REVIEW ARTICLE

Lung Cancer in India

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ABSTRACT

Background. Lung cancer is one of the commonest malignant neoplasms all over the world. It accounts for more cancer deaths than any other cancer. It is increasingly being recognized in India.

Methods. We did a systematic review of the published studies on epidemiology, diagnosis and treatment of lung cancer in India. Literature from other countries was also reviewed.

Results. With increasing prevalence of smoking, lung cancer has reached epidemic proportions in India. It has surpassed the earlier commonest form of cancer, that of oropharynx, and now is the commonest malignancy in males in many hospitals. In addition to smoking, occupational exposure to carcinogens, indoor air pollution and dietary factors have recently been implicated in the causation of lung cancer. Squamous cell carcinoma is still the commonest histological type in India in contrast to the Western countries, although adenocarcinoma is becoming more common. Molecular genetics of lung cancer has opened up new vistas of research in carcinogenesis. Various modalities for early detection through screening are being investigated. Majority of the patients have locally advanced or disseminated disease at presentation and are not candidates for surgery. Chemotherapy applied as an adjunct with radiation improves survival and the quality of life. New anticancer drugs, which have emerged during the last decade, have shown an improved efficacy- toxicity ratio.

Conclusions. In view of our large population, the burden of lung cancer will be quite enormous in India. Drastic measures aimed at discouraging people from smoking must be taken to reduce the morbidity and mortality due to lung cancer.

Key words : *Lung Cancer, Epidemiology, Smoking, Air pollution, Chemotherapy.*

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INTRODUCTION

Lung cancer was considered to be rare in the beginning of the century[1] but has now reached almost epidemic proportions. It is the leading cause of cancer deaths in developed countries and is also rising at alarming rates in developing countries[2]. Deaths due to lung cancer are more than those due to colorectal, breast and prostate cancers put together. Incidence and mortality from lung cancer in females is rising while it is declining in males in developed countries. This is the single most devastating cause of cancer-related deaths[2] with

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approximately 1.5 million cases world-wide and more than 1.3 million cancer-related deaths in 2001. The five-year survival rate for lung cancer has improved only marginally from 5% in the late 1950s to 14% by 1994. This is in contrast to the five years survival rate of 52% for some other cancers. Lung cancer is responsible for about one million deaths per year at present and it will rise to three millions per year by the year 2010.

WORLD SCENARIO

There is a great variation in the prevalence of lung cancer in different geographical areas. Nearly 70% of all the new cases of lung cancer in the world occur in the developed countries[3]. USA, Canada, New Zealand (Maori population) and Europe have the highest incidence (>50 per 10^5 population) followed by China, Ireland, Malta, Spain, Australia, and New Zeland (non - Maori population) with a moderate incidence (35-50 per 10^5 population) and low incidence (<35 per 10^5 population) countries include Utah (USA), Latin America, most Asian countries, lceland, Norway and Sweden[4]. This is the most frequent tumour in males, and 2nd or 3rd most common in females. In the US alone, there were about 1,64,100 new cases in 2000, of which 70, 000 were in the metastatic stage (stage IV) and another 70,000 were locally advanced (stage IIIA and IIIB disease)[2]. In the European Union, the crude incidence of lung cancer is 52.2 cases per 10^5 per year and the death rate is 48.7 per 10^5 per year. For men, the rates are 79.3 and 78.3 and for women, 21.6 and 20.5 respectively per 10^5 per year. Non-small cell lung cancer accounts for about 80% of all lung cancer cases[5,6].

The incidence rates in France are close to the average rates observed in Europe. Between 1985 and 1995, as a result of changes in tobacco consumption, the incidence rates increased by 56% in women and by 5% in men under the age of 65. In 1995, lung cancer led to 23,900 deaths in France (mortality rate standardised to Europe: $36.6/10^5$). Eighty-five percent of deaths due to lung cancer occurred among men. Prognosis of lung cancer remains poor and has not improved appreciably over the last few decades. Fifty-eight per cent of all patients died during the first year and 82% during the three years following the diagnosis[7].

During 1977-86, the incidence and mortality of lung cancer ranked first among cancers at all sites in Beijing and has been on the increase from year to year[8]. The annual average crude incidence rate of cancer was $31.3/10^5$ in males during 1982-84 compared to a world standard rate of $33.0/10^5$. Incidence due to lung cancer accounted for 20.3% of all male cancer cases. The crude incidence rate was $22.8/10^5$. Incidence due to lung cancer accounted for 16.1% among all female cancer cases. Female mortality rate due to lung cancer in Beijing is the highest compared to other countries of the world.

Janssen-Heijinen *et al*[9] did a survival analysis of 173,448 lung cancer cases diagnosed between 1985 and 1989 in 44 population-based cancer registries, participating in the EUROCARE study in Europe. Relative one-year survival rates for patients with lung cancer varied from 24% to 40%, being the highest in Finland, France, the Netherlands and Switzerland and lowest in Denmark, England, Poland and Scotland. Half of all the patients under the age of 45 years died within one year of the diagnosis, increasing to almost 80% for those aged 75 years or older. Whilst the prognosis for patients with non-small cell carcinoma remained more or less constant between 1978 and 1989 (25% in Denmark and 44% in Finland), that for patients with small cell carcinoma improved slightly, especially in the Netherlands and Switzerland. A fairly large variation in lung cancer related survival rates existed between European countries. The most likely explanation for the differences is the variation in access to specialised care. Except for a slight improvement in short-term survival for patients with small cell lung cancer, survival has remained poor since 1978.

Retrospective analysis of data from the New South Wales Cancer Registry and Australian Bureau of Statistics population data for NSW for 1985-1995 revealed that increased smoking

cessation has halved lung cancer rates in men. The distribution of histological subtypes of lung cancer in women was different from that in men[10]. In a large series of autopsy cases of lung cancer in 41,988 males and 13,818 females consecutively registered between 1958 and 1987 in Japan, the percentage was found to be 9% for males and 5% for females. The percentage of lung cancer cases among all malignant tumours was about 17% for males and 9% for females. Among fatal malignant tumours, gastric cancer and lung cancer showed the highest frequency. The relative incidence of gastric cancer was seen to decrease, whereas that of lung cancer was observed to increase. Of the histological types of lung cancer in both sexes, adenocarcinoma was the most frequent, followed by squamous cell carcinoma. During the period studied the peak age of patients with lung cancer shifted from the seventh to eighth decade, and a significant elevation of mean age was demonstrated for all of the major histological types in both the sexes. The male to female ratio for all lung cancer cases was 3.0, which was much lower than those for the United States and Europe, but very similar to the ratios of mortality statistics in Japan and other Asian countries[11].

Some of the increases compared to that prior to 1950, may be due to improved diagnosis but changes more recently reflect an actual increase. In 1980, it was estimated to cause 15.8% of all new cancer cases in males varying between 4.5% in Africa to 23.3% in Europe. In females lung cancer is rare. However, the increase between 1975 and 1980 was 10.1% in males, but 16% in females. The situation was different in 1985. Ignoring the non-melanoma skin cancers, lung cancer was estimated to be the most common cancer in men in the world around 1985. It comprised 17.6% of all new cancers in men and 5.8% in women. In men there were about 667,000 new cases in 1985, and 219,000 in women[12-15]. The age adjusted mortality trends in 14 countries show that the increase is universal, at rates between one to five percent a year. Although the overall mortalities are less in females, marked increases have been seen in some countries, such as Canada, Denmark, and USA.

INDIAN SCENARIO

Lung cancer was initially thought to be infrequent in India[16]. Lung cancer constituted 14.4% of all cancers in a review of 9210 consecutive autopsies by Banker[17]. Sirsat[18] reported that lung cancer formed one per cent of all cancers in Tata Cancer Hospital. Viswanathan *et al*[19] collected information from different hospitals of the country and found that the incidence of lung cancer in hospital population was 27.4 per million in 1950 and in 78.6 per million in 1959. They also found an increase in the incidence of bronchogenic carcinoma (16.1 in 1950 to 26.9 in 1961 per 1000 malignancies), following analysis of the records of 15 teaching institutions in India over a period of 10 years. According to Wig *et al*[20], lung carcinoma was a frequent diagnosis amongst all types of chest diseases. The survey conducted in Uttar Pradesh in 1966 by Misra and others showed that the incidence was 4.2 per 10,000 hospital admissions and 2.1 per cent of all malignancies[21].

The National Cancer Registry Programme of the Indian Council of Medical Research, which collected data from six different parts of the country, both rural and urban areas, showed varying figures in different areas[22]. While cancer of the trachea, bronchus and lungs was the most common form of malignancy in males in 1989 from Bombay, Delhi, and Bhopal, it was the second most common in Madras and third in Bangalore, and was most unusual in Barshi, a rural area. The disease was uncommon in females and only in Bombay it was the sixth common malignancy while in Bhopal, it was the seventh in rank. International comparison of incidence rates of lung cancer with that seen in India showed a low figure (age adjusted rates of 66.5-100.4 in Europe and USA *versus* 2.0 to 14.6 per 10^5 in India males; the same is 16.1 to 33.3 *vs* 0 to 3.7 in females). However because of the overall population size, the absolute number should be large.

Hospital data from different parts of the country has also shown different patterns. Behera and Kashyap[23] analyzed the pattern of malignancy in patients admitted to PGIMER,

Chandigarh from 1973 to 1982 and found that of the 223,930 hospital admissions, there were 863 lung cancer cases (0.38%). Lung cancer was the fifth common cancer after lympho-reticular malignancy carcinoma cervix, oropharyngeal cancer and carcinoma of breast. The total number of lung cancer admissions steadily rose from 1973.

As of 1st July 2002 a total of 41,000 cases of lung cancer would have been diagnosed for that year in India as per the ICMR data from its Cancer Registry[22]. Table 1 summarizes the published data on lung cancer from different parts of India[19-21, 24-46]. Jindal and Behera have reported the largest series of 1009 lung cancer cases[38]. They reported that both the mean and peak ages of lung cancer were lower compared to the West (54.3 years). The smoker to non-smoker ratio was 2.7:1. However, the smoker to non-smoker ratio is high, up to 20:1 in some other studies. Up to 40 years of age small cell type predominates and has a weaker association with smoking. After the age of 40 years squamous cell type is the commonest type in smokers and adenocarcinoma, in non-smokers[47-51]. When the cases reported from India before 1985 are compared with those reported after 1985, a marginal increase was seen in frequency of adenocarcinoma (Figures 1 and 2).

Table 2 shows the demographic data of lung cancer patients from all the Indian studies divided broadly into two groups, *i.e.* studies before and after 1985. Lung cancer has remained predominantly a disease of males with a male-

Table 1. *Comparative clinical features and cell type patterns in different Indian studies*

Authors	Total	M:F	Age (yrs)	Sm:NS	Squam	Anapla	Adeno	Uncla
1. Viswanathan *et al*[19] 1962	95	-	-	-	50.5	-	28.4	21.1
2. Wig *et al*[20] 1961	65	4.9	55.8	-	-	-	-	-
3. Basu *et al*[21] 1971	24	7	48.3	5	62.5	8.3	25	4.2
4. Sinha[24] 1961	33	4.5	57.1	-	-	-	-	-
5. Karai *et al*[25] 1967	100	24	52.1	-	41	-	20	39
6. Shankar[26] 1967	20	All M	54	5.7	73.3	6.7	20	-
7. Nagrath *et al*[27] 1970	35	4	47.7	1.9	25.7	-	34.3	40
8. Reddy *et al*[28] 1970	46	6.4	50	0.1	50	25	25	-
9. Guleria *et al*[29] 1971	120	7.6	57.2	2	46.2	36.5	17.3	-
10. Jha *et al*[30] 1972	25	2.9	46.6	5.3	44	20	20	20
11. Nafae *et al*[31] 1973	25	All M	51	7.3	56	20	12	12
12. Malik *et al*[32] 1976	136	5.2	48.5	3.5	40.4	21.3	16.9	7.3
13. Narang *et al*[33] 1977	58	8.7	51.3	4.8	37.9	51.8	10.4	-
14. Jindal *et al*[34] 1979	150	5.5	51.7	2.4	32.5	19.3	15.8	21.9
15. Notani *et al*[35] 1974	520	-	-	3.9	27.5	11.3	7.3	53.4
16. Garg *et al*[36] 1973	82	-	-	-	46.3	28	20.7	-
17. Malhotra *et al*[37] 1986	70	7.8	49.6	4.8	50	17	14.3	17.1
18. Jindal and Behera[38] 1990	1009	4.5	54.3	2.7	34.3	27.6	25.9	12.2
19. Arora *et al*[39] 1990	100	4.05	40-60	1.2	27	1	21	41
20. Rao *et al*[40] 1992	539*	-	-	-	-	-	-	-
21. Rajasekaran *et al*[41] 1993	232	7.9	53	2.7	72	4.3	3.9	15.1
22. Gupta *et al*[42] 1998	279	7.41	56.7	4.5	42.3	32.2	19.9	5.6
23. Thippanna *et al*[43] 1998	160	8.4	40-60	4	67.5	8.8	18.7	5.1
24. Arora *et al*[44] 1998	200*	-	-	-	-	-	-	-
25. Gupta *et al*[45] 2001	265	7.8	50-70	3.6	60	21.5	16.2	2.3
26. Kashyap *et al*[46] 2001	638**	6.17	54.6	2.4	58.3	-	10.81	-

*Data described only for those below 40 years of age; **:Personal communication. Data reported for 281 cases of *bidi* smokers, quoted in Ref No. 46; M:F=Male: Female; Sm: NS=Smoker: non-smoker; squam=Squamous cell carcinoma; Adeno=Adenocarcinoma; Anapla=Anaplaste carcinoma; Uncla=Unclassified.

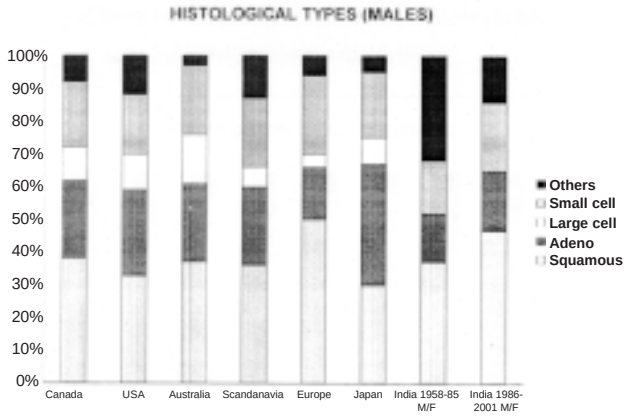

Figure 1. Distribution of histological types of lung cancer in males in various countries[1,16,18-51].
Sex-wise data on histological types in Indian patients is not available. Therefore, it is shown as combined data for males and females

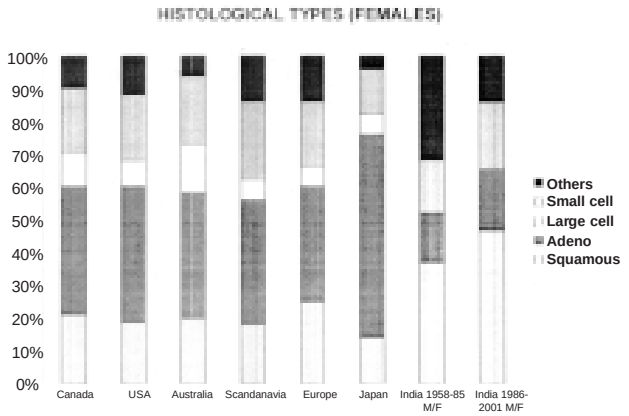

Figure 2. Distribution of histological types of lung cancer in females in various countries[1,16,18-51].
Sex-wise data on histological types in Indian patients is not available. Therefore, it is shown as combined data for males and females

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[38]. Around 80% of lung cancer patients come from the rural areas. The demographic pattern of lung cancer in India is similar to that observed in Western countries 40 years ago. Forty per cent of patients of lung cancer are less than 50 years of age and 11% are less than 40 years.

SMOKING AND LUNG CANCER IN INDIA

Smoking is the most important contributory factor in the causation of lung cancer[52]. In patients with lung cancer a history of active tobacco smoking is present in 87% of males and in 85% of females. History of passive tobacco exposure is found in only three per cent.

Table 2. *Summary of demographic data of lung cancer reported from Indian studies[18-51]*

Details	1958-1985	1986-2001
Total cases	1735	2973
M:F	6.67:1	5.76:1
Mean age (yrs)	52.16	54.6
SM:NS	2.5:1	2.7:1
Urban:Rural	19.6–81.6	18.4–80.4
Occupation	Farmers	13.9-48%
	Labourers	21.0–27.3%
	Clerks / teachers	16.7%
	Businessmen	21.3%
	Housewives	8.0–14.7%
	Others	23%
Religion		
	Hindus	75.1%
	Muslims	18.9%
	Christians	5.9%

SM: small cell carcinoma; NS: non-small cell carcinoma.

The relative risk of developing lung cancer is 2.64 for *bidi* smokers and 2.23 for cigarette smokers with 2.45 as the overall relative risk[35]. *Bidi* is more carcinogenic as has been shown in studies by Jussawalla and Jain[49] and Pakhale *et al*[51]. *Hooka* smoking has also been associated with lung cancer as reported by Nafae *et al*[31].

In a recent study by Gupta *et al*[45], 80% of men and 33% of women among the patients were ever-smokers as compared to 60% of men and 20% of women among controls. The odds ratio (OR) for ever-smoking was 5.0 (95% CI=3.11-8.04) among men and 2.47 (95% CI=0.79-7.75) among women. Smoking of *bidi* and *hooka* as well as cigarettes had similar ORs for cumulative consumption. The risk increased with both the duration and quantity of all smoking products[45].

PASSIVE SMOKING AND LUNG CANCER

Environmental tobacco smoke is a known

lung carcinogen. A meta-analysis of 41 studies showed that environmental tobacco exposure carries a relative risk of development of lung cancer of 1.48 (1.13-1.92) in males and 1.2 (1.12-1.29) in females[53]. Risk increases with increase in exposure. Exposure at work place results in a relative risk of 1.16. In a study on non-smoking lung cancer patients, environmental tobacco exposure during childhood carried an OR of 3.9 (95% CI-1.9-8.2). There was an increasing risk with increase in number of smokers in the household and the duration of exposure. Women had a higher OR of 5.1. Work place, and vehicular pollutant exposure have shown a weak association. Another study by Rapiti *et al*[54] has shown that environmental tobacco smoke exposure during childhood is strongly associated with the risk of later development of lung cancer (OR 3.9, 95% CI=1.9-8.2).

OCCUPATIONAL RISK FOR LUNG CANCER

Certain occupations carry a higher risk of lung cancer[55,56]. The following occupational exposures are known to be associated with an increased risk: *(a) Asbestos:* insulation workers and shipyard workers are exposed to asbestos. There is some increase in the risk of lung cancer after 10 years of exposure and a substantial risk after 20 years of exposure. Concurrent smoking increases the risk to 90 fold; *(b) Arsenic :* smelter workers and vineyard workers are exposed to arsenic. The risk is dose related. Lung cancers have an upper lobe predominance and there may be multiple primaries; *(c) Nickel refinery workers :* squamous cell carcinoma is more common; *(d) Radiation (Uranium mining):* oat cell carcinoma is more common; *(e) Haematite mining:* due to radon exposure; *(f) Hard rock mining; (g) Chromium exposure in ore mining and pigment manufacturing*: squamous cell variety is most common; *(h) Chloromethyl exposure in workers in industries:* oat cell carcinoma is most common; *(i) Ethers and mustard gas:* squamous and undifferentiated carcinomas are most common; *(j) Soot, tars exposure in coke oven workers* and *(k) Oils and coke exposure in Gas house workers, roofers and rubber workers*.

Other occupational exposures that are suspected include those to acrylonitrite, berrylium, and dimethyl sulphate. No systematic information on occupational risk for lung cancer patients is available in India.

GENETICS OF LUNG CANCER

Cytogenetic studies have identified many chromosomal changes in lung cancer with numerical abnormalities, and structural aberrations including deletions and translocations. These mutations include activation of the dominant cellular protooncogenes (which promote oncogenesis) of the *ras* and *myc* family and inactivation of the recessive or tumour suppressor genes (these genes help suppression of tumour development). Small cell lung cancer is associated with oncogenes, like *c-myc*, L-*myc*, N-*myc*, c-*raf* and tumour suppressor genes, like p53 and Rb. Non-small cell lung cancer is associated with K-*ras*, N-*ras*, H-*ras*, c-*myc*, c-*raf* and tumour suppressor genes like p16 and Rb genes[57-58].

FHIT is a tumour-suppressor gene and is frequently altered in lung cancer[59]. Apoptosis or programmed cell death is altered in lung cancers due to changes in the anti-(BCL-3, Bel-xl) and proapoptotic members (Bax, Bad)[60]. The protein level expression of bCl-2, bax and bel-xl shows a variable expression ranging from negative to moderate positivity. Singh *et al*[61] reported that presence of arginine homozygous genotype of p53 codon 72 contributes to susceptibility for lung cancer and patients with proline homozygous genotype present early and may have a better prognosis. To elucidate that molecular mechanisms of chemotherapeutic effects, Sen *et al*[62] in an *in vitro* study concluded that while Bax was unaffected, there was downregulation of anti-apoptotic BCl-Xl during treatment.

DIET AND LUNG CANCER

There is some evidence that certain dietary factors may be protective for lung cancer, and others may increase the risk. There are

conflicting reports about the role of beta-carotene and lung cancer, although most reports suggest a protective effect. Case control studies from China have shown that vegetable intake is a protective factor for lung cancer[63]. Sankaranarayanan[64] found that green vegetables and bananas have a protective effect on the development of lung cancer. Pumpkins and onions had the most consistent protective effect. On the other hand, animal food products and diary products have a predisposing effect on lung cancer. Dietary cholesterol and animal fat increases the risk of lung cancer. Behera *et al*[65], however, reported that β-carotene and vitamin A levels and vitamin C levels in patients with lung cancer compared to healthy controls were not significantly different.

AIR POLLUTION AND LUNG CANCER

Urban air contains many known carcinogens and exposure to this has been shown to predispose to lung cancer in UK and US. Lung cancer is more frequent in subjects residing in neighbourhoods where outdoor air is smoky. Studies from China[66] have shown that coal burning at home is a significant risk factor for the development of lung cancer in non-smoking females. Coal smoke contains many potential carcinogens like radon and thoron.

Gupta *et al*[45] reported that among risk factors for lung cancer, cumulative exposure of > 45 years to indoor air pollution in women from use of coal or wood for cooking or heating showed an OR of 1.43 (95% CI=0.33-6.30)[45]. Residence in urban areas, however, did not entail an increased risk for developing lung cancer.

REACTIVE OXYGEN SPECIES AND ANTIOXIDANT DEFENSE SYSTEM IN LUNG CANCER

Studies by Sharma *et al*[67] have shown that there is a significant increase in *in vitro* superoxide anion and hydrogen peroxide formation in alveolar macrophages from malignant lobe and neutrophils of lung cancer patients. The activities of catalase and glutathione peroxidase were decreased. The assays of antioxidant vitamins such as retinal and α-tocopherol revealed that their levels in alveolar macrophages from malignant lobe were significantly decreased. This oxidant / antioxidant imbalance in the malignant lobe of lung cancer patients could potentially enhance the neoplastic behaviour by augmenting both the genetic instability of a tumour and its capacity to injure and penetrate the host tissues. Further, Sohi *et al*[68] and Bhardwaj and Khanduja[69] have also emphasized the role of oxidant and antioxidant balance in the pathogenesis of lung cancer.

CLINICAL SPECTRUM OF PRIMARY LUNG CANCER IN INDIA

There are important differences in the clinical spectrum of lung cancer patients in India compared to those in the West[38]. Both the mean and peak ages of lung cancer are lower. The smoker: non-smoker ratios have been lower in most of the Indian studies as compared to those in the West. Most of the patients have advanced disease at diagnosis and 51.8% have evidence of metastases. The commonest presentation has been a mass lesion with or without collapse in 68% while 25% had a pleural effusion and 16.7% had superior vena cava compression syndrome[38, 70]. Squamous cell carcinoma has been found in 34.3%, anaplastic in 27.6%, adenocarcinoma in 25.9% and unclassified in 12.2 per cent.

DIAGNOSIS OF LUNG CANCER

Clinical Presentation (Table 3)[18-51]

Symptoms such as fever, cough, expectoration, hemoptysis, weight loss and anorexia are common to both tuberculosis and lung cancer. In India, where tuberculosis is rampant it is not uncommon to find a lung cancer patient being treated for tuberculosis initially. However, age of the patient, smoking history, mediastinal symptoms such as hoarseness of voice, SVC

obstruction and dysphagia favour the diagnosis of lung cancer. On examination, there may be signs of collapse or mass, clubbing and metastatic and non-metastatic complications of lung cancer. The duration of symptoms before lung cancer is diagnosed is reported to be < 3 months in 32.6 – 44% cases, 3-6 months in 16.0-34.3% and > 6 months in 21.0 - 24.0 per cent.

Table 3. *Presenting features of Indian lung cancer patients (%)*[18-51]

Symptoms	Jindal and Behera (1990)	Other-Indian studies (range)
Cough with expectoration	88	40-94.3
Chest pain	52.2	16-66.7
Loss of weight	90	11.4-77
Breathlessness	Not reported	24-59
Weakness	90	4-60
Haemoptysis	69.2	8-60
Fever	19.6	22-68.6
Anorexia	90	20.5-70
Hoarseness of voice	29.9	9-33
Nausea and vomiting	6	25.0
Puffiness of face	19.8	2.9-8.3
Dysphagia	20.8	2.9-6
Others	30.5	-

Radiological Findings

Mass with or without collapse is the commonest radiological finding in lung cancer[70]. Other findings include pleural effusion in 25.1%, rib erosion in 4.8% and lymphangitis in 2.8 per cent. A normal chest x-ray is found in 0.4% of cases of lung cancer. Upper zone is involved in most cases followed by mid zone (32.7%), lower zone (16%) and the entire lung (8.8%). Adenocarcinoma presents as a peripheral mass in 61% cases and in 38.3% as a central lesion. Presentation as a central mass (72.2% cases) is more common among squamous cell carcinoma than as a peripheral lesion (27.8%). Small cell cancer also presents more commonly as a central lesion (83.6%) than as a peripheral lesion (16.4%). Isolated pleural effusion has been reported in 3.8% in squamous cell lung cancer, 22% in adenocarcinoma and only 4% in small cell lung cancer[70].

Other Investigations

Tissue diagnosis and categorisation of the cell type is required before treatment can be planned in a case of lung cancer. With experienced personnel and using multiple, diagnostic techniques, 70-90% of all lung cancers can be diagnosed by cytopathological examination. Any mass lesion demonstrable on radiology can be subjected to bronchoscopy or transthoracic fine-needle aspiration cytology biopsy. The procedural yield is 93% and a firm diagnosis can be established in 78 per cent[71]. For peripheral lesions fluoroscopic guidance is required and an adequate yield is obtained in 75 per cent. The overall diagnostic yield of transbronchial needle aspiration is 75% and exact categorisation is possible in 82% of cases[72]. The diagnostic yield of bronchial biopsy specimens varies from 70 to 90 per cent depending on the site and type of the tumour, number of specimens examined, and experience of the pathologist and the endoscopist. Central lesions, with visible tumours and multiple samples give a better diagnostic yield.

Malignant cells especially small cell cancer type produce and release several hormones, enzymes and tissue antigens. Among the commoner hormones are ACTH, beta-hCG, FSH and LH. These are, however, not diagnostic.

SCAR CARCINOMA

Some authors define a scar carcinoma as a peripherally located tumour with no evidence of bronchial origin, occurring around a true hyalinized scar tissue. Others include tumours superimposed on chronic regional or diffuse interstitial fibrosis. Scar cancers are almost always of the non-small cell type, with a preponderance of adenocarcinomas. Some of the conditions that are described to be associated with a scar carcinoma are tuberculosis, pulmonary infarction, emphysema, systemic sclerosis, bronchiectasis, idiopathic pulmonary fibrosis and asbestosis[75].

There are conflicting reports about the association of tuberculosis and lung cancer. In

an analysis of 1009 patients with lung cancer from Chandigarh only 1.2% had clinical evidence of tuberculosis and 3.8% had radiological evidence of tuberculosis[38]. In a prospective study from same centre only two out of 280 patients with past tuberculosis and two out of 272 controls were found to have lung cancer[76]. The authors concluded that subjects with a past history of tuberculosis are not at are increased risk of lung cancer. In a study from Bangalore sputum was positive for acid-fast bacilli (AFB) in 290 patients with malignancy, out of which 13.8% had lung cancer[77]. Unlike sear carcinomas lung cancer in a patient with old tuberculosis is predominantly of the squamous cell variety[78].

MANAGEMENT OF LUNG CANCER

Surgery, radiotherapy and chemotherapy are the various options available for the management of lung cancer. In the early stages of NSCLC (Stage I to IIIA), surgery if feasible is the treatment of choice. The five-year survival rate after surgery are as follows: Stage I: 60-70%, State IA: (T1N0), 80%, Stage II: 35-40%, Stage IIIA (N2): 10-15%.

As most cases of lung cancer present in an advanced and inoperable stage, and radiotherapy is only a local form of therapy, chemotherapy has an important role in the management of lung cancer. Several regimens of chemotherapeutic agents have been studied in lung cancer. In a recent meta-analysis of randomized trials that compared chemotherapy with good supportive care, chemotherapy showed a modest benefit[5]. There is an improvement in the quality of life, prolongation of median survival by 1.5-3 months, increased survival at one year by 10% and a reduction in the risk of death by 27 percent. In our experience, chemotherapy results in a modest but significant improvement in survival in patients with inoperable lung cancer compared to good supportive care alone[79].

Newer chemotherapeutic agents that have increased one-year survival up to 40% and median survival of about 8-9 months are being increasingly used now a days . These include Gemeitabine, Docetaxel, Paclitaxel, Vinorelbine, Topotecan, Irinotecan, and Newer Platinum agents (carboplatin, Oxaloplatin, etc)[5]. Combinations of a platinum agent with a new generation cytotoxic agent have become the standard of care for first-line chemotherapy of advanced non-small cell lung cancer. In the presence of contraindications for platinum-based chemotherapy, platinum-free chemotherapy might be a reasonable option. There is not enough evidence to support the use of triple-drug chemotherapy. Administration of single-agent gemcitabine or vinorelbine can be considered in patients with poor performance status and in elderly patients. In case of non-progression and lack of severe toxicity, the administration of four to six cycles of chemotherapy is recommended. There is no evidence that prolongation of treatment has an impact upon survival. Second line chemotherapy using docetaxel should be considered for chemotherapeutically pre-treated patients with good performance status in order to relieve

Table 4. *Chemotherapy with median survival in weeks in lung cancer at a tertiary care centre (PGIMER-Chandigarh)[79-87]*

Regimen	No.	SCLC	NSCLC	Total survival	1-year survival
SFRT	28	-	-	5	-
CTX	24	-	-	7.5	-
Combination	38	26	9.5	16	8.3-12%
V+C+B	26	-	18	-	26.5%
V+C+M	20	23.5	31	-	33%
V+C+A	27	23.5	23	-	25-36%
VB+MIT+C	27	-	16-28	24	12%
E+V+C+CC	22	22.5-39	-	24	12.5%
IFO+V	16	35.5	-	-	26.5%

SFRT: Single fraction radiotherapy of 1000 rads; CTX: Cyclophosphamide; V: vincristine; C: Cisplatin; B:bleomycin; M: methotrexate; A: adriamycin; VB: vinblastin; MIT: mitomycin; CC: CCNU; IFO: Ifosfamide, E: etoposide.

Table 5. *Median survival (in weeks) in lung cancer with newer chemotherapeutic agents*[84-87].

Regimen	NSCLC	SCLC	6 M	1 Yr
MIC (n=299)	22 (24-36)	-	30%	15.5%
VIE (n=98)	-	31	44.4%	12.7%
DOC + CISP (n=50)	38+	(30-32)	93.3%	23.3%
GCB + CISP (n=16)	36	-	Response Rate-69%	

MIC: Mitomycin, Ifosfamide, Cisplatin; VIE: VP-16, Ifosfamide, Etoposide; DOC: Docetaxel; CISP: Cisplatin, GCB: Gemcitabine.

symptoms, prolong survival and improve quality of life.

Studies from India have shown that without chemotherpay the median survival of unresectable NSCLC is five weeks, with a single agent it is 7.5 weeks (Tables 4 and 5), with less effective chemotherapy it is 9.5 weeks and with modern chemotherapy it is 23 weeks to more than 40 weeks[80-87]. The problems with chemotherapy in India include a large number of dropouts, because of the costs and the side effects.

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