

Prevalence of Lung Cancer in Non Smoker Patients Attending Al-Diwaniyah Teaching Hospital

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Abstract

Background: Smoking is a well known risk factor that is implicated in a number of human malignant disorders.

Aim of the Study: To study the prevalence of lung cancer in a sample of Iraqi non smoker patients and the main risk factor implicated in such malignant tumor.

Patients and Method: In this hospital based study, in order to explore the prevalence rate of bronchogenic carcinoma in non smoker patients ,it retrospectively collected data about those patients for the last four years, starting from January 2016 through June 2019. These information were retrieved from patients records that are already present in oncology and respiratory units in Al-Diwaniyah teaching hospital, Al-Diwaniyah province, Mid-Euphrates region of Iraq. The following variables were included in the questionnaire form: Age, gender, occupation, education level, residency, socioeconomic status, marital status history of smoking, history of second hand smoking, number of household smokers, type of smoking, history of alcoholism, history of chronic illness, the main presenting clinical features and clinical features of carcinoma and finding in examination as well as those obtained from investigations.

Results: In the current study, the prevalence rate of all cases of lung cancer during the period of study was 61 out of 403 (15.1 %). the rate of lung cancer in none smokers, in the current study, was 39.3 %. Old age individuals were the main age group affected and there was female predilection. there was also no significant difference in the distribution of patients and control subjects according to residency, occupation, level of education marital status and socioeconomic status ($P > 0.05$). In the current study, the prevalence rate of passive smoking in patients was significantly higher than that in control subjects, 70.8 % versus 40 %. Moreover, the number of household smokers was significantly higher inpatients group than in control group.

Conclusion: Lung cancer in non smokers appears to be significantly correlated with passive smoking in addition to increase incidence in old age and women.

Key words: Prevalence; Lung Cancer, Non Smoker, Iraq.

Introduction

The term, *never smokers*, refers to persons who have smoked fewer than 100 cigarettes in their lifetime, including lifetime nonsmokers. Most studies that track the trend of lung cancer rates often include both smokers and never smokers, and few studies independently study the trends over time for never smokers because of the limited longitudinal collection and the limited reliability of smoking information in population-based registries. From what is available, however, the overall global

statistics estimate that 15% of lung cancers in men and up to 53% in women are not attributable to smoking, with never smokers accounting for 25% of all lung cancer cases worldwide ¹. If lung cancer in never smokers were considered separately, it would rank as the seventh most common cause of cancer death worldwide before cervical, pancreatic, and prostate cancer ². In countries in South Asia, up to 80% of women with lung cancer are never smokers ³. In the United States, one study estimated that 19% of lung cancer in women and 9% of

lung cancer in men occurs in never smokers⁴. The age-adjusted rate for lung cancer in never smokers (ages 40–79 years) ranged from 11.2 to 13.7 per 100,000 person-years for men and from 15.2 to 20.8 per 100,000 person-years for women. The rates are 12 to 30 times higher in current smokers of the same age group. Lung cancer included heterogeneous group of malignant epithelial disorders that comprises squamous cell carcinoma, adenocarcinoma, small cell carcinoma and large cell carcinoma as well as a number of rare histopathological subtypes such as bronchoalveolar carcinoma. The most common subtype by far is squamous carcinoma and is mainly attributed to smoking but a number of cases have been reported in life time non smokers. Because of the shortage of Iraqi literatures dealing with lung cancer in non smokers since most published Iraqi articles deal with smoking related lung cancer, and because we are interested in making an idea about the prevalence rate of lung cancer in non smokers and to outline its possible risk factors in our community we planned and conducted the current study to one of leading articles in the Mid-Euphrates region dealing with this important human cancer.

Patients and Method

In this hospital based study, in order to explore the prevalence rate of bronchogenic carcinoma in non smoker patients we prospectively interviewed 5 cases during 2019 and retrospectively collected data about those patients for the last 3years, starting from January 2016 through June 2018. These information were retrieved from patients records that are already present in oncology and respiratory units in Al-Diwaniyah teaching hospital, Al-Diwaniyah province, Mid-Euphrates region of Iraq. However for purpose of comparison in order to evaluate possible risk factors in association with non smoker bronchogenic carcinoma we included in the study 25 apparently healthy individuals serving as control group. Records of all patients with established diagnosis of bronchogenic carcinoma were included in the present study. Variables were registered concerning those patients who are never smokers. Although records of smoker patients with bronchogenic carcinoma were retrieved, information about them were used for calculation of prevalence rate of lung cancer in non smoker only, and the rest of information were excluded. The total number of patients with all kinds of malignant tumor was also obtained to calculate the prevalence

rate of bronchogenic carcinoma out of all malignant tumors. The following variables were included in the questionnaire form: Age, gender, occupation, education level, residency, socioeconomic status, marital status history of smoking, history of second hand smoking, number of household smokers, type of smoking, history of alcoholism, history of chronic illness, the main presenting clinical features and clinical features of carcinoma and finding in examination as well as those obtained from investigations. The study was approved by the institutional ethical approval committee and formal agreement was obtained from the directorate of Health in Al-Diwaniyah province, the formal representative of Iraqi Ministry of health. Data were collected and transformed into a spread sheet of Microsoft Office Excel 2010 and then into an SPSS (statistical package for social sciences) version 23. Numeric quantitative data were expressed as mean, range and standard deviation (SD), whereas, qualitative data were expressed as number and percentage. Comparison of mean between any two groups was done according to independent sample t-test, while chi-square test was used to evaluate association between any two categorical variables. The level of significance was considered at $P \leq 0.05$.

Results

During that period the number of cases with malignant tumors, including lung cancer, accounted for 403. In addition, the total number of cases with lung carcinoma during the period of study, irrespective of smoking, was 61. Therefore, the prevalence rate of all cases of lung cancer during the period of study was 61 out of 403 (15.1 %), out of which 24 cases were associated with evidence of passive smoking (39.3 %). Table .1 outlines the comparison of age between control and patients group. There was no significant difference in mean age between patient and control group, 61.63 ± 15.31 years versus 68.28 ± 8.50 years, respectively ($P = 0.065$). The age range of patients with bronchogenic carcinoma was from 30 – 85 years. In addition the frequency distribution of patients according to 10 years intervals was as following: 8.3 %, 16.7 %, 4.2 %, 41.7 %, 12.5 % and 16.7 % as 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years and ≥ 80 years, respectively. Thus, the highest incidence rate was observed at age interval of 60-69 years, table 1.

Table 1: Mean age and age range of patients and control subjects

Age (years)	Control group n = 25	Patients group n = 24	P
30-39	0 (0.0)	2 (8.3)	
40-49	0 (0.0)	4 (16.7)	
50-59	2 (8.0)	1 (4.2)	
60-69	13 (52.0)	10 (41.7)	
70-79	6 (24.0)	3 (12.5)	
≥ 80	4 (16.0)	4 (16.7)	
Mean ±SD	68.28 ±8.50	61.63 ±15.31	0.065 †
Range	55 - 90	30 - 85	NS

n: number; data were presented as mean standard deviation or number (%); †: independent samples t-test; NS: not significant at $P \leq 0.05$

With respect to gender, women accounted to 15 out 24 patients with bronchogenic carcinoma thereby accounting for 62.5 %, making the male to female ratio 1:1.7. Control group included 12 men and 13 women; therefore there was no significant difference in the distribution of patients and control subjects according to gender, as shown in table 2. There was also no significant difference in the distribution of patients and control subjects according to residency, occupation, level of education marital status and socioeconomic status ($P > 0.05$), as shown in table 3. Regarding bad habits, none of patients or control subjects admit to be alcoholic of experience cigarette smoking.

Table 2: Frequency distribution of patients and control subjects according to gender

Gender	Control group n = 25		Patients group n = 24		χ^2	P
	n	%	n	%		
Male	12	48	9	37.5	0.551	0.458 ¥ NS
Female	13	52	15	62.5		

n: number of cases; ¥: Chi-square test; NS: not significant at $P \leq 0.05$

Table 3: Demographic characteristics of control subjects and patients with bronchogenic carcinoma

Characteristic n	Control group n = 25		Patients group n = 24		χ^2	P	
	%	n	%	n			
Residency	Urban	19	76.0	14	58.3	1.738	0.187 ¥ NS
	Rural	6	24.0	10	41.7		

Cont... Table 3: Demographic characteristics of control subjects and patients with bronchogenic carcinoma

Occupation	Employee	4	16.0	3	12.5	5.654	0.341 ¥ NV
	Farmer	0	0.0	4	16.7		
	Housewife	10	40.0	7	29.2		
	Private Job	1	4.0	2	8.3		
	Teacher	4	16.0	2	8.3		
	No job	6	24.0	6	25.0		
Level of Education	Illiterate	13	52.0	15	62.5	0.656	0.883 ¥ NV
	Primary	2	8.0	2	8.3		
	Secondary	3	12.0	2	8.3		
	University	7	28.0	5	20.8		
Marital status	Single	0	0.0	2	8.3	---	0.235 F NS
	Married	25	100.0	22	91.7		
Socioeconomic status	Poor	2	8.0	3	12.5	1.147	0.564 ¥ NV
	Moderate	11	44.0	13	54.2		
	Good	12	48.0	8	33.3		

n: number of cases; ¥: Chi-square test; F : Fischer exact test; NS: not significant; NV: not valid since > 20 % of cells have expected count < 5 .

Table 4: Chronic disorders in control and patients with bronchogenic carcinoma

Characteristic	Control group n = 25		Patients group n = 24		χ^2	P
	n	%	n	%		
HT	14	56.0	9	37.5	1.683	0.195 ¥ NS
DM	8	32.0	4	16.7	4.307	0.201 ¥ S
IHD	1	4.0	0	0.0	---	1.000 F NS
Asthma	3	12.0	0	0.0	---	0.235 F NS

n: number of cases; ¥: Chi-square test; F : Fischer exact test; NS: not significant; S: significant

Table 5: Prevalence rate of passive smoking in patients and control subjects

Passive smoking	Control group n = 25		Patients group n = 24		χ^2	P
	n	%	n	%		
Positive	10	40.0	17	70.8	4.705	0.030 ¥ S
Negative	15	60.0	7	29.2		

n: number of cases; ¥: Chi-square test; S: significant at $P \leq 0.05$

Table 6: Number of household smokers in patients and control groups

Group	Mean ± SD	Median (IQR)	Range	P
Control group	0.64 ± 0.86	0.00 (2.00)	0.00 - 2.00	0.027 † S
Patients group	1.38 ± 1.25	1.00 (3.00)	0.00 - 4.00	

SD: standard deviation; IQR: inter-quartile range; †: Mann Whitney U test; S: significant at $P \leq 0.05$

Discussion

In the current study, the prevalence rate of all cases of lung cancer during the period of study was 61 out of 403 (15.1 %). It has been estimated that lung cancer accounts for about 16 % of all cancers ⁵, a proportion that is nearly similar and in total agreement with our finding. On the other hand, the rate of lung cancer in none smokers, in the current study, was 39.3 %. Most published articles indicated that the proportion of non smokers with lung cancer ranges between 10 to 25 % (6,7, 8,9). This indicates that a significant proportion of patients with bronchogenic carcinoma, in our study, have acquired the disease irrespective with cigarette smoking. Therefore, identifying other possible risk factors in association with lung cancer in those patients was the main aim of the current study. Indeed, we supposed that passive smoking may play a principal role in the development of lung cancer in patients who are not habitual smokers. Unfortunately lung cancer in never-smokers has been studied far less extensively than tobacco-related lung cancer ⁷. This indicates that age by itself may be a risk factor. Indeed, most published articles dealing with lung cancer in non smokers has linked age as a potential risk factor for such malignant disorder (10, 11, 12,13). Older age is associated with cancer development due to biologic factors that include DNA damage over time and shortening telomeres. Accordingly, the median

age of lung cancer diagnosis is 70 years for both men and women ¹⁴. On the other hand and with respect to gender, in the current study, women accounted to 15 out 24 patients with bronchogenic carcinoma thereby accounting for 62.5 %, making the male to female ratio 1:1.7. There are conflicting data regarding the possibility that women may be more susceptible to developing lung cancer ¹⁵. There is a higher rate of lung cancer in non-smoking women compared with non-smoking men, a higher proportion of epidermal growth factor receptor (EGFR) mutations in female NSCLC, and a higher incidence of adenocarcinoma with lepidic features in women (16, 17). Some genetic mutations found to be more common in females may predispose toward lung cancer development in women, including over-expression of the CYP1A1 gene, mutation of the glutathione S-transferase M1 enzyme, mutations of the p53 tumor suppressor gene, and over-expression of X-linked gastrin-releasing peptide receptor (15, 16,17). Moreover, in the current study, there was also no significant difference in the distribution of patients and control subjects according to residency, occupation, level of education marital status and socioeconomic status ($P > 0.05$). In agreement with our results, a number of authors have denied any association between residency, rural versus urban and lung cancer (18,19). Exposure to pollutant in association with occupation is the main hazard precipitating to lung cancer. The occupational

and environmental exposure to carcinogenic agents is an everyday phenomenon²⁰.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Medicine/ University of Al-Qadisiyah, Iraq and all experiments were carried out in accordance with approved guidelines.

References

- Parkin DM, Bray F, Ferlay J. Global cancer statistics, 2002. *CA Cancer J Clin.* 2005;55(2):74–108.
- Rudin CM, Avila-Tang E, Samet JM. Lung cancer in never smokers: a call to action. *Clin Cancer Res.* 2009;15(18):5622–5625.
- Sun S, Schiller JH, Gazdar AF. Lung cancer in never smokers--a different disease. *Nat. Rev. Cancer.* 2007;7(10):778–790.
- Wakelee HA, Chang ET, Gomez SL, Keegan TH, Feskanich D, Clarke CA, Holmberg L, Yong LC, Kolonel LN, Gould MK, West DW. Lung cancer incidence in never smokers. *J. Clin. Oncol.* 2007;25(5):472–478.
- Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin.* 2011;61:69–90.
- Okazaki I, Ishikawa S, Ando W. Lung Adenocarcinoma in Never Smokers: Problems of Primary Prevention from Aspects of Susceptible Genes and Carcinogens. *Anticancer Res* 2016;36:6207-24.
- Sisti J, Boffetta P. What proportion of lung cancer in never-smokers can be attributed to known risk factors?. *Int J Cancer.* 2012;131(2):265–275.
- Thun MJ, Hannan LM, Adams-Campbell L. Lung cancer occurrence in never-smokers: an analysis of 13 cohorts and 22 cancer registry studies. *PLoS Med.* 2008;5(9):e185.
- US. Center for Disease Control Annual smoking-attributable mortality, years of potential life lost, and productivity losses--United States, 1997-2001. *MMWR Morb Mortal Wkly Rep.* 2005;54:625–8.
- Pronk A, Coble J, Ji BT, Shu XO. Occupational risk of lung cancer among lifetime non-smoking women in Shanghai, China. *Occup Environ Med.* 2009;66:672–8.
- Zeka A, Mannetje A, Zaridze D, Szeszenia-Dabrowska N, Rudnai P, Lissowska J, Fabianova E, Mates D, Bencko V, Navratilova M, Cassidy A, Janout V, et al. Lung cancer and occupation in nonsmokers: a multicenter case-control study in Europe. *Epidemiology.* 2006;17:615–23.
- Kreuzer M, Gerken M, Kreienbrock L. Lung cancer in lifetime nonsmoking men – results of a case-control study in Germany. *Br J Cancer.* 2001;84:134–40.
- Pohlabeln H, Boffetta P. Occupational risks for lung cancer among nonsmokers. *Epidemiology.* 2000;11:532–8.
- Torre LA, Siegel R. Lung Cancer Statistics. *Adv Exp Med Biol* 2016;893:1-19.
- Kligerman S, White C. Epidemiology of lung cancer in women: risk factors, survival, and screening. *AJR Am J Roentgenol* 2011;196:287-95.
- Patel A, Jacobs E, Dudas D. The American Cancer Society's Cancer Prevention study 3 (CPS-3): Recruitment, study design, and baseline characteristics. *Cancer* 2017;123:2014–24.
- Planchard D, Loriot Y, Goubar A. Differential expression of biomarkers in men and women. *Semin Oncol* 2009;36:553-65.
- Atkins GT, Kim T, Munson J. Residence in rural areas of the United States and lung cancer mortality: Disease incidence, treatment disparities, and stage-specific survival. *Ann Am Thorac Soc* 2017;14: 403-11.
- Shugarman LR, Sorbero ME, Tian H. An exploration of urban and rural differences in lung cancer survival among medicare beneficiaries. *Am J Public Health.* 2008;98(7):1280–1287
- Spyratos D, Zarogoulidis P, Porpodis K. Occupational exposure and lung cancer. *J Thorac Dis.* 2013;5 Suppl 4(Suppl 4):S440–S445.