



Original Article

Role of Bronchial Brush Cytology in Diagnosis of Bronchopulmonary Lesions

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Abstract

Bronchial carcinoma is currently the most common cause of cancer-related mortality worldwide. The increasing incidence could be due to increased smoking habits, change in lifestyles, increased environmental pollution, and the availability of different modalities to detect lung cancer. Fibreoptic bronchoscopy was introduced in 1968 to evaluate bronchopulmonary lesions. Since then, various methods for obtaining good specimens have become available apart from sputum. A higher positive rate was obtained from specimens collected by fiberoptic bronchoscope. We aimed to assess the sensitivity and specificity of brushings compared with the biopsy of lung lesions. The study was done on 100 patients, of which bronchial brush cytology was done in all 100 cases, and endobronchial biopsy was carried out in 20 cases. This study showed sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of brushing to be 87.5%, 75%, 85%, 93.13%, and 60%, respectively.

TAJ 2022; 35: No-1: 107-115

Introduction

Bronchial carcinoma is one of the leading cause of cancer-related deaths in both men and women internationally.¹ Lung cancer incidence and mortality are tightly linked to cigarette smoking patterns. As smoking rates peak, incidence and mortality of lung cancer also increases.²⁻⁴

In Bangladesh, lung cancer is 16.7% of all cancers and the most common cancer (25%) among male cancer patients, with a 6:1 male-female ratio.⁵ The incidence of bronchial cancer is increased due to an increase in smoking habit, change in lifestyles, increased environmental pollution, and also the availability of different modern diagnostic modalities to detect lung cancer.⁶ Fifteen percent of lifetime smokers develop lung cancer, but 10% of lung cancers occur in non-smokers.⁷

Several investigations to be carried out through the flexible fibreoptic bronchoscope, but bronchial brushing is thought to be most useful as the results obtained by it are considered better than those obtained by bronchial washings, biopsy, or sputum examination, especially for distal bronchial lesions.

Studies done using bronchial brushing for the cytodiagnosis of lung cancer have emphasized its high accuracy rate in evaluating neoplastic and nonneoplastic pulmonary lesions.⁸⁻¹³

The present study is based on the cytologic evaluation of bronchial brushings for diagnosing bronchopulmonary lesions and to correlate with the cytologic findings with the clinical diagnosis and histopathologic examination wherever possible. Dudgeon and Barret realized first that bronchial carcinoma could be accurately

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diagnosed and typed by the microscopic study of expectorated cells.¹⁴

Materials and Methods

A cross-sectional comparative study was conducted in the Department of Respiratory Medicine and Department of Pathology, Rajshahi Medical College Hospital, Rajshahi, from July 2017 to June 2018. One hundred patients aged 25 to 85 years were selected from those admitted to the Department of Respiratory Medicine, Rajshahi Medical College Hospital, Rajshahi. In addition, patients were also selected from a private clinic in Rajshahi. Patients were selected based on history, physical examination, chest X-ray, and those who fulfilled the inclusion and exclusion criteria.

Inclusion Criteria

- Radiological lesion (chest X-ray) suggestive of the centrally placed lesion.
- Prominence of a hilar shadow with a whiskering appearance.
- Hilar / parahilar masses
- Mediastinal widening
- Complete or partial collapse of a lung.
- Central bronchial cancer on endoscopic findings visible by fiberoptic bronchoscopy.
- Age more than 18 years
- Both sex
- Clinical symptoms refractory to medication or visible endobronchial mass

Exclusion Criteria

- All bronchial lesion approaching carina
- All peripheral lung lesion

Results

The study group consisted of 100 cases selected based on clinical, radiological, and bronchoscopic findings. The age of the patients varied from 20 years to 85 years, and the M: F ratio was 9:1. The age range was given in Table-I.

- Significantly disabled patients due to poor general condition.
- Patient who refused to enroll in the study.

Technique of Brushing Cytology

Informed written consent was obtained from the patients or attendants after a full explanation of the details of the disease process. Detailed clinical history, physical examination, blood test, chest X-ray, and bronchoscopy were performed in all 100 cases. Bronchoscopy was performed through the transnasal approach, using an Olympus BF-2TR fiberoptic bronchoscope.

Bronchial brushing (BB) was performed using straight brushes. After the sampling, the brush was smeared on 5-6 clean slides; these were fixed in 95% ethyl alcohol for H&E staining.

Endobronchial biopsy was performed in 22 cases using flexible long biopsy forceps, and tissue samples were fixed in 10% formalin and processed for histopathological examination.

Complications were negligible. One patient had a mild pneumothorax which required no therapy, and two patients had transient hemoptysis that consisted of faint blood streaking of the sputum. Those patients who had the procedure performed on an outpatient basis returned home the same day.

Data recording and calculation

All necessary and relevant data were recorded methodically and meticulously. All the cases were numbered chronologically; the same number was given to cytology slides and biopsy slides for each case. All the data were evaluated by standard statistical methods.^{15,16} Various indices were calculated: false positive, false negative, sensitivity, specificity, accuracy, positive predictive value, and negative predictive value.

Table-I: Age distribution

Age groups (Years)	Total	%
20-30	03	03
31-40	03	03
41-50	20	20
51-60	34	34
61- 70	27	27
71-80	11	11
81-85	02	02

Regarding smoking, 79 cases were smokers, and 21 were nonsmokers, with a smoker-to-nonsmoker ratio of 3.8:1.

Among the male patients, 58 lesions were in the right lobe, and 32 lesions were in the left lobe. Among the female patients, 07 were in the right lobe, and 03 were in the left lobe (Table-II).

Table-II: Site of the lesion in both sexes

Site	Male	%	Female	%
Right	58	48.00	07	7.00
Left	32	42.00	03	3.00

On histopathological examination, the biopsy specimens were inadequate for interpretation in 02 cases that were not included in the study. Among the 20 cases, 03 were diagnosed as inflammatory, 01 as tuberculosis, 01 as small cell carcinoma, 04 were adenocarcinoma, and squamous cell carcinoma was detected in 10 cases (Table-III).

Table-III: Distribution of histopathological diagnosis of 20 cases.

Diagnosis	Total number	Percentage
Inflammatory	03	15 %
Tuberculosis	01	05 %
Small cell carcinoma	01	05 %
Adenocarcinoma	05	25 %
Squamous cell carcinoma	10	50 %

The histopathology of adenocarcinoma and squamous cell carcinoma are shown in the following figures 1 & 2.

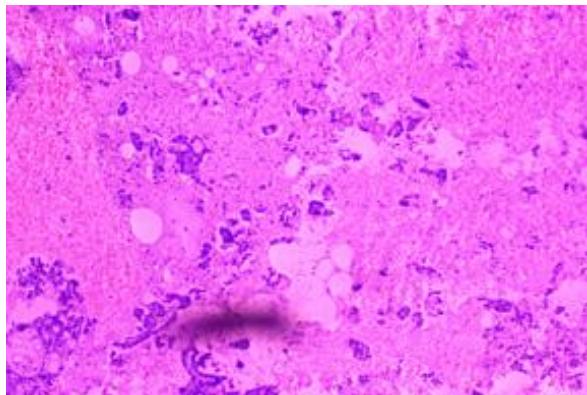


Fig 1: Histopathology of adenocarcinoma

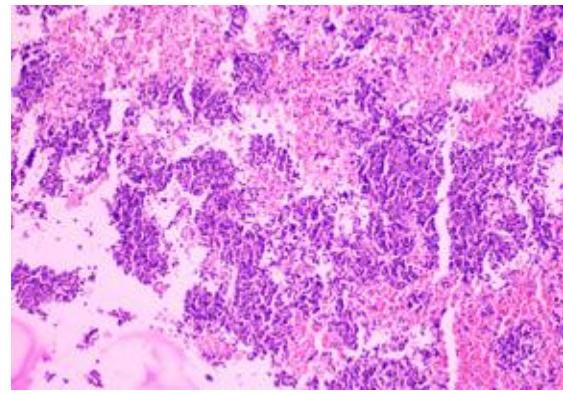


Fig 2: Histopathology of squamous cell carcinoma

Among brush cytology of 100 cases, satisfactory smears were obtained in 98 cases, and 02 smears were unsatisfactory. On cytological examination, 05 were diagnosed as inflammatory, 02 were diagnosed as tuberculosis, 02 were atypical, 03 small cell carcinoma, 04 metastatic, 02 Non-Hodgkin's Lymphoma, 22 adenocarcinomas, 18 undifferentiated carcinomas, and 40 were squamous cell carcinoma (Table-IV).

Table-IV: Cytological Diagnosis Of 100 cases

Diagnosis	Number	%
Unsatisfactory	02	2.0
Inflammatory	05	5.0
Tuberculosis	02	2.0
Atypical	02	2.0
Small cell carcinoma	03	3.0
Metastatic undifferentiated carcinoma	04	4.0
Non-Hodgkin lymphoma	02	2.0
Adenocarcinoma	22	22.0
Undifferentiated carcinoma	18	18.0
Squamous cell carcinoma	40	40.0

Cytological findings are shown in the following figures 3-8.

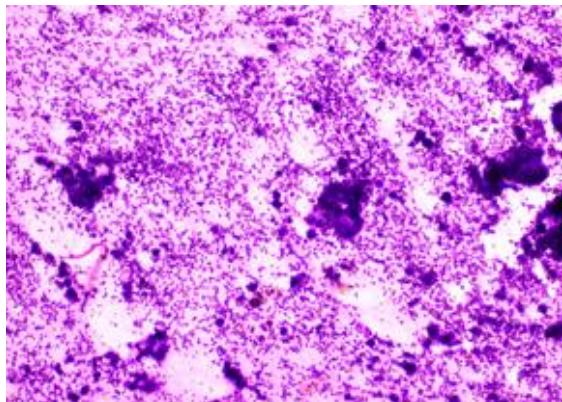


Fig 3: Cytology of adenocarcinoma

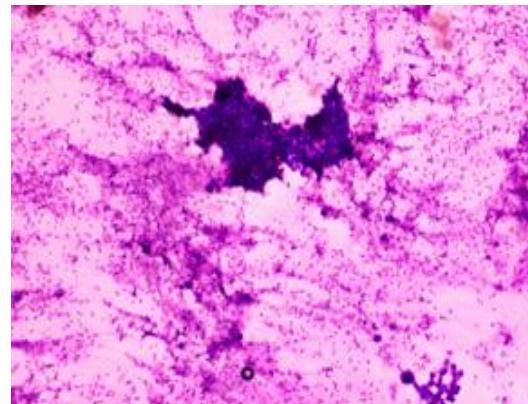


Fig 4: Cytology of squamous cell
Carcinoma

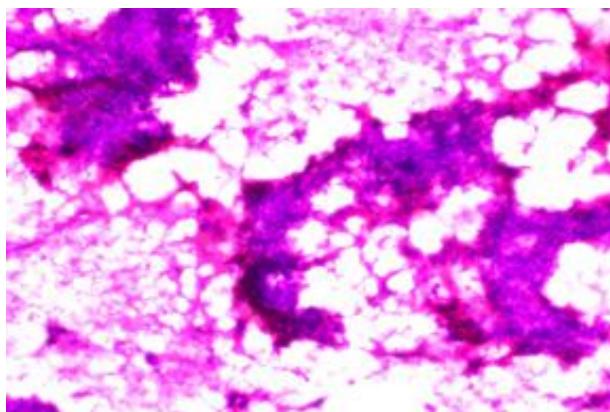


Fig 5: Cytology of large cell undifferentiated
carcinoma

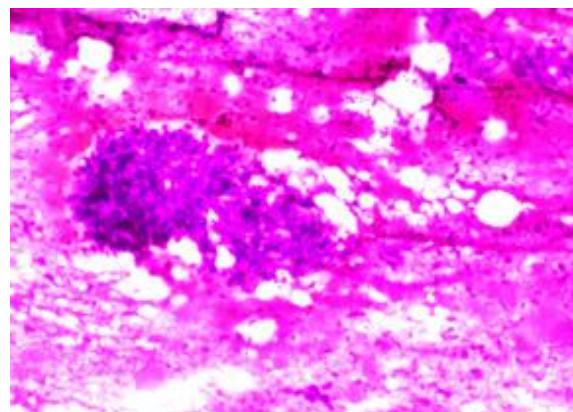


Fig 6: Cytology of malignant mesenchymal
tumor

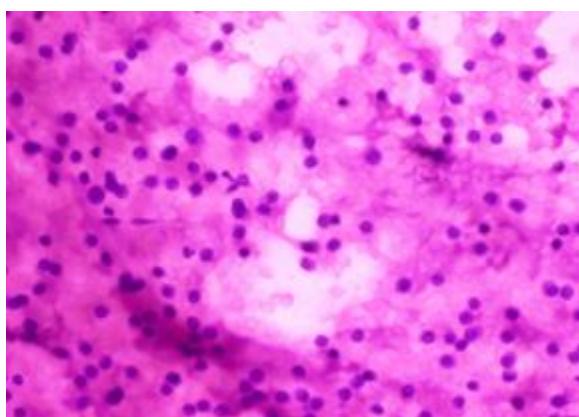


Fig 7: Cytology of Non-Hodgkin lymphoma

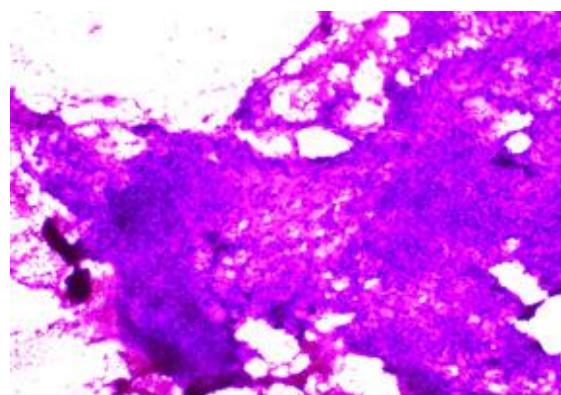


Fig 8: Cytology of tuberculosis

Table V shows the findings of brush cytology in relation to histopathology.

Table-V: Findings of brush cytology in relation to histopathology in 20 cases.

Histopathological diagnosis	No. Patients	Cytology	
		+ve	-ve
Inflammatory	03		03
Tuberculosis	01		02
Small cell carcinoma	01	01	
Adenocarcinoma	05	04	
Squamous cell carcinoma	10	10	
False positive =	01 (Disease negative but test positive)		
False negative =	02 (Disease positive but test negative)		
True positive =	14 (Those who are both test positive and disease positive)		
True negative =	03 (Those who are both test negative and disease negative)		

Table-VI: Statistical analysis of brush cytology in 20 cases

Diagnostic Methods	Brush cytology
True positive	14
True negative	03
False positive	01
False negative	02
Sensitivity (%)	87.50
Specificity (%)	75.00
PPV (%)	93.33
NPV (%)	60.00
Accuracy (%)	85.00 %

Discussion

Lung cancer is the commonest cause of cancer-related deaths worldwide. So early diagnosis and management are the key to preventing mortality.⁶

Fibreoptic bronchoscopy was introduced in 1968 as a diagnostic procedure. Since then, different methods for obtaining satisfactory specimens have become available apart from sputum. The specimens collected by fibreoptic bronchoscope yield a higher positive rate. The sensitivity of

bronchial aspirates in diagnosing lung cancer has been 75 to 88.1 % by various studies.^{17,18} Bronchoscopy and guided techniques have a definitive role in the diagnosis of endobronchial lesions, and a combination of washings and brushings with forceps biopsy increased the sensitivity from 83.17 to 85.64% and 90.65%, respectively.⁸

In the present study, the mean age is 52.5 years. Ahmed Z et al. studied age groups from 25 years

to 90 years with a mean age of 54.34 years which is more or less similar to this study.¹⁹ The age incidence also correlates well with D Raiza's study.⁶

In this study about location, 65 was in the right lung & 35 in the left lung, which also has similarity with Ahmed Z et al.¹⁹ In a study by Alam MA et al., 122 were in the right lung, and 44 were in the left lung.²⁰ The present study differed with the study by Alam MA.²⁰

In this study, there were 90 male patients & 10 female patients with a ratio of 9:1. In the study by Alam MA, the M: F was 4:1.²⁰ In the study by Sultana B et al., the M: F was 17.5:1.²¹ D. Raiza studied M: F was 6:1.⁶ The male preponderance is observed in all the studies. This could be due to the higher prevalence of smoking in males in our society.

In this study, the endobronchial biopsy and histopathology revealed bronchial carcinoma in 16 cases (80%) and inflammatory in 04 cases (20%). About cell typing, squamous cell carcinoma was diagnosed in 10 cases (50%), adenocarcinoma in 05 cases (25%), small cell carcinoma in 01 cases (05%), inflammatory in 03 patients (15%), and tuberculosis in 01 cases (05%). Squamous cell carcinoma was the most common malignant tumor, followed by adenocarcinoma and small cell carcinoma. Sultana B et al. showed squamous cell carcinoma 48.6%, adenocarcinoma 10.8 %, small cell carcinoma 08%, and no malignancy in 32.4% of cases.²¹ The frequency of squamous cell carcinoma is similar to the study by Sultana B et al.²¹, but it differs from other types.

Choudhury M et al. showed squamous cell carcinoma 51.42%, small cell carcinoma 5.71%, adenocarcinoma 2.85%, and inflammatory in 14 cases (40%).²² This study correlates well with squamous cell carcinoma, but the frequency of small cell carcinoma and adenocarcinoma do not connect with this study.

Adenocarcinoma is the most common histologic subtype of lung cancer in men and women.²³ Before the 1990s, squamous cell lung carcinoma was the most common histologic subtype, particularly among men. Since then, the incidence

of adenocarcinoma rose to be greater than that of squamous cell carcinomas in the US, Canada, many European countries, and Japan.²⁴ However, this switch has not yet been observed in other countries such as Spain and Netherlands.²⁵

The higher rates of adenocarcinoma relative to squamous and small cell lung cancer are greater in women.³

Among brush cytology of 100 cases, 02 (2%) smears were unsatisfactory, 05(5.0%) were inflammatory, 02(2.0%) were tuberculosis, 02(2.0%) were atypical, 02(2.0%) were small cell carcinoma, 04(4.0%) were metastatic, 02(2.0%) was Non-Hodgkin's Lymphoma, 22(22.0%) were adenocarcinoma, 18(18.0%) were undifferentiated carcinoma and squamous cell carcinoma was diagnosed in 40(40%) cases.

In the study of brush cytology, Sultana B et al. showed squamous cell carcinoma 67.6%, adenocarcinoma 10.8%, small cell carcinoma 10.8%, and non-conclusive 10.8%²¹. Although regarding frequency, this study correlates well with Sultana's study, regarding cell typing, this study varies from her research.

Choudhury M et al. studied brush cytology of 35 cases in which she showed squamous cell carcinoma in 18(51.42%), small cell carcinoma in 02(5.71%), adenocarcinoma in 01(2.85%) & inflammatory 14(40%).²² In this study, the frequency of squamous cell carcinoma is high, which is similar to that study, but it differed from other types of lesions.

In this study, two cases were falsely diagnosed as tuberculosis in brush cytology. This is due to extensive necrosis in squamous cell carcinoma. During collection, the brush tip probably touched the necrotic area, and the specimen collected was only necrotic material. Opposite matter also occurred in one case of tuberculosis which was falsely diagnosed as undifferentiated carcinoma due to the aggressive appearance of macrophages. Reactive macrophages may sometimes look similar to malignant cells.

Accuracy was highest in the squamous cell type, which was in general agreement with the results of

studies conducted by Bedrossian et al.²⁶ However, Tuladar A et al. found that BB was the most sensitive technique for diagnosis of small cell carcinoma (80%), followed by squamous cell carcinoma.¹³

Small cell carcinoma tumor cells showed slight variation in size and shape, high nuclear/cytoplasmic ratio, frequent molding, salt, pepper chromatin, and crush artifact. Sturgis CD et al. identified nuclear molding and salt and pepper chromatin as essential features for distinguishing small cell carcinoma from non-small cell carcinoma.²⁷

This study aimed to evaluate the justification of using a cytologic examination as an alternative to histopathological confirmation of the diagnosis.

In this study bronchial brushing showed sensitivity 87.5%, specificity 75%, accuracy 85%, PPV 93.13%, NPV 60%. Choudhury M et al. showed a sensitivity of brush cytology was 80.9%, specificity 85.7%, accuracy 82.85%, PPV 89.47%, and NPV 75%. This was similar to Choudhury M et al.²²

Similar observations were made by Gaur DS et al. 10, who mentioned sensitivity, specificity, PPV, NPV, and brushing accuracy to 87.3%, 97.6%, 95.4%, 93.10%, and 93.90%, respectively.¹¹ Rawat J reported endobronchial brushing sensitivity to 69.15% and that of washing to 47.66%.¹¹

Jay et al. showed a sensitivity of 87%, specificity of 90%, and PPV of 79%.²⁸ The diagnostic efficacy of cytology in this series established a sensitivity of 87.50%, specificity of 75.00%, and PPV 93.33%. This study showed similarity in Jay's sensitivity but differed in the case of specificity and PPV. The overall accuracy of bronchial cytology was 75% and 75.4% in two other studies by Thuong et al.²⁹ and Chaudhary et al.³⁰ respectively, whereas, in the present study, it was slightly higher (85.00%).

We attempted to confirm with these findings the concept that pulmonary cytology has improved to the point that its sensitivity is high enough to

justify its use as a definitive diagnostic tool in those cases where tissue diagnosis is not possible.

Conclusion:

This study showed sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of brushing are pretty high, thus making it a useful diagnostic tool for bronchopulmonary lesions.

Conflict of interest: None declared

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