STAGES AND METHODS OF DIAGNOSIS OF BRONCHOGENIC CARCINOMA IN HIWA CANCER HOSPITAL IN SULAIMANI CITY

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ABSTRACT

Background

Lung cancer is usually suspected in individuals who have an abnormal chest radiograph finding or have symptoms caused by either local or systemic effects of the tumour. The method and stage of diagnosis of suspected lung cancer depend on the type of lung cancer (i.e., small cell lung cancer [SCLC] or non-SCLC [NSCLC]), the size and location of the primary tumour, the presence of metastasis, and the overall clinical status of the patient.

Objectives

To determine the stage and method of diagnosis of bronchogenic carcinoma in Hiwa cancer hospital.

Patients and Methods

A cross-sectional study, at which three hundred patients with lung cancer in Hiwa cancer hospital from 1st Jan. 2016 to 1st Feb. 2018 were evaluated, and as much as possible as data were collected and analyzed for stage, method, and histological type.

Results

The mean age for lung cancer was 65.7±10.7 years. Male: female ratio was 3.4:1. Smoking was present in (88%) of cases. Most of our cases (61.7%) were diagnosed by bronchoscopy, and most of them were non-small cell lung cancer was stage III & IV. There was a significant relationship between the method of diagnosis and stages of lung cancer (P-value=0.016).

Conclusion

Most of our cases were males between 60–69-year-old, and smokers, without a family history, they presented with cough and were diagnosed by bronchoscopy (wash & biopsy) with metastatic disease, and their histological type was Non-small cell.

Keywords: *Bronchogenic carcinoma, Bronchoscopy, Non-small cell lung cancer, Small cell lung cancer.*

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INTRODUCTION

Lung cancer is the most common cancer in the world for several decades. Data from GLOBOCAN 2012 estimated a figure of 1.8 million new cases in 2012 (12.9% of the total diagnosed cancer), 58% of which occurred in the less developed regions. Lung cancer is the most common cause of death from cancer worldwide, estimated to be responsible for nearly one in five (1.59 million deaths, 19.4% of the total) [1].

In the United States, lung cancer (both small cell and non-small cell) is the second most cancer in both men and women (not counting skin cancer). In men, prostate cancer is more common; while in women breast, cancer accounts for about l3% of all new cancers [2].

Lung cancer incidence rates and mortalities are still low in the Arab world as compared to Europe or the US; though it is gradually increasing in the region [3].

In Iraq, lung cancer ranked as the second commonest cancer after breast with an incidence rate of about 4.96 /100,000 population, but it was first cancer among males in 2009 with an incidence rate of about 7.23 /100,000 population [4].

The WHO divides lung cancer into 2 major classes based on its biology, therapy, and prognosis: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC accounts for more than 85% of all lung cancer cases, and it includes 2 major non-squamous carcinomas (including adenocarcinoma, large-cell carcinoma, and types other cell types); and squamous cell (epidermoid) carcinoma. Most of the cases are stage IV at diagnosis due to adaptation of the symptoms by patients because most of them are smokers [5, 6].

The diagnosis of lung cancer depends on the stage, size, type, and location of the tumour, bronchoscopy is still the most usable and accurate tool for the diagnosis of lung cancer especially centrally located masses, which followed CT-percutaneous FNA for the peripheral masses [7].

EBUS-TBNA was an accurate, safe, and cost-effective tool in lung cancer staging. The selection of patients who had positive results of suspected lymph node metastasis in CT or PET may improve the sensitivity of EBUS-TBNA. High-quality prospective studies regarding EBUS-TBNA in lung cancer staging are still needed to be conducted [8].

The sensitivity and specificity of the CT-scan for identifying mediastinal lymph node metastases were approximately 55% and 81%, respectively, confirming that CT scanning has limited ability either to rule in or exclude mediastinal metastasis. For PET scanning, estimates of sensitivity and specificity for identifying mediastinal metastasis were approximately 77% and 86%, respectively. These findings demonstrate that PET scanning is more accurate than CT scanning, but a tissue biopsy is still required to confirm PET-scan findings. The needle techniques endobronchial ultrasound-needle aspiration, endoscopic ultrasound-needle aspiration, and combined endobronchial ultrasound and endoscopic ultrasound-needle aspiration have sensitivities of approximately 89%, 89%, and 91%, respectively. [9].

PATIENTS AND METHODS

A cross-sectional analytic study was performed in the Hiwa cancer center which is the only tertiary cancer center for Sulaymaniyah and Halabja provinces over a period starting from (1st JAN 2016 until 1st FEB 2018). Three hundred bronchogenic carcinoma patients attending our hospital were recruited for purpose of this study.

Institutional ethical approval was obtained from the authorities of the Hiwa cancer center. All were diagnosed with bronchogenic carcinoma thorough medical investigation, clinical examination, imaging (chest x-ray, CT-scan, and pet-scan), bronchoscopy (wash and biopsy), open lung biopsy, CT-guide biopsy, and histopathology result with immunohistochemistry at Shorsh armed-forces hospital in the city.

A data collection form (questionnaire) has been constructed and we brought all histopathology results of lung cancer patients from Shorsh armed-forces hospital and our hospital database system, and then correlated their stage and method of diagnosis with their age, sex, and type of smoking.

Statistical analysis

Data entry was performed using Microsoft Excel 2010 spreadsheet. Data analysis was performed to present the data in tabular and diagrammatic forms (using Pie charts and bar charts) and measurement of central tendency (Arithmetic mean) plus the measurement of dispersion (standard deviation) calculated for the variables. P-value obtained using (Chi-square and Fisher's exact test). A P-value of less than 0.05 is statistically significant.

RESULTS

In this study, three hundred cases of bronchogenic carcinoma were analyzed, over two years (1st Jan. 2016 until 1st Feb. 2018) at Hiwa cancer Teaching hospital. The results were as follow:

Age Distribution

Among our 300 cases, age ranged from 27 years to 100 years. The peak age of presentation was (60-69 years), the median age was 65.7±10.7, Table 1.

Gender Distribution

In this study, 231 patients (77%) were male and the remaining 69 patients (23%) were female. The male: female ratio was 3.4:1, Table 2.

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Family History of Bronchogenic Carcinoma

In this study, 20 cases (6.7%) had a family history of lung cancer while the remaining 280 cases (93.3%) had no family history, Table 3.

In our study, 264 cases (88%) had a history of smoking while the remaining 36 cases (12%) had no smoking history, Table 4.

In our study, 173 cases (57.7%) were current smokers (continue smoking at presentation), 90 cases (30%) were ex-smokers, and 36 cases (12%) were non-smoker, Table 5.

Clinical Presentation

Most of the study sample presented with cough, followed by chest pain, weight loss& loss of appetite, bone pain, neurological deficit, and lastly had hoarseness of the voice and syndromes (SIADH, SVCO), (84.7%, 46.7%, 32%, 17.3%, 12%, 10.3%, 1.3%, respectively), Table 6.

Methods of Diagnosis

In the present study, 165 cases (61.7%) were diagnosed by Bronchoscopy (biopsy and wash), 52 cases (17.3%) were diagnosed by CT-guided FNA, 42 cases (14%) were diagnosed by US-guided FNA, 20 patients (6.7) were diagnosed by Open lung biopsy, and only one case (0.3%) was diagnosed by Thoracoscopy and biopsy, Table 7.

Histological Types and Stages

Among 293 cases (97.7%) were diagnosed as Non-small cell lung cancer while the remaining 7 cases (2.3%) were diagnosed as small cell lung cancer.

Regarding Non-small cell lung cancer 117 cases (39%) were diagnosed as stage 4B, 76 cases (25.3%) were diagnosed as stage 4A, 46 cases (15.3%) were diagnosed as stage 3B while regarding the small cell lung cancer,

6 cases (2%) were diagnosed as extensive small cell lung cancer, and the remaining 1 case (0.3%) was diagnosed as limited small cell lung cancer, Table 8.

There was a significant relationship between stage and age at diagnosis (P-value=0.022). 72 cases (24%) stage IV were between (60-69) years old, and 55 cases (18.4%) were between (70-79) years old, Table 9.

Lastly, there was a significant relationship between the stage of diagnosis and smoking history (P-value<0.001), 172 cases (57.4%) with stage IV at diagnosis were smokers, while only 21 cases (7%) were non-smoker, and 77 cases (25.7%) with stage III at diagnosis were smoker, while only 7 cases (2.3%) were a non-smoker., Table 10.

Table 1. The distribution of age groups (year) among the participants

Age groups (year)	Frequency	Percent (%)
<19	0	0
20-29	1	0.3
30-39	2	0.7
40-49	21	7
50-59	47	15.7
60-69	114	38
70-79	92	30.7
80-above	23	7.6
Total	300	100

Table 2. Distribution of gender.

Gender	Frequency	Percent (%)
Male	231	77
Female	69	23
Total	300	100

Table 3 Family history of lung cancer.

Family history	Frequency	Percent (%)
Yes	20	6.7
No	280	93.3
Total	300	100

Table 4: Distribution of smoking history among the patients.

Smoking history	Frequency	Percent (%)
Yes	264	88
No	36	12
Total	300	100

Table 5. Smoking patterns among the patients.

Types of smoking	Frequency	Percent (%)
Current smoker	173	57.7
Ex-smoker	90	30
Passive smoker	1	0.3
No smoking	36	12
Total	300	100

Table 6. Distribution of different clinical presentations.

Symptoms	Frequency	Percentage (%)
Cough	254	84.7
Chest pain	140	46.7
Loss of appetite and weight	96	32
Hoarseness of the voice	31	10.3
Bone Pain	52	17.3
Neurological symptoms	36	12.0
Syndromes	4	1.3

Table 7. Methods of diagnosis for patients with lung cancer.

Method of diagnosis	Frequency	Percent (%)
Bronchoscopy (biopsy and wash)	185	61.7
CT-guided FNA	52	17.3
US-guided FNA	42	14
Open lung biopsy	20	6.7
Thoracoscopy and biopsy	1	0.3
Total	300	100

CT = computerized tomography; FNA = fine needle aspiration; US = ultrasound.

Table 8: Types and Stages at presentation.

Stages of lung cancer		Frequency (%)	Total (%)
Non-small cell lung cancer	1 B	1 (0.3%)	293 (97.7%)
	2 A	9 (3%)	
	2 B	6 (2%)	
	3 A	18 (6%)	
	3 B	46 (15.3%)	
	3 C	20 (6.7%)	
	4 A	76 (25.3%)	
	4 B	117 (39%)	
Small cell lung cancer	Limited	1 (0.3%)	7 (2.3%)
	Extensive	6 (2%)	
Total		300 (100%)	300 (100%)

Table 9. Relationship between the age groups and the stage.

Age groups (year)	Stages of lung cancer										Total	P-value
	Non-small cell lung cancer								Small cell lung cancer			
	1 B	2 A	2 B	3 A	3 B	3 C	4 A	4 B	Limited	Extensive		
20-29	0 0%	0 0%	0 (0%)	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	1 0.3%	1 0.3%	**0.022**
30-39	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	2 0.7%	0 0%	0 0%	2 0.7%	
40-49	0 0%	0 0%	0 0%	1 0.3%	5 1.7%	0 0%	4 1.3%	10 3.3%	0 0%	1 0.3%	21 7%	
50-59	0 0%	0 0%	2 0.7%	3 1%	5 1.7%	6 2%	15 5%	16 5.3%	0 0%	0 0%	47 15.7%	
60-69	1 0.3%	8 2.7%	2 0.7%	8 2.7%	12 4%	9 3%	23 7.7%	49 16.3%	1 0.3%	1 0.3%	114 38%	
70-79	0 0%	1 0.3%	1 0.3%	5 1.7%	22 7.3%	5 1.7%	26 8.7%	29 9.7%	0 0%	3 1%	92 30.7%	
80-above	0 0%	0 0%	1 0.3%	1 0.3%	2 0.3%	0 0%	8 2.7%	11 3.6%	0 0%	0 0%	23 7.6%	
Total	1 0.3%	9 3%	6 2%	18 6%	46 15.3%	20 6.7%	76 25.3%	117 39%	1 0.3%	6 2%	300 100%	

Table 10. Shows a significant relationship between the smoking history and the stage

Stages of lung cancer		Smoking history		Total	Total	P-value
		Yes	No			
Non-small cell lung cancer	1 B	1 (0.3%)	0 (0%)	1 (0.3%)	293 (97.7%)	<0.001
	2 A	7 (2.3%)	2 (0.7%)	9 (3%)		
	2 B	4 (1.3%)	2 (0.7%)	6 (2%)		
	3 A	15 (5%)	3 (1%)	18 (6%)		
	3 B	42 (14%)	4 (1.3%)	46 (15.3%)		
	3 C	20 (6.7%)	0 (0%)	20 (6.7%)		
	4 A	62 (20.7%)	14 (4.7%)	76 (25.3%)		
	4 B	110 (36.7%)	7 (2.3%)	117 (39%)		
Small cell lung cancer	Limited	0 (0%)	1 (0.3%)	1 (0.3%)	7 (2.3%)	
	Extensive	3 (1%)	3 (1%)	6 (2%)		
Total		264 (88%)	36 (12%)	300 (100%)	300 (100%)	

DISCUSSION

The incidence of lung cancer is higher among men than women worldwide. In a ratio that differs widely between different regions and countries [10]. Among men, the incidence rate in the United States, Canada, Denmark, and Australia have already reached the peak, but they continue to rise in Spain, China, and Japan. Among women, incidence rates have been considerably lower; an increase has been noticed lately but the rate in most areas has not peaked yet. Male: Female ratio varied from less than 2 in Iceland, U.S. whites, Canada, Denmark, and Sweden to more than 6 in Slovenia, Italy, and France [11]. In European countries, the lowest Male: Female ratio is in Denmark (1:7), the highest in Spain (13:4) [10]. In our study, the ratio was 3.4:1 which is similar to that of the neighboring countries like 3.01:1 in Kuwait and 2.8:1in Iran [12, 13]. At a population level, the high male-to-female ratio in the occurrence of lung cancer is primarily due to the historically higher prevalence of cigarette smoking in men than women. [14].Therefore, a higher male to female ratio in our study can be explained by the lower prevalence of smoking among women in Iraq as published in the Smoking Control Committee reports (prevalence of smoking in Iraq is 40% for males over the age of 16 years and less than 5% of females) [15].

Age is a major determinant of cancer risk [16]. In this study the mean age of patients was 64.5± 36 years, similar to that observed in another local study from Baghdad in which the mean age was 62 years, but in Iran it was 65.7years [17]. According to SEER the median age at diagnosis in the USA was 70 years with most patients diagnosed among people aged 65-74 years [18]. In our study the median age was 65 years and most patients were diagnosed at age intervals of 60 to 69 years. (Table1). This could reflect the higher life expectancy in the more developed countries compared with less developed countries.

Among the patients of the current study, NSCLC comprises most of the histological types & it constitutes 97.7% (293) of cases the remaining 2.3% were had small cell types. In comparison with SEER data, we notice that non-small cell type is much more common in our population than in western countries as non-small cell type constitutes only 85% of cases of US population [18].

According to the UK Cancer Research, at the time of lung cancer diagnosis approximately (36%) of patients presented at stage IV, (31%) presented at stage III and 22% were in early stages l or II [19]. In our study among NSCLC nearly 64% were stage IV, 28% were stage III and only 5% were stage I or II, and the remaining was SCLC among them 1 case was limited stage and 6 cases were extensive stage (Table 8). This variation in stages between our results and the UK Cancer research study group reflects variation in the health care and sophistication in the diagnostic approach

between the two populations. Also, implementation of the screening program in some parts of the world and health awareness and education.

The initial presenting symptoms in patients with lung cancer may be respiratory but are often constitutional and attributable to metastatic disease. Cough is reported to be the most common presenting symptom of lung cancer; other respiratory symptoms include dyspnea, chest pain, and hemoptysis [20].

In Saudi Arabia: A four-year prospective study showed that the most common presenting symptoms of lung cancer were cough 76%, followed by dyspnea 67.5% [19]. Ehsan Elliah and colleagues from Pakistan showed that the most common symptoms were cough (70%), dyspnea 64%, chest pain 52%, hemoptysis 39%, and loss of weight 29% [21]. In our study cough was witnessed in 84.7% of cases and represented the most common symptom followed by chest pain 47%.

There have been many published studies showing familial aggregation of lung cancer in first-degree relatives of probands with lung cancer [22, 23]. In a systematic review and meta-analysis of 53 studies on family history and lung cancer risk, Matakidouet al. found a significantly increased lung cancer risk among those who have at least one affected relative [24]. In our study family history of lung cancer was found in 20(6.7%) cases, (Table 3)

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 [25]. In countries in South Asia, up to 80% of women with lung cancer are never-smokers [26]. In the US, one study estimated that 19% of lung cancer in women and 9% of lung cancer in men occurs in never-smokers [27]. In our study, 12% of all patients were non-smoker regardless of their gender, (Table 4)

A second-hand smoker can contribute to an increased risk for lung cancer with a dose Second dependent relationship between the degree of exposure and the relative risk. Some reports showed an increased risk for lung cancer in non-smoking women married to men who smoke [28]. A summary analysis of a large number of epidemiologic studies on the risk for lung cancer in non-smokers found an excess risk for lung cancer of 24% in non-smokers who lived with a smoker [29]. In our study we found that only 0.3% of patients were passive smokers.

The method of diagnosis of suspected lung cancer depends on the type of lung cancer, size and location of the primary, the presence of metastasis, and overall clinical status of the patient. In our study, we find that 185 (61.7%) cases have been diagnosed by bronchoscopy, 94 (31.3%) cases by imaging-guided FNA, and 20 (6.7%) by open lung biopsy [7, 30].

Also, there was a significant relationship between stage and age at diagnosis (P-value=0.022). 72 cases (24%) stage IV were between (60-69) years old, and 55 cases (18.4%) were between (70-79) years old.

Lastly, there was a significant relationship between the stage of diagnosis and smoking history (P-value<0.001), 172 cases (57.4%) with stage IV at diagnosis were smokers, while only 21 cases (7%) were non-smoker, and 77 cases (25.7%) with stage III at diagnosis were smoker, while only 7 cases (2.3%) were a non-smoker.

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