



Original Research Article

HISTOPATHOLOGICAL TYPES AND CLINICAL PROFILE OF PRIMARY LUNG CANCER DIAGNOSED IN A TERTIARY CARE CENTRE IN KERALA –A CROSS SECTIONAL STUDY

Ok Mani¹, Safa VP²

¹Assistant Professor, Department of Pulmonary Medicine, Government Medical, College Thrissur Kerala, India

²Senior Resident, Department of Pulmonary Medicine, Government Medical College Thrissur Kerala, India.

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Corresponding Author:

Dr. OK Mani

Assistant Professor, Department of Pulmonary Medicine, Government Medical, College, Thrissur, Kerala, India.

Email: drokmani@gmail.com

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ABSTRACT

Background: The second most common cancer and the main cause of death from cancer worldwide is lung cancer. The stage of the cancer, mutation, and histological type all affect the prognosis and course of treatment. There is no adequate data about histological subtypes lung cancer in our area. The aim of this study is to evaluate the smoking status, histological subtypes, clinico-epidemiological profile, and interdependencies among those suffering from lung cancer.

Materials and Methods: This cross-sectional study was conducted in Department of Pulmonary Medicine, Government Medical College, Thrissur, Kerala, India. From May 2, 2021, until May 7, 2022. Histopathologically confirmed lung cancer patients were studied. The data was collected by using a semi-structured proforma, and SPSS 20 was used for analysis.

Results: The mean age of the patients (n=124) was 63.42 + 9.11 (SD) years. The common symptoms were cough (71.8%), breathlessness (62.9%), chest pain (35.5%), and loss of weight (31.5%). Among the patients 86.3% are males and 80.6% are smokers. Adenocarcinoma was the commonest histopathological subtype (45.9%) followed by squamous cell carcinoma (37.9%), small cell carcinoma (10.5%) and other neuroendocrine tumors (5.6%). Squamous cell carcinoma was the commonest subtype among males (42.1%) and smokers (44.6%). Adenocarcinoma remained commonest among females (82.3%) and non-smokers (87%). Cough was significantly higher in squamous cell and small cell carcinomas (p=0.04). Dyspnea remained the most prevalent symptom in adenocarcinoma (64.9%).

Conclusion: Adenocarcinoma was the commonest subtype. Squamous cell carcinoma had higher prevalence among males and smokers; adenocarcinoma was higher among females and non-smokers. The commonest symptom was cough. Cough was significantly higher in squamous cell and small cell carcinomas. Dyspnoea was the most prevalent symptom in adenocarcinoma.

Keywords: Lung cancer, Smoking, Adenocarcinoma, Squamous cell carcinoma, small cell carcinoma.

INTRODUCTION

Lung cancer is the second commonest malignancy and the leading cause of cancer deaths worldwide.^[1] The global lung cancer burden was estimated by the International Agency for Research on Cancer (IARC) and the Global Cancer Observatory (GLOBOCAN) to be 2.2 million new cases and 1.8

million deaths in 2020.^[1] The most significant modifiable risk factor for lung cancer is tobacco smoking.^[2] Tobacco Smoking is responsible for 85% of all lung cancer cases.^[3] Symptoms of lung cancer reported are cough, chest pain, shortness of breath, haemoptysis, fatigue and weight loss.^[3] More than 90% of patients with lung cancer will be symptomatic at presentation. A minority present with

symptoms related to the primary tumor,^[4] A chest x-ray is often the initial imaging test.^[5] The abnormalities are more clearly demonstrated with contrast-enhanced CT scans or combined PET-CT scans, but for confirmation of lung cancer, a histopathological and immunohistochemistry examination is needed.^[5,6] The procedure most frequently used to diagnose lung cancer is bronchoscopy bronchial washing, endobronchial or transbronchial biopsy.^[5] Small-cell lung cancer (SCLC) is about 15% and non-small-cell lung cancer (NSCLC) is about 85% of all lung cancers. These are the two subtypes of lung cancer, based on histologic characteristics.^[7,8] Histologically adenocarcinoma, squamous cell carcinoma, and large cell carcinoma are different subtypes of non-small cell lung cancer (NSCLC).^[8] Most patients with lung carcinoma have advanced disease when they are diagnosed.^[9,10] Patients with advanced lung cancer are reported to have a relatively low overall survival rate.^[10] The treatment and prognosis of lung cancer are largely influenced by histo-pathological type, disease stage, and mutation.^[10] There is a dearth of information about histological subtypes in our region.

Objectives

1. To assess the clinico-epidemiological profile, histological subtypes and smoking status of primary lung cancer patients
2. To find out association of gender, smoking status and clinical presentation with histopathological subtypes.

MATERIAL AND METHODS

This was a cross-sectional study which was conducted in the Department of Pulmonary Medicine, Government Medical College, Thrissur, Kerala, India.

Inclusion Criteria

We included patients with confirmed histopathological or cytological diagnosis of primary lung cancer, those aged between 30–80 years, those who were willing to participate in the study were included. We excluded those,^[1] who had synchronous extra pulmonary malignancy,^[2] who were unwilling and unfit for the diagnostic procedures like bronchoscopy bronchial washing, endobronchial or transbronchial biopsy or true cut lung biopsy and,^[3] who had lung metastasis from other organs.

Study Procedure

A semi-structured proforma was administered by the investigators, after getting written informed consent from the patients. Baseline socio-demographic details of the patients, such as age, sex, occupation, and socioeconomic status were noted. The presence of risk factors like smoking, environmental tobacco smoke, family history of cancer, occupational exposure and biomass fuel exposure were recorded. Data regarding symptoms, signs elicited on clinical examination, baseline investigations, and radiological investigations were also noted. Details

of the diagnostic procedures like bronchoscopy, bronchial washing, endobronchial or transbronchial biopsy or true cut lung biopsy. Histopathological subtypes and details of immunohistochemistry were recorded.

Statistical Analysis

The collected data were analysed by using SPSS version 20. Categorical variable was summarised as proportion / percentage; quantitative data were summarised as the mean with a standard deviation.

Ethical Aspects

The present study was approved by Institutional Ethics Committee, Government Medical College, Thrissur, Kerala vide letter no. IEC/GMCTSR/095/2021. From each patient a Written informed consent was obtained before the study. Patient's details were kept confidential throughout the study. There was no any kind of financial burden to any patients.

RESULTS

Baseline characteristics

A. Socio-demographic profile

There was a total of 124 patients, with a mean age of 63.42 ± 9.11 (SD) years. The patients age ranged from 37 to 79 years. The majority of the patients (41.9 %) belonged to the age group of 60–69 years. Of the total 124 patients, the majority were males, accounting for 86.3% of the patients. In terms of education, high school was the most common level achieved among patients (54.8%). A significant proportion of the study population (65.3%) were manual labourers. The majority of participants belonged to Below Poverty Level (BPL) 75.8%.

B. Co-morbidities

Among the 124 patients 14.5% had Chronic Obstructive Pulmonary Disease (COPD). 12.1 % had Hypertension (HTN) and 12.1% had Diabetes Mellitus (DM) and 6.5% gave history of treatment for pulmonary Tuberculosis.

Presence of risk factors: The majority of the patients were smokers 100 (80.6%), with smoking index more than 300 in 91 patients (78.2%). Other risk factors were being an environmental tobacco smoke (4.8%) and exposure to biomass fuel (7.3%). Baseline features of the patients studied is given in Table 1. [Table 1]

Clinical profile

Presenting Symptoms

Out of the total 124 patients, the majority (71.8%) presented with cough. Breathlessness (62.9%) and chest discomfort in 35.5%, weight loss in 31.5%, haemoptysis in 29%, loss of appetite in 27.4% and hoarseness of voice in 10.5% were the other symptoms

General examination findings (clinical signs)

Among the total 124 patients, 78 had (62.9%) clubbing, 29 had (23.4%) had cervical lymphadenopathy, 5 (4%) had pedal oedema, and 4 had (3.2%) pallor. Distribution of symptoms and

signs among the participants is given in table no.2. [Table 2]

Imaging investigations (Chest X- ray)

The most common imaging investigation was chest X-ray, which shows mass lesion in 101 participants (81.45%) it was followed by pleural effusion (11.29%), consolidation (4%) and collapse (3.23%) are given in Figure no.1. [Figure 1]

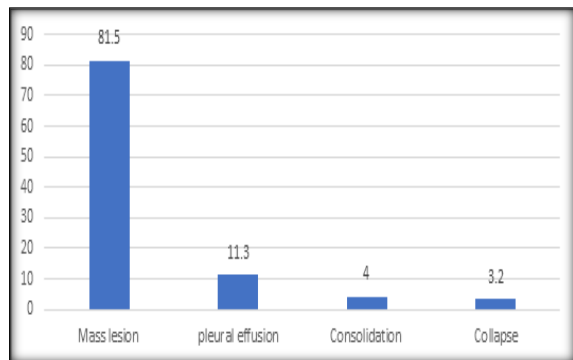


Figure 1: Chest X-ray Distribution of findings in (%) (N=124)

Contrast Enhanced CT (CECT) Thorax

All the participants were undergone for CECT Thorax showed mass lesion in 118 (95.2%), Hilar lymphadenopathy in 29 (23.4%), pleural effusion in 16 (12.9 %), consolidation in 9 (7.3 %), collapse in 8 (6.5), bony involvement in 3 (2.4%).

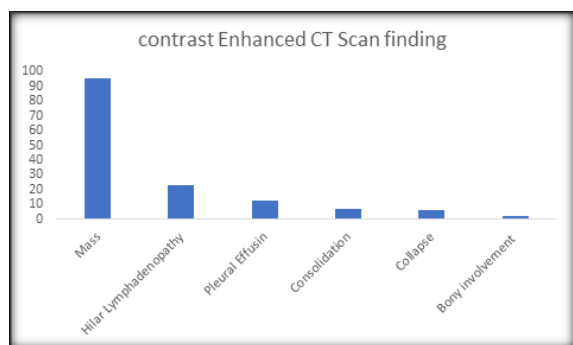


Figure 2: Distribution of findings in CECT Thorax results (%) (N=124)

Diagnostic procedures

The histopathological diagnosis was made by different diagnostic procedures, most commonly used procedure was bronchoscopy done in 52 patients (41.9%). Followed by USG-guided trucut lung biopsy in 20(16.1%), CT-guided lung biopsy in 15(12.1%), and Lung FNAC in 14 (11.3%). peripheral lymph node FNAC in 14 (11.3%), pleural fluid cytology 6 (4.8%) pleural biopsy in 2(1.6%) The distribution of diagnostic procedures is given in Fig 3. [Figure 3]

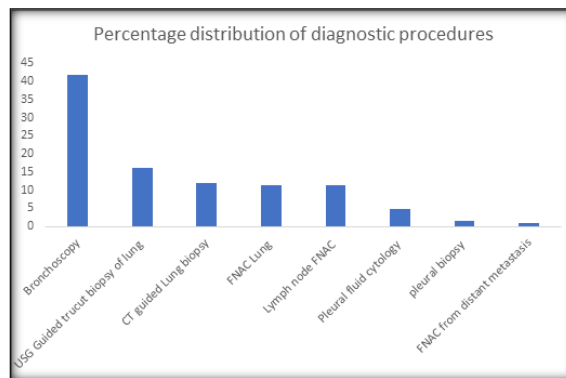


Figure 3: Distribution of diagnostic procedures Percentage (N=124)

Histological Subtype

Adenocarcinoma was the commonest histological subtype (45.9%, no = 57) of participants followed by Squamous cell carcinoma (37.9%, n = 47), Small cell carcinoma (10.5%, n = 13), and other neuroendocrine tumors (5.6%, n = 7). The histologic subtypes distribution is shown in Figure no 4. [Figure 4]

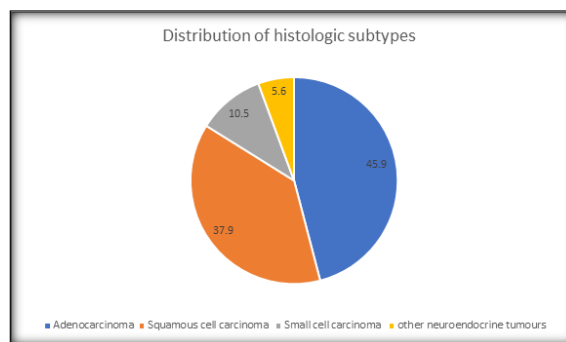


Figure 4: Distribution histological subtype percentage (N=124)

Compared to females males had a higher prevalence of squamous cell carcinoma (42.5% vs. 11.1%) and small cell carcinoma (11.3% vs. 5.6%), But females had a higher prevalence of adenocarcinoma (77.8% vs. 40.6%) (p=0.028). Prevalence of other neuro- endocrine tumors was comparable among both males and females (5.6% vs 5.9%).

A similar trend which was statistically significant also seen across smoking status, which showed, a higher prevalence of squamous cell carcinoma (45 % vs.8.3%) and small cell carcinoma (12 % vs. 4.2%) among smokers compared to non-smokers. Higher prevalence of adenocarcinoma among non-smokers (83.3 % vs. 37%) (p=0.001). Prevalence of other neuro- endocrine tumors were comparable among both smokers and non-smokers (5.9% vs 4.3%).

When all other carcinomas were considered together, males had a significantly higher prevalence of squamous carcinoma, compared to females (chi-square =6.42, p=0.011). Similarly, females had a significantly higher prevalence of adenocarcinoma,

compared to males (chi-square =8.58, p=0.003). The prevalence of squamous cell carcinoma among males and females is compared in fig. 5. The prevalence of adenocarcinoma among males and females is compared in fig.6. [Figure 6]

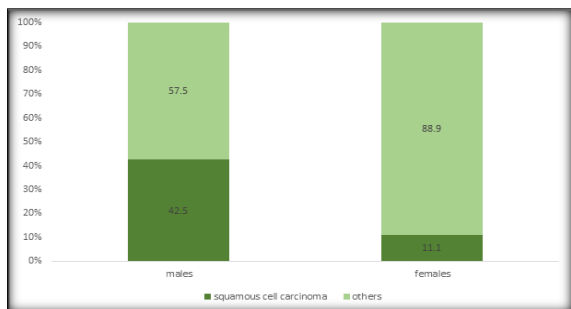


Figure 5: comparison of prevalence of squamous cell carcinoma among males and females (%) (p=0.011)

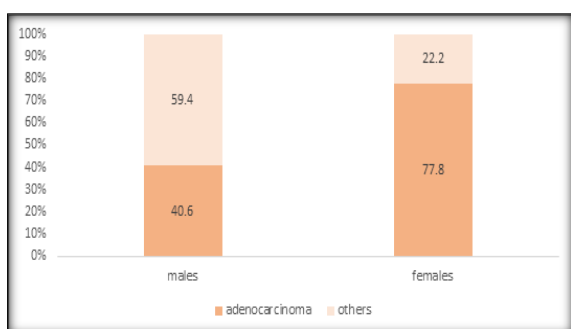


Figure 6: Comparison of prevalence of adenocarcinoma among males and females (%). (p=0.003).

When all other carcinomas were considered together, smokers had a significantly higher prevalence of squamous cell carcinoma, compared to non-smokers (chi-square =11.06, p=0.001). Similarly, when all other carcinomas were considered together non-smokers had a statistically significant higher prevalence of adenocarcinoma, compared to smokers (chi-square =16.73, p=0.000). The comparison of squamous cell carcinoma and adenocarcinoma among smokers and non-smokers with respect to the rest of carcinomas are shown in fig.no 8 and 7 respectively.

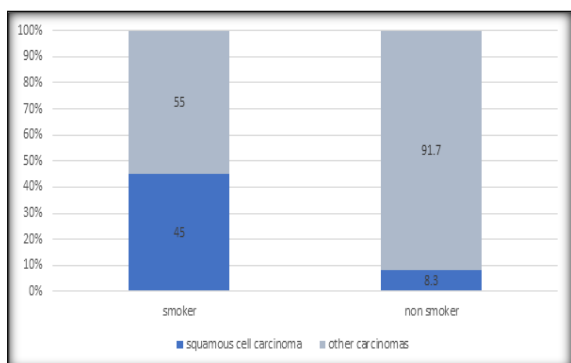


Figure 7: comparison of prevalence of squamous cell carcinoma among smokers and non-smokers (%) (p=0.001)

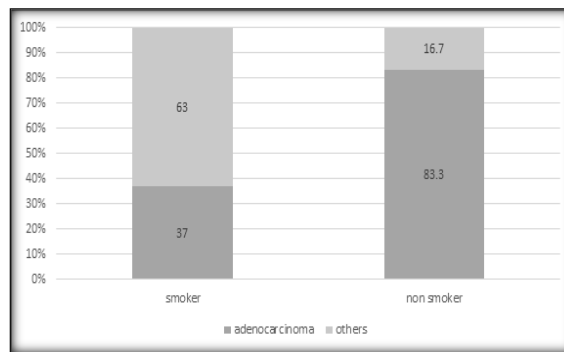


Figure 8: Comparison of prevalence of adenocarcinoma among smokers and non-smokers (%) (p=0.000)

There was a high prevalence of cough in small lung carcinoma (84.6%) compared to squamous cell carcinoma (82.9%) and other neuroendocrine tumors (71%) which was found to be statistically significant (p=0.04). Dyspnoea was the most prevalent symptom in small cell lung carcinoma (84.6%) compared to the adenocarcinoma group (64.9%) and squamous cell lung carcinoma (57.4%), though it was not significant statistically (p=0.21). The prevalence of chest pain was higher among those with neuroendocrine tumors (57%) compared to the other tumors; this was also not a statistically significant association (p=0.64). [Table 4]

Signs and histological subtypes

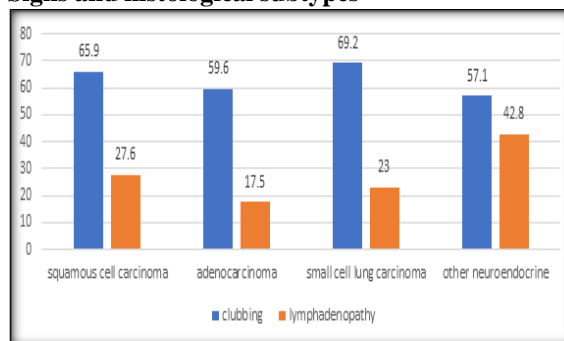


Figure 9: Prevalence of clubbing and lymphadenopathy among different histological types of lung carcinomas (%)

Among the general examination findings, Clubbing was the most common finding in all lung carcinoma groups. The prevalence was comparable across different groups (p = 0.885) (Fig.no.9) with respect to all other clinical signs. The prevalence of lymphadenopathy was higher among neuroendocrine tumors (42.8%) compared to other lung carcinomas, though this was not significant statistically (p value = 0.336) (Fig.9).

Clubbing was common in adenocarcinoma (43.5%), followed by Squamous cell carcinoma (39.7%), and other lung carcinomas. peripheral lymphadenopathy more found in squamous cell carcinoma (44%), followed by Adenocarcinoma (34%) and others. [Table 5]

Table 1: The Baseline characteristics of the study population (N=124)

Variable	Number	Percentage
Age groups		
30-39	1	0.8
40-49	8	6.5
50-59	28	22.6
60-69	52	41.9
70-79	35	28.2
Gender		
Male	107	86.3
Female	17	13.7
Educational status		
Uneducated	4	3.2
1to 4 th std	14	11.3
5 to 7 th	27	21.77
8 to 10 th	68	54.83
Above 10 th std	11	8.87
Occupation		
Manual labourer	81	65.3
Homemaker	17	13.7
Expert worker	22	17.7
Not working	4	3.2
Socio-economic status		
BPL	94	75.8
APL	30	24.2
Co-morbidities		
COPD	18	14.5
H/O old pulmonary TB	8	6.5
Diabetes Mellitus	15	12.1
Hypertension	15	12.1
Coronary Artery Disease	5	4
Cerebrovascular Accident	2	1.6
None	61	49.2
Risk factors		
Smoker	100	80.6
Passive smoking	6	4.8
Biomass fuel	9	7.3
None	9	7.3

Table 2: Distribution of symptoms and signs

Variable	Number	Percentage
Cough	89	71.8
Breathlessness	78	62.9
Chest pain	44	35.5
Loss of weight	39	31.5
Haemoptysis	36	29
Loss of appetite	34	27.4
Hoarseness of voice	13	10.5
General examination signs		
Clubbing	78	62.9
Lymphadenopathy	29	23.4
Pedal oedema	5	4
Pallor	4	3.2

Associations

Gender and smoking habit show in table no 3.

Table 3: Distribution of gender and smoking status across different histological subtypes of lung carcinoma percentage (N=124)

Variables	Squamous Cell Carcinoma Number (%)	Adeno Carcinoma Number (%)	Small Cell Carcinoma Number (%)	Other Neuro Endocrine Tumour Number (%)	Total (N=124)	Chi square (p)
Gender						
Male	45(42.5)	43(40.6)	12(11.3)	6(5.7)	107	9.11 (0.028)
Female	2(11.1)	14(77.8)	1(5.6)	1(5.6)	17	
Smoking status						
Smoker	45(45)	37(37)	12(12)	6(6)	100	17.15 (0.001)
Non smoker	2(8.3)	20(83.3)	1(4.2)	1(4.2)	24	

Pattern of symptoms and histological subtypes

Table 4: Distribution of symptoms across various histopathological subtype

Presenting complaint	Squamous Cell Carcinoma (n-47)	Adeno Carcinoma (n-57)	Small Cell Lung Carcinoma (n-13)	Other neuroendocrine tumours (n-7)	Total	p value
Cough	39(82.9%)	34(59.6%)	11(84.6%)	5(71%)	89	0.040
Dyspnoea	27(57.4%)	37(64.9%)	11(84.6%)	3(42%)	78	0.212
Chest pain	16(34%)	19(33.3%)	5(38.4%)	4(57%)	44	0.639
Hoarseness of voice	7(14%)	4(7%)	0	2(18%)	13	
Haemoptysis	18(38.2%)	11(19.2%)	5(38.4%)	2(28%)	36	0.131

Table 5: Cross tab of clinical signs versus histological subtypes of lung cancer

Histological subtypes	Digital clubbing Number (%)	Peripheral lymphadenopathy Number (%)	pedal edema Number	Pallor Number
Squamous Cell Carcinoma	31 (39.7%)	13 (44.8%)	1	2
Adenocarcinoma	34 (43.5%)	10 (34.5%)	2	1
Small Cell Carcinoma	9 (11.5%)	3 (10.3%)	1	1
Other neuro endocrine tumours	4(5.1%)	3(10.3%)	1	
Total	78 (100)	29(100)	5(100)	4(100)

DISCUSSION

The male to female ratio in this study was 6.29:1, which reinforces the male predominance in lung cancer which is already established by many researchers.^[11,12] Mean age of lung cancer was 63.42years (+/- 9.11) years, which is slightly higher than many other studies from tertiary care centres in India, which identified average age at diagnosis as below 60 years.^[13-15] A clinico-epidemiological profile of lung cancers in India based on the National Cancer Registry Programme in India, identifies the median age at presentation ranged from 54 to 70 years in different geographic areas (16). As age is one of the major prognostic factors affecting survival in lung cancer patients, all efforts to be made to diagnose lung cancer as early as possible.^[17]

The prevalence of smoking in the present study (80.6%) is comparable to study conducted by Gupta R C et al (81.6%) and is slightly lower than most western data (87%-93%).^[13,18,19] In the present study the commonest symptom was cough (71.8%), followed by breathlessness (62.9%), chest pain (35.5%), loss off weight (31.5%), haemoptysis (29%), loss of appetite (27.4%), hoarseness of voice (10.5%). These findings are similar to findings in a study by Sawhney et al.^[20] It is important to note that the prevalence of these symptoms may vary among individuals and can be influenced by various factors such as the stage and cell type of lung cancer.^[21] The current study partly exemplifies this fact as cough was the most common symptom in small cell carcinoma (84.6%) and squamous cell carcinoma (82.9%) and dyspnoea was the commonest symptom in Adenocarcinoma group (64.9%). Small cell carcinoma group had both cough and dyspnoea as the most common symptoms in the present study. In smokers and patients with age more than 70 years the positive Predictive Values for each symptom are higher.^[22] Awareness of symptoms leads to early diagnosis and best treatment outcome

Digital Clubbing was the most common clinical examination finding, present in 62.9% of patients in the current study. Peripheral lymphadenopathy was seen in 23.4% in our study. Study by Pandhi et al found out the prevalence of digital clubbing as 50% and peripheral lymphadenopathy as 30%.^[23] The current study identifies lymphadenopathy more with neuroendocrine tumours (42.8%) followed by squamous cell carcinoma (27.6%), small cell carcinoma (23%) and adenocarcinoma (17.5%). The study by Deng H Y et al found out that patients with adenocarcinoma had significantly more mean positive Lymph nodes (2.2 and 0.7; P = 0.008) and a higher rate of Lymph nodes metastasis (53% and 29%; P = 0.016) than those with Squamous Cell Carcinoma (24). According to Huang L et al, among the patients with lung Squamous Cell Carcinoma of 3 cm or less in diameter, there are certain risk factors such as age <60 years, tumour location of central-type, tumour long axis >2cm but ≤3cm which significantly increased the rate of lymph node metastasis.^[25]

Bronchoscopy is one of the most effective and precise diagnostic procedures for evaluating suspected cases of lung cancer. In the present study, bronchoscopy and related procedures like bronchial biopsy brushing and bronchial wash provided diagnosis in 41.9% followed by USG Guided true-cut lung biopsy (16.1%), CT Guided lung biopsy (12.1%) and Lung FNAC (11.3%). These results are consistent with the findings in the study conducted by Singh M.P et al.^[26]

In the present study, adenocarcinoma remained the commonest histological subtype (45.9%) followed by Squamous cell carcinoma (37.9%), Small cell carcinoma (10.5%) and another Neuroendocrine tumour (5.6%). In a similar study done by Sheema S in tertiary care hospital in Kashmir on a total of 783 cases over a 10 years period (1996-2006) the most common histological type of tumour in both sexes was squamous cell carcinoma (71.3%), followed by small cell carcinoma (20.8%), adenocarcinoma (2.6%), bronchioalveolar carcinoma (1.8%) while other tumours constituted 3.6%.^[27] In the 3-year

clinico-pathological study done in AIIMS, where a total of 434 pathologically confirmed lung cancer were analysed, there were 85.3% of NSCLC cases and 14.7% of SCLC cases. Adenocarcinoma was the most common histological subtype among NSCLCs (45.41%).^[26] Few other studies also report similar trend in cancer epidemiology.^[28,29] Recently the adeno carcinoma is become more common than squamous cell carcinoma in western and Asian countries. This may be due to the changed smoking pattern and incidence of lung cancer in women.^[30]

In this study, all the females were non-smokers. The study found that squamous cell carcinoma was more prevalent in males (42.1% vs 11.8%) and smokers (44.6% vs 8.7%), while adenocarcinoma was more prevalent in females (82.35% vs 40.1%) and non-smokers (87% vs 36.6%). These findings align with previous research by Gupta et al.^[31] When read in line with increasing trends in adenocarcinoma, incidence of female/non-smokers lung cancer and their strong interdependencies worth investing in research. The exploration of other than cigarette smoke environmental risk factors could bring health-related legal regulations too. High prevalence of adenocarcinoma among the females needs detailed evaluation including genetical aspects.^[32]

CONCLUSION

Cough remained as the commonest symptom. Adenocarcinoma was the commonest histopathological subtype. Squamous cell carcinoma had higher prevalence among males and smokers; adenocarcinoma was higher among females and non-smokers. Cough was significantly higher in squamous cell carcinoma and small cell carcinomas. Dyspnoea was the most prevalent symptom in small cell carcinoma.

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