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Original Research Article

Role of bronchoalveolar lavage in the diagnosis of lung cancer

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ABSTRACT

Background: Early diagnosis of lung cancer plays a vital role in reducing the lung cancer death rate. Different modalities can be applied e.g. radiology, bronchoscopy, bronchoalveolar lavage (BAL), and fine needle aspiration cytology. Cytological diagnostic techniques are safer, economical, and provide quick results. The aim of the study was to find out diagnostic yields of bronchoalveolar lavage in diagnosing lung cancer, and to determine the sensitivity, and specificity of BAL fluid cytology considering the bronchial biopsy as the gold standard.
Methods: This cross-sectional study was carried out in the Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period from November 2018 to March 2020 with a total of 38 participants.
Results: 33 (86.84%) patients were male, and 5 (13.16%) were female; the mean age was 58.29±13.11 years. In clinical presentations, cough was present in all 100% of the patients, and some more frequent presentations were shortness of breath in 26 (68.4%), hemoptysis in 24 (63.15%), and chest pain in 21 (55.26%). Majority of the patients (78.95%) were smokers. Considering histopathological findings, maximum patients had squamous cell carcinoma 13 (38.23%), then adenocarcinoma 11 (32.35%), small cell carcinoma 5 (14.70%), large cell carcinoma 3 (8.82%), and poorly differentiated non-small cell carcinoma 2 (5.88%). The sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of BAL were 70.59%, 100%, 100%, 28.57%, and 73.68% respectively.
Conclusions: BAL fluid cytology is a useful tool for the diagnosis of lung cancer. It has good sensitivity, and specificity, and shows nearly identical information as biopsy.

Keywords: Bronchoalveolar, Cancer, Lesion, Lavage, BAL

INTRODUCTION

Lung cancer is a major health problem worldwide.[1] There have been over six million new cases of lung cancer which corresponds to 12.7% of the world's cancer incidence that was diagnosed in 2008.[2] It is the leading cause of death in developed countries, accounting for 17.8% of all cancer deaths, and is increasing at alarming rates in developing countries.[3] Lung cancer is more prevalent in the male population compared to the female population, but the difference is decreasing. It is the most common malignant neoplasm in the Asian Pacific area.[4] According to the hospital cancer registry of the National Institute of Cancer Research and Hospital, Dhaka, Bangladesh, the prevalence of lung cancer is 16.7% of all cancers, and it is the most common cancer (25%) among male cancer patients, with a 6.1: 1 male-female ratio.[5] Most of the people of Bangladesh do not even know they have lung cancer, and the majority of cases are diagnosed at late stages when a cure is impossible. The overall prognosis of lung cancer is

very poor, and the 5-year survival rate is only 6-8%. Therefore, the early diagnosis of lung cancer plays a vital role in reducing the lung cancer death rate but the diagnosis is costly in developing countries. This situation demands a cheap, and effective modality of investigation for the diagnosis of lung cancer. While the early stage of lung cancer is a potentially curable disease, it is often clinically silent, and therefore goes unrecognized. Even after patients recognize the presence of new or changing symptoms, there is often a substantial delay in seeking medical advice, and then an additional delay in making the correct diagnosis, and in referral to a cancer specialist.[6] Late detection is an important factor for high mortality rates related to lung cancer.[7] For the treatment of lung cancer in the best possible, and successful way, accurate diagnosis is the key. For the diagnosis, different modalities can be applied, e.g. radiology, fine needle aspiration cytology, bronchoscopy with bronchial washing, bronchoalveolar lavage (BAL), bronchial brushing, bronchial biopsy etc. In 1968 fiber-optic bronchoscopy was first used as a diagnostic procedure.[8] With the advent of flexible fiber-optic bronchoscopes, respiratory cytology has taken a new turn as samples like bronchial washings, broncho-alveolar lavage, and bronchial brushings could be collected from the respiratory tract, yielding a significant amount of cytological material. With this, the emphasis shifted from diagnosis of malignancy in operable patients and confirmation of metastases, to the use of cytology as a first-line diagnostic procedure on which management decisions could be based.[9] Flexible bronchoscopy with bronchial biopsy is one of the main methods used in the diagnosis of suspected central lung cancer.[10] In the case of peripheral pulmonary lesion which is inaccessible to bronchial biopsy, a histological diagnosis of malignancy is possible by fine-needle aspiration cytology which is also contraindicated if there is extensive coexisting emphysema.[11] BAL is a minimally invasive procedure and may be used for the diagnosis of both central, and peripheral lung cancers. The diagnostic yield of BAL is higher for central lung lesions.[12] The sensitivity of BAL for central, and peripheral lung cancer is 31 to 78%, and 12 to 65% respectively. It was originally developed as a therapeutic tool for pulmonary conditions like pulmonary alveolar proteinosis, cystic fibrosis, and intractable asthma, now it has gained acceptance, and steady popularity as a tool for diagnosing lung cancer.[9] Few studies have shown that a definitive diagnosis of lung cancer is possible by cytology alone.[13] Our aim was to see the role of bronchoalveolar lavage fluid cytology in the diagnosis of lung cancer by considering the histopathological diagnosis by bronchial biopsy as the gold standard.

Objectives

General objective

General objective was to determine the role of BAL fluid cytology in the diagnosis of lung cancer.

Specific objectives

To assess the morphological type of lung cancer by BAL, to see the morphological type of lung cancer by bronchial biopsy, and to calculate the role of BAL in the form of sensitivity, and specificity.

METHODS

This cross-sectional study was conducted at the Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh. The study duration was 15 months, starting from November 2018 to March 2020. Consecutive sampling was done to select a total of 120 participants who had undergone bronchoscopy at the initial screening. After following the inclusion, and exclusion criteria of the study, the final sample size was determined to be 38. All patients were informed about the purpose of the study, and written consent was obtained from the participants. Ethical approval was also obtained from the ethical review committee of the study hospital. A Structured questionnaire containing demography, clinical, and laboratory characteristics of the patients was used for data collection. After collecting the data, it was checked and rechecked for omission, inconsistencies, and improbabilities. Means and standard deviations (SD) were used to summarize continuous variables, while percentages were used for categorical variables. The role of BAL fluid cytology was expressed by sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy. Data analysis was performed by statistical package for social science (SPSS), version-25.

Inclusion criteria

All suspected lung cancer patients who had undergone a bronchial biopsy, and BAL, and patients who had given consent to participate in the study.

Exclusion criteria

Mentally ill patients who underwent only BAL, patients who underwent only bronchial biopsy, unable to answer the criteria question and those affected with other chronic diseases were excluded.

RESULTS

Figure 1 showed the sex distribution of the study patients, maximum patients (86.84%) were male, and 5 (13.16%) patients were female. Male: female ratio was 6.6:1.

Table 1 showed the age distribution of the study patients, the mean age of the participants was 58.29±13.11 years, range 25-80 years. Among the 33 male patients, a maximum (45.45%) was from the age group of 61-70 years. Among the 5 female patients, a maximum (60%) was from the age group of 61-70 years. The mean age for

the male population was 56.34±13.86 years, and for females, it was 64.56±8.05 years.

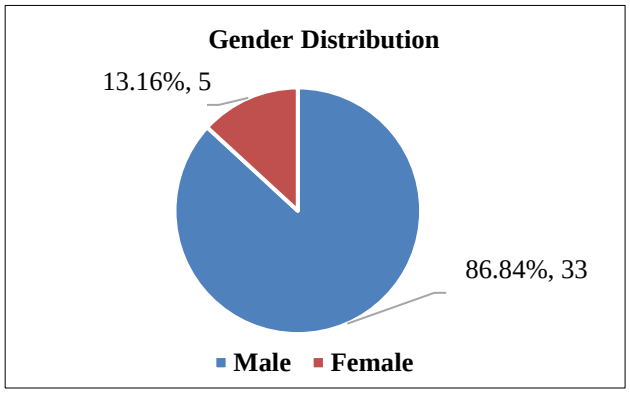

Figure 1: Gender distribution of the participants (n=38).

Table 1: Age, and gender distribution of the participants (n=38).

Age group (years)	Male (%)	Female (%)	Total (%)
20–30	1 (3.03)	0 (0.0)	1 (2.63)
31–40	1 (3.03)	0 (0.0)	1 (2.63)
41–50	3 (9.09)	0 (0.0)	3 (7.89)
51–60	8 (24.24)	1 (20)	9 (23.68)
61–70	15 (45.45)	3 (60)	18 (47.37)
71–80	5 (15.15)	1 (20)	6 (15.79)
Total	33 (100.0)	5 (100.0)	38 (100.0)
Mean± SD	56.34±13.86	64.56±8.05	58.29±13.11

All 38 patients (100%) had cough, 68.42% had shortness of breath, 63.15% had hemoptysis, 21 (55.26%) had chest pain, 14 (36.84%) had weight loss, 11 (28.9%) had hoarseness of voice, 1 (2.63%) had engorged neck vein, and clubbing and fever were present in 5.26% each (Table 2).

Table 2: Distribution of the study patients by clinical features (n=38).

Clinical features	Frequency	Percentage (%)
Cough	38	100
Shortness of breath	26	68.42
Hemoptysis	24	63.15
Chest pain	21	55.26
Weight loss	14	36.84
Hoarseness of voice	11	28.94
Engorged neck vein	1	2.63
Fever	2	5.26
Clubbing	2	5.26
Family history of lung cancer	1	2.63

Table 3 showed the chest x-ray findings of the patients. Maximum patients (42.10%) had mass lesions. followed by pleural effusion in 15 (39.47%), lung collapse in 9 (23.68%), and raised hemidiaphragm in 9 (23.68%).

Table 3: Distribution of the study patients by chest X-ray findings (n=38).

Chest examination	Frequency	Percentage (%)
Pleural effusion	15	39.47
Lung collapse	9	23.68
Mass lesion	16	42.1
Raised hemidiaphragm	9	23.68

Considering the CT chest findings, maximum patients (42.10%) had mass lesions, followed by pleural effusion in 15 (39.47%), lymphadenopathy in 15 (39.47%), and lung collapse in 10 (26.3%) (Table 4).

Table 4: Distribution of the study patients by CT chest findings (n=38).

CT chest findings	Frequency	Percentage (%)
Pleural effusion	15	39.47
Lung collapse	10	26.32
Mass lesion	16	42.1
Lymphadenopathy	15	39.47

Histopathological findings confirmed 34 out of 38 cases. Among those 34, maximum patients (38.23%) had squamous cell carcinoma, then 11 (32.35%) had adenocarcinoma, 5 (14.70%) had small cell carcinoma, 3 (8.82%) had large cell carcinoma, and 2 (5.88%) had poorly differentiated non-small cell carcinoma (Table 5).

Table 5: Distribution of lung cancer patients by bronchial biopsy findings (n=34).

Histopathological findings	Frequency	Percentage (%)
Squamous cell carcinoma	13	38.23
Adenocarcinoma	11	32.35
Small cell carcinoma	5	14.7
Large cell carcinoma	3	8.82
Poorly differentiated carcinoma	2	5.88
Total	34	100

BAL fluid cytology found 24 out of 38 lung cancer patients. Among those 24, maximum patients (45.83%) had squamous cell carcinoma, then 10 (41.66%) had adenocarcinoma, 1 (4.16%) had small cell carcinoma, and 2 (8.33%) had poorly differentiated non-small cell carcinoma (Table 6).

Table 6: Distribution of lung cancer patients by BAL fluid cytology findings (n=24).

Cytological findings	Frequency	Percentage
Squamous cell carcinoma	11	45.83
Adenocarcinoma	10	41.66
Small cell carcinoma	1	4.16
Poorly differentiated carcinoma	2	8.33
Total	24	100

Holding the bronchial biopsy as the gold standard, Table 7 showed that 24 patients had a true positive, 10 patients had a false negative, 4 patients had a true negative, and no one was a false positive.

Table 7: Diagnostic validity test results (gold standard bronchial biopsy).

Sample	Test result				Total
	True positive	True negative	False positive	False negative	
BAL	24	4	0	10	38

Table 8 showed the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of BAL at 70.59%, 100%, 100%, 28.57%, and 73.68% respectively.

Table 8: Performance indices of BAL fluid cytology.

Indices	BAL cytology (%)	
	Values	95% CI
Sensitivity	70.59	52.52 to 84.90
Specificity	100	39.76 to 100
PPV	100	
NPV	28.57	19.20 to 40.24
Accuracy	73.68	56.90 to 86.60

DISCUSSION

This descriptive cross-sectional study was conducted in the Department of Respiratory Medicine, BSMMU, Dhaka for one year, and five months. The aim of this study was to know the sensitivity, and specificity of bronchoalveolar lavage fluid cytology in the diagnosis of lung cancer. Male predominance was observed in the present study, which was similar to the findings of other studies.[5] This male predominance might be explained by the increased smoking and occupational exposure among males in our society. Age-wise, the majority of both male and female participants were found to be from the sixth or seventh decade of life. This might be due to older people getting prolonged period of exposure to carcinogenic materials over their lifetime. Cough was a common clinical presentation in all the participants, while some of the more prevalent complications included shortness of breath, hemoptysis, chest pain, weight loss, and hoarseness of voice. These results were consistent with the findings of another study that similar common symptoms.[14] Among the radiological findings, the mass lesion was the most common. Other common findings of the present study included pleural effusion, lung collapse, raised hemidiaphragm, and mediastinal lymphadenopathy. bronchial biopsy revealed lung cancer in thirty-four patients out of thirty-eight where maximum patients had squamous cell carcinoma, and adenocarcinoma. Other detected lung cancer included small cell carcinoma, large cell carcinoma, and poorly differentiated non-small cell carcinoma. These findings were similar to the observation done by multiple other studies, where squamous cell carcinoma and adenocarcinoma were the most common lung cancer.[15,16] Some studies also had a higher incidence of adenocarcinoma compared to squamous cell carcinoma.[17] These dissimilarities in the subtype of lung cancer might be related to gender, smoking history, and the site of origin of lung cancer. Squamous cell carcinoma is more common in males with a smoking history, and central lung lesion. Adenocarcinoma is more common in females, non-smokers, and peripheral lung lesions. The BAL fluid cytology identified malignancy in 24 among the 38 participants of our study. Among these 24, the majority had squamous cell carcinoma followed by adenocarcinoma, small cell carcinoma, and poorly differentiated non-small carcinoma. This was different from the findings of Sharma et al who found poorly differentiated carcinoma as the commonest lung cancer followed by adenocarcinoma, squamous cell carcinoma, and small cell carcinoma on BAL cytology.[15] The present study revealed ten false negative cases. The reasons for false negative results could be superadded inflammation, scanty cellular aspirates, or bad material preservation. Since cytological sampling by BAL technique depends mainly on cells 'exfoliated' from the malignant lesion in the bronchial epithelium, the adequacy of its samples relies on several factors, especially: the degree of differentiation of malignant tumor; preservation of the morphology of cytological material collected; and technical skill of the pulmonologist who is collecting the lavage fluid from the bronchus. Generally, less differentiated, anaplastic lesions have more loosely cohesive cells in comparison to well-differentiated lesions.[18] Thus, such lesions exfoliate a larger number of cells into the bronchial cavity than the well-differentiated lesions. In our study, the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of BAL were 70.59%, 100%, 100%, 28.57%, and 73.68% respectively. These findings were supported by other studies like Shenoy, and Shetty who showed a sensitivity of 72%, specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 53.3%.[19] But contradictory results were also observed in some studies, like a study by Choudhury et al where they found the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of BAL at 88.1%, 97.98%, 94.7%, 95.1%, and 95.03% respectively.[20] The sensitivity was more prominent in these discrepancies. This might be related to the number of attempts at obtaining BAL sampling. A

higher number of attempts can improve the sensitivity, specificity, PPV, and overall accuracy. In our study, the sample parameters were calculated using a single sample. This might be the reason for being of our sensitivity less than the previous studies. As BAL fluid cytology has good sensitivity and high specificity, it promises to be a very convenient cytological technique that can be confidently used for the diagnosis of lung cancer, as it saves the time needed for the processing of biopsy specimens. However, if BAL fails to show morphological classification of lung cancer, it may lead to biopsy to confirm the morphological type of the malignant lesion for the planning of treatment.

Limitations

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

BAL fluid cytology is a useful tool for the diagnosis of lung cancer. It has good sensitivity, and specificity, and shows nearly identical information as biopsy.

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

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