

Histopathological Patterns of Lung Cancer along with Clinico-Radiological Correlation in a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Lung cancer is the most common fatal neoplastic disease and the leading cause of cancer-related deaths worldwide. In Bangladesh, lung cancer has been on the rise, possibly due to an increase in smoking and air pollution. So, it is essential to understand the natural history of this disease.

Aim: This study aimed to find out the correlation between Clinico-radiological profiles with histopathological patterns of lung cancer in Bangladesh.

Material and Methods: A total of 100 confirmed cases of lung cancer were included in this cross-sectional observational study between January 1, 2021, to December 31, 2021. The complete socio-demographic characteristics, smoking status, previous history of COPD, details of radiological imaging findings, pathological characteristics of the tumor, and the performance status of patients were recorded in this study. Data were entered and analyzed using SPSS software.

Results: A total of 100 (86 male, and 14 female) confirmed lung cancer patients were included in our study with a mean \pm SD age of 59.57 ± 10.41 years. Cough (87%), breathlessness (61%), and chest pain (58%) were the most common symptom and mass lesions (83%) followed by collapse (8%) was the most common radiological presentation. Among the histopathological types adenocarcinoma (48%) was the most common type followed by squamous cell carcinoma (35%). Correlation showed that mass lesion was the most common radiological finding in both adenocarcinoma and squamous cell carcinoma. ECOG performance status 2, and status 3 were about 36% and 35% respectively. Multivariate logistic regression analysis shows male gender with COPD independently had a 1.681-fold risk of developing lung cancer.

Conclusion: The Clinico-histopathological pattern of lung cancer has changed recently. The incidence of adenocarcinoma is increasing, and becoming the most common cause in both smokers and non-smokers.

Keywords: Lung cancer, Clinico-radiological profile, ECOG, Bangladesh.



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Introduction

Lung cancer had become one of the leading causes of preventable death worldwide at the end of the 20th century. Increasing lifespan along with exposure to etiological agents have made this once a rare disease a very serious health problem. It is the leading cause of cancer death (18.0% of the total cancer deaths) and the second most commonly diagnosed cancer in both sexes worldwide.¹

In Bangladesh, a new study suggests that lung cancer cases have been on the rise, experts attributing this to an increase in smoking and air pollution. According to the latest Hospital

Cancer Registry Study, there is a reportedly near 200% rise in the country's lung cancer cases in just three years. A total of 5,887 people with lung cancer were admitted to the National Institute of Cancer Research and Hospital (NICRH) from January 2015 to December 2017. In 2014, the figure was 1983, which indicates a nearly 200% rise in cases in just three years.²

Lung cancer is caused by mutations, causes abnormal proliferation of the mutated cells, and the formation of a tumor. Previously, lung cancer was broadly classified into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The availability of newer histology-guided targeted molecular therapies for lung cancer has made this classification inadequate. So, histopathological and genomic characterization of lung cancer has now become the topic of interest.³ Targeted therapy or immunotherapy is mainly based on subtype analysis for mutation. Another changing trend has been observed in the morphological variety, with adenocarcinoma becoming equal to or even overtaking squamous cell carcinoma sometimes in some Asian and most Western countries.⁴

A great majority of cases are directly linked to smoking. About one-third of patients present with symptoms resulting from loco-regional growth of the tumor as well as hematogenous and lymphatic spread and para-neoplastic manifestations. In others, bronchial carcinoma is diagnosed by radiology done for unrelated health problems followed by histopathology.

This study aimed to evaluate the histopathological patterns of lung cancer in relation to Clinico-radiological features.

Material and Methods

This was a cross-sectional observational study. Patients with histopathologically confirmed lung cancer in the Department of Respiratory Medicine of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh between January 1, 2021, and December 31, 2021, were included. Patients who had lung metastasis from a non-pulmonary primary tumor, lymphoproliferative disorder, and the patient already received treatment for lung cancer were excluded from this study. Prior approval was taken from Institutional Review Board (IRB).

Complete sociodemographic characteristics, smoking status, previous history of COPD, radiological, and histopathological characteristics of the tumor were recorded in the study. The performance status of patients was documented using the Eastern Cooperative Oncology Group scale (ECOG). CT scan of the chest was done in the majority of the patient. CT-guided or fibre-optic bronchoscopic guided tissue sampling from lung lesions followed by histopathological examination was done to diagnose the appropriate tumor type.

Results

A total of 100 histopathologically confirmed diagnosed patients with lung cancer in the Department of Respiratory Medicine between January 1 to December 31, 2021, were included in this study, which comprises 86 males and 14 females. There were 35% and 34% of patients who belonged to age between 51-60year and 60-70year respectively. The average age of the study population was 59.57years. Out of 100 patients, 80 patients were smokers, 44 patients had a prior history of COPD, and lymphadenopathy was present in 10 patients. While evaluating ECOG performance status 36% of patients remained on scale 2, followed by 35% on scale 3 (Table 1). When we look for clinical symptoms, cough (87%), breathlessness (61%), chest pain (58%) followed by hemoptysis, sputum production, voice change, and superior vena cava obstruction. Radiological examination shows mass lesion was the most common finding (83%) followed by collapse (8%) and pleural effusion (6%) (Table 2).

Table 1. Demographic and baseline characteristics of the study subjects (n=100)

Characteristic	Total (n=100) (%)
Sex	
Male	86 (86.0)
Female	14 (14.0)
Age(years)	
≤40	6 (6.0)
41-50	14 (14.0)
51-60	35 (35.0)
61-70	34 (34.0)
>70	11 (11.0)
Mean ± SD	59.57 ± 10.41
Smoking status	
Never smoker	20 (20.0)
Current smoker	80 (80.0)
COPD	
No	56 (56.0%)
Yes	44 (44.0)
Lymphadenopathy	
No	90 (90.0)
Yes	10 (10.0)
ECOG	
1	4 (4.0)
2	36 (36)
3	35 (35.0)
4	16 (16.0)
5	9 (9.0)

COPD: Chronic Obstructive Pulmonary Disease; ECOG: Eastern Cooperative Oncology Group

Non-small cell carcinoma was diagnosed in 84% of patients while 16% of patients had small cell carcinoma. The most common histopathological type found in adenocarcinoma (48%) followed by squamous cell carcinoma (35%) (Figure 1). Both smoker and nonsmoker adenocarcinoma was the predominant lung cancer 46.3% and 55% respectively. Adenocarcinoma was the most histopathological type in non-COPD (53.6%) patients, and adenocarcinoma and squamous cell carcinoma were equal (40.9%) in COPD patients (Table 3 and Figure 2). Correlation of histopathological types with radiological findings showed that mass lesion was the major finding in both adenocarcinoma and squamous cell carcinoma 44.6% and 37.3% respectively. Pleural effusion was about half of the patients with adenocarcinoma, 37.3% in small cell carcinoma, and 16.7% in small cell carcinoma. Lymphadenopathy was only present in adenocarcinoma (Table 4 and figure 3). Multivariate logistic regression analysis shows male gender with COPD independently had a 1.681-fold risk of developing lung cancer, OR: 5.369(CI: 1.040-27.727; p-0.045) (Table 5).

Table 2: Distribution of the study subjects according to clinical findings (n=100)

Symptoms	Total (n=100) (%)
Cough	87 (87.0)
Breathlessness	61 (61.0)
SVO	6 (6.0)
Voice change	14 (14.0)
Sputum	37 (37.0)
Hemoptysis	38 (38.0)
Chest pain	58 (58.0)
Radiological presentation	
Pleural effusion	6 (6.0)
Mass lesion	83 (83.0)
Collapse	8 (8.0)
Lymphadenopathy	3 (3.0)

SVO: Superior vena caval obstruction.

Table 3. Histopathological diagnosis of the study subjects among smokers, non-smokers, COPD and Non-COPD:

Histopathological type	Total (n=100) (%)	Smoker (80%)	Non-smoker (20%)	COPD (44%)	Non-COPD (56%)
Small cell carcinoma	16	14 (17.5)	2 (10.0)	7 (15.9)	9 (16.1)
Squamous cell carcinoma	35	28 (35.0)	7 (35.0)	18 (40.9)	17 (30.4)
Adenocarcinoma	48	37 (46.3)	11 (55.0)	18 (40.9)	30 (53.6)
Undifferentiated carcinoma	1	1 (1.3)	0 (0.0)	1 (2.3)	0 (0.0)

Chi-Square test was done

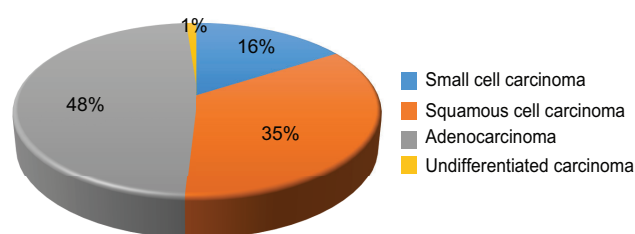


Figure 1: Distribution of lung cancer patients by histopathological type

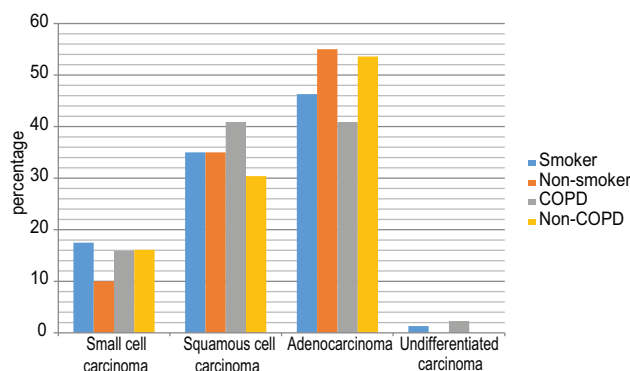


Figure 2: Distribution of lung cancer patients among smokers, non-smokers, COPD, and non-COPD

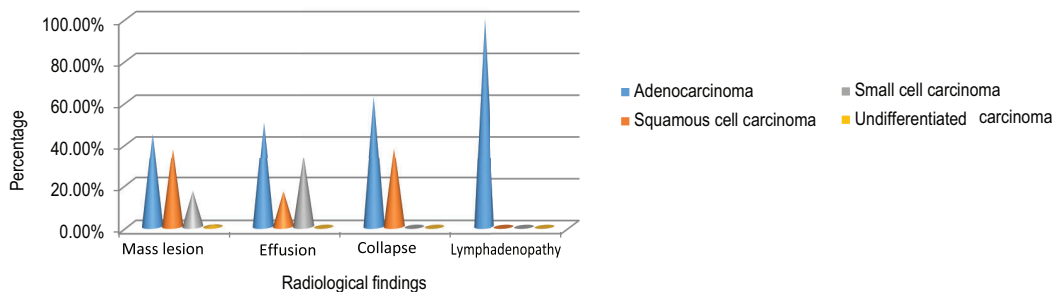


Figure 3: Correlation of radiological findings with the histopathological type of lung cancer

Table 4: Association of histopathological diagnosis with CXR/CECT findings (n=100)

Histopathological diagnosis	CXR/CECT findings			
	Effusion(n=6)	Mass(n=83)	Collapse(n=8)	LN(n=3)
Small cell carcinoma	2 (33.3)	14 (16.9)	0 (0.0)	0 (0.0)
Squamous cell carcinoma	1 (16.7)	31 (37.3)	3 (37.5)	0 (0.0)
Adenocarcinoma	3 (50.0)	37 (44.6)	5 (62.5)	3 (100.0)
Undifferentiated carcinoma	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)

Table 5: Factors associated with COPD and Lung cancer among study subjects; results from multivariate analysis

	B	SE	p-value	OR	95% CI OR	
					Lower	Upper
Age	0.039	0.022	0.077	1.040	0.996	1.086
Gender (Male)	1.681	0.838	0.045	5.369	1.040	27.727
Smoking status	-0.604	0.604	0.317	0.546	0.167	1.786

Discussion

Lung cancer is a serious health problem and the leading cause of cancer-related deaths worldwide. This reflects disparities in demographic variables, socioeconomic status, and geographic variations. That’s why it is very much required to correlate epidemiology and clinicopathological profile for a better understanding of tumor biology, prevention, and control.

Primary lung cancer cases in Bangladesh have been on the rise. There is an almost 200% rise in the country’s lung cancer cases within just 3 years.² Despite the increasing trend in our country and worldwide, histopathological data is scant in our region. Keeping this in mind, we tried to highlight the demographic profile, frequency, and histopathological features of lung cancer in 100 cases.

Age is one of the most important factors determining the risk of cancer. In our study, the age ranged from 31 to 88 years, with a mean age of 59.57 years. This showed that lung cancer is relatively a disease of older age. The age group in our study is similar to previous studies.^{4,5,6} Studying the age range in our work shows that the highest incidence of lung cancer was in the 6th and 7th decade of life with 69% of cases found in these two decades of life which is similar to the study.⁷ As life expectancy is increasing, increase the risk of cancer with aging.⁸ Similarly, the male predominance in our study is similar to observations done previously.^{9,10} It can be explained by the fact that in Bangladesh, females have a lower prevalence of smoking. There have been many studies done in various parts of the world showing a

relationship between smoking and lung cancer. The smoking habit as revealed from our study shows that the number of smokers (80%) is 4-fold that of non-smokers (20%). The risk of lung cancer development is 20-40 times higher in lifelong smokers compared to non-smokers.¹¹ The risk for the development of lung cancer increased with the duration of smoking and the number of cigarettes smoked per day. Average smoking in males had an approximately 9- fold to 10-fold risk for lung cancer, whereas heavy smokers had at least a 20-fold risk.¹² In our study, smoking can be connected with all types of histologic varieties of lung cancer. This relation was most evident between adenocarcinoma and squamous cell carcinoma. This finding is different, as adenocarcinoma was thought to be the most common subtype less related to smoking. But from our study, it was also observed that adenocarcinoma was the most common subtype amongst the non-smokers (55%).

In our study, adenocarcinoma surpassed squamous cell carcinoma. This is similar to the observations^{13, 14, 15} but is contrary to most Indian studies. Mohan et al.⁴ observed this very well in their 10-year trend in lung cancer (2008-2018) and reported that in the initial year squamous cell carcinoma dominated, but was overtaken by adenocarcinoma in 2012, and this trend remained like this till 2018. They also gave a probable explanation for this shift and attributed this partly to the changed smoking pattern (inhaling smoke more vigorously so that it goes to the periphery of the lung, where adenocarcinoma is the commonest) and the increasing incidence of lung cancer cases among female and non-smokers. There may be ethnic differences which can also be

a contributory factor. Behera et al stated that small cell carcinoma is the predominant cell type weakly associated with smoking up to 40 years of age. After 40 years, squamous cell carcinoma predominates in smokers and adenocarcinoma in non-smokers.¹⁶

In our study cough was found as the most common symptom (87%), followed by shortness of breath (61%), chest pain (58%), hemoptysis (31%), and others. According to Aki et al.⁷ and Rawat et al.¹⁷ cough was the most common symptom. Cough receptors were stimulated by an intraluminal tumor, particularly if it is in the trachea or a mainstream bronchus. Obstruction of airflow produces the sensation of dyspnea. Extra-luminal compression of a large airway more frequently causes dyspnea without cough. Obstruction of the airway may cause post-obstructive pneumonia, which may have been associated with cough.¹⁸ 44% of the study subjects had a prior history of COPD in our study. Distribution of histopathological type according to COPD revealed that 30 patients (53.6%) who had no prior history of COPD developed adenocarcinoma, while 18 of them (40.9%) were having COPD. Squamous cell carcinoma was found almost equally in both COPD and non- COPD patients in 18 and 17 cases, respectively. No statistically significant association was found between histologic subtype and smoking or COPD.

The radiological findings showed that the commonest picture was mass lesion (83%), followed by collapse (8%), pleural effusion (6%), and hilar lymphadenopathy (3%). A similar observation regarding finding out mass lesions was made by Aki et al.⁷ and Rawat et al.¹⁷ Distribution of histopathological type according to radiological findings showed that pleural effusion was most commonly detected in adenocarcinoma, followed by small cell carcinoma. Sarfraz et al.⁵ also noted that adenocarcinoma was most commonly associated with pleural effusion. The presence of mass lesion was noted in 37 cases (44.6%) of adenocarcinoma, followed by 31 cases (37.3%) of squamous cell carcinoma. The collapse was observed in adenocarcinoma and squamous cell carcinoma only. The mass lesion was the major radiological finding in our study.

The majority of study subjects had not a reasonably good performance status at the time of diagnosis, 36% remained on scale 2, followed by 35% on scale 3. The prevalence of poor performance status in lung cancer was higher overall in a study done by Lilenbaum et al.¹⁹ and Wakelee et al.²⁰ but this is contrary to the finding of Mohan et al.⁴ This might be because most patients seek medical care when they already their disease got advanced.

In our study multivariate logistic regression analysis shows male gender with COPD independently risk of developing

lung cancer is more, [OR: 5.369 (95% CI: 1.040-27.727; p-0.045)]. COPD and lung cancer are major worldwide health problems, that occur mainly due to cigarette smoking. Lung cancer is about five times more common in smokers with airflow obstruction than with normal lung function. The high prevalence of lung cancer in COPD patients may be due to premature aging in the lungs, genetic predispositions, Oxidative stress that cause DNA damage, and inflammation which leads to numerous cytokine release associated with the development of lung cancer.²¹

Conclusion

Our study appears to be following the current trend in the world with increasing new cases of adenocarcinoma both in smokers and non-smokers. The highest incidence of cancer was found in the sixth and seventh decades. Males still predominated. Smoking remains the major risk factor in aetiopathogenesis. In all subtypes, the mass lesion was the major radiological finding.

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