Diagnostic Efficacy of Bronchoalveolar Lavage in a Rural Industrial Hospital in Madhya Pradesh, India

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ABSTRACT

BACKGROUND
The incidence of lung carcinomas is on rise and it is the second most common cause of death due to carcinomas in the West. Due to rise in air pollutants other lung diseases are also on rise. The use of cytological methods in the diagnosis of pathological lesions of respiratory tract has been generally acclaimed as one of its most successful application. Flexible fibre optic bronchoscope revolutionised respiratory cytology because techniques like broncho alveolar lavage, brush cytology, bronchial biopsy, and fine needle aspiration cytology (FNAC) have become easier and more acceptable, shifting the emphasis from advanced inoperable malignancy to use of cytology as first line diagnostic and management tool. Broncho alveolar lavage (BAL) which was originally developed as a therapeutic tool for pulmonary alveolar proteinosis, cystic fibrosis and intractable asthma also has gained acceptance and steady popularity as a tool for diagnosis of lung pathology. We wanted to analyse BAL examined in the Department of Pathology, Nehru Shatabdi Chikitsalaya (NSC), NCL and establish its utility as a diagnostic tool in our setup and reduce referral to higher centres.

METHODS
36 BAL samples were examined from August 2006 to December 2007. Bronchoscopy was performed by ENT specialists among all patients who were not relieved by the medical treatment and their X-ray lung showed some findings, as an outdoor procedure. Patients were asked to come in an empty stomach, and X-ray chest was done before bronchoscopy. All bronchoscopies were performed under local anaesthesia (LA) except for a 2 yrs. old child. BAL fluid was subjected to cytological studies and Ziehl-Neelsen staining wherever required.

RESULTS
Out of 36 cases, nonspecific inflammation was seen in 13 cases, tuberculosis in 8 cases, where in three samples of sputum were negative for acid-fast bacillus (AFB) and BAL showed bacteria in many fields. Two cases were found to have aspergillosis, to rule out contamination, serum antibodies against aspergillosis were estimated which was very high ruling out contamination. Out of 8 cases of malignancy one was metastasis from mature teratoma testis. Two cases of adenocarcinoma (both females) and two cases of squamous cell carcinoma were found, in one case of adenocarcinoma and two cases of squamous cell carcinoma (SCC), BAL was found negative. No history was available regarding tobacco smoking in females with adenocarcinoma.

CONCLUSIONS
Study of BAL obtained by simple non-invasive technique has improved the diagnostic accuracy of lung diseases. Carcinomas can be diagnosed at an early operable stage. The combination of BAL with brush cytology increases the accuracy. To conclude, in all bronchoscopic examination BAL should be performed and should be subjected to microscopic examination irrespective of the age of patient.

KEY WORDS
Fiberoptic Bronchoscope, Lung, BAL, Tuberculosis, Adenocarcinoma Lung, SCC Lung
BACKGROUND

Lung malignancies are one of the leading causes of cancer related deaths in men and women. Bronchial irrigation with saline solution via a catheter passed through a rigid bronchoscope was first reported in 1927 and the term bronchial lavage was given by Stitt in 1932.1 The use of cytological methods in the diagnosis of pathological lesions of respiratory tract has been generally acclaimed as a safe, well tolerated one and most successful application. BAL which was originally developed as a therapeutic tool for pulmonary alveolar proteinosis, cystic fibrosis and intractable asthma, it also gained acceptance and steady popularity as a tool for diagnosis of lung pathology inflammatory as well as malignancy. Flexible fibre optic bronchoscope revolutionised respiratory cytology because techniques like Broncho alveolar lavage, brush cytology, bronchial biopsy and fine needle aspiration cytology have become easier and more acceptable, shifting the emphasis from advanced inoperable malignancy to use of cytology as first line diagnostic and management tool.

Lung is the organ which is always in contact with surrounding atmosphere and its contaminants. We breathe litres of air and there are chances that some organism may start growing in it and is more liable in coal mines workers. Due to limitation of x-rays, many of pathological lesions cannot be seen on plain chest x-rays. Moreover, in many cases inflammatory and neoplastic pathology cannot be differentiated.

We wanted to analyse BAL examined in the Department of Pathology, Nehru Shatabdi Chikitsalaya (NSC), NCL and establish its utility as a diagnostic tool in our setup and reduce referral to higher centres.

METHODS

This is a retrospective study done in a 300-bed secondary care hospital developed for the treatment of coal field’s workers and surrounding population, situated in a small town of Madhya Pradesh, Singrauli. All cases were followed up properly. The nearest town with facilities of computed tomography (CT) and magnetic resonance imaging (MRI) was situated approx. 300 Kms.

36 BAL samples were examined from August 2006 to December 2007. Sample size was taken based on the convenience of the study. Bronchoscopy was performed by ENT specialists as an outdoor procedure, in all patients who were not relieved by medical treatment or X-ray lung showed some findings. Patients were asked to come in an empty stomach, X-ray chest was done before bronchoscopy. All bronchoscopies were performed under LA except in one 2 yr. old child. 10 % lignocaine was sprayed in throat.

Xylocaine jelly was applied in the nostril and at the top of bronchoscope. At the level of vocal cord 2 % xylocaine was pushed through the working channel. Colour of mucosa, carina, mucosal rugosities, mobility of mucosa and any abnormal nodule or growth were the things observed. Lavage was performed from the affected lobe of the lung. For this fibre optic bronchoscope was fixed at the orifice of lobar or segmental bronchus.

20 ml of normal saline was pushed, waited for one minute, suction was performed, and fluid collected in the trap. The fluid was sent to the laboratory within half an hour along with a proforma containing details of clinical history provisional diagnosis and radiological findings of the patient. Fluid was immediately processed for examination. One part was centrifuged at slow speed (250 g) for 10 minutes for cytological study and another part was centrifuged at high speed (1500 RPM) for 5 minutes for microbiological examination. Slides were prepared. No any available material was wasted.

Slides for examination were alcohol fixed and air dried. The air-dried smears were stained with May-Grunwald Giemsa stain and Ziehl-Neelsen stain and alcohol fixed with PAP stain. Slides were then examined under microscope. All the cases were followed up, cases diagnosed as malignant lesions were referred to a tertiary care centre and cases diagnosed as inflammatory lesions were given specific treatment at our setup. The study was approved by ethics committee and informed consent was obtained.

Statistical Analysis

The Statistical Package for Social Science (SPSS) version 20 was used for data analysis. Mean, median, and standard deviation (SD) were used to describe quantitative data. Qualitative data were summarised using frequency and percentages.

RESULTS

In our study of 36 cases most of the cases were above 20 yrs. (78 %) and only 22 % (8 cases) were below 20 years as shown in Table 1. All samples were subjected to Ziehl-Neelsen stain along with May-Grunwald stain and PAP stain. It was observed that out of 36 cases, inflammatory pathology was the most common finding (23 cases). Nonspecific inflammation (13 cases), eight cases of tuberculosis were diagnosed on the basis of presence of AFB, though all of them were AFB negative in three consecutive samples of sputum. Tuberculosis was observed mostly above 20 yrs. (7 cases). Two cases of fungal pathology with mycelia of aspergillosis in BAL were found. All cases of tuberculosis and nonspecific inflammation were followed up and follow up X-ray chest showed resolution of pathology. In cases of fungal pathology to rule out contamination, serum antibodies were estimated by sending sample to a referral lab and in both cases antibody titre was very high which ruled out contamination. Table II

| Sl. No. | Age Group | No. of Cases |
|---------|------------|--------------|
| 1       | 0 - 5 yrs. | 1            |
| 2       | 5 -10 yrs. | 1            |
| 3       | 10 - 20 yrs | 6            |
| 4       | 20 - 40 yrs | 14           |
| 5       | 40 - 60 yrs | 7            |
| 6       | 60 yrs and above | 7       |

Table I. Age Wise Distribution of Cases

Both the cases of aspergillosis were above 60 yrs. and were immunocompromised. In malignancy group, only one young boy of 18 years was found positive for malignancy showing benign group of cells in adenomatous arrangement. He had four round opacities in Rt lung, because he was a young boy,
his testes were examined and on ultrasound 2 cm mass was
found in Rt testis, fine needle aspiration cytology (FNAC) of
which revealed non seminomatous germ cell tumour. The final
histological diagnosis was mature teratoma.

The cells of moderately or poorly differentiated tumours
show larger nuclei with coarse and granular chromatin texture
and cyanophilic cytoplasm (with Papanicolaou stains); they
are often arranged in thick groups. Keratinisation is rare or
absent.

Out of eight cases of squamous cell carcinoma two were
found false negative. As the patients were not improving with
medical treatment, they were referred to higher centre on
follow-up it was observed that our cytological diagnosis was
wrong. Table IV.

### DISCUSSION

Flexible fibre optic bronchoscopy has become very useful tool
in patient care and medical research since its introduction in
1968 by Ikeda et al. Proper selection of patient is necessary to
ensure effective and safe procedure. Role for flexible bronchoscope with collection of BAL and its study has
provided increased scope in research on respiratory tract
pathology.

The significant clinical presentations, and x-ray findings in
many cases of tuberculosis in our study with sputum negative
smears for AFB, though suggest that the signs and symptoms,
and radiographic findings are suggestive of pulmonary
tuberculosis, but cannot confirm the diagnosis of pulmonary
tuberculosis. Therefore, patients with radiographic and
clinical findings compatible with Pulmonary Tuberculosis (PTB)
but negative for sputum smear are a challenge to the
physician to start with Anti-tubercular treatment (ATT). It has
been reported that 74 % of these patients develop active
tuberculosis in five years if not treated. Flexible fibre optic
bronchoscopy is considered as a safe diagnostic and
interventional tool, even in young or extremely premature
infants. Caminero et al. concluded that bronchoscopy should
be conducted on all patients without expectoration and
negative sputum bacilloscopy and that BAL collection should
be a routine procedure as it was simple and usually
uncomplicated technique.

Wallace et al. as well as Kennedy et al and Vijayan et al. 586
have demonstrated lower yield whereas Baughman et al.
reported 87 % of bronchoscopy sample positivity in sputum
smear negative cases.5 A study by Mohan et al. confirmed
PTB in 22 of the 50 patients from BAL. BAL had significant
sensitivity and specificity in a study by Conde et al. and was
useful in diagnosis of PTB in 72 % cases.11 In our study, the
sensitivity was 34.7 % little lesser than the study by Mohan et
al and Conde et al. Small sample size of our study could be the
reason for it. Mustaq Ahmad et al. detected 61 / 190 (32.1 %)
cases of pulmonary tuberculosis who were sputum negative
which was lower than the findings of our study. Thus BAL is
considered best for diagnosis of TB.

In our study, malignant patients had slight male
dominance with male to female ratio of 1:6:1, which was very
much lower compared to other studies by Reddy AS et al.
(2:4:1), Bhat N et al. (6:3:1), Sareen R et al. (8:4:1), but was
little more in comparison to study of Shubhra T et al.16
(1:29:1). The mean age of the malignancy was 57.57 years with
commonest age group of 5th decade which was higher in our
study as we found most of the cases in 6th decade of life.

We found one case of metastatic carcinoma out of 13 cases
of malignancy. Shubhra et al. also found on case of metastatic

### Table II. Age Wise Distribution of Inflammatory Lesions

| Sl. No | Age Group | Non-specific Inflammation | Tuberculosis | Fungal |
|-------|-----------|---------------------------|--------------|--------|
| 1     | 0 - 5 yrs. | 1                         | 2            | 1      |
| 2     | 5 - 10 yrs. | 1                         | 2            | 1      |
| 3     | 10 - 20 yrs. | 2                         | 7            | 5      |
| 4     | 20 - 40 yrs. | 2                         | 1            | 1      |
| 5     | 40 - 60 yrs. | 1                         | 1            | 1      |
| 6     | 60 yrs. and above | 1                         | 3            | 2      |
| Total |           | 13                        | 08           | 02     |

### Table III. Age & Sex Wise Distribution of Malignant Lesions

| Sl. No | No. of Cases | Cytological Diagnosis | Histopathological Diagnosis |
|--------|--------------|-----------------------|----------------------------|
| 1      | 1            | Metastatic deposits of NSGCT | Mature teratoma with lung metastasis |
| 2      | 2            | Adenocarcinoma BAC | BAC |
| 3      | 4            | Normal cytology | BAC |
| 4      | 2            | Well differentiated squamous cell carcinoma | Well differentiated squamous cell carcinoma |
| 5      | 2            | Normal | Well differentiated squamous cell carcinoma |
| Total  | 13           |                  |                          |

All the other cases of malignancy were above 50 yrs. of age.
Out of thirteen cases of malignancy, females were less than
males, 5:8 cases, and were found to be having BAC at an early
age of 50 - 60 yrs. Squamous cell carcinoma (SCC) was found
in older age group of 65 yrs. and above. History of cigarette /
 bidi smoking was present in all cases of SCC. Table III

Smeared with clean background, 3-dimensional clusters, flat
sheets, papillae, orderly arrangement of cells with round
uniform nuclei, predominance of mucinous cells, overlapping
nuclei, irregular nuclear membranes, fine granular chromatin,
macro nuclei, intranuclear cytoplasmic inclusions, and
nuclear grooves were diagnosed as bronchoalveolar carcinoma.2
Out of four cases of bronchoalveolar carcinoma one was found false negative, may be because it was a case of
typical BAC which showed cytological features in dudging
background, absence of 3-dimensional clusters, neoplastic
cells in flat sheets, orderly arrangement of cells with round
uniform nuclei, absence of nuclear overlap, absence of
irregular nuclear membranes, fine granular chromatin, and
nuclear grooves.3

Smeared with an abundant granular debris, necrosis and
abundant dyscohesive cells, that may be polygonal, rounded or
elongated, dense cytoplasmic orgranellin in Papanicolaou
stain, pleomorphic hyperchromatic and often pyknotic nuclei,
obscured nucleoli and chromatin detail, Tadpole or fibre-like
cells, frequent anucleate cells twisted keratin strands
(Herzheimer spirals) were diagnosed as cases of squamous
cell carcinoma.

Tadpole or fibre-like cells are bizarre, elongated, spindle-
shaped cells which can often be seen.
cancer of the lung. Squamous cell carcinoma is the most common type of carcinoma of the lung followed by adenocarcinoma (17.40%) of lung which was similar to the results by Shubhra et al. and Kotadia TP et al. Whereas studies by Reddy AS et al. showed adenocarcinomas as the most common malignancy and Bhat N et al. showed small cell carcinoma as the second most common malignancy.

**Table V. Type of Malignant Lesions on Biopsy in Different Studies**

| Studies          | Squamous Cell Carcinoma | Adeno-Carcinoma | Small Cell Carcinoma | Metastatic Deposits | Others |
|------------------|-------------------------|-----------------|----------------------|---------------------|--------|
| Kotadia TP et al.| 39.43%                  | 21.21%          | 13.63%               | -                   | 16.65% |
| Reddy AS et al.  | 68.55%                  | 4.93%           | 23.02%               | -                   | 4.23%  |
| Shubhra et al.   | 31.02%                  | 8.82%           | 6.91%                | -                   | 27.09% |
| Present study    | 29.6%                   | 12.7%           | 21.13%               | 3%                  | 36.62% |

In our study, the sensitivity, was 76.9%. Shubhra et al. reported sensitivity of 47.8% and 39.40% respectively, while Sareen R et al. reported a sensitivity as high as 72.69% for BAL. Higher sensitivity in our study may be because we have not wasted any material and examined all slides thoroughly. Table VI.

**Table VI. Sensitivity of BAL in Various Studies of Malignancies**

| Studies          | Sensitivity |
|------------------|-------------|
| Sareen R et al.  | 72.69%      |
| Bhat N et al.    | 35.5%       |
| Gaur DS et al.   | 39.60%      |
| Shubhra et al.   | 47.03%      |
| Present Study    | 76.9%       |

**CONCLUSIONS**

Due to good yield of cytological material directly collected from respiratory tract by means of BAL or brush cytology, bronchial biopsy and trans bronchial FNA directly from the lesion, the examination of sputum for malignant cells became obsolete.

Cytological material is better obtained by brush cytology as in BAL exfoliated cells are collected. Exfoliation is poor in well differentiated carcinomas and more with poorly differentiated ones. The exfoliated cells start degeneration and we may get degenerated cells which makes it difficult to differentiate malignant cells from non-malignant cells.

For inflammatory lesions BAL is richer in causative organism and inflammatory cells. Therefore, study of BAL is very useful for inflammatory pathology as we can also subject the available material for bacterial or fungal culture as per requirement and can also be subjected to gene expert. Multidrug-resistant (MDR) tuberculosis with culture and sensitivity can be diagnosed.

For diagnosis of malignancies, if BAL brush cytology and FNAC is done it might increase the accuracy.

Study of BAL obtained by simple non-invasive technique has improved diagnostic accuracy of lung diseases. Sputum negative samples can be subjected to GeneXpert along with Zeil Neelsen stain and demonstration of AFB. Carcinomas can be diagnosed at an early operable stage.

In a secondary care hospital if we can rule out malignancy in a major group of cases, it decreases load on higher centres and also avoids inconvenience to patients as major group of patients will get treatment in their local hospital and only few patients require treatment at higher centre that too with proper diagnosis.

To conclude all bronchoscopic examination, BAL should be performed and should be subjected to microscopic examination irrespective of the age of patient.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

Disclosure forms provided by the authors are available with the full text of this article at jemds.com.

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