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Original Research Paper

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CLINICAL PROFILE, RADIOLOGICAL, PATHOLOGICAL AND MOLECULAR MARKERS IN LUNG CANCER PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND: Cancer is perhaps one of the biggest challenges faced by modern medicine and its research is rife with challenges as well as opportunities. Carcinoma lung is one of the most common varieties of cancer worldwide more so in India. The changing trends in epidemiology and the varied clinical and radiological presentation are crucial especially for the primary physician. The fact that many cases of carcinoma lung have been falsely diagnosed as TB especially in endemic areas is a case in point.

AIMS AND OBJECTIVES: To assess the epidemiology as well as the clinical and radiological features of various types of lung cancer. Assess the recent trends in the demographic patterns and symptomatology along with its pathological and radiological correlation in our local study population. To assess the prevalence of ALK positivity in adenocarcinoma patients in the study group.

MATERIALS AND METHODS: This is an observational study done on patients with an established diagnosis of carcinoma lung. The study is done on patients admitted in General Medicine wards or IMCU of tertiary care centre from a period of January 2013 to August 2016.

RESULTS AND DISCUSSION: Our study composed of 100 patients who were treated in the General Medicine or Medical oncology departments of our hospital for primary lung cancer. In squamous cell carcinoma, 19 of the 25 patients had mass lesion on imaging. 7 showed consolidation and 2 had pleural effusion. Likewise, in adenocarcinoma, 27 patients had a mass lesion and 17 showed collapse consolidation on x-ray or CT of the chest. Likewise, in small cell, large cell and undifferentiated lung carcinomas also mass lesion was the most common radiological finding. Out of 100 patients 38 patients had adenocarcinoma, 25 had squamous cell carcinoma, 8 patients had large cell carcinoma and 9 had small cell variety. 20 patients had undifferentiated lung cancer on histologic examination.

CONCLUSION: There is a change in the demographic pattern of lung cancer. While smoking still remains the primary risk factor, a significant number of non-smokers are being affected. Though males are more affected, there is a rise in the number of females with the disease. An overwhelming majority of males with the disease were smokers. The mean age of disease onset is also less than what is classically thought to be. Adenocarcinoma is the most common histological type of lung cancer in the population followed by squamous cell carcinoma. More females and non-smokers and those in the younger age group had contracted adenocarcinoma compared to the other subtypes.

KEYWORDS : Lung Carcinoma, ALK

1. INTRODUCTION

Cancer is perhaps one of the biggest challenges faced by modern medicine and its research is rife with challenges as well as opportunities. Carcinoma lung is one of the most common varieties of cancer worldwide more so in India.[1]There has been a significant shift in the epidemiology of carcinoma lung with more and more cases of the disease in females as well as non-smokers being reported.[10]

There have been some path breaking developments of late in chemotherapy with highly targeted molecules which offers a promise of significant cure rates or better standard of life especially if the disease is diagnosed early enough.

In this context knowing the changing trends in epidemiology and the varied clinical and radiological presentation is crucial especially for the primary physician. The fact that many cases of carcinoma lung have been falsely diagnosed as TB especially in endemic areas is a case in point.[11]

In the case of non-small cell carcinomas especially adenocarcinoma lung newer targeted therapies offer great promise. Rearrangements of the gene encoding anaplastic lymphoma kinase (ALK) have been implicated in many adenocarcinoma cases[3]. The most common ALK rearrangement reported is in EML 4 ALK. The tyrosine kinase arising from mutant ALK like EML 4 have been targeted with newer drugs like Crizotinib and they have shown some promise too. In the era of highly personalized medicine, identifying these markers helps to start targeted therapy at the earliest.

2. AIMS AND OBJECTIVES

- To assess the epidemiology as well as the clinical and radiological features of various types of lung cancer.
- Assess the recent trends in the demographic patterns and symptomatology along with its pathological and radiological correlation in our local study population.
- To assess the prevalence of ALK positivity in adenocarcinoma patients in the study group.

3. MATERIALS AND METHODS

This is an observational study done on patients with an established diagnosis of carcinoma lung. The study is done on patients admitted in General Medicine wards or IMCU of tertiary care centre from a period of January 2013 to August 2016. The details of the patients referred to Medical Oncology department of the hospital are recovered from the data maintained in that department. Patients referred directly to Medical Oncology from other centres or other departments are also included. The details of the patients with a diagnosis of Carcinoma lung that expired/ were referred to outside centres/ went against medical advice for various reasons were recovered from the case sheets in the Medical Records directory of the hospital.

The age, sex and smoking status of the patient were noted. Smokers were classified as never smokers and those who have smoked before. The initial radiological presentation was also recorded. Though a plain chest x-ray was used as the

initial screening imaging technique, the findings were always confirmed by a Computed Tomography of the thorax. High Resolution CT scans or Contrast Enhanced CT scans were used as required.

The histopathological tissue diagnosis of each patient was obtained. The final pathologic diagnosis was arrived at by meticulous histologic studies and molecular markers. Medical records of each patient were studied to note any history of ATT prior to the diagnosis of the malignancy.

The patients with adenocarcinoma were also tested for ALK rearrangements using immuno histochemistry techniques on the tissue blocks.

PATIENT SELECTION

INCLUSION CRITERIA:

- All patients with a histologically confirmed diagnosis of primary carcinoma lung treated at the General Medicine or Medical Oncology Departments of Government Stanley Medical College.

EXCLUSION CRITERIA:

- Patients with clinically/radio logically suspected carcinoma lung but not histologically proven are excluded.
- Patients with secondaries in the lung from other sites are excluded.

The various data obtained are finally matched for age, sex, smoking status and other variables to establish the aims and objectives proposed in the stud

a. DURATION OF STUDY: January 2013 to August 2016

b. PLACE OF STUDY: Tertiary care centre, Chennai

c. SAMPLE SIZE: 100

d. STUDY DESIGN: Observational study

4. RESULTS AND DISCUSSION

Our study composed of 100 patients who were treated in the General Medicine or Medical oncology departments of our hospital for primary lung cancer.

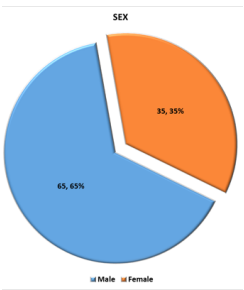
Out of the 100 patients, 65 were males and 35 were females. The incidence of lung cancer in males was nearly double of that in females. As per our study even though the incidence of lung cancer is more in males, women do form a considerable proportion of the cases affected by the disease.

TABLE 1 Age & Sex distribution

SEX	N	MEAN AGE	STD. DEVIATION	P-VALUE¥
MALE	65	55.37	10.590	0.335
FEMALE	35	53.20	10.868	

Independent T-test
P<0.05 – significant

Figure 1 Sex distribution in the study population



The mean age at which lung cancer was diagnosed was found to be around 55 years. The mean age of diagnosis of lung cancer in males was 55.4 and that in females was found to be 53.2 years.

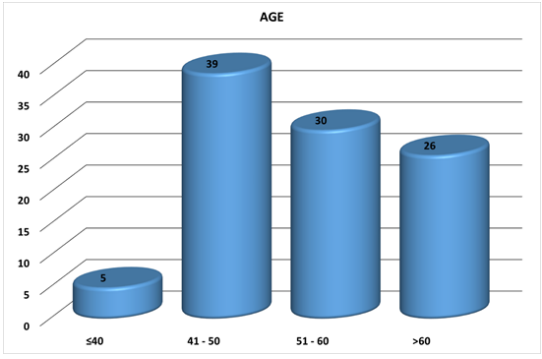
The P value is 0.335. There is no statistical evidence to say that the sex has any impact on the age at which lung cancer occurs as per our study even though the mean age in females is less than in males

Table 2 Age and smoking status amongst the study population

SMOKING STATUS	N	MEAN AGE	STD. DEVIATION	P-VALUE¥
YES	50	56.54	9.871	0.07
NO	50	52.68	11.206	

¥ Independent T-test
P<0.05 – significant

Figure 2 Age distribution in the study population



Most of the patients were above the age of 50 years. Overall mean age at which lung cancer occurs is 54.6 years as per the study. Only 5 patients out of the total of 100 were less than 40 years. 39 were in the 41 to 50 age group; 30 in the 51 to 60 group and 26 were above 60. More than half the patients were diagnosed after 50 years of age.

50% of the study subjects were smokers and 50% were non smokers. This shows the emerging trend of non smokers getting lung carcinoma. It is interesting to note that none of the women in the study were smokers.

Out of 100 patients 38 patients had adenocarcinoma, 25 had squamous cell carcinoma, 8 patients had large cell carcinoma and 9 had small cell variety. 20 patients had undifferentiated lung cancer on histologic examination.

Figure 3 Smoking status amongst the male population in the study group

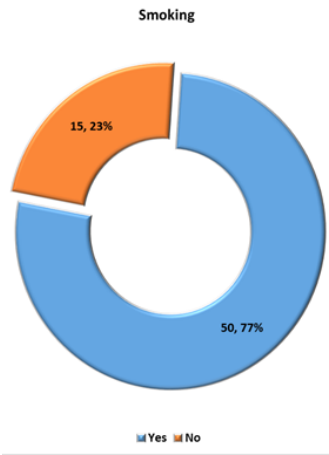


Table 3 Distribution of types of malignancy in the study population

SUB TYPE	NO. OF PATIENTS	PERCENTAGE (%)
SQUAMOUS CELL	25	25.0%
ADENOCARCINOMA	38	38.0%
LARGE CELL	8	8.%
SMALL CELL	9	9.%
UNDIFFERENTIATED	20	20.%

Table 4 Age distribution of adenocarcinoma in the study population

AGE		N	MEAN	STD. DEVIATION	P-VALUE¥
ADENOCARCINOMA	YES	38	48.16	8.056	<0.001
	NO	62	58.56	10.201	

¥ Independent t-test
P<0.05 – significant

Small cell carcinoma and squamous cell carcinoma occur at a higher age compared to the other types of cancer. Mean age of squamous cell carcinoma is found to be 60 and that in small cell type 61.

Adenocarcinoma tends to occur in a younger age group with a mean age of 48 years as shown in the table. The p vale for the above distribution is statistically significant. This assumes special significance especially in the case of adenocarcinoma.

50 of the 100 lung cancer patients were smokers. All of them were males. None of the 35 females in the study had ever smoked.

64% of patients with squamous cell carcinoma were smokers. More than half of those with small and large cell carcinomas were smokers and half of those in the undifferentiated category were smokers. However majority of the patients with adenocarcinoma had never smoked. It is interesting to note that females were more afflicted by adenocarcinoma than other types and that all thefemales were non smokers.

Table 5 Smoking status and type of cancer in males

SUB TYPE	SMOKING STATUS		TOTAL
	YES	NO	
SQUAMOUS CELL	16(32%)	3(20%)	19(29.2%)
ADENOCARCINOMA	14(28%)	8(53.3%)	22(33.8%)
LARGE CELL	5(10%)	1(6.7%)	6(9.2%)
SMALL CELL	5(10%)	1(6.7%)	6(9.2%)
UNDIFFERENTIATED	10(20%)	2(13.3%)	12(18.5%)
TOTAL	50	15	65

As all the females were non smokers in our study and as it was reflective of our society, the distribution of various types of malignancies in male smokers and male non smokers was studied. It showed that more than 80% of males with squamous cell carcinoma were smokers. Almost all the male patients with small cell,large cell and undifferentiated lung carcinomas were smokers.

Compared to the other types, the percentage of smokers in males with adenocarcinoma was less – around 65%.

Table 6 Gender distribution of different types of lung cancers in the study population

SUB TYPE	SEX		TOTAL	P-VALUE¥
	MALE	FEMALE		
SQUAMOUS CELL	19(29.2%)	6(17.1%)	25(25%)	0.6
ADENOCARCINOMA	22(33.8%)	16(45.7%)	38(38%)	
LARGE CELL	6(9.2%)	2(5.7%)	8(8%)	
SMALL CELL	6(9.2%)	3(8.6%)	9(9%)	
UNDIFFERENTIATED	12(18.5%)	8(22.9%)	20(20%)	
TOTAL	65	35	100	

¥ Chi square test
P<0.05 – significant

As per the sex distribution charts shown above, adenocarcinoma tends to occur more in females. Almost half of the female patients with lung cancer had this subtype. In males squamous cell and adenocarcinoma were almost equally distributed. Adenocarcinoma was the most common type of cancer in both the sexes.

However 76% of the patients with squamous cell carcinoma were males. Overall 65% patients were also male. But adenocarcinoma showed a trend favouring females compared to the other subtypes as around 45% cases were females in this type. This trend is supported by a studyin annonc. [12]

In females, after adenocarcinoma, undifferentiated malignancy was the most common followed by squamous cell carcinoma. Most of the patients had more than one presenting complaint. Overall the most common presenting complaint was cough. 61% of the patients in the study had cough. This was followed by dyspnoea and loss of appetite at 40 and 32 % respectively.20% had haemoptysis at presentation.

Fever, symptoms S/O of SVC syndrome, low back ache, hoarseness of voice etc. was some of the rarer presenting complaints.

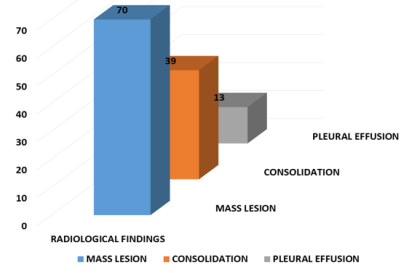
Loss of appetite was not a common complaint in their study unlike our observation. SVC syndrome at presentation showed an incidence of 6% in that study also. Other common presenting complaints followed the trends in our observation. Cough and dyspnoea are the predominant complaints in almost all types of cancer. Loss of appetite and weight are also seen in a significant proportion all the types. Patients presenting with back pain or lower limb weakness due to spinal metastases were seen only in small cell carcinoma and adenocarcinoma.

Chest pain is particularly more in adenocarcinoma. Higher percentage of patients with squamous cell carcinoma had haemoptysis than other types.

2 cases each of squamous cell carcinoma, small cell carcinoma and adenocarcinoma had SVC syndrome.

A patient might have more than one feature on chest imaging. Overall, mass lesion was the most common radiological finding. 70% of the patients in the survey had mass lesion on chest xray and CT scans. This was followed by collapse/ consolidation.39% of the people had this finding on chest imaging.Pleural effusion was a rather rare finding.Only 13% of the patients had pleural effusion.Mediastinal lymphadenopathy has not been included as a feature in the study per se.

Figure 4 Frequency distribution of radiological features in the study population



In squamous cell carcinoma, 19 of the 25 patients had mass lesion on imaging. 7 showed consolidation and 2 had pleural effusion. Likewise, in adenocarcinoma, 27 patients had a mass lesion and 17 showed collapse consolidation on x-ray or CT of the chest. Likewise, in small cell, large cell and undifferentiated lung carcinomas also mass lesion was the most common radiological finding. Some patients had a combination of the above findings.

Table 7 Frequency distribution of history of Anti-tuberculosis therapy(ATT) in the study population

SUB TYPE	ATT		TOTAL	P-VALUE¥
	YES	NO		
SQUAMOUS CELL	3(30%)	22(24.4%)	25(25%)	0.149
ADENOCARCINOMA	5(50%)	33(36.7%)	38(38%)	
LARGE CELL	0(0%)	8(8.9%)	8(8%)	
SMALL CELL	2(20%)	7(7.8%)	9(9%)	
UNDIFFERENTIATED	0(0%)	20(22.2%)	20(20%)	
TOTAL	10	90	100	

p<0.05 - significant

A total of 10 patients out of the 100 lung cancer patients studied had a history of prior ATT. Most of these cases were of the adenocarcinoma subtype. Of the 38 patients with adenocarcinoma 5 had a history of ATT. Out of 25 squamous cell carcinoma cases 3 had taken prior ATT.

EML4/ ALK TRANSLOCATION:

All the 38 patients with adenocarcinoma were subjected testing for the presence of EML4/ALK translocation in their biopsy specimens. Immunohistochemistry techniques were used for the same. Of all the 38 specimens tested none of them turned out to be positive for the above translocation. Overall the prevalence of Anaplastic Lymphoma Kinase mutation in adenocarcinoma lung is shown to be less than 5%

CONCLUSION

There is a change in the demographic pattern of lung cancer. While smoking still remains the primary risk factor, a significant number of non-smokers are being affected. Though males are more affected, there is a rise in the number of females with the disease. An overwhelming majority of males with the disease were smokers. The mean age of disease onset is also less than what is classically thought to be. Adenocarcinoma is the most common histological type of lung cancer in the population followed by squamous cell carcinoma. More females and non-smokers and those in the younger age group had contracted adenocarcinoma compared to the other subtypes.

Patients usually present with vague multiple symptoms. The classically described respiratory symptoms would be present in a majority of the patients. But quite a few of them may have atypical features like systemic symptoms and symptoms related to metastases at the time presentation. Even radiologically there may be only vague features. A high index of suspicion is required to make an early diagnosis which is very crucial to the patient's final diagnosis.

None of the patients with adenocarcinoma were positive for ALK mutations in the study population. A higher sample size may be required to assess the exact prevalence of ALK mutations in the community.

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