

## Original Research Article

# Comparative analysis of fiberoptic bronchoscope aided cytohistological techniques in diagnosis of benign and malignant lesions of lung

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## ABSTRACT

**Background:** Morbidity and mortality from chronic lung diseases are increasing worldwide. A combination of various cytological and histopathological techniques are required for the high diagnostic accuracy. This study aims to evaluate and compare diagnostic accuracy of fiberoptic bronchoscope aided cytohistological techniques such as BAL (bronchoalveolar lavage), TBNA (Transbronchoscopic needle aspiration) and FB (forceps biopsy) in diseases of lung.

**Method:** A prospective study conducted on 100 patients with symptoms and signs of various respiratory diseases who underwent fiberoptic bronchoscopy. Diagnostic accuracy of various samples alone and in combination were analysed.

**Results:** Sensitivity of BAL-24%, TBNA 64% and FB 66%. Addition of BAL to FB increased the sensitivity to 69%. Addition of BAL to TBNA increased the sensitivity to 70%. Sensitivity of cytological methods (FB and TBNA) 90%. Addition of both BAL and TBNA to FB increased overall sensitivity to 93%. FB the most specific amongst the three techniques with specificity of 94% followed by TBNA (59.4%) and BAL (50%).

**Conclusions:** There are variable results regarding diagnostic yields and utilities of various fibre-optic bronchoscope aided cytohistological techniques but there combination adds the yields. Thus a combination of various cytohistological samples should be taken in a patient undergoing fiberoptic bronchoscopic examination to increase the diagnostic yield, to cut short the diagnostic time and early start of treatment.

**Keywords:** Lung, BAL, TBNA, FB

## INTRODUCTION

Morbidity and mortality from chronic lung diseases are increasing worldwide.<sup>1</sup> It has been observed that over past century lung cancer has gone from obscure disease to one of the leading causes of cancer related death worldwide.<sup>2</sup>

A variety of benign and malignant tumors arise in the lung but the vast majority (90-95%) are carcinomas, about 5% are bronchial carcinoids and 2-5% are mesenchymal and other miscellaneous neoplasms.<sup>3</sup> With current and projected smoking patterns, it is anticipated that lung cancer will remain the leading cause of death in the world for decades to come.<sup>2</sup> With increasing

prevalence of smoking patterns lung cancer has reached epidemic proportions in India. About 80% of lung cancer patients come from rural areas.<sup>4</sup>

A combination of various cytological and histopathological techniques are required for the high diagnostic accuracy. Cytopathological examination of different materials obtained from the respiratory system greatly helps in diagnosing pulmonary diseases. The diagnostic accuracy is enhanced by the newer cytopreparation and immunocytochemical techniques.<sup>5,6</sup>

A wide variety of pulmonary specimens can be examined cytohistologically. Commonly obtained specimens include: spontaneously produced sputum, induced

sputum, BAL, bronchial brushings, post bronchoscopy sputum, transbronchial needle aspiration (TBNA), transthoracic needle aspiration (TTNA), and FB.

Keeping in view the above facts, technical difficulties in accessing the site of lesions in lungs and variable results of different diagnostic techniques a prospective study was planned to evaluate the relative efficacy of different cytological, histological samples obtained by fibre-optic bronchoscopy (viz FB, endobronchial fine needle aspirate, BAL fluid) in diagnosis of pulmonary diseases

## METHODS

A prospective study was conducted on 100 patients in department of pathology and department of respiratory medicine, Pt B. D. Sharma PGIMS Rohtak from July 2020-July 2021. The study group included patients with symptoms and signs of various respiratory diseases having some radiological abnormality who underwent fibreoptic bronchoscopy. Patients with respiratory diseases who underwent fiberoptic bronchoscopy, but specimens obtained were inadequate were excluded from the study. Ethical approval was taken from institutional ethical committee. Statistical analysis was done using SPSS software.

With the advent of flexible fibreoptic bronchoscope (FOB), a number of pulmonary specimens can be examined cytohistologically. The commonly obtained specimens are spontaneously produced sputum, induced sputum, BAL, bronchial brushings, post bronchoscopy sputum, transbronchial needle aspiration, transthoracic needle aspiration, FB. A satisfactory specimen should be representative of the lesion, adequate in quantity, well preserved and well prepared for staining.

**Spontaneously induced sputum:** After rinsing the mouth and cleaning the throat, the patient should take a deep breath, hold it for 20 seconds and cough out the specimen forcefully in a wide mouthed container.

**Induced sputum:** Induction of sputum is useful in patients who are unable to produce satisfactory sputum by deep coughing. Hypertonic saline or a mucolytic agent is administered and the patient is asked to cough.

**BAL:** The technique consist of wedging the tip of FOB as far as possible into a distal airway. Normal saline in aliquots of 20-60ml is introduced and aspirated through the suction channel of FOB. Aspirated fluid is pooled and sent for analysis. After withdrawing the fluid was processed immediately in most cases and when it was not possible, it was refrigerated until processed. It was centrifuged at 600G for 10 min and multiple smears prepared. Smears were air dried and at least 1 was fixed in alcohol. Air dried and alcohol fixed smears stained with may Grunwald giemsa (MGG) and hematoxylin and eosin (H and E) stain and examined under light microscope.

**TBNA:** TBNA is done by introducing an aspirating needle and directed to the area of interest.

**FB:** Biopsy of endobronchial lesions and of distal lung parenchyma can be performed with the same instruments used for endobronchial sampling. Biopsy forceps can be passed through the bronchoscope into the small airways, where they penetrate the alveolar wall, allowing biopsy of peribronchial alveolar tissue. Specimens were processed and paraffin sections obtained as per standard procedure of tissue processing. Routine hematoxylin and eosin sections were examined in every case.

Specific cytochemical /histochemical stains were employed wherever necessary to reach a final diagnosis. Specific stains employed were periodic acid Schiffs, ZN stain for acid fast bacilli, gomorimethamine silver stain (GMS), Grocotts stain, mucicarmine and reticulin stain.

## RESULT

Out of total 100 cases, 88 were male and 12 were female. 79 patients came from rural background and 21 from urban dwellings. The age of the patients ranged from 14-80 years. Maximum number of patients were in the age group of 41 to 50 years that is 35 patients followed by 30 patients in the age group of 51-60 years (Table 1).

**Table 1: Age wise distribution of patients, (n=100).**

| Age (Years)  | Males | Females | Total |
|--------------|-------|---------|-------|
| <b>0-10</b>  |       |         |       |
| <b>11-20</b> |       | 1       | 1     |
| <b>21-30</b> | 1     |         | 1     |
| <b>31-40</b> | 6     |         | 6     |
| <b>41-50</b> | 34    | 1       | 35    |
| <b>51-60</b> | 27    | 3       | 30    |
| <b>61-70</b> | 16    | 4       | 20    |
| <b>71-80</b> | 4     | 3       | 7     |
| <b>Total</b> | 88    | 12      | 100   |

Most common symptoms with which patients presented included cough (72), dyspnoea (69), chest pain (69), on and off fever (25), hemoptysis (18), hoarseness of voice (11), shoulder pain (4) and back pain (3) (Table 2).

**Table 2: Presenting symptoms.**

| Presenting symptoms                                              | N  |
|------------------------------------------------------------------|----|
| <b>Cough with expectoration</b>                                  | 64 |
| <b>Dyspnoea</b>                                                  | 69 |
| <b>Chest Pain</b>                                                | 69 |
| <b>Fever</b>                                                     | 25 |
| <b>Hemoptysis</b>                                                | 18 |
| <b>Hoarseness of voice</b>                                       | 11 |
| <b>Dry cough</b>                                                 | 8  |
| <b>Shoulder pain</b>                                             | 4  |
| <b>Back pain</b>                                                 | 3  |
| <b>Swelling feet, facial puffiness, cervical lymphadenopathy</b> | 1  |

Of 100 patients in study group, 91 smokers. Of these, on final analysis, amongst a total of 84 (94%) malignant lesions 78 patients were smokers. There was no statistically significant association of smoking between benign and malignant disorders. However, it could be inferred that smoking, in general associated with increased incidence of respiratory disorders (Table 3). Fibreoptic bronchoscopy showed endobronchial mass in bronchus in 67 cases, abnormal mucosa in 20, nodular growth in 5 cases while growth ill-defined in 2 cases. In 1 case, bronchoscopy showed fungal ball while in 5 cases, no abnormality could be detected on bronchoscopic examination.

**Table 3: Association of smoking with pulmonary diseases.**

| Lesions                   | Total      | Cases with smoking | Percent (%) |
|---------------------------|------------|--------------------|-------------|
| Squamous cell carcinoma   | 31         | 29                 | 93.5        |
| Adenocarcinoma            | 13         | 9                  |             |
| Small cell carcinoma      | 13         | 13                 | 100         |
| Non small cell carcinoma  | 7          | 7                  | 100         |
| Large cell carcinoma      | 1          | 1                  | 100         |
| carcinoma unclassified    | 17         | 17                 | 100         |
| Metastatic carcinoma      | 1          | 1                  | 100         |
| Lymphoma                  | 1          | 1                  | 100         |
| Tuberculosis              | 4          | 3                  | 75          |
| Chronic bronchitis        | 2          | 2                  | 100         |
| Non specific inflammation | 2          | 2                  | 100         |
| Fungal infection          | 1          | 1                  | 100         |
| Undiagnosed cases         | 7          | 5                  | 71.4        |
| <b>Total</b>              | <b>100</b> | <b>91</b>          | <b>91</b>   |

By using all, cytohistological techniques final diagnosis could be arrived in 93 cases, while in rest 7 cases findings were suggestive of an inflammatory lesion but could not be correlated conclusively with other investigative or clinical data, so were considered inadequate.

There were a total of 9 benign lesions, 84 malignant lesions and 7 cases remained undiagnosed. Benign lesions include TB (4 cases), chronic bronchitis (2 cases), non specific inflammation (2 cases) and one case of aspergillosis. Malignant lesions included squamous cell carcinoma (31 cases), small cell carcinoma (13 cases), adenocarcinoma (8 cases) and one case each of large cell carcinoma and metastatic carcinoma. In 7 cases diagnosis of non small cell carcinoma was made and in 17 cases, the lesion could be identified as carcinoma but could not

be categorized further. There was one (1.2 %) case of non hodghkin lymphoma (Table 4).

**Table 4: Number of cases diagnosed by BAL, TBNA and FB.**

| Variables                        | BAL      | TBNA      | FB        |
|----------------------------------|----------|-----------|-----------|
| <b>Malignant lesions</b>         |          |           |           |
| Squamous cell carcinoma, (n=31)  | -        | 4         | 7         |
| Adenocarcinoma, (n=8)            | -        | 1         | 4         |
| Small cell carcinoma, (n=13)     | -        | 1         | 4         |
| Non small cell carcinoma, (n=7)  | -        | 2         | 1         |
| Large cell carcinoma, (n=1)      | -        | 1         | -         |
| Carcinoma unclassified, (n=17)   | 3        | 8         | 2         |
| Metastatic carcinoma, (n=1)      | -        | 1         | -         |
| Lymphoma, (n=1)                  | -        | 1         | -         |
| <b>Total, (n=84)</b>             | <b>3</b> | <b>19</b> | <b>18</b> |
| <b>Benign lesions</b>            |          |           |           |
| Tuberculosis, (n=4)              | -        | 2         | 2         |
| Chronic bronchitis, (n=2)        | -        | -         | 2         |
| Non specific inflammation, (n=2) | -        | -         | -         |
| Fungal infection, (n=1)          | -        | -         | 1         |
| <b>Total, (n=9)</b>              | <b>-</b> | <b>2</b>  | <b>5</b>  |

Amongst various cytohistological techniques, BAL was diagnostic in 3 cases while TBNA alone was positive in 21 cases and FB in 23 cases. BAL and TBNA both were positive in 3 cases. BAL and FB in 3 cases, TBNA and FB in 25 cases and in 15 cases all the three techniques were diagnostic (Table 5).

**Table 5: Efficacy of various cytohistological techniques alone and in combination.**

| Technique           | Diagnostic | Percent of diagnosed cases, (n=93) (%) | Percent of total cases (%) |
|---------------------|------------|----------------------------------------|----------------------------|
| <b>BAL</b>          | 3          | 3.2                                    | 3                          |
| <b>TBNA</b>         | 21         | 22.6                                   | 21                         |
| <b>FB</b>           | 23         | 24.7                                   | 23                         |
| <b>BAL+ TBNA</b>    | 3          | 3.2                                    | 3                          |
| <b>BAL+FB</b>       | 3          | 3.2                                    | 3                          |
| <b>TBNA+ FB</b>     | 25         | 26.9                                   | 25                         |
| <b>BAL+TB NA+FB</b> | 15         | 16.1                                   | 15                         |

Out of total 93 cases diagnosed, 76 were centrally located while 17 were located peripherally. Five centrally located lesion and two peripheral lesions remained undiagnosed.

Statistical analysis revealed that sensitivity of BAL was 24%, of TBNA 64% and FB 66%. Addition of BAL to FB increased the sensitivity to 69%. Addition of BAL and TBNA increased the sensitivity to 70%. Overall sensitivity of cytological methods (FB and TBNA) was 90%. Addition of both BAL and TBNA to FB increased the overall sensitivity to 93%. FB was the most specific amongst the three techniques with specificity of 94% followed by TBNA and BAL.

In centrally and peripherally located lesions, BAL showed a sensitivity of 26 and 15.8% and a specificity of 52.4% and 33.3% respectively. TBNA showed sensitivity of 61.2% in centrally placed lesions and 73.7% in peripheral lesions while specificity of 93% and 88.8% respectively. The p value was significant in case of forcep biopsy evaluation. Thus, TBNA was more useful in peripheral lesion as compared to centrally placed lesions. While FB was more sensitive in central lesion and most specific amongst all the technique in both central and peripheral lesions (Table 6-8).

**Table 6: Sensitivity of various FOB aided cytohistological techniques.**

| Technique   | Sensitivity |
|-------------|-------------|
| BAL         | 24          |
| TBNA        | 64          |
| FB          | 66          |
| BAL+FB      | 69          |
| BAL+TBNA    | 70          |
| TBNA+FB     | 90          |
| BAL+TBNA+FB | 93          |

**Table 7: Specificity of FOB aided cytohistological techniques.**

| Technique | Specificity |
|-----------|-------------|
| BAL       | 50          |
| TBNA      | 59.4        |
| FB        | 94          |

**Table 8: Efficacy of various cytohistological techniques alone and in combination, (n=93).**

| Technique   | Diagnostic | Percent of diagnosed cases, (n=93) (%) | Percent of total cases, (%) |
|-------------|------------|----------------------------------------|-----------------------------|
| BAL         | 3          | 3.2                                    | 3                           |
| TBNA        | 21         | 22.6                                   | 21                          |
| FB          | 23         | 24.7                                   | 23                          |
| BAL+TBNA    | 3          | 3.2                                    | 3                           |
| BAL+FB      | 3          | 3.2                                    | 3                           |
| TBNA+FB     | 25         | 26.9                                   | 25                          |
| BAL+TBNA+FB | 15         | 16.1                                   | 15                          |

## DISCUSSION

Diseases of lung are common and are important cause of morbidity and mortality world-wide. Primary respiratory infections, such as bronchitis and pneumonias etc. are common. In India, both neoplastic and non neoplastic chronic lung diseases are increasing in both adults and paediatric population.<sup>2,3</sup>

Various clinical, laboratory and radiological techniques are employed to arrive at a diagnosis in pulmonary diseases. Fiberoptic bronchoscope permits to visualise the bronchi directly and to obtain various pathological samples including for tissue diagnosis. Various fiberoptic bronchoscope assisted cytohistological techniques include bronchial aspiration, washings, BAL, bronchial brushings, TBNA, FB etc., but the data available in literature is variable regarding efficacy of various FOB assisted cytohistological techniques.

In the present study mean age was 54.3 years, male to female ratio was 7.3:1. out of 100 cases 79 patients came from rural settings and 21 patients were from urban dwellings. The difference of pulmonary disease among rural and urban population cannot be considered significant if we take into consideration the fact that 80% of population of India lives in rural areas.

Maximum number of patients presented with cough followed by dysnoea, chest pain, fever and hemoptysis. Other studies have reported similar presenting symptoms. Association with smoking was seen in 93.5% cases of squamous cell carcinoma, 75% cases of adenocarcinoma and 100% in small cell carcinoma, large cell carcinoma, carcinoma unclassified, lymphoma and metastatic carcinoma. The association of smoking between benign and malignant lesion was not statistically significant, it reflects overall increased incidence of respiratory disorders in smokers. Carcinoma of lung and chronic obstructive pulmonary disease (COPD) are most important smoking associated respiratory diseases.

FOB findings include endobronchial mass, abnormal mucosa, nodular growth, ill-defined growth and fungal ball. Endobronchial mass was seen in 67cases, abnormal mucosa in 20 cases, nodular growth in 5 cases, ill defined growth in 2 cases and fungal ball in 1 case while in 5 cases no endobronchial lesion was identified. Reichenberger et al observed in their study that out of 172 patients analysed by bronchoscopy, 73.6% were having malignant lesions and 26.4% were having benign lesions.<sup>7</sup> Chechani in his study shown mass, growth with sharp and fuzzy borders as findings on bronchoscopy.<sup>8</sup> Garg et al revealed that most common FOB finding as mass in 46.7% cases, followed by bleeding to touch in 25%, narrowing in 20% and increased secretions in 6.7% cases.<sup>9</sup> According to literature, there was operator based differences in naming the lesions seen on bronchoscopy but a mass lesion was commonest amongst neoplastic lesions.

Samples were adequate in 93 cases and inadequate in 7 cases. Rate of inadequacy of samples using FOB has been reported to be 2.55-11.2%. Amorim et al pointed in their study that no diagnosis was possible inspite of all techniques used in some cases though exact number of patients and nature of inadequacy not mentioned.<sup>10</sup>

Amongst malignant lesions, squamous cell carcinoma (31) was the most frequent diagnosis, followed by carcinoma unclassified (17), small cell carcinoma (13), adenocarcinoma (8) and non small cell carcinoma (7), large cell carcinoma (1), metastatic carcinoma (1) and lymphoma (1). Similar trends have been reported in many other studies.<sup>9,11,12</sup>

In our study BAL showed a sensitivity of 24% with 50% specificity, TBNA 64% sensitivity and 59.4% specificity and FB 66% sensitivity and 94% specificity. Combined sensitivity of all the 3 procedures was 93%. Comparison of diagnostic yield with different techniques as reported by various authors are as follow:

**Table 9: Comparison studies.**

| Authors                       | BAL    | TBNA  | FB     | All combined |
|-------------------------------|--------|-------|--------|--------------|
| Jay <sup>13</sup>             | 63%    |       |        | 87%          |
| Schenk et al <sup>14</sup>    | 29%    | 45%   | 56%    | 64%          |
| Buirski et al <sup>15</sup>   |        | 80%   | 67%    | 92%          |
| Xing <sup>16</sup>            |        | 70.9% | 69%    | 93.6%        |
| Chechani <sup>8</sup>         | 35%    | 51%   | 57%    |              |
| Govert et al <sup>17</sup>    | 63.2 % | 82.5% | 73.7 % | 95%          |
| Gupta et al <sup>5</sup>      | 27%    | 85%   | 60%    | 96%          |
| Karahalli et al <sup>18</sup> | 31.6 % |       | 68.6 % |              |
| Present study                 | 24%    | 71.4% | 70.2 % | 93%          |

In present study cytological methods (BAL and TBNA) gave more diagnostic yield than FB in peripheral lesions while FB was most sensitive in centrally located lesions. There specificities not significantly changed by location of tumour. Similar results have been reported by few reports available in literature.

After analysis of the results of our study alone and comparison with results of other studies by various authors it can be concluded that although there are variable results regarding diagnostic yields and utilities of various fibre-optic bronchoscope aided cytohistological techniques but there combination adds the yields and specially addition of TBNA to conventional diagnostic technique like BAL and FB can increase the diagnostic yield more than 90% and is even closer to 100%. Thus, a combination of various cytohistological samples should be taken in a patient undergoing fiberoptic bronchoscopic

examination to increase the diagnostic yield, to cut short the diagnostic time and early start of treatment.

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