

Lung Cancer in Non- Smoker Patients in Baghdad Teaching Hospital

Hamza Abdullah Al Sabah*, Asaad Abdal Hameed**,
Abdulla Janger Alfarttoosi***

ABSTRACT:

BACKGROUND:

Despite the predominance of tobacco smoking as its presumed etiology, lung cancer is also a significant health problem in those with no history of smoking.

OBJECTIVE:

To assess the clinical and epidemiological characteristics of lung cancer in non smokers patients.

PATIENTS AND METHODS:

This was a retrograde across-sectional study conducted at Baghdad teaching hospital during the period from 14th February 2012 to 8th January 2013. Including 100 patients with proved lung cancer all were never smokers. Medical records of those patients were revised, data were collected regarding sociodemographic characteristics of patients and medical history in addition to the clinical characteristics. Data analyzed with SPSS software, and the results were presented in tables and figures accordingly.

RESULTS:

In the current study 100 patients with different types of lung cancer were included, all were never smoker.

Female gender was more common than males .In this study majority of the cases were aged 60 years and more. The prevalence of passive smoking among studied group was (39%), Urban residence was the dominant, 74%.

On X-ray examination all the patients had positive findings; (99%) had unilateral findings and only one with bilateral. Adenocarcinoma was the predominant type, (51%) of the cases, which is much higher than the prevalence of other types. Adenocarcinoma was significantly predominant among females than males (64.7%) vs. (35.3%) respectively, $P= 0.003$.

majority of the cases were of stage IV (78%) and stage III (22%), this reflected the late presentation of the patients. Vast majority of dead cases (96.5%) were died within 2 years, and only 3 patients were survived for three years while none of the cases were survived for more than 3 years.

CONCLUSION:

The prevalence of lung cancer in non smoker women was higher than in men. In this study the prevalence of lung cancer seemed to be increased with the advancing age. Passive smoking was an important risk factor for lung cancer in more than one third of studied group, and women were more likely to be affected.

KEY WORDS: Lung cancer , non smoken .

INTRODUCTION:

Lung cancer is the most common cancer worldwide, with an estimated 1,600,000 new cases and 1,380,000 deaths in 2008⁽¹⁾. In the

United States, there was 221,000 new cases of lung cancer and 157,000 deaths in 2010⁽²⁾.

Despite the predominance of tobacco smoking as its presumed etiology, lung cancer is also a significant health problem in those with no history of smoking⁽³⁾. Emerging information supports the notion that lung cancer in never smokers is distinct enough from an

*Baghdad Teaching Hospital.

**Baghdad Teaching Hospital.

***College of Medicine, Baghdad University.

epidemiologic and biologic standpoint to be considered a separate entity⁽⁴⁾. In general, the term "never smoker" refers to individuals who have smoked fewer than 100 cigarettes in their lifetime⁽⁵⁾.

Worldwide, lung cancer in never smokers comprises an estimated 15 to 20 percent of cases in men and over 50 percent in women. There are major geographic differences, particularly in Asia, where 60 to 80 percent of women with the disease are never smokers⁽³⁾. The incidence of small cell lung cancer in never smokers is exceedingly small⁽⁶⁾.

The age-adjusted mortality rate from lung cancer among never smokers was higher in men than women in two American Cancer Society cancer prevention study cohorts⁽⁷⁾.

Risk factors for lung cancer among never smokers include: Second hand smoke, Radon, Environmental exposures (Common toxins of this sort include asbestos, chromium, and arsenic), underlying lung disease and Genetic factors^(8,9).

More recent series of lung cancer in never smokers continue to report adenocarcinoma as the most common histology^(10,11,12). Whether or not patients with non-small cell lung cancer who are never smokers have a better response to standard treatment and/or a better prognosis than those with a positive smoking history is uncertain. Some observational studies have demonstrated a better outcome, although this has not been true in all studies^(13,14).

AIM OF THE STUDY:

To assess the clinical and epidemiological characteristics of lung cancer in never smokers patients.

PATIENTS AND METHODS:

A cross-sectional study; a retrospective review of records of diagnosed patients during 2008-2012. This study was conducted at the department of medicine, floor 9 unit 2, in Baghdad teaching hospital, medical city, Baghdad-Iraq, during a period from 14th of February 2012 to 8th January 2013. Records of 100 never smoker patients all with lung cancer, diagnosed and proved by professional specialists via clinical examination and investigations (radiological and bronchoscopic) including cytology and or biopsy. Data were collected using a pre-constructed data collection form which gathered the data of the patients including the following:

1.Socio-demographic data: which included age, gender, job, residence, level of education, marital status, drinking habits, history of

chronic diseases; hypertension, diabetes, tuberculosis, carcinomas in other sites of the body, or other diseases.

2.Patients complaint and duration: This included chief complaint of the patient (symptoms), duration of symptoms (categorized into three groups < 6 months, 6months - 1 year and > 1 year.

3.Physical and clinical findings: include the chest examination findings (unilateral or bilateral), extrapulmonary findings, neurological findings and lymph nodes findings.

4.Investigations: Included laboratory and clinical tests and examination:

Haematological laboratory investigation: (Hb. and ESR),

B. Radiological investigations : Chest X-ray and CT scanning

C. Bronchoscopic examination:

D. Histopathological examination: this included type of lung cancer.

Treatment data; chemotherapy, radiotherapy or surgery.

Data analyzed with SPSS software, and the results were presented in tables and figures accordingly.

RESULTS:

Socio-demographic characteristics:

There were 100 patients recruited in this study, their socio-demographic characteristics is summarized in table 1, the studied group included 38 (38%) men and 62 (62%) women, figure 1. The mean age of studied group was (62.7 ± 11.9) years, with a range of (35 – 88) years, from other point of view, lung cancer was high prevalent in those with age (60-69) years figure 2, on the other hand, the prevalence tend to increase with the advancing age particularly above the age of 60 years, among study group, represented (67%) of all cases, figure 3.

Majority of cases (80%) were married while (18%) were widowed and only (2%) were single. Out of all cases (41%) were illiterate, and only (4%) were complete their higher education. None of the patients gave a history of alcohol consumption. Regarding the residence and job, as it shown in table 3.3, (74%) of the cases were of urban origin, and (44%) were housewife, (16%) were farmer, (12%) were military, retired, drivers, employee and other jobs, represented (10%), (4%), (4%) and (10%) respectively.

Passive smoking: Passive smokers were (39%) of the cases, on the other hand it was more prevalent among women, rather than men (59% vs. 41%) respectively, table 2.

Table 1: Socio-demographic characteristics of study population (N=100).

Variable		N	%
Gender	Men	38	38%
	Women	62	62%
Age (year)	<40	6	6%
	41-49	7	7%
	50-59	20	20%
	≥ 60	67	67%
	Mean ± Standard deviation	62.7 ± 11.9	
	Range	35 - 88	
Marital	Married	80	80%
	widowed	18	18%
	Single	2	2%
Education	Illiterate	41	41%
	Read and write + Primary	22	22%
	Preparatory and secondary	33	33%
	Higher education	4	4%
Alcohol drinking	Non	100	100%
Passive smoker	Yes	39	39%
	No	61	61%

Table 2: Distribution of passive smoking among study group.

Passive smoking	Male	Female	Total
Yes	16	23	39
	41%	59%	100%
No	22	39	61
	36.1%	63.9%	100%
Total	38	62	100
	38.0%	62.0%	100%

Table 3: Distribution of residence and job of patients (N=100).

Variable	N	%
Residence		
Urban	74	74%
Rural	26	26%
Job		
Housewife	44	44%
Farmer	16	16%
Military	12	12%
Retired	10	10%
Driver	4	4%
Employed	4	4%
Other	10	10%

History of chronic diseases

Is summarized in table 4, (43%) of the patients were hypertensive, (32%) were diabetic, (28%) had CHDs, (3%) had history of carcinomas in other sites. and (3%) had history of other diseases including, TB, cerebellar ataxia and renal failure.

Table 4: History of chronic diseases among study group.

Variable	N	%
Hypertension	43	43%
DM	32	32%
CHDs	28	28%
Carcinomas	3	3%
Others	3	3%

Distribution of chief complaint

Is shown in table 5, all cases had complained of cough, (89%) chest pain, (83%) presented with SOB, (64%) presented with loss of weight, (63%) anorexia, (52%) with sputum , (27%) with fever, (23%) with hemoptysis and only (13%) were presented with loss of energy.

The Majority of the cases (78%), had their symptoms for less than 6 months, (15%) had symptoms for 6 month to one year and (7%) for more than 1 year, with a mean duration of symptoms of (3.6 ± 2.4) months.

Table 5: Distribution of chief compliant among study population (N=100).

Variable	N	%	
Chief complaint	Cough	100	100%
	Chest pain	89	89%
	SOB	83	83%
	Loss of weight	64	64%
	Anorexia	63	63%
	Productive Cough	52	52%
	Fever	27	27%
	Hemoptysis	23	23%
	Loss of energy	13	13%
Duration of complaint	< 6months	78	78%
	6months - 1 year	15	15%
	>1 year	7	7%
Duration between compliant and diagnosis (mean ± SD) months		3.6 ± 2.4	

Physical finding:Table 6, demonstrates the physical findings of the patients; all patients had pulmonary findings on clinical examination, (99%) of them with unilateral findings and only

one patient with bilateral findings. Extra pulmonary findings were present in (4%), neurological findings in (3%) and (8%) had lymph nodes involvement.

Table 6:Distribution of physical finding among study population (N=284).

Physical finding		N	%
Pulmonary Finding	Unilateral	99	99%
	Bilateral	1	1%
Extra Pulmonary		4	4%
Neurological		3	3%
Lymph node		8	8%

Hematological tests:

The mean hemoglobin level of patients was (11.6 ± 1.4) gm\dl with a range of (8 - 14.3) gm\dl. The mean ESR value was (81 ± 21) with a range of (30 - 135), table 3.7.

Table 7:Mean hemoglobin and ESR of patients.

Test	Range		Mean ± SD
Hb. gm\dl	8	14.3	11.6 ± 1.4
ESR	30	135	81 ± 21

Radiological and Bronchoscopic findings:

The frequencies and percentage of radiological finding, were presented in table 8, chest X-ray revealed positive finding in all patients (100%), of them 99 (99%) were unilateral and only 1 (1%) with bilateral funding. CT scan findings

were positive in all patients (100%).Bronchoscopy was performed for 97 patients, in 80 patients of them positive findings had been found, while it not performed for 3 patients was diagnosed by fine needle or pleural aspiration.

Table 8:Radiological and Bronchoscopic findings of study group.(N=100).

Test		N	
X-ray	Positive finding	100	
	Side	Unilateral	99
		Bilateral	1
CT-scan		Positive 100	
Bronchoscopy	Performed	Positive	80
		Negative	17
		Not performed	3
MRI	Not performed		100

Distribution of types of lung carcinoma:

According to the frequency distribution of types of carcinoma, presented in table 9, adenocarcinoma was the more prevalent type, it was present in (51%) of the

cases, followed by squamous cell carcinoma in (23%), Small cell carcinoma in (17%) and the least frequent was the large cell carcinoma which present in (9%).

Table 9: Distribution of types of lung carcinoma among study group.

Type of Carcinoma	N	%
Adenocarcinoma	51	51%
Squamous cell carcinoma	23	23%
Small cell carcinoma	17	17%
Large cell carcinoma	9	9%
Total	100	100%

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Distribution of types of carcinoma by gender: In table 10, it had been significantly found (P=0.003), that female gender was more common among patients with adenocarcinoma

rather than males (64.7% vs. 35.3%) respectively. On the other hand, no statistically significant differences had been found in between both gender regarding the other types, P>0.05.

Table 10: Comparison of types of carcinoma by gender among study group.

Type of lung cancer	Sex		Total	P
	Male (n=38)	Female (n=62)		
Adenocarcinoma	18 35.3%	33 64.7%	51 100%	0.003
Squamous cell carcinoma	11 47.8%	12 52.2%	23 100%	0.5
Small cell carcinoma	6 35.3%	11 64.7%	17 100%	0.08
Large cell carcinoma	3 33.3%	6 66.7%	9 100%	0.17
Total	38 38%	62 62%	100 100%	

Treatment:

Chemotherapy was the dominant treatment type it was used in (47%) of the cases, then

radiotherapy in (38%), and surgery was done for only one patients, table 3.11.

Table 11: Distribution of treatment types among study group.

Type of treatment	Frequency	Percent
Chemotherapy	47	47%
Radiotherapy	38	38%
Both	14	14%
Surgery	1	1%
Total	100	100%

Staging:

It had been observed that all cases were of advanced stages, all with stages III or IV which, 22 patients (22%) were of stage III and 78 (78%) were of stage IV.

Outcome:

As it shown in figure 6, 85 patients (85%) were died at different time period after detection of their disease, while 15 (15%) were lost to follow

up and their outcomes were missed. In table 3.12, Out of the 85 died patients, (96.5%) were died within less than 2 years after detection; those who were died within one year were (25.9%) and those who were died within 2 years were (70.6%). The remaining 3 patients (3.5%) of the 85 dead patients were died within three years and none of the patients were survived for more than three years.

Table 12: Frequency distribution of outcome of patients with lung cancer.

Outcome		Frequency	Percent
Died	within ≤ 1 year	22	25.9%
	within 2 years	60	70.6%
	within 3 years	3	3.5%
	within 4 years	0	0.0%
	Total	85	100%

DISCUSSION:

Lung cancer is an important and serious public health problem with an increasing in incidence and prevalence in Iraq. The majority of cases of lung cancer in Iraq are detected in advanced stages.⁽¹⁵⁾

Female gender was more common than males among studied group represented (62%) vs. (38%) respectively, this agreed with the earlier studies findings and supporting the observations that women are more likely than men to have never-smoking-associated lung cancer, in an analysis of 6 large cohort studies, Wakelee H.A. et al,⁽¹⁶⁾ found lung cancer age-adjusted incidence rates in these six cohorts were significantly lower in never smokers than former or current smokers., age-adjusted rates in current smokers are roughly 12 to 30 times higher than never smokers.⁸⁷ similar findings were also reported by other four studies.^(3,10,17)

Evaluating comparable groups of males and females, rates of never smokers-associated lung cancer were consistently higher among females. The higher rate among females suggests sex-based differences in either susceptibility or exposure to risk factors (such as secondhand smoke, burning coal and wood for cooking), also this might be attributed to the higher proportion of females gender among never smoker, this finding was consistent with other studies worldwide; it had been reported that the higher percentage of women with lung cancer are never smoker compared to men.⁽¹⁶⁾

In this study majority of the cases were aged 60 years and more, this consistent with recent cohort studies in Western populations.⁽¹⁰⁾ In a study from USA in 2009, Samet et al.,⁽¹⁸⁾ suggested that Lung cancer risk increases with age in both smokers and never smokers cohorts.

In contrast to our study and the western studies, inconsistent findings were reported in some Asian studies; it had been suggested that a younger age at diagnosis is characteristic of lung cancer in never smokers while it was the opposite in the Western population⁽⁹⁾.

The prevalence of passive smoking among studied group was (39%), this reflected that passive smoking was an important risk factor for

developing lung cancer among never smoker, many studies had been suggested similar finding of ours, in a study from UK they suggested that the risk of lung cancer among never-smoker women increased by 23% per 10 cigarettes/day smoked by the husband.⁽¹⁹⁾

Urban residence was the dominant, (74%), many studies and literatures suggested that lung cancer is a disease of modern man. and this finding is consistent with the distribution in the USA and UK that might be attributed to the effect of environmental pollution.⁽²⁰⁾

All patients in the current study were presented with cough, while (89%) of patients were presented with chest pain, and (64%) with SOB this came in line with what was previously reported in Iraq²¹ and Qatar.⁽²²⁾

On X-ray examination all the patients had positive findings; (99%) had unilateral findings and only one with bilateral, this consistent with and very close to findings of an Indian study, by Kumar et al, 2010.⁽²³⁾ where it was reported that unilateral positive finding in 98% of the cases while bilateral in 2%.

The lung cancer types among never smokers is quietly different than that among smokers, our study reported that among the studied group, Adenocarcinoma was the predominant type, (51%) of the cases, which is much higher than the prevalence of other types. The sequence in the prevalence of the other types in this study was; (23%) squamous cell carcinoma, (17%) Small cell carcinoma and the least frequent (9%) large cell carcinoma. this consistent with other studies of lung cancer among never smokers, Definite epidemiologic differences exist between never-smokers and smokers, this might be attributed to the suggestion that there was a difference in the biology underlying the pathogenesis and behaviour of lung cancer in between smokers and never smoker. In a study from Singapore published in 2006,⁽²⁴⁾ never-smokers comprised a high proportion of NSCLC patients, furthermore, they found the prevalence of different types of lung cancer among never smoker was as follow; 69.9% with

adenocarcinoma , 5.9% with squamous cell carcinoma and (24%) of other types. Also our findings regarding the types distribution was close to that of other study by Sun S. et al.⁽³⁾ in 2007, found adenocarcinoma was more common than SqCLC among never smoker, (62% vs. 18%). Recent series of lung cancer in never smokers continue to report adenocarcinoma as the most common histology.^(10,25)

From other point of view, on comparison of types of lung cancer in between both genders, Adenocarcinoma was significantly predominant among females than males (64.7%) vs. (35.3%) respectively, $P= 0.003$, and this agreed the Indian study,⁽²³⁾ furthermore, the adenocarcinoma is predominant in females in both smokers and never smokers.

At the Gulf Cooperation Council (Bahrain, Oman, Saudi Arabia, Kuwait and Qatar), the predominant types were squamous cell carcinoma in males (except in Qatar) and adenocarcinoma in females.⁽²⁶⁾

Chemotherapy was the treatment used in (59%) of the cases while radiotherapy represented (40%). Surgery was the least choice in treatment; only used in one patient. This might be attributed to the reluctance of the patients from surgical option of treatment caused by the low chance rate of cure and the majority of cases were presented in advanced stages.

Our findings regarding treatment was consistent , in part, with a previous Iraqi study by Al-Rahim Y.A.,⁽²¹⁾ he suggested Chemo-therapy and/ or radiotherapy were used in (75.9%) of the cases. While disagreed the same Iraqi study regarding the surgical treatment, in which surgery was the decision in (24.1%) of the patients.⁽²¹⁾

It had been observed that majority of the cases were of stage IV and stage III, (78%) and (22%) respectively, this reflected the late presentation of the patients . In approximately (70%) of patients, the disease has spread to regional lymphatic and other sites at the time of diagnosis.⁽²⁷⁾

Our findings were in line with previous study from Qatar; Ibrahim W et al reported stage IV of about 64% of the cases and stage III of (22%).⁽²⁸⁾ In 2010, Debieuvre D et al (French) found that the more advanced stage (stage IV) was found in 64% of the cases.⁽²⁹⁾

Despite major advances in understanding and treating lung cancer, it still had a higher mortality rates , in the present study it had been found that (85%) of the patients, were died within 3 years, while (15%) were lost to follow up. Vast majority of dead cases (96.5%) were died within 2 years, and only 3 patients were survived for three years

while none of the cases were survived for more than 3 years. In most countries, the survival rate is low, , the 5-year relative survival rate in North Africa and the Middle East is only 8%.⁽²⁷⁾

One of the limitation of this study was the cross-sectional study design so the incidence of lung cancer couldn't be calculated as in cohort study design that used in majority of studies worldwide which is inapplicable in our situation because limitation in time and cost.

CONCLUSION:

Lung cancer in never smoker is an important and serious public health problem with an increasing in incidence and prevalence in Iraq. The prevalence of lung cancer in never smoker women was higher than in men. In this study the prevalence of lung cancer seemed to be increased with the advancing age. Passive smoking was an important risk factor for lung cancer in more than onethird of studied group, and women were more likely to be affected .Adenocarcinoma was the more prevalent type of lung cancer among study group and it was about more than double the prevalence of squamous cell carcinoma. It was also more common in women.

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