

# Clinical, Radiological and Histological profile of Primary Lung Carcinomas

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## Abstract

The present prospective study was conducted on 170 patients of lung carcinoma, over a period of two years, to study the clinical features, radiological manifestations and histological types of primary lung carcinoma. These were investigated according to a study protocol which included a detailed history regarding the onset and progress of the disease, smoking habits, detailed examination of the respiratory system, routine laboratory investigations, chest roentgenogram, computed tomography of thorax, fiberoptic bronchoscopy and others. The mean age of the patients was 55.94 years (range 29 to 85 years). Eighty seven percent were males. The smoker to non-smoker ratio was 3.9:1. The average duration of symptoms was three months. Cough was the most common presenting symptom (90%). A history of anti-tubercular treatment was present in 42.5% patients. A mass lesion was the most common radiological finding (30.6%), followed by collapse consolidation in 13.5%. Combination presentation was observed in 43.5% patients. Squamous cell carcinoma presented more commonly as a central mass (75%), while adenocarcinoma as peripheral mass lesion (64.5%). Squamous cell carcinoma was the most common histological type diagnosed (45.3%) although adenocarcinoma was the more common in females (39.1%) and non-smokers (51.4%). In India Squamous cell carcinoma is still the most common cell type. Carcinoma lung is still being misdiagnosed as tuberculosis and many patients are wrongly put on antitubercular treatment. Thus there is a need to create awareness about carcinoma lung among the general practitioners.

## Key Words

Lung cancer, Radiographic patterns, Histologic types

## Introduction

Lung cancer is one of the commonest cancers and cause of cancer related deaths all over the world. It accounts for 13% of all new cancer cases and 19 % of cancer related deaths worldwide. (1).

About 85% to 90% of patients with lung cancer have had direct exposure to tobacco. The strongest associations are with small cell and squamous cell carcinomas (2). An estimated 2% to 9% of lung cancers are related to occupational exposures. An inherited genetic predisposition has epidemiologic support as a risk factor (3). Differences in the metabolism of tobacco-related carcinogens and their metabolites or an effect of hormone differences are believed to account for the increased susceptibility (4). Pathologic features, visible on light

microscopy, are used to categorize lung cancers. Lung cancers are divided into two major groups, small cell and non-small cell. The clinical manifestations of lung cancer result from the effects of local growth of the tumor, regional growth or spread through the lymphatic system, hematogenous distant metastatic spread and remote paraneoplastic effects from tumor products or immune cross-reaction with tumor antigens (5). Approximately 85% of patients with lung cancer are symptomatic at presentation. In the remainder, lung cancer is detected by radiographic evaluation initiated for an unrelated problem. (6) The present study explored the clinico-radiographic spectrum of lung cancer in relation to its various pathological subtypes.

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## Material and Methods

The present, prospective study was conducted over a period of two years on patients, with a high clinical or radiological suspicion of lung malignancy, referred to GMC, Jammu. Of these, 170 patients diagnosed with lung malignancy were included in the study. The study protocol included a detailed history regarding the onset and progress of the disease and smoking habits and other associated risk factors. The clinical symptoms were recorded. The patient was thoroughly examined with a detailed reference to the general physical examination pertaining to the respiratory diseases and emaciation along with a detailed examination of the respiratory system. Besides routine laboratory investigations all the patients were subjected to chest roentgenogram, postero-anterior (PA) and lateral view. Radiographs were evaluated based on number, location, distribution and other characteristics of the lesions including details of calcification, cavitation, satellite lesions and involvement of adjacent structures if any. In patients who showed clinical and radiological evidence of pleural effusion, fluid was aspirated and sent for cytopathological examination. Transthoracic needle aspiration of lung mass was done in patients who had a peripheral lung mass or a central growth big enough to be approached by a percutaneous needle. The slides thus prepared were fixed in 95% alcohol and transported to the laboratory for staining and cytopathological examination.

Computed tomography (CT) Thorax (SIEMENS Somatom Balance Spiral) was done in 153 patients to confirm the diagnosis and stage the tumor. FNAC was needed in 43 patients to establish the diagnosis. Following radiographic evaluation 98 patients who were having a central tumor radiologically, underwent fiberoptic bronchoscopy, using single channel bronchoscope (Olympus BF type 2). Mucosal brushings were obtained with a protected brush from the area surrounding the endobronchial lesion and suspected abnormal segments (on radiological basis) in case of patients without endobronchial involvement. Bronchial aspirate was also obtained. Endobronchial biopsy was obtained in patients with endobronchial lesions. Transbronchial needle aspiration was performed in patients with no endobronchial involvement. If indicated, patients were subjected to percutaneous lymph node aspiration cytology and biopsy and pleural biopsy to establish a diagnosis. The specimens were subjected to laboratory procedures by preparing paraffin blocks. After processing 3-5 micron thick sections were cut and stained with H&E. The

histological typing was based on the WHO classification of lung tumors (7).

## Results

Initially, a total of 180 patients were selected for the present open prospective study. Diagnosis proved to be other than bronchogenic carcinoma in 10 patients and these patients were excluded from the study group. Thus, the study group comprised of 170 patients.

The mean age of the patients was 55.94 (range 29 to 85 years) years. Only 18 (10.6%) cases were below the age of 40 years, youngest being 30 years old. Majority of the cases 138 (81.2%) were between 41 to 70 years. Out of 170 cases, 147 (86.5%) were males and 23 (13.5%) were females. One hundred and thirty-five (79.4%) were smokers. The smoker to non-smoker ratio was 3.9:1 (*Table 1 & 2*). Amongst smokers, the average number of pack-years was 25. Smoking of 20 pack-years and more showed a significant increase in incidence of squamous cell carcinoma ( $p < 0.05$ ) over the other cell types. The average duration of symptoms was 3 months. Cough was the most common presenting symptom and was present in 153 (90%) of cases. Seventy-two (42.4%) out of 170 patients of the study group had a history of anti-tubercular treatment. Clubbing was present in 34 (20%), while hypertrophic pulmonary osteoarthropathy was seen only in 5 (2.9%) patients. All these five patients were later diagnosed as having squamous cell carcinoma. Signs suggestive of superior vena caval (SVC) obstruction were present in 24 (14.1%) cases while 3 (1.7%) had Horner's syndrome. Out of the 24 patients having SVC syndrome, 12 (50%) were later found to have small cell carcinoma while 6 each had squamous cell and adenocarcinoma. Evidence of metastasis to supraclavicular/cervical lymph nodes was present in 51 (30%) cases. Six (3.5%) patients each had the presence of subcutaneous nodules and hepatomegaly. Gynaecomastia was present in 3 (1.7%) cases while 2 (1.1%) had deep vein thrombosis (*Table 3*). A mass lesion was the most common radiological finding (30.6%), followed by collapse consolidation in 13.5%. Combination presentation was observed in 43.5% cases. Twenty-one (12.4%) cases had pleural effusion, most of them having adenocarcinoma. A solitary pulmonary nodule was found in 7 (4.1%) cases. Pancoast tumour was diagnosed in 9 cases all of whom were later found to have squamous cell carcinoma (*Table 4*). CT thorax was done in 153 patients. Out of these, mass lesion was detected in 148 (96.7%). Mediastinal lymphadenopathy was detected in 121 (79.1%) cases and in 27 of these it was bilateral. A

**Table 1. Distribution of Patients According to Smoking Habits**

Group	Males	Females	Total
	Number (%)	Number (%)	Number (%)
Smoker	126 (85.7)	9 (39.1)	135 (79.4)
Non-smoker	21 (14.3)	14 (60.9)	35 (20.6)
Total	147 (100.0)	23 (100.0)	170 (100.0)

**Table 2. Level of Smoking in Pack-Years**

Pack-years	Number of patients (%)
>40	19/135 (14.1)
>20	116/135 (85.9)
Non smoker	35 (20.6)

solitary pulmonary nodule was seen in 5 (3.3%) cases. Local infiltration of the mass to aorta, oesophagus and pleura was present in 15 (9.8%) cases. Bony erosion of ribs and/or vertebra was detected in 55 (35.9%) cases while metastasis to opposite lung was found in seven cases. The features detected on CT thorax are shown in Table 5. Fibreoptic bronchoscopy was done in 98 (57.6%) cases. Intrabronchial growth was visible in 60 (61.2%) cases. Extrabronchial compression was present in 25 (25.5%) cases. Squamous cell carcinoma was found to be the most common type of carcinoma lung and was found in 77 (45.3%) cases, followed by adenocarcinoma which was present in 60 (35.3%) cases. The most common cell type amongst smokers was squamous cell carcinoma (54%), followed by adenocarcinoma (31.7%). Amongst non-smokers (35 patients) the most common pathological diagnosis was adenocarcinoma (51.4%) (Table 6). Majority (60%) of the cases had involvement of right side. Upper zone was involved in 43 (25.3%) cases, mid zone in 55 (32.4%), lower zone in 24 (14.1%) and entire lung in 19 (11.2%) cases. Squamous cell carcinoma presented more commonly as a central tumor with or without lung collapse (75% cases), while adenocarcinoma presented more commonly as peripheral mass lesion (64.5% cases). Pleural effusion was seen in 21 (12.4%) cases of which 13 had adenocarcinoma. Calcification of the lesion was seen in seven cases, five of whom had squamous cell and two small cell lung cancer. Cavitating lesion was present in 10 cases, 70% of them had squamous cell carcinoma. Metastasis involving the ribs was seen in 20 cases most of whom had squamous cell carcinoma. The radiological findings in the various histologic types of lung cancer are shown in Table 4.

**Discussion**

Lung cancer is now the leading cause of cancer mortality(8). The mean age of carcinoma lung patients in the present study was 55.94 years. This showed that

carcinoma lung is the disease of the older age. In the study of Wagner *et al.* (9), the age ranged between 37 to 82 years which is comparable to the age group in the present study. The average age of the carcinoma lung patients in the present study is also comparable to some of the major Indian studies (10-12). The sex ratio reported

**Table 3. Clinical Features (n=170)**

Clinical features	No. of cases (%)
Cough	153 (90.0)
Loss of appetite and weight loss	136 (80.0)
Expectoration	135 (79.4)
Non-specific constitutional symptoms	127 (74.7)
Chest pain / Discomfort	115 (67.6)
Shortness of breath	93 (54.7)
Fever	72 (42.3)
Lymphadenopathy	51 (30)
Haemoptysis	48 (28.2)
Hoarseness of voice	42 (24.7)
Neurological signs	25 (14.7)
SVC syndrome	24 (14.1)
Bone pain	20 (11.7)
Puffiness of face	16 (9.4)
Asymptomatic	6 (3.5)
Subcutaneous nodules	6 (3.5)
HPOA	5 (2.9)
Dysphagia	3 (1.7)
Horner's syndrome	3 (1.7)
Gynaecomastia	3 (1.7)
Deep Vein Thrombosis (DVT)	2 (1.1)

in various Indian studies ranged from 4.5:1 to 8.2:1 (12-15). In a study from USA the male: female ratio was 5:1 (16). The sex ratio in our study was 6.5:1 with a clear male preponderance. This could be explained because of still lower incidence of female smokers in India as compared to that in the West. In our study, 85.7% males were smokers and only 14.3% were non-smokers. This is comparable with the WHO 1986 survey in which 92-94% lung cancer deaths were attributed to tobacco smoking in males. The smoker to non-smoker ratio in our study was 3.9:1 which is comparable with the study of Gupta *et al.*, (13) and Rawat *et al.* (15). Cough was the most common symptom and was present in 90% patients in the present study. This is similar to other studies from India and abroad (12, 13, 15, 17, 18, 19, 20).Haemoptysis has been reported to be present in 11% to 24% carcinoma lung patients in various studies (11, 15, 17). Pandhi *et al.*

**Table 4. Radiological Findings in the Various Histologic Types of Lung Cancer Patients**

	Squamous cell carcinoma No. (%)	Adenocarcinoma No. (%)	Small cell carcinoma No. (%)	Others No. (%)	Total No. (%)
No. of patients	76 (44.7)	62 (36.5)	18 (10.6)	14 (8.2)	170 (100.0)
<b>Site of Tumor</b>					
Right lung	51 (67.1)	33 (53.2)	12 (66.7)	6 (42.9)	102 (60.0)
Left lung	22 (29.0)	24 (38.7)	4 (22.2)	8 (57.1)	58 (34.1)
Bilateral	3 (3.9)	5 (8.1)	2 (11.1)	-	10 (5.9)
<b>Location</b>					
Central	57 (75.0)	15 (24.2)	9 (50.0)	5 (35.7)	86 (50.6)
Peripheral	12 (15.8)	40 (64.5)	3 (16.7)	2 (14.3)	57 (33.5)
Central + Peripheral	7 (9.2)	7 (11.3)	6 (33.3)	7 (50.0)	27 (15.9)
Upper zone	30 (39.5)	11 (17.7)	2 (11.1)	0 (0)	43 (25.3)
Mid zone	33 (43.4)	15 (24.2)	4 (22.2)	3 (21.4)	55 (32.4)
Lower zone	3 (4.0)	12 (19.4)	6 (33.3)	3 (21.4)	24 (14.1)
Entire lung	2 (2.6)	11 (17.7)	3 (16.7)	3 (21.4)	19 (11.2)
Other / combinations	8 (10.5)	13 (21.0)	3 (16.7)	5 (35.8)	29 (17.0)
<b>Lesions</b>					
Collapse	16 (21.0)	4 (6.5)	3 (16.7)	-	23 (13.5)
Mass	12 (15.8)	25 (40.3)	9 (50.0)	6 (42.9)	52 (30.6)
Pleural effusion	5 (6.6)	13 (21.0)	-	3 (21.4)	21 (12.4)
Combinations	43 (56.6)	20 (32.3)	6 (33.3)	5 (35.7)	74 (43.5)
<b>Special features</b>					
Cavitation	10 (13.1)	3 (4.8)	-	2 (14.3)	15 (8.8)
Calcification	5 (6.6)	-	-	2 (14.3)	7 (4.1)
Rib involvement	12 (15.8)	6 (9.7)	2 (11.1)	-	20 (11.8)
Satellite lesions	10 (13.1)	14 (22.6)	6 (33.3)	-	30 (17.6)

**Table 5. CT Finding of the Patient (n=153)**

CT findings	No. of cases (%)
Mass	148 (96.7)
Lymphadenopathy	121 (79.1)
Collapse	62 (40.5)
Rib/Vertebral Involvement	55 (35.9)
Effusion	36 (23.5)
Consolidation	33 (21.6)
Diaphragmatism palsy	30 (19.6)
Bilateral	27 (17.6)
Cavitation	24 (15.7)
Local soft infiltration	15 (9.8)
Pericardial effusion	10 (6.5)
Calcification	9 (5.9)
SPN	5 (3.3)
<b>Metastasis:</b>	
Ipsilateral Lung	22 (14.4)
Opposite/Bilateral	7 (4.6)
Liver	38 (24.8)
Adrenal	16 (10.4)

(11), Jindal and Behera (12) and Patel *et al.* (20) have reported a higher percentage of haemoptysis in their studies (50%, 69.2% and 35-50% respectively). In the present study haemoptysis was present in 28.2% patients. Hoarseness of voice has been reported as a fairly common symptom of lung cancer. Jindal & Behera (12) and Chhajed *et al.* (19) reported it to be present in 29.9% and 21% respectively. In the present study 24.7% patients

complained of hoarseness of voice. Bronchogenic carcinoma is one of the most common causes of SVC syndrome and is most commonly reported with small cell carcinoma with incidence ranging between 7 to 17% in various published studies (12, 13, 17-19). The incidence of SVC syndrome in the present study was 14.1% with small cell carcinoma the most common cause.

Bronchogenic carcinoma especially squamous cell type is one of the most common respiratory causes of clubbing (12, 17, 19, 20). In the present study the incidence of clubbing was 20.3%. Paraneoplastic syndromes have been reported in a large number of cases of carcinoma lung especially of the small cell type but in this study only three cases of gynecomastia were observed. One important observation that, 43% of the cases in our study were misdiagnosed as tuberculosis and treated at various other centers, thereby causing a delay in the diagnosis and time of presentation. This emphasizes the need for more effective methods for early detection of lung cancer and to increase the awareness among general practitioners. Rawat *et al.* (15) also reported delay in presentation of patients to their attending physician. Majority of the cases were misdiagnosed as tuberculosis and treated at various other centers, thereby causing a delay in seeking treatment which varied from 4-6 months. Radiographic analysis in patients with lung cancer in various published

**Table 6. Histologic Types According to Sex and Smoking Habits**

Histologic type	Males		Females		Total No. (%)
	Smokers No. (%)	Non-smokers No. (%)	Smokers No. (%)	Non-smokers No. (%)	
Squamous cell carcinoma	68 (54.0)	5 (23.8)	4 (44.4)	0 (0)	77 (45.3)
Adenocarcinoma	40 (31.7)	11 (52.4)	2 (22.2)	7 (50.0)	60 (35.3)
Small cell carcinoma	10 (7.9)	3 (14.3)	2 (22.2)	3 (21.4)	18 (10.6)
Large cell carcinoma	3 (2.4)	2 (9.5)	1 (11.1)	2 (14.3)	8 (4.7)
Undifferentiated carcinoma	3 (2.4)	0 (0)	0 (0)	0 (0)	3 (1.8)
Adenocarcinoma carcinoma	2 (1.6)	0 (0)	0 (0)	2 (14.3)	4 (2.3)
<b>Total</b>	<b>126</b>	<b>21</b>	<b>9</b>	<b>14</b>	<b>170</b>

studies has revealed a preponderance of right lung involvement with upper lobe especially anterior segment described as the commonest site of involvement (21, 22). This was noticed in the present study also. It is well known that squamous cell carcinoma presents mostly as a central tumour. In this study 75% of squamous cell carcinoma patients had central lesion. In Mayo clinic study about 53% of the patients with squamous cell carcinoma had central tumours (20). Adenocarcinoma most commonly manifests as peripheral mass or a malignant pleural effusion. In this study only 24.2% had central lesion while about 64.5% had peripheral lesion. This again is in concordance with most reports published from elsewhere. Rawat *et al.* (15) in their study observed that adenocarcinoma commonly manifested as peripheral mass or a malignant pleural effusion. Swett *et al.* (23) reported that greater than 50% of the patients of adenocarcinoma presented as peripheral mass. Thus the statement that "adenocarcinoma usually develops in the periphery" (21) is again confirmed by the results from this study. In this study small cell lung cancer presented most commonly as central masses, which is similar to both Mayo clinic (20) and Marshfield studies (25) where 77% and 78% patients with this histological subtype presented with central masses as well as in major Indian studies by Gupta *et al.* (13) and Sharma *et al.* (22) where 94.9% and 83.6% small cell carcinoma patients presented with central masses. Rawat *et al.* (15) also observed that small cell lung cancer presented commonly as central lesion.

Cavitation is seen most commonly in squamous cell cancers (22). Carr *et al.* (26) found over two-third of radiographs showing cavitating lung malignancy had squamous cell lung cancer. In the present study too, 66.7% of cavitating lesions were of squamous cell subtype. Sharma *et al.* (22) in their study on 373 lung cancer patients also found that 66% of cavitating lung malignancy was of squamous cell type.

Patients showing calcification of lesions, rib involvement as well as those having Pancoast's tumour, more commonly had squamous cell carcinoma.

Involvement of ipsilateral hemidiaphragm or cardiac enlargement/pericardial effusion was more commonly seen with small cell carcinoma. This is similar to reports published in the literature (21). Computed tomography of the chest and upper abdomen has already been shown to be an important tool in the diagnosis and staging of lung cancer (27, 28). In our study the computed tomography of chest and upper abdomen (including adrenals) was done in 153 patients. In this group, chest roentgenogram diagnosed rib or vertebral involvement in 20 patients as compared to 55 patients diagnosed by computed tomography. The reported incidence of adrenal metastasis diagnosed by computed tomography is 10-15 per cent (21). Sharma *et al.* (22) found metastasis involving ribs in 7.2% patients, most of whom had squamous cell carcinoma. In our study computed tomography diagnosed adrenal metastasis in 10.4% patients and was most commonly seen in adenocarcinoma (54.5%). Moreover computed tomography of chest diagnosed significant mediastinal lymphadenopathy in 121 patients which was not evident on chest roentgenogram. Chhajed *et al.* (19) reported mediastinal lymphadenopathy in about 34% patients and liver metastasis in 23% cases.

The pattern of lung cancer has been changing in the West. Lung cancer is being increasingly diagnosed in women, and adenocarcinoma has overtaken squamous cell carcinoma as the commonest histological type (25). In Indian studies, however, the pattern is different with squamous cell carcinoma still being the most common histologic subtype (7, 12, 13, 14, 29). In our study also squamous cell carcinoma was found to be the commonest histological subtype (45.3%) followed by adenocarcinoma (35.3%). There could be several reasons for this difference in cell patterns between the Western and Indian studies. Firstly, smoking is less prevalent among women in India, as opposed to the West, where it is rising. Secondly, socio-cultural considerations may have modified the pattern

and there may be ethnic/racial differences in disease pattern, which seems to resemble the distribution seen in the West in 1950s and 1960s (22). The cell type pattern also varies with smoking habits, age and sex (30). Upto 40 years of age, small cell carcinoma predominates and has a weaker association with smoking. After the age of 40 years, squamous cell type is the commonest type in smokers and adenocarcinoma in non-smokers (31).

### Conclusion

The study points towards a need to create an awareness about carcinoma lung, its presenting features, risk factors and radiological pattern among the general practitioners for an early detection of lung cancer.

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