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REVIEW

Clinico-pathological profile of bronchogenic carcinoma cases presented to Chest Department, Cairo University in the last 10 years

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KEYWORDS

Clinico-pathological;
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Abstract *Introduction:* Lung cancer was the most commonly diagnosed cancer as well as the leading cause of cancer death in males in 2008 globally.

Aim of the work: To evaluate the clinico-pathological profile of the bronchogenic carcinoma cases in the Chest Department, Cairo University.

Patients and methods: Retrospective study was carried out in the Chest Department, Cairo University, in which four hundred and four confirmed cases of bronchogenic carcinoma were admitted during July 2002 till July 2012. Data regarding demographics, smoking, histology, clinical presentation, radiographic findings are reported.

Results: Our study included 404 confirmed cases of bronchogenic carcinoma. Male to female ratio was 4.6:1. The highest incidence was in the sixth and seventh decades of life (63.6%). Smoking was found to be the main risk factor in 75.7% of patients. Cough was the most common symptom found in 347 patients (85.9%), followed by dyspnea in 276 patients (68.3%). Most common radiological finding was mass lesion (49.8%). Majority of cases were diagnosed by bronchoscopy (68.1%). Four types of bronchogenic carcinoma were found: squamous cell carcinoma 37.4% adenocarcinoma 29.5%, small cell carcinoma 14.9%, large cell carcinoma 7.2% and undifferentiated carcinoma 11.1%. In females, adenocarcinoma was the predominant cell type (54.2%) while in males, squamous cell carcinoma was the predominant cell type (42.5%).

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Conclusion: Bronchogenic carcinoma is more frequent beyond the middle age. Smoking is still the major risk factor. Adenocarcinoma is more common in females and was the most frequent tumor in non-smokers, while in males, squamous cell carcinoma is still the predominant cell type. © 2013 Production and hosting by Elsevier B.V. on behalf of The Egyptian Society of Chest Diseases and Tuberculosis. Open access under CC BY-NC-ND license.

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Introduction

At the end of the 20th century, Bronchogenic Carcinoma had become one of the leading causes of preventable death. It was a rare disease at the start of that century, but exposures to new etiologic agents and an increasing life span combined to make lung cancer a scourge of the 20th century. Lung cancer is the most common malignancy worldwide and is the leading cause of cancer deaths in men and women [1].

Lung cancer was the most commonly diagnosed cancer as well as the leading cause of cancer death in males in 2008 globally. Among females, it was the fourth most common diagnosed cancer and the second leading cause of cancer death. Lung cancer accounted for 13% (1.6 million) of the total cases and 18% (1.4 million) of the death in 2008 [2].

Patients and methods

This retrospective study was carried out in the Department of Chest Medicine of Cairo University Hospital, in which four hundred and four (404 cases) histopathologically and/or cytologically confirmed cases of bronchogenic carcinoma were included in the study. These patients were admitted during the last 10 years (from 2001 to 2010).

Data regarding demographics (age of the patients, sex), smoking status, histopathological type, clinical presentation, radiographic findings, the method of diagnosis and clinical stage of the disease were obtained from the files of confirmed cases of bronchogenic carcinoma.

Radiological assessment was done in all cases. The diagnosis of bronchogenic carcinoma was based on positive histopathological or cytological examination. Patients without histopathological confirmation were excluded from this study. For confirmation of diagnosis of bronchogenic carcinoma, majority of patients were subjected to fibro-optic bronchoscopy and/or CT-guided biopsy. Other diagnostic methods were open biopsy, thoracoscopy, pleural fluid and supraclavicular lymph node biopsy.

All case data were tabulated. Statistical analysis was performed using descriptive statistics of the collected data.

Results

The results are shown in Tables 1–10 and Figs. 1–9.

Discussion

Accurate epidemiological data on lung cancer in Egypt are not available since a comprehensive national population-based cancer registry is lacking. However, official statistics as well as institution and hospital-based studies show that it is the second most common cancer in men and second leading cause of cancer death, after bladder cancer [3].

As regards to the sex distribution of bronchogenic carcinoma cases, Table 1 shows that 82.2% of cases were males and 17.8% of cases were females with a male to female ratio of 4.6:1 which is near to that reported by Elattar from the National Cancer Institute (NCI) in Egypt [3]. According to Bahader and Jazieh study the male:female ratio was 3:1 [4].

In many of the more developed countries, the incidence of lung cancer in men has reached a plateau and is now decreasing, whereas the number of new cases in women continues to increase [5,6].

According to Devesa et al., male:female rate ratios varied from less than 2 in Iceland, US whites, Canada, Denmark and Sweden to more than 6 in Slovenia, Italy, and France and more than 10 in Spain [7].

Generally, lung cancer trends among females lag behind males lung cancer rates in females are increasing in many countries [2]. In recent years, adenocarcinoma has increased as a proportion of all lung cancers diagnosed [8]. Women are

Table 1 Sex distribution of the bronchogenic carcinoma cases.

Sex	Frequency (No.)	Percentage	Ratio
Male	332	82.2	4.6
Female	72	17.8	1.0
Total	404	100.0	4.6:1

Table 2 Mean age of incidence in males and females and in both sexes.

Sex	No.	Minimum	Maximum	Mean	Std. Deviation
Male	332	26	90	58.50	10.98
Female	72	35	75	53.42	8.92
Total	404	36	90	57.54	10.81

Table 3 Relation between age groups and histological cell type.

Age group	SCC No.	SCLC No.	Adeno CA No.	LCC No.	Undiff. No.
26–40	5 (3.3%)	3 (5.0%)	8 (6.7%)	4 (13.8%)	4 (8.9%)
41–50	19 (12.6%)	22 (36.7%)	34 (28.6%)	11 (37.9%)	6 (13.3%)
51–60	42 (27.8%)	20 (33.3%)	42 (35.3%)	5 (17.2%)	19 (42.2%)
61–70	70 (46.4%)	15 (25.0%)	26 (21.8%)	6 (20.7%)	12 (26.7%)
> 70	15 (9.9%)	0 (0.0%)	9 (7.6%)	3 (10.3%)	4 (8.9%)
Total	151 (100%)	60 (100%)	119 (100%)	29 (100%)	45 (100%)

Table 4 Incidence of different histopathologic cell types in smokers and in non-smokers.

Histopathological cell type	Smoking status				Total	
	Smoking		Non-smoking		No.	%
	No.	%	No.	%		
Squamous cell carcinoma	134	88.7	17	11.3	151	37.4
Small cell carcinoma	49	81.7	11	18.3	60	14.9
Adenocarcinoma	63	52.9	56	47.1	119	29.5
Large cell carcinoma	26	89.7	3	10.3	29	7.2
Undifferentiated carcinoma	34	75.6	11	24.4	45	11.1
Total	306	75.7	98	24.3	404	100

Table 5 Distribution of histopathological cell types according to the radiological findings.

Histopathologic cell type	Lung mass	Apical opacity	Pleural effusion	Hilar mass	Cavitary lesion	Pulmonary nodule	Total
Squamous cell carcinoma	67 (44.4%)	25 (16.6%)	11 (7.3%)	38 (25.2%)	9 (6.0%)	1 (0.7%)	151 (100%)
Small cell carcinoma	40 (66.7%)	3 (5.0%)	2 (3.3%)	11 (18.3%)	2 (3.3%)	2 (3.3%)	60 (100%)
Adenocarcinoma	64 (53.8%)	10 (8.4%)	25 (21.0%)	11 (9.2%)	7 (5.9%)	2 (1.6%)	119 (100%)
Large cell carcinoma	15 (51.7%)	2 (6.9%)	6 (20.7%)	2 (6.9%)	3 (10.3%)	1 (3.4%)	29 (100%)
Undifferentiated carcinoma	15 (33.3%)	13 (28.9%)	5 (11.1%)	2 (4.4%)	9 (20%)	1 (2.2%)	45 (100%)
	201 (49.8%)	53 (13.1%)	49 (12.1%)	64 (15.8%)	30 (7.4%)	7 (1.7%)	404

more frequently diagnosed with adenocarcinoma, and this may explain the narrowing of the gap between men and women in the incidence of bronchogenic carcinoma in our study.

Studying the age distribution in this work shows that, the highest incidence of bronchogenic carcinoma was in the sixth and seventh decades of life with 63.6% of the cases found in these two decades of life (Fig. 1).

The incidence declined before the age of 40 with 5.9% of cases and after the age of 70 with 7.7% of cases, and no cases were found before age of 26 years, indicating that bronchogenic carcinoma was less common in these age groups.

Similarly, a study carried out by Karlikaya and Cakir Edis [9] and another study by Suliman et al. [10] also proved that maximum patients were in their sixth and seventh decade at the time of diagnosis of bronchogenic carcinoma.

The average age at the time of diagnosis that was reported by the Radzikowska study was 61.94 years [11]. In our study, age ranged from 26 to 90 years with 58.59 years being the average age (Table 2). This may be explained by that patients started smoking early in their life. The mean age in males was 58.50 years and it was 53.42 years in females.

The relation between age groups and histological cell type (Table 3) shows that the squamous cell carcinoma was common after the age of 50 years (84.1%) while the small cell carcinoma was common in the age period between 40 and 60 years (70%) and also adenocarcinoma cell type was common in the age period between 40 and 60 years (63.9%).

As regards to smoking status, there have been many studies in many parts of the world which showed a relationship between smoking and bronchogenic carcinoma. In our study,

Table 6 Different cell types of cases that present with pleural effusion.

Cell type	No. and % of cases present with pleural effusion	
Squamous cell carcinoma	11	22.4%
Small cell carcinoma	2	4.1%
Adenocarcinoma	25	51%
Large cell carcinoma	6	12.2%
Undifferentiated carcinoma	5	10.2%
Total	49	100%

Table 7 Different cell types of cases that present with hilar shadow.

Cell type	No. and % of cases present with hilar shadow	
Squamous cell carcinoma	38	59.4%
Small cell carcinoma	11	17.2%
Adenocarcinoma	11	17.2%
Large cell carcinoma	2	3.1%
Undifferentiated carcinoma	2	3.1%
Total	64	100%

Table 8 Different methods of diagnosis of bronchogenic carcinoma and their percentages.

Methods of diagnosis	No.	%
FOB	275	68.1
CT guided biopsy	86	21.3
Supraclavicular LN biopsy	2	0.5
Pleural fluid	9	2.2
Thoracoscopy	15	3.7
Open biopsy	17	4.2
Total	404	100

smoking habit of the patient (Fig. 2), revealed that, the number of smokers (75.7%) is 3 folds that of non-smokers (24.3%). Study of Rawat et al., reported that smoking was the main risk factor in 81.77% patients [12].

In our study of 72 females with bronchogenic carcinoma, a high percentage of them were non-smokers (97.25% non-smokers versus 2.8% smokers). And this explains the relatively high percentage (42.3%) of non-smokers in our study.

In male cases, the percentage of smokers was 91.6% while the percentage of non-smokers was 8.4% of male (Fig. 3).

In our study, the percentage of non-smoking females was 97.2% versus only 2.8% of smoking females, so other risk factors other than smoking, should be considered that include exposure to environmental tobacco smoke (ETS), fumes and smoke from certain cooking fuels and environmental pollution.

In our study smoking is associated with all types of bronchogenic carcinoma. The connection between smoking and bronchogenic carcinoma was most evident among patients with squamous cell carcinoma, small cell carcinoma and large cell carcinoma and less evident among patients with adenocarcinoma (Fig. 4).

The strength of the association between cigarette smoking and bronchogenic carcinoma varies by cell type, with the largest for squamous and small cell carcinomas and somewhat smaller for adenocarcinoma. This result is similar to that reported in another study [13].

The different clinical presentations of the patients (Fig. 5) revealed that cough was the most frequent symptom in the whole group, as 347 patients (85.9%) had this complaint. According to Rawat et al. study cough was the common symptom (72.90%) [12].

Cough is present in >65% of patients at the time lung cancer is diagnosed [14].

In this study cough was the most common symptom (347 patients; 85.9%) and was followed by dyspnea (276 patients; 68.3%), expectoration (270 patients; 66.8%), chest pain (241 patients; 59.7%), hemoptysis (142 patients; 35.1%) weight loss (115 patients; 28.5%), and hoarseness of voice (85 patients; 21%) was also a frequent symptom. Other symptoms, as fever (16.3%), dysphagia (9.2%) and supraclavicular lymph node (1%) were not so frequent clinical presentations. In our study the incidence of symptoms was high compared to those described in the literature (Fig. 5) and this explained by that our patients presented late in their disease.

The radiological findings (Fig. 6), showed that, lung mass was the commonest radiological picture, as it occurred in 201 cases (49.8%) near to that percentage (46.31%) that was reported by Rawat et al. study [12] followed by hilar shadow (15.8%), apical opacity (13.1%), and pleural effusion (12.1%).

Cavitary lesion was found in 7.4% of cases. A prospective study by Shetty et al., found that cavitary lesion incidence was 8.6% of lung cancer [15]. Pulmonary nodule in our study occurred in 1.7% of cases, this may be explained by that most cases were presented in late stages.

Distribution of histopathologic cell types according to the radiological findings (Table 5), showed that 44.4% of cases of squamous cell carcinoma presented with mass lesion followed by 25.2% of cases presented with hilar shadow and 16.6% presented radiologically with apical opacity while pleural effusion and cavitary lesion presented in 7.3% and 6% of the squamous cell carcinoma cases, respectively.

In our study, 53.8% of cases of adenocarcinoma presented with mass lesion followed by 21% of cases of adenocarcinoma presented with pleural effusion while hilar shadow incidence was 9.2% of adenocarcinoma cases. Most of cases of small cell carcinoma presented radiologically with mass lesion 66.7% followed by hilar shadow in 18.3% of small cell carcinoma cases. 51.7% of large cell carcinoma presented with mass lesion and 20.7% of large cell carcinoma with pleural effusion.

In all cell types of bronchogenic carcinoma, the mass lesion was the major radiological picture, in this study (Fig. 8).

Table 6 shows that pleural effusion was more frequent with adenocarcinoma, as 51% of cases that presented with pleural effusion were adenocarcinoma and this may be due to that most of adenocarcinoma located peripherally and it can cause pleural invasion.

Table 7 shows that hilar shadows were common with squamous cell carcinoma, as 59.4% of cases presented with hilar shadows were squamous cell carcinoma followed by small cell carcinoma and adenocarcinoma (17.2%).

Apical opacity incidence was more frequent with squamous cell carcinoma, 47.2% of cases that presented with apical

Table 9 Distribution of bronchogenic carcinoma cell types according to the method used for diagnosis.

Diagnosis method		Histopathology					Total
		SCC	SCLC	Adeno-CA	LCC	Undiff	
FOB	Count	107	52	60	21	35	275
	% within diagnosis method	38.9	18.9	21.8	7.6	12.7	100.0
	% within histopathology	70.9	86.7	50.4	72.4	77.8	68.1
CT guided biopsy	Count	36	5	38	3	4	86
	% within diagnosis method	41.9	5.8	44.2	3.5	4.7	100.0
	% within histopathology	23.8	8.3	31.9	10.3	8.9	21.3
Supraclavicular LN biopsy	Count	0	1	0	0	1	2
	% within diagnosis method	0.0	50.0	0.0	0.0	50.0	100.0
	% within histopathology	0.0	1.7	0.0	0.0	2.2	0.5
Pleural fluid	Count	2	0	3	4	0	9
	% within diagnosis method	22.2	0.0	33.3	44.4	0.0	100.0
	% within histopathology	1.3	0.0	2.5	13.8	0.0	2.2
Thoracoscopy	Count	2	0	9	1	3	15
	% within diagnosis method	13.3	0.0	60.0	6.7	20.0	100.0
	% within histopathology	1.3	0.0	7.6	3.4	6.7	3.7
Open biopsy	Count	4	2	9	0	2	17
	% within diagnosis method	23.5	11.8	52.9	0.0	11.8	100.0
	% within histopathology	2.6	3.3	7.6	0.0	4.4	4.2
Total	Count	151	60	119	29	45	404
	% within diagnosis method	37.4	14.9	29.5	7.2	11.1	100.0
	% within histopathology	100.0	100.0	100.0	100.0	100.0	100.0

Table 10 Stage of disease.

Stage	Frequency (No.)	Percentage
Operable stage	11	9.8
Inoperable stage	101	90.2
Total	112	100.0

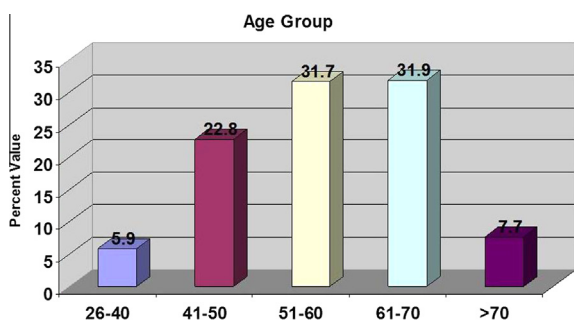


Figure 1 Age distribution of the bronchogenic carcinoma cases.

opacity were squamous cell carcinoma, followed by 24.4% undifferentiated carcinoma.

Table 8 and Fig. 7 illustrate different methods of diagnosis that had been performed in this study, in our study, diagnosis of bronchogenic carcinoma was made by fiberoptic bronchoscopy in 275 patients (68.1%), and this percentage is near to that reported in another study which was 61.7% [16]. An important role in improving the diagnostic relevance of the fiberoptic bronchoscopy was assumed by the more frequent adoption of biopsies and trans-bronchial needle aspiration on parenchyma and mediastinal lymph nodes.

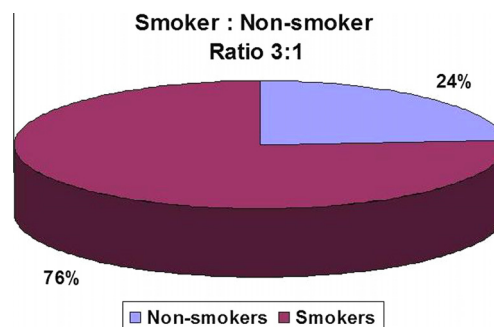


Figure 2 Incidence of bronchogenic carcinoma in smokers and in non-smokers.

Table 9 shows that bronchoscopic biopsy was positive in 107 of 151 patients (70.9%) of the squamous cell carcinoma cases, also in 52 of 60 patients (86.7%) of cases of the small cell carcinoma, in 60 of 119 patients (50.4%) of cases of adenocarcinoma, in 21 of 29 patients (72.4%) of cases of the large cell carcinoma and. in 35 of 45 patients (68.1%) of cases of undifferentiated carcinoma.

The cases of bronchogenic carcinoma that was diagnosed by CT guided biopsy were 86 cases (21.3% of all cases). Table 9 shows that most cases that were diagnosed by FNAB (FNAB done under CT) was adenocarcinoma (38 patients; 44.2%), followed by squamous cell carcinoma (36 patients; 41.9%), while only 5 cases (5.8%) of the small cell carcinoma, 3 cases (3.5%) of the large cell carcinoma and 4 cases (4.7%) of the undifferentiated carcinoma were diagnosed by CT guided biopsy.

Supraclavicular lymph node biopsy was performed in 2 cases (0.5% of all cases), 1 of these cases proved to be

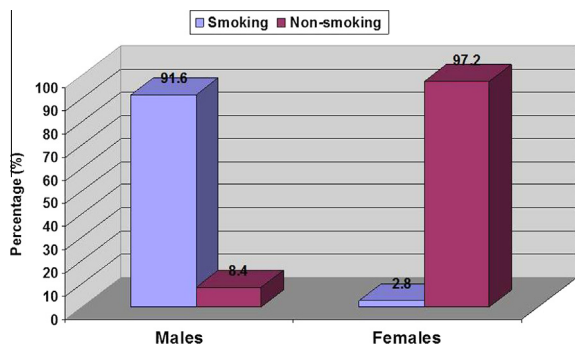


Figure 3 Smoking status distribution in males and females.

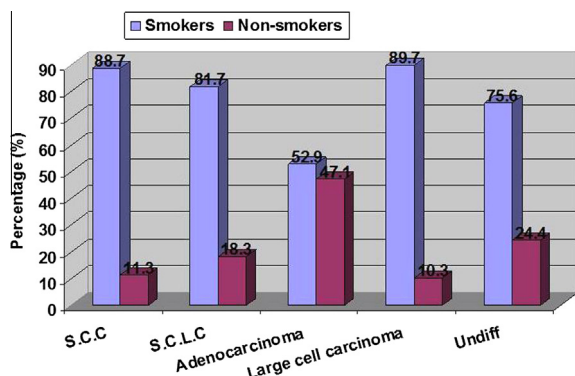


Figure 4 Incidence of different histopathological cell types in smokers and in non-smokers.

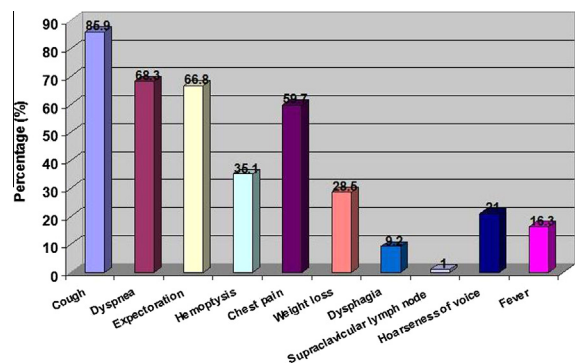


Figure 5 Percentages of different clinical presentations.

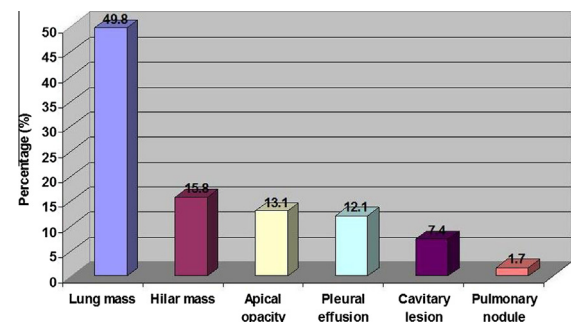


Figure 6 Radiological findings of bronchogenic carcinoma.

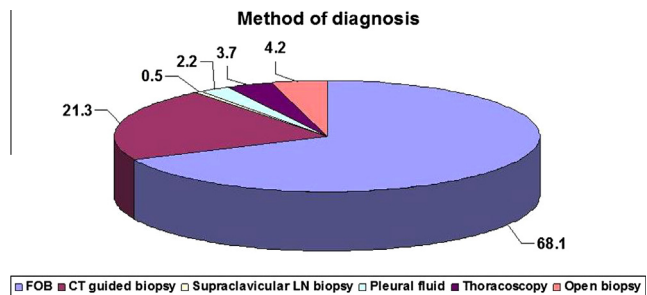


Figure 7 Methods of diagnosis and their percentages.

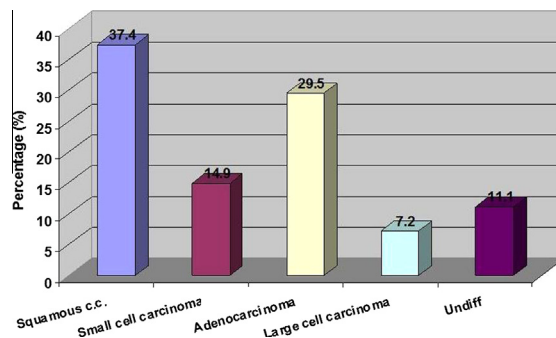


Figure 8 Percentage of different pathologic cell types in this study.

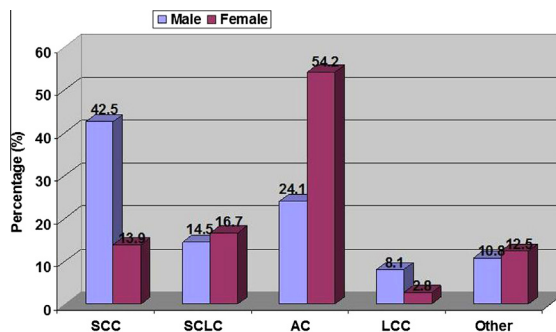


Figure 9 Distribution of histopathologic cell type in males and females.

squamous cell carcinoma, while other case was undifferentiated carcinoma. Pleural fluid cytology was positive in 9 cases (2.2% of all cases), 3 cases were adenocarcinoma, 4 cases were large cell carcinoma and 2 cases were squamous cell carcinoma.

Thoracoscopy was the diagnostic procedure in 15 cases (3.7% of all cases), 60% of them were adenocarcinoma, 13.3% were squamous cell carcinoma and 20% were undifferentiated carcinoma.

Open biopsy was performed in 17 cases (4.2% of all cases), as regards the histologic cell type, that most cases were adenocarcinoma (52.9%) followed by squamous cell carcinoma (23.5%).

In our study the most common histopathological cell type was squamous cell carcinoma (37.4%), followed by adenocarcinoma (29.5%), small cell carcinoma (14.9%), large cell

carcinoma (7.2%) and undifferentiated carcinoma (11.1%) (Fig. 8).

In the cell type distribution reported by Radzikowska, squamous cell carcinoma had the highest cell type incidence (52.1%) followed by small cell carcinoma (20.8%) while adenocarcinoma represented only 11.3% of the cases [11].

According to Shetty et al., study, squamous cell carcinoma also presented 44.5% of cases followed by adenocarcinoma (18.5%) and small cell carcinoma (17.2%) [15].

In another study by Rawat et al., they reported that 44.8% of cases were squamous cell carcinoma followed by adenocarcinoma (19.7%) and small cell carcinoma (16.75%) [12].

In our study the incidence of squamous cell carcinoma (37.4%) is less than that reported in a previous study and close to percentage reported in study by Lam et al., (39%) [17].

The incidence of adenocarcinoma in our study (29.5%) is higher than that reported in other studies 11.3%, 18.5% and 19.7% by Radzikowska et al. [11], Shetty et al. [15] and Rawat et al. [12], respectively.

There was a shift in the incidence of squamous cell carcinoma and adenocarcinoma, up to the late 1980s, squamous cell carcinoma was the most common subtype, which was then surpassed by adenocarcinoma. In recent years adenocarcinoma is the most common histologic subtype of lung cancer in most countries, accounting for almost half of all lung cancers [18].

The shift in the incidence of squamous cell carcinoma and adenocarcinoma may be associated with the switch from non-filtered to filtered cigarettes, the depth of inhalation had been altered [19].

In particular, smoke from unfiltered strong cigarettes may be shallowly inhaled, resulting in chemical carcinogen deposition centrally in the bronchial area and giving rise to squamous cell carcinomas. Smoke from filtered milder cigarettes may be more deeply inhaled, resulting in carcinogen deposition more peripherally and giving rise to adenocarcinomas. Reducing the nicotine content may also promote deeper inhalation as smokers attempt to compensate [20]. The changes in cigarette composition reduced the yield of carcinogenic polycyclic aromatic hydrocarbons (PAHs), inducers of squamous cell carcinomas, while increasing the yields of carcinogenic tobacco-specific N-nitrosamines (TSNAs), inducers of adenocarcinomas [21].

Other possible explanations that the increasing use of mucin stains and immunocytochemical staining for antibodies to CEA has contributed to enhanced recognition of adenocarcinomas [15].

These factors have contributed to the emerging predominance of adenocarcinoma in the lung cancer rates.

Fig. 9 shows that adenocarcinoma was the predominant type (54.2%) in females followed by small cell carcinoma (16.7%) and squamous cell carcinoma (13.9%). In males the predominant type was squamous cell carcinoma (42.5%) followed by adenocarcinoma (14.5%).

The criteria of inoperability in our cases included: X-ray finding of chest wall invasion, finding of bilateral hilar or mediastinal enlargement suggestive of lymph node involvement, pleural effusion, mediastinal invasion and signs of vital structures involvement, presence of extrathoracic metastasis, bronchoscopic finding as vocal cord paralysis and tracheal or carinal involvement and the presence of supraclavicular lymph nodes metastasis.

The high percentage of inoperable cases in our study may be attributed to that some of the cases were misdiagnosed as tuberculosis and treated by anti-tuberculous treatment at other centers and after long time, the patients were referred to our chest department, thereby causing a delay in diagnosis, the smokers often explain any cough they experience as smoker's cough and this wrong belief may mask presence of tumor for a long time before diagnosis and thus delay diagnosis until the disease is at a more advanced. Lack of diagnostic facilities at peripheral health centers could be another cause for delay in diagnosis of bronchogenic carcinoma.

Conclusion

We can conclude from the study:

1. In this work, the highest incidence of bronchogenic carcinoma was in the sixth and seventh decades of life. The incidence declined before the age of 40 years and after the age of 70 years.
2. Smoking still remains the major risk factor in the pathogenesis of bronchogenic carcinoma.
3. On histological examination, squamous cell carcinoma was relatively more frequent than any other tumor type followed by adenocarcinoma and then by small cell carcinoma.
4. In all cell types of bronchogenic carcinoma, the mass lesion was the major radiological finding and the majority of cases were diagnosed by fibro-optic bronchoscopy.

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