DIAGNOSTIC EVALUATION OF PRIMARY LUNG CANCER AMONG WOMEN IN CHENNAI

Davidson Nancy Glory

1Associate Professor, Department of Respiratory Medicine, Government Stanley Medical College, Chennai, Tamil Nadu.

ABSTRACT

BACKGROUND
Lung cancer is rapidly emerging as a serious cause of mortality among all the cancers across the globe. Though it was linked to tobacco smoking for several decades, recent research has demonstrated that its incidence is similar among smokers and non-smokers; and also, among men and women alike. This study was done to evaluate the various diagnostic modalities in diagnosis of primary lung cancer among females from non-smoking population of Chennai.

MATERIALS AND METHODS
This cross-sectional study was carried out among 31 female patients who were diagnosed with lung cancer by Computerized Tomography (CT), chest radiography and ultrasound, and also by Fiber Optic Bronchoscopy (FOB). The histological classification was carried out and TNM staging was done.

RESULTS
The mean age of the participants was 49 years. A majority of the participants (71%) were diagnosed with adenocarcinoma followed by 19.4% who were diagnosed with squamous cell carcinoma. Among the participants with adenocarcinoma, 95.4% of them were diagnosed at advanced stages, beyond stage II. Adenocarcinoma was best diagnosed using CT, while squamous cell carcinoma and small cell carcinoma were best diagnosed with FOB.

CONCLUSION
Fiber optic bronchoscopy is a significant modality in diagnosing centrally located tumour and for staging purposes. It is essential that regular screening is carried out, among the suspected cases, without any gender bias.

KEYWORDS
Adenocarcinoma, Fiberoptic Bronchoscopy, Keratinization, Squamous Cell Carcinoma.

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BACKGROUND
Lung cancer is a major health problem worldwide. The mortality of lung cancer is on a steady rise across the world, irrespective of the gender. It is the leading cause of cancer mortality in most of the countries in the world. It remains the most lethal form of cancer in men and has now surpassed breast cancer in women as well. In India, the incident of lung cancer are approximately 63,000 per year. Studies have demonstrated that the incidence of lung cancer in women is on par with smoking related cancers.

Despite advances in imaging techniques and treatment modalities, the prognosis of lung cancer remains poor, with a five-year survival of less than 5% in locally advanced stages. Most of the patients present at later stages, resulting in inoperable conditions. As far as diagnosis and management of lung cancers are concerned, the aetiology of the cancer determines the location and type of malignancy. For example, while smoking related cancers involve proximal and distal airways alike, the lung cancers of non-smokers involve distal airways. Moreover, these carcinomas are often adenocarcinoma. It has been well established that adenocarcinoma and squamous cell carcinoma are the most common types of lung cancer.

There is a growing need for classification of primary lung cancers, based on the etiological factors and time of presentation. The new classification of lung cancers adopted by World Health Organization was based on the 2011 International Association for the Study of Lung Cancer/ American Thoracic Society/ European Respiratory Society (IASLC/ATS/ERS) for lung adenocarcinoma classification. This classification focuses on distinguishing squamous cell carcinoma from adenocarcinoma and on molecular testing for mutations like EGFR and ALK rearrangement. Studies have proven that non-smoking status is a strong clinical predictor of EGFR tyrosine kinase inhibitors. It is therefore pertinent that a histopathological evaluation is carried out, especially among women belonging to the non-smoking population, in order to assess the molecular basis and histopathological basis of primary lung cancers.
Objectives
To evaluate the histopathological diagnosis and staging of primary lung cancers among women in Chennai.

MATERIALS AND METHODS
Study Setting
This study was carried out as a cross sectional study among the female patients attending the outpatient clinic of the Respiratory Medicine Department of our Government hospital, Chennai. The duration of the study was for a period of 15 months.

Study Population
All the female patients who presented with clinical symptoms suggestive of primary lung cancer during the study period were selected for the study. A histopathological diagnosis was made on these patients and all those participants were confirmed to have primary lung cancer were taken up for this study. Staging of the tumours were done using TNM staging. Males were excluded. Female patients with other respiratory symptoms who were negative for primary lung cancer by histopathology were excluded from the study.

Sample Size and Sampling Technique
The participants were selected by convenient sampling. A total of 31 females participated in this study.

Ethical Approval and Informed Consent
Approval from the Institutional Ethics Committee was obtained prior to the commencement of the study. Each participant was explained in detail about the study and informed consent was obtained prior to data collection.

Data Collection
The study protocol included a detailed history regarding the onset and progress of the disease, and risk factors. A detailed general and systemic examination was performed. Chest X-Ray was done to obtain radiological diagnosis. The modalities used to obtain the specimen were Computerized Tomography guided needle biopsy, Fiber optic bronchoscope Brushing/Washing and biopsy and Ultrasound guided needle biopsy

Computerized Tomography / Ultrasound guided needle biopsy was done in patients to detect peripherally located tumours. The biopsy was done using Atovac Gun core biopsy needle. The needle size was 18G, 10 cm to 15 cm in length with 1 cm markings. The distal tip is ultrasound sensitive. The needle also has a over sheath cannula for Computerized Tomography guidance. The needle length was adjusted using pins. With computerized Tomography, Ultrasound guidance the lesion was localized, under cover of local anaesthesia the needle length was adjusted according to the lesion and core biopsy obtained which was 2 cm to 2.5 cm bit.

Fiber optic bronchoscopy was performed with the single channel bronchoscope to detect centrally located tumours and for TNM staging. Under local anaesthesia, 2 ml of 2% lignocaine was injected transtracheally after test dose along with spraying of 4% lignocaine using hand atomizer just prior to the procedure. Lignocaine jelly was applied to the effective length of fiber optic bronchoscope. The fiber optic bronchoscope was passed transnasally/transorally in the supine position. The normal side was visualized first and then the suspected abnormal side. Biopsy was performed in patients with obvious endo bronchial lesion. Mucosal brushings and washings were obtained from the area surrounding the abnormal segments on radiological basis in case of patients without endo bronchial lesion. A central tumor is defined as a tumor that is evident within the bronchial tree at fibre optic bronchoscope and a peripheral tumor as one that is not visualized at bronchoscopy. X-ray wise, central tumor is defined as tumor arising at (or) close to the hilum, peripheral tumor as tumor arising beyond the hilum. Post bronchoscopic sputum was sent for cytological examination. Patients were subjected to FNAC / Excision biopsy of peripheral Lymph node.

Smears for cytology were fixed in isopropyl alcohol for 30 minutes and stained with Haematoxylin and eosin stain. Smears were air dried and fixed in methanol for 30 minutes. Air dried smears were fixed with MGG (Maygrunwald Giemsa) stain, slides were mounted and reported under microscope by cytopathologist. Biopsy specimens were fixed in formaldehyde (10%) for 24 hours. These slides were stained with Haematoxylin and eosin and reported by pathologist. Pleural fluid was centrifuged, and smears stained in Haematoxylin and eosin.

Data Analysis
Data was entered and analysed using Microsoft Excel Spreadsheet 2010. The prevalence of histological types and stages of the tumours were computed as percentages.

RESULTS
This study was carried out among 31 women who were diagnosed with primary lung cancers. The mean age of the study participants was 49 years. The age distribution of the study participants is given in figure 1. Majority of the participants (38.7%) belonged to 41-50 years of age.
The histopathological classification of the primary lung cancers is given in table 1. A majority of the participants (71%) were diagnosed with adenocarcinoma, followed by squamous cell carcinoma (19.4%).

<table>
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<th>(%)</th>
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<td>Adeno Carcinoma</td>
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<td>71.0</td>
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<tr>
<td>2.</td>
<td>Squamous cell Carcinoma</td>
<td>6</td>
<td>19.4</td>
</tr>
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<td>3.</td>
<td>Small cell Carcinoma</td>
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<td>3.2</td>
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Table 1. Histopathological Diagnosis of Primary Lung Cancer Among Study Participants

The staging of lung cancers was based on clinical, radiological, histological and bronchoscopic findings. Non-small cell carcinoma patients were staged based on TNM classification whereas small cell carcinoma patient was staged in a simple fashion into two categories like limited disease and extensive disease. It was observed that majority of the patients in adenocarcinoma belonged to stage III, followed by stage IV. In squamous cell carcinoma, majority of the patients belonged to stage III, followed by stage IV. Only one participant from squamous cell carcinoma belonged to stage I at the time of diagnosis. Most of the patients were in stage III B (33.3%) and IVA (33.3%) at the time of presentation (n=20).

The TNM staging of lung cancers is given in table 2.

<table>
<thead>
<tr>
<th>Cell Type</th>
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<td>B</td>
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<td>1(3.3)</td>
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</table>

Table 2. TNM Staging of Lung Cancers Among the Study Participants

*1 Patient with small cell carcinoma was at extensive stage of disease at the time of diagnosis.

The histopathological presentation of adenocarcinoma and squamous cell carcinoma are given in figure 2 and 3. While adenocarcinoma was characterized by heterogeneous differentiation within the same tumor, squamous cell carcinoma was characterized by the presence of cytokeratin differentiation with keratinization and presence of intercellular bridges.

Figure 2: Adenocarcinoma histological picture (L)
Figure 3: Squamous cell carcinoma histological picture (R)

The radiological diagnostic findings among the study participants is given in table 3. The most common presentation was mass lesion 54.84% (n=17) followed by pleural effusion 35.48% (n=11).
Comparison of diagnostic modalities for detection of primary lung cancers is given in Table 4. Computerized Tomography helped in histopathological diagnosis by way of computerized Tomography guided needle biopsy of suspected mass in 12 patients (38.71%). Bronchus cut off sign was positive in 3 patients. Computerized Tomography diagnosed 4 patients with mediastinal nodes, 2 patients with rib/vertebral metastasis and 2 patients with nodules in the lung which were not seen on the chest X-ray. Fiber optic bronchoscopy was done in 26 patients (83.87%). Bronchial brushing cytology yield was 26.92% (n=7). Endobronchial biopsy yield was 15.38% (n=4). Ultrasonography of the chest was useful in identifying peripheral tumours close to the chest wall. It helped in the histopathological diagnosis by the way of guided needle biopsy of suspected mass in 8 patients (25.81%). Supra clavicular Node FNAC/Biopsy yielded positive results in 6 patients (19.35%).

<table>
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<tr>
<td>Total</td>
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<td>12</td>
<td>11</td>
<td>8</td>
</tr>
</tbody>
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Table 4. Primary Diagnostic Modalities for Histopathological Documentation

DISCUSSION
Lung Cancer is one of the most serious and fatal neoplasms in India both in males and females. Complex circumstances like genetic predisposition, environmental exposure, life style habits combine over a lifetime to initiate and promote tumor growth in the lung. In this study of 31 patients, 30 patients had confirmed pathological diagnosis, but in 1 patient malignant cell could be identified but cell type was not possible. The age range was from 28 to 68 years. Maximum number of patients in this study was between 41 and 50 years. Mean age was 49 years. This is less than the study conducted by Jindal SK and Behera D where the mean age was 42 years.8

The most common histopathological type in this study was Adeno Carcinoma (70.96%). The second most common type was Squamous cell Carcinoma (19.35%). This is in corroboration with the study done by T. Behera, T. Balamugesh.8

Fibre optic bronchoscopy was done in 26 patients (83.87%). It helped in diagnosis by the way of endo bronchial biopsy in 4 patients (15.38%) and by bronchial brushing cytology in 7 patients (26.92%). This is in corroboration with the study conducted by Gupta Pk et al Rajasthan, in which the combined yield of bronchial biopsy and brush cytology was 45%.10 Post bronchoscopy sputum cytology was positive in 2 patients (6.45%) and the most common tumor associated was squamous cell carcinoma. Supraclavicular Lymph node FNAC/biopsy yielded positive results in 6 patients (19.35%) whereas in the study conducted by Jindal SK and Behera D, the yield was 10.7%.8 In this study majority of the patients (83.33%) were in the advanced stages of the disease (IIIIB and beyond) at the time of presentation. In the study conducted by Rajendra Prasad et al, 74.2% of patients were in the advanced stage. In the study conducted by Rajashekar et al, 96% were in the advanced stage of the disease.11,12

The most common radiological presentation was mass lesion, which was seen in 17 patients (54.84%) followed by pleural effusion in 11 patients (35.48%). Adeno Carcinoma present as a peripheral mass is 68% and as a central lesion in 13% of patients. Squamous cell carcinoma presented as a peripheral mass in 16% and as a central lesion in 66% of patients. Only one patient of small cell carcinoma was present as a central lesion (100%). This is in corroboration
with the study done by D. Behera, T. Balamugesh 2004.9 About two Patients with bronchioloalveolar sub type of Adeno Carcinoma presented as consolidation in X-ray.

Post bronchoscopic sputum cytology was positive in 2 patients (6.45%) and the most common tumor associated was squamous cell carcinoma. Computerized Tomography study was done in all 31 patients. Computerized Tomography guided needle biopsy of suspected mass was done in 14 patients. Positive results were obtained in 12 patients (85.71%). USG guided needle biopsy of suspected mass lesion was positive in all patients who underwent the procedure (100%). CT/USG guided needle biopsy helped in the diagnosis of 20 patients (65%) out of 31 patients. Whereas in the study conducted by Payne CR et al, the yield was much higher (88%).13

Fibre optic bronchoscopy was done in 26 patients (83.87%). It helped in diagnosis by the way of endo bronchial Biopsy in 4 patients (15.38%) and by bronchial brushing cytology in 7 patients (26.92%). This is in corroborations with the study conducted by Gupta PK et al Rajasthan where the combined yield of bronchial biopsy and brush cytology was 45%.14 Supraclavicular Lymph node FNAC/biopsy yielded positive results in 6 patients (19.35%) whereas in the study conducted by Jindal SK and Behera D, the yield was 10.7%.8

CONCLUSION
This study has shown that there is definitely an increasing trend in the incidence of Primary Lung Cancer in females when compared with the previous studies conducted in our institution. This disturbing trend is in line with global situation and needs further evaluation. Most common pathological cell type in females in our study was adenocarcinoma. Moreover, 83% of patients were in the advanced stages of disease at the time of presentation. Fibreoptic Bronchoscope Biopsy and Brushing/Computerized Tomography / Ultrasound guided core needle biopsy were valuable tools to get a tissue diagnosis. It is therefore essential that lung lesions in females in high risk age group of 40 years and above are investigated without gender bias thoroughly to rule out malignancy. This approach may result in diagnosing malignancy at an early stage.

REFERENCES

[9] D Behera, T Balamugesh, Department of Pulmonary Medicine, Post Graduate Institute of Medical Education and Research, Chandigarh, India. Indoor air pollution as a risk factor for lung cancer in woman. JAPI 2005; 53: 190-192