

ORIGINAL ARTICLE

Histological Pattern of Bronchial Carcinoma in Tertiary Care Hospital in Bangladesh

Mousumi Podder¹, Farzana Mahejabin², S.M. Abdur Razzaque³, Shayela Farah⁴, Manoranjan Roy⁵, Gourab Podder⁶

Abstract:

Background: Lung cancer is the most common malignant neoplasm worldwide. Among all human cancers, carcinoma of the lung has the highest mortality rate and is the leading cause of all cancer deaths. However, histological types may vary with the changes in geographical region, smoking status and other social factors. Among the few published reports, squamous cell carcinoma of lung is more common in male smokers.

Aim: This study was aimed to find out the specific histological type of lung cancers patients of Bangladeshi people.

Methods: This was a cross-sectional study and was conducted on bronchial carcinoma patients who had been admitted and diagnosed at the department of respiratory medicine, National Institute of the diseases of the Chest & Hospital (NIDCH). Total 120 diagnosed case of bronchial carcinoma were included in the study. The respondents were divided into two groups, smokers and non-smokers. Following informed written consent, 100 smoker and 20 non-smoker patients were interviewed and information was recorded in the questionnaire. The laboratory investigations were collected from patients or attendants. Ethical issues were maintained and the results of histological diagnosis were obtained to complete the data sheet and analyzed by SPSS, Z test, t test, chi-square test.

Results: A total of 120 patients were interviewed. Among them, 86.7% were males and 13.3% were females and ratio were 6.5:1. The mean age of the patients were 59.41±2.89 years. Out of the 120 patients, 100 patients (83.3%) had history of smoking in their life time and 20 patients (16.7%) were non-smoker. In case of male, majority of patients were smokers (82.5%) and in case of female, majority of patients (12.5%) were non-smokers. Among smokers, squamous cell carcinoma (44.1%) was the most common histological type followed by adenocarcinoma (6.7%). In case of non-smokers, the status was entirely different and here adenocarcinoma was the most common type and which constituted 11.7% and squamous cell carcinoma in non-smokers was less and only 1.7%. Among male patients 45% had squamous cell carcinoma which was higher than other histological types of cancer. In case of female patients 10.83% had adenocarcinoma, which was higher than other histological types of lung cancer.

Conclusion: In male smokers, squamous cell carcinoma is still the most frequent histological type of bronchial carcinoma in present study. In case of females and non-smokers adenocarcinoma is the predominant histological type.

Key words: Histological Pattern, Bronchial carcinoma.

[Chest Heart J. 2021; 45(1) : 12-18]

DOI: <http://dx.doi.org/10.33316/chab.j.v45i1.2019631>

1. MPH (Community Medicine, BSMMU), Dhaka Community Medical College, Dhaka.
2. Professor, Department of Community Medicine, Dhaka Community Medical College, Dhaka.
3. Associate Professor, Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
4. Associate Professor, Department Community Medicine, Dhaka Community Medical College, Dhaka.
5. Assistant Professor, Department of Respiratory Medicine, NIDCH, Dhaka.
6. Medical Officer (Ex), ICDDBB, Mohakhali, Dhaka, Bangladesh.

Correspondence to: Dr. Mousumi Podder, MPH (Community Medicine), Dhaka Community Medical College, Dhaka. Mobile-01716846350, E-mail- mousumi19850@gmail.com

Submission on: 10 December, 2020

Accepted for Publication: 26 December, 2020

Available at <http://www.chabjournal.org>

Introduction:

Among all human cancers, carcinoma of the lung has the highest mortality rate and is the leading cause of all cancer deaths. Lung cancer is a leading cause of morbidity and mortality globally, accounting for 2,094 million cases and 1.8 million deaths per year.¹ Lung cancer is the most common malignant disease in developed countries, causing more deaths than breast, colorectal, prostate and pancreatic cancer combined. It is one of the health problems in Bangladesh of which smoking plays the most vital role. Lung cancer mainly originates from the basal epithelial cells and is mainly classified into two types, non-small cell lung cancer and small cell lung cancer. Among these non-small carcinomas is more common and which accounts for around 85% of lung cancer cases.² The main histological types of lung cancer are adenocarcinoma, squamous cell carcinoma, large cell carcinoma and small cell carcinoma.³ All the diverse histological types are somehow associated to tobacco smoking. However, the intensity of association between smoking and adenocarcinoma is much lesser than between smoking and squamous cell carcinoma or small cell carcinoma. In the mid-1900s lung carcinoma was an uncommon disease. Now it is in relevant proportions and is presently the prominent cause of cancer related deaths in the western countries.^{4,5} In the recent decades, the percentage of squamous cell carcinoma (which was predominant) has decreased and the trend shows an increase of adenocarcinoma in both genders. Histological gradation of the bronchial carcinoma in order of frequencies were squamous cell carcinoma 54.7 %, small cell carcinoma 24.1%, adenocarcinoma 16.9% and large cell carcinoma 4.3%.⁶ In another study, squamous cell carcinoma was found 31.7%, adenocarcinoma 30.9%, and large cell carcinoma 26%.⁷ Although squamous cell carcinoma has for many years been the most common. Adenocarcinoma has been increasing in incidence over last 20 years.⁸ Adenocarcinoma has become today the most frequent histological type of lung cancer and is responsible for 50% of all lung cancers.⁹ However, it is also possible that the increase in lung adenocarcinoma cases, in fact, may be caused also by increasing smoking prevalence. A direct association between smoking and various histologic types of lung cancer has been observed

for measures of intensity, duration and dose. Studies conducted in the USA, Western Europe and China observed a higher smoking related risk of squamous cell carcinoma and small cell carcinoma than that of adenocarcinoma of the lung. The largest of these studies suggested that intensity of cigarette exposure has less distinct effect on all cell type than duration of use with duration more strongly associated with SQCC and SMCC than adenocarcinoma. The distribution of lung cancer by histological type differs between smokers and non- smokers and even among smokers, is different for man and woman. In both sexes adenocarcinoma is much more common among non-smokers than smokers.¹⁰ But regardless of smoking status, squamous cell carcinoma is much more common among men and adenocarcinoma is more common among women.¹¹ Lung cancer has a tremendous impact on US mortality, with an estimated total 142670 deaths in 2019 in men and women combined.¹² It is the common malignant disease in developed countries, there approximately 228150 new patients per year in the USA and 85000 patients per year in the UK; the incidence is increasing rapidly in developed countries. The disease is more common in men than women, although this difference has become smaller; in USA and the UK the male/female ratio was approximately 2.5:1.¹³ But in 2019 in USA male/female ratio was around 1.04:1. Risk of developing lung cancer increases with duration of smoking and the number of cigarettes smoked per day and is diminished by discontinuing smoking. In the United States, current estimates indicate that 87% of all cases of lung cancer are directly attributable to cigarette smoking. This includes 51.03% of lung cancer in men and 48.96% of cases in women. The lifetime risk for developing lung cancer in a nonsmoker is probably about 1% less. Environmental, or secondhand, tobacco smoke, is also implicated in causing lung cancer. Environmental tobacco smoke has the same components as inhaled mainstream smoke, although in lower absolute concentrations, between 1% and 10%, depending on the constituent. It has been estimated that cigarette smokers are 8-20 times more likely to develop lung cancer than life long nonsmokers and the extent of this risk correlates closely with the number of cigarettes smoked.¹⁴ In Bangladesh out

of all cancer patients, 8.2% is newly diagnosed with lung cancer, the number might seem insignificant but that is about 12,374 people. A new study suggests that cases of lung cancer have been on the rise in Bangladesh, with the number of smokers and air pollution levels rising. The report claimed that from January 2015 to December 2017, a total 5,887 people with lung cancer were admitted in National Institute of Cancer Research and Hospital. Their study also reported that 81.56% lung cancer in male smoker. Squamous cell carcinoma was most frequent type among the males and smokers, but adenocarcinoma more in females and nonsmokers.¹⁵Data on histological pattern of bronchial cancer is limited in Bangladesh pointing out to the need of more researches for prevention and treatment. Therefore, this study was aimed to identify histological pattern of bronchogenic carcinoma in tertiary care hospital in Bangladesh.

Materials and methods:

This was a cross-sectional type of Descriptive study, was conducted in the Department of Respiratory Medicine, National Institute of the Diseases of the chest & Hospital (NIDCH), located in the Mohakhali, Dhaka-1212, Bangladesh, during the period of 1 year (January 2020-December2020). Total 120 patients were enrolled consecutively who was confirmed as a case of bronchial carcinoma. The information regarding bronchial carcinoma was collected from each patient in whom the diagnosis was confirmed by CT guided FNAC of chest and FNAC of the cervical lymph nodes, biopsy reports. Exclusion criteria were 1. Patients who refused to be part of the study.2. Patients having major concomitant diseases i.e., recent MI, CVD, serious cardiac dysrhythmias, unstable angina etc.3. Patients having bleeding

diathesis.4.Sputum positive for acid-fast bacilli (AFB).Written informed consent was obtained from patient. Before requesting consent, the individual was explained in an understandable language about the aims of the study, the methods of conduct, expected duration of subject participation, benefits, foreseeable rights or discomfort, the extent of investigators responsibility, the right to refuse to participate and withdraw from the study without affecting further medical care. All information were properly documented in the data sheet. All questionnaires were checked for completeness, accuracy and consistency to exclude missing or inconsistent data. Data were checked, cleaned and edited properly before analysis and for this analysis recent version of worldwide well accepted statistical software SPSS (Statistical Package for Social Science) were used. During analysis, age, sex and other baseline characteristic differences were analyzed by Z test, t test and chi-square test whenever necessary. Results were presented by choosing variable form of tables, graph, percentage, and chart. In all cases, p-value <0.05 was considered statistically significant.

Results:

In this study 120 patients with bronchial carcinoma, squamous cell carcinoma (44.1%) was the most common histological type among the smokers followed by adenocarcinoma (6.7%). In case of non -smokers, the status was entirely different and here adenocarcinoma was the most common type and which constituted 11.7% and squamous cell carcinoma in non-smokers was less and only 1.7%. Among male patients 45% had squamous cell carcinoma which was higher than other histological types of cancer. In case of female patients 10.83% had adenocarcinoma which was higher than other histological types of lung cancer.

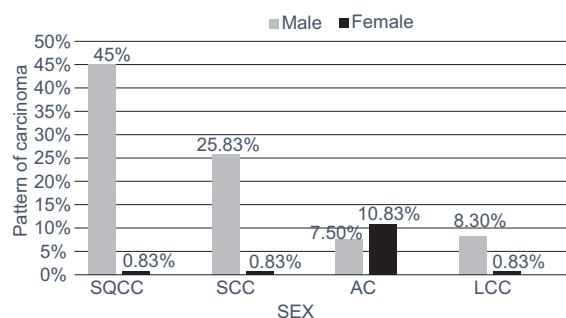
Table-I
Age and sex distribution of study respondents (n=120)

Age (in years)	Male		Female		Total		P value
	Number	%	Number	%	Number	%	
35-44	7	5.8	2	1.7	9	7.5	
45-54	22	18.33	10		32		26.7
55-64	35	29.17	2	1.7	37	30.83	0.00001
65-74	34	28.33	1	0.83	35	29.1	
75-84	6	5	1	0.83	7	5.83	
Total	104	86.7	16	13.3	120	100.0	

[Analysis done by t test and SPSS. P value-0.00001]

It is observed that most of the male patients were in the age range of 55-64 years 35(29.17%), followed by 65-74 years 34(28.33%), 45-54 years 22(18.33%) and 75-84 years 6(5%). Among female patients majority were in the age range of 45-54 years 10(8.3%) followed by 65-74 years and 75-84 years 1(0.83%); 35-44 years and 55-64 years 2(1.66%). The mean age of the patients were 59.41 years with SD±2.89. In case of male the mean age of the patients were 60.46 years with SD ±3.11& in case female the mean age of the patients were 52.62 years with SD ±9.07; Male: Female were 6.5:1. It was evident that statistically significant age difference was found between male and female patients (p<0.05).

Figure 1- It was found that major proportion of squamous cell carcinoma 54(45%) were in male



[SQCC-Squamous Cell Carcinoma, SCC-Small Cell Carcinoma, ACC-Adenocarcinoma, LCC-Large Cell Carcinoma]

Fig.-1: Distribution of the respondents by histologic pattern and sex of the patients.

respondents and majority 13(10.83%) adenocarcinoma were found in female respondents.

The table shows distribution of study subjects by histologic pattern and age of the patients. It was found that among squamous cell carcinoma majority 20(16.7%) were in the age group of 55-64 years and 5(4.1%) were found in large cell carcinoma in the same age group. Among the patients of small cell carcinoma 12(10%) were found 65-74 years age group, adenocarcinoma 11(9.1%) were found in 45-54 years age group.

Figure 'I- It was found that majority 55(45.83%) respondents had squamous cell carcinoma, followed by 32(26.7%) had small cell carcinoma, 22(18.33%) had adenocarcinoma, 11(9.2%) had large cell carcinoma.

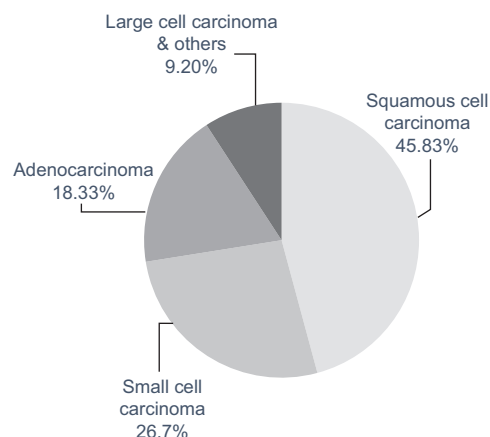


Fig.-1: Distribution of the respondents by histologic patterns of carcinoma

Table-II

Distribution of the respon	Pattern of carcinoma				Total	P value
	SQCC	SCC	AC	LCC		
35-44	5(4.1)	2(1.7)	1(0.83)	1(0.83)	9(7.5)	0.847
45-54	12(10)	7(5.8)	11(9.1)	2(1.7)	32(26.7)	
55-64	20(16.7)	10(4.3)	2(1.7)	5(4.1)	37(30.83)	
65-74	15(12.5)	12(10)	6(5)	2(1.7)	35(29.2)	
75-84	3(2.5)	1(0.83)	2(1.7)	1(0.83)	7(5.83)	
Total	55(45.83)	32(26.7)	22(18.3)	11(9.1)	120(100)	

[Analysis done by t test and SPSS. P value-0.847]

[SQCC-Squamous Cell Carcinoma, SCC-Small Cell Carcinoma, ACC-Adenocarcinoma, LCC-Large Cell Carcinoma]

Discussion

It has been observed by different studies that in both developed and developing countries, tobacco smoking is widely prevalent. It is found in all classes of people from very high to low class, which is one of the important preventable causes of premature death. In developing countries, it has been estimated that nearly 50% of man are dependent on some form of tobacco use whereas less than 50% of women are smokers.^{12,16} The main objective of present study was to find out the different histological types of lung cancer in tertiary care hospital in Bangladesh. This was a cross-sectional type of descriptive study conducted in the NIDCH Dhaka during the period of January 2020-December 2020. A total of 120 histologically proven primary lung cancer patients were included in the study.

In this study, out of 120 patients, 104 (86.7%) were male and 16 (13.3%) were female and Male: Female ratio was 6.5:1. The number of female patients were small in this study which can be explained by the fact that in our country females are dependent mostly on husband and or guardian, religious and social grounds act as a barrier; over and above bronchogenic carcinoma is uncommon in females of our country. In the Jonathan M S, Erika A T study showed that male and female ratio among smokers was 32:1 and among non-smokers 1:1.9.¹⁷ In Navin P, Balbin M study found that male and female ratio was 5:1.¹³ The frequency of tobacco habits among females is very low compared to male. The increasing percentage of smoking in males was consistent with the study reports from developing countries.¹⁸ These studies were almost similar with present study. But it was not similar with the statistics of the American Cancer Society in 2019 which reveals that among 235760 new cases of lung cancer-119,100 (50%) were found in men and 116,660 (49%) in women. This might be due to fact that tobacco smoking in women of this country (USA) became increasingly popular day by day.¹²

In the present study, it was found that most of the patients belonged to the age range of 55-64 years among smokers 35(29.1%) and in case of non-smokers majority 12(10%) of the patients belonged to the age range of 45-54 years. These findings were consistent with the Tsugaway, Hashimoto K study which showed that out of 473 patients 51%

were above 50-60 years of age. Lung cancer mainly occurs in older people. Most of the patient were diagnosed with lung cancer above 60 years of age, a very small number of patients were diagnosed below 45 years of age.¹⁶

In the present study, it was found that among the smoker patients highest percentage were among the farmers (32.5%). This was because more than 70% of the population of our country belong to cultivation. Among the non-smokers, most of the patients were housewives (10.8%). These findings were almost similar with the Dubey N, Julka Arti study which showed that most of the smoker patients were farmers (72.3%) and non-smokers were housewives.¹⁸

In the present study, out of 120 patients among the smoker patients 68(56.7%) had monthly family income below 20,000 BDT followed by 27(22.5%) between 20,000-40,000 BDT. Among the non-smoker patients, 10(8.3%) had monthly family income between 20,000-40,000 BDT, followed by 5(4.1%) had monthly family income below 20,000 BDT. This was quite similar with Elahi MQE, Razzak MA study. They found that majority of smoker patient's (85.93%) monthly family income was below 10,000 BDT.¹⁹

In the present study, highest percentage of patients had squamous cell carcinoma 55(45.8%) followed by small cell carcinoma 32(26.7%) and adenocarcinoma 22(18.3%). It was observed that among the smoker patients majority of bronchial carcinoma were squamous cell carcinoma 53(44.1%) followed by small cell carcinoma 32(26.7%) and adenocarcinoma 22(18.33%). Among the non-smoker patients, most of the bronchial carcinoma were adenocarcinoma 14(11.7%), followed by squamous cell carcinoma 2(1.7%). Similar findings were observed in C. Muhas, Palur Ramakrishnan Anand Vijaya Kumar study. They found among the smoker patients, squamous cell carcinoma (63.25%) was the most common histological type followed by adenocarcinoma (22.89%). In case of non-smoker patients, the status was entirely different and here adenocarcinoma was the most common type which constituted 66.67% and the presence of squamous cell carcinoma in non-smokers were very less only 15.27%.²⁰

In the present study, it was found that major proportion of squamous cell carcinoma 54(45%),

small cell carcinoma 31(25.8%) were higher in male respondents whereas adenocarcinoma 13(11.0.8%) was proportionately higher among female respondents. In C. Muhas, Palur Ramakrishnan study, it was observed that in case of male patients squamous cell carcinoma was the predominant histologic type of lung cancer (55.84%) followed by adenocarcinoma (29.95%) and small cell carcinoma (10.15%). In case of female patients, adenocarcinoma was the most prevalent histologic type (65.85%) and squamous cell carcinoma was 14.63%.²⁰ These findings were similar with the present study.

In the present study it was found that mean number of smoking was 22.79±1.4 sticks/day. The mean number of smoking 26.89±1.9 sticks/day for squamous cell carcinoma, followed by 21.16±2.7 sticks/day for small cell carcinoma, 24.61±4.8 sticks/day for large cell carcinoma. It was almost similar with Yelena Y, Kevin Mc Donnell study which showed that number of smoking more than 30 sticks/day for squamous cell carcinoma and 20 to 29 sticks/day smoking for small cell and large cell carcinoma.²¹

It was observed in the present study that among squamous cell carcinoma majority 20(16.7%) were in the 55-64 years age group and 5(4.1%) were found in large cell carcinoma in the same age group. Among the patients of small cell carcinoma 12(10%) were 65-74 years age group, adenocarcinoma 11(9.1%) were found in 45-54 years age group. These findings were consistent with AL. Hashimi MMY, C. Muhas, Rahul G study. These studies found increasing number of lung cancer patients were in older age group, particularly in the sixth and seventh decades of life. Highest percentage of squamous cell carcinoma were in the 61-80 years age group.^{20,22,23}

In the present study, it was found that highest percentage of squamous cell carcinoma 30(25%) and small cell carcinoma 27(22.5%) had monthly family income below 20,000 BDT, whereas large cell carcinoma 5(4.2%) patients had monthly family income between 20,000-40,000 BDT, adenocarcinoma 12(10%) monthly family income above 40,000 BDT. These findings were almost similar with Rahul G, Ishfaq C study. These studies found smokers of low socioeconomic status (low household income) were associated with an increased risk of squamous cell carcinoma.²³

In the present study, it was found that squamous cell carcinoma was more frequent in male smoker respondents in 55-64 years age group and adenocarcinoma was more in non-smokers and female respondents in 45-54 years age group. These findings were supported by SEER Cancer statistics 2017 and WHO 2019.^{24,25,26}

Conclusion:

In this present study, out of 120 respondents 104 patients were males and 16 patients were females and ratio were 6.5:1. It was found that among the smokers, most of the patients belonged to the 55-64 years age group and in case of nonsmokers majority were 45-54 years age group. Out of 120 respondents, 100 patients had history of smoking in their life time and 20 patients were nonsmoker. It was found that among the smoker patients highest percentage were the farmers. Among the nonsmokers, most of the patients were housewives. Among the smokers, squamous cell carcinoma was the most common histological type of cancer. In case of nonsmokers adenocarcinoma was the most common type of cancer. Among male patients 45% had squamous cell carcinoma which was higher than other histological types of lung cancer. In case of female patients 10.83% had adenocarcinoma which was higher than other histological types of lung cancer.

Data of the present study confirmed a marked relationship between smoking and all histological types of lung cancer under the study and also showed that squamous cell carcinoma is more frequent among male smokers and adenocarcinoma in non-smoking females. However, the association of smoking and adenocarcinoma remain unclear at the moment. Further work in this field should be encouraging.

References:

1. Bray F, Ferlay J, Soerjomataram I, Siegel R, Torre L, Jemal A. Global cancer statistics. GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; 68:394-424.
2. Reck M, Heigener D F, Mok T, Soria J C and Rabe K F. Management of non-small-cell lung cancer: recent developments. *Lancet* 2013; 382:709-19.
3. Binukumar B, Saina SK and Satheesan B. Lung cancer in Malabar Cancer Center in

- Kerala -A Descriptive analysis. *Asian Pacific J Cancer Prev* 2012; 13:4639-43.
4. Parvaiz A K, Satish K K, Mohammad MS, Reyaz A T and Azra S. Lung cancer in the Kashmir valley. *Lung India* 2010; 27:131-7.
 5. Alberg A, Wallace K, Silvestri G and Brock M. The etiology of lung cancer in men compared with women. *Am J Epidemiol* 2013; 177:613-6.
 6. Gupta R, Chowdhury I, Singh P. Clinical, Radiological and Histological profile of Primary Lung Carcinomas. *JK Science* 2015; 17(3):146-51.
 7. Abo-Elkheir OI, Hafez MR. Characteristics, risk factors and histopathological types of bronchogenic carcinoma among cases presented to chest Department, Al-Zahraa Hospital, Al-Azhar University. *Int J Community Med Public Health* 2018;5:1281-90.
 8. Akl YM, Emam RH, Sabry IM, Ali AA. Clinicopathological profile of bronchogenic carcinoma cases presented to chest department, Cairo University in the last 10 years. *Egyptian J Chest Diseases Tuberculosis* 2013; 62:705-12.
 9. Kader A, Albasri M. A histopathological analysis of lung cancer. *Saudi Med J*. 2019 ;40(5): 503-506.
 10. Hathilia N, Goswami D. Radiological evaluation of various types of primary bronchogenic carcinoma: a study of 65 cases. *Int J Med Sci Public Health*. 2016 ;5(5):1.
 11. Gupta V, Bhardwaj S, Bhagat OK. Pattern of transbronchial lung biopsy-proven lung malignancies in tertiary care hospital in north India: a clinicopathological study. *Int J Adv Med* 2016;3(4):804-7.
 12. ACS 2019 cancer facts and figures. Atlanta, Ga; American cancer society 2019.
 13. Navin P, Balbir M, Nirmalchand K, Rahul RP, Nagaraja CL and Nidhi M. Clinicopathological profile of patients with lung cancer visiting chest and TB hospital Amritsar. *Sch J App Med Sci* 2015; 3(2D): 802-9.
 14. Dubey AK, Gupta U, Jain S. Epidemiology of Lung cancer and approaches for its prediction: a systematic review and analysis. *Chinese J Cancer* 2016;35(1):71.
 15. Globacon 2018: Bangladesh. [Internet; cited 2019, October].
 16. Tsugaway Y, Hashimoto K, Tabuchi T, Shibuya K. Non small cell lung cancer treatment. *Lancet* 2017 ;390 :933-939.
 17. Samet J M, Tang E A, Boffetta P, Hannan L M, Rudin C M. Lung cancer in never smokers and clinical epidemiology and environmental risk factor. *Clin cancer Res* 2010; 5(18): 5626-5645.
 18. Dubey N, Julka A, Varudkar H G, Agarwal J C, Bhandari D. A clinicopathological profile of primary lung cancer patients presenting in a rural medical college of central India. *Panacea Journal of medical science* 2015;5(3);124-129.
 19. Elahi MQE, Razzak MA, Islam MA. Demography of Lung cancer patients. *Journal of Armed Forces Medical College* 2019; 15(1):32-34.
 20. Muhus C, Ramakrishnan P, Kumar A V, Sreenivasan P, Raja D. Correlational of age and gender with different histological subtypes of primary lung cancer. *IJPSR* 2018;9(12): 5490-5495.
 21. Yelena Y J, Kevin M D, Gregory J R. Pack years of Cigarette Smoking as a Prognostic factor in patients with non-small cell lung cancer. *IJPSR* 2010;116(3):670-675.
 22. AL-Hashimi MMY and Wang XJ. Trend analysis of lung cancer incidence rates in Ninawa province, Iraq, from 2000 to 2010-decrease and recent stability. *Asian Pac J Cancer Prev* 2014; 15:385-90.
 23. Rahul G, Ishfaq C and Pritpal S. Clinical, Radiological and Histological profile of primary lung carcinomas. *JK Science* 2015; 17:146-51.
 24. SEER Cancer Statistic Review,1975-2014.National cancer Institute 2017. [Available <https://seer.cancer.gov/csr/1975-2014>. Updated April 2, 2018.]
 25. World Health Organization. Global health risk: mortality and burden of disease attributable to selected major risks. Geneva: World Health Organization 2010.
 26. An estimated 12.6 million deaths each year are attributable to unhealthy environments. WHO 2019. [Available <https://www.who.int/news/room/detail>. Updated 15-03-2016.]