Original Article

Clinical Spectrum of 106 Cigarette and *Bidi* Smokers and Non-smokers with Lung Cancer at a Tertiary Care Centre in India

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Abstract

Background. There is a paucity of data from India on changing trends in lung cancer.

Objective. In this study, we analysed the spectrum of lung cancer patients in cigarette and *bidi* smokers and non-smokers presenting to a tertiary care centre.

Methods. A retrospective analysis of lung cancer cases diagnosed at the Vallabhbhai Patel Chest Institute between 2001 and 2013 was done.

Results. Out of a total of 106 patients with lung cancer, 35 (33%) were non-smokers. Their mean age was 51.7±14.9 years [non-smokers (39.4±14.3), *bidi* smokers (57.5±10.9) and cigarette smokers (58.1±11.2)] ($p<0.0001$). Cigarette smoking was common among patients (34.9%). Smoking was predominantly seen in males (n=80, 77.5%) ($p<0.05$). History of biomass fuel exposure was observed in 9 (25.7%) non-smokers. Cough was the commonest symptom (n=90; 84.9%) followed by dyspnoea (n=80; 75.5%) and haemoptysis (n=48; 45.3%). On chest radiograph, right lung (n=52; 49%) was the most common site. Mass was the commonest radiological presentation. The bronschoscopy showed no visible abnormality in 51.4% of non-smokers. Endobronchial mass seen in 32.3%, 54%, 25.7% of *bidi* smokers, cigarette smokers and non-smokers, respectively. Non-small cell lung carcinoma was seen in 82.1%, squamous cell carcinoma in 59.8% and adenocarcinoma in 40.2% patients. Squamous cell carcinoma was the predominant subtype amongst smokers, while adenocarcinoma was the commonest histological subtype in non-smokers ($p<0.05\%$).

Conclusions. The study concludes that *bidi* smoking poses a similar risk for lung cancer as with cigarette smoking. The focus of tobacco control programmes should be extended to all types of tobacco users to reduce the increasing incidence of lung cancer in India. **[Indian J Chest Dis Allied Sci 2017;59:69-74]**

Key words: Lung cancer, Cigarette, *Bidi*, Non-smoker, Bronchoscopy.

Introduction

Lung cancer, a rare disease in the beginning of twentieth century, is now a leading cause of death in both men and women worldwide[1] and has reached epidemic proportions. As per data of GLOBOCAN project in 2012, there were 1.8 million new cases of lung cancer accounting for 12.9% of the 14.1 million new cancer cases worldwide. In India, lung cancer constitutes 6.9% of all new cancer cases and 9.3% of all cancer related deaths.[2]

With an increase in adoption of cancer-causing behaviours, particularly smoking in economically developing countries,[3] together with the aging and growth of world population, a surge in the incidence of lung cancer is being observed in developing countries also. In addition, there have been important changes in incidence trends amongst men and women, histology of lung cancer, and incidence in non-smokers.[4]

Cigarette smoking is the most common cause of lung cancer among both men and women, as 85% to 90% of all patients with lung cancer are current or past smokers.[5] Regional variation in the smoking patterns in India also influence the occurrence of lung cancer due to variations in tobacco content. Tobacco is smoked in different forms with prevalence of type of tobacco use varying with regions. The prevalence of use varies as follows: *bidi* (28.4% - 79.0%), cigarettes (9.0% - 53.7%), *hookah* (3.4% - 77.3%), and mixed (7.5% - 13.6%).[6] In addition to exposure to tobacco smoke, domestic exposure to biomass fuel in Indian households is another important risk factor in the causation of lung cancer among women.[7]

In this present study, a retrospective analysis and correlation of the demographic profile, clinical presentation and smoking patterns in patients with

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lung cancer was done. The aim of the present study was to analyse and correlate the clinical profile, radiological pattern, bronchoscopic evaluation and histopathological diagnosis amongst patients with different smoking practices.

Material and Methods

The study is a retrospective analysis of lung cancer cases diagnosed in a unit of the Department of Respiratory Medicine at the Vallabhbhai Patel Chest Institute between 2001 and 2013. Ethical approval for the study was obtained from the Institutional Ethical Committee. The case records were retrospectively reviewed for clinical presentation, radiological and bronchoscopic findings, and histopathological diagnosis.

A detailed assessment of the patients was done through a questionnaire, that comprised of details regarding age, sex, social/economic status, history of smoking with duration, smoking pattern (main stream/side stream smoke), type of smoking (cigarette/ *bidi*) and biomass fuel exposure. Definition of smoking status was adopted from the guidelines of the Centers for Disease Control and Prevention, USA. Current smokers were defined as respondents, who reported to smoke at least 100 cigarettes in their lifetime and who, at the time of survey, smoked either every day or some days. Former smokers were defined as respondents who reported smoking at least 100 cigarettes in their lifetime and who at the time of the survey did not smoke at all. Never smokers were defined as the individuals who never smoked or have smoked less than 100 cigarettes in his or her lifetime. A pack-year for cigarettes was calculated as 20 cigarettes smoked every day for one year (pack years = number of cigarettes per day × years of smoking/20). One *bidi* as equivalent of one cigarette was considered for pack-year calculation, as it takes into consideration more factors than merely grams of tobacco in *bidis* and cigarettes, such as nicotine, tar, carbon monoxide.[9]

Biomass fuel exposure assessment was done by surveying fuel/stove type, type of house, location and type of kitchen, and location of cooking place (indoor/ outdoor). However, no quantitative measurement, like $PM_{2.5}$ was performed at the households.

Past history of tuberculosis and treatment with anti-tuberculosis treatment (ATT), co-existing chronic obstructive pulmonary disease (COPD) and other comorbidities, like diabetes, hypertension and coronary artery disease were also evaluated. History of symptoms (cough, expectoration, haemoptysis, breathlessness, weight loss, loss of appetite, chest pain and fever) with their duration was recorded. Clinical examination findings of pallor, icterus, cyanosis, clubbing and lymphadenopathy were recorded. Radiological assessment included location of tumour, presence of mass, collapse, pleural effusion, cavitation and calcification. Presence of lesions in hilar and para-hilar regions were designated as central lesions. On bronchoscopic evaluation, endoscopic findings were categorised according to the classification of Ikeda *et al*[10] (endoscopically visible and endoscopically invisible tumours), together with some of the criteria used by the Japan Lung Cancer Society[11,12] in order to classify mucosal injury and secretion findings. Endoscopically visible tumours were also classified according to their location in the tracheobronchial tree.

The same specialist performed all bronchoscopic procedures, and transbronchial lung biopsy (TBLB), endobronchial biopsy (EBB) and transbronchial needle aspiration (TBNA) and reports were correlated with the histopathological pattern. The final diagnosis was classified into non-small-cell lung cancer (squamous cell carcinoma and adenocarcinoma) and small cell lung carcinoma.

Statistical Analysis

Statistical analysis was done using Statistical Software Package for Social Sciences (SPSS for Microsoft Windows, package version 10; SPSS Inc; Chicago, IL). Mean (±SD) or the median (range) was calculated for continuous variables. The categorical variables were compared using the Chi-square test, while continuous variables were compared using the Mann–Whitney U-test or Kruskal–Wallis tests, as applicable. Statistical significance was taken at a p value of <0.05.

Results

We studied 106 patients (80 males) with lung cancer diagnosed on the basis of clinical, radiological, bronchoscopy and pathological characteristics. The overall mean age at presentation was 51.7±14.9 years, (39.4±14.3 years in non-smokers, 57.5±10.9 years in *bidi* smokers and 58.1±11.2 years in cigarette smokers). The difference in mean age between the three groups was statistically significant ($p<0.0001$). In all, 35 (33%) patients were never smokers and 71 (67%) patients had smoked at some point. Amongst the smokers, cigarette smoking was more common (35%) than *bidi* smoking (32%). The mean pack years of smoking were 34.7±7.2 and 33.8±12.1 for *bidi* and cigarette smoking, respectively. In female smokers, *bidi* smoking (n=8) was more commonly seen than cigarette smoking. History of biomass fuel exposure was observed in 9 (25.7%) non-smokers. However, there was no statistically significant association between smoking status and exposure to biomass fuel. Most frequent presenting symptom was cough

(90, 85%) followed by dyspnoea (80, 75%) and haemoptysis (48, 45%) (Table 1). Loss of weight and fever was observed in 38.3% (n=43) and 21.7% (n=23), respectively (Table 1). There was no statistically significant association between the presenting symptoms and smoking status. A total of 40 (37.7%) patients had received ATT in the past (63% of non-smokers and 25% of smokers). This association was statistically significant (p<0.05) (Table 1). Amongst smokers and non-smokers clubbing was observed in 39% and 23%, respectively.

Table 1. Clinical characteristics of 106 patients with lung cancer

Characteristics	Smokers		Non-smokers (n=35)	p value
	Bidi (n=34)	Cigarette (n=37)		
Age (years) (Mean±SD)	57.5±10.9	58.1±11.2	39.4±14.3	<0.0001
Male/Female	26/8	34/3	20/15	<0.05
Symptoms				
Cough, n (%)	32 (94%)	30 (81%)	28 (80%)	NS
Dyspnoea, n (%)	29 (85%)	26 (70%)	25 (71%)	NS
Haemoptysis, n (%)	10 (29%)	26 (70%)	12 (34%)	NS
Loss of weight, n (%)	16 (47%)	16 (43%)	11 (31%)	NS
Fever, n (%)	6 (18%)	9 (24%)	8 (23%)	NS
Signs				
Clubbing, n (%)	13 (38%)	15 (41%)	8 (23%)	NS
History of ATT, n (%)	8 (24%)	10 (27%)	22 (63%)	<0.05
History of smoking				
Pack years	34.8	33.8		<0.0001
History of biomass fuel exposure, n (%)	6 (18%)	3 (8%)	9 (26%)	NS

Definition of abbreviations: NS=Not significant; ATT=Anti-tuberculosis treatment

None of the 106 patients had any occupational risk factors for lung cancer.

A summary of the radiological, bronchoscopic and histopathological findings is given in table 2. Right lung was the most common site (49%), followed by left lung (38%) and both lungs (13%). However, in *bidi* smokers, left lung was more commonly involved (47%). Overall, hilar region was more involved than the periphery, and upper zone involvement was the most common in all the three subgroups. The most common radiological presentation was mass in all the three subgroups. Cavitation was observed in 12 (35%) *bidi* smokers, in 16 (43%) cigarette smokers and 8 (23%) non-smokers (Table 2). Calcification was seen in 2.9% and 2.7% of *bidi* and cigarette smokers, respectively (Table 2). Association of radiological features of cavitation and calcification with smoking pattern was found to be statistically significant (p<0.05). Bronschoscopy showed no visible abnormality in 51% of non-smokers (Table 3). Overall, endobronchial mass was the most common endoscopically visualised presentation, seen in 32%, 54%, 26% of *bidi* smokers, cigarette smokers and non-smokers, respectively (Table 3). Overall, non-small cell lung carcinoma was found to be the predominant histology (87 [82%] patients)— the most common histology being squamous cell carcinoma (60%) followed by adenocarcinoma (40%). Adenocarcinoma was found to be commonest subtype (34%) in non-smokers, while among *bidi* and cigarette smokers, squamous cell carcinoma was the predominant subtype observed in 53% and 65%, respectively. However, the difference was not significant statistically (Table 3).

Table 2. Radiographic features of 106 patients with lung cancer.

Radiographic Finding	Smokers		Non-smokers (n=35)	p value
	Bidi (n=34)	Cigarette (n=37)		
Site				
Right	15 (44%)	20 (54%)	17 (49%)	NS
Left	16 (47%)	10 (27%)	14 (38%)	
Bilalteral	3 (9%)	7 (19%)	4 (11%)	
Location				
Hilar	16 (47%)	18 (49%)	10 (29%)	NS
Peripheral	2 (6%)	—	3 (9%)	
Upper zone	20 (59%)	15 (41%)	19 (54%)	
Middle zone	9 (26%)	6 (16%)	9 (26%)	
Lower zone	6 (18%)	1 (3%)	1 (3%)	
Entire lung	3 (9%)	7 (19%)	6 (17%)	
Lesions				
Collapse	5 (15%)	6 (16%)	10 (29%)	NS
Mass	25 (74%)	30 (81%)	19 (54%)	
Effusion	2 (6%)	1 (3%)	0	
Combination	6 (18%)	4 (11%)	6 (17%)	
Other findings				
Cavitation	12 (35%)	16 (43%)	8 (23%)	<0.05
Calcification	1 (3%)	1 (3%)	—	

Percentage figures shown as rounded off to the nearest number.
Definition of abbreviation: NS=Not significant

Table 3. Bronchoscopic and histopathological findings in 106 patients with lung cancer.

Characteristics	Smokers		Non-smokers (n=35)	p value
	Bidi (n=34)	Cigarette (n=37)		
Bronchoscopy findings				NS
Normal	9 (26%)	10 (27%)	18 (51.4%)	
Endoscopically visible tumour				
Endobronchial mass	11 (32%)	20 (54%)	9 (26%)	
Mucosal infiltration	1 (3%)	1 (3%)	1 (3%)	
Micronodules in the mucosa	1 (3%)	1 (3%)	—	
Endoscopically invisible tumour				
External compression	1 (3%)	1 (3%)	—	
Luminal narrowing/ constriction	7 (21%)	3 (8%)	4 (11%)	
Vocal cord paralysis	1 (3%)	1 (3%)	1 (3%)	
Widening of the main carina	3 (9%)	—	2 (6%)	
Final diagnosis				<0.05
Squamous cell carcinoma	18 (53%)	24 (65%)	10 (29%)	
Adenocarcinoma	6 (18%)	3 (8%)	12 (34%)	
Bronchoalveolar cell carcinoma	2 (6%)	4 (11%)	1 (3%)	
Small cell carcinoma	6 (18%)	3 (8%)	10 (29%)	
Lymphangitic carcinomatosa	2 (6%)	3 (8%)	2 (6%)	

Data presented as number of patients (percentage); Percentage figures shown as rounded off to the nearest number.

Definition of abbreviation: NS=Not significant

Discussion

Studies have observed a statistically significant variation in the age at presentation and smoking status of patients suffering with lung cancer. Behera *et al*[1] reported the mean age of diagnosis of lung cancer was 52.2 years before 1985 and this remained nearly the same, about 54.6 years, when cases diagnosed after 1985 were analysed.[1] Krishnamurthy *et al*[13] observed that mean age of smokers with lung cancer was 56.9 years and of non-smokers was 53.3 years. They also found a statistically significant association between the age at presentation and the smoking status.[13] In our study, we found that non-smokers had an early presentation with a mean age of 39.4 years followed by *bidi* smokers at 57.5 years, cigarette smokers at 58.1 years and the association was statistically significant. Studies have also shown that *bidi* smoking was more carcinogenic than other forms of smoking.[14,15] However, smoking of *bidi* and cigarettes had similar odds ratio for cumulative consumption.[16] The occurrence of lung cancer in non-smokers can be due to complex interplay of genetic and environmental mechanisms that lead to progressive accumulation of genetic lesions.

Studies have shown that the prevalence of smoking is higher amongst men than women, though the difference is found to be narrowing.[17] With respect to India, studies have reported that 87% of men and 85% of women with lung cancer have a history of active tobacco smoking.[1] In our study, we found that 75% of the men and 42.3% of the women had a history of smoking. These findings were similar to the study by Gupta *et al*[16] where 89% of men and 33% of women were ever smokers as compared to 60% of men and 20% of women among controls. We tried to assess the influence of smoking and gender in patients with lung cancer and observed that male smokers and female non-smokers are at a risk of developing lung cancer and the association was statistically significant. This was in concordance with the study of 607 patients by Dey *et al*.[18]

The cumulative lung cancer risk among heavy smokers can be as high as 30% compared with a life-time risk of less than 1% in non-smokers. The lung cancer risk is proportional to the quantity of cigarette consumption because factors, such as number of packs smoked per day, age of onset of smoking, degree of inhalation, tar and nicotine content of cigarettes, and use of unfiltered cigarettes are important factors.[19,20] In our study 71 patients (66.9%) were smokers. Studies from India have observed that the type of tobacco consumption influences the risk of lung cancer.[7] In the present study, amongst the smokers, cigarette smoking was more common (34.9%) than *bidi* smoking (32%). However, in female smokers, *bidi* smoking was more commonly seen than cigarette smoking. Studies have reported a higher odds ratio of *bidi* smoking in comparison with cigarette smoking.[21-24]

The most common clinical presentation in our study was cough irrespective of the smoking status followed by dyspnoea and haemoptysis. Haemoptysis and clubbing were more common in cigarette smokers than *bidi* smokers though statistically not significant in the present study. These findings were similar to findings of other studies.[7,25]

In the present study, radiologically right lung was most commonly involved in cigarette smokers (54%) and non-smokers (48.5%). However, left lung involvement was predominantly seen in *bidi* smokers (47%). Hilar and para-hilar region involvement was

seen predominantly. Similarly, Mandal *et al*[26] observed that the right lung was involved commonly followed by the left lung. Also upper zone involvement was seen most commonly in our study amongst both smokers and non-smokers. This was similar to the assessment of radiological pattern in a study by Sharma *et al*[27], where they observed involvement of upper zone in maximum number of cases (42%), followed by mid zone, lower zone in 32.7% and 16%, respectively. In the present study, mass lesion was the most common presentation among both smokers and non-smokers. This was followed by collapse, effusion and combination of these findings. Similar observations were made in two other studies.[18,26] In the present study, cavitation was predominantly observed in smokers than non-smokers, and the relation was statistically significant.

In the present study, non-smokers with lung cancer predominantly had normal findings on bronchoscopy (51.4%). Endoscopically visible tumours presented predominantly as endobronchial mass and was the commonest bronchoscopic finding in cigarette and *bidi* smokers. However, in endoscopically non-visible tumours, constriction with luminal narrowing was the predominant presentation in both smokers and non-smokers.

Non-small-cell lung cancer (NSCLC) was the predominant histology seen in 87 (82.1%) patients and small cell carcinoma in 19 (17.9%) patients. Overall, squamous cell carcinoma was the commonest histopathology observed in both *bidi* and cigarette smokers and the association was statistically significant. This is in agreement with other studies from India.[7,18,28-30] In the present study, adenocarcinoma was found predominantly in non-smokers and had a statistically significant association. Noronha *et al*[4] and Krishnamurthy *et al*[13] made similar observations, where adenocarcinoma occurred in 44.8% and 52.72% of non-smokers. Mandal *et al*[26], in their study from North Eastern India, also observed adenocarcinoma to be predominant among non-smokers. Other published studies also support the increased incidence of adenocarcinoma amongst non-smokers.[31-33] The above association highlights the importance of assessing non-smoking related risk factors for lung cancer. It has been observed that factors like environmental tobacco smoke,[34,35] mineral dusts like asbestos and arsenic,[36,37] indoor air pollutants, especially exposure to biomass fuel exposure in rural India[38] are associated with increased risk for lung cancer.

The absence of data on staging, mutation and follow-up is the major limitation of the present study. The study patients were referred to cancer specialty hospital due to infrastructure limitation at the place of study.

Conclusions

We observed that *bidi* smoking poses a similar risk for lung cancer as cigarette smoking. Prevalence of adenocarcinoma was highest in non-smokers. We suggest that focus of tobacco control programmes should be expanded to all types of tobacco users, including *bidi*, to reduce the increasing prevalence of lung cancer in India. Presentation with symptoms of cough and dyspnaea in patients with lung cancer does not differ between *bidi* and cigarette smokers. *Bidi* smokers had a significantly higher number of pack years as compared to cigarette smokers. Presence of cavitation is significantly high in cigarette smokers on radiological evaluation. The bronchoscopic findings of cigarette smokers and *bidi* smokers are similar except that endobronchial mass is commonly seen in cigarette smokers.

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