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Original Article

Clinical and Radiological Profile of Lung Cancer – Data from Southwestern Part of India

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Abstract

Background: Lung cancer is one of the most common cancers and causes of cancer-related deaths worldwide. The disease shows varied epidemiological, clinico-radiological, and pathological profile. With the changing trends of chronic benign lung conditions and better diagnostic modalities available for detection and staging of lung cancer, especially with the advent of metabolic imaging, the current clinico-radiological profile in a tertiary care center was analyzed.

Aims and Objectives: The aim of the study was to study the clinico-radiological profile of lung cancer patients in a tertiary care center in Southwestern part of India.

Materials and Methods: This is a prospective descriptive study done between November 2016 and November 2017. A total of 125 of histopathologically proven primary lung cancer patients were enrolled and analyzed. Their history, demographic profiles, clinical details, histopathological, and radiological findings were obtained and analyzed using SPSS software.

Results: A total of 125 patients were analyzed in our study. The mean ± SD of the age of cases studied in the study group was 58.1 ± 12.1 years with an overall male predominance with male/female ratio of 1.84:1. A total of 66 patients (52.8%) were smokers (active) with an average duration of smoking being 24.5 pack years. Cough (82.4%) and dyspnea (76.8%) were the most common symptom while pallor (56.8%) and clubbing (39.2%) were the most common physical findings. Mass lesion (80%) was the most common radiological presentation. Adenocarcinoma (72.8%) was the most common histopathological type followed by squamous cell carcinoma (20.8%). Most common site of metastasis was bones (52.8%) followed by metastasis to adrenals (20.8%) and liver (19.2%). Nodal upstaging after positron emission tomography (PET) scan was demonstrated in 32% of the patients.

Conclusion: Carcinoma lung remains one of the most prevalent causes of cancer-related mortality in the world. Smoking continues to be an important risk factor for the development of carcinoma lung with cough still being the most common clinical presentation. The radiologically mass lesion is the most common presentation. ^{18}Flurodeoxyglucose-PET imaging has emerged as an inescapable modality to be used in evaluation and staging in patients of primary lung cancer.

Key words: Lung cancer, PET-CT, FDG, Adenocarcinoma

INTRODUCTION

Lung cancer is the most common cancer in the world since 1985.[1] Since then, it remains the leading cause of cancer-related mortality in the developed world and its incidence is rising in developing countries. Lung cancer accounts for 11.6% of all new cancer cases diagnosed per year and is becoming the most common fatal neoplastic condition in the world today, accounting for 18.4% deaths related to all cancer-related mortality in the world.[2] Approximately 85% of patients with lung cancer are symptomatic at presentation with symptoms usually appearing at the fairly advanced and non-curable stage of the disease. The early symptoms of the lung (persistent cough, chest pain, and shortness of breath) are similar to other lung problems such as an infection or long-term effects of smoking and thus the diagnosis is often delayed. Now with the changing prevalence of various chronic infections better diagnostic

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modalities for early detection of neoplastic processes including high-resolution imaging and metabolic imaging positron emission tomography (PET), this study was done to explore the present day clinico-radiological profile of lung cancer cases reporting to tertiary care center in Southwestern part of India.

MATERIALS AND METHODS

The cross-sectional descriptive study was conducted over 1 year period from November 2016 to October 2017. A total of 145 consecutive cases of histopathologically proven primary lung carcinoma (all types) were included in the study. A total of 10 patients could not undergo all requisite evaluations required for study and hence were not included for further analysis and 5 patients were lost to follow-up. Thus, finally 125 primary lung cancer cases were included in the study. Patients with secondary lung cancer, lymphoproliferative, and granulomatous disease of the lung and with any other malignancy were excluded from this study. These patients were analyzed for their clinical presentation, exposure to risk factors, histopathological type, stage at presentation, and sites of metastasis. A written informed consent was obtained from the study participants fulfilling the inclusion criteria. Study was cleared by the Institutional Ethical Committee.

Histopathological diagnosis was based on endobronchial/Computed tomography (CT)-guided biopsy or needle aspiration cytology. The suitable mode was used as per tumor location and performance status of the patient. For staging, conventional imaging (including CT Thorax, ultrasonography [USG] abdomen, and magnetic resonance imaging [MRI] Brain [wherever applicable]) and whole-body PET-CT imaging was done. Patients were staged in tumor-node-metastasis (TNM) classification (8th edition) according to tumor size, nodal spread, and sites of metastasis. CT scan was performed with Siemens Somatom Emotion 16 slice using following parameters –250 mAs, 120 kV, pitch 1, 1.2 mm slice thickness, single breath hold, 1 ml/kg iodinated contrast IV at a rate of 2.5 ml/s and imaging after 30 s of injection. PET-CT imaging was done with GE Discovery 690 VCT Std. Radiopharmaceutical used was ^{18}flurodeoxyglucose (^{18}FDG) in the doses of 6–10 mci. The scan was performed head to mid-thigh after 45 min of FDG injection. The integrated CT was done with standard protocol – non-contrast, 120 kv, 200 mAs, and 3.75 mm slice thickness.

Chi-square test was used for intergroup statistical comparison of the distribution of categorical variables. The statistical agreement between two diagnostic methods was tested using Cohen kappa technique. All the results are shown in tabular as well as a graphical format to visualize the statistically significant difference more clearly. $P < 0.05$ was considered to be statistically significant. All the hypotheses were formulated using two-tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data were statistically analyzed using Statistical Package for the Social Sciences (SPSS version 21.0, IBM Corporation, USA) MS Windows.

RESULTS

A total of 125 confirmed lung cancer cases were available for clinico-radiological analysis. The demographic profile of the patients is as shown in Table 1. The mean ± SD of the age of cases studied in the study group was 58.1 ± 12.1 years, and the age range was 29–90 years. There was an overall male predominance with a male/female ratio of 1.84:1. Out of the total population, 66 patients (52.8%) were smokers (active) with an average duration of smoking being 24.5 pack years. 35 patients out of 125 patients had exposure to indoor pollution in the form of chulha use at home for cooking. 11 (8.80%) patients had exposure to passive smoke with a history of at least one family member smoking at home. The eastern cooperative oncology group (ECOG) functional status is depicted in Table 1.

Clinical profile of the patient analyzed in the study is as shown in Figures 1 and 2. Cough (82.4%, 103 out of 125) was the most common complaint followed by dyspnea (76.8%, 96 out of 125) and weight loss (60.8%, 76 out of 125). At presentation, 56.8% (71 out of 125) patients had pallor and 39.2% (49 out of 125) had clubbing while lymphadenopathy was present in 27.2% (34 out of 125) patients.

The most predominant histopathological subtypes were adenocarcinoma 72.8% (91 out of 125) and squamous cell

Table 1: Demographic profile of patients

Patient's characteristics	Total patients (*n*=125) (%)
Gender	
Male	81 (64.8)
Female	44 (35.2)
Age (in years)	
<50	25 (20.0)
50–70	78 (62.4)
>70	22 (17.6)
Smoking status	
Smoker	66 (52.8)
Non-smoker	59 (47.2)
Mean duration of smoking (in pack-years)	24.5
ECOG status	
0–2	82 (65.8)
3–4	43 (34.2)

ECOG: Eastern cooperative oncology group

carcinoma 20.8% (26 out of 125) followed by small cell lung carcinoma and undifferentiated carcinoma [Figure 3].

The various patterns of radiological presentation as demonstrated on Chest X-ray and PET-CT scan are depicted in Figure 4. On Chest X-ray, 64.8% (81 out of 125) patients were detected with a mass lesion, while 33.6% (42 out of 125) had pleural effusion and 14.4% (18 out of 125) had nodular opacities. Other presentations included cavitation, consolidation, and collapse. On CT scan imaging, 80% (100 out of 125) patients had a mass lesion which was followed by 60.0% (75 out of 125) patients being detected with lymphadenopathy and pleural effusion was present in 41.6% (52 out of 125) patients. Whole-body PET CT scan revealed mass lesion in 80% (100 out of 125) patients, lymphadenopathy in 81.6% (102 out of 125), and pleural effusion in 40.8% (51 out of 125) patients, followed by nodular opacities, cavitation, and consolidation.

Sites of extrathoracic metastatic deposits are shown in Table 2. A most common site was bones (52.8%, 66 out of 125) followed by metastasis to adrenals (20.8%, 26 out of 125) and liver (19.2%, 24 out of 125). Other sites of extrathoracic metastatic deposits were brain, spleen, and kidneys. Figures 5 and 6 show image of PET scan of patients with skeletal and liver metastasis, respectively.

The distribution of nodal stage by CT was significantly associated with nodal stage by PET CT ($P < 0.001$). However, nodal upstaging was seen in 40 (32%) patients after PET scan as demonstrated in Table 3. Figure 7 shows PET-CT showing metabolically active subcarinal lymph node, not detected positive on conventional imaging. Change in TNM staging was seen in 68 (54.4%) of patients after PET scan. The distribution of TNM staging by conventional imaging was significantly associated with TNM staging by PET CT ($P < 0.001$).

Table 2: Sites of extrathoracic metastasis

Sites of metastasis	*n* (%)
Skeletal (bone)	66 (52.8)
Adrenals	26 (20.8)
Liver	24 (19.2)
Brain	18 (14.4)
Kidney	1 (0.8)
Spleen	1 (0.8)

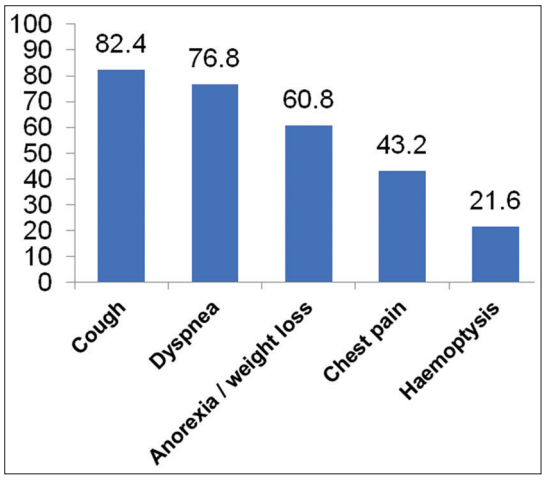

Figure 1: Clinical presentation

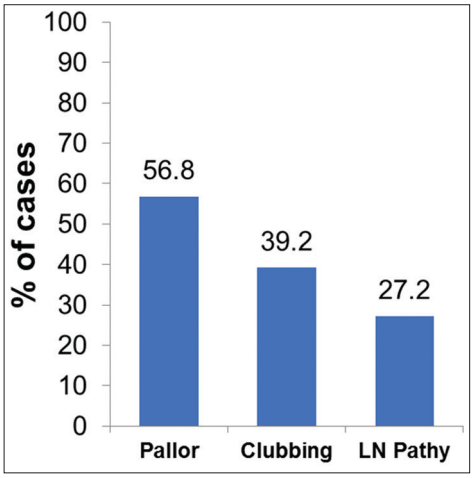

Figure 2: Physical findings

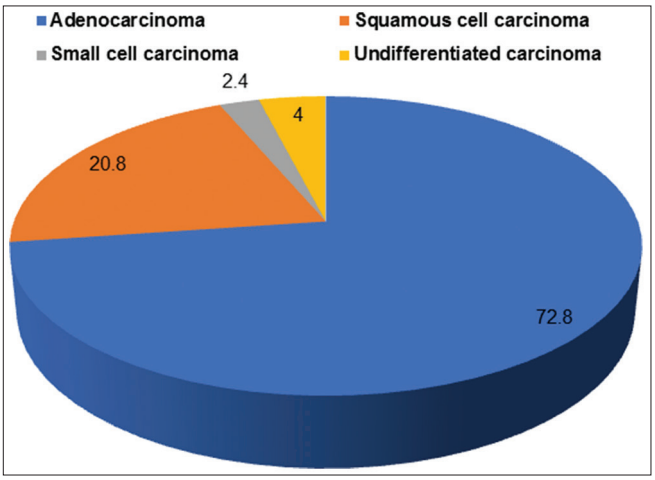

Figure 3: Histological distribution of cases

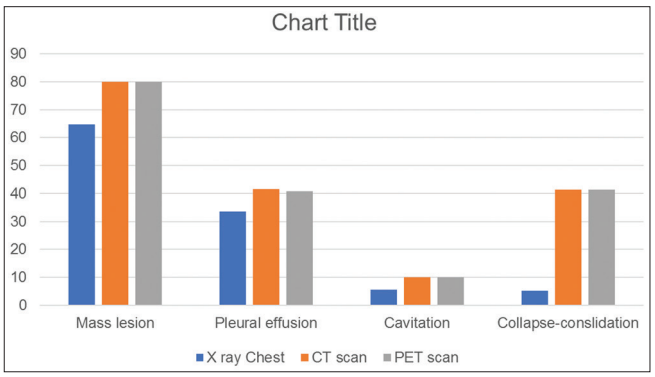

Figure 4: Radiological manifestations

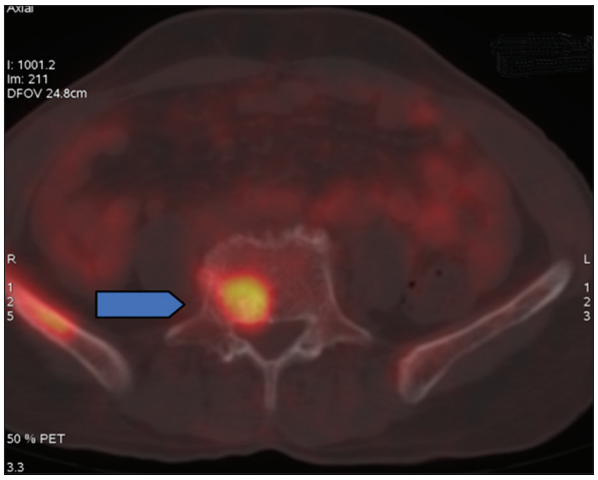

Figure 5: Positron emission tomography-computed tomography showing skeletal metastasis to lumbar vertebral body

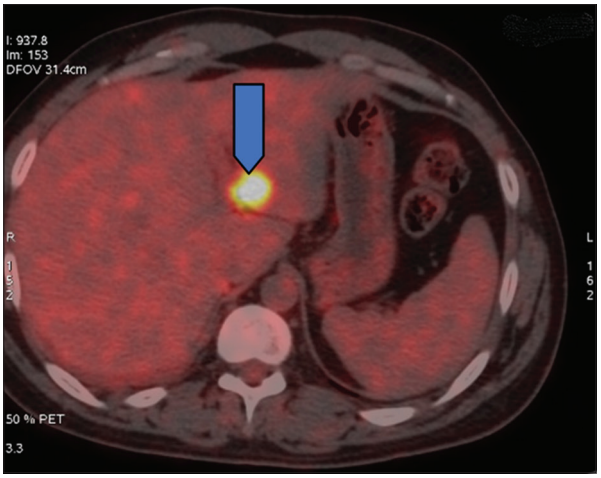

Figure 6: Positron emission tomography-computed tomography shows metabolically acive lesion in the left lobe -liver metastasis

Table 3: Change of nodal staging after PET-CT scan

Nodal stage on CT scan	Nodal stage on PET-CT scan	Change of staging
N0–28	N0–07 N1–04 N2–12 N3-05	Upgraded: 21
N1–28	N1–15 N2–12 N3 – 01	Upgraded: 13
N2–67	N2–61 N3–06	Upgraded: 06
N3–02	N3–02	Upgraded: 00
Total–125	Total–125	Total upgraded on PET-CT=40 (32%)

PET-CT: Positron emission tomography-computed tomography

DISCUSSION

Carcinoma lung remains the leading cause of cancer-related mortality in the developed world and its incidence is rising in developing countries. The epidemiology and clinic-radiological spectrum of lung cancer are changing all over the world from the late 1940s to the current time especially with the changing prevalence of chronic lung conditions and availability of better diagnostic modalities. The present study had explored the clinical and radiological profile in patients of primary lung cancer in patients presenting to our center.

Mean age at presentation was 58.1 years. Majority of the patients (62.4%) were in the age group of 51–70 years while only 10.4% of patients were younger than 40 years. Mean age of our patients is comparable to the studies done on clinical profile in lung cancer patients in other countries.[3,4] Most of the previous studies in India have reported similar mean age.[5-9]

Out of 125 cases of primary lung cancer studied, 81 (64.8%) were males and 44 (35.2%) were females. The male to female ratio in our study is 1.84:1. In a retrospective audit conducted by Maasdorp *et al.* in 2011 in South Africa where the clinical profile of lung cancer patients was analyzed, male to female ratio was reported as 3:1.[4] Most of the Indian literature has also reported higher male to female ratio.[6,7,9]

Among risk factors, smoking was the most common risk factor in which cigarette was used by most of the patients followed by bidi and hookah. Of the total patients, 66 out of 125, 52.8% had a history of active smoking. Among smokers, the average number of pack-years was 24.5. Among all the smokers in the study 93.6% were males. The smoker to non-smoker ratio was 1.12:1. In other Indian studies, the range of this ratio varies from 1.7:1 to 3.9: 1.[7,9] This could be explained by the high percentage of females in the study and less prevalence of smoking among the female population.

Cough was the most common presenting symptom and was present in 103 out of 125 (82.4%) patients who were included in the study, followed by dyspnea (76.8%), anorexia and weight loss (60.8%), and chest pain (42.8%). The most frequently observed physical signs were pallor (56.8%) followed by clubbing (39.2%) and clinical lymphadenopathy (27.2%). Other Indian and western studies have shown similar clinical presentation.[3,6-9]

In our study, we found adenocarcinoma to be the most common histological subtype, accounting for 72.8% of all lung cancer cases. Squamous cell carcinoma accounted for 20.8%. Over the past few years, there has been a shift of histological profile toward adenocarcinoma. This shift might be partly due to smoking habits, particularly filtered cigarettes and also there is also an increasing incidence of lung cancer in females and non-smokers.[10] Table 4 demonstrates histological subtypes reported in various studies conducted in India and western countries.[3,4,6,9,11]

Most of the patients (111 out of 125, 88.8%), in our study, had metastatic disease (Stage IV) at the time of presentation. Bony (Skeletal) metastasis was detected in 52.8%, 66 out of 125 patients, followed by metastasis to adrenals (20.8%), liver (19.2%), and brain (14.4%). Dey *et al.* in his study of 607 lung cancer patients conducted in two tertiary hospitals of the eastern part of India in 2012, reported liver as the most common site of metastasis in patients of lung carcinoma.[6] Various other Indian and Western studies had shown bony (skeletal) metastasis as the most common site followed by liver and adrenals.[3,9,12] Table 5 demonstrates a comparison between the various studies.

Radiologically, the mass was the most common lesion of primary lung cancer (100 out of 125, 80%) followed by pleural effusion (51 out of 125, 40.8%), followed by nodular opacities, cavitation, and consolidation. In a prospective study conducted by Alamoudi where140 patients were analyzed, lung mass was the most common radiological finding followed by pleural effusion.[3] Most of the previous Indian studies as demonstrated in Table 6 have reported similar frequency of radiological presentations.[3,6,7,9]

Out of total of 125 patients analyzed in our study, 93.6% (117 out of 125) presented at advanced stage (Stages III B and IV) as diagnosed on PET-CT imaging. In a retrospective analysis published in 2017, Rai *et al.* reported 93.3% of cases presenting in advanced stages (Stages III B and IV).[7] However, western literature shows <50% of patients presenting at advanced stages and diagnosis of the patients at early stages.[4,13-15] This could be explained by better awareness of disease symptoms among people in western countries and better cancer screening strategies.

In our study, we analyzed change of stage after PET-CT scan in comparison to staging by conventional imaging. Out of 125 patients studied, 54.4% of patients had a change of stage after whole-body PET-CT imaging. Hicks *et al.* in their prospective analysis of 153 patients of primary lung cancer in 2001 reported 43% change in staging after PET-CT scan as compared with conventional imaging.[16] In the preoperative analysis of 102 patients of non-small cell lung carcinoma by Peiterman *et al.* 62% patients had change in staging after PET scan compared to conventional imaging.[17] Table 7 demonstrates various studies in western literature having reported a similar difference in staging with use of PET-CT imaging in cases of primary lung cancer.[15-18]

Change in overall staging of the patients was related to the detection of unexpected distant metastatic lesions by PET imaging mainly as compared to conventional imaging. Conventional imaging methods used for staging included CT scan abdomen and pelvis, MRI brain, and USG in some patients. In contrast, PET imaging with FDG allowed scanning the entire body and thus detecting unexpected

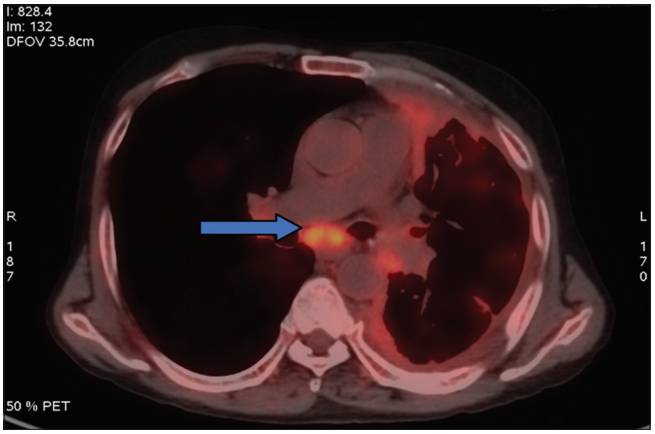

Figure 7: Positron emission tomography-computed tomography axial section showing subcarinal node

Table 4: Histological subtypes in various studies

Study by	Adenocarcinoma (%)	Squamous cell carcinoma (%)
Alamoudi 2010[3]	27.2	51.8
Maasdorp *et al*. 2011[4]	32.6	34.8
Dey *et al*. 2012[6]	30.8	35.1
Noronha *et al*. 2012[11]	43.8	26.2
Gupta *et al*. 2015[9]	42.6	35.1
Present study	72.8	20.8

Table 5: Extrathoracic metastasis sites reported in various studies

Study by	Sites of metastasis
Shetty *et al*. 2005[12]	Skeletal (19.7%) >Liver (18.5%) > Adrenal (6.1%)
Alamoudi 2010[3]	Skeletal (49.1%) > Liver (29.8%) > Adrenal (8.8%)
Dey *et al*. 2012[6]	Liver (7.7%) > Skeletal (4.4%) > Adrenal (3.2%)
Gupta *et al*. 2015[9]	Skeletal (35.9) > Adrenal (10.4%) > Liver (9.4%)
Present study	Skeletal (52.8%) > Adrenal (20.8%) > Liver (19.2%)

Table 6: Radiological lung lesions in various studies

Study by	Radiological appearance
Alamoudi 2010[3]	Mass (82.5%) > Pleural effusion (36%) > Collapse (33.3%)
Dey *et al*. 2012[6]	Mass (77.3%) > Pleural effusion (27.8%) > Collapse (18.6%)
Gupta *et al*. 2015[9]	Mass (30.6%) > Collapse (13.5%) > Pleural effusion (12.4%)
Deependra *et al*. 2017[7]	Mass (86.6%) > Pleural effusion (53.3%) > Collapse (20%)
Present study	Mass (77.3%) > Pleural effusion (27.8%) > Collapse (18.6%)

Table 7: Change in stage after PET-CT scan in comparison with conventional imaging in various studies

Study by	Change in staging (%)
Lewis *et al*. 1994[18]	41
Pieterman *et al*. 2000[17]	62
Hicks *et al*. 2001[16]	43
Fischer *et al*. 2009[15]	31.6
Present study	54.4

Table 8: Change in nodal staging after PET-CT scan in comparison to conventional imaging

Study by	Change in nodal (n) staging(%)
Gupta *et al*. 1998[19]	36.8
De Wever *et al*. 2007[20]	17.5
Yang *et al*. 2008[21]	17.6
Ceylan *et al*. 2012[13]	21.3
Present study	32

metastatic lesions.

Nodal upstaging was reported in 40 (32%) patients. Our results were consistent with previously reported observations in Indian as well as western literature as shown in Table 8. In the study conducted by Ceylan *et al.,* in 2012, where he analyzed a total of 57 patients comparing contrast enhanced CT versus integrated PET-CT in nodal staging of non-small cell lung carcinoma, he reported a change in nodal staging in 21.3% cases.[13] Gupta *et al*., in his study of 103 patients, reported a change in nodal staging in 36.8% patients.[19] Most of the other studies reported similar changes in nodal staging after PET-CT in comparison to CT scan.[20,21] The anatomical imaging modalities rely on size criteria for nodal assessment. However, with metabolic imaging, the PET scan detects changes early hence gives early positivity.

CONCLUSION

Carcinoma lung remains one of the most prevalent and leading causes of cancer-related mortality in the world. In our study, adenocarcinoma was the most common variety. The higher incidence is likely related to a higher proportion of non-smokers. Smoking, however, continues to be an important risk factor. Radiologically mass lesion remains the most common presentation. FDG-PET imaging has emerged as an excellent tool in the diagnostic armamentarium for staging and evaluation, and a large proportion of patients get upstaged after PET.

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