

Research Article**Clinicopathological Profile of Patients with Lung Cancer Visiting Chest and TB Hospital Amritsar****Navin Pandhi¹, Balbir Malhotra², Nirmalchand Kajal³, Rahul R. Prabhudesai^{4*}, Nagaraja C.L.⁵, Nidhi Mahajan⁶**¹Assistant Professor, Chest and TB Department, Govt Medical College, Amritsar, Batala Road, Amritsar-143001, India²Professor, Chest and TB Department, Govt Medical College, Amritsar, Batala Road, Amritsar-143001, India³Professor and Head cum DMS, Chest and TB Department, Govt Medical College, Amritsar, Batala Road, Amritsar-143001, India⁴⁻⁶Junior Resident, Chest and TB Department, Govt Medical College, Amritsar, Batala Road, Amritsar-143001, India***Corresponding author**

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Abstract: Lung cancer is presently the most common malignant disease in the world. The relative frequency and clinicopathological profile of different histological subtypes of primary lung cancer have been changing in recent years. The present study was conducted to document the clinicopathological and radiological features of patients hospitalized with carcinoma lung to our center. A total of 150 patients with histopathologically proven cases of lung cancer, hospitalized between 2012 and 2014 at a tertiary care Hospital in Punjab, were analyzed. Out of the total 150 histologically proven cases of lung cancer, 73% were males with a male: female ratio was 2.7:1. Most patients were in the age group of 50-70 years with an overall mean age of 59.3 years. 60% of the patients were smokers and all of them were males. Cough (80%) and breathlessness (65%) were the commonest symptoms. Clubbing was the most common finding (50%) followed by vocal cord paralysis (43%). Squamous cell carcinoma (SCC) was the commonest histological type (41%) followed by Adenocarcinoma (36%). SCC most commonly presented in male smokers and adenocarcinoma in females and non-smokers. Most common radiological presentation was solitary pulmonary mass (97%) followed by pleural effusion (60%). Fibreoptic bronchoscopy (42%) and Transthoracic needle aspiration (33%) were the most efficient diagnostic procedures. SCC is the most common histological subtype of primary lung cancer. The relatively increased frequency of adenocarcinoma in our study as compared to other studies from India is probably due to higher proportion of nonsmokers.

Keywords: Lung cancer, Clinicopathological, Radiological, Smoking.

INTRODUCTION

Lung cancer has been reported to be presently the most common malignant disease (12.34% of all cancers) and the leading cause of cancer deaths (17.8% of all cancer deaths) in the world [1] in both sexes [2, 3] with the peak incidence between age 55 and 65 years [4]. It has been reported that in the developed countries, incidence and mortality from lung cancer in females is rising, whereas it has been found to be declining in males [5].

Lung cancer has been categorized into small cell carcinoma (SCLC) or non-small cell (NSCLC) lung carcinoma. The major histologic classes of NSCLC carcinoma include adenocarcinoma, squamous cell (SCC) carcinoma, large cell carcinoma and other less common tumor subtypes [4].

In India, lung cancer was initially thought to be infrequent [6]. In a study by Banker [7] in 1957 reported that lung cancer constituted 14.4% of all cancers in a review of 9,210 consecutive autopsies. Sirsat [8] in 1958 reported that it constituted one per cent of all cancers [8]. Viswanathan and Sengupta [9] reported that the incidence of lung cancer in hospital population was 27.4 per million in 1950, and in 1959 it increased to 78.6 per million. Later, many sporadic reports on the clinical and pathological features of lung cancer from different parts of the country have been reported [10-14].

Hospital based studies have also shown variability regarding risk factors, clinical presentations, radiological findings and histological diagnosis [4]. Progressive survival extension and increasing cigarette smoking has led to increased primary lung cancer in

India [15]. Smoking is reported to be the cause for more than 85% of the bronchogenic carcinoma cases [16].

The present study was conducted to document the clinicopathological and radiological features of patients hospitalized with carcinoma lung to our center.

MATERIALS AND METHODS

This study is a retrospective analysis of 150 lung cancer cases diagnosed from December 2012 to December 2014 in Chest and TB hospital. This is a tertiary care hospital which caters to one third of population of Punjab. Only those cases with confirmed histological or cytological diagnosis of primary bronchogenic carcinoma according to WHO classification and complete available data related to demographic profile, smoking status, clinicopathological and diagnostic details, are included in our database. Patients with secondary lung cancer, lymphoproliferative disease, malignant pleural effusion of unknown primary, or nonpulmonary site, sarcomatoid tumors and other rare varieties were excluded from this study. Radiological assessment was done in all patients. The diagnosis of primary bronchogenic carcinoma was established by fiberoptic bronchoscopy (FOB) and/or USG or CT-guided tissue sampling from lung mass, supplemented by pleural fluid analysis and cytological examination of regional lymph nodes and metastatic deposits as appropriate. Postero-anterior and lateral view of chest radiograph was taken in all patients. CT scan of thorax was done in majority of cases. But CT scan of abdomen, brain or other parts of body were done in restricted cases if suggestive symptoms of involvement was there as appropriate due to economic constrains. Hence data related to the exact item smoked (bidi/cigarette/hookah/cigar), family history of cancer and history of cancer in other regions of body are lacking from our database.

RESULTS

Our study included 150 histologically proven cases of lung cancer. Most patients were in the age group of 50-70 years. The youngest patient was aged 40 years and the oldest was aged 80 years. The overall mean age of the study subjects was 59.3 years. For male patients, the mean age was 61.77 and for female patients, it was 52.5 years. Of the 150 subjects, 110 were males (73%) and 40 were females (27%). The male: female ratio was 2.7:1.

Majority of the patients were current or ex smokers. Overall, 90 patients (60%) were smokers while 60 (40%) were non smokers. 82% of males were smokers (90 out of 110) and none of the females were smokers. The overall smoker: non-smoker ratio was 1.5:1. Of the 90 smokers encountered in the present study, 85 (94.4%) were exclusive beedi smokers, none of the patients were exclusive cigarette smokers and 5 patients (5.6%) smoked both beedi as well as cigarette.

None of the patients gave history of smoking any other forms of tobacco.

Cough with or without expectoration was the commonest symptom, being present in 120 patients (80%) followed by breathlessness in 98 patients (65%). Other common symptoms were chest pain (60%), loss of appetite (50%), loss of weight (46.6%) and hemoptysis (50%). Less common symptoms include fever, change of voice and dysphagia. Duration of symptoms was less than 3 months in 85 patients (56.6%), 3-6 months in 34 patients (23.3%) and more than 6 months in 30 patients (20%). In most cases, the duration of chest pain, hemoptysis, dysphagia or hoarseness of voice was less than 3 months where as cough, loss of appetite and breathlessness were present for varying periods of time, sometimes more than 6 months.

The most common finding was clubbing found in 50% of the cases. This was followed by vocal cord paralysis (hoarseness of voice) and atelectasis each in 43% of cases. Hoarseness of voice is mostly associated with left sided lesion. SCC being central lesion is the most common type noted causing hoarseness (46%). Peripheral lymphadenopathy was seen in 30 % cases in which supraclavicular lymph nodes were the most commonly involved. Other findings were mass lesion (26% cases), pleural effusion (20%), Superior Vena Cava (SVC) obstruction (13%), chest wall invasion (10%) and pneumothorax (3.3%).

SCC was the commonest histological subtype encountered(41%) although adenocarcinoma also occurred with a comparable frequency(36%). SCC presented at a later age (61 years) compared to adenocarcinoma (53.3 years) and was the most common carcinoma in males (52 out of 110 cases i.e. 46%) and smokers(60 out of 90 patients i.e. 66%). Adenocarcinoma was most common carcinoma in females (22 out of 40 cases i.e. 55%) and non-smokers (44 out of 60 patients i.e. 73%). SCC presented at a slightly older age than adenocarcinoma (62.3 years v/s 54 years). There were 20 cases(13%) of small cell carcinoma, 10 cases(6%) of poorly differentiated carcinoma and 4 cases (2%) of large cell carcinoma.

All the 150 patients had an abnormal chest radiograph at presentation. Most common pattern observed was solitary pulmonary mass in 145 cases (97%) followed by pleural effusion in 90 cases (60%), atelectasis or post obstructive consolidation in 60 cases (40%), unilateral hilar prominence in 50 cases (33%) and multiple nodules in 45 cases (30%). Less commonly observed appearances include mediastinal widening (20%), rib destruction (16%), pericardial effusion (10%), pancoast tumor (6%), solitary pulmonary nodule (3%). CT thorax was useful in confirming the chest x ray findings, especially hilar

prominence, pericardial effusion, rib destruction, mediastinal lymphadenopathy etc.

Fibreoptic bronchoscopy with endobronchial biopsy or brushing was the most useful investigation which yielded results in 64 out of 150 cases (42%). Sensitivity was highest for central tumors. Transthoracic needle aspiration of the tumour mass by

FNAC was the next most useful investigation. It detected malignancy in 49 cases (33%). It was very useful in detecting peripheral tumours. FNAC or biopsy of supraclavicular lymph nodes revealed malignancy in 24 cases (16%). Pleural fluid cytology was positive in 4 cases, whereas cytology from malignant sites led to diagnosis in 9 cases.

Table 1: Age and sex distribution of patients with lung carcinoma

Age group	Number of males	Number of females
<50 years	10	15
50-70 years	80	20
>70 years	20	5
Total	110(73%)	40(27%)

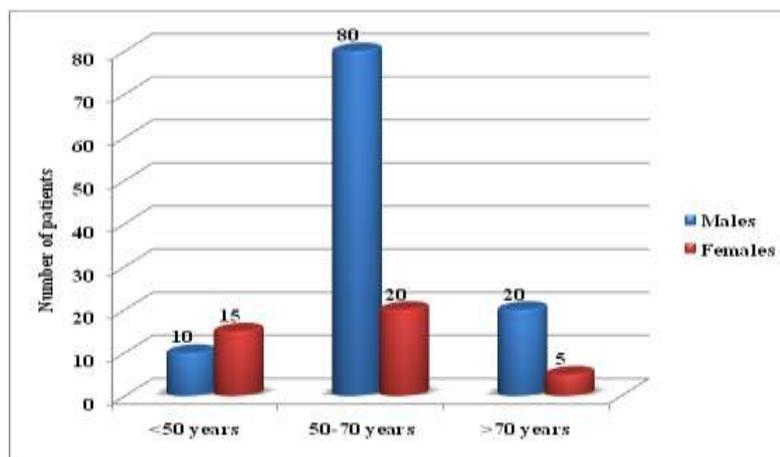


Fig. 1: Age and sex distribution of patients with lung carcinoma

Table 2: Symptoms of patients with lung carcinoma at presentation

Symptom	Number of cases	Percentage
Cough	120	80.0
Loss of appetite	75	50.0
Loss of weight	70	46.6
Breathlessness	98	65.3
Chest pain	90	60.0
Hemoptysis	75	50.0
Fever	35	23.0
Change of voice	65	43.0
Dysphagia	30	20.0
Others	45	29.5

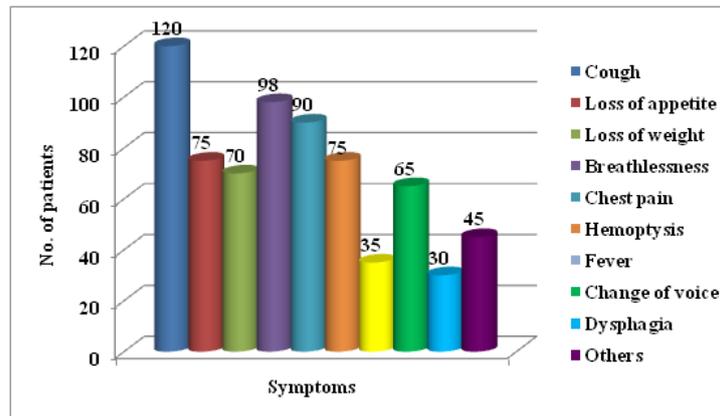


Fig. 2: Bar graph showing Symptoms of patients with lung carcinoma at presentation

Table 3: Examination findings of patients with lung carcinoma

Findings	Number of cases	Percentage
Clubbing	75	50
Peripheral lymphadenopathy	45	30
Superior venacaval occlusion	20	13.3
Stridor	0	0
Vocal cord paralysis	65	43.3
Chest wall invasion	15	10
Atelectasis/ post obstructive pneumonia	65	43.3
Mass lesion	40	26
Pleural effusion	30	20.1
Pneumothorax	5	3.3

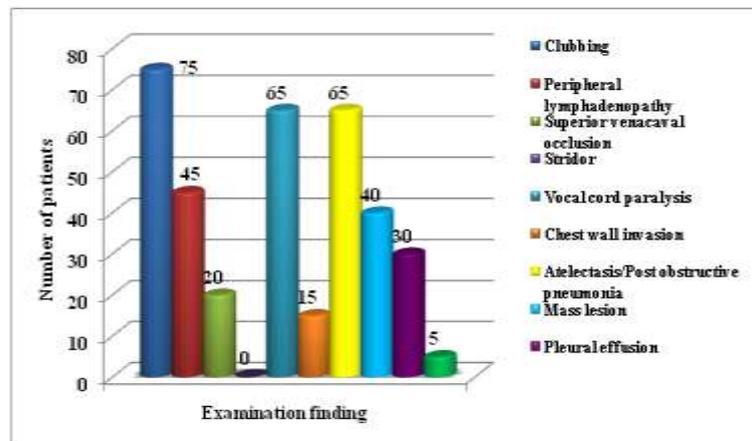


Fig. 3: Bar graph showing Examination findings of patients with lung carcinoma

Table 4: Radiological features of patients with bronchogenic carcinoma

Appearance	Number of cases	Percentage
Atelectasis/post obstructive consolidation	60	40
Solitary pulmonary mass	145	97
Solitary pulmonary nodule	5	3
Hilar prominence	50	33
Pleural effusion	90	0.6
Pneumothorax	5	3
Mediastinal widening	30	20
Cavitation	0	0
Multiple nodules/masses	45	30
Lymphangitis carcinomatosa	0	0
Pericardial effusion	15	10
Rib destruction	25	16.6
Pancoast tumour	10	6.6

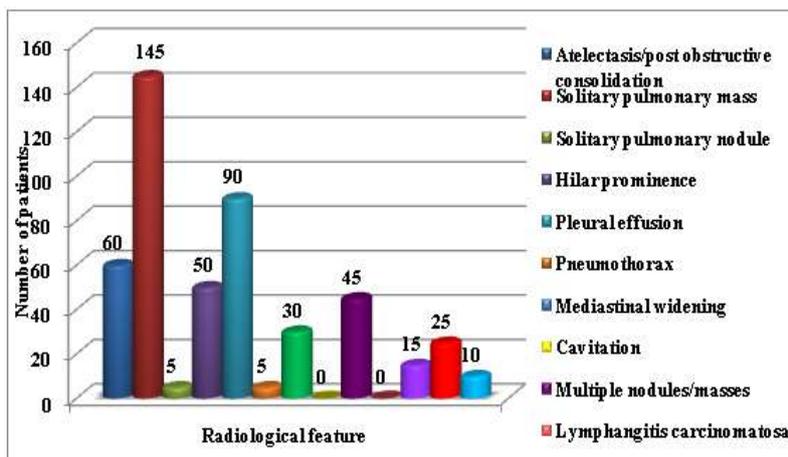
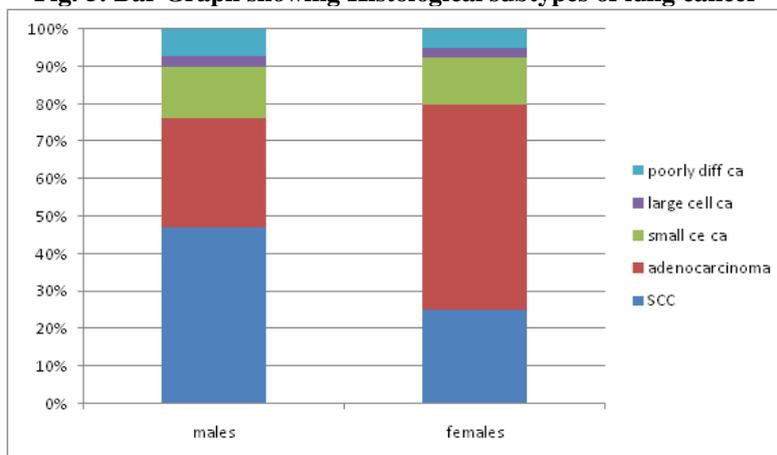


Fig 4: Bar graph showing Radiological features of patients with lung cancer

Table 5: Histological subtypes of carcinoma lung

Types	Males	Females	Total with percentage
Squamous cell carcinoma	52	10	62 (41%)
Adeno carcinoma	32	22	54 (36%)
Small cell carcinoma	15	5	20 (13%)
Large cell carcinoma	3	1	4 (3%)
Poorly differentiated carcinoma	8	2	10 (7%)

Fig. 5: Bar Graph showing Histological subtypes of lung cancer



DISCUSSION

Lung carcinoma is the most common carcinoma with a wide range of clinical symptoms. The symptoms of lung cancer can be nonspecific and thus it delays the diagnoses for patients who present with this disease [17]. Though most are nonspecific, however, some clues can be obtained from the history, thus raising the clinician's suspicion regarding the presence of lung cancer [18].

The mean age of patients with lung carcinoma has remained relatively constant over the years. The mean age in this study was 59.3 years which is similar to that reported by Guleria *et al.* [19], Dey *et al.* [20] and Bhurgri *et al.* [21]. The higher mean age reported by T Kanematsu *et al.* [22] may be attributed to the longer life expectancy in Japan.

The male: female ratio of patients of lung carcinoma has varied in different studies. The present study observed a male: female ratio of 2.7: 1 which was similar to that reported by T Kanematsu *et al.* [22]. This may be because of less prevalence of smoking among our study population because of religious prohibitions. A rising incidence in females is being observed in recent years. This may be due to increasing smoking habits in females. Secondly, the practice of cooking by these women is of the traditional style, using biomass fuel like cow dung and firewood.

The present study showed a smoker: non-smoker ratio of 1.5:1 in patients of lung carcinoma similar to Guleria *et al.* [19] and Jindal *et al.* [23] who have reported ratios of 2:1 and 2.4:1 respectively. These studies were conducted in areas with a high degree of

urbanisation with associated industrial and atmospheric pollution, patients being exposed to a variety of chemical carcinogens other than tobacco smoke. The present study has been conducted in that part of the country where the population is relatively non-smoking due to religious prohibitions. Smoking is also banned by law in public places and institutions.

Cough was the commonest presenting symptom in the present study, being present in 80% of cases. The result was similar to that reported by Jindal *et al.* [23] and Arora *et al.* [24]. This may be due to the fact that even early mucosal changes induced by the tumor can result in cough. Another explanation is that most patients are smokers and have associated chronic bronchitis. Breathlessness was the next common symptom in the present study, being present in 65% cases. Other symptoms like chest pain, loss of appetite, loss of weight and hemoptysis are also comparable in frequency to other studies [25, 26].

The most common examination finding in the present study was finger clubbing (50%) while Jindal *et al.* reported it in 35% of their patients [23]. The next most common sign was atelectasis/post obstructive consolidation seen in 43% cases similar to that reported by Arora *et al.* [24]. Vocal cord paralysis was also seen in similar number of cases.

Peripheral lymphadenopathy was seen in 30% of patients while Jindal *et al.* [23] and Arora *et al.* [24] reported it in 37.9% and 26% of their patients respectively. Mass lesion was found in 26% cases. Pleural effusion was present in 20% of patients in the present study and 25% of patients in the study conducted by Jindal *et al.* [23].

The most common finding on radiological examination observed in the present study was solitary pulmonary mass (97%) which was almost similar to that reported by various studies [27, 28]. This may be because most of the patients presented to us at advanced stage.

Second most common radiological finding was pleural effusion seen in 60% of patients in the present study while Jain *et al.* [29], Jindal *et al.* [23] and Dey *et al.* [20] reported it in 24%, 25% and 28% of their patients respectively. Left sided pleural effusion was most commonly seen (67%).

The incidence of atelectasis/post obstructive consolidation in the present study (40%) was similar to that found by Gupta *et al.* [30]. The other common findings were hilar prominence (33%) and multiple nodules (30%). Pericardial effusion was seen in 3 cases (10%) and was most commonly associated with adenocarcinoma.

The present study has observed that squamous cell carcinoma accounted for 41% of tumors, adenocarcinoma for 36%, small cell carcinoma for 13%, poorly differentiated carcinoma for 7% and large cell ca 3%. There has been some variation in the relative proportion of various histological subtypes in different studies. An increase in the relative proportion of adenocarcinoma has occurred in recent years. This may be due to changing smoking pattern, exposure to carcinogen other than tobacco smoke, change in the histologic criteria employed etc.

Lung cancer is being increasingly diagnosed in women. Adenocarcinoma has over taken SCC as the most common histological cell type [31]. However, in our hospital, SCC was still the commonest cell type seen, followed by adenocarcinoma and SCLC. This is similar to reports from other part of India [32-34]. The shift in the incidence of squamous cell carcinoma to adenocarcinoma may be associated with the switch from non-filtered to filtered cigarettes; the depth of inhalation had been altered [35]. Particularly, smoke from unfiltered strong cigarettes may be shallowly inhaled that results in chemical carcinogen deposition centrally in the bronchial area, giving rise to squamous cell carcinomas. Smoke from filtered milder cigarettes may be more deeply inhaled that result in deposition of carcinogen more peripherally, giving rise to adenocarcinomas [36]. Reduction in the nicotine content may also promote deeper inhalation as smokers attempt to compensate. The changes in cigarette composition has reduced the yield of carcinogenic polycyclic aromatic hydrocarbons (PAHs), inducers of squamous cell carcinomas, but increasing the yields of carcinogenic tobacco-specific N-nitrosamines (TSNAs) that are inducers of adenocarcinomas [37].

In our study, Fiberoptic bronchoscopy (FOB) achieved diagnosis in 42% of lung cancer patients. The high number of cases diagnosed by FOB in our study is due to the fact that almost three-fourth (76%) of the tumors were central.

According to simoff MJ [38] more than 50% of patients with advanced-stage lung cancer will have involvement of the central airways either by bulky endobronchial disease, extension into the airways, or extrinsic compression of the airways by the tumor or by lymphadenopathy. According to Popovich J [23], the yield with three or more bronchial biopsies should approach 100% for centrally located lesions.

Also the easy availability of fiberoptic bronchoscope and highly skilled bronchoscopists in our hospital, has increased the sensitivity of bronchoscopy.

TTNA has contributed to 33% of diagnosis of malignancy which is similar to that observed by Miravet *et al.* [39]. The lower sensitivity of TTNA as compared to bronchoscopy in our study is due to the

fact that only one fourth of the lesions were peripheral and this procedure depended on experienced radiologists for doing CT or USG guided aspiration. FNAC lymph node has led to diagnosis in 16% cases which is somewhat similar to that obtained by Jha *et al.* [40].

CONCLUSION

Squamous cell carcinoma is still the most common histological type of lung cancer in India mainly presenting in male smokers. Over the past few decades, adenocarcinoma is emerging as a dominant histological type with increased incidence in females due to the changing trends in smoking habits.

REFERENCES

1. Stewart BW, Kleihues P; World Cancer Report. IARC Press, Lyon, 2003: 265-269.
2. Emstein VL, Mustaechi P, Osanm KE; Epidemiology of lung cancer. In Murray JF, Nadel JA editors; Text Book of Respiratory Medicine. 2nd edition, Volume II, Saunders Company, Philadelphia, 1994: 1504-1552.
3. Blot WJ, Fraumeni JF Jr.; Changing patterns of lung cancer in the United States. *Am J Epidemiol.*, 1982; 115: 664-673.
4. Sundaram S, Sanyal N; Clinicopathological profile of bronchogenic carcinoma in a tertiary care hospital in eastern part of India. *Clinical Cancer Investigation Journal*, 2014; 3(3): 220-224.
5. Rawat J, Sindhvani G, Gaur D, Dua R, Saini S; Clinico-pathological profile of lung cancer in Uttarakhand. *Lung India*, 2009; 26(3): 74-76.
6. Nath V, Grewal KS; Cancer in India. *Ind J Med Res.*, 1935; 23: 149-190.
7. Banker DD; *J Post Grad Med.*, 1955; 1 : 108.(Quoted in Nagrath SP, Hazra DK, Lahiri B, Kishore B, Kumar R; Primary carcinoma of the lung: Clinicopathological study of 35 cases. *Indian J Chest Dis.*, 1970; 12 : 15-24)
8. Sirsat MV; Some aspects of the pathology of primary carcinoma of the lung. *J Postgrad Med.*, 1958; 4 : 6-14.
9. Viswanathan R, Gupta S, Iyer PVK; Incidence of primary lung cancer in India. *Thorax*, 1962; 17 : 73-76
10. Nagrath SP, Hazra DK, Lahiri B, Kishore B, Kumar R; Primary carcinoma of lung: Clinicopathological study of 35 cases. *Indian J Chest Dis.*, 1970; 12: 15-24.
11. Jindal SK, Malik SK, Dhand R, Gujral JS, Malik AK, Datta BN; Bronchogenic carcinoma in Northern India. *Thorax*, 1982; 37: 343-347.
12. Garg UK, Srivastava VK, Rajvanshi VS, Maheshwari BB; Carcinoma of the lung-A correlative cytological and histopathological study. *Indian J Cancer*, 1973; 10: 204-211.
13. Notani P, Sanghvi LD; A retrospective study of lung cancer in Bombay. *Br J Cancer*, 1974; 29: 477-482.
14. Narang RK, Dubey AL, Gupta MC, Raju S; Primary bronchial carcinoma-A clinical study. *Indian J Chest Dis Allied Sci.*, 1977; 19: 120-123.
15. Ginsberg RJ, Vokes EE, Raben A; Cancer of the lung. In DeVita VT, Hellman S, Rosenberg SA editors; *Cancer: Principles and practices of oncology*. Lippincott-Raven, Philadelphia, 1999: 849-950.
16. Carr DT, Holoye PY, Hong WK; Bronchogenic carcinoma. In Murray JF, Nadel JA editors; *Textbook of respiratory medicine*. 2nd edition, WB Saunders Company, Philadelphia, 1994: 1528-1596.
17. Hamdan Al Jahdali; Evaluation of the patient with lung cancer. *Annals of Thoracic Medicine*, 2008; 3(6): 74-78.
18. Mason RJ, Broaddus VC, Martin T, King TE Jr., Schraufnagel D, Murray JF, Nade JA; Murray and Nadel's *Textbook of Respiratory Medicine*. Elsevier Health Sciences, 2010.
19. Guleria JS, Gopinath N, Talwar JR, Bhargave S, Pande JN, Gupta RG; Bronchial carcinoma-An analysis of 120 cases. *J Assoc Physicians India*, 1971; 19: 251-255.
20. Dey A, Biswas D, Saha SK, Kundu S, Sengupta A; Comparison study of clinicoradiological profile of primary lung cancer cases: An Eastern India experience. *Indian J Cancer*, 2012; 49: 89-95.
21. Bhurgri Y, Bhurgri A, Usman A; Patho-epidemiology of Lung Cancer in Karachi (1995-2002). *Asian Pacific J Cancer Prev.*, 2006; 7: 60-64.
22. Kanematsu T, Hanibuchi M, Tomimoto H; Epidemiological and clinical features of lung cancer patients from 1999 to 2009 in Tokushima Prefecture of Japan. *The Journal of Medical Investigation*. 2010; 57:326-33.
23. Jindal SK, Behera D, Dhand R; Flexible fiberoptic bronchoscopy in clinical practice – A review of 100 procedures. *Ind J Chest Dis.*, 1990; 27:153-158.
24. Arora VK, Sitaraman ML, Ramkumar S; Bronchogenic carcinoma. Clinicopathological-pattern in South Indian population. *Lung India*, 1990; 7: 133-138.
25. Popovich J, Kvale PA, Eichenhorn MS; Diagnostic accuracy of multiple biopsies from flexible FOB: A comparison of central versus peripheral carcinoma. *Am Rev Respir Dis.*, 1982; 12: 5521-5523.
26. Cerfolio RJ; Perioperative care of the patient undergoing lung resection . In Grippi MA, Fishman AP, Elias JA, Fishman JA, Grippi MA, Senior RM, Pack AI; *Fishman's pulmonary diseases and disorders*, 4th edition, New York. Mc Graw Hill, 2008: 1740-1755.
27. Behera D, Balamugesh T; Lung cancer in India. *Indian J Chest Dis Allied Sci.* 2004; 46: 269-281.

28. Fraser RG, Pare JP, Pare PD. Neoplastic disease of the lung. In Fraser RG editor; *Diagnosis of diseases of the chest*. 3rd edition, WB Saunders, Philadelphia, 1989: 1327–4175.
29. Jain NK, Madan A, Sharma TN. Bronchogenic Cracinoma – Histologic Diagnosis and Roentgenographic Relationship. *Ind J Chest Dis*. 1987; 29:202-6.
30. Gupta RC, Behera D, Malik SK; Bronchogenic carcinoma in young adults below the age of 35 years. *Ind J Chest Dis.*, 1987; 29: 192-197.
31. Daniel Q, Gianlupi A, Broste S; The changing radiographic presentation of bronchogenic carcinoma with reference to cell type. *Chest*, 1996; 110: 1474–1479.
32. Jindal SK, Malik SK, Malik AK, Singh K, Gujral JS, Sodhi JS; Bronchogenic carcinoma: A review of 150 cases. *Indian J Chest Dis Allied Sci.*, 1979; 21: 59–64.
33. Notani P, Sanghvi LD; A retrospective study of lung cancer in Bombay. *Br J Cancer*, 1974; 29: 477–482.
34. Jindal SK, Malik SK, Datta BN; Lung cancer in Northern India in relation to age, sex and smoking habits. *Eur J Respir Dis.*, 1987; 70: 23–28.
35. Wynder E, Hoffmann E; Cigarette smoking and the histopathology of lung cancer. *J Natl Cancer Inst.*, 1998; 90: 1486–1488
36. Gadigil V, Krishnamurthy A, Ranganathan R, Sagar TG, Vijayalakshmi R; The relevance of Nonsmoking-associated lung cancer in India: A single-centre experience. *Indian Journal of Cancer*, 2012; 49(1): 82-88.
37. Djordjevic MV, Hoffmann D, Hoffmann I; Nicotine regulates smoking patterns. *Prev Med.*, 1997; 26: 435–440.
38. Simoff MJ: Endobronchial management of advanced lung cancer. *Cancer Control*. 2001; 8:337,
39. Miravet L, Paradis A, Pelaez S, Arnal M. Evolution of Lung Cancer in the North of the Province of Castellon, Spain, 1993-2002. *Arch Bronconeumol*. 2004; 40(12):553-7.
40. Jha VK, Roy DC, Ravindran P. Bronchogenic Carcinoma- A Clinicopathologic Study. *Ind J Chest Dis*. 1972; 14:78-85.