Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 3
Open Access

Clinicopathological and Histomorphological Profiling of Primary Lung Carcinoma: A Tertiary Care Center Prospective Study in Central India

Kartavya K. Verma[1*], Amit Bugalia[2], Ajoy Kumar Behera[3], Nighat Hussain[4]
[1]Senior Resident, Department of Pathology and Lab Medicine, All India Institute of Medical Sciences, Raipur Chhattisgarh, India.
[2]Associate professor, Department of Pathology and Lab Medicine, All India Institute of Medical Sciences, Raipur Chhattisgarh, India.
[3]Additional professor, Department of Pulmonary Medicine, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India
[4]Professor, Department of Pathology and Lab Medicine, All India Institute of Medical Sciences, Raipur Chhattisgarh, India.
Corresponding author: Dr Kartavya Kumar Verma (*dr.kartavya123@gmail.com*)

Cite this paper as: Kartavya K. Verma, Amit Bugalia, Ajoy Kumar Behera, Nighat Hussain (2024) Clinicopathological and Histomorphological Profiling of Primary Lung Carcinoma: A Tertiary Care Center Prospective Study in Central India. *Frontiers in Health Informatics, 13* (3), 6940-6950

ABSTRACT
Introduction: *Lung cancer is one of the most lethal types of organ-specific cancers. Diagnosis with a small biopsy is a difficult task for the pathologist. In recent years, the treatment scenario and prognosis for lung cancer have changed depending on the type of cell morphology. This study aims to provide data to help diagnose suspected lung cancer cases as early as possible so they can be treated effectively.*
Material and Methods: *We conducted this prospective observational study in the Department of Pathology and Lab Medicine at the All-India Institute of Medical Sciences in Chhattisgarh, India. We collected our data from case records, demographic profiles, and histomorphological profiles of patients diagnosed with primary lung carcinoma from March 2019 to March 2020.*
Results: *All histopathology samples (N = 48) were taken from small biopsies, and 38 of these were from endobronchial biopsies. The mean age of patients in our study was 58.1 ± 12.2 (mean ± SD). Cough (35/48, 72.95%) and pallor (44/48, 91.76%) were the most common symptom and sign, respectively. Adenocarcinoma (ADC) was the most common morphological type (31/48, 64.5%), and the majority of the patients were nonsmokers (30/48, 62.5%). Furthermore, solid pattern (17/31, 54.83%) was the most common subtype among ADC cases.*
Conclusion: *ADC was the most common morphological subtype. In the region where our study was conducted, most patients were nonsmokers. The clinical profiles of the lung carcinoma patients were similar to those in the previously documented literature. We found that immunohistochemistry is useful in the diagnosis of lung carcinoma in small biopsies.*

Keywords: *Central India, Diagnosis, Lung Cancer, Histological Profile, Clinical Profile*

INTRODUCTION

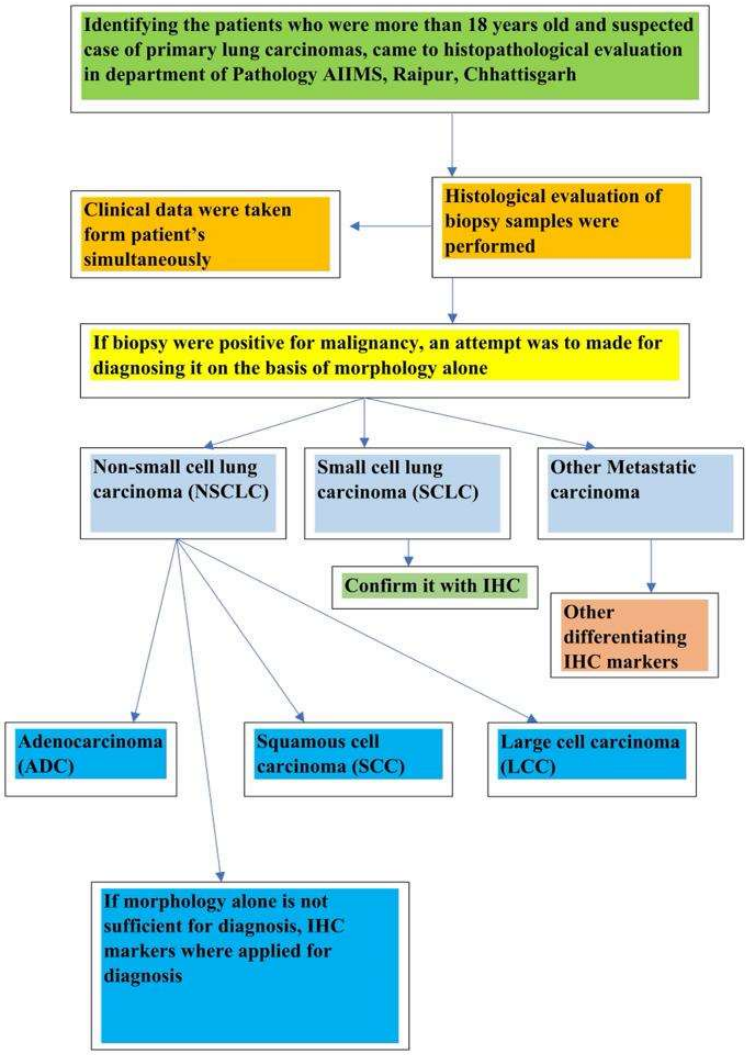
The increasing prevalence of lung cancer in Asian populations has become problematic from a human health perspective [1]. It is now the leading cause of cancer-related mortality in developing countries [2]. Diagnosing lung cancer in its earliest stages is advantageous for treatment, limits the course of the disease, and aids in survival. A biopsy examination is minimally invasive and is the current method of choice for diagnosing lung carcinoma. Biopsies are then correlated with clinical, radiological, and histological findings. Clinical suspicion

of lung carcinoma depends on a proper clinical history and thorough examination. According to the National Comprehensive Cancer Network, clinical signs and symptoms are peculiar for lung carcinoma.

Modalities for treatment of lung cancer include surgery, chemotherapy, or targeted therapies. At the time of diagnosis, approximately 70% of lung carcinomas are inoperable because they have been found at a late stage [3]. The treatment scenario and prognosis differ according to the type of lung carcinoma. The use of anticancer drugs targeted to particular mutations improves the prognosis. A precise and accurate diagnosis and the correct typing of lung carcinoma are essential for a decreased disease burden and possible surgical removal of the tumor.

MATERIALS AND METHODS

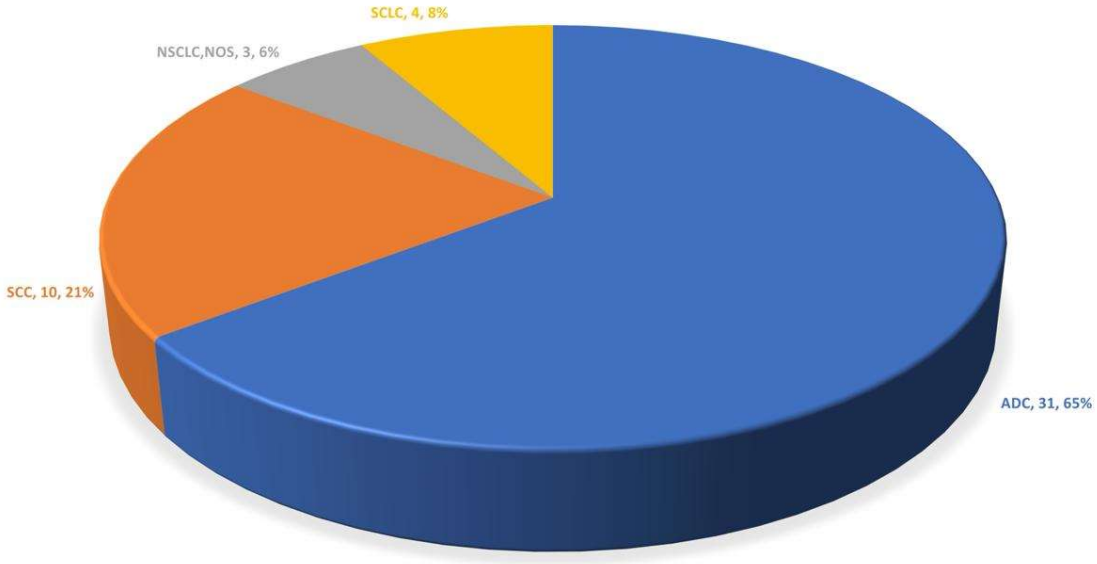
To begin our study, we first sought and received approval from an institutional ethics committee All India Institute of Medical Sciences (AIIMS) Raipur (AIIMSRPR/IEC/2019/241). Then, from March 2019 to March 2020, we followed up on AIIMS cases that were suspicious for lung carcinoma based on clinical history, signs, and symptoms. We then performed radiological examinations and clinical staging of those cases according to recommendations from the International Union Against Cancer and the 8th edition of the American Joint Committee on Cancer's staging system. We also assessed socioeconomic status using a BJ Prasad classification scale [4]. Biopsy samples were followed up of those cases. We then fixed the specimens in 10% neutral-buffered formalin and left them for fixation for 6-24 hours. We cut and processed embedded tissue sections with a Leica tissue processor and 4-micron thick paraffin. We prepared the initial slides using hematoxylin and eosin stain per protocol. We also attempted to classify tumors based on morphology, and when possible, we subcategorized the adenocarcinomas. We undertook further sectioning if there was no evidence of a tumor on the initial sectioning. If the biopsy was positive and showed morphological evidence of adenocarcinoma (ADC), squamous cell carcinoma (SCC), or small cell lung carcinoma (SCLC), we did not perform diagnostic immunohistochemistry (IHC) unless there was a question regarding the primary site. Cases that were difficult to diagnose on morphology alone required IHC validation. Then, we used SCC-specific (e.g., P40 or P63 and CK5/6) and ADC-specific (TTF-1 and Napsin A) markers on the unstained sections (Figure 1).



Two pathologists interpreted the IHC panel as per the World Health Organization's 2015 guidelines [5]. We conducted our data analysis with the help of SPSS statistical software. The data were compiled in Microsoft Excel (2019) (Microsoft®). We summarized the data using descriptive statistics, frequencies, and percentages. We assessed statistical differences between categorical variables using the chi-square or Fisher's exact test (if the cell value was < 5) and compared means using the student's t test. A p value of < 0.05 was considered statistically significant.

RESULTS

After applying inclusion and exclusion criteria, we studied 48 primary lung carcinoma cases using small biopsies. Approximately 65% (31/48) of cases were ADC, 21% (10/48) were SCC, 6% (3/48) were non-small cell lung carcinoma, not otherwise specified (NSCLC, NOS), and 8% (4/48) were SCLC. No Large cell carcinoma (LCC) was diagnosed in these 48 cases (Figure 2).



Out of 31 ADC cases, 17 (54.83%) were solid, eight (25.80%) mucinous, six (19.35%) showed lepidic pattern. Out of 10 SCC cases, one (10%) was keratinizing and nine (90%) were non-keratinizing. The mean age in our study was 58.1 ± 12.2 years old, and patients' ages ranged from 22 to 80. The proportions for different age ranges in our study were as follows: 51-60 years old 16 (33.3%), 61-70 years old 13 (27.1%), 41-50 years old 10 (20.8%), 71-80 years old six (12.5%), 31-40 years old two (4.2%), and 21-30 years old one (2.1%). Most patients (16, 33.3%) that we observed came from the 51-60 age group. The ratio of men to women was 4.33:1. The predominant pattern in both genders was ADC. All four (8.3%) cases of SCLC were men. No significant statistical association was found (p value of 0.198). In our study, 31 (64.6%) of patients resided in urban areas. No significant statistical association was found, with a p value of 0.198. The majority of patients were in private-sector jobs (11, 22.9%). Most of the women were homemakers (eight, 16.6%), and no significant statistical association was found, with a p value of 0.12. The majority of the patients were middle class (21, 43.75%). No significant statistical association was found, with a p value of 0.113.

In addition, 20 (41.6%) of patients had a history of tobacco chewing, 21 (43.8%) were alcoholics, and 18 (37.5%) had a history of smoking. A significant correlation was found between a history of alcohol and smoking and the development of SCC lung carcinoma, with a p value of 0.02. Two (4.2%) smokers with >30 pack years were diagnosed as SCC. Also, with same history one (2.1%) diagnosed as ADC and one (2.1%) as SCLC respectively. The association was statistically significant, with a p value of 0.05. Nine (18.6%) patients showed a history of a previous lung infection in the form of tuberculosis, histoplasmosis, or bacterial infection. Seven (14.5%) had a history of mycobacterial infection, and one (2.1%) had a bacterial infection in the form of an abscess. One (2.1%) SCLC patient had a history of histoplasmosis. A history of previous lung infection was not statistically significant, with a p value of 0.164. A history of chronic obstructive pulmonary disease (COPD) was found in 13 (27.1%) of patients. The association was not statistically significant, with a p value of 0.123 (Table I).

Table I: Clinicopathological profile of studied cases

Clinical and demographic factors	Variables	ADC (n=31)	SCC (n=10)	NSCLC, NOS (n=3)	SCLC (n=4)
Age wise Distribution	21-30	1 (2.1%)	0	0	0
	31-40	1 (2.1%)	1 (2.1%)	0	0
	41-50	7 (14.6%)	3 (6.3%)	0	0
	51-60	9 (18.8%)	2 (4.2%)	2 (4.2%)	3 (6.3%)
	61-70	9 (18.8%)	2 (4.2%)	1 (2.1%)	1 (2.1%)
	71-80	4 (8.3%)	2 (4.2%)	0	0
Gender wise Distribution	Female	8 (16.7%)	0	1 (2.1%)	0
	Male	23 (47.9%)	10 (20.8%)	2 (4.2%)	4 (8.3%)
Residency wise Distribution	Urban	19 (39.6%)	7 (14.6%)	2 (4.2%)	3 (6.3%)
	Rural	12 (25%)	3 (6.3%)	1 (2.1%)	1 (2.1%)
Occupation wise Distribution	Private job	9 (18.8%)	2 (4.2%)	0	0
	Government job	2 (4.2%)	2 (4.2%)	1 (2.1%)	0
	Housewife	7 (14.6%)	0	1 (2.1%)	0
	Driver	4	0	0	2 (4.2%)
	Farmer	7 (14.6%)	2 (4.2%)	1 (2.1%)	0
	Carpenter	1 (2.1%)	0	0	0
	Student	1 (2.1%)	0	0	0
	Labour	0	2 (4.2%)	0	1 (2.1%)
	Teacher	0	2 (4.2%)	0	1 (2.1%)
Socio-economic status wise Distribution	Upper class	8 (16.7%)	4 (8.3%)	1 (2.1%)	0
	Upper middle class	4 (8.3%)	2 (4.2%)	0	0
	Middle class	16 (33.3%)	2 (4.2%)	2 (4.2%)	1 (2.1%)
	Lower middle class	2 (4.2%)	2 (4.2%)	0	3 (6.3%)
	Lower class	1 (2.1%)	0	0	0
History of tobacco chewing	Present	8(16.6%)	9(18.6%)	0	3(6.25%)
	Not present	23(47.9%)	1(2.1%)	3(6.25%)	1(2.1%)
History of alcohol	Present	9(18.6%)	8(16.6%)	1(2.1%)	3(6.25%)

	Not present	22(45.83%)	2(4.2%)	2(4.2%)	1(2.1%)
History of smoking	**Present**	7(14.6%)	7(14.6%)	1(2.1%)	3(6.25%)
	Not present	24(50.0%)	3(6.25%)	2(4.2%)	1(2.1%)
Pack years	**3**	1(2.1%)	0	1(2.1%)	0
	10	4(8.4%)	1(2.1%)	1(2.1%)	0
	15	0	2(4.2%)	0	1(2.1%)
	20	2(4.2%)	1(2.1%)	0	1(2.1%)
	25	0	1(2.1%)	0	0
	30	1(2.1%)	2(4.2%)	0	1(2.1%)
	Nonsmokers	24(50.0%)	3(6.25%)	2(4.2%)	1(2.1%)
History of infectious agent	**Abscess**	1(2.1%)	0	0	0
	Histoplasmosis	0	0	0	1(2.1%)
	Mycobacterium Tuberculosis	5(10.4%)	2(4.2%)	0	0
	Not present	25(52.1%)	8(16.6%)	3(6.25%)	3(6.25%)
History of other lung disease	**History of COPD present**	6 (12.5%)	5(10.4%)	0	2(4.2%)
	Not present	25(52.1%)	5(10.4%)	3(6.25%)	2(4.2%)
Symptom	**Cough**	24(50.0%)	7(14.6%)	1(2.1%)	3(6.25%)
	Chest pain	13(27.0%)	6(12.5%)	2(4.2%)	0
	Haemoptysis	8(16.6%)	3(6.25%)	1(2.1%)	2(4.2%)
	Dyspnoea	7(14.6%)	4(8.4%)	1(2.1%)	0
	Hoarseness of voice	5(10.4%)	1(2.1%)	0	1(2.1%)
	Fever	9(18.6%)	4(8.4%)	0	1(2.1%)
	Loss of appetite	7(14.6%)	3(6.25%)	2(4.2%)	1(2.1%)
	Loss of weight	7(14.6%)	1(2.1%)	1(2.1%)	0
	Vomiting	1(2.1%)	0	0	0

Sign	**Clubbing**	1(2.1%)	3(6.25%)	0	2(4.2%)
	Pallor	28(58.33%)	10(20.83%)	2(4.2%)	4(8.4%)
	Icterus	3(6.25%)	2(4.2%)	0	1(2.1%)
	Cyanosis	2(4.2%)	1(2.1%)	0	0
	Peripheral lymphadenopathy	12(25.0%)	8(16.6%)	2(4.2%)	2(4.2%)

Adenocarcinoma (ADC), Squamous cell carcinoma (SCC), Non-Small cell lungcarcinoma, not otherwise specified (NSCLC, NOS), Small cell lung carcinoma (SCLC)

In addition, cough was the most common symptom, found in 35 (72.9%) of patients, followed by chest pain 21 (48.8%), hemoptysis 14 (29.2%), and fever 14 (29.2%). Weight loss was found in nine (18.8%) of cases. Hemoptysis was most commonly reported with ADC and was found in eight (16.6%) of patients. All histological variants had a cough as the most common presenting symptom. Pallor was found in most patients 44 (95.7%), followed by clubbing in six (13.0%). Clubbing was mainly associated with three SCC cases (6.25%). However, two SCLC patients also had clubbing (4.2%). Peripheral lymphadenopathy was found in 24 (52.2%) in the form of supraclavicular and cervical lymphadenopathy. The majority 30 (62.5%) presented with a right- sided lesion. Bilateral lesions were found in two patients (4.2%) (Table II).

Table II: Specimen laterality and tumour site of studied cases

Radiological findings	**Variable**	**ADC (n=31)**	**SCC (n=10)**	**NSCLC, NOS (n=3)**	**SCLC (n=4)**
Tumor Laterality	**Left**	9(18.6%)	2(4.2%)	1(2.1%)	3(6.25%)
	Right	20(41.6%)	7(14.7%)	2(4.2%)	1(2.1%)
	Bilateral	2(4.2%)	1(2.1%)	0	0
Tumor site	**Upper lobe**	11(22.9%)	3(6.3%)	0	1(2.1%)
	Upper and middlelobe	1(2.1%)	0	0	0
	Upper lobe, lower lobe and bronchus	1(2.1%)	0	0	0
	Middle lobe	3(6.3%)	3(6.3%)	0	3(6.3%)
	Middle and lowerlobe	1(2.1%)	0	0	0

Lower lobe	12(25.0%)	4(8.4%)	0	0
Not specified	1(2.1%)	0	0	0
Not available	1(2.1%)	0	3(6.3%)	0

Adenocarcinoma (ADC), Squamous cell carcinoma (SCC), Non-Small cell lungcarcinoma, not otherwise specified (NSCLC, NOS), Small cell lung carcinoma (SCLC)

DISCUSSION

Several studies across various demographic cohorts in India have shown that lung cancer contributes significantly toward cancer morbidity and mortality [6]. In a study from Chhattisgarh, it was reported to be the third most common cancer in men after oral cavity and stomach cancers [7].

In our study, we analyzed 48 cases of lung carcinomas diagnosed from histopathology using small biopsies. Thirty-eight (79.2%) of these were endobronchial biopsies, two (4.2%) were transbronchial biopsies, and eight (16.7%) were CT/USG guided biopsies. Based on morphology and IHC examination, 44 (91.66) % were NSCLC, and four (8.3) % were SCLC. NSCLC cases needed to be further categorized into specific cell types for therapeutic reasons. Accordingly, we further classified the NSCLC cases morphologically using IHC.

We found that 65% (31/48) of cases were ADC, 21% (10/48) were SCC, and 6% (3/48) were NSCLC or NOS. Thus, the predominant histological type in our study was ADC, followed by SCC. In Western countries and most Asian countries, ADC has surpassed SCC as the most common histologic variant of lung cancer [8-10]. This shift seems to be attributable in part to the changing trends in smoking patterns and the increasing incidence of lung cancer in women and nonsmokers. However, most of the older and some recent publications from India still report SCC as the most common histological subtype [11].

Identification of the different subtypes is important for surgeons. However, the accuracy of small-biopsy subtyping of adenocarcinoma has not yet been completely validated [12]. The most common morphological pattern in ADC was solid (17, 54.83% of cases), followed by mucinous and lepidic (14, 45.17% of cases). The most common morphological pattern in SCC was nonkeratinizing (nine, 90% of cases), followed by keratinizing (one, 10% of cases). The solid subtype is associated with a poorer prognosis [13]. Routine adoption of subtype classification in clinical diagnosis and prospective validation in future studies is warranted [14].

Most of the cases in our study (16, 33.3%) came from the 51-60 age group. The mean age of diagnosis was 58.1 ± 12.2. To the best of our knowledge, lung carcinoma trends in relationship to age appear to have remained the same as in previous studies from India [15,16], in which the mean age reported is almost ten years less than in most Western studies [17,18].

In our study, the ratio of men to women was 4.3:1. Male predominance in our study was similar to that in other Indian reports but higher than in Western studies [15-18]. This may be a reflection of higher female smoking rates in the West or because men seek medical attention less frequently than women in India [19]. However, Mandal et al. found a men-to-women ratio of 1.09:1 [15].

In our study, the majority of patients were from urban areas (31, 64.6%), held private jobs (11, 22.9%), were middle-class (21, 43.75%), were nonsmokers (30, 62.5%), and had a history of COPD. Our findings contrasted with other studies from India where the study population belonged to a low socioeconomic status and showed a high prevalence of smoking (53%-89% in Indian studies and 87%-93% in Western studies) [17,18,20,21]. Other factors may contribute to lung cancer etiology, such as genetic predisposition, passive smoking, urban air pollution, and fumes from the traditional chulhas commonly used in rural India [22,23]. Additionally, in a prospective cohort study, Cohen et al. found a 30% to 50% increase in lung cancer rates associated with exposure to respirable particles [24]. Air pollution may have also been a contributing factor in the causation of lung cancer in the urban population in our study.

In our study, two smokers (4.2%) who had more than 30 pack-year smoking history were diagnosed with SCC. Other two cases which have same history diagnosed as ADC (2.1%) and one as SCLC (2.1%) respectively. The

association was statistically significant, with a p value of < 0.05. A history of smoking for more than 30 years has been reported to be the greatest risk factor for lung carcinoma [25]. Furthermore, a high prevalence of SCC was found in studies with a high prevalence of smoking, and a high prevalence of ADC was found in studies with a predominant population of nonsmokers [6-10,15]. This matches the predominance of ADC cases in our study.

Our study also found a history of previous lung infection in nine patients (18.6%) in the form of tuberculosis, histoplasmosis, and bacterial infection. Of these patients, seven (14.5%) had a history of mycobacterial infection, and one (2.1%) had a bacterial infection in the form of an abscess. However, this association was not statistically significant, with a p value of 0.164. Cicènas et al. also found that lung cancer was not significantly associated with mycobacterial tuberculosis infection [26]. However, a meta-analysis by Brenner et al. found that there was an increased risk of lung cancer in cases of COPD, emphysema, chronic bronchitis, pneumonia, and tuberculosis [27]. In our study, one patient with SCLC had a previous history of histoplasmosis.

We found that cough was the most common symptom in all histological variants (35, 72.9% of cases), followed by chest pain (21, 48.8%), hemoptysis (14, 29.2%), and fever (14, 29.2%). Hemoptysis was most commonly seen in

ADC (eight, 16.6%). Cough was the most common presenting symptom in all studies carried out in India related to lung carcinoma [2,6-11,15-17]. Furthermore, patients who presented with hemoptysis had predominantly lower- lobe lesions. Pallor was the most common sign, seen in 44 cases (95.7%), followed by clubbing in six cases (13.0%). It was most commonly associated with SCC. The majority of patients, 30 (62.5%), presented with a right-sided lesion. Hyun Woo Lu et al. reported a poor prognosis in left-sided adenocarcinomas [28]. However, Bio Jia could not find any difference in prognosis between left- and right-sided lesions [29]. In our study, three patients (75%) with SCLC presented with a left-sided lesion. Sahmoun et al. found more aggressive behavior with right-sided SCLC [30]. We found metastasis in four cases, of which three (75%) were ADC and one (25%) was SCC. The majority of patients (33.3%) had a lesion in the lower lobe.

LIMITATIONS OF STUDY

The institutional data may not represent the data from whole of Chhattisgarh. This was a cross-sectional study of one year duration so long-term follow-up was not possible.

CONCLUSIONS

Profiling of clinical signs and symptoms gives data that is useful for the early detection of lung carcinoma and is important because of the disease's aggressive nature. The onus of final diagnosis falls on the pathologist. However, the data from our study may be useful for the early screening of primary lung carcinoma. The literature also suggests that ADC is the most common variant. However, the risk factors for developing ADC are not as clear as the risk factors for SCC, namely smoking. We suggest further study on molecular profiling and treatment response for specific immunotherapy regimens in central India.

Conflict Of Interest: Nil

REFERENCE

1. Siegel R, Naishadham D, Jemal A: Cancer statistics, 2012. CA Cancer J Clin. 2012, 62:10-29. 10.3322/caac.20138
2. Dela Cruz CS, Tanoue LT, Matthay RA: Lung cancer: epidemiology, etiology, and prevention. Clin Chest Med. 2011, 32:605-44. 10.1016/j.ccm.2011.09.001
3. Hirsch FR, Wynes MW, Gandara DR, Bunn PA: The tissue is the issue: personalized medicine for non-small cell lung cancer. Clin Cancer Res. 2010, 16:4909-11. 10.1158/1078-0432.CCR-10-2005
4. Debnath D, Kakkar R: Modified BG Prasad Socio-economic Classification, Updated - 2020. Indian Journal of Community Health [Internet. 2020, 32:124-5. 10.47203/IJCH. 2020.v32i01.024

5. Travis WD, Brambilla E, Nicholson AG, et al.: The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification. J Thorac Oncol. 2015, 10:1243-1260. 10.1097/JTO.0000000000000630
6. Viswanathan R, Sen Gupta null, Iyer PV: Incidence of primary lung cancer in India. Thorax. 1962, 17:73-6. 10.1136/thx.17.1.73
7. Thakur H, Kawale S, Dhruw V, Singh L: Morbidity and mortality trend and pattern of cancer in newly started cancer unit of tertiary care hospital in Bilaspur, Chhattisgarh. Int J Med Sci Public Health. 2018, 7:638. 10.5455/ijmsph.2018.0102428042018
8. Mohan A, Garg A, Gupta A, et al.: Clinical profile of lung cancer in North India: A 10-year analysis of 1862 patients from a tertiary care center. Lung India. 2020, 37:190-7. 10.4103/lungindia.lungindia_333_19
9. Dhandapani S, Srinivasan A, Rajagopalan R, Chellamuthu S, Rajkumar A, Palaniswamy P: Clinicopathological Profile of Lung Cancer Patients in A Teaching Hospital in South India. J Cardiothorac Med. 2016, 4:440-443. 10.22038/JCTM.2016.6954
10. Dattatreya SP, Bansal R, Vamsy M, et al.: Clinicopathological profile of lung cancer at a tertiary care center. Indian Journal of Cancer. 2018, 55:273. 10.4103/ijc.IJC_455_17
11. Noronha V, Pinninti R, Patil VM, Joshi A, Prabhash K: Lung cancer in the Indian subcontinent. South Asian J Cancer. 2016, 5:95-103. 10.4103/2278-330X.187571
12. Huang KY, Ko PZ, Yao CW, et al.: Inaccuracy of lung adenocarcinoma subtyping using preoperative biopsy specimens. The. Journal of Thoracic and Cardiovascular Surgery. 2017, 154:332-339. 10.1016/j.jtcvs.2017.02.059
13. Paesmans M, Berghmans T, Dusart M, et al.: European Lung Cancer Working Party, and on behalf of the IASLC Lung Cancer Staging Project. Primary tumor standardized uptake value measured on fluorodeoxyglucose positron emission tomography is of prognostic value for survival in non-small cell lung cancer: update of a systematic review and meta-analysis by the European Lung Cancer Working Party for the International Association for the Study of Lung Cancer Staging Project. J Thorac Oncol. 2010, 5:612-9. 10.1097/JTO.0b013e3181d0a4f5
14. Tsao MS, Marguet S, Le Teuff G, et al.: Subtype Classification of Lung Adenocarcinoma Predicts Benefit from Adjuvant Chemotherapy in Patients Undergoing Complete Resection. JCO [Internet. 2015, 33:3439-46. 10.1200/JCO.2014.58.8335
15. Mandal SK, Singh TT, Sharma TD, Amrithalingam V: Clinico-pathology of lung cancer in a regional cancer center in Northeastern India. Asian PacJ Cancer Prev. 2013,14:7277-81. 10.7314/apjcp.2013.14.12.7277
16. Kaur H, Sehgal IS, Bal A, et al.: Evolving epidemiology of lung cancer in India: Reducing non-small cell lung cancer-not otherwise specified and quantifying tobacco smoke exposure are the key. Indian J Cancer. 2017, 54:285-90. 10.4103/ijc.IJC_597_16
17. Gadgeel SM, Ramalingam S, Cummings G, et al.: Lung cancer in patients < 50 years of age: the experience of an academic multidisciplinary program. Chest. 1999, 115:1232-6. 10.1378/chest.115.5.1232
18. Fu JB, Kau TY, Severson RK, Kalemkerian GP: Lung cancer in women: analysis of the national Surveillance, Epidemiology, and End Results database. Chest. 2005, 127:768-77. 10.1378/chest.127.3.768
19. Kabir Z, Connolly GN, Clancy L: Sex-differences in lung cancer cell-types? An epidemiologic study in Ireland. Ulster Med J. 2008:31-5.
20. Sharma PK, Bansal R: Profile of lung cancer in predominantly Bidi smoking rural population of northern Himachal Pradesh. Indian J Chest Dis Allied Sci. 2013, 55:75-8.

21. Baburao A, Narayanswamy H: Clinico-Pathological Profile and Haematological Abnormalities Associated with Lung Cancer in Bangalore, India. Asian Pacific Journal of Cancer Prevention. 2016, 16:8235-8. 10.7314/apjcp.2015.16.18.8235
22. Bruce N, Dherani M, Liu R, et al.: Does household use of biomass fuel cause lung cancer? A systematic review and evaluation of the evidence for the GBD 2010 study. Thorax. 2015, 70:433-41. 10.1136/thoraxjnl- 2014-206625
23. Chen G, Wan X, Yang G, Zou X: Traffic-related air pollution and lung cancer: A meta-analysis. Thorac Cancer. 2015, 6:307-18. 10.1111/1759-7714.12185
24. Cohen A J, Pope C A: Lung cancer and air pollution. Environmental Health Perspectives. 1995, 103:219-24.10.1289/ehp.95103s8219
25. Ettinger DS, Wood DE, Aisner DL, et al.: Non-Small Cell Lung Cancer, Version 5.2017, NCCN Clinical PracticeGuidelinesinOncology.JNatlComprCancNetw.2017,15:504-535. 10.6004/jnccn.2017.0050
26. Cicėnas S, Vencevičius V: Lung cancer in patients with tuberculosis. World Journal of Surgical Oncology. 2007, 5:22. 10.1186/1477-7819-5-22
27. Brenner DR, McLaughlin JR, Hung RJ. Previous Lung Diseases and Lung Cancer Risk: A Systematic Review and Meta-Analysis. PLoS One. 2011, 6: 10.1371/journal.pone.0017479
28. Lee H, Park YS, Park S: Poor prognosis of NSCLC located in lower lobe is partly mediated by lower frequency of EGFR mutations. Scientific reports. 2020, 10:14933. 10.1038/s41598-020-71996-7
29. Jia B, Zheng Q, Qi X, et al.: Survival comparison of right and left side non-small cell lung cancer in stage I- IIIA patients: A Surveillance Epidemiology and End Results (SEER) analysis. Thorac Cancer. 2019, 10:459- 71. 10.1111/1759-7714.12959
30. Sahmoun AE, Case LD, Santoro TJ, Schwartz GG: Anatomical distribution of small cell lung cancer: effects of lobe and gender on brain metastasis and survival. Anticancer Res. 2005, 25:1101-8.