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Original Research Article

Diagnostic efficacy of bronchoalveolar lavage (BAL) in lung malignancies

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ABSTRACT

Background: Lung malignancies are the leading cause of cancer related deaths in men and in women it has surpassed even breast cancer. With the development of flexible fiber-optic bronchoscope, respiratory cytology has newer approach as samples like bronchial washings, bronchial brushings, bronchoalveolar lavage and trans-bronchial needle aspirations could be collected from the respiratory tract, yielding significant amount of cytological material.
Methods: A prospective study conducted in department of pathology in MGM Medical College and Hospital, Aurangabad during a period from November 2015 to October 2017. 48samples of bronchoalveolar lavage received and patient data collected.
Results: About 48 cases included in the study comprised of 23 (47.92%) malignancies, 16 (33.34%) DLDs and 9 (18%) cases of tuberculosis. In our study, 23 cases of malignancy included 15 male and 8 female patients (male:female ratio= 1.87). Mean age for malignancy was 57.57 years with median age of 60 years. Among 23 cases of malignancies 11 were given as positive/suspicious/atypical cells on BAL, whereas 10 out of 11 bronchial brushing were given as positive/suspicious or suggestive of malignancy.
Conclusions: Bronchoalveolar lavage is useful procedure. Efficacy of BAL is increased when used in combination with bronchial brushing.

Keywords: Bronchoalveolar lavage, Bronchial brushing, Malignancies, Lung

INTRODUCTION

Broncho-alveolar lavage (BAL) is the saline lavage of a portion of lower respiratory tract which explores large areas of the alveolar compartment providing cellular as well as non-cellular constituents from the lower respiratory tract.[1]

Bronchial irrigation with saline solution via a catheter passed through a rigid bronchoscope was first reported in 1927, and the term "bronchial lavage" was coined by Stitt in 1932.[2] Now it has been established as a safe and well tolerated procedure as research tool as well as for diagnostic and therapeutic purposes.

BAL, which was originally developed as a therapeutic tool for pulmonary conditions like pulmonary alveolar proteinosis, cystic fibrosis and intractable asthma, also gained acceptance and steady popularity as a tool for diagnosing lung cancer and other inflammatory disorders.[3,4]

Lung malignancies are the leading cause of cancer related deaths in men and in women it has surpassed even breast cancer. The increase in number of the deaths related to lung malignancies are mainly because of detection in late stage. Early detection of disease plays an important role

in the management and long term survival of patients, and pulmonary cytology and histopathology are valuable tools in the diagnosis of lung malignancies.[5]

With the development of flexible fiber-optic bronchoscope, respiratory cytology has newer approach as samples like bronchial washings, bronchial brushings, bronchoalveolar lavage and trans-bronchial needle aspirations could be collected from the respiratory tract, yielding significant amount of cytological material.

Aim of this study was to assess the efficacy of cytology of broncho-alveolar lavage in neoplastic lesions and the correlation with clinico-radiological findings.

METHODS

This was a prospective study conducted in MGM Medical college and hospital, Aurangabad during a period of November 2015 to October 2017. Total of 48 of bronchoalveolar lavage samples were received and clinico-radiological findings of consecutive patients were collected. Bronchoalveolar lavage fluid (BALF) received was subjected to centrifugation at the speed of 250g for 10 minutes and five smears were prepared from the cell pellet obtained. Air dried smears were stained with Field's A and B and Giemsa stain of air dried smears; and alcohol fixed smears were stained with haematoxylin and eosin.

Results were correlated with bronchial brushing in 11 cases and histopathology of lung biopsy was considered as gold standard of diagnosis.

Exclusion criteria

A BAL fluid is regarded non-representative if it fulfills one of the following criteria[4]

- Volume <20ml,
- Total cell count <60.000cells/ml,
- Alveolar Macrophages <10cells/10hpf
- Presence of >1% squamous epithelial cells,
- Presence of >5% bronchial epithelial cells.

RESULTS

Our study of 48 bronchoalveolar lavage fluid cytology showed, 28 cases (58.33%) were males and 20 cases (41.67%) were females (Male:Female ratio = 1.4:1). The mean age was 52.02 years and median was 56 years. The age sex distribution is shown in Table 1.

The study revealed, 24 (50%) out of 48 lesions were of right lung, 16 (33.34%) of left lung and 8 (16.67%) were bilateral. The commonest site was right upper lobe. Radiographic findings of 48 cases included, lung mass, consolidation (opacity), fibrocavitatory lesion, solid cystic lesion, nodular opacities etc. Lung mass was seen in 21 (43.75%) cases followed by 19 (39.58%) cases of consolidation.

Table 1: Age and sex distribution of cases.

Age group (years)	Male	Female	Total Number of patients
< 20	1	1	2
21-30	4	3	7
31-40	1	2	3
41-50	3	4	7
51-60	9	4	13
>60	10	6	16
Total	28	20	48

Table 2: Cytological impression of BALF in malignancies.

Impression on Cytology	No. of cases	Percentage
Positive for malignancy	2	8.70%
Suspicious of malignancy	7	30.43%
Atypical cells	2	8.70%
Negative for malignancy	12	52.17%

About 48 cases included in the study comprised of 23 (47.92%) malignancies, 16 (33.34%) diffuse lung disease (DLDs) and 9 (18%) cases of tuberculosis. In our study, 23 cases of malignancy included 15 male and 8 female patients (male:female ratio= 1.87). Mean age for malignancy was 57.57 years with median age of 60 years.

Amongst 23 cases of malignancies, 22 were primary tumors of lung and one case was of metastatic deposits from breast carcinoma. All the final diagnoses were confirmed on histopathology accompanied with immuno-histochemistry where ever required. Cytology of BALF in these 23 cases were reported as positive/suspicious/negative for malignancy and atypical cells only. The number of cases with respective impressions are shown in the Table 2. Bronchial brushing was received in eleven cases and the results were given depicted in Table 3.

Table 3: Cytological impression of bronchial brushing in malignancies.

Impression	Number of cases
Positive for malignancy	5
Suspicious for malignancy	4
Suggestive of malignancy	1
Negative for malignancy	1

Cytological findings of BALF and bronchial brushings were compared in these 11 cases. The comparative findings of these are shown in the Table 4.

Final diagnosis was based on histopathological findings supported with immuno-histochemistry in the cases

where it was necessary. Spectrum of the histopathological diagnoses included 22 cases of primary tumors and one case of metastatic deposits from carcinoma breast. The distribution of histological type of malignancies is shown in Table 5.

Table 4: Impression on bronchial brushing in malignancies.

Impression on BALF cytology	Positive	Suspicious	Suggestive	Negative	Total
Positive	1	0	0	0	1
Suspicious	3	2	0	0	5
Atypical cells	0	1	0	0	1
Negative	1	1	1	1	4
Total	5	4	1	1	11

Table 5: Spectrum of malignant lesions.

Histological type of malignancy	Male	Female	Total number of patients
Squamous cell carcinoma	13	2	15 (65.21%)
Adenocarcinoma	0	4	4 (17.40%)
Small cell carcinoma	2	1	3 (13.04%)
Metastatic deposits	0	1	1(4.34%)
Total	15	8	23

Table 6: Comparison of cytological findings of BALF with histopathological impression.

Histo-pathological diagnoses	Positive on BALF	Suspicious on BALF	Atypical Cells on BALF	Negative on BALF	Total
Squamous cell carcinoma	1	6	1	7	15
Adenocarcinoma	1	0	1	2	4
Small cell carcinoma	0	0	0	3	3
Metastatic deposits	0	1	0	0	1
Total	2 (8.69%)	7 (30.40%)	2 (8.69%)	12 (52.17%)	23

Comparison between the BALF cytology findings and histopathological diagnosis showed that 12 cases (52.17%) were falsely negative on BALF, distribution of lesions and BALF cytology findings is shown in Table 6.

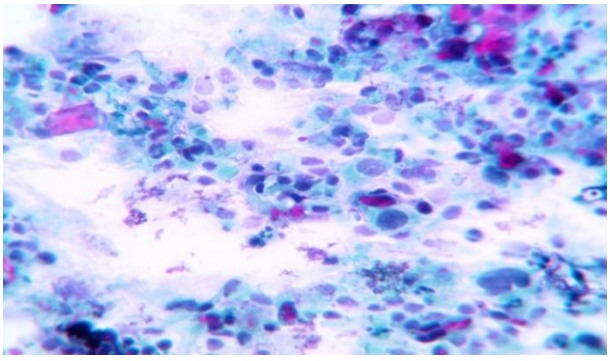

Figure 1: 40x; Giemsa stain: Photomicrograph of BAL cytology, positive for malignancy; non small cell carcinoma.

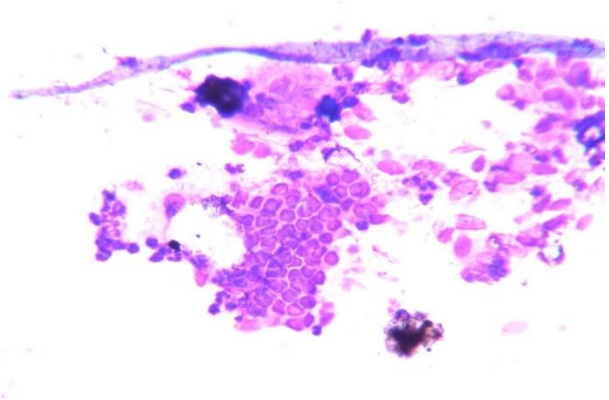

Figure 2: 40x; Haematoxylin and eosin stain; Photomicrograph of BAL cytology suspicious of malignancy.

Study showed a sensitivity of 47.83% and specificity of 100% and accuracy of 75%. Statistical analysis of data is shown in Table 7.

Table 7: Indices in BALF cytology in malignancies.

Parameters	Percentage
Sensitivity	47.83%
Specificity	100%
Positive predictive value	100%
Negative predictive value	37%
Accuracy	75%

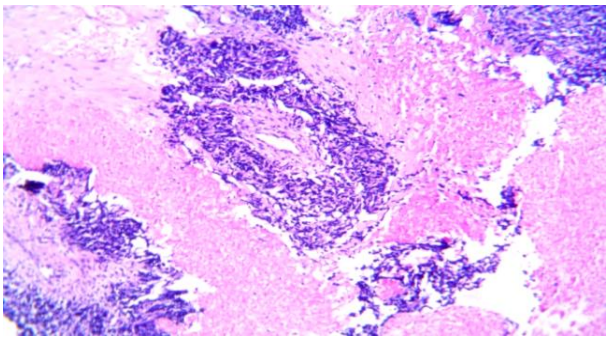

Figure 3: 10x; Haematoxylin and eosin stain: photomicrograph of lung mass biopsy showing small tumor cells and large areas of necrosis; Small cell carcinoma. (inset: 40x; haematoxylin and eosin stain).

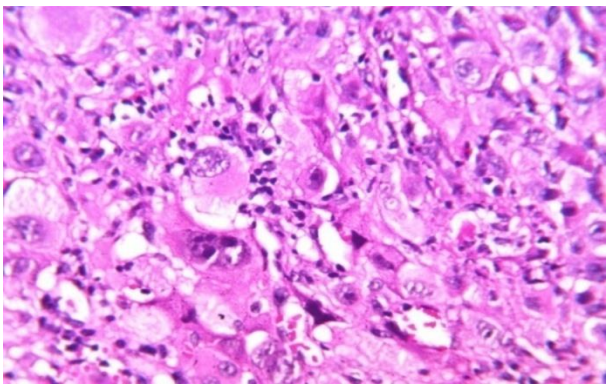

Figure 4: 40x; Haematoxylin and eosin stain: photomicrograph of lung mass biopsy showing large tumor cells with high N:C ratio and intracellular keratin arranged in sheets; squamous cell carcinoma.

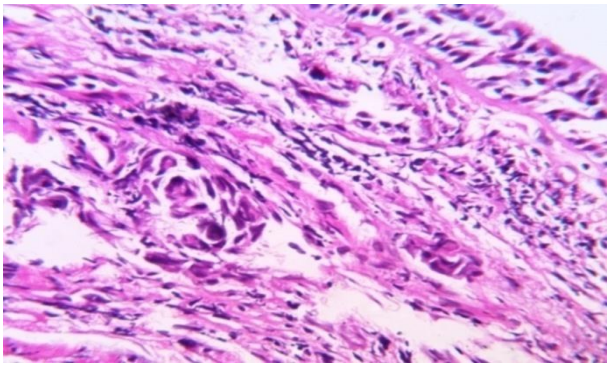

Figure 5: 40x; Haematoxylin and eosin stain: lung mass biopsy showing tumor cells in ill-formed gland pattern; adenocarcinoma of lung.

DISCUSSION

In our study, in patients of malignancy, slight male dominance was seen with male to female ratio of 1.29:1, which was very much lower compared to other studies by Reddy AS et al, (2.64:1), Bhat N et al (6.3:1), Sareen R et al (8.4:1).[10,5,8] The mean age of the malignancy, was 57.57 years with commonest age group of 5th decade which was consistent with other Indian studies. Cough and dyspnea were found to be the most common presenting complaints and mass and opacities were the most common radiographic findings in malignant cases of our study and the results were consistent with the findings by Sareen R et al.[8] The commonest site of malignancy was right upper lobe followed by left lower lobe which was consistent with the findings by Sareen R et al.[8]

Our study showed, squamous cell carcinoma (65.21%) as the commonest type of carcinoma of lung followed by adenocarcinoma (17.40%) of lung which were similar to the results by Kotadia TP et al.[9] Whereas studies by Reddy AS et al, showed adenocarcinomas the most common malignancy and Bhat N et al, showed small cell carcinoma as the second most common malignancy.[7,5] In our study, the sensitivity, specificity and accuracy of BAL samples were 47.83%, 100% and 75% respectively. Gaur DS et al, reported Sensitivity of 39.40%; while Sareen R et al, reported a sensitivity as high as 72.69% for BAL.[10,8]

Comparison of demographic factors, radiographic findings and spectrum of lesions, between various studies is shown in Table 8, 9 and 10, respectively.

In our study, bronchial brushing gave higher sensitivity of 90%. Since cytological yield by BAL technique relies mainly on cells 'exfoliated' in the bronchial epithelium from the malignant lesion, the adequacy of its samples depends on several important factors, especially:

- The degree of differentiation of malignant growth;
- Preservation of the morphology of cytological material obtained;
- Technical skill of the pulmonologist who is retrieving the lavage fluid from the bronchus.

In general, poorly differentiated, anaplastic lesions have more discohesive cells in to well differentiated lesions.[12] Thus, such lesions exfoliate larger number of cells into the bronchial cavity than the well differentiated lesions, therefore giving a better yield. Also, these exfoliated cells start developing degenerative changes while they are lying in the bronchus, thus losing their morphological details which are important in differentiating them from non-malignant cells shed off by the normal bronchial epithelial lining.[13,14]

All these factors, present individually or together, affect the overall yield and diagnostic value of BAL specimens

(Figure 6). Whereas, in bronchial brushing technique the surface of the suspicious lesion is scraped by the help of a brush passed in through the bronchoscope, therefore managing to 'dislodge' the cells from the surface of those well differentiated malignant lesions too, which do not exfoliate cells readily, therefore giving a better yield (Figure 7) than BAL and thereby giving less false negative. This technique not only manages to give better cellular yield, but, it also preserves the morphological details of cells better. Comparison of cytological characters of bronchial brushings and lavage showed that cellularity of the smear in brushings largely comprises of numerous columnar cells against a clear background whereas bronchial lavage samples tends to shed mostly single malignant cells with occasional cell clusters which were larger in brush than in lavage samples. All these factors contribute in the increased diagnostic yield of BB samplings.[10]

Table 8: Demographic factors in various studies in malignancies.

	Bhat N et al[5]	Reddy AS et al[7]	Sareen R et al[8]	Present study
Mean age (years)	58.62	-	57.6	57.57
Commonest age group	6th decade	5th decade	6th decade	5th decade
Male to female ratio (M:F ratio)	6.3:1	2.64:1	8.4:1	1.88:1
Laterality	-	Right- 56.6% Left- 43.3%	Right- 58.69% Left- 34.27% Bilateral -6.57% Lower end trachea- 0.47%	Right- 56.52% Left- 43.47%

Table 9: Radiological findings in various studies in malignancies.

	Sareen R et al[8]	Present study
Mass	80 (26.67%)	20 (86.96%)
Pleural effusion	60 (20%)	1 (4.35%)
Collapse	8 (2.67%)	
Opacity	38 (12.67%)	2 (8.70%)
Others	113 (37.99%)	-

In our study, the sensitivity, specificity and accuracy of BAL samples were 47.83%, 100% and 75% respectively (Table 8). Gaur DS et al, reported sensitivity of 39.40%; while Sareen R et al, reported a sensitivity as high as 72.69% for BAL.[10,8] Studies have shown that increasing the number of attempts at obtaining BAL sampling can improve its sensitivity, specificity and accuracy.[10,14] However, the inconvenience caused to the patient, in spite of BAL technique being noninvasive, outweighs the benefits of multiple samplings, especially when other techniques like bronchial brushing and bronchial biopsy are available.

In our study, the values of sensitivity and overall accuracy of BB were 90 % respectively, which were much superior to those of BAL (Table 11).

Table 10: Spectrum of malignant lesions on biopsy in various studies.

Studies	Squamous cell carcinoma	Adeno-carcinoma	Small cell carcinoma	Metastatic deposits	Others
Radke JR et al[11]	39.43%	28.17%	5.63%	2.81%	7.04%
Kotadia TP et al[9]	39.9%	21.21%	13.63%	-	16.65%
Bhat N et al[5]	68.55%	4.93%	23.02%	-	4.23%
Reddy AS et al[7]	31.02%	34.82%	6.91%	-	27.09%
Gaur DS et al[10]	29.6%	12.7%	21.13%	-	36.62%
Present study	65.21%	17.40%	13.04%	4.34%	-

Various studies have tried to combine the two techniques of BAL and BB, in order to improve the yield of diagnostic cytological material. Govert et al, reported 85.3% Sensitivity on combining these two techniques; while Bedrossian et al, reported a higher Sensitivity of 92%.[15,16] However, this combination has not gained much popularity since the cost of two cytological procedures are need to borne by the patient or laboratory for a little increase in sensitivity when compared to bronchial brushing alone.[16]

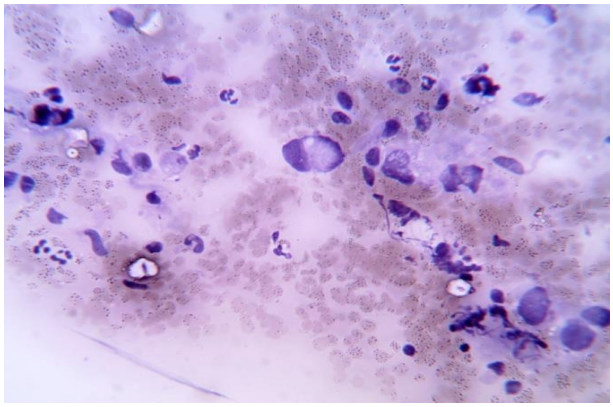

Figure 6: 100x; oil immersion; Papincolaou stain: bronchial brushing cytology showing cells pleomorphic cells with karyomegaly, positive for malignancy.

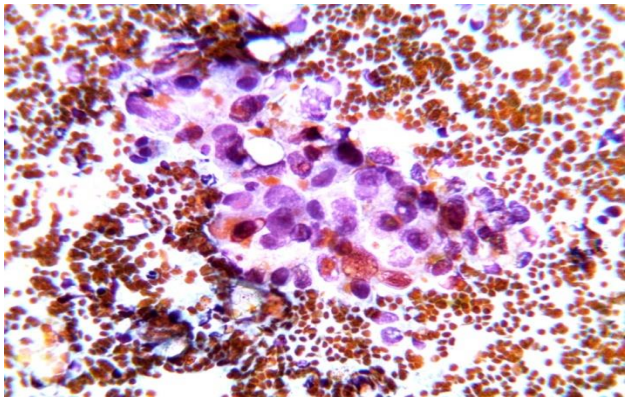

Figure 7: 100x; oil immersion; papincolaou stain: bronchial brushing cytology, positive for malignancy; non small cell carcinoma, suggestive of adenocarcinoma.

Table 11: Indices in BAL in various studies in malignancies.

	Sareen R et al[8]	Bhat N et al[5]	Gaur DS et al[10]	Present study
Sensitivity	72.69%	35.50%	39.40%	47.83%
Specificity	100.00%	78.16%	89.60%	100.00%
Positive predictive value	100.00%	89.70%	68.30%	100.00%
Negative predictive value	76.95%	18.46%	72.30%	37.00%
Accuracy	83.67%	43.23%	71.40%	75.00%

With a good sensitivity (87.3%) and accuracy (93.9%), bronchial brushing seems to be a more convenient cytological technique than BAL. It can be utilized for screening of doubtful cases and early diagnosis of lung cancer, since it saves the time needed for the processing of biopsy specimens. However, as BB lacks accuracy in morphological classification of lung cancers, only cases positive for malignancy may later be biopsied to confirm the morphological type of the malignant lesion. This study showed the maximum yield of 53.3% in squamous cell carcinoma and minimum in small cell carcinoma among primary tumors.

CONCLUSION

Malignancies showed low sensitivity for BAL due to relatively less cell retrieval and decreased cell viability in the bronchial pathway. As compared to BAL, bronchial brushing shows better sensitivity and specificity, even in cases of well differentiated carcinomas because of better cellular yield and better preservation of morphology.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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