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# Cytohistological Correlation of Fibreoptic Bronchoscopy Specimens with Added Value of Immunohistochemistry in Diagnosis of Lung Tumors

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***Abstract***
***Aim****: To correlate bronchial cytology specimens with endobronchial biopsies along with immunohistochemistry , taking the latter as confirmatory method.*
***Materials and Methods****: The study was done at Institute of Pathology , Madras Medical College for a period of two years from June2014 to May2016. A total of 172 cases with lung mass were taken up for the study. Bronchial washings,bronchial brushings and biopsies were obtained by fibreoptic bronchoscope from all the cases.*
***Results****:Out of 172 cases of suspected lung mass, 139 cases were positive for malignancy by cytology and was confirmed for 142 cases by biopsy. The total number of false positives was 9 and false negative cases were 13. Sensitivity of bronchial cytology was found to be 90.9% and specificity 68.97%. Immunohistochemistry has helped to subtype nonsmall cell carcinomas in 12 cases.*
***Conclusion*** *:Bronchial cytology is a valuable tool in early diagnosis of lung cancer. However to increase the specificity of the results, it should be used concurrently with bronchial biopsy along with immunohistochemistry to further subtype the lung cancer which carries therapeutic and prognostic significance in the current era of targetted therapy.*
***Keywords****: bronchial biopsy, bronchial washings, bronchial brushings, fibreoptic bronchoscope, lung cancer*

## I. Introduction

Carcinoma of the lung is increasing in incidence and it is one of the most common cause of cancer deaths during the past few decades[1]. Although clinical and radiological evaluations like CT Scan etc, plays an important role in diagnosis of lung masses, they do not provide a conclusive diagnosis on the nature of the lesion whether it is benign or malignant[2]. Bronchoscopy is very effective for detecting lung cancer at a very early stage[3]. The samples such as bronchial washings , brushings, and lavage may not only provide the accurate diagnosis but also help in recognising its type[4]. The sampling techniques for biopsies include transbronchial forceps biopsy and endobronchial forceps biopsies. These biopsies along with immunohistochemistry form a gold standard for diagnosis of lung tumors and thereby to plan appropriate treatment for the patient . The cytology specimens offer accurate information regarding the site of the lesion and especially bronchoalveolar lavage is of great use in providing adequate material from peripheral lesions[5]. The current study was done to ascertain the diagnostic importance of endobronchial cytology specimens by correlating with biopsy samples , and confirming it with immunohistochemistry taking the latter as the confirmatory method . As the latest classification of lung cancers[6] on small biopsies mainly rely on immunohistochemistry for the accurate diagnosis and rarity attempt has been made to validate whether a combination of biopsy and immunohistochemistry is more effective than cytological methods in detecting lung cancers in our setup .

## II. Materials And Methods

Two year prospective study was done in our Institute of Pathology, Madras medical college from June 2014 to May 2016. Samples were collected from 172 patients in whom clinical, radiological and bronchoscopic examination suggested the presence of lung mass. Using flexible fibreoptic bronchoscope, the samples were obtained from our thoracic medicine department. Bronchial washings and lavage specimens were centrifuged and smears were made. Direct smears were made with bronchial brush material. Both were subjected to H&E and MGG Stain. Endobronchial biopsies were fixed in 10 % neutral buffered formalin,processed and stained with H&E. All neoplastic lesions were subjected to Immunohistochemistry by routine antigen retrival technique for confirmation and typing of lesion. All cases with clinical, radiological and bronchoscopic findings suggestive of lung mass were included in this study. Inflammatory lesions were excluded from this study.

## III. Results

172 patients were taken up for the study. Majority of them were males with male female ratio of 2.6:1. The mean age was 60 years with the range of 32 -70 years. The most common site of lesion being the right upper lobe . Cytological examination revealed 139 malignant cases including 9 suspicious cases . Malignancy was confirmed in 143 out of 172 samples by biopsy and immunohistochemistry. Among these the commonest was squamous cell carcinoma(40.69%), followed by adenocarcinoma (29.65%) and then small cell carcinoma (4.65%). Correlation of cytology with biopsy and immunohistochemistry is given in table

**Table 1:** Comparison of bronchial cytology and endobronchial biopsy

| Tumor Type | Cytology | Biopsy | Ihc |
|---|---|---|---|
| Squamous | 62 | 70 | 74 |
| Adeno | 48 | 51 | 57 |
| Small Cell | 9 | 8 | 8 |
| Adenosquamous | - | - | 2 |
| Carcinoid | - | 1 | 1 |
| Lymphoma | 1 | 1 | 1 |
| Nsclc | 4 | 12 | - |
| Positive | 6 | - | - |
| Suspicious | 9 | - | - |
| Negative | 33 | 29 | 29 |
| Total | 172 | 172 | 172 |

True positives :130
True negatives : 20
Falsepositives : 9
False negatives :13
Sensitivity between cytology and biopsy was 90.9%, and specificity was 68.97%.

**Table 2:** Sub categorisation of lung carcinoma using immunohistochemistry with incidence

| Subtype | Biopsy | Immuno Histochemistry | Incidence (%) |
|---|---|---|---|
| Squamous Cell Carcinoma | 70 | 74 | 51.75 |
| Adenocarcinoma | 51 | 57 | 39.86 |
| Amall Cell Carcinoma | 8 | 8 | 5.6 |
| Adenosquamous Carcinoma | | 2 | 1.43 |
| Carcinoid | 1 | 1 | 0.7 |
| Lymphoma | 1 | 1 | 0.7 |
| Nonsmall Cell Carcinoma | 12 | | |
| Total | 143 | 143 | |

## IV. Discussion

The frequency of lung cancer has increased dramatically over a few decades and advent of fibre optic bronchoscope has brought a great revolution in detection of lung cancers at a very early stage. The male to female ratio in our study was 2.6: 1, which is closer to the study done by Bodh et al [7] . The age range was between 32 and 75 years with the mean age falling in the $6^{th}$ decade, which was similar to a study done by Ahmad M et al [8] and Upama et al [9].

The present study was done with the purpose of assessing the sensitivity and specificity of broncoscopic cytological material with that of biopsy tissue from the tumor site. Our study could detect malignancy in 139 cases out of 172 cases by cytology (Table 1)(fig 1) , with a sensitivity of 90.9% and specificity of 68.97% which was similar to the study done by Bodh et al [7] thereby proving that the samples were very effective in detecting lung cancer. In our study 9 cases were false positives. False positivity may occur due to chronic inflammatory cells , epithelioid cells, atypical histiocytes and squamous metaplasia along with dysplasia . 13 cases were false negative. False negative was due to superadded inflammation and hypocellular aspirates and nonrepresentative samples .

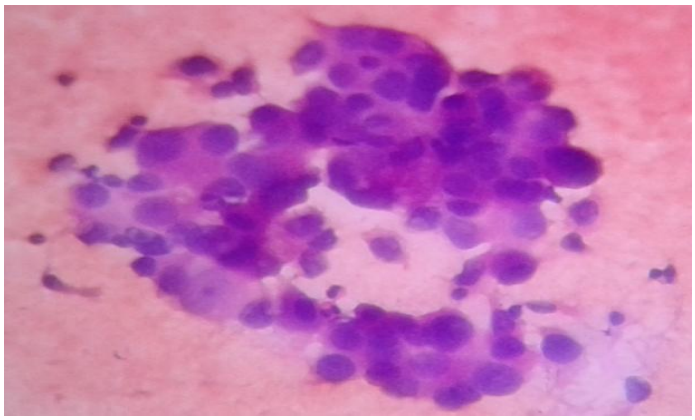

**Figure1:** H&E Stain : 40xview: Bronchial cytology positve for malignant cells

Although studies by Trevisani et al[10] , Karahalli et al[11], reported that diagnostic yield did not increase by adding bronchial washing to biopsy , authors like Mak VH et al [12 ] and Jones et al[13] had recommended combination of biopsy with cytology using both washing and brushing for maximum diagnostic yield.To classify the tumor accurately according to the histologic type, biopsy and immunohistochemistry gains its importance especially in the current era of targetted therapy for certain histologic types of lung cancers. In biopsy samples out of 172 cases, 143 cases were malignant ,of which 12 cases could not be subtyped and were categorized as non small cell carcinomas (Fig 2). Using Immunohistochemistry (Table 2), they were subclassified into adenocarcinoma, squamous cell (Fig 3) and adenosquamous carcinomas. Lymphomas and small cell carcinomas were confirmed by immunohistochemistry with respective markers. This justifies the use of immunohistochemistry in diagnosis of lung cancer especially when the histopathological diagnosis is equivocal as therapeutic decisions are mainly based on specific diagnosis. Earlier there has been no therapeutic implications to classify non small cell carcinomas. This has changed dramatically over the past few years with the advent of epidermal growth factor(EGFR ) mutations and anaplastic lymphoma kinase rearrangements (ALK) rearrangements as effective targets for advanced lung adenocarcinomas(6).

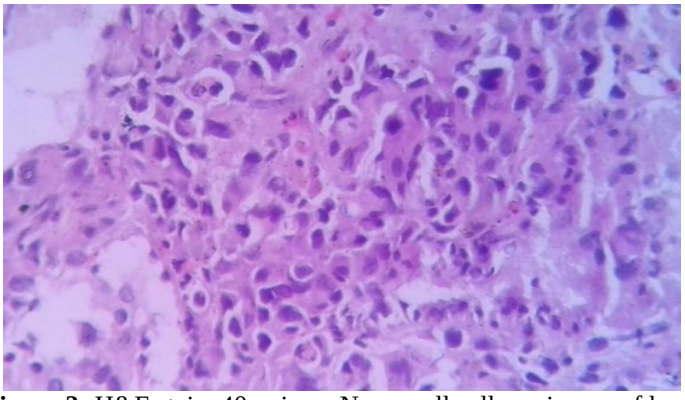

**Figure 2:** H&E stain, 40x view : Non small cell carcinoma of lung

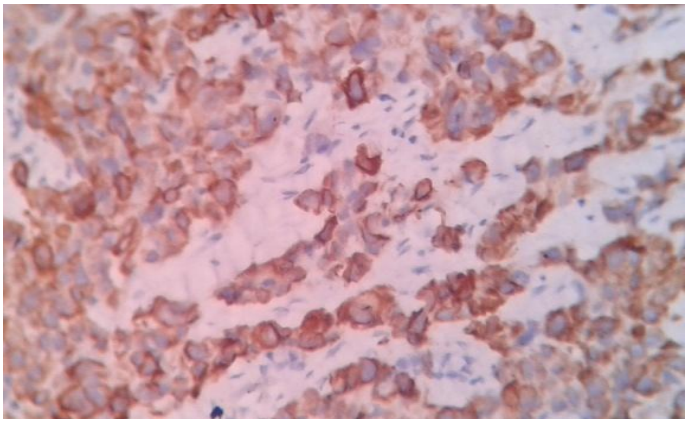

**Figure 3:** P63immunohistochemistry positivity in squamous cell carcinoma

In our study majority of cases were squamous cell carcinomas (51.75%) followed by adenocarcinoma (31.86%) and then small cell carcinoma (5.6%). Though worldwide adenocarcinoma has replaced squamous cell carcinoma as the most prevalent lung malignancy, dominance of the latter is even seen in few areas including our study population . In studies done by Reddy et al [14] ,Sharma et al [15] and Upama et al [9], squamous cell carcinoma predominated adenocarcinoma . Two cases of nonsmall cell carcinoma(fig 3) was reported as adenosquamous carcinoma with the help of immunohistochemistry markers such as TTF -1 and p63(fig 4). Lymphomas and carcinoids accounted for 0.7%. As for typing of lung cancers by cytology was concerned,it was less accurate than histopathology along with immunohistochemistry.

## V. Conclusion

In our study of comparing endobronchial cytology and biopsy specimens , the sensitivity and specificity was 90.9% and 68.97% respectively. Thereby we arrived at a conclusion that bronchial cytology has excellent sensitivity, specificity,and predictive values in diagnosing malignancies. It yields nearly the same information as that of biopsy . However for further subtyping of tumors and in suspicious cases it must be concurrently used with biopsy and immunohistochemistry to arrive at an accurate diagnosis of therapeutic and prognostic significance.

**Conflict of Interest:** Nil
**Acknowledgement:** Nil

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