

Original paper

Bronchogenic Carcinoma in Patients Younger Than 40 Years

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Abstract

B **ackground:** lung cancer is the most frequent cancer related cause of death for both gender, currently 10 millions new lung cancer are diagnosed each year worldwide. **Objective:** To determine the different clinical characteristics and other features of lung cancer in the different age groups.

Methodology: This was descriptive retrospective study carried on 32 patients with histological proven lung cancer under the age of 40 years from three medical centers. All patients underwent full clinical assessment including history (particularly smoking) and full physical examination. Bronchoscope was done to all patients except those unfit. pleural effusion cytology and pleural biopsy done to all patients with pleural effusion. FNA Cytology done under ultrasound guide and was of great help in those patient in whom the histological diagnosis was difficult to be obtained by other methods.

Results: The age of studied group ranged between (10_40 years) with a mean of 25. From the thirty two patients, there were 18 males patients (56%) and 14 females patients (44%), with 1.3:1 male: female ratio. History of smoking in the young age group was present in 19 patients (60%), 13 were males (68.5%) and 6 patients (31%) were females, and 13 patients (40%) never smoked. Undifferentiated carcinoma is much more common in males than females (20% and 8% respectively). The most common histological types of lung cancer in both sex of young group was adenocarcinoma (44% of cases) occurring 50% of females and 40% of male.

Conclusion: Cigarette smoking is an important cause of the current epidemic of lung cancer among our young patients, so it is preventable rather than curable medical problem. Adenocarcinoma was the most frequent histological type of lung cancer in Iraqi young patients.

Keyword: lung cancer, young patient, sex, smoking, histopathology.

Introduction

Lung cancer is the most common cause of cancer death among American men and women ⁽²⁾. Currently 10 millions new lung cancers are diagnosed each year worldwide ^(4, 5). In Iraq, lung cancer is the most commonly occurring cancer in men (16.7%) and the 5th in women (4.2%) ⁽⁶⁾. Lung cancer is rare below age 40, with rates increasing until age 80, after which the rate tapers off ⁽²⁾. It is estimated that cigarette smoking is responsible for approximately 85 to 90% of all cases of lung cancer, including 90% of cases in men

and 80% in women. More than 40 carcinogens have been identified in cigarette smoke. Exposure to environmental tobacco smoke (i.e., passive smoking) by nonsmokers, especially in the workplace, increases the risk for the development of lung cancer. Women who smoke have a 1.2- to 1.7-fold higher risk ratio than men, especially for adenocarcinoma and SCLC. First-degree relatives of patients with lung cancer have a two- to six-fold increase in the risk for lung cancer after adjusting for tobacco use ⁽¹⁾. Bronchial carcinomas arise from the bronchial epithelium or mucous glands.

The common cell types are listed in the following table (9).

Cell type %

Squamous 30

Adenocarcinoma 40

Small-cell 20

Large-cell 10

More than half of all patients diagnosed with lung cancer present with advanced disease at the time of diagnosis. Lung cancer arising in a lifetime never smoker is more common in women and East Asians. Such patients also tend to be younger than their smoking counterparts at the time of diagnosis. The clinical presentation of lung cancer in never smokers tends to mirror that of current and former smokers. The propensity of small-cell lung cancer to metastasize early dictates that patients with this tumor type are usually not suitable for surgical intervention. In patients with other cell types, subsequent investigations should focus on determining whether the tumor is operable, because complete resection may be curative ⁽²⁾.

Patient and method

This descriptive retrospective study carried on 32 patients with histological proven lung cancer under the age of 40 years from a total sample 787 patients that had attending Baghdad hospitals (Baghdad medical city, Al-Kadhymia medical city, Al-Yarmuk & Al-Amal (radiotherapy) hospitals) reviewed between 2007 to 2012, a sample of 32 patients over the age of 40 years were used for comparison. All patients underwent full clinical assessment including: Histories (particularly smoking) and full physical examination, especially of the chest and for palpable lymph nodes and features of metastases.

Chest X ray results in two views (PA and LAT) have been evaluated. Sputum cytology of three early morning samples were taken. Bronchoscope was done for all irrespective to the result of sputum cytology, bronchoscope was taken to all patients except those unfit for this

procedure and its one of the main available way of diagnosis, staging and assessing operability. During this procedure biopsies for intrabronchial tumors, bronchial wash and brush, also postbronchoscopic sputum were taken for histopathology and cytopathology pleural effusion cytology and pleural biopsy done to all patients with pleural effusion for whom thoracostomy tube was done as a diagnostic procedure. Supraclavicular and Scalene node biopsy was performed in patients with palpable cervical lymph nodes.

FNA Cytology the procedure done under ultrasound guide and was of great help in those patient whom the histological diagnosis was difficult to be obtained by other methods.

Open lung biopsy: is the last choice to establish the diagnosis when other means fail to do so and those patients already have the criteria of inoperability.

Results

Thirty two patients with lung cancer who were under the age 40 years involved in this study, there was 18 males patients (56%) and 14 females patients (44%), with 1.3:1 male: female ratio. In the sample of 32 patients older than 40 years, there was 27 males patients (84.4%) and 5 females patients (15.6%) with 5.4:1 ratio as shown in the (Table1) with significant increase in lung cancer older males in comparison to the younger group ($p < 0.001$). The age of studied group ranged between (10_40 years) with a mean of 25, the highest number of cases was in these between the age of (30_40 years), while the lowest number of cases was in the age between (10_19 years) as shown in the (table 2).

History of smoking in the young age group was present in 19 patients (60%), 13 were males (68.5%) and 6 patients (31%) were females, and 13 patients (40%) never smoked, while In the older age group 90.6% of patients were smoker as shown in (table 3).

Clinical feature were less prominent in younger group (72%) of patients had cough and (60%) had dyspnea, both are the main presenting symptoms in younger group as shown in (table 4).

Clubbing is present less frequently in the younger group 19% compared to 56% in the older group; other signs are shown in (table 5).

Twenty seven patients (84.5%) in the younger group had right side radiological shadow with or without pleural effusion, while left side shadow with or without pleural effusion was present in 15 patients (47%) as shown in (table 6) which shows that right side lung cancer is more common than the left with (1.8:1) and upper lobes more frequently involved than the lower with ratio of (1.9:1). Table 7 and fig.1 show the results of different investigations, 15 patients had sputum cytology done looking for malignant cells only 7 patients had positive results (46.6%). Bronchoscope was done for 27 patients, 15 patients had positive cytological or histological

diagnosis for staging and operability assessment, and 15 patients (55.5%) had abnormal results. Fine needle aspirate was done for 17 patients with peripheral tumors and 12 patients had positive results (70.5%). Seven patients had pleural fluid analysis and 2 patients (29%) had malignant cells in their pleural fluid.

Open lung biopsy was done in 2 patients were previous methods of investigations failed to show positive results with 100% sensitivity rate, all of them found to be unresectable during surgery.

Undifferentiated carcinoma is much more common in males than females (20% and 8% respectively).

The most common histological types of lung cancer in both sex of young group was adenocarcinoma (44% of cases) occurring 50% of females and 40% of male, but in the older group squamous cell carcinoma was the commonest type (50%) of cases and small cell carcinoma (16%) are more common than in the younger patients, with significant difference ($p < 0.05$) (table 8).

Table 1. Lung cancer distribution by age and gender type.

gender	<40 years*	%	≥ 40 years**	%
male	18	56	27	84.4
female	14	44	5	15.6
total	32	100	32	100

P value of total male to female above 40 = 0.001, P value of total male to female under 40 = 0.159

*male: female= 1.3:1, **male:female=5.4:1

Table 2. Age distribution of 32 young patients

	male	%	female	%	total	%
10-19	1	5.5	0	0	1	3
20-29	2	11	5	36	7	22
30-40	15	83	9	64	24	75
T0tal	18	100	14	100	32	100

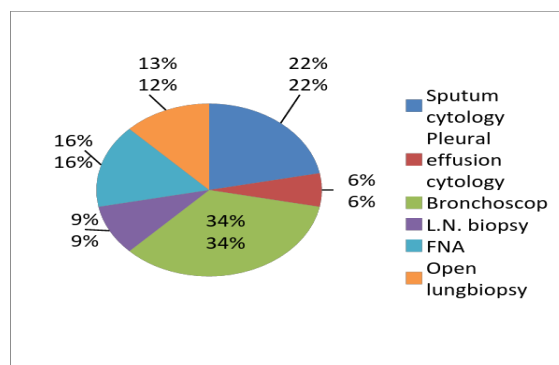


Fig 1. The value of different methods of investigations for diagnosis of lung cancer in young patients.

Table 3. Smoking habit in patient with lung cancer

Gender type	< 40 years				≥ 40 years			
	smoker	Non smoker	total	% smoking	smoker	Non smoker	total	% smoking
male	13	5	18	40.625	25	2	27	78.1
female	6	8	14	18.75	4	1	5	12.5
total	19	13	32	60	29	3	32	90.6

Table 4. Symptomatology of patients with lung cancer under 40 years in comparison to aged patients.

	< 40 years	%	≥ 40 years	%	P value
cough	23	72	29	90.6	0.017
sputum	14	43	25	78	0.003
haemoptysis	11	34	23	71	0.001
Chest pain	8	25	24	75	0.012
dyspneo	19	60	26	81	0.001
fever	9	28	20	62.5	0.001
Weight loss	12	37.5	28	87.5	0.001

Table 5. Significant physical finding in young and aged group.

	< 40 years	%	≥ 40 years	%	P value
clubbing	6	19	18	56	0.001
Lymph node	5	16	11	34	0.113
hepatomegaly	7	21	15	45	0.083
Horner syndrome	3	9.5	4	12.5	1
Pleural effusion	11	35	10	31	0.876

Table 6. Chest radiological findings in patients <40 years old

	< 40 years	%
Right side lung shadow	20	62.5
Left side lung shadow	12	37.5
Right pleural effusion	7	22
Left pleural effusion	3	9.4
Upper lobes	21	65.6
Lower lobes	11	34.4
Central lesion	15	46.88
Peripheral lesion	17	53.13

Table 8. Histological diagnosis in males and females of the young study group.

Type of cancer	male	%	female	%	Total	%
adenocarcinoma	8	40	6	50	14	44
Squamous cell carcinoma	4	20	3	25	7	22
Small cell carcinoma	2	10	1	8	3	9
Undifferentiated cancer	4	20	1	8	5	16
Large cell carcinoma	2	10	1	8	3	9
total	20	100	12	100	32	100

Table 7. The value different method of investigation for diagnosis of lung cancer in young patients.

	< 40 years	%
Sputum cytology	7	21.88
Pleural effusion cytology	2	6.25
Bronchoscope	15	47
L.N biopsy	3	9.38
FNA	12	37.5
Open lung biopsy	2	6.25

Discussion

In this study we focused on the difference between the young and older lung cancer patients and compare it with other studies to determine the different clinical characteristics and other features of lung cancer in the different age groups.

Thirty-two (4.06%) patients from a total sample of 787 patients with lung cancer were under the age of 40 year old in comparison with other studies as that of Schonfeld N in Germany 1999 was (2.1%)⁽¹⁰⁾, chih-wei in Taiwan 2000 was (2.1%)⁽¹¹⁾, Shimono in Japan 1994 was (2.9%)⁽¹²⁾, Capewell S. in UK 1992 was (1.3%)⁽¹³⁾, Netali F in France 1991 was (4%)⁽¹⁴⁾ & Joseph in USA 1989 (3%)⁽¹⁵⁾, so the percentage of Iraqi young patients with lung cancer can be considered to be higher than in other studies.

The female to male ratio was 1:1.3 in younger group higher than that in older one 1:5.4 in comparison to that conducted by schonfeld N.⁽¹⁰⁾ (1:1.4 in young & 1:2.4 in older), Jiang wei⁽¹⁶⁾ (1:2 in young & 1:2.1 in older), MARUYAMA⁽³¹⁾ (1:1.5 in young & 1:3.2 in older), but slightly lower than that of Leon S. Green⁽¹⁷⁾ (1:1 young & 1:2.7 older), This high picture of female involvement in contrast to other series of patient with lung cancer were male gender is more prevalent & male : female ratio is often higher than 3⁽²⁷⁻²⁹⁾ and to other Iraqi studies conducted by El_hassani in 1987 found the ratio was 9:1⁽²⁶⁾, this difference between our results & previous studies is probably caused by the recent increasing incidence of lung cancer in women as a result of increase smoking in the female population (either active or passive) & improved female health consciousness with more vigorous pursuit of diagnosis & treatment of the disease in recent decades . One of the irrefutable risk factor for lung cancer is tobacco, So cigarette smoking apparently is an important risk factor in all age groups, but to less extent in the younger patients⁽¹⁵⁻¹⁷⁾ .

We found that 60% of our younger group had history of current smoking which was lower than that of other studies; Heland A study was (80%)⁽¹⁸⁾, TurutH study was (61.2%)⁽¹⁹⁾ but the association between lung cancer & smoking in young American & young Chinese (43.7% & 51.27%) respectively were weaker^(16,17,24), on the other hand in the Iraqi older group, the smoking habit has more prominent role (90.6%) in this sampled study.

The identification of cases in young never smokers is of concern & suggest the need for more research in air pollution & lung cancer in our country; in this study 40% of young patients were never smoker, so as a result the Aetiology of lung cancer in never smoker remain indefinite although many risk factors have been described including 2nd hand smoking, occupational exposure, preexisting lung disease, diets, estrogen exposure, etc.⁽²⁰⁾.

In both classical signs & sympt of lung cancer are present but in general much less pronounced in younger than older group, still persistent cough & dyspnea are the commonest presenting symptoms (72 %, 60% respectively) and these findings agree with Iraqi, American and Chinese young patients studies^(2,4,11,29).

Pleural involvement was present in (34.5%) of our young patients & this consistent with Leon S Green that show early pleural involvement was a usual finding in adenocarcinoma cases⁽¹⁷⁾.

CXRs finding in young patients revealed right lung shadow in (62%) & right pleural effusion in (22%), and this result is comparable with JIANG Wei study that show the tumors were more frequently detected in the right lung & upper lobes than in the other sites⁽¹⁶⁾. The sensitivity of sputum cytology ranging from 20% to 80%, the least for peripheral and the greatest for central, especially if associated with haemoptysis⁽³⁰⁾, and this fact explain the finding of our study as (47%) were positive for malignant cells in sputum cytology much more lower than that of yousif study⁽²¹⁾ in patients more than 40 years

where the squamous was dominant and mainly centrally located and has invaded the airways and adenocarcinoma mainly peripherally located that was dominant in our study.

Bronchoscope was done in 27 patients in this study, abnormalities revealed in 55.5% of them and this result agree with that of Jiang Wei study that show 58% have such abnormalities⁽¹⁶⁾.

Pleural biopsy is much less yielding in young group confirming diagnosis in (20%), in comparison to AL_Alusi study (67%) in older patients⁽²²⁾.

Fine needle aspirate was done for 17 patients with peripheral tumours and 12 patients had positive results (70.6%) that were closed to Yousif study (73.8%)⁽²¹⁾

Open lung biopsy proves the diagnosis in 2 patients in this study group with (100%) positive results. In this study adenocarcinoma was the commonest histological type (44%) in the younger group with slight predominance in male gender then squamous cell carcinomas that was present in (22%) and small cell carcinoma in (9%) and these results agree with that of Jiang, Leons, Tsai CM, Mauri, and Maruyama studies^(16,17,24,25,,31) that show the predominance of adenocarcinoma, then squamous cell carcinoma & small cell carcinoma in order of frequency in patients under the age of 40 & similar to the study of Joseph G in 1987 in New York report that in (44%) of CA lung were of adenocarcinoma type⁽¹⁵⁾, but in contrast to Turut H which show that squamous cell carcinoma was on the top to be followed by adenocarcinoma, and this explained by the predominant gender was male (87%) and high percentage of smoking habit in the last study (61.2%)⁽¹⁹⁾. This study show squamous cell carcinoma was the commonest type (50%) in older followed by adenocarcinoma (19%) & small (16%) and this results was consistent with other series which confirm that squamous is the leading type, in Iraq F.A. AL Alusi's study in 1987 found that squamous cell in (47%), adenocarcinoma

in (23%) and (17%) for small type⁽²²⁾ and Yousif A. Al- Rahim study 2007 show that squamous cell (42.6%), adenocarcinoma in (27.7%), and small cell (14.9%)⁽²¹⁾.

Conclusion

The gender is a risk factor to determine the prevalence of lung cancer for those patients ≥ 40 years. Our result confirm that cigarette smoking is an important cause of the current epidemic of lung cancer among our young patients, so it is preventable rather than curable medical problem. However there still are unknown factors that appear to favor the development the disease in young. In this study we found adenocarcinoma was the most frequent histological type of lung cancer in Iraq young patients, in contrast to previous studies.

References

1. DAVID S. ETTINGER; lung cancer and other pulmonary neoplasm, LL GOLDMAN I. SCHAFE Cecil Textbook of medicine 24th edition, 2012, chapter 197 page 1264-1271.
2. John w. Adamson; Neoplasm of the lung; LONGO FAUCI KASPER JAMESON Harrison's principle of internal medicine; 18th Edition; 2012; chapter 89 page 828-902.
3. ROBERT J.C. STEEL AND ALASTAIR J. MUNRO; primary lung cancer; NORMAN S. WILLIAMS Bailey and Love's short practice of surgery 25th Edition 2008; 52.884.
4. Anthony J. Alberg, Jonathan M. Samet, Epidemiology of lung cancer, Murry J.F. and Nadal J.A., Textbook of Respiratory Medicine, 5rd edition, 2010. Vol.2, chap.46, P. 2026-2037
5. Coleman T. Smoking cessation: integrating recent advances into clinical practice. Thorax. 2001 Jul 1; 56:579-82.
6. MOH, Iraqi cancer Registry center, Baghdad, Iraq; 2002.
7. Waxman H.A.; the future of the global tobacco. England J. Med. 2002. vol.346 no.12.
8. Jose Angelo A. et al: chest journal 2011, 140:1378-1381.
9. P.T. Reid, J.A. Innes; tumor of the bronchus and lung, Church Livingstone, Davidson's principles and practice of medicine 21th Ed.; 19 pages 698-705.

10. Schonfeld N , Lienert ... et al ; Bronchial carcinoma in young adults ; Article in German October 1999 ; 53; 480-4
11. Chih – wei kuo , Yuh – min chen , et al ; Non-small cell lung cancer in very young and very old patient; chest Journal; 2000; 117; 354 – 357.
12. Shimono –T ; surgical treatment of primary lung cancer in patient less than 40 years , Journal clinical – oncology, 1994, may 12: 981 – 5.
13. Capewell S.; lung cancer in young patients, Respiratory medicine 1992 , Nov. 86: 499-502
14. Natali F, Guigay J, Laamim M, Vaylet F, L'Her P, Genero-Gygax ML, Allard P. Primary bronchial cancer in subjects aged 40 or younger. Revue de pneumologie clinique. 1990 Dec; 47:80-4.
15. Joseph G. Antkowiak; Bronchogenic carcinoma in patient under age 40, Ann Thoracic surgery 1989; 47; 397-3
16. Jiang W, Kang Y, Shi GY, Zhang HY, Cai L, Sun XW, Sun LC, Sui GJ. Comparisons of multiple characteristics between young and old lung cancer patients. Chinese medical journal. 2012 Jan; 125:72-80.
17. Leon S Green; Teresa I. For toul ... et al; Bronchogenic cancer in patients under 40years, the experience of Latin American country; chest journal 1993; Nov. 104: 1477 – 81.
18. Helland A, Brustugun OT; lung cancer in smokers and never smoker; article in Norwegian 2009 sep. 24; 129: 1859 - 62.
19. Turut H, Tastepe I... et al: Surgical results and prognosis of patients with primary bronchogenic carcinoma aged less than 36 years: Respirology 2007 Sep; 12: 707-11.
20. Yano T, Haro A, Shikada Y, Maruyama R, Maehara Y. Non-small cell lung cancer in never smokers as a representative 'non-smoking-associated lung cancer': epidemiology and clinical features. International journal of clinical oncology. 2011 Aug 1; 16:287-93.
21. Al Rahim YA. Lung Cancer in a sample of Iraqi patients. Al-Kindy College Medical Journal. 2007;53-9.
22. Al- Alusi, F, A: lung cancer in Iraq, analysis of 576 cases. J. Fac. Med. Baghdad 1987 , vol. 29 ,No.1; 87-92
23. John H. pemberton; bronchogenic carcinoma in patients younger than 40 years, the Annuals of thoracic surgery, November; 1993 vol. 36, No.5, 509-515.
24. Tsai–CM. lung cancer in young Chinese cancer detection and prevention 1988, 11, 235-8.
25. Mauri D, Pentheroudakis G, Bafaloukos D, Pectasides D, Samantas E, Efsthathiou E, Kalofonos HP, Syrigos K, Klouvas G, Papakostas P, Kosmidis P. Non-small cell lung cancer in the young: a retrospective analysis of diagnosis, management and outcome data. Anticancer research. 2006 Jul 1; 26:3175-81.
26. El-hassani N.B., “Bronchogenic Carcinoma in Iraq”. J. Fac. Med. Bag., 29, 1, PP: 87-93, 1987.
27. Minami H, Yoshimura M, Miyamoto Y, Matsuoka H, Tsubota N. Lung cancer in women: Sex-associated differences in survival of patients undergoing resection for lung cancer. Chest 2000; 118: 1603-1609.
28. Jemal A, Travis WD, Tarone RE, Travis L, Devesa SS. Lung cancer rates convergence in young men and women in the United States: Analysis by birth cohort and histologic type. Int J Cancer 2003; 105: 101-107.
29. Belani CP, Marts S, Schiller J, Socinski MA. Women and Chinese Medical Journal 2012; 125:72-80 79 lung cancer: Epidemiology, tumor biology, and emerging trends in clinical research. Lung Cancer 2007; 55: 15-23.
30. Ali H.H., “Sputum Lung Cancer”. J. Fac. Med. Bag., 34, 5 P: 415, 1992.
31. Maruyama R, Yoshino I, Yohena T, Uehara T, Kanematsu T, Kitajima M, Teruya T, Ichinose Y. Lung cancer in patients younger than 40 years of age. Journal of surgical oncology. 2001 Jul 1; 77:208-12.