

Diagnostic Accuracy of Endobronchial Washings in Patients of Lung Malignancies

Hafiz Muhammad Hamza Arshad, Muhammad Usman Rathore, Bushra Parveen, Adeel Arif,
Umair Aslam Shahzad, Wajahat Ahmed Khan

Department of Histopathology, Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

ABSTRACT

Objective: To evaluate diagnostic accuracy of endobronchial washings of patients presenting with lung malignancy.

Study Design: Cross sectional study

Place and Duration of Study: Armed Forces Institute of Pathology Rawalpindi, Pakistan from Aug 2024 to Feb 2025.

Methodology: Specimens of 146 patients undergoing both procedures of endobronchial washings and endobronchial biopsy were included in the study. Patients who underwent bronchoscopy for only one procedure, patients unwilling for informed consent and samples with poorly fixed tissue and broken cytology slides were excluded. Slides of endobronchial washings and endobronchial biopsy were examined and the results were recorded.

Results: The study included specimens of 146 patients, with a male to female ratio of 3:1. The ages of the patients ranged from 21 to 84 years with median age 54 years. (IQR 65 – 37 years) Majority of malignant cases occurred in the 5th and 6th decades of life. The endobronchial washings showed a sensitivity of 46%, specificity of 91%, positive predictive value of 85%, and negative predictive value of 61%. Diagnostic accuracy was achieved in 99 cases (67.7%).

Conclusion: Based on the results obtained, it has been observed that bronchial washings cytology demonstrated low sensitivity when it comes to the diagnosis of lung tumors. Therefore, it cannot be used as a reliable diagnostic test for lung malignancies.

Keywords: Bronchoscope, Diagnostic accuracy, Endobronchial biopsy, Endobronchial washings, Lung cancers

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INTRODUCTION

Lung cancer remains the leading cause of cancer related deaths globally. It is particularly common in individuals living and working in industrialized regions. This type of cancer accounts for 30% of cancer deaths in men and 26% in women worldwide. Annually, an estimated 1.38 million people die because of lung cancer.¹ Smoking, lifestyle changes, and rising environmental pollution may be the possible contributing factors responsible for increase in lung cancer cases.² Lung cancer is a significant public health concern in Pakistan. It is responsible for 10,538 newly diagnosed cases across all age groups and both genders, representing around 5.9% of all cancer cases. This data makes it the second most prevalent cancer in men and the third most common cancer overall in Pakistan.³ Diagnosis of lung cancer cases at earliest possible stage can help in the effective management. The main aim of cancer researchers is to develop tools and procedures that would help in the early diagnosis and treatment of lung cancer, thereby reducing the mortality rate.⁴

Detailed clinical and radiological examination is performed in patients who are having suspicion of lung cancer. A variety of diagnostic tools and procedures are used for this purpose. Endobronchial washings (EBW) and endobronchial biopsy (EBB) are the two commonly used procedures in evaluation of lung cancer. In endobronchial washings, cells from the bronchial airways are collected by inserting a bronchoscope into the lower respiratory tract. During the process, 10-20 ml of normal saline is instilled, and then the fluid is re-aspirated using a suction device, with the sample collected in a mucus extractor, followed by smear preparation and cytological examination.⁵ In endobronchial biopsy, tissue sample from the bronchial mucosa or lung parenchyma is obtained by using a core needle biopsy through bronchoscope followed by histopathological examination.

In 2016, the Papanicolaou Society of Cytopathology introduced a 6-tier lung cytopathology reporting system.⁶ This was followed by a 4-tier system proposed by the Japan Lung Cancer Society and the Japanese Society of Clinical Cytology in 2020.⁷ The latest reporting system, developed by the International Academy of Cytology (IAC) in

Correspondence: Dr Hafiz Muhammad Hamza Arshad, Department of Histopathology, Armed Forces Institute of Pathology, Rawalpindi Pakistan
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collaboration with the International Agency for Research on Cancer (IARC), represents a global consensus on lung cytopathology reporting. This system is adaptable to various clinical settings and accounts for the diversity of different institutions. The five categories in the WHO system are "Non-diagnostic," "Benign," "Atypical," "Suspicious for malignancy," and "Malignant".⁸

Endobronchial biopsy is considered the gold standard for diagnosis of lung cancer; however, it is both invasive and costly. In contrast, endobronchial washings offer a less invasive and more affordable alternative. Despite this, no comprehensive study has been conducted in Pakistan over the past 15 years to assess the diagnostic accuracy of endobronchial washings. This study is aimed to assess the sensitivity, specificity, and diagnostic accuracy of endobronchial washings keeping the endobronchial biopsy as the gold standard if proven reliable, this technique could serve as a valuable substitute for endobronchial biopsy, particularly in resource-limited settings like Pakistan.

METHODOLOGY

This was a cross sectional study, conducted over the period of six months from August 2024 to February 2025 at the Department of Histopathology, Armed Forces Institute of Pathology Rawalpindi, Pakistan after approval of Institution Review Board (16 Aug 2024, FC-HSP23-17/READ-IRB/24/3554).

Inclusion Criteria: All patients with clinical suspicion of lung malignancy undergoing both procedures of endobronchial washings and endobronchial biopsy during bronchoscopy were included in the study.

Exclusion Criteria: Patients who underwent bronchoscopy for only one procedure either endobronchial washings or endobronchial biopsy, patients unwilling for informed consent and samples with poorly fixed tissue and broken cytology slides were excluded.

Specimens of 146 patients fulfilling the inclusion criteria, were calculated through Buderer's formula for diagnostic accuracy study, with 95% confidence level and expected precision of ± 0.10 by using sensitivity and specificity of bronchial cytology 60% and 89% respectively with 66.67% prevalence of lung cancer in suspected cases (Out of 63 suspected cases, 42 were ultimately diagnosed as malignant) from previous study.^{1,9} Patients were recruited from the pulmonology clinic of tertiary care hospital and

provided with detailed information about the study. Informed consent was obtained. During bronchoscopy, a needle of 18G is inserted through the main bronchus into the lung lesion through bronchoscope and biopsy sample was obtained and sent in laboratory in 10% Formalin fixative. Tissue specimens were processed in the histopathology department, where 3 mm thick sections were prepared using the Paraffin embedding technique. Hematoxylin and eosin staining was performed on the tissue sections for morphological assessment and immunohistochemistry (IHC) was applied for confirmation. Special stains, such as ZN stain (for Acid-Fast Bacilli) and PAS (Periodic Acid-Schiff) were applied if required. Endobronchial washings were collected by introducing a fiber-optic bronchoscope into the lower respiratory tract. Approximately 10-20 ml of Normal Saline was infused, and this fluid was re-aspirated using a suction device. The bronchial washings were then centrifuged in the laboratory, and the sediments were placed in a clean petri dish against a black background. Solid particles or bloody material were carefully picked and smeared onto the slides, ensuring the smears were slightly thicker than a blood smear and evenly spread. These smears were then fixed in 95% alcohol.^{10,11} May-Grünwald-Giemsa (MGG) staining was used for air-dried smears, while Papanicolaou (PAP) staining was used for wet-fixed smears.^{12,13} These slides were analyzed under microscope for morphological evaluation. Both cytological and histopathological slides were seen by two consultant histo-pathologists independently. In case of any discrepancy, opinion from third consultant was taken. Results of both procedures were recorded. Figure-1 shows patients flow chart.

Data was analyzed using Statistical Package for Social Sciences version 27.0. The Shapiro-Wilk test was employed to assess the normality of continuous variable such as age of the patients. Data analysis showed skewed results, so median (IQR) were calculated. Percentages were calculated for qualitative variables including tumor type and gender of patients. The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of endobronchial washing were calculated. Concordance was evaluated using Cohen's kappa coefficient.

RESULTS

The study included histopathological and cytological specimens of 146 patients. One hundred

and eight patients were males (74%) and 38 were females (26%) with a male-to-female ratio of 3:1. The patients age ranged from 21 to 84 years with median age 54 years. (IQR 65-37 years) The majority of malignant cases occurred in the 5th and 6th decades of life. The majority of malignant cases occurred in the 5th and 6th decades of life. On endobronchial washings, 41(28%) cases were diagnosed as malignant/ suspicious while 105(72%) cases were labeled benign. On the other hand, endobronchial biopsy diagnosed 76(52%) cases as malignant and 70(48%) cases as benign shown below in the Figure-2.

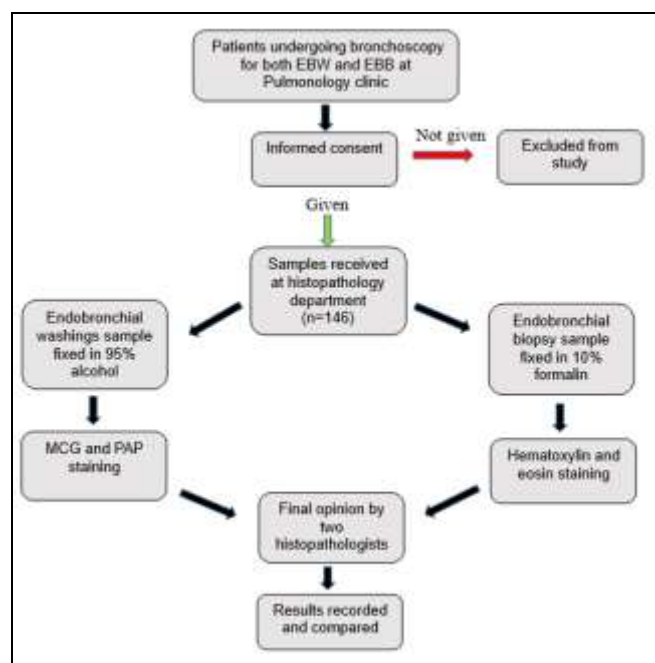


Figure-1: Patients Flow Chart

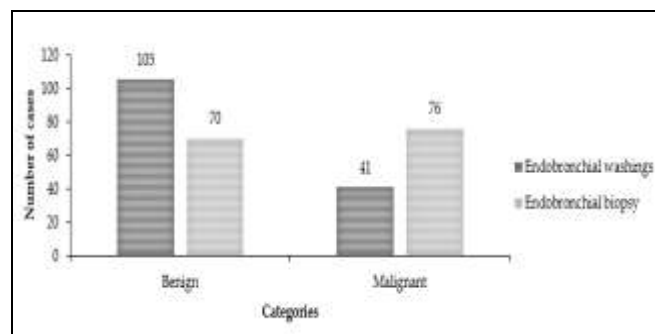


Figure-2: Benign and malignant cases on endobronchial washing and endobronchial biopsy (n=146)

Out of 41 malignant/ suspicious cases identified on cytological examination, 32 cases were labeled definite malignant while 9 cases were identified as suspicious for malignancy. All 32 malignant cases on

cytology proved to be malignant on histopathology whereas only 3 suspicious cases on cytology were proved to be malignant on histopathology, bringing the total number of true positive cases to 35. 70(48%) cases were confirmed as benign on endobronchial biopsy. 64 cases out of 70 were correctly labeled benign on endobronchial washings, these cases were labeled as true negative. Additionally, 41(28%) false negative cases were identified, where cytology showed benign features, but histopathology confirmed these cases as malignant. The cytology of endobronchial washings showed a sensitivity of 46%, specificity of 91%, positive predictive value of 85%, and negative predictive value of 61%. Cytological and histopathological concordance was achieved in 99 cases (67.7%). The Cohen's Kappa coefficient was approximately 0.369 indicating the fair agreement between endobronchial washing and endobronchial biopsy which means endobronchial washing cannot be used as an alternative to endobronchial biopsy.

Table-I: Diagnosis Parameters (n=146)

		Endobronchial biopsy	
		Positive	Negative
Endobronchial washings	Positive	35(46%)	6(9%)
	Negative	41(54%)	64(91%)

Sensitivity= $35/35+41=46\%$

Specificity= $64/64+6=91\%$

Positive predictive value= $35/35+6=85\%$

Negative predictive value= $64/64+41=61\%$

Diagnostic accuracy= $35+64/146=67.7\%$

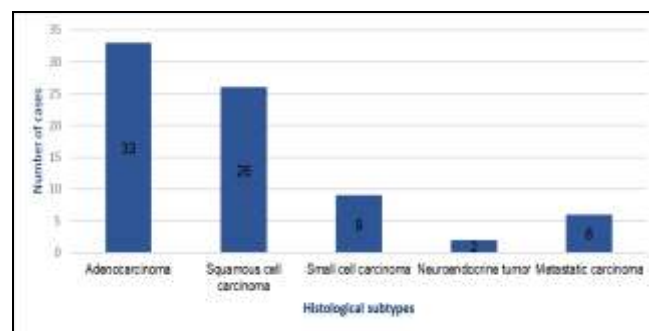


Figure-3: Frequency of histological subtypes of malignant cases on endobronchial biopsy (n=76)

Table-II: Comparison of current study with previous studies

	Sensitivity	Specificity	Diagnostic accuracy
Present study	46%	91%	67%
Rawat J <i>et al.</i> , 2007 ¹⁵	47.6%	-	-
Zainudeen F <i>et al.</i> , 2021 ¹⁴	51.9%	90.9%	56.8%
Goel S <i>et al.</i> , 2022 ¹	60%	89%	71%
Khandelwal R <i>et al.</i> , 2018 ¹⁸	70.8%	88.9%	73.8%
Abbasi F <i>et al.</i> , 2017 ¹⁷	32.1%	96.4%	65%
Mrudula K <i>et al.</i> , 2019 ¹⁶	11.8%	-	-

Tissue biopsy revealed that 76 cases (52%) were malignant, and 70 cases (48%) were benign. Among the malignant cases, adenocarcinoma was the most common malignancy found in 33 cases (43.4%), followed by squamous cell carcinoma in 26 cases (34.2%). Frequency of other malignant neoplasms is summarized in Figure-3. In the benign category, 24 cases exhibited chronic granulomatous inflammation, likely due to tuberculosis, while 46 cases demonstrated acute on chronic nonspecific inflammation.

DISCUSSION

In this study majority of lung cancer patients were in their 5th and 6th decades of life, which aligns with existing literature. Male to female ratio was 3:1 which is also comparable to other studies.^{1,10} This could be due to the higher prevalence of habitual smoking among males compared to females. Endobronchial washings were able to correctly diagnose 35 out of 76 malignant cases in present study with sensitivity of 46%. While out of 70 benign cases, 64 were correctly identified as benign on endobronchial washings with specificity of 91%. Cytological and histological concordance was achieved in 99 cases of the total 146 cases with diagnostic accuracy of 67%. There has been ongoing debate regarding the routine use of endobronchial washings. Previous studies by Zainudeen F *et al.*, and Rawat J *et al.*, obtained almost similar results for sensitivity of endobronchial washing which was 51.9% and 47.6% respectively.^{14,15} While studies by Mrudula K *et al.*, and Abbasi F *et al.*, had achieved much lower sensitivity of 11.8% and 32.1% respectively.^{16,17} However Goel S *et al.*, and Khandelwal R *et al.*, had achieved a higher sensitivity of 60% and 70.8% respectively, which differed from the findings of this study.^{1,18} Table-II is showing comparison of sensitivity, specificity and diagnostic accuracy of present study with previous studies. The sensitivity and diagnostic accuracy in this study is therefore very low, which is comparable to the results of most studies done in the region.

Adenocarcinoma was the most prevalent malignancy in our study, accounting for 43.4% of the cases, followed by squamous cell carcinoma (34.2%) cases which is in agreement with Mrudula K *et al.*, and Reddy A *et al.*, in which adenocarcinoma was diagnosed in 54% and 34% cases and squamous cell carcinoma was identified in 27% and 31% cases.^{16,19} In some other studies squamous cell carcinoma was the most common type. In Goel S *et al.*, and Khandelwal R

et al., squamous cell carcinoma was diagnosed in 74% and 45% cases while adenocarcinoma was present in 25% and 16% cases respectively.^{1,18} Possible cause of more prevalence of lung adenocarcinoma in our population could be exposure to environmental toxins like asbestos, radon, air pollution, and diesel exhaust, which can be inhaled even by non-smokers.

Endobronchial washings is a minimally invasive, cost-effective procedure that requires less technical expertise compared to endobronchial biopsy. This study aimed to evaluate whether the diagnostic sensitivity of endobronchial washings has improved sufficiently to serve as a viable alternative to endobronchial biopsy in the diagnosis of lung malignancies. However, the findings revealed that the sensitivity of endobronchial washings remains significantly lower than that of biopsy. Consequently, it is suggested that further studies should be conducted to assess the sensitivity and diagnostic accuracy of other non-invasive cytological techniques such as endobronchial brushings which may potentially serve as effective alternatives to endobronchial biopsy in the detection of lung cancers.

LIMITATION OF STUDY

This study is limited by a relatively small sample size and low sensitivity, likely attributable to sampling errors, inflammation, and the presence of debris. Our results demonstrate that endobronchial biopsy remains the most reliable modality for diagnosing endobronchial lesions. In contrast, cytological analysis from endobronchial washings appears to offer limited diagnostic value. Additionally, accurate tumor subtyping essential for guiding appropriate therapy, cannot be consistently achieved through endobronchial washings alone.

CONCLUSION

Based on the results obtained, it has been observed that bronchial washings cytology demonstrated a relatively low sensitivity when it comes to the diagnosis of lung tumors. Therefore, it cannot be used as a reliable test for diagnosis of lung malignancies. Furthermore, a combination of both bronchial washings and bronchial brushings could be employed together in order to increase the sensitivity and accuracy of lung tumor detection, ultimately improving the likelihood of early and precise diagnosis.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

HMHA & MUR: Data acquisition, data analysis, critical review, approval of the final version to be published.

BP & AA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

UAS & WAK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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