Clinical profile of lung cancer in a tertiary care teaching hospital in north india with special reference to acceptance and outcome of treatment

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BACKGROUND: Lung cancer is the commonest cancer and among the biggest cause of cancer mortality worldwide. Tobacco Smoking remains the biggest risk factor. As most of the patients are diagnosed at an advanced stage of the disease, treatment largely remains palliative and prognosis grim.

AIMS: This study was designed to observe the clinic-radiological and pathological presentations of lung cancer, diagnostic yields of various procedures and acceptance of treatment.

RESULTS: A total of 393 patients were included in the study. Majority of them (n= 324; 82.44%) were male and were smokers (n=299; 76%). A large number of patients (n=142, 36.1%) were receiving anti-tubercular therapy. The most common radiological finding was a mass lesion (n=166), followed by pleural effusion (n=135). Adenocarcinoma was found to be commonest type (n=115, 29.26%), followed by squamous cell ca (n=86, 21.88%) and small cell ca (n=50; 12.8%). Among NSCLC, 218 (75.4%) patients were presented in stage IV (distant metastasis). Of 28 patients of stage I, II & IIIA NSCLC or Limited Disease SCLC, 12 (42.8%) patients came for follow-up. Only 37 (11.9%) of 311 patients in stage IIIB, IV NSCLC or extensive SCLC came for follow-up.

CONCLUSION: Most patients were smoker males of 50-70 years of age, presented in poor general condition and with disseminated disease as many of them were misdiagnosed outside as a case of tuberculosis or other benign diseases. Only a few could receive treatment with curative intent and one year survival was dismally low.

Key Words: *Lung cancer; diagnosis; staging; treatment.*

Lung cancer is the commonest cancer and the biggest cause of cancer mortality worldwide. Every year lung cancer causes more than 1.6 million deaths, more than breast, colon, and prostate cancers combined (1). Tobacco smoking remains the biggest risk factor for development of lung cancer (1). Other factors include occupational exposures, air pollution and old pulmonary scar. Cough with or without sputum production, heamoptysis, chest pain, dyspnoea, hoarseness of voice and fever are the main presenting features. Non-specific nature of symptoms and high prevalence of tuberculosis in our country, often leads to misdiagnosis and delayed diagnosis of lung cancer (2). Many patients present with various co-morbidities which adversely affect diagnosis and prognosis (2). Most patients are diagnosed at an advanced stage of the disease, unfit for curative treatment (2). Treatment largely remains palliative and prognosis grim. There are few Indian studies on lung cancer, showing shift of commonest lung cancer type from Squamous cell carcinoma to Adenocarcinoma. At our tertiary care hospital we receive a large number of lung cancer patients, mostly in poor general conditions, so we decided to conduct this study.

SUBJECTS AND METHODS

This prospective observational study was designed to study the clinical, radiological and pathological presentations of lung cancer, diagnostic yields of various pathological procedures and acceptance of treatment and was conducted in the department of TB and Respiratory Diseases, SRMS IMS, Bareilly over a period of five years from January 2012 to December 2016. All the patients of lung cancer (confirmed by at least one pathological specimen) diagnosed during a period of 5 years were included in present study. A few referred patients diagnosed outside or other departments were also included. A total of 393 patients of Lung cancer were included in study after written consents of all the patients. Prior approval of Hospital's Ethical committee was taken. To define socio-economic status of the patient, we simplified Kuppuswami indices into 3 groups; Upper (I), Middle (II, III) and Lower (IV & V). A detailed history, clinical examination, routine blood investigations and chest radiographs were obtained in all the patients. Contrast-enhanced CT scan thorax, USG abdomen and other relevant imaging studies were done. Sputum cytology, fibre-optic bronchoscopy and procedures including bronchial wash, brush and biopsy, and/or USG/CT guided FNA/biopsy of the lung lesions were performed. Patients presenting with pleural effusion were subjected to pleural fluid analysis and pleural biopsy (closed or image guided) and/or thoracoscopy. Once confirmed for lung malignancy, search for metastasis was done. Treatment was offered in each patient depending on stage. A follow-up was done for a minimum of 12 months.

RESULTS

A total of 393 patients were included in the study. Majority of them (n= 324; 82.44%) were male (Tables 1 and 2). Most patients (n=245; 62.34%) were in 5th to 7th decades. Most patients (n=311, 79.1%) belong to rural areas. Majority of them (n=279, 71%) belong to low socio-economic condition. Most of them (n=299; 76%) were smokers. Most male were smokers (86.4%), while only 27.5% female were smokers. A large number of patients (n=142, 36.1%) were receiving anti-tubercular therapy (ATT) for at least 1 month duration. Many patients were suffering from other co-morbid conditions. Mean duration of the symptoms was 6.5 months (range, 1- 18 months).

TABLE 1

Clinic-radiological profile of lung cancer patients

Gender			Number	%age
	Male	Male	324	82.44
	Female	Female	69	17.56
Age	Mean		63.3 yr	
		<30 yrs	15	3.8
		30-40 yrs	15	3.8
		40-50 yrs	57	14.5
		50-60 yrs	156	39.7
		60-70 yrs	89	22.6
		70-80 yrs	55	14
		>80 yrs	6	1.5
	Rural	Rural	311	79.1
	Urban	Urban	82	20.8

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Socio-economic				
	Poor		279	71
	Middle class		81	20.6
	Upper class		33	8.4
Smoking habit				
	Smokers		299	76
		Male	280	
		Female	19	
		Heavy (>20 pack years)	139	
		Moderate (10-20 pack years)	81	
		Light (<10 pack years)	53	
	Non-smokers		94	24
Co-morbidity				
		Diabetes mallitus	65	16.5
		COPD	50	12.7
		Pulmonary Tuberculosis	17	4.3
		Ischemic heart disease	15	3.8
		Renal failure	12	3
		hypothyroidism		
Symptoms				
		Cough	276	70.2
		Breathless	242	61.5
		Chest pain	224	57
		Fever	134	34
		Hemoptysis	81	20.6
		HOV	61	15.5
		Wt. Loss	248	63
		Appetite Loss	256	65
	Anaemia		162	42
	Palpable LN		88	22.4
	Clubbing		44	11.2
	Pleural Effusion		135	34.3
	Facial swelling/ SVCO		32	8.1
Radiological features				
	Right		205	52.2
	Left		146	37.1
	Bilateral		42	10.7
		Mass	166	42.2
		(Peripheal)	98	59
		(Central/hilar)	68	41
		Mass+ Collapse	47	12
		SPN	13	3.3
		Cannon balls	8	2
		Pleural effusion	135	34.3
		(with Mass)	112	83
		(with collapse)	10	7.4
		(alone)	13	9.6
		Diffuse	12	3
		Lymphangitic	8	2

Cough was the commonest symptom (n=276, 70.2%). Loss of appetite, weight loss, breathlessness and chest pain (and bony pain) occurred in 256 (65%), 248 (63%), 242 (61.5%) and 224 (57%) patients respectively. Fever, heamoptysis, hoarseness of voice, and neurological symptoms (altered sensorium, seizures or hemiplagia) occurred in 134 (34%), 81 (20.6%), 61 (15.5%) and 21 (5.3%) patients respectively.

TABLE 2

Histopathological profile of lung cancer and yield of various sampling processes

Histologic types			Number	%age
	Squamous cell Ca		86	21.9
	Adenocarcinoma		115	29.3
	Small cell Ca		50	12.7
	NSCC/ Poor Diff		47	11.9
	Others		16	4.1
	Metastatic		25	6.4
	Type not confirm		54	13.7
	Total		393	100
Diagnostic Procedures				
	CT Fna/ biopsy (231)	Definitive	159	68.8
		Positive cytology	42	18.2
		Negative	30	13
	FOB-Combine (338)	Definite	180	53.3
		(Biopsy)	142	
		(BW/Brush)	78	
		Positive cytology	93	27.5
		Negative	65	19.2
	Sputum cytology (271)		106	39.1
		Central (156)	89	57.1
		Peripheral (115)	17	14.8
	Fna lymph node (88)		88	100
	Pleural Fluid (135)	Positive	79	58.5
		Negative	56	41.5
	Pleural biopsy (28)		20	71.4
	Thoracoscopy (42)		36	85.7
Metastasis				
	Liver		28	
	Lymph node		88	
	Ribs		17	
	Vertebra		14	
	Brain		16	
	Ant chest wall		3	
	Pleura		135	
	Others		6	

Anaemia, clubbing, facial swelling and jaundice were present in 165 (42%), 44 (11.2%), 32 (8.1%) and 17 (4.3%) patients respectively. Supraclavicular and axillary lymph nodes were enlarged in 83 (21.1%) and 5 (1.2%) patients respectively. The most common radiological finding was a mass lesion (n=166) followed by pleural effusion (n=135). Mass with collapse was seen in 47 (12%) patients. Solitary Pulmonary Nodule, Cannon ball lesion, Diffuse lesions and Lymphangitic Carcinomatosis were found in 13(3.3%), 12(3%) 12(3%) and 8 (2%) patients respectively. Rib erosion, Superior sulcus tumour and Pericardial effusion was seen in 47 (12%), 30 (7.6%) and 12 (3%) cases respectively. Adenocarcinoma was found to be commonest type 15, 29.26%), followed by squamous cell ca (n=86, 21.88%) and small cell ca (n=50, 12.8%). In 47 (12%) patients report was poorly differentiated NSCLC. In a large number of patients (n=54, 13.7%), type of cancer could not be confirmed. Fibre-optic bronchoscopy was performed in 338 patients

and yielded positive results in 273 (80.8%) patients. CT guided FNAC/ biopsy were performed in 231 patients and yielded positive results in 201 (87%) patients. Sputum yield was positive in 106 (39.1%) patients. CT head was done in 45 (11.5%) patients with 16 patients turning positive for brain metastasis. A large number of the patients (n=197; 50%) were presented with distant metastasis, a few with multiple metastasis. Apart from pleura (n=135, 34.6%) and lymph nodes (n=88, 22.4%) other sites were liver (n=28, 7.1%)), ribs (n=17, 4.3%), brain (n=16, 4.1%), vertebra (n=14, 3.6%), adrenal gland (n=8, 2%) anterior chest wall (n=3, 0.76%) and others (n=6, 1.5%).

DISCUSSION

Epidemiology- Lung cancer was uncommon and a rare diagnosis in the early 1900s (3), but since then it has become more prevalent with nearly 1.8 million cases worldwide each year and is the most common cause of cancer death in the world (1). Present study comprises of a total of 393 patients. Majority of them (n= 324; 82.44%) were male. The male to female ratio shows national variation and our data of 4.7:1 is similar to other regional studies (4, table 3). Comparison shows that the gap in incidence between male and female is gradually decreasing. There is some evidence that women have an increased susceptibility to lung carcinogen. Lung cancer is typically a disease of elderly patients, with a peak incidence at around 70-80 years of age (4). In our study too, majority of the patients (n=245, 62.34%) were in age group 50-70 years. The average age of presentation in our study is 63.3 years and this is higher than the most other studies (4, Table 3), reason for this may be the fact that we receive patients from a large geographic area and a large number of ex-service army personnel as well. Smoking is estimated to be the cause of 85% of lung cancer deaths (1, 5). The relative risk of developing lung cancer for cigarette smoker is 2.23 while for bidi smoker is 2.64 (6). In our study most of the patients (n=299; 76%) were smokers, thus the smoker to the non-smoker ratio was 3:1 and almost similar ratio (range 3:2 to 4.6:1) were found by other Indian studies (4, 6, Table 3). Among 324 males, 280 (86.4%) were smokers, while only 19 (27.5%) female had tobacco smoking history.

In present study a significant number of patients were non-smokers and most of them were either female or young males (age <30 years). History of chulha smoke (biomass fuel or kerosene use) was present in almost all the females except one. Other causative factors like exposure to arsenic, chromium, nickel and asbestos, cicatricial lesions of tuberculosis and familiar history of lung cancer are also implicated as risk factor (7). There were many patients with past history of pulmonary tuberculosis and cicatricial scars on chest x-ray. 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 (8). It has shown been that environmental tobacco smoke exposure during childhood is strongly associated with the risk of development of lung cancer (OR 3.9, 95% CI=1.9-8.2) (9). In our study, most patients (n=311, 79.1%) belong to rural areas, and lower socio-economic strata (n=279, 71%), this can explain continuous exposures of smoke and fumes and lack of awareness and lack of medical care which might have led to delay in diagnosis. Clinical presentations- Many patients remain asymptomatic for very long time owing to slow and silent growth of lung cancer or non-specific natures of lung cancer symptoms and present in advance stages (11, 12). A large number of patients (n=142, 36.1%) were receiving anti-tubercular therapy (ATT) for at least 1 month duration (range 1 month- 12 months). In our study, mean duration of the symptoms was 6.5 months (range, 1- 18 months). Mean delay for diagnosis of lung cancer in patients, who were on ATT, was 2.4 months. Tuberculosis presents as a big confounder for lung cancer (11, 12). Cough (dry or productive) (n=276, 70.2%) was the commonest symptom followed by loss of appetite (65%) and weight loss (63%). Breathlessness, chest pain (and other pain), heamoptysis and hoarseness of voice occurred in 242 (61.5%), 224 (57%), 81 (20.6%) and 61 (15.5%) patients respectively. Fever was found in a large number (n=134, 34%) of patients, many of these patients were receiving ATT and had diffuse or bilateral disease. Many patients were suffering from other co-morbid conditions, namely diabetes mellitus, COPD, ischemic heart disease, chronic renal failure, gastro-esophageal reflux, hypothyroidism and rheumatoid arthritis. Co-morbidities too led to delayed seeking of medical care. Worldwide, adenocarcinoma had replaced squamous cell carcinoma as most common histological subtypes (13). Most studies from India (6, 14-20) had reported squamous cell carcinoma as most dominant subtype, but many recent studies from India (21-23, 25) too showing changing trends and reporting adenocarcinoma as the predominant subtype (Table 3). This shift may be attributable to the changing smoking pattern and increasing incidence of lung cancer in females and nonsmokers (21). In our study too, adenocarcinoma was found to be commonest type (n=115, 29.26%), followed

TABLE 3
Comparison of various Indian studies on lung cancer

Authors (Ref. No.)	Year	Cases	Male: Female	Age (in year)	Smoker %	Histopathological Distribution				
						Adeno Ca	Sq Cell Ca	Small Cell Ca	NSC L	Undetermined/ Other
Viswanathan 1962 (15)		2444	6.86	50-60	67.6	21.0	50.5	24.2	-	-
Guleria (16)	1971	120	7.6	57.2	67	17.3	46.2	-	-	36.5
Notani (8)	1974	520	5.5	55	79.6	7.3	27.5	11.3	-	53.4
Malik (17)	1976	136	5.2	48.5	77.8	16.9	40.4	-	-	-
Jindal 1990 (14)		1009	4.5	54.3	73	25.9	34.3	27.6	-	12.2
Gupta (18)	1998	279	6.1	57	81.6	20	42	14	-	24
Prasad (19)	2004	400	5.2	-	71.4	18.5	46.5	18.2	4.0	12.8
Mandal (20)	2013	466	1.1	-	78.7	30.8	49.1	14.8	3.7	1.5
Malik (21)	2013	434	4.6	55.0	69.7	37.3	32.1	28.0	2.8	0.5
Sunderam (22)	2014	60	4.3	63.0	71.4	43.3	31.7	10.0	3.2	-
Pandhi (23)	2015	150	2.7	59.3	60.0	36	41	13	3	7
Baburao (24)	2015	96	3.1	-	69.7	28.1	47.9	12.0	3.1	-
Mahendra (25)		110	5.6	58.1	82	40.9		20.0	2.7	1.8
Present		393	4.7	63.3	76	29.3		12.8	12	24

by squamous cell carcinoma (n=86, 21.88%) and small cell carcinoma (n=50, 12.8%). Poorly differentiated non-small cell lung cancers (NSCLC) were reported in 47 (12%) patients. In our study, sixteen (4%) patients had other cell type including large cell cancer, lymphoma and sarcoma. Twenty five (6.4%) patients were diagnosed to have metastatic lung cancer; the major primaries were breast, colon, testis, thyroid, pancreas and stomach. No other study recorded metastatic lung cancer. In a large number of patients (n=54, 13.7%), type of cancer could not be confirmed owing to poor general or financial condition. Imaging- On chest radiograph (PA view) and/or CT thorax, 205 (52.2%) patients had lesion on right side, 146 (37.1%) on left side while 42 (10.7%) patients had bilateral lesions. The commonest radiological lesion was a single mass, found in 166 (42.2%) patients. A large number of patients (n=135, 34.3%) presented with pleural effusions, of which majority (n=112) had a mass also. Many studies find pleural effusion to be major presenting feature of lung malignancies (10, 21-26). Thirteen (3.3%) patients had well defined solitary pulmonary nodules (SPN). Twelve (3%) patients had bilateral diffuse nodular infiltrations. Eight (2%) patients each had bilateral multiple cannon balls. or lymphangitic pattern. CT head was advised in all the patients presented with neurologic symptoms and the patients diagnosed with small cell cancer. A total of 45 patients undergone CT head and 16 (4.1%) patients were found to have Brain metastasis. Sputum cytology is a simple, cost-effective and noninvasive procedure for the assessment of pre-invasive and invasive pulmonary malignancies (27). In our study, 89 of the 156 (57.1%) patients with central lesions and 17 out of 115 (14.8%) with peripheral lesions were positive for malignancy on sputum cytology. In the present study, the sensitivity of sputum cytology was 56.9% (49 out of 86 cases) for squamous cell carcinoma compared with 18.2% (21 out of 115 cases) for adenocarcinoma. The diagnostic yield of bronchoscopic procedures for a centrally-located tumour by using endobronchial biopsies is quite high (80-90%), followed by bronchial brushing (50 to 77%) (28, 29). In our study, Fibre-optic bronchoscopy was performed in 338 patients and yielded positive results in 273 (80.8%) patients. Fine needle aspiration cytology (FNAC) of intrathoracic localized lesions can be performed using various imaging modalities such as fluoroscopy, ultrasonography, and computed tomography (30). CT guided FNAC/Biopsy were performed in 231 patients and yielded positive results in 201 (87%) patients. Our results are comparable with other studies (25, 30). In patients with pleural effusion, Pleural fluid cytology yielded positive results in 79 (58.5%) cases. Image (CT/USG) guided pleural biopsy yielded positive results in 17 (65.4%) patients. Thoracoscopy yielded positive results in 39 (81.3%) patients. Lymph node FNAC/Biopsy was done in all the 88 patients presented with lymphadenopathy. A large number of the patients (n=246; 62.6%) were presented with distant metastasis, a few with multiple metastasis. Apart from pleura (135 cases) and lymph nodes (88 cases) other common sites were liver, ribs, brain, vertebra, adrenal gland and chest wall. Staging-out of total 393 patients, 50 were small cell cancer and most (42, 84%) were extensive disease. Histo-pathologic typing and staging could not be done in 54 patients as these patients refused any further investigations or treatment. Of remaining 289 patients, majority 218 (75.4%) presented in stage IV (distant metastasis). Eight patients belonged to stage IA, 3 patients each in stage IIA and IIB, 6 patients in stage IIIA and 51 (17.6%) patients in stage IIIB (TNM 2015). Our results match with other Indian studies (21, 22). At presentation, ECOG performance status of 1, 2, 3 and 4 were seen in 58 (14.8%), 175 (44.5%), 128 (32.6%) and 32 (8.1%) patients respectively. All the patients were offered stage-appropriate treatment. Many (n=178; 66.2%) patients of stage IIIB and IV NSCLC registered for treatment (chemotherapy/chemo-radiation), only 116 patients were found to be fit for chemotherapy and 87 patients completed their chemotherapy. Platinum based chemotherapy was administered in the department of Oncology and radiotherapy of our hospital. Remaining 91 (33.8%) patients of stage IIIB and IV managed conservatively including pleural aspiration/ intercostals drainage +/- chemical pleurodesis for malignant effusion. A total of 53 (39.3%) patients required repeated (2 or more) pleurocentesis. Twenty nine (21.5%) patients required intercostals drainage. Chemical pleurodesis with doxycycline was done in 23 patients, complete response was seen in 15 (65.2%) patients, 4 (17.4%) patients each had partial response or failed. Twenty patients of stage I, II and IIIA were sent for surgical resection and adjuvant chemotherapy (radiotherapy). Eight patients of limited disease Small Cell Lung Cancer (SCLC) sent for possible surgery followed by adjuvant chemotherapy. Of the remaining 42 patients, only 18 patients received chemotherapy. We sent samples of 56 patients of NSCLC for EFGR mutation in the last two years of study. Only 13 patients came out to be positive for EFGR Mutation, and received Tyrosine Kinase Inhibitor (TKI) Geftinib. At present more than 50 per cent of lung adenocarcinomas and about a third of squamous cell carcinomas can be characterized based on the mutation profile. Recent studies have focused their efforts into incorporating tumor genotyping into clinical decision making. Molecular biomarker EGFR is included as standard care for NSCLC patients (31, 32). Phenotype associated with EFGR mutation and response to the TKIs (geftinib and erlotinib), includes adenocarcinoma, never smoker, female and East Asian descent. First generation ALK- TKI, crizotinib, has been found to be effective against anaplastic lymphoma kinase (ALK) fusion gene which is the second most common driver mutation. Acceptance of any kind of therapy was poor, owing to disease spread, poor general condition, poor financial condition, and poor tolerance of chemotherapy. In hospital mortality was quite high. Forty three patients died during 1st hospital stay while still being investigated or receiving treatment. One year follow-up was done and we found that most patients either died or lost follow-up. Of 28 patients of stage I, II and IIIA NSCLC or Limited Disease SCLC, 12 (42.8%) patients came for follow-up. Only 37 (11.9%) of 311 patients in stage IIIB, IV NSCLC or extensive SCLC came for follow-up after one year.

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