

Common risk factors of Lung cancer, an observational study in a National Institute, Dhaka

Bodiuzzaman MM¹, Hussain MZ², Morshed SMM³, Islam MR⁴, Akhtaruzzaman M⁵
Asaduzzaman M⁶, Khatun N⁷, Akhter PS⁸

Abstract

Lung cancer is the most prevalent malignant neoplasm in most of the countries, and is leading cause of mortality worldwide. Till date tobacco consumption is the main etiological factor in lung carcinogenesis. Other factors such as genetic susceptibility, poor diet, occupational exposures and air pollution may act independently. Treatment of lung cancer is time consuming, costly and need special care during its management. Post treatment complications also more and sometimes it is more serious and becomes life threatening to the patients. The study was done to find out the most common risk factors of lung cancer, for this we can take necessary preventive measure from those risk factors to prevent health burden and mortality from lung cancer. This observational study was done in the department of Medical Oncology, National Institute of Cancer Research and Hospital (NICRH), Mohakhali, Dhaka, from January 2012 to May 2012. One hundred and six (106) patients, aged over 30 years, included all sexes, were diagnosed as a lung cancer by histopathology and came for chemotherapy, were selected randomly in this study after informed written consent. In this study we found males are predominantly affected (92.45%) by lung cancer and common age groups affected are between 51-60 years (39.62%). Among the occupation farmers are more affected (77.35%) and most of them were active smokers (64.15%). In our study we found that right side of lung is more affected (58.49%) than left side and adenocarcinoma was predominant (35.84%). Control of tobacco smoking is the most important preventive measure. This study may help us to identify the etiological aspect and future preventive efforts and research be needed to focus on tobacco smoking and non-cigarette tobacco smoking products, as well as better understanding of risk factors underlying lung carcinogenesis in never-smokers.

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Introduction

Lung cancer is the most frequent malignant neoplasm among men in most countries and the main cause of cancer death in both sexes. Despite the success in delineation of tobacco smoking as the major risk factor for lung cancer, this highly preventable disease remains among the most common and most lethal cancers globally. 1.38 million Deaths (18.2% of the total) by 2008 in the world (Ferlay et al., 2010)¹ and almost half (49.9%) of the lung cancer cases occur in the developing countries (Siegel et al., 2013).² Accounting for an estimated 27% of total cancer deaths in the USA in 2015 and 20% in the European Union (EU) in 2016.³

According to GLOBOCAN (Global Cancer Observatory), in 2012 lung cancer accounted for an estimated 1242000 new

1. Dr. M. M. Bodiuzzaman; Assistant Professor (Medicine); Faridpur Medical College.
2. Dr. Muhammad Zubaer Hussain; Assistant Professor (Medicine); Sher E Bangla Medical College, Barishal.
3. Dr. S. M. Munawar Morshed; Assistant Professor (Radiotherapy), Faridpur Medical College.
4. Dr. Md. Rafiqul Islam; Assistant Professor (Medical Oncology) NICRH; Mohakhali, Dhaka.
5. Dr. Md Akhtaruzzaman; Registrar (Medical Oncology) NICRH; Mohakhali, Dhaka.
6. Dr. Md Asaduzzaman; Assistant Registrar (Medical Oncology) NICRH; Mohakhali, Dhaka.
7. Dr. Nazrina Khatun; Associate Professor (Medical Oncology) NICRH; Mohakhali, Dhaka.
8. Dr. Parveen Sahida Akhter; Professor & Head (Medical Oncology), NICRH; Mohakhali, Dhaka.

Address of correspondence:

Email: drbodiuzzaman72@gmail.com
Mobile: 01763-771144

cases among men, which is 17% of all cancers excluding non-melanoma skin cancer, and 583000 (9%) of new cancer cases among women.³ Approximately 58% of all cases occur in middle- and low-income countries.⁴ Lung cancer also accounts for 19% of all cancer deaths.⁵ Among both women and men, the incidence of lung cancer is low in people aged <40 years and increases up to age 60 years and above.

Tobacco smoking is the major cause of all major histological types of lung cancer. Approximately 20 potential carcinogens of ~3,500 chemicals have been detected in a burning cigarette. The most established are the polycyclic aromatic hydrocarbons (PAH) like benzo(a) pyrenes, and the tobacco-specific N-nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), while others include Asz-arenes, Dibenz(a,h) acridine, inorganic compounds like cadmium, chromium, nickel, arsenic, radioactive polonium (Po210) and organic compounds like butadiene.⁶ Nitrates in the tobacco are reduced to NH₂⁻ and NH₃ while smoking. Air-cured tobacco contains higher concentrations of aromatic amines as compared to flue-cured tobaccos (e.g. the urinary bladder carcinogens β₂-naphthylamine and 4-aminobiphenyl).⁷ Cigarette smoke contains high levels of acrolein, which is toxic to the ciliated lining of the lungs, and other agents such as nitrogen oxides, acetaldehyde, phenols, and formaldehyde, which may contribute indirectly to pulmonary carcinogenicity in animals and humans. Cigarette smoke also contains free radicals (FR) (e.g. hydrogen peroxide [H₂O₂], hydroxyl ion [OH⁻], sulfoxide anion) which induce oxidative damage in animal models as well as humans, while catechol and hydroquinone play their roles in single strand DNA breaks caused by the release of FR.⁸

There is evidence from case-control studies that a diet rich in vegetables and fruits, especially cruciferous vegetables, may exert some protective effect against lung cancer.^{9,10} Here is evidence from

observational studies that low levels of vitamin D are associated with lung cancer risk¹¹ however, results of randomized trials do not provide supportive evidence. Coffee drinking has been associated with lung cancer as coffee drinkers were more likely to be smokers than non-coffee drinkers.¹² Also, no evidence of an increased risk has been reported in studies of never-smokers.¹⁰ There is some evidence of a chemo preventive effect of tea, notably green tea, in smokers.¹³ However, the overall evidence is not consistent.

Patients with chronic obstructive pulmonary disease are at increased risk for lung cancer, and a number of studies have suggested that this is independent of smoking.¹⁴⁻¹⁶ Patients with pulmonary tuberculosis have been found to be at increased risk of lung cancer.¹⁷

Exposure to ionizing radiation increases the risk of lung cancer.¹⁸ This increased risk has been reported in atomic bomb survivors, as well as patients treated with radiotherapy (RR 1.5-2 for cumulative exposure in excess of 100 cGy).¹⁹

Occupational exposures play a significant role in lung cancer aetiology, and the risk of lung cancer is increased among workers employed in a number of industries and occupations.²⁰ Two studies have reported an estimate of the proportion of lung cancer cases attributable to occupational agents in the UK to be 14.5% overall²¹ and 12.5% in men in France.²² The most important occupational lung carcinogens are reported to be asbestos, silica, radon, heavy metals and polycyclic aromatic hydrocarbons.²³

Material and Methods

This retrospective observational study was done in the department of Medical Oncology, National Institute of Cancer Research and Hospital (NICRH), Mohakhali, Dhaka, from January 2012 to May 2012. One hundred and six (106) patients, aged over 30 years were diagnosed as lung cancer by histopathology and came for chemotherapy, were selected randomly. Informed written consent was taken during

data collection in a questioner form. Patients were included in this study, who gave voluntary consent, clear history regarding risk factors and whose histopathological reports support confirm diagnosis. Patients were excluded from this study those didn't give voluntary consent, clear history about risk factors and whose histopathological reports were not adequate. A proforma was designed to collect information regarding various parameters like age, sex, occupation, risk factors, diagnostic tools, site of cancer and histopathological types. All relevant data were collected, edited, organized into tables and analyzed by SPSS computerized program.

Results

Age and sex distribution:

Age (in years)	No. of patients(%)
<40	04(3.77)
40-50	24(22.64)
51-60	42(39.62)
61-70	30(28.30)
70-80	06(5.66)
Sex	
Male	98(92.45)
Female	08(7.54)

Table I: Age and sex distribution

Table I shows, among the patients diagnosed as lung cancer age ranges from 35 - 80 years with median age 55 years. Age less than 40 years were 04 (3.7%), 40-50 years 24 (22.64%), 51-60 years 42 (39.62%), 61-70 years 30 (28.3%) and 70-80 years 06(5.6%). Regarding gender distribution male 98(92.45%) and female 08(7.54%).

Occupation profile:

Occupation	No. of patients(%)
Farmer	82(77.35)
Businessman	11(10.37)
Official worker	09(8.49)
Housewife	04(3.77)

Table II: Occupation chart

Table II shows, Farmer 82(77.35%), Businessman 11(10.37%), Official worker 09(8.49%) and Housewife 04(3.77%).

Risk factors:

Risk factors	No. of patients(%)
Active smoker	68(64.15)
Ex-smoker	20(18.86)
Nonsmoker(n=18) 16.98%	
No cause found	07(6.60)
Use of biofuel	05(4.71)
COPD	04(3.77)
Evidence of arsenicosis	02(1.88)
Pack year(among smokers)	
>40	58(54.71)
30-40	19(17.92)
<30	11(10.37)

Table III: Distribution of risk factors

Table III shows active smoker 68 (64.15%), ex-smoker 20 (18.86%), non-smoker 18 (16.98%) and among this no cause was found in 07(6.60%) patients. Among smokers most of the patients smokes >40 pack year (54.71%)

Site and types of lung cancer:

Site of lung involvement	No. of patients (%)
Right lung	62(58.49)
Left lung	44(41.50)
Histopathological types	
Small cell lung cancer (SCLC)	22(20.25)
Non-small cell lung cancer (NSCLC)	84(79.25)
Adenocarcinoma	38(35.84)
Squamous cell carcinoma	18(16.98)
Large cell carcinoma	15(14.15)
Anaplastic carcinoma	09(8.50)
Others	04(3.77)

Table IV: Site and major histo-pathological type

Table IV shows Right sided lung cancer was 62(58.49%), and left sided 44(41.50%). Among the histo-pathological types of lung cancer, Small cell lung cancer 22(20.25%) and non-small cell lung cancer 84 (79.24%). Adenocarcinoma 38 (35.84%), Squamous cell carcinoma 18 (16.98%), Large cell carcinoma 15(14.15%), Anaplastic cell carcinoma 09(8.50%) and others 04 (3.77%).

Discussion:

Lung cancer mainly occurs in older person and most people diagnosed with lung cancer are 65 years and above, very small number of people is younger than 45 years. But in our study we found lung cancer more in under age of 60 years. This may be due to we have no actual birth registration at the time of birth so the patients have no idea about their actual age. Most of them hide their age to doctors. They start smoking at early age and smoke more than usual. They use cigarette without filter. Genetic factors also may be the cause of early lung cancer and patient with genetic susceptibility who smoke increase the risk of lung cancer. But in western countries they are well educated and have birth registration at the time of birth and their life expectancy is more than our country.

In this study male affected predominantly (92.45% male compared to 7.54% female) because male consume more cigarette than female. Due to religious background of our country, most of Muslim women avoid smoking. Males start smoking in early part of their life and consume more than female. Male persons are also exposed to outside dusts and other biohazards than to female. But in western country this figure is different because they smoke more cigarette than our female population. In western countries the incidence of lung cancer is also higher among men (34%) as compared to women (13.5%). The age-standardized ratio for cancer incidence is 33.81%, and for mortality is 29.2% in men alone.²⁴ But in our country smoking habit in female is increasing day by day especially in affluent society. Female who smoke got chance more to become a lung cancer. This emphasizes that females may respond differently to tobacco-specific carcinogens for certain cell-types.^{25,26} Several molecular studies have also suggested that sex-differences in lung cancer biology do exist. Examples include, females having higher DNA adduct levels,²⁷ an increased *CYP1A1* expression,²⁷ a decreased DNA repair capacity²⁸ and an

increased incidence of *K-ras* gene mutations.²⁹ A novel estrogen receptor β was also detected in lung tumours,³⁰ although both exogenous and endogenous estrogens might be involved in lung cancer development.³¹ All these indicate that estrogen signaling could have a biological role in lung carcinogenesis. Another factor of lung cancer in female is genetic factor called GRPR (Gastrin releasing peptide receptor) is linked to abnormal growth lung cells is more found in women in both smoker and non-smoker than it is in men.

In our study smoking is most common risk factor and among these, active smoker (64.15%), ex-smoker (18.86%), non-smoker including male and female (16.98%). In female, smoking is also common risk factor. Also there is definite relationship between smoking in pack year and lung cancer. In our study people with lung cancer consume cigarettes >40 pack year risk is 54.17%, 30- 40 pack year risk is 17.92% and <30 pack year least risk (10.37%). In other study tobacco smoking is also major cause of all major histological types of lung cancer. In the USA, tobacco use is responsible for nearly 1 in 5 deaths. In 2012, the estimated percentage of new lung cancers in males (116,470 cases) and females (109,690 cases) was 14% each. Among these lung cancers, 29% of male and 26% of female cases were estimated to be fatal. Smoking accounts for at least 30% of all cancer deaths and 87% of lung cancer deaths.³²

A carcinogenic effect of tobacco smoke on the lung was demonstrated in epidemiological studies conducted since the early 1950s and has been recognized by public health and regulatory authorities since the mid-1960s.³³ The geographic and temporal patterns of the disease largely reflect tobacco consumption accumulated during previous decades.^{34,35} The excess risk among continuous smokers relative to that among never-smokers is in the order of 20 to 50 fold. Duration of smoking should be considered the strongest determinant of lung cancer risk in smokers.³⁶ The relative risk decreases in ex-smokers, and a

favorable effect of stopping is apparent even for cessation later in life. However, an excess risk throughout life probably persists even in long-term quitters.³⁵

In our study lung cancer occurs more in right site 58.49% than to left site 41.50%. Probably this is due to nature of right bronchus, which is shorter, wider and more nearer to major bronchus. For this smoking tar and other form of carcinogen enters easily more in right site.

In our study small cell lung cancer 20.75% and non-small cell lung cancer 79.25%. Adenocarcinoma 35.85%, Squamous cell carcinoma 16.98%, Large cell carcinoma 14.15%, Anaplastic cell carcinoma 8.50% and others 3.77%. Among other cases, lymphoma (n=02), neuroendocrine tumor (n=01), sarcomatoid tumor (n=01). This results are almost similar with other established data, where small cell lung cancer 15%, and non-small cell lung cancer 85%, Adenocarcinoma 35-40%, Squamous cell carcinoma 25-30%, Large cell carcinoma 10-15%.³⁷

In our study adenocarcinoma is also more than others type of lung cancer. Adenocarcinoma occurs both in current and ex-smoker but also more seen in nonsmoker, for this reason we found all female patient including smoker and nonsmoker are adenocarcinoma variety. The Irish National Cancer Registry Board based in Cork has been registering lung cancer incident cases from January 1st, 1994.³⁸ In total, 10,514 lung cancer incident cases (6,823 in males, 3,691 in females) were registered in the Republic of Ireland from 1994 to 2000. Of these, Squamous cell carcinoma was the most frequent cell-type in both males (34%) and females (22%), while adenocarcinoma was relatively high among female populations across all the periods studied (18% vs. 14% in males). The frequency of Small cell lung cancer was also high in females (17% vs. 12% in males); large cell carcinoma was the least frequent cell-type across both sexes (3%).

Occupational exposures play a significant role in lung cancer etiology, and the risk of

lung cancer is increased among workers employed in a number of industries and occupations.³⁹ Two studies have reported an estimate of the proportion of lung cancer cases attributable to occupational agents in the UK to be 14.5% overall⁴⁰ and 12.5% in men in France.⁴¹ The most important occupational lung carcinogens are reported to be asbestos, silica, radon, heavy metals and polycyclic aromatic hydrocarbons. But in our study we are unable to detect any relation of specific occupational agents associated with lung cancer.

Conclusion

For lung cancer prevention, control of tobacco smoking is the most important preventive measure. While the effects of tobacco control in the past few decades on the incidence and mortality of the disease can be appreciated, much remains to be done, in particular among women and in the area of lung cancer screening in smokers using low-dose computed tomography scans. Other priorities for the prevention of lung cancer include control of occupational exposures, as well as indoor and outdoor air pollution, and understanding the carcinogenic and preventive effects of dietary and other lifestyle factors.

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