Section: Pathology

Original Research Article

HISTOPATHOLOGICAL SPECTRUM OF MALIGNANT LUNG TUMORS IN A TERTIARY CARE HOSPITAL OF NORTH INDIA: A RETROSPECTIVE STUDY

Bharti Sharma[1], Ritesh K Sheorain[1]

[1]Specialist, Department of Pathology, Pt. B D Sharma PGIMS, Rohtak, India.

Received *: 20/06/2026*
Received in revised form *: 12/08/2026*
Accepted *: 27/08/2026*

Corresponding Author:
Dr. Bharti Sharma,
Specialist, Department of Pathology, Pt. Neki Ram Sharma govt. medical college, Bhiwani, India..
Email: bhartisharma405@gmail.com

DOI: 10.70034/ijmedph.2026.3.661

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 4229-4233

ABSTRACT

Background: Lung cancer (LC) is a major health problem and is the most common cancer in the world. It is more common in males. LC is classified into small cell lung cancer and non-small cell lung cancer based on pathological diagnosis. Lung tissue biopsy is the gold standard for LC diagnosis. Histopathological examination enables proper classification of lung malignancies. The objective is to see the spectrum of lung cancer on histopathology in the region of north India.

Materials and Methods: We conducted a retrospective study, in the department of Pathology, PGIMS, Rohtak over a period of two years. Records of all the malignant lung tumors, diagnosed on histopathological examination along with immunohistochemistry (IHC) where ever required from transbronchial lung biopsy, endobronchial lung biopsy and pleural biopsy specimen were reviewed. Total of 212 cases were included in which lung tumor was diagnosed on histopathology.

Results: There were 212 cases of LC. Male is to female ratio was 3.8:1, and the mean age was 60.9 years. 79.2 % were male and 20.8 % were female patients. 88.6 % cases were smokers and 11.4 % cases were non-smokers. Occupational hazard history were present in 15.5 % cases. Family history of LC was present in 5.7% cases. The most common histological type of LC was squamous cell carcinoma comprising of 63.7% followed by poorly differentiated carcinoma 13.8%. IHC was used in only 30% of cases for LC subtyping. Analysis revealed a significant association between smoking status and the specific cancer subtype (Chi-square=46.99, $p<0.0001$).

Conclusion: Squamous cell carcinoma is still the most common histological type of LC in north India. It is more common in males having history of smoking.

Keywords: Lung cancer, Histopathology, Small cell lung cancer, non-small cell lung cancer, Histopathological spectrum.

INTRODUCTION

Lung cancer (LC) is a major public health problem and continues to be the leading cause of cancer mortality worldwide.[1] It is more common in males, having male is to female ratio of 2:1. This is the second most common cancer in males, while in females, it is ranked 6th.[2]

According to histopathological classification LC is broadly classified into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). SCLC represent about 15% of LC cases and is characterized microscopically by small, round to spindle-shaped, with scant cytoplasm and granular chromatin, and frequent necrosis.[3] NSCLC, comprising nearly 85% of LC cases, and includes adenocarcinoma, squamous cell carcinoma and large cell carcinoma, with adenocarcinoma and squamous cell carcinoma being the most common subtypes.[4]

Lung tissue biopsy is the cornerstone of LC evaluation. These biopsies are obtained through thoracotomy or needle biopsy, followed by pathological examination.[5-7] Histopathological examination along with immunohistochemistry

(IHC) enables precise classification of lung malignancies and guide subsequent management.[8]

Objective: To assess the histopathological spectrum of lung cancer in North India.

Need of the study: To establish regional epidemiological patterns and identifies high risk demographics like male smokers aged 40-60.

Novelty of the study: This study document the dominance of squamous cell carcinoma driven by high regional smoking rates, alongside a younger than average age presentation and a real-world audit of low IHC utilization in a resource limited North Indian setting.

MATERIALS AND METHODS

We conducted a retrospective study, in the department of Pathology, PGIMS, Rohtak over a period of two years. Records of all the malignant lung tumors, diagnosed on histopathological examination along with immunohistochemistry (IHC) where ever required, from transbronchial lung biopsy, endobronchial lung biopsy and pleural biopsy specimen were reviewed. Total of 212 cases were included in which lung tumor was diagnosed on histopathology.

Following IHC markers were used where ever required: CK5/6, CK7, TTF-1, p63, Synaptophysin, Chromogranin A and Pan-cytokeratin. A staining was scored as negative, focal (minority of tumor cells) and diffuse (majority of tumor cells). The staining pattern of different IHC markers was as follow.[9]

- CK5/6, CK7 & pan-keratin: cytoplasmic positivity.
- TTF-1, p63: nuclear positivity.
- Synaptophysin, Chromogranin A: granular cytoplasmic positivity.

Both morphological and IHC profile needed for NSCLC subtyping in some cases.

- Adenocarcinoma – TTF-1 and/or CK7 positive. CK5/6 and p63 typically negative.
- Squamous cell carcinoma- CK5/6 and p63 positive. TTF-1 and CK7 negative.
- Small cell carcinoma- synaptophysin, chromogranin A and pan-keratin positive.

Sampling method: A non-probability consecutive sampling method was used. All consecutive cases of primary malignant lung tumors diagnosed histopathologically over the two-year study period that met the inclusion criteria were sequentially enrolled in the study. This approach ensured the inclusion of all available data within the study timeframe to eliminate selection bias.

Inclusion criteria

All the definitively diagnosed primary malignant lung tumors on histopathological examination along with the help of IHC where ever required from transbronchial lung biopsy, endobronchial lung biopsy and pleural biopsy specimen were included in the study.

Exclusion criteria

All those cases where definitive histopathological diagnosis cannot be reached or where the tumor was not a primary malignant lung tumor were excluded from the study.

Primary outcome: Squamous cell carcinoma is the most common histological type of LC in the north India.

Secondary outcome: Squamous cell carcinoma occurrence is more common among tobacco smokers.

Statistical Analysis: Total of 212 cases were included in which lung tumor was diagnosed on histopathology. The collected data was categorized and coded properly and the data was compiled, tabulated and analyzed using SPSS 20 software. Statistical tests applied were percentages, proportions, chi-square test and unpaired t test where ever applicable.

Ethics: This study was a retrospective clinical audit/evaluation. According to the policies of the ethical committee of our institution, formal ethical review and informed consent were not required for this type of observational, non-interventional study. All the patient data was fully anonymized and kept confidential prior to analysis.

All the procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation and with the Helsinki Declaration of 1975, revised in 2008.

RESULTS

A total of 212 cases of LC were analyzed. The overall male-to-female ratio was 3.8:1, and the age of patients ranged from 29 to 89 years, with a mean age of 60.9 years. The majority of the patients, 73.5 % (n=156) belonged to the 40-to-60-year age group [Table1]. Males constituted 79.2 % (n=168) and females 20.8 % (n=44) of the cohort [Table 2].

Table 1: Age distribution

Age group (years)	No. of patients	Percentage
0-20	0	0
20-40	26	12.2 %
40-60	156	73.5 %
60-80	28	13.2 %
80-100	2	1.2 %
Total	212	100

Table 2: Gender distribution

Gender	No. of patients	Percentage
Males	168	79.2 %
Females	44	20.8 %
Total	212	100 %

Smoking history was present in 88.6 % (n=188) of cases, while 11.4 % (n=24) were non-smokers, giving a Smoker-to-non-smoker ratio of 7.8:1. Occupational exposure was recorded in 15.5 % (n=33) cases. A positive family history of LC was present in 5.7% (n=12), whereas 94.3% (n=200) had no significant family history [Table 3].

Table 3: Personal and family history.

Smoking history	No. of patients	Percentage
Present	188	88.6 %
Absent	24	11.4 %
Occupational history		
Present	33	15.5 %
Absent	179	84.5 %
Family history of lung cancer		
Present	12	5.7 %
Absent	200	94.3 %

The most common histological type of LC was squamous cell carcinoma comprising of 63.7% (n=135) followed by poorly differentiated carcinoma (13.8% [n=29]), adenocarcinoma (11.7% [n=25]) and small cell carcinoma (10.8% [n=23]) [Figure 1-4] [Table 4].

Table 4: Classification of lung cancer based on histopathological findings

Findings	No. of patients	Percentage
Small cell carcinoma	23	10.8 %
Non- small cell carcinoma		
Squamous cell carcinoma	135	63.7 %
Adenocarcinoma	25	11.7 %
Poorly differentiated carcinoma	29	13.8 %
Total	212	100

IHC was performed in only 30% of cases (n=64) for LC subtyping. Out of these 64 cases, 68.7% (n=44) were diagnosed as squamous cell carcinoma, 17% (n=11) were diagnosed as adenocarcinoma and 14% (n=9) were diagnosed as small cell lung cancer [Table 5].

Table 5: Number of cases where IHC was performed.

IHC marker	Squamous cell carcinoma (n)	Adenocarcinoma (n)	Small cell cancer (n)
CK5/6 & p63	44	0	0
CK7, TTF-1	0	11	0
Synaptophysin, Chromogranin A & pan- keratin	0	0	9

[Table 6] shows the distribution of different histological subtypes of LC among smokers and non-smokers. A chi-square test of independence was conducted to evaluate the relationship between smoking history and histological subtypes of lung cancer. The analysis revealed a highly significant association between smoking status and the specific cancer subtype (Chi-square=46.99, $p<0.0001$). The strength of this relationship was strong, as indicated by a Cramer's V of 0.471. The prevalence of smoking was exceptionally high among patients with squamous cell carcinoma (94.8%), poorly differentiated carcinoma (93.1%) and small cell lung cancer (91.3%). In striking contrast, less than half of the patients with adenocarcinoma had a history of smoking (48%), meaning non smokers comprised the majority of the adenocarcinoma sub-cohort.

Table 6: Distribution of different histological subtypes of Lung cancer among smokers and non-smokers.

Histological type	Smokers n (%)	Non-Smokers n (%)	Total n (%)
Squamous cell	128 (94.8%)	7 (5.2%)	135 (100%)
Poorly differentiated	27 (93.1%)	2 (6.9%)	29 (100%)
Small cell	21(91.3%)	2 (8.7%)	23 (100%)
Adenocarcinoma	12 (48%)	13 (52%)	25 (100%)
Total cohort	188 (88.6%)	24 (11.4%)	212 (100%)

To further quantify the risk association, Odds ratios (OR) were calculated using adenocarcinoma as the reference category. Compared to patients with adenocarcinoma, the odds of having a history of

smoking were 19.81 times higher in patients with squamous cell carcinoma (95% CI, p<0.0001). Patients with poorly differentiated carcinoma and small cell lung cancer also demonstrated markedly elevated odds of tobacco exposure with ORs of 14.63 (95% CI, p=0.0016) and 11.38 (95% CI, p=0.0051) respectively.

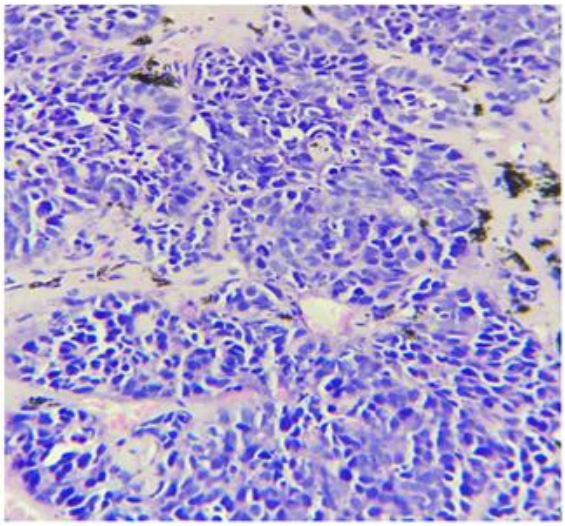

Figure 1: H & E stained photomicrograph of squamous cell carcinoma lung (400 X).

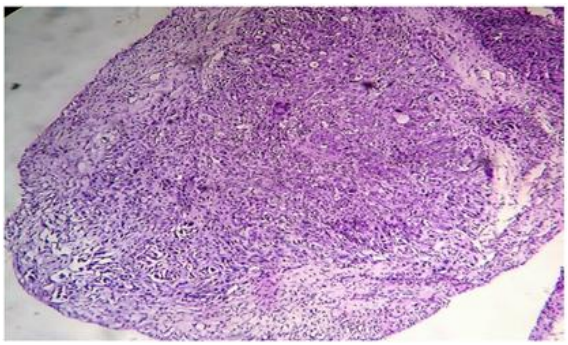

Figure 2: H & E stained photomicrograph of poorly differentiated carcinoma lung (400X).

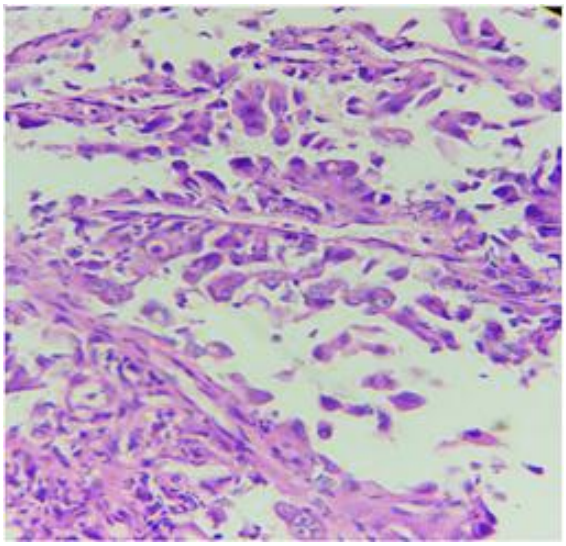

Figure 3: H & E stained photomicrograph of adenocarcinoma lung (400X).

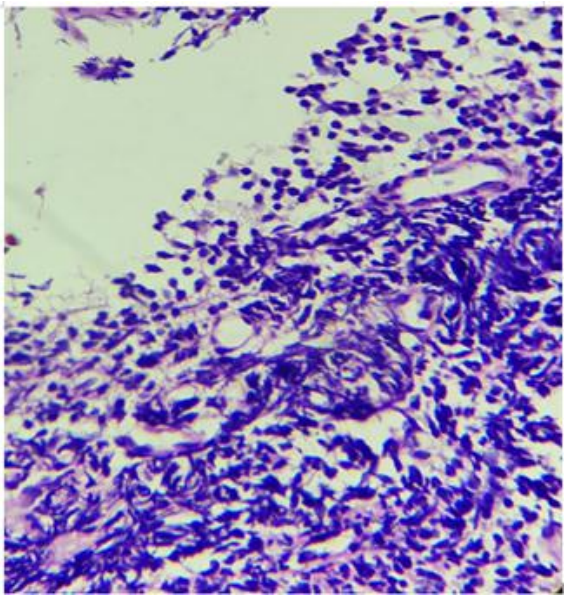

Figure 4: H & E-stained photomicrograph of small cell carcinoma lung (400 X).

DISCUSSION

This two-year retrospective study of 212 LC cases provides an overview of the histopathological pattern seen in a North India tertiary care setting.

The male predominance observed in our cohort, with a ratio of 3.8:1, which is slightly higher as compared to the other studies. This is attributed to smoking behavior which is more widespread among males in north Indian population [Table 5].[10,11]

The mean age of presentation was 60.9 years, which is slightly higher than that reported in some other Indian studies. This is attributed to tobacco smoking habit in north Indian population which started in early 20's and this is consistent damage over periods to manifest as LC as a result of which most of the cases were in age group of 60.9 plus minus 11 years [Table 5].[10-12]

We all are well aware that tobacco smoking has direct positive correlation with LC cases. In our study 88.6 % cases were tobacco smokers. This high percentage of smoking history in this study itself shows a positive correlation between smoking and lung cancer.

Santana et al,[13] study consist of an integrative literature review, that enables the synthesis of knowledge by the analysis of different previously published scientific studies and this study showed that occupational exposure remains a relevant factor in the development of LC among the workers in various sector. In our study only 15.5 % cases had occupational hazard history, this proportion is lower than that reported in some occupational studies, possibly because many patients in our setting were engaged in occupations with limited exposure to known carcinogens. Nonetheless, workplace exposure remains an important contributor to LC risk and should not be overlooked.[13]

A positive family history was present in 5.7 % of LC cases, which is higher than the study conducted by Kishida et al,[14] this may reflect a combination of shared environmental habits, especially smoking and possible genetic susceptibility. Smoking, a major risk factor for LC, often spreads from siblings and parents due to their shared environment from childhood to adolescent.

In the present study, squamous cell carcinoma was the most common histological subtype. This is in contrast to the global trend in which adenocarcinoma has become more frequent in many regions. As cigarette smoking is strongly associated with squamous cell carcinoma and small cell carcinoma, in our study 88.6 % of LC patients were smokers because of which, squamous cell carcinoma is also the most common type of lung cancer in our study [Table 7].

The changing epidemiological trend of LC subtypes in which adenocarcinoma is the most common subtype could be related to change in cigarettes designs, tobacco composition and inhalation patterns, although other factors may also contribute.[15]

The results of our study in context of smoking association with LC and distribution of different histological subtypes among smokers and non-smokers matches with the global pattern and the study conducted by Khuder et al.[16]

Table 7: Demographic profile and distribution of histological subtypes of lung carcinoma in various studies.

	M: F	Mean age	Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma	Others
Present study	3.8:1	60.9	63.7 %	11.7 %	10.8 %	13.8 %
Noronha et al,[9]	3.5:1	56	24.1 %	40.3 %	8.0 %	27.6 %
Krishnamurthy et al,[10]	3.5:1	56	15.9 %	42.6 %	13.2 %	28.3 %
Singh et al,[11]	4.4:1	57.9	34.8 %	26 %	18.4 %	20.8 %

Strength of the study: Being a tertiary care center in North India, the study likely benefits from a large volume of cases over several years, this study establishes clear patterns regarding the prevalence of different histological subtypes specific to the regional demography.

Limitation of the study: This type of study usually focuses only on tissue diagnostics and staging at presentation. They frequently lack long-term follow-up data or treatment outcomes.

CONCLUSION

Squamous cell carcinoma remains the most common histological subtype of LC in the North India. This disease is seen predominantly in men, having smoking history with mean age of 60.9 years.

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