RESEARCH COMMUNICATION

Histological Pattern of Primary Malignant Lung Tumours Diagnosed in a Tertiary Care Hospital: 10 Year Study

Sheema Sheikh[1*], Azra Shah[1], Aijaz Arshed[2], Romana Makhdoomi[1], Rais Ahmad[1]

Abstract

Lung cancer is the most frequently diagnosed cancer in the world and is the second commonest cancer according to hospital based data from Kashmir, India. The objective of this study was to assess the histopathological pattern of primary malignant tumours of lung at a tertiary care hospital among smokers and non-smokers of both sexes. A total of 783 cases over a 10 years period, were studied, including 685 males and 98 females with a mean age at presentation of 57.8 years. The most common histological type of tumour in both sexes was squamous cell carcinoma (71.3 per cent), followed by small cell carcinoma (20.8 per cent), adenocarcinoma (2.6 per cent), bronchioalveolar carcinoma (1.8 per cent) while other tumours constituted 3.6 per cent. The two main histological subtypes of lung cancer found among smokers was squamous cell carcinoma (72.2 per cent) and small cell carcinoma 22.9 per cent. The smoker to non-smoker ratio was 2.14:1.

Keywords: Lung cancer histopathology - tertiary hospital - Kashmir, India

Asian Pacific J Cancer Prev, **11**, 1341-1346

Introduction

Lung cancer is the most frequently diagnosed major cancer in the world and is the leading cause of cancer-related mortality in both men and women(Brambella et al., 2001; Hussain, 2010). This is largely due to carcinogenic effects of cigarette smoke. Over the coming decades, changes in smoking habits will greatly influence lung cancer incidence and mortality as well as prevalence of various histological types of lung cancer (Travis, 2004; Hussain, 2010). Deaths due to lung cancer are more than those due to colorectal, breast and prostate cancers put together (Parkin et al., 1988; Khuri et al., 2001). Nearly 70 per cent of all new cases of lung cancer in the world occur in developed countries (Parkin et al., 1988) but incidence is rising at an alarming rate in developing countries also (Parkin, 1935).

In India, lung cancer was thought to be infrequent (Nath and Grewal, 1935), but as per the data given in first All India Report (AIR) 2001-2002, in males the lung cancer is leading site of cancer in 8 of the 12-population based cancer registries (PBCR's) (ICMR, 2001-2002). Lung cancer was reported to be the second most common malignancy in an earlier hospital based study from Kashmir valley (Dhar et al., 1993), the first being cancer of the upper gastrointestinal tract (Shah and Jan, 1990; Dhar et al., 1993). However, a recent study by Koul et al., (2010) reported that Srinagar, the summer capital of Jammu & Kashir has the highest incidence of lung cancer among males in India (Koul et al., 2010).

Lung cancer is almost exclusively a smoker's disease and both incidence and mortality are directly related to the degree of cigarette use that occurs in a population (Doll and Hill, 1954; Doll, 1956; Wingo et al., 1999) and this causal relationship has been shown in several studies (Doll and Hill, 1954; Doll, 1956; Peto et al., 1996; Wingo et al., 1999)

Materials and Methods

This study was conducted in the Department of Pathology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, over a 10 year period (1st July 1996 to 30th June, 2006). The study included a retrospective eight and a half and prospective one and a half years. 783 cases of malignant primarly lung tumours were studied during this period. For retrospective period (1st July 2006 to 31st December, 2004), all diagnosed cases of malignant primary tumours of lung were taken out from the records of the department and slides were reviewed according to W.H.O. 1999 histological classification of lung tumours. (16) In the prospective period (1st January 2005 to 30th June, 2006), all the resected specimens and bronchial biopsies received were followed, lung specimens operated for the diseases other than cancer and bronchial biopsies which turned out to be negative for malignancy were excluded from the study. All the metastatic lesions to the lung were likewise excluded from the study in both retrospective as well as prospective group. The patient particulars were recorded in detail on proformas which

*[1]Department of Pathology, [2]Department of Medicine, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, India. *For correspondence : drsheema7@gmail.com*

included age, sex, clinical findings, history of primary tumours anywhere else in the body, investigations like CT scan, USG and other relevant investigations were also noted. The smoking history was taken in prospective group and included 179 cases of which 122 were smokers and 57 non-smokers. However, no exact quantitative estimation of the lung cancer risk associated with number of cigarette smoked and the duration of smoking was done. Lung specimens were examined in detail grossly and a minimum of three sections were taken from the tumours. Bronchial biopsies were examined in detail included the number and size of bits. The tissue was processed as per standard procedure; 4-5µm thick sections were cut on a rotary microtome. Special stains like periodic acid Schiff's, reticulin and Masson's Fontana were performed where needed. Immunohistochemistry was also done wherever needed especially to rule out metastatic lesions.

Results

The present study was conducted on 700 bronchial biopsies (including CT guided and open lung biopsies) and 83 surgical specimens (Lobectomy, pneumonectomy).

Sex ratio

Males constituted 87.5 per cent (685 cases) and females 12.5 per cent (98 cases) of all malignant primary lung tumours and male to female ratio was 6.98:1

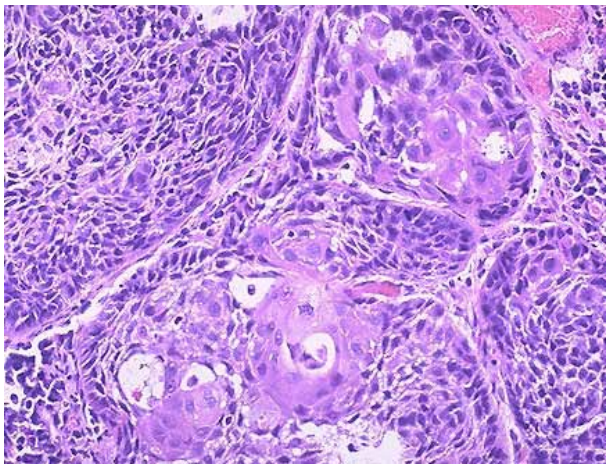

Figure 1. Squamous Cell Carcinoma

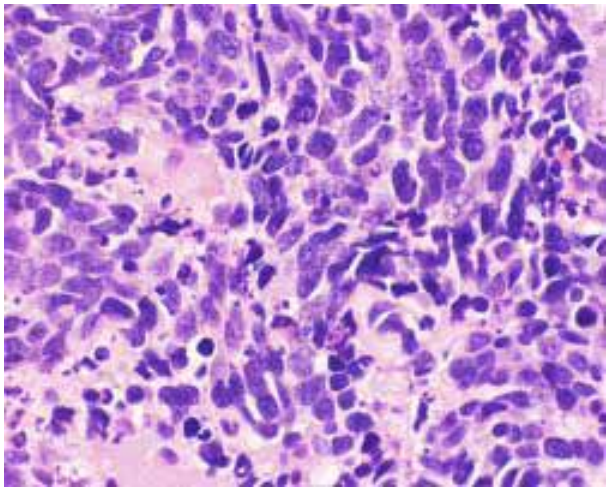

Figure 2. Small Cell Carcinoma

Age

The overall mean age of patients of primary lung cancer was 57.8 years with maximum number of cases seen between 60-69 years. The mean age for men was 58.3 years and for females, it was 53.9 years. The peak incidence of the disease was seen in age group of 60-69 years which constituted 47.9 per cent of all cases. The next peak was seen between 50 to 59 years (26.9 per cent). Minimum age among males was a 5 year old child diagnosed as hemangiopericytoma, minimum age among females was 20 years diagnosed as a malignant carcinoid. In both males as well as females, maximum age seen was 85 years. Only 3.5 per cent of cases were seen in patients less than 30 years old.

Histopathological type

The most common histological type of lung cancer was squamous cell carcinoma 71.26 per cent (558 cases), of which 48.57 per cent (271 cases) were well differentiated, 44.08 per cent (246 cases) were moderately well differentiated and 7.35 per cent (41 causes) were poorly differentiated. The second most common type of lung cancer was small cell carcinoma 20.81 per cent (163 cases), followed by adenocarcinoma 2.55 per cent (20 cases) and bronchoalveolar carcinoma 1.78 per cent (14 cases). Large cell anaplastic carcinoma, malignant carcinoid and miscellaneous tumours constituted 1.02 per cent (8 cases) each. Besides, there was a group of unclassifiable tumours; 0.5 per cent (4 cases) - Table 1. Among the miscellaneous group, there were 2 fibrosarcomas, 3 mature teratomas, 2 adenoid cystic carcinomas and 1 case of hemangiopericytoma.

Comparison between males and females in histological type of lung cancer

Majority of lung cancer in males in our study were having squamous cell carcinoma (74 per cent), followed by small cell carcinoma (20 per cent), adenocarcinoma (including bronchioalveolar type 3.06 per cent), whereas in females squamous cell carcinoma was seen in 52.04 per cent, followed by small cell carcinoma 27.5 per cent and adenocarcinoma including bronchioalveolar type (13.26 per cent) - Table 2. Carcinoid tumour was seen comparatively more commonly among females 4.08 per cent versus 0.58 per cent in males. Large cell anaplastic carcinoma comprising 1.02 per cent (8 cases) was seen

Table 1. Histological Distribution of Lung Cancer Cases Over 10 Year Period (July 96 to June 06)

Histological Diagnosis	Frequency	Percent
Squamous Cell CA	558	71.26
Small Cell CA	163	20.81
Adenocarcinoma	20	2.55
Bronchioalveolar CA	14	1.78
Large Cell Anaplastic CA	8	1.02
Carcinoid Tumour	8	1.02
Miscellaneous Tumours	8	1.02
Unclassifiable Tumours	4	0.54
Total	783	100

The most common histological type of Lung cancer is squamous cell carcinoma (71.26%) followed by small cell carcinoma (20.81%).

Table 2. Distribution of Malignant Lung Tumours by Age, Sex and Histological Diagnosis

Age	Squamous Cell CA			Small Cell CA			Adenocarcinoma		
(Years)	Male	Female	Total	Male	Female	Total	Male	Female	Total
0-19	0	0	0	0	0	0	0	0	0
	1	1	2				1	1	2
20-29	(50%)	(50%)	(100%)	0	0	0	(50%)	(50%)	(100%)
	0.19%	1.96%	0.35%				8.3%	12.5%	10%
	9	2	11	2	3	5	1	1	2
30-39	(81.8%)	(18.2%)	(100%)	(40%)	(60%)	(100%)	(50%)	(50%)	(100%)
	1.77%	3.93%	1.97%	1.47%	11.2%	3.06%	8.3%	12.5%	10%
	57	9	66	17	6	23	3	1	4
40-49	(86.3%)	(13.7%)	(100%)	(73.9%)	(26.1%)	(100%)	(75%)	(25%)	(100%)
	11.3%	17.6%	11.82%	12.5%	22.2%	14.11%	25%	12.5%	20%
	138	12	150	41	7	48	3	1	4
50-59	(92%)	(8%)	(100%)	(85.4%)	(14.6%)	(100%)	(75%)	(25%)	(100%)
	27.2%	23.5%	26.9%	30.1%	25.9%	29.4%	25%	12.5%	20%
	254	22	276	67	9	76	4	1	5
60-69	(92%)	(8%)	(100%)	(88.2%)	(11.8%)	(100%)	(80%)	(20%)	(100%)
	50.1%	43.1%	49.5%	49.3%	33.3%	46.7%	33.4%	12.5%	25%
	44	4	48	6	2	8		3	3
70-79	(91.6%)	(8.4%)	(100%)	(75%)	(25%)	(100%)	0	(100%)	(100%)
	8.67%	7.85%	8.6%	4.4%	7.4%	4.9%		37.5%	15%
	4	1	5	3		3			
≥80	(80%)	(20%)	(100%)	(100%)	0	(100%)	0	0	0
	0.78%	1.96%	0.89%	2.2%		1.8%			
	507	51	558	136	27	163	12	8	20
Total	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)
	90.9%	9.14%	71.3%	83.4%	16.6%	20.8%	60.0%	40%	2.55%

Table 3. Distribution of Total Lung Cancer Patients from 1st Jan 05 to 30th June 06 as per Histological Diagnosis, Gender and Smoking History

Histological Diagnosis	Male			Female			Overall Total		
	Smoker	Non-Smoker	Total	Smoker	Non-Smoker	Total	Smoker	Non-Smoker	Total
	86	29	115	2	16	18	88	45	133
Squamous Cell CA	(74.8%)	(25.2%)	(100%)	(11.2%)	(88.8%)	(100%)	(66.2%)	(33.8%)	(100%)
	72.8%	87.8%	76.15%	50%	66.6%	64.3%	72.2%	78.9%	74.3%
	27	3	30	1	5	6	28	8	36
Small Cell CA	(90%)	(107%)	(100%)	(16.7%)	(83.3%)	(100%)	(77.7%)	(22.3%)	(100%)
	22.9%	9.1%	19.86%	25%	20.9%	21.4%	22.9%	14.04%	20.1%
	5	1	6	1	3	4	6	4	10
Others	(83.3%)	(16.7%)	(100%)	(25%)	(75%)	(100%)	(60%)	(40%)	(100%)
	4.3%	3.1%	3.99%	25%	12.5%	14.3%	4.9%	7.02%	5.6%
	118	33	151	4	24	28	122	57	179
Total	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)
	78.2%	21.8%	100%	14.3%	85.7%	100%	68.15%	31.85%	100%
χ^2	3.325 (P>0.05)			0.551 (P>0.05)			2.085 (P>0.05)		

only in males.

Smoking and histological type

Smoking parameter was studied in the prospective group only (1½ years) and included 179 cases of which 122 were smokers and 57 non-smokers. The smoker to non-smoker ratio was 2.14:1. the two main histological sub-types of lung cancer found among smokers were: squamous cell carcinoma 72.2 per cent and small cell carcinoma 22.9 per cent. The smoker to non-smoker ratio among males was 3.57:1, whereas among females, it was 0.6:1 (Table 3).

Discussion

Primary lung cancer in India was reported from rare to extremely infrequent in the earlier part of 20th century (Nath and Grewal, 1935). An increasing trend in its incidence was recognized by Vishwanathan et al (1962) who analysed 1570 cases admitted during 1950-59 in several teaching hospital of Delhi (Vishwanathan et al., 1962) and now with increasing prevalence of smoking, lung cancer has reached epidemic proportions in India (Behera and Balamugesh, 2004). In Kashmir valley, a study of 462 patients of lung cancer by Koul et al., (2010) revealed crude incidence of disease to be 4.01 per 100,000 of population and Srinagar district has the highest incidence of lung cancer among males in Kashmir. The present study was undertaken as our Institute is a tertiary care hospital and most of the patients of suspected lung malignancy are referred to our Institute for further evaluation and treatment. Table 4 shows the comparative clinical features and cell type pattern in different Indian studies. Of the 783 cases of primary malignant lung tumours, the most common histological type was squamous cell carcinoma (71.26 per cent), followed by small cell carcinoma (20.81 per cent), adenocarcinoma (2.55 per cent), bronchioalveolar

Table 4. Comparative Clinical Features and Cell Type Patterns in Different Indian Studies

S. No.	Authors	Total	M:F	Age (Yrs.)	Sm:NS	Per cent of histological types			
						Squam	Anapla	Adeno	Uncla
01.	Vishwanathan et al 1962[17]	95	-	-	-	50.5	-	28.4	21.1
02.	Wig et al 1961[28]	65	4.9	55.8	-	-	-	-	-
03.	Basu et al 1971[29]	24	7	48.3	5	62.5	8.3	25	4.2
04.	Sinha 1961[30]	33	4.5	57.1	-	-	-	-	-
05.	Karai et al 1967[31]	100	24	52.1	-	41	-	20	39
06.	Shankar 1967[32]	20	All M	54	5.7	73.3	6.7	20	
07.	Nagrath et al 1970[33]	35	4	47.7	1.9	25.7	-	34.3	40
08.	Reddy et al 1970[27]	46	6.4	50	0.1	50	25	25	-
09.	Guleria et al 1971[34]	120	7.6	57.2	2	46.2	36.5**	17.3	-
10.	Jha et al 1971[35]	25	2.9	46.6	5.3	44	20	20	20
11.	Malik et al 1976[36]	136	5.2	48.5	3.5	40.4	21.3	16.9	7.3
12.	Narang et al 1977[37]	58	8.7	51.3	4.8	37.9	51.8	10.4	-
13.	Jindal et al 1979[38]	150	5.5	51.7	2.4	32.5	19.3	15.8	21.9
14.	Nafae et al 1973[19]	25	All M	51	7.3	56	20	12	12
15.	Notani et al 1974[39]	520	-	-	3.9	27.5	11.3**	7.3	53.4
16.	Garg et al 1973[40]	82	-	-	-	46.3	28	20.7	-
17.	Malhotra et al 1986[41]	70	7.8	49.6	4.8	50	17**	14.3	17.1
18.	Jindal and Behera 1990[26]	1009	4.5	54.3	2.7	34.3	27.6**	25.9	12.2
19.	Arora et al 1990[42]	100	4.05	40-60	1.2	27	1	21	41
20.	Rajasekaran 1993[25]	232	7.9	53	2.7	72	4.3	3.9	15.1
21	Gupta et al 1998[43]	279	7.41	56.7	4.5	42.3	32.2	19.9	5.6
22.	Thippanna et al1998[44]	160	8.4	40-60	4	67.5	8.8	18.7	5.1
23.	Gupta et al 2001[45]	265	7.8	50-70	3.6	60	21.5	16.2	2.3
24.	Koul et al 2010[11]	462	6.1:1	57.6	4.6:1	67.5	20.8	3.03	4.7
25.	Present study	783	6.98	57.88	2.14	71.2	21.8**	4.3	0.54

M:F= male:female, Sm = Smoke, NS = No- smoker, Squam = Squamous cell carcinoma; Adeno = Adenocarcinoma, Anaplastic = Small cell (OAT cell type) carcinoma; **includes large cell carcinoma, +++ for 179 cases only

carcinoma (1.78 per cent) and other constituted 3.75 per cent. Nafae et al., (1997) and Khan et al., (2006) from Kashmir valley also showed squamous cell carcinoma to be most common followed by small cell carcinoma and adenomacarcinoma. In the initial decades of smoking caused epidemic of lung cancer worldwide, squamous cell carcinoma was most frequent type of lung cancer among smokers and small cell carcinoma was the next most frequent (Alber and Samet, 2003). In the last 1970's, the first evidence of a shift towards a predominance of adenocarcinoma was noted and now adenocarcinoma of the lung is the most common histological type of lung cancer in women and in many studies in men(Vincent et al., 1977; El-Torky et al., 1990; Alber and Samet, 2003) as well in Western countries. Thun et al concluded that increase in lung adenocarcinoma since the 1950's is more consistent with changes in smoking behaviour and cigarette design than with diagnostic advances (Thun et al., 1997). In India, squamous cell carcinoma is still the commonest histological type of lung cancer in contrast to Western countries, although adenocarcinoma is becoming more common (Behera and Balamugesh, 2004). Two studies conducted by Rajasekaran (1993) and Jindal and Behera () showed almost comparable results, regarding the distribution of various major histological types of primary malignant lung tumours as that of ours.

The sex ratio in our study was 6.98:1 (685 males and 98 females). Nafae et al. (1997) and Khan et al. (2006) from the valley also showed males being predominantly affected by the disease. Koul et al., (2010) from the valley reported a male to female sex ratio of 6.1:1. It is a global observation that lung cancer has a higher incidence in men than in women. The high sex ratio in our study correlates well with other studies from rest of the country (Jindal and Behera), Rajasekaran et al., (1993) and that of Reddy et al., (1972).

The overall mean age in our patients was 57.86 years being 58.33 years in males and 53.94 years in females. The peak incidence of the disease was seen in age group of 60-69 years (47.9 per cent) and next peak was seen between 50-59 years (26.9 per cent). Koul et al., (2010) reported mean age for men as 58.28 years and for females as 53.26 years, whereas in most of the reported studies from India, the average age lung cancer in approximately 55 years (Jindal and Behera). Behera and Balamugesh, (2004) divided the demographic data of lung cancer patients from all the Indian studies into two groups i.e. studies before and after 1985 and concluded that lung cancer has remained predominantly a disease of males with a male to female ratio ranging from 5.76:1 to 6.67:1. The mean age was 54.6 years in males and 52.8 years in females which has remained more or less the same over the years (Jindal and Behera). The demographic pattern of lung cancer in India is similar to that observed in Western countries 40 years ago (Behaea and Balamugesh, 2004; Jindal and Behera)

In our study, squamous cell carcinoma is the most common histological type in both sexes. The relative frequency of small cell cancer and adenocarcinoma is higher in females as compared to males in our study.

Regarding sex distribution of other histological types of tumours, carcinoid tumour was seen comparatively more commonly among females (4.08 per cent) versus 0.58 per cent in males. Besides, in our study, large cell anaplastic tumour comprised 1.02 per cent and was seen

only in males. Regarding smoking, this parameter was studied in the prospective group only (1½ years) and included 179 non-smokers. The smoker to non-smoker ratio was 2.14:1. The two main histological sub-types of lung cancer among smokers was squamous cell carcinoma: 72.2 per cent and small cell carcinoma: 22.9 per cent). The two histological types of lung cancer are largely influenced by smoking which is evident in our study also. Our smoker to non-smoker ratio correlates well with that of Jindal and Behera and Rajasekaran et al., (1993).

In conclusion, although the advantage of present study is that sample used for assessment of the data is assumed to be closest approximation of the patients attending our tertiary care hospital. The main limitation of our study is that not all the cases treated in our Institute reach the Pathology department as many are diagnosed at other places and referred here or many patients will be diagnosed on clinical and radiological findings and may be terminally ill and thus not subjected to biopsy. Such cases will be missing in our study. Another limitation is that smoking history was not available in retrospective group. Only small number of patients in prospective group were studied and also the exact amount and duration of cigarettes smoked was not assessed.

This study shows that lung cancer is predominantly a disease of males in Kashmir, peak incidence is seen in sixth and seventh decade of life. Squamous cell carcinoma is most common histological type in both sexes and in both smokers as well as non-smokers.

References

Alber Anthony J and Samet JM (2003). Epidemiology of lung cancer. *Chest*, **123**, 21S-49S.

Arora VK, Seetharaman ML, Ramkumar S, et al (1990). Bronchogenic carcinoma: clinicopathologic pattern in South Indian population. *Lung India*, **7**, 133-8.

Basu BK and Gosh TN (1971). A study of bronchogenic carcinoma. *Ind J Chest Dis*, **13**, 1-9.

Behera D and Balamugesh T (2004). Lung cancer in India. *Indian J Chest Dis Allied Sci*, **46**, 269-81.

Brambella E et al (2001). The new world health organization classification of lung tumours. *Eur Respir J*, **18**, 1059-68.

Dhar GM, Shan GN, Nahsed B, et al (1993). Epidemiological trend in the distribution of cancer in Kashmir valley. *J Epidemiol Commu Hlth*, **47**, 290-2.

Doll R (1956). Lung cancer and other causes of deaths in relation to smoking. A second report in the mortality of British doctors. *Br Med J*, **2**, 1071-81.

Doll R, Hill AB (1954). The mortality of British doctors in relation to their smoking habits: a preliminary report. *Br Med J*, **1**, 1451-5.

El-Torky M, et al (1990). Significant changes in distribution of histologic types of lung cancer: a review of 4928 cases. *Cancer*, **65**, 2361-7.

Garg UK, Srivastava VK, Rajwanshi VS, et al (1973). Carcinoma of lung. A correlative cytological and histopathological study. *Ind J Cancer*, **10**, 204-11.

Guleria JS, Gopinath N, Talwar JR, et al (1971). Bronchial carcinoma: an analysis of 120 cases. *J Ass Phy Ind*, **19**, 25-5.

Gupta D, Boffeta P, Gab Orieau V, et al (2001). Risk factors of lung cancer in Chandigarh, India. *Ind J Res*, **113**, 142-50.

Gupta RC, Purohit SD, Sharma MP, et al (1998). Primary bronchogenic carcinoma: clinical profile of 279 cases from Mid-West Rajasthan. *Ind J Chest Dis Allied Sci*, **40**, 109-16.

Hussain Aliya N (2010). The lung Robbin's and Cotran's pathologic basis of disease. *Saunders Company*, **8**, 721-34.

ICMR (2001-2002). Cancer incidence and leading sites of cancer in population based cancer registries: development of an atlas of cancer in India. *ICMR*, First AIR 2001-2002, 11-8.

Jha VK, Roy DC and Ravindran P (1972). Bronchogenic carcinoma: a clinicopathological study. *Ind J Chest Dis*, **14**, 78-85.

Jindal SK Behera D (1994). Clinical spectrum of primary lung cancer. Review of Chandigarh experience of 10 years. *Lung India*, **8**, 94-8.

Jindal SK, Malik SK, Malik AK, et al (1979). Bronchogenic carcinoma. A review of 150 cases. *Ind J Chest Dis Allied Sci*, **21**, 59-64.

Karai GS, Nath HK, Paul G, et al (1967). Carcinoma of the lung: a record and analysis of 100 cases. *Ind J Cancer*, **4**, 105-13.

Khan NA, Afroz F, Lone MM, et al (2006). Profile of lung cancer in Kashmir, India: a 5-year study. *Indian J Chest Dis and Allied Sci*, **48**, 187-190.

Khuri FR, Herbst RS, Fossella FV (2001). Emerging therapies in non-small cell lung cancer. *Ann Oncol*, **12**, 739-44.

Koul PA, Kaul SK, Sheikh MM, et al (2010). Lung cancer in Kashmir valley. *Lung India*, **25**, 131-7.

Malhotra V, Malik R, Beohar PC, et al (1986). Tumours of the lung: histomorphological study. *Ind J Chest Dis Allied Sci*, **28**, 28-40.

Malik AK, Aikat BK (1976). Primary pulmonary neoplasms. A histopathological study. *Ind J Cancer*, **13**, 149-55.

Nafae A, Misra SP, Dhar SN, et al (1973). Bronchogenic carcinoma is Kashmir valley. *Ind J Chest Dis*, **15**, 285-95.

Nagrath SP, Hazra DK, Lahiri B, et al (1970). Primary carcinoma of lung: clinicopathological study of 35 cases. *Ind J Chest Dis*, 15-24.

Narang RK, Dubey AL, Gupta MC, et al (1977). Primary bronchial carcinoma. A clinical study. *Ind J Chest Dis Allied Sci*, **19**, 120-3.

Nath V, Grewal KS (1935). Cancer in India. *Ind J Med Res*, **23**, 149-90.

Notani P, Sanghavi LD (1974). A retrospective study of lung cancer in Bombay. *Br J Cancer*, 477-82.

Parkin DM (1989). Trends in lung cancer incidence. *Worldwide Chest*, **96**, 55-9S.

Parkin DM, Laara E, Muir CS (1988). Estimates of the worldwide frequency of sixteen major cancers in 1980. *Int J Cancer*, **41**, 184-93.

Peto R, Lopez AD, Boreham J, et al (1996). Mortality from smoking worldwide. *Br Med Bull*, **52**, 12-21.

Rajasekaran, Manickam S, Visanthan, et al (1993). Pattern of primary lung cancer: a Madras study. *Lung India*, **11**, 7-11.

Reddy DB, parasthamurthy D and Satyavathi S (1972). Bronchogenic carcinoma. A clinicopathologic study. *Ind J Chest Dis*, **14**, 86-9.

Shah Azra and Jan GM (1990). Pattern of cancer at Srinagar (Kashmir). *Ind J Pathol Microbiol*, **33**, 119-23.

Shankar PS (1967). Bronchogenic carcinoma. *Ind J of Chest Dis*, **9**, 161-4.

Sinha BC (1961). Lung cancer: clinical features. *Ind J Chest*, **3**, 219.

Thippana G, Venu K, Gopal KV, et al (1999). A profile of lung cancer patients in Hyderabad. *J Indian Med Assoc*, **97**, 357-9.

Thun MJ, Lally CA, Flannery JT, et al (1997). Cigarette smoking and changes in the histopathology of lung cancer. *J Natl Cancer Inst*, **89**, 1580-6.

Travis WD (2004). World Health Organization classification of tumours. Lyon, IARC Press.

Travis WD, Colby TV, Corrin B, Shimosato Y, Brambilla E, for

the World Health Organization. Histologic types of lung and pleural tumours, 3rd ed. Berlin: Springer 1999.

Wig KL, Lazaro EJ, Gadekar NG, et al (1961). Bronchogenic carcinoma (Clinical features and diagnosis). *Ind J Chest Dis*, **3**, 209-18.

Wingo PA, Ries LA, Giovino GA, et al (1999). Annual report to the nation on the status of cancer, 1973-1996, with a special section on lung cancer and tobacco smoking. *J Natl Cancer Inst*, **91**, 675-90.

Vincent RG, Pickren JW, Warren W, et al (1977). The changing histopathology of lung cancer: a review of 1682 cases. *Cancer*, **39**, 1647-55.

Vishwanathan R, Gupta Sen, Krishna PV (1962). Incidence of primary lung cancer in India. *Thorax*, **17**, 73-6.