study. Distribution may vary in other centre and cities. As data was collected by document review, due to non-uniformity of information, other socio-demographic characteristics couldn't be embodied.

CONCLUSION

This study assessed the characteristics of patients with metastatic lung cancer receiving osimertinib therapy. The mid-age group with a male preponderance had the highest frequency. Due to the limited sample size, the findings are

not definitive, but it was demonstrated that the site of metastasis varied according to the patient's age and sex. Extensive studies on this ground can be conducted to support the results for evidence generation. There is a lack of data in our country on the role of sex and age in distant metastasis of lung cancer, although both have a significant impact on prognosis, treatment response, and overall survival.

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