Diagnostic Efficacy of Bronchial Brush and Bronchoalveolar Lavage Cytology in Bronchopulmonary Lesions

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Abstract

Context: Cytopathological assessment of bronchoscopy specimens plays a crucial role in the diagnosis of bronchopulmonary lesions. *Aim:* Our study was aimed to assess the diagnostic efficacy of cytological techniques in bronchopulmonary lesions in correlation with histopathological examination findings. *Settings and Design:* Correlative study. *Methods and Material:* 250 patients with symptoms and signs of pulmonary lesions were selected for the study and bronchoscopy was performed. Specimens from bronchial brush followed by bronchio-alveolar lavage were collected and routinely stained with Papanicolaou, Hematoxylin & eosin and Giemsa stains and studied. Special stains like Per-iodic acid Schiff and Ziehl-Neelson were performed as per requirement. Endobronchial biopsy specimens were processed as per routine histopathological techniques and stained. *Statistical analysis used:* Sensitivity, Specificity, Positive Predictive value, Negative Predictive value and Diagnostic Accuracy. *Results:* The age of the patients ranged from 20 to 87 years. The male to female ratio was 3.2:1. Out of 250 cases, neoplastic lesions were seen in 48 cases and non-neoplastic lesions were observed in 202 cases. Bronchoalveolar lavage cytology showed 36 true positive cases and 202 true negative cases, Bronchial brushing cytology showed 46 true positive cases and 202 true negative cases as confirmed by Bronchial biopsy. *Conclusion:* Diagnostic efficacy levels of cytological techniques in pulmonary lesions have acquired sensitivity levels high enough to be recommended for use as routine and definitive diagnostic tools in the evaluation of bronchopulmonary lesions.

Keywords: Bronchoscopy; Endobronchial Biopsy; Cytopathological Assessment; Sensitivity; Specificity.

Introduction

Bronchopulmonary lesions are the major causes for morbidity and mortality affecting larger population worldwide. In developing countries like India, Tuberculosis and Bronchogenic carcinoma are the leading causes of death. Hence, early diagnosis of both these lesions are mandatory for successful treatment [1].

Development of flexible fibre-optic bronchoscopy has literally revolutionized pulmonary cytology just as diagnostic techniques like Bronchoalveolar Lavage (BAL) cytology, Bronchial Brushings (BB) and Bronchial biopsy became popular and easily accessible, thus shifting the emphasis from diagnosis of advanced malignancy to the increased use of cytological techniques as the first line diagnostic and management tools [2].

The application of cytological techniques in the diagnosis of malignant bronchopulmonary lesions has been routinely accepted as one of its most successful implementations [3]. In the current scenario, the cytological techniques are established, identified and acknowledged as vital diagnostic procedures in the evaluation of pulmonary lesions. They are widely acclaimed as safe, economical and rapid diagnostic methods in the evaluation of lung lesions.

A long standing goal of researchers has been, to develop techniques that would facilitate early diagnosis and treatment especially in malignant lung lesions, since the only hope of combating them successfully depends on diagnosis at the earliest

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possible stage, preferably before the lesion has reached the stage of a visible and palpable tumour [4].

Bronchoalveolar Lavage (BAL) was originally developed as a therapeutic tool for pulmonary conditions like pulmonary alveolar proteinosis, cystic fibrosis and intractable bronchial asthma. But in the current scenario, it has gained acceptance and steady popularity as a very useful tool in the diagnosis of pulmonary lesions [3].

Bronchial brushing (BB) is a technique wherein, the surface of a suspected lesion which is visualized through a bronchoscope is scraped for cytological study.

The present study was undertaken with an aim to study and compare the efficacy of these two very popular cytological techniques in diagnosing pulmonary lesions by correlating them with the histological diagnosis by bronchial biopsy.

Materials and Methods

This study was conducted in the department of pathology, DM Wayand Institute of medical sciences, Meppadi, Wayanad, Kerala during the period from May 2015 to April 2017.

The BAL, BB and Bronchial biopsy specimens were received at the department of pathology. The clinical, radiological and bronchoscopic data were recorded. Only the cases where BAL, BB and bronchial biopsy specimens were all available simultaneously were taken up for the study. Cases with improperly preserved specimens having disturbed cellular morphological details, inadequate material and those cases without proper clinical history, provisional diagnosis and radiological findings were excluded from the study. 250 cases which fulfilled all these criteria constituted the material for this study.

The BAL fluid received in the department within half an hour of the procedure was immediately centrifuged at 1500 revolutions per minute. A minimum of four slides were prepared from the sediment out of which, two were fixed in absolute alcohol for half an hour and two were air- dried. One of the alcohol- fixed slides was stained with Hematoxylin & Eosin (H&E) stain and the other slide was stained with Papanicolaou stain. The two air-dried smears were stained with Giemsa and Zeihl-Neelson stains. All the slides were thoroughly screened under the light microscope by the cytopathologist and the diagnosis formulated.

The BB samples were received as air-dried and wet-fixed smears from two or three brushings and smeared directly onto clean glass slides. The air-dried smears were stained with Giemsa and wet-fixed smears were stained with Papanicolaou and H&E stains. All the BB slides were thoroughly screened and studied by the cytopathologist. The Bronchial biopsy specimens were processed in the automatic tissue processor and paraffin blocks were prepared. From each block, 2-3 micron thick sections were prepared by using a rotary microtome. The slides were stained with H&E stain and thoroughly studied by the histopathologist.

Results

Out of the total 250 cases taken up for the study, 191 were male and 59 female patients. The male: female ratio being 3.2:1, showed a strong male predominance. The patient's age ranged from 20 to 87 years. Malignancy was diagnosed in 48 cases and the remaining 202 cases were non-neoplastic bronchopulmonary lesions which included tuberculosis, fungal and non-specific inflammatory lesions and with no significant pathology. Among the inflammatory lesions, Tuberculosis was observed in 36 cases contributing to the highest number of specific inflammatory conditions diagnosed in this study by BAL cytology. One case of fungal infection diagnosed on BAL cytology was found to be Cryptococcus neoformans (Table 1) (Figure 1&2).

Nineteen (52.78%) of the 36 malignant cases diagnosed by BAL cytology could be morphologically subtyped. Thirty five (76.09%) of the 46 malignant cases diagnosed by BB cytology could be specifically subtyped and the remaining 11 (33.01%) cases could be only broadly classified as Small cell and Non-small cell carcinomas. Whereas, all the 48 malignancies diagnosed on Bronchial biopsy could be specifically subtyped as Adenocarcinoma (Figure 3, 4 & 5) Squamous cell carcinoma (Figure 6 & 7), and Small cell carcinoma (Figure 8 & 9).

BAL cytology showed 36 true positive cases and 202 true negative cases as confirmed by biopsy. BB cytology showed 46 true positive cases and 202 true negative cases. 12 cases were diagnosed as false positive by BAL cytology whereas BB cytology showed 2 false negative cases (Table 1).

BB cytology showed a better sensitivity of 95.83% (85. 75 to 99.49%) when compared to BAL cytology which showed a sensitivity of 75% (60.40 to 86.36%). Both BAL cytology and BB cytology showed 100% (98.19 to 100) specificity (Table 2).

Diagnostic accuracy of BB cytology was 97.9%, while that of BAL cytology was 87.5% (Graph 2).

**Table 1**: Distribution of Pulmonary lesions as confirmed on bronchial biopsy

	Lesions	BAL Cytology	BB cytology	Bronchial biopsy
1	Non-Specific Inflammation	162	151	149
2	Tuberculosis	36	36	36
3	Fungal	01	01	01
4	Malignancy	36	46	48
5	No Specific Pathology	15	16	16
	Total cases	250	250	250

Table 2: Comparative Statistical indices of BAL cytology and BB cytology

	BAL cytology	BB cytology
Sensitivity	75% (60.40 to 86.36)*	95.83% (85.75 to 99.49)*
Specificity	100% (98.19 to 100)*	100% (98.19 to 100)*
PPV	100%	100%
NPV	94.39% (91.16 to 96.49)*	99.02% (96.3 to 99.75)*
Diagnostic Accuracy	87.5%	97.9%

* 95% confidence interval
Abbreviations: [PPV = Positive Predictive Value, NPV = Negative Predictive Value]
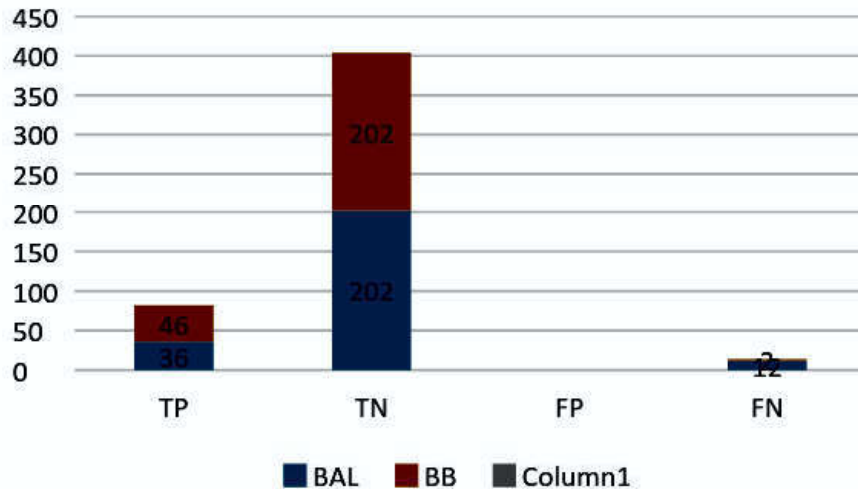
Abbreviations: [TP = True positive, TN = True negative, FP = False positive, FN = False negative]

Graph 1: Comparative Analysis of Bronchial washings and Bronchial brushing cytology results
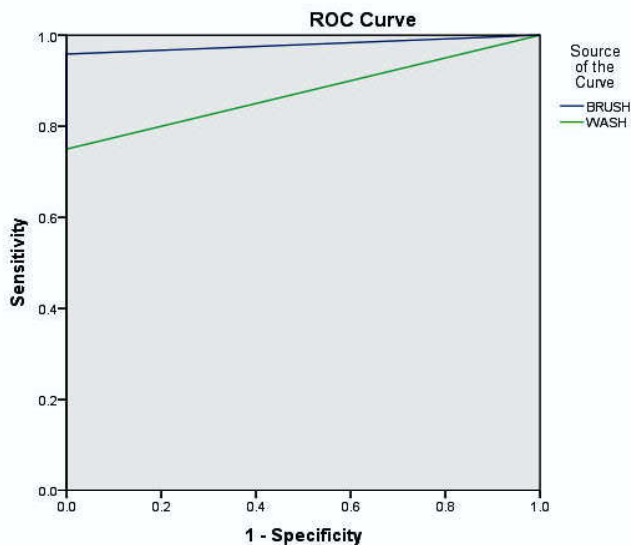
Abbreviations: [ROC = Receiver Operating Characteristic curve]

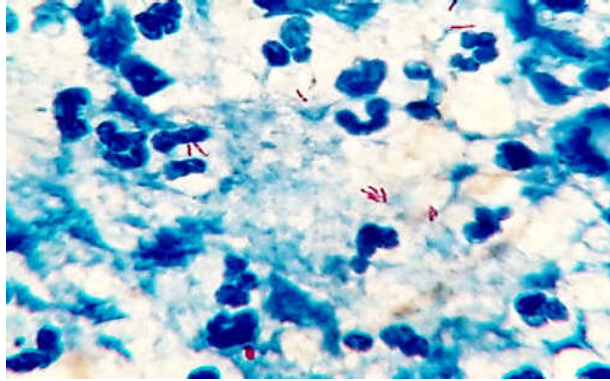**Graph 2**: Comparison of Diagnostic accuracy between BAL cytology and BB Cytology

Fig. 1: Photomicrograph of BAL cytology smear showing Acid Fast Bacilli (ZN Stain, X100)
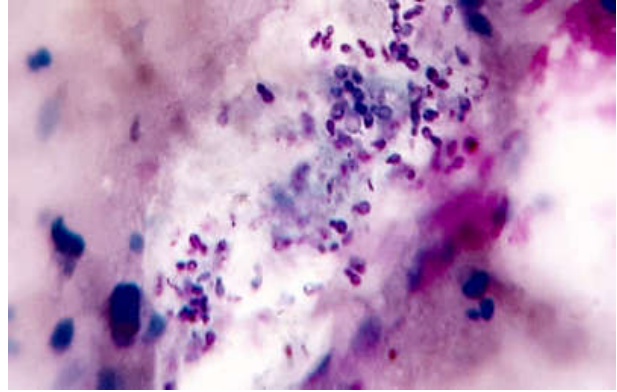

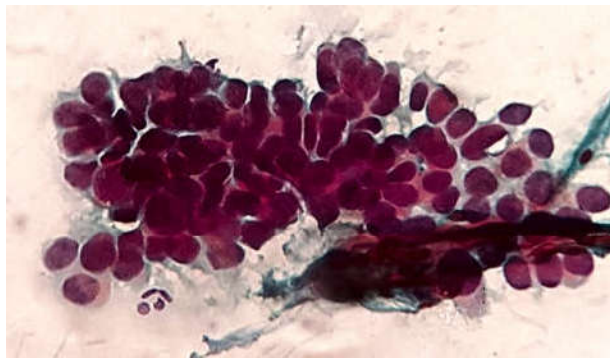**Fig. 2**: Photomicrograph of BAL cytology smear showing Cryptococcus neoformans (H&E, X40)
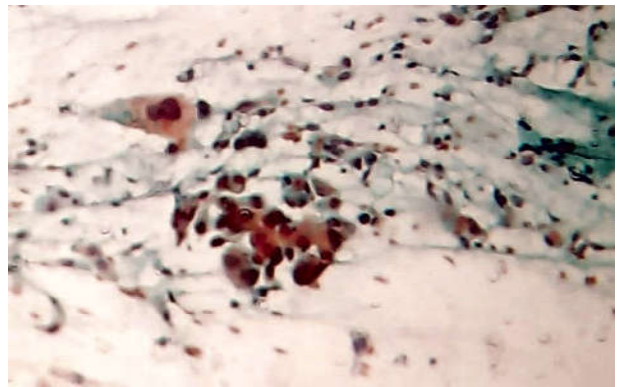

Fig. 3A:

Fig. 4A:

Fig. 3B:

Fig. 4B:

Fig. 4: Photomicrographs from a case of squamous cell carcinoma: **(A)**-[BAL cytology, PAP X40], **(B)**-[Bronchial biopsy, H&E X10]
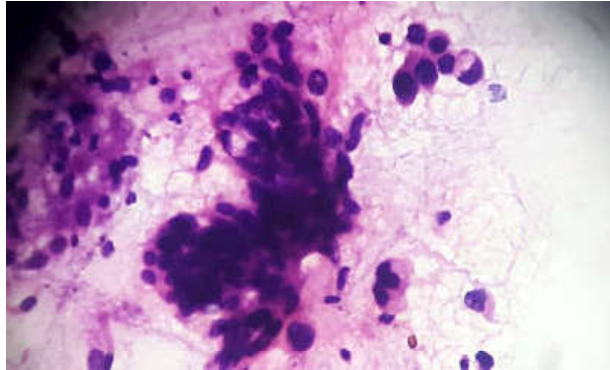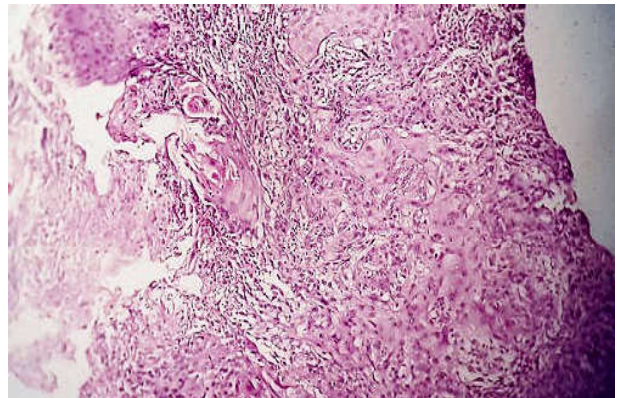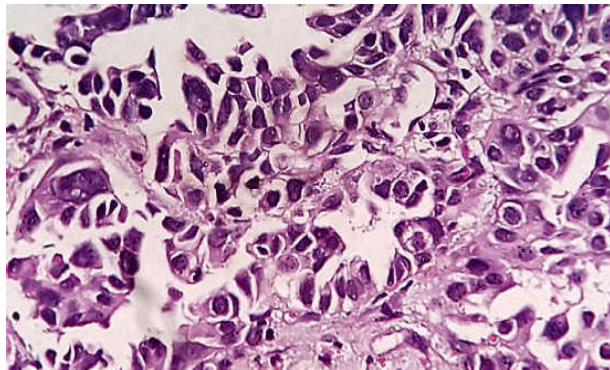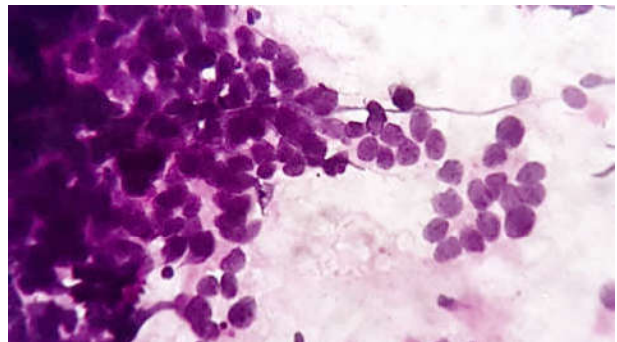

Fig. 3C:

Fig. 3: Photomicrographs from a case of moderately differentiated adenocarcinoma **(A)**-]BAL cytology, PAP X40], **(B)**-[BB cytology, H&E X10], **(C)**-[Bronchial biopsy, H&E X40]
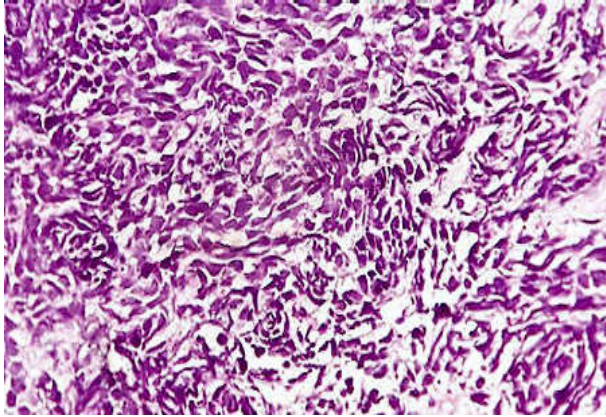

Fig. 5A:

Fig. 5B:

Fig. 5: Photomicrographs from a case of small cell carcinoma: **(A)**-[BAL cytology, H&E X40], **(B)**-[Bronchial biopsy, H&E X10]

Discussion

A variety of diagnostic modalities are available for the early diagnosis of bronchopulmonary lesions at the present time. Bronchoscopy and guided techniques have a commendable role in the diagnosis of endobronchial lesions ever since the combination of BAL cytology, BB cytology and Bronchial biopsy had come into vogue [5].

A lot of variations were observed from center to center, since most of these techniques and their interpretation depend on the expertise of the concerned speciality. It may be hard for a center to excel in all the three techniques and their interpretation [6]. It may not be practical and feasible to perform all the techniques in every patient and hence the quest for the single best and reliable technique will go on.

BAL cytology is a valuable diagnostic and research tool in bronchopulmonary lesions [7]. Yamamoto et al reported in their comparative study of BAL cytology and open lung biopsy that, BAL cytology played an almost equal role [8].

A number of studies have tried out different permutations and combinations of diagnostic techniques in order to improve the diagnostic accuracy. In the present study, though the overall diagnostic accuracy rate of BAL cytology was not as high as BB cytology, we observed that BAL cytology was extremely helpful in the diagnosis of the specific inflammatory conditions like tuberculosis and the fungal infection like Cryptococcus neoformans, (Figure 1 & 2). Besides this, BAL cytology was found to be useful in diagnosis of two cases of lung cancers which was not demonstrable in bronchial brushings. This upholds the fact that, the combination of

diagnostic techniques wherever feasible will surely yield better diagnostic accuracy.

Our study have no false positivity in malignancies on BAL cytology, which is in concurrence with the findings by Linder J et al suggesting that the rarity of false positivity is the actual strength of BAL cytology [9]. False negative cases on BAL cytology in our study was 12. The reasons attributable could be superadded inflammation and poor cellular morphology or hypocellularity. Similarly Wongsurakiat et al reported a very high rate of false negativity in BAL cytology [10].

Poletti V et al reported their experience with BAL cytology and its value in the diagnosis of malignant lung infiltrates which detected malignancy in 76% of their subjects [11]. This is in discordance with our study which showed very high false negativity rate in BAL cytology.

BB technique has an added advantage as the surface of the suspicious lesion is scraped with the help of a brush passed through a bronchoscope [3]. Thus, this technique manages to dislodge the cells from the surface of the lesions. Thus, the chance of getting adequate diagnostic cytological sample by BB greatly increases in comparison with BAL sampling. The cells freshly retrieved by BB show better morphological details in contrast to the exfoliated cells in the bronchial cavity which might be old and degenerated when retrieved by BAL. All these factors contribute to the increased diagnostic yield of BB samplings as observed in our study.

In the present study, it was observed that, the morphological subtyping of malignancies were possible on brushings but not on BAL samplings. BB cytology was useful in specifically subtyping malignancies in majority of the cases. Whenever definitive subtyping was not possible, we diagnosed the malignancies under two broad categories as Small cell and Non-small cell carcinomas which was found useful and adequate in the management of these cases. However, Bronchial biopsy was the best method for definite morphological subtyping of malignancies

In our study, the statistical indices including sensitivity, specificity and overall diagnostic accuracy rates of BB cytology were 95.83%, 100% & 97.9% respectively which were far superior to those of BAL cytology (Table 3). This is in concordance with the other studies by Chopra SK et al [12] and Jay SJ et al [13]. With a better sensitivity, specificity and diagnostic accuracy rate BB cytology promises to be a more convenient and reliable diagnostic tool for all the bronchopulmonary lesions.

Diagnostic accuracy of BAL cytology and BB

cytology can be estimated by measuring the area under Receiver Operating Characteristic curve (ROC). ROC graph is constructed by plotting the data (1- specificity) on the X-axis and sensitivity values on Y-axis. The Area Under the Curve (AUC) indicates the diagnostic accuracy, it can range from values 0 to 1. A value of 0.9 to 1 indicates excellent diagnostic accuracy, value 0.8 to 0.9 indicates good diagnostic accuracy and a value of 0.7 to 0.8 shows good diagnostic accuracy [14]. In our study, BB cytology showed a value of 0.979 indicating excellent diagnostic accuracy rate when compared to very good accuracy rate (0.875) of BAL cytology.

Govert JA et al combined the two techniques of BAL & BB cytology in order to improve the overall yield of diagnostic material [15]. However, the combination has not gained much popularity, since the cost of the procedures hikes up for the patient in exchange for very little improvement in the sensitivity. But in our study, BAL cytology was especially useful in diagnosing specific inflammatory conditions like Tuberculosis and Cryptococcosis and two cases of malignancies which were not demonstrable on BB cytology. We recommend that, since BAL and BB cytology are complimentary to each other, the combination if affordable to the patient offers the most accurate diagnostic results.

Conclusion

We conclude that, BB cytology has a better diagnostic accuracy as compared to BAL cytology. However, the combination of these two techniques improve the overall diagnostic accuracy and contribute towards more effective and appropriate management of patients with bronchopulmonary lesions.

Acknowledgement

Conflict of Interest: No

Key Messages

Bronchoalveolar lavage cytology is highly sensitive in detecting Tuberculosis and fungal lesions.

Diagnostic accuracy of Bronchial brush is far superior to Bronchoalveolar lavage cytology. Bronchial brush cytology is extremely efficacious in classifying malignant pulmonary lesions.

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