

Original Research Article

Epidemiological snapshot of carcinoma lung at a tertiary cancer centre of Bihar, India

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ABSTRACT

Background: According to the GLOBOCAN 2020 report, the estimated incidence of lung cancer in India was 72,510 in all ages and both sexes. In incidence, lung cancer ranked fourth overall among the various types of cancer. To study epidemiological profile in terms of clinical presentation, stage, risk factors and factors associated with late stage presentations at a newly established tertiary cancer care hospital Bihar

Methods: This was a retrospective-prospective analysis of collected data of histopathologically proven lung cancer cases in the Outpatients department (OPD) of Department of Radiotherapy, All India Institute of Medical Sciences (AIIMS), Patna over a period of 2.5 years from March 2018 to October 2020.

Results: There were 140 patients, with a median age of 56 years, 59.28% (n=83) were smokers, 37.14% (n=52) used chewing tobacco, 24.28% (n=34) worked on earthen stoves and 15% (n=21) had passive smoking exposure. The male-to-female ratio was 1.64:1. Non-small cell lung carcinoma comprised 87.85% (n=123), stage IV presentation in 76.42% (n=107) cases with the most common site of metastases being bone (35.51%, 38 patients). IHC was performed on 64 patients (45.71%) of total 140 patients of which 51 patients were of adenocarcinoma histology. 35.29% (n=18) were EGFR positive and 28.57% (n=4) tested ALK positive. 4 patients tested for ROS-1 were negative. 32.14% (n=45) cases were treated empirically for Tuberculosis on the finding of chest X-ray only.

Conclusions: Majority of the patients were males in advanced stage. Bone is the most common site of metastases. Long empirical treatments lead to late presentations.

Keywords: Lung cancer, Epidemiology, Tuberculosis, Anaplastic lymphoma kinase

INTRODUCTION

A consistent and comparative description of the burden of diseases and injuries, and risk factors that cause them, is an important input to health decision-making and planning processes. At the global level, 7 of the 10 causes of death in 2019 were non-communicable diseases. These seven causes made up 44% of all deaths or 80% of the top 10. However, all non-communicable diseases accounted for 74% of deaths worldwide by 2019. The death toll from Trachea, bronchus and lung cancers has risen from 1.2

million to 1.8 million and is now ranked 6th among the leading causes of death.¹ According to the GLOBOCAN 2020 report, the estimated incidence of lung cancer in India was 72,510 in all ages and both sexes. In terms of incidence rates, lung cancer ranked fourth overall among the various types of cancer (excluding non-melanoma skin cancer).² The top five cancers in men and women account for 47.2% of all cancers; these cancers can be prevented, screened for and/or detected early and treated at an early stage. This could significantly reduce the death rate from these cancers.³ Tracy et al concluded from her study that patients

with localised NSCLC are most likely to have no potentially curative surgery if they live distant from a specialist hospital and attend a general hospital for their care.⁴ Some studies have shown that as the distance of the patient's residence increases from the tertiary care hospitals, there is an incidence of patients presenting in higher stage of the disease, mostly attributed to empirical tubercular treatments based on chest x-rays only, that they continue for 2-6 months before being referred or presenting to higher centres. Of all cancers, rural people had lower rates of local cancer and higher rates of long-term cancer. The incidence of long-term lung cancer was higher in all rural groups.⁵

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.

The changing epidemiological profile of lung cancer is portrayed by increasing incidence of adenocarcinoma variety of lung cancer among both smokers and non-smokers. Various factors responsible include smoking tobacco, non-smoking tobacco both among males and females and also passive smoking and cooking of earthen chulhas predominantly among female population. In Bihar household using clean fuel for cooking in rural areas are only 30%.⁶ Another study by Bahara and Balamugesh showed a significant contribution of biomass fuel exposure in the development of lung cancer. This association is present even after adjusting for smoking.⁷

Molecular genetics of lung cancer has opened up new vistas of research in carcinogenesis.[8] Due to increasing occurrence of adenocarcinoma, there is a shift towards testing for the molecular markers as there is a relation between the molecular markers positivity (EGFR/ALK/ROS1) in adenocarcinoma group with feasibility of treatment offered and the response rate. Also in other histopathological subtypes, the trend towards molecular studies are increasingly being popular and various treatment modalities targeting the molecular alterations had given promising results.

Objective

Studying the epidemiological profile could help us formulate policies about healthcare system and treatment approaches. It will give an insight into the presentation, cause, factors responsible, molecular trends to some extent.

METHODS

This was a retrospective-prospective analysis of collected data of histopathologically proven lung cancer cases registered in the Outpatients department (OPD) of Department of Radiotherapy, All India Institute Of Medical Sciences (AIIMS), Patna over a period of 2.5 years retrospectively from March, 2018 to July 2020 and prospectively from August 2020 to October 2020. Diagnostic modalities like CECT thorax, bronchoalveolar lavage, CT-guided or bronchoscopy guided tumor tissue biopsy for histopathology and immunochemistry and/or molecular studies.

All histopathologically confirmed lung cancers patients who attended the Department of Radiotherapy, AIIMS, Patna from March 2018 to October 2020 were included in the study. These patients were treated according to the department protocol and prior informed consent was obtained regarding use of their data for departmental research. Patient data with incomplete investigations or workup were excluded from the analysis. Institutional Ethics Committee was obtained.

The following information was extracted from the database: age, gender, place of residence, use of smoking or smokeless tobacco, use of earthen chulhas or any history of passive smoking. The database was also used to gather information regarding the histological subtype of lung cancer, the stage at presentation, site of metastases if any, any history of tuberculosis or any empirical treatment for tuberculosis taken at peripheries due to lack of access to proper healthcare system.

Histological subtype and stage of lung cancer

Histological subtype was established on the basis of morphology or relevant immunohistochemistry wherever feasible. The staging was done according to the American Joint Committee on Cancer (AJCC), 8th classification.⁹ These patients were treated according to the department protocol and prior informed consent was obtained regarding use of their data for departmental research.

Inclusion criteria

All the Histopathologically proven Lung cancer were taken for the study.

Exclusion criteria

Patients who has diagnosed more than once cancer. Patient not giving consent.

Statistical analysis

Quantitative variables were summarized as mean and standard deviation while nominal/categorical variables were presented as proportions (%). Statistical package for

social sciences (SPSS) 22.0 version software was used for all statistical calculations.

RESULTS

Demography

Out of the total 140 patients, the majority belonged to the 51-60 years of age group, comprising 32.85% (46 patients) of the total patients with the mean age of presentation 56.171 years with 13.1143 SD. The male to female ratio was 1.64:1. Smoking continues to stand in the first place among cases of lung cancer with 59.28% (83 patients) of total patients, giving a history of smoking. Non-smoking tobacco or as we call 'chewing addiction' was found among 52 patients who accounted for 37.14% of the total. The following two factors were found to be limited to the female group, firstly the use of a clay stove (chulha) among 34 patients (24.28%) and secondly, the passive smoking among 21 patients (15%) of total patients. (Table 1)

Histopathological type of cancer

The majority of the cases comprised of Non-Small Cell Lung Cancer (NSCLC) consisting of 87.85% (123 patients) of the total number. Small cell lung cancer (SCLC) comprised only 10.71% (15 patients) and some other histologies combined to 1.42% (2 patients).

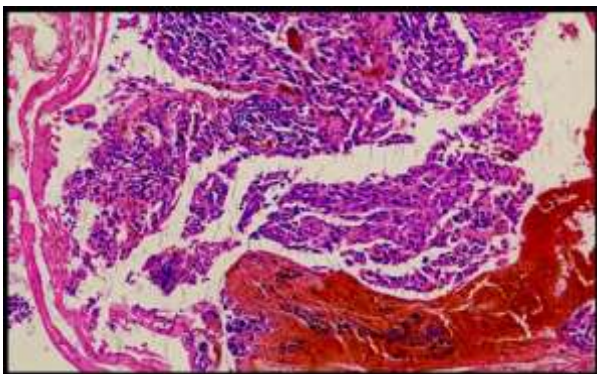


Figure 1: Hematoxylin and Eosin stain for squamous cell carcinoma (100X).

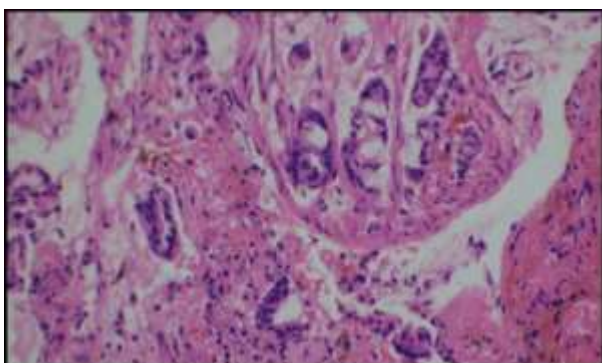


Figure 2: Hematoxylin and Eosin stain for adenocarcinoma (100X).

Upon further analysis of the histopathological components, the Adenocarcinoma ranked first among the NSCLC (75 patients, 53.57%) followed by Squamous cell carcinoma (40 patients, 28.57%). Other histologies included Adeno-squamous, Mesothelioma and Neuro-endocrine tumor comprising of 2.85% (4 patients) each and inflammatory myo-fibroblastic tumor and Poorly differentiated synovial sarcoma consisting 0.71% (1 patient) each. (Figure 1, 2 and Table 1)

Stage of presentation

The majority of the population presented in the stage IV (76.42%, 107 patients) i.e., metastasis at diagnosis was present and the rest in stage IIIB (17.14%, 24 patients) and IIIA (6.42%, 9 patients). Metastases percentage for individual age groups as compared to total number of patients who presented in that particular age group was maximum in the >70 years (12 out of 15 patients, 80% of patients in this age group), followed by 31-40 years (10 out of 13 patients, 76.92%), 41-50 years (20 out of 27 patients, 74.07%), 51-60 years of age (32 out of 46 patients, 69.56%), 61-70 years (23 out of 34 patients, 67.64%) and 21-30 years (3 out of 5 patients, 60%). The most common site of metastases was found to be bone (35.51%, 38 patients) followed by liver, malignant pleural effusion, contralateral lung, supra-clavicular lymph node and adrenal glands. The major histopathology of the metastases at diagnosis was that of NSCLC (94 patients, 87.85%) and especially that of adenocarcinoma (60 patients, 56.07% of total 107 patients presenting with metastases) and squamous cell carcinoma (30 patients, 28.03% of total 107 patients presenting with metastases) followed by adeno-squamous, mesothelioma, neuroendocrine tumor and small cell carcinoma. (Table 1, 2)

Immuno-histochemistry (IHC) study

IHC was performed on 64 patients (45.71%) of total 140 patients. Of these 64 patients 51 patients (79.7% of IHC tested patients) were of adenocarcinoma histology. Rest 13 belonged to squamous cell carcinoma (8 patients), neuroendocrine tumour (2 patients), small cell carcinoma (2 patients), and low grade inflammatory myofibroblastic tumour (1 patient).

Out of the 51 adenocarcinoma patients tested for IHC, EGFR was performed on all of them, 14 patients were tested for both EGFR and ALK and 4 patients were tested for EGFR, ALK and ROS-1. 18 patients (35.3% of 51 adenocarcinoma patients tested for EGFR) were EGFR positive and 33 patients (64.7% of 51 adenocarcinoma patients tested for EGFR) were negative. 4 patients (28.6% of 14 ALK tested patients) were ALK positive and 10 patients (71.4% of 14 ALK tested patients) were negative. ROS-1 was tested for 4 patients out of the 51 adenocarcinoma patients tested for IHC and all of them were negative for it. 8 patients were both EGFR and ALK negative and 3 patients were EGFR negative but ALK positive (Table 3).

Table 1: Patient data.

	Variables	Number (N)	%
No. of patients		140	
Median age		56.17 years	
Age of presentation (years)	21-30	5	3.57
	31-40	13	9.29
	41-50	27	19.29
	51-60	46	32.86
	61-70	34	24.29
	>70	15	10.71
Sex	Male	87	62.14
	Female	53	37.86
	Male:female	1.64 : 1	
Past history of tuberculosis		22 patients	15.71
Patients who underwent empirical TB treatment based of Chest X-ray only	No	95	67.86
	Yes (1 month-6 month)	45	32.14
Risk factors	Smoking	83 patients	59.29
	Passive smoking	21 patients	15.00
	Earthen stove (chulhas)	34 patients	24.29
	Non-smoking tobacco	52 patients	37.14
	Alcohol	10 patients	7.14
Histopathological classification of major subtypes	NSCLC	123	87.86
	SCLC	15	10.71
	Others	2	1.43
Stage of presentation of patients with lung cancer	IIIA	9	6.43
	IIIB	24	17.14
	IV	107	76.43

Table 2: Tumour characteristics.

	Variable	Number (N)	%
Histopathological subtypes of lung cancers	Adenocarcinoma	75	53.57
	Squamous cell carcinoma	40	28.57
	Small cell carcinoma	11	7.86
	Adeno-squamous carcinoma	4	2.86
	Mesothelioma	4	2.86
	Neuro-endocrine tumor	4	2.86
	Inflammatory myo-fibroblastic tumor,	1	0.71
	PD synovial sarcoma	1	0.71
Site of metastases at diagnosis (including multiple sites of metastases)	Adrenal gland	4	3.73
	Bilateral lung nodules	19	17.76
	Bone	38	35.51
	Liver	24	22.42
	Supraclavicular lymph node	7	6.54
	Malignant pleural effusion	23	21.50
Histopathological relation of patients presenting with metastases at diagnosis	Brain	8	7.48
	NSCLC	94	87.85
	SCLC	9	8.41
	Other	4	3.74
NSCLC subtype associated with metastases at diagnosis	Adenocarcinoma	60	63.83
	Adeno-squamous carcinoma	4	4.26
	Squamous cell carcinoma	30	31.91
Poorly differentiated synovial sarcoma		1	0.93

Continued.

Variable	Number (N)	%
Mesothelioma	3	2.80
Small cell carcinoma associated with metastases at diagnosis	9	8.41

Table 3: Immunohistochemistry profile.

Variable	Number(N)	Percentage (%)
IHC	No	54.28
	Yes	45.72
EGFR	Negative	64.7
	Positive	35.3
ALK	Negative	71.4
	Positive	28.6
ROS1	Negative	100
	Positive	0.00

Risk factors associated with lung cancer

Smoking was present among 71.42% (100 patients) of the patients who presented with metastases at the first visit. Nonsmoking tobacco and alcohol also accounted for 71.43% (100 patients) each but passive smoking and earthen stoves were minimal contributors. Although metastases was also found among 30 patients of those who had no history of exposure to these factors (Table 1).

Tuberculosis and lung cancer

Actual history previous TB was found in 22 patients (15.71%) and among whom only 50% (11 patients) took completed Anti-tubercular therapy (ATT). Rest 50% defaulted from ATT.

45 patients (32.14%) were treated empirically for TB based on the finding of chest X-ray only for a period ranging about 1 month to 6 months and later presented to higher centres when the symptoms were not relieved (Table 1).

DISCUSSION

Lung cancer is the fourth most common cancer worldwide in terms of incidence according to the GLOBOCON 2020 report. It spreads to other parts of the body through the blood and lymphatic system, a process called metastasis, which in turn quickly causes the growth of secondary tumors. Other risk factors such as smoking, breathing polluted air, and living in a contaminated environment can adversely affect the prognosis and quality of life of patients with lung cancer.

Out of the 140 patients that presented to our newly established tertiary cancer care centre between March 2018 to October 2020, it was found that majority of the patients were males and belonged to the age group of 51-60 years. The mean age of presentation for lung cancer patients (both males and females) was 56 years. The finding of concern was that almost 76.42% presented in stage IV (i.e.,

metastases at diagnosis). Rest of the patients presented in stage IIIB (17.14%) and IIIA (6.42%). None of the patients that presented to our OPD were diagnosed to be stage I or II. The reason for this late presentation was undetermined but after some research into the census of the state, according to 2020 data, literacy rate was 71.20% for males and 51.50% for females.¹⁰ Some studies had suggested that long distance between the place of residence and the nearest tertiary cancer care centre is also one of the factors for late presentation.⁴ But among the patients who presented to our institute this factor was not significant because those who resided in the city versus those who presented from the peripheries, majority were in the advanced stage already. There was no sex preference for the metastases and percentage being nearly equal among both males and females. Metastases percent was maximum in the >70 years (80% of patients in this age group), followed closely by age-group of 31-40 years (76.92%).

For the history of Tuberculosis, it was found that 32.14% of the patients were treated empirically for TB based on the finding of chest X-ray only for a period ranging about 1 month to 6 months and later presented to higher centres when the symptoms were not relieved. This factor also contributed to the finding of presentation at advanced stage of the disease. Actual history previous TB was found in 22 patients (15.71%) and among whom only 50% (11 patients) took completed ATT. Rest 50% defaulted from ATT.

In agreement with the changing global pattern of lung cancer, Adenocarcinoma ranked first among the various histopathological diagnosis (53.57%) followed by squamous cell carcinoma (28.57%).¹¹ As evident by these data NSCLC was the major histopathology of diagnosis (87.86% overall). Other lesser percentage of diagnosis belonged to adenosquamous, mesothelioma, neuroendocrine tumors, inflammatory myo-fibroblastic tumor and poorly differentiated synovial sarcoma.

Smoking remains ahead in the race of risk factors with 59.29% of total population involved in smoking tobacco. Smoking was also associated with 71.43% of the cases that presented with metastases at diagnosis. Smokeless tobacco (or chewing tobacco) was next. Working on earthen stoves (chulhas) and passive smoking were less significant factors and were exclusively confined to the female population. Nonsmoking tobacco and alcohol also accounted for 71.43% each. Passive smoking and earthen stoves were minimal contributors. Metastases was also reported in 28.57% of patients, who had no history of exposure to these factors.

Bone was site of metastases in majority of the cases, followed by liver, malignant pleural effusion, contralateral lung, supra-clavicular lymph node and adrenal glands. The major histopathology of the metastases at diagnosis was that of NSCLC (87.85%) and especially that of Adenocarcinoma (63.8% of total NSCLC presenting with metastases at diagnosis), followed by squamous cell carcinoma (30 patients, 31.9% of total NSCLC presenting with metastases at diagnosis) followed by adeno-squamous, mesothelioma, neuroendocrine as equal contributors of 75% each of their total respective subtypes. 81.8% total small cell carcinoma presented with metastases at diagnosis accounting for 8.41% of total cases with metastases with all histologies included.

Immunohistochemical marker study was started later at our institute in the year 2019. Due to higher cost of this investigation as compared to other investigations, though it was offered to the patients but only 64 patients (45.71%) opted for it. We did some research again in the economic census of Bihar it was found that the poverty ratios using the Tendulkar Committee methodology of Bihar was 34.1% for the rural and 31.2% for the urban areas in 2011-12. The overall poverty ratio was 33.7%, which is much higher than at the all-India level. That justifies the unwillingness of the patients for the test. Weighing the economic status of the patients against cost of IHC marker study, at minimum EGFR analysis was offered to all the adenocarcinoma patients so that they could be put to atlas some therapy rather than no therapy due to financial constraints altogether. Of these 64 patients tested for IHC, 51 patients (79.7% of IHC tested patients) were of adenocarcinoma histology. Rest 13 belonged to other histologies. Out of the 51 adenocarcinoma patients tested for IHC, EGFR was performed on all of them, 14 patients were tested for both EGFR and ALK and 4 patients were tested for EGFR, ALK and ROS-1. 35.3% of patients were EGFR positive which is in accordance with other studies stating that there is a large variation in the EGFR mutation rate across various ethnicities and geographies. The mutation rate ranges from 10% to 15% in Caucasians and 30% to 51% in Asian population.¹² There are significant differences in the number of EGFR mutations across different races and regions. The conversion rate ranges from 10% to 15% in the Caucasus and 30% to 51% in the Asian population.¹² In our study also 55.5% of EGFR positive patients were non-smoker females. Another study

was in agreement with this data which concluded the incidence of EGFR mutation in NSCLC is 33% from Kolkata and is typically more common in females and nonsmokers.¹²

Limitations

This study has potential limitations. The patient data for the retrospective period was stored with many incomplete information and so they had to be excluded from the analysis. The IHC for all the patients was not feasible due to limitation of resources and financial constraints of the patients. Also patient number in the prospective period is limited due to covid pandemic and less number of patients visiting hospitals for treatment.

CONCLUSION

Majority of the patients presenting to our centre were in advanced or metastatic stage with one-third of them treated empirically for tuberculosis without actual confirmation. Low level of awareness at the peripheries and financial constrains for seeking treatment were the major culprits behind this which needs to be addressed at grass root level in the state.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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