

Changing trends in histopathology of lung cancer in a tobacco prevalent area of South India

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Abstract:

Background: Lung cancer is the most devastating disease of mankind among all cancers in the world with 1.8 million cases. In the west, adenocarcinoma of lung is the most common type, accounts for 38.5% followed by squamous 23% and large cell carcinoma. In India, squamous cell carcinoma was common until few recent studies which described the changing trends. Present study is done at a tertiary care hospital where tobacco cultivation and consumption is rampant in its surrounding places. An attempt to assess the histological trends in this area is made.

Methodology: Total of 450 lung cancer patients, were studied in a span of 7 years.

Results: Out of 450360 cases were histopathologically proven, 255 (70.83%) were males and 95 (26.38) were females with a male to female ratio of 2.7:1. Adeno carcinoma was found in 215 (59.72%) being most common, followed by squamous cell carcinoma 81(22.50%), small cell 23 (6.38%), large cell 12 (3.3%), and others 31(7.5%). Adenocarcinoma is the most common histopathological type seen in both males and females with 147 (57.64) cases, and 63 (66.31%) cases respectively. Adenocarcinoma is the most common histopathological type seen in both smokers and non-smokers with 246 (68.33%) and 114 (31.66%) respectively.

Conclusions: Adenocarcinoma is evolving to be the most common histological type in both smokers and non-smokers in India. Tobacco cessation and change to filtered cigarettes has globally reduced tobacco related histological types of lung cancers. The aetiology of adenocarcinoma should be further evaluated in order to achieve an overall prevention.

Keywords: Adenocarcinoma; Lung cancer; Squamous cell carcinoma.

Introduction:

Worldwide, lung cancer is the cause of major cancer incidence and mortality in men, where as in women it is the third most common cause of cancer incidence and the second most common cause of cancer mortality [1]. In the past several decades, the incidence of adenocarcinoma has increased greatly, and adenocarcinoma has replaced squamous cell carcinoma as the most prevalent type of non-small cell carcinoma in many western countries. In India it is still squamous cell carcinoma in both males and females [2-5].

Lung cancer is the foremost contributor to cancer-related mortality, resulting in 1.38 million cancer deaths per year worldwide [6]. According to the Globocon 2012 report, the estimated incidence of lung cancer in India was 70275 in all ages and both sexes; males predominate with a M:F ratio of 4.5:1 and this ratio varies with age and smoking status. The ratio increased progressively up to 51-60 years and then remained same. The smoker to non-smoker ratio is high up to 20:1 in various studies. Up to 40 years of age small cell type predominates and has less association with smoking. After the age of 40 years squamous cell type is commonest in smokers and adenocarcinoma in non-smokers. The demographic pattern of lung cancer in India is similar to those of Western countries 40 years ago. While in Western countries adenocarcinoma has become the commonest histological type of lung cancer

in India it is still squamous cell carcinoma in both males and females [7].

The World Health Organization estimates that lung cancer deaths worldwide will continue to rise, largely as a result of an increase in global tobacco use. Especially in Asia, tobacco use is the principal risk factor for lung cancer. This study is conducted especially in the area which is famous for cultivation of tobacco. Tobacco consumption in the form of beedis, cigars, cigarettes, and tobacco chewing are rampant in this locality and surrounding districts. By this study we will be able to know the various histological types of lung cancers, analyse the risk factors and recommend preventive measures.

Materials and Methods:

This was a prospective cross sectional study to diagnose histopathological types of lung cancer in patients attending our hospital. The present study was carried out in the Department of Pulmonary Medicine, NRI General Hospital, Chinankakani, Guntur, Andhra Pradesh, during the period from June 2010 to July 2017. Patients attending Pulmonary Medicine department with a suspected diagnosis of lung cancer were included in the study. An ethical committee approval and consent of patients was obtained. Suspicion of cancer was based on both clinical symptoms and radiological abnormalities, suspected in individuals who have an abnormal chest radiograph

finding or have symptoms and signs caused by either local or systemic effects of the tumour. All the cases admitted to hospital were thoroughly investigated by detailed history; smoking status and occupational history were stressed. Clinical examination routine blood investigations, sputum examination, chest X-rays, CT chest, USG chest were done accordingly. They are further evaluated for histopathological diagnosis by either of the method by CT guidance, USG guidance; bronchoscopic guided biopsy, bronchoalveolar lavage, bronchial washings, post bronchoscopic sputum for malignant cytology or FNAC of lymph node, pleural fluid analysis for malignant cytology. Cases of primary mediastinal mass, primary pleural tumours and lymphoproliferative malignancies were excluded.

Results:

Sex: In the present study there were a greater number of male patients than female patients. Males constituted 70.83% and females 26.38%. Male to female ratio was 2.7:1. This ratio was slightly lower to the previous Indian studies which varied from 4.5:1 to 7.8:1.

Age: The mean age of patients with proven diagnosis of lung cancer in our study was 58.97 years with a range of 33 to 82 years. It is similar to the previous studies of Jindal et al. 1990 and Prasad et al. 2004 which were 54 and 57 years respectively [8,9]. The ratio is significantly higher in older population in comparison to younger population. The mean age in males was 60.66 years and female was 53.16 years. Female in our study group are younger than males which very similar to previous studies.

Prasad et al. (2004) showed the mean ages of male and female patients were 57 and 54 year, respectively [9]. The mean age among smokers is 60.95 years and in non-smokers is 54.37 years. There was statistically significant difference between average of male and female patients and lung cancer ($p=0.04$ by Z test,) occurring at an early age in females. In our study, most cases 255(70.83%) presented between 50- 69 years of age. Peak age group is 50-69 years.

Smoking Status: In our study 68.33% were smokers and 31.66% were non-smokers. Smoker to non-smokers ratio was 2.15:1. None of the female patients were smokers. Smoking status had a strong correlation with lung cancer. Overall male smokers and female non-smokers were at increased risk of lung cancer.

Study by Smith et al., reported that smoking is the principal risk factor for lung cancer and more than 80% of lung cancer occurs in smokers [14]. In our study 87% of males were smokers.

Occupation: Most of the participants in our study were agricultural workers and daily wagers explaining their habit of smoking and incidence of lung cancer among them.

Residence: In our study 296 (82.22) belonged to rural area and 64 cases (17.77%) belonged to urban area.

Symptoms: Most common presenting complaint was cough in 84.52%, followed by breathlessness in 72.62%, chest pain in 32.14%, haemoptysis in 21.43%, fever in 19.05%, wheeze in 15.48%, appetite loss in 14.29%, hoarseness of voice in 11.90%, loss of weight in 5.95%, superior vena cava obstruction in 5.95%, dysphagia in 1.19% respectively in decreasing order.

Radiology: In the present study right side of the lung was involved in 53.57% left side of the lung is involved in 41.67%, bilateral lesions were seen in 4.67%. Upper lobe was involved in 61.90%, middle lobe in 7.14%, lower lobe in 26.190%. As also studied by Sharma et al., our most common presentation on X-ray is mass lesion, which was present in 71 cases (84.52%) [10]. Collapse was seen in 4 cases (4.7%), consolidation in 2 cases (2.35%), cavitatory lesions in 5 cases, (5.95%) massive pleural effusion in 2(2.35%) cases. Behera and Balmugesh have done an analysis of Indian studies and found mass in 72% with or without collapse and is the commonest radiological finding in lung cancer [11]. They also showed that pleural effusion was seen in 25.1% of cases and rib erosion was seen in 4.8% of cases.

Histopathology: Out of 360 cases in our study, adenocarcinoma accounted for 59.72%, squamous cell carcinoma for 22.50%, small cell and large cell 6.38%, 3.33% respectively.

Discussion:

Over the past decades there was a shift in pathological distribution of non-small cell carcinoma. Prior to 1970's squamous cell carcinoma was most common histological type of non-small cell carcinoma. However since 1975 there has been a dramatic increase in the incidence of adenocarcinoma making it the predominant histological type of non-small cell carcinoma worldwide. In India, previous studies till 2004 showed predominance of squamous cell carcinoma [11].

In the present study 246 cases were smokers. Predominant histological type in smokers in our study was adenocarcinoma 147 (59.75%), followed by squamous cell carcinoma in 46 (18.69%), small cell carcinoma in 23 (9.34%), large cell carcinoma in 7 (2.84%). 114 cases were non-smokers in present study. Among them the predominant histological type is adenocarcinoma 68 (59.64%), followed by squamous cell carcinoma 35 (30.70%), large cell in 5 (4.28%). Among 114 non-smokers 21 (18.42%) had history of passive smoking. Small cell carcinoma was exclusively found in smokers. There was higher incidence of adenocarcinoma which was similar to previous studies of Fonthametal, Tohetal, Nornaha et al. [12-14]. There was a higher incidence of all types of carcinomas in smokers ($p=0.02$ by Chi-square test).

In our study out of 151 male patients most common histopathological type was adenocarcinoma (48.34%), followed by squamous cell carcinoma in 28.47%, small

cell carcinoma in 7.94%, large cell carcinoma in 3.97%, poorly differentiated in 5(3.31%), undifferentiated 3(1.98%) and adeno-squamous in 3 respectively. In females out of 39 case 48.71% were adenocarcinoma, 25.64% squamous cell carcinoma, 15.38% large cell carcinoma, poorly differentiated and adenoid cystic in 10.25%. From our study there is no statistical correlation with histological type of cancer and gender. In present study both males and females adenocarcinoma is the most common histopathological type.

Table 1: Gender distribution age wise

Age group	No. of patients		Total	Percentage
	Male	Female		
30-39	3	7	10	2.70
40-49	15	35	50	13.88
50-59	125	5	130	36.11
60-69	82	43	125	34.72
70-79	27	5	32	8.88
80-89	3	0	3	0.83
Total	255	95	360	

Table 2: Gender distribution in smokers and non-smokers

Gender	Smokers	Non smokers
Male	246	19
Female	0	95
Total	246	114
%	68.33	31.66

Table 3: Histopathological types

Type of carcinoma	No. of cases	Percentage
Adenocarcinoma	215	59.72
Squamous cell	81	22.50
Small cell	23	6.38
Large cell	12	3.33
Poorly differentiated	10	2.77
Non Hodgkins	5	1.38
Undifferentiated	7	1.94
Adeno-squamous	5	1.38
Adenocystic	2	0.55
Total	360	100

Table 4: Histopathological types in females

Histological type	No. of cases	Percentage
Adenocarcinoma	63	66.31
Squamous cell	20	21.05
Large cell	6	6.31
Poorly differentiated	4	4.21
Adenoid cystic	2	2.10
Total	95	100

Table 5: Histopathological types in Males

Type of carcinoma	No. of cases	Percentage
Adenocarcinoma	147	57.64
Squamous cell	61	23.92
Small cell	23	9.01
Large cell	6	2.35
Poorly differentiated	6	2.35
Non Hodgkins	5	1.96
Undifferentiated	7	2.74
Adeno-squamous	5	1.96
Total	255	100

Table 6: Histopathological type in non-smokers

Histopathological type	No of cases	Percentage
Adenocarcinoma	68	59.64
Squamous cell	35	30.70
Large cell	5	4.38
Poorly differentiated	4	3.50
Adenoid cystic	2	1.75
Total	114	100

Table 7: Histopathological type in smokers

Histological type	No. of cases	Percentage
Adenocarcinoma	147	59.75
Squamous cell carcinoma	46	18.69
Small cell carcinoma	23	9.34
Large cell carcinoma	7	2.84
Poorly differentiated	6	2.43
Undifferentiated	7	2.84
Non Hodgkins	5	2.03
Adenosquamous	5	2.03
Total	246	100

Table 8: Comparison of cell type patterns in different Indian studies:

Authors	Total	M:F	Age (yrs)	Smokers: non smokers	Squamous	Anaplastic	Adenocarcinoma	Un-classified
Viswanathan et al. 1962 ¹⁵	95	-	-	-	50.5	-	28.4	21.1
Jindal et al. 1979 ¹⁶	150	5.5	51.7	2.4	32.5	19.3	15.8	21.9
Jindal and Behera 1990 ⁸	1009	4.5	54.3	2.7	34.3	27.6	25.9	12.2
Arora et al. 1990 ¹⁷	100	4.05	40-60	1.2	27	1	21	41
Rajasekarn et al. 1993 ¹⁸	232	7.9	53	2.7	72	4.3	3.9	15.1
Gupta et al. 1998 ¹⁹	279	7.41	56.7	4.5	42.3	32.2	19.9	5.6

Thippanna et al. 1998 ²⁰	160	8.4	40-60	4	67.5	8.8	18.7	5.1
Gupta et al. 2001 ²¹	265	7.8	50-70	3.6	60	21.5	16.2	2.3
Kashyap et al. 2001 ²²	638	6.17	54.6	2.4	58.3	-	10.81	-
Noronha et al. 2012 ¹⁴	255	-	-	-	26.3	8	43.8	-
Current Study	360	2.68	60.6	12.86	22.50	-	59.72	-

Conclusions:

This study suggests that a pathological shift may have emerged in India as well. Traditionally squamous cell carcinoma of lung was thought to be related to smoking than adenocarcinoma. The increase in the incidence of adenocarcinoma can be attributed to tobacco cessation and change to filtered cigarettes which has globally reduced tobacco related major histological types of lung cancers like squamous cell carcinoma and small cell carcinoma. Smoke from filtered cigarettes may be more deeply inhaled, resulting in carcinogen deposition in lung periphery and hence leading to adenocarcinomas. Ours being a single centre study, more studies are warranted to correlate with this new epidemiological trend.

Conflicts of Interest: None

Acknowledgements: Nil

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