Evaluation of the diagnostic yield of lung cancer on various Bronchoscopic modalities.

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ABSTRACT

Background: The application of cytological techniques in identifying malignant respiratory tract lesions has been widely praised as a significant achievement. Flexible fiberoptic bronchoscopy has greatly transformed respiratory cytology, making procedures such as bronchial brushings, broncho-alveolar lavage, and bronchial forceps biopsy more convenient, accessible, and popular.

Methodology: All the suspected cases of lung cancer from 1st Jan, 2020 - 31st Dec, 2022 fulfilling inclusion criteria who have undergone flexible bronchoscopy in our center have been analyzed and enrolled in the study.

Results: Out of 90 patients, 85 were found to be malignant. Squamous cell carcinoma was the most common carcinoma (31.1%) followed by adenocarcinoma (26.7%), non-small Cell Lung Carcinoma (17.8%) and small cell carcinoma (12.2%), majority of the cases were of 6-7th decade of life and were smoker. Sensitivities of Bronchoalveolar Lavage (BAL), Bronchial brush, Endobronchial forceps Biopsy (EBB), Transbronchial Lung Biopsy (TBLB) and Transbronchial Needle Aspiration (TBNA) were found to be 32%, 87%, 83%, 55% and 69% respectively. Diagnostic accuracy of BAL, bronchial brush, EBB, TBLB and TBNA were found to be 36%, 87%, 83%, 55% and 61% respectively.

Conclusion: With a greater sensitivity (87%) and diagnostic accuracy (87%), bronchial brushing shows great promise as a convenient cytological technique suitable for screening ambiguous cases and early detection of lung cancer, as it saves the time required for processing biopsy samples.

Keywords: Bronchial Brush; Bronchoalveolar lavage; Diagnostic accuracy; Endobronchial forceps biopsy; Fiberoptic bronchoscopy; Lung cancer.

INTRODUCTION

Lung cancer is one of the common cancers worldwide and is the commonest cancer in Nepal, with an incidence of 16%.[1] It is the most common cancer in men (18% of new cases diagnosed) and third most common cancer in women (7.7%) in Nepal.[2] The increase in the incidence of lung cancer follows the increasing adoption of cigarette smoking. The incidence of lung cancer among people who never smoked in Asia is high compared with their Western counterparts.[3] Epidemiological studies have shown that lung cancer in never-smokers is consistently more common in females than in males. 83% of female lung cancer cases in eastern and southern Asia, are never-smokers, compared to 15% in the USA.[4]

Early and precise diagnosis of lung cancer is vital for effective treatment and improved patient outcomes. Bronchoscopy, a minimally invasive procedure, plays a crucial role in diagnosing lung cancer by allowing direct visualization and sampling of suspicious lesions within the airways and lung parenchyma. A diverse range of cytological samples, such as bronchial washings, bronchial brushings, and bronchoalveolar lavage, can now be collected for diagnostic purposes. Moreover, transbronchial fine-needle aspiration can be conducted during fiberoptic bronchoscopy, thus avoiding the need for more invasive open biopsies.[5] The sampling techniques performed for histopathological diagnosis of lung cancer include endobronchial forceps biopsy and transbronchial lung biopsy for more peripheral tumors.[6] Though histopathological diagnosis is considered the gold standard for diagnosis of lung tumors, it has certain drawbacks such as invasive procedure, time consuming and more expertise is required. The yield is higher in patients with endoscopically-visible tumors than those not visible endoscopically.[7] Thus, this study is conducted to evaluate the diagnostic yield of bronchial brushings,

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transbronchial needle aspiration, bronchial biopsy and bronchoalveolar lavage in diagnosing lung cancer, to share early experiences with the use of bronchial brushings, TBNA, BAL and bronchial biopsy for lung cancer diagnosis such as : discussing the practical application of each procedure, evaluating how effectively these procedures detect lung cancer, enhancing the understanding of the effectiveness and utility of these diagnostic modalities in clinical practice, providing a comprehensive overview of the experiences and insights from our center and to identify the common types of lung cancer.

METHODS

This is three years (1st Jan, 2020 - 31st Dec, 2022) retrospective study conducted in the department of Pulmonary, Critical Care and Sleep Medicine at B.P. Koirala Institute of Health Sciences, Dharan. 90 patients with clinical and radiological suspicions of lung cancer were included in the study and the patients who were feasible of Ultrasound guided and CT-scan guided lung biopsy were excluded. The study protocol was submitted for ethical approval to the Institutional Ethical Review Board (IERB) and ethical clearance to conduct the study was obtained before doing the study.

The results were broadly categorized into malignant, benign, suspicious and inadequate. The malignant cases were further classified as Non Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC) , with NSCLC further divided into Adenocarcinoma and Squamous Cell Carcinoma. In some cases, where cytological distinction between squamous cell carcinoma and adenocarcinoma were not possible, were classified under non-small cell carcinoma and those where further tumor typing could not be done at all were classified simply as positive for malignancy. Unsatisfactory and inadequate smears were those which showed poor cellularity, degenerated cells, too much blood or necrotic debris. All the cases which were unequivocally positive on any test (BAL, TBLB, EBB, Brushing Cytology and TBNA cytology) were considered malignant (True positives). True negatives were the cases which were both cytologically and histologically benign or negative for malignancy. Any case with positive on cyto-diagnosis later which on histopathology turned out to be benign/negative was labeled as false positive. False negative was a case diagnosed benign or negative for malignancy on cytology but later on histopathology turned out to be malignant.

Procedure Details: After taking informed and written consent, patient preparation was done with 2% xylocaine used as nebulization or aerosol spray. Premedication was done with 1mg of midazolam and 20 mcg of fentanyl. Additional 2 ml of 2% lignocaine were instilled through the bronchoscope for topical bronchial anesthesia. The bronchoscope was inserted via trans-nasal route in about 85% of cases, while in the remaining cases, the transoral route was used. When the tumor was visible with bronchoscope, Bronchial washing was obtained by aspiration of any secretion and instillation, followed by immediate aspiration of two-three aliquots of 20 ml of sterile isotonic 0.9% saline solution. Following this, Endobronchial biopsy was performed with biopsy forceps, at least three biopsies were obtained from the center of the most abnormal area and the specimens were immediately fixed in 10% formalin. Using a cytology brush, brushing specimens were taken from the surface of bronchoscope-visible lesions. Brushing samples were smeared on clean glass slides and immediately fixed in 95% ethanol for cytological examination. At least six smeared samples from the brushing were obtained from each patient. When the tumor was not bronchoscope-visible, BAL was performed by instilling aliquots of 20 ml sterile isotonic 0.9% saline solution and aspirating by suction into a plastic specimen trap. Using a cytology brush, brushing specimens were taken blindly from anatomical segments suspected to be involved with tumors, as determined by chest CT. Transbronchial biopsy using biopsy forceps guided by chest CT findings was performed. Transbronchial needle aspiration was done in visible endobronchial lesion, widened main carina (station 7 lymph node), secondary carina or at the area of 4R station lymph node. TBNA cytology samples were smeared on clean glass slides and immediately fixed in 95% ethanol for cytological examination. At least six smeared samples from the TBNA cytology.

RESULTS

Majority of the positive cases were found in females. The age of the patient ranged from 30 to 90 years with 73.3% patient was in 61 to 80 age group (Table no.1) and 44% male patients were positive for malignancy whereas 49% female patients were positive for malignancy as shown in Table no. 2. The commonest tumor type was Squamous cell carcinoma 28 (31%) followed by Adenocarcinoma 24 (26.7%) as shown in Figure 1. Squamous cell carcinoma was common in both male and female patients. Majority of patients were smokers with a history of exposure to indoor air pollution via biomass fuel exposure (74%).

Table No.1: Age distribution of lung cancer

Age	Frequency	Percent (%)
30-40	4	4.4
41-50	5	5.6
51-60	12	13.3
61-70	36	40.0
71-80	30	33.3
81-90	3	3.3
Total	90	100.0

Table No.2: Sex wise distribution of lung cancer

No.	Sex	No of cases	Positive for malignancy (n,%)	Negative for malignancy (n,%)
1.	Male	42	40 (44.44%)	2 (2.22%)
2.	Female	48	44 (48.88%)	4 (4.44%)
	Total	90	84	6

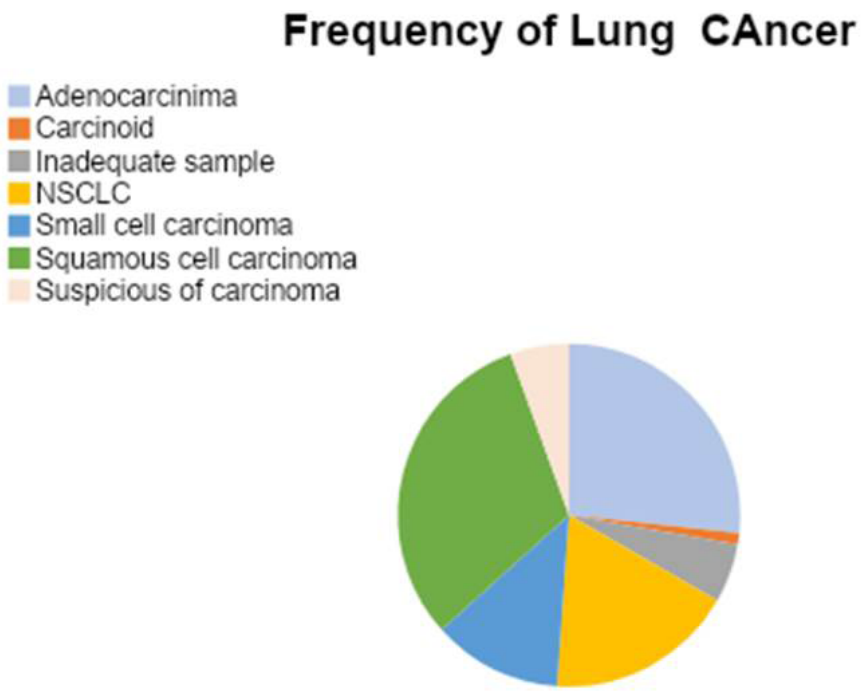

Figure 1: Frequency of different types of lung cancer

Table No.3: Frequency of different types of tumors in male and female.

		Final Diagnosis							Total
		Adenocarcinoma	Carcinoid	Inadequate sample	NSCLC	Small cell carcinoma	Squamous cell carcinoma	Suspicious of carcinoma	
Sex	Female	13	1	3	6	8	15	2	48
	Male	11	0	2	10	3	13	3	42
Total		24	1	5	16	11	28	5	90

Table No.4: Statistical analysis of various bronchoscopy techniques

Specimen	True Positive	False Positive	True Negative	False Negative	Total
BAL	16 (30.18%)	0	3 (5.66%)	34 (64.15%)	53
EBB	33 (80.48%)	0	1 (2.4%)	7 (17.07)	41
TBLB	16 (51.6%)	1 (3.2%)	1 (3.2%)	13 (41.9%)	31
Bronchial Brush	40 (83.33%)	1 (2.08%)	1 (2.08%)	6 (12.5%)	48
TBNA	22 (61.11%)	4 (11.1%)	0	10 (27.77%)	36

Table no. 4 elaborates the broad categorization of different specimens on microscopic examination and different specimen yields were compared with the final diagnosis of the patient to calculate the true positive, false positive, true negative and false negative. In BAL cytology 16 cases were true positive whereas false negative was 34 and true negative were found in 3 cases and no cases of false positive. In Brush cytology 40 cases were true positive, 6 cases were false negative and one case each in true negative and false positive. In TBNA cytology, 22 cases were found to be true positive, 4 cases were false positive and 10 cases were false negative and no cases of true negative. In EBB, 33 cases were true positive, no cases of false positive, 7 cases were false negative and 1 case was true negative. In TBLB, 16 cases were found to be true positive, 13 cases of false negative and 1 case each in both false positive and true negative.

Table no.5: Comparisons of indices of various techniques

Method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic Accuracy (%)
BAL	32%	100%	100%	8%	36%
EBB	83%	100%	100%	13%	83%
TBLB	55%	50%	94%	7%	55%
Bronchial Brush	87%	50%	98%	17%	87%
TBNA	69%	0%	85%	0%	61%

Table 5 compares the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy for BAL, EBB, TBLB, Bronchial brush, and TBNA. Bronchial brushing and endobronchial forceps biopsy were found to be the best screening test with highest diagnostic accuracy (87% and 83% respectively).

DISCUSSION

Lung cancer is a significant public health concern, causing a considerable number of deaths globally. GLOBOCAN 2020 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer (IARC) show as lung cancer remains the leading cause of cancer death, with an estimated 1.8 million deaths (18%) in 2020.[8]

Cancer accounts for 9% of total annual deaths and is the third leading cause of noncommunicable disease death in Nepal.[9] Lung cancer is one of the common cancers worldwide, and is the commonest cancer in Nepal, with an incidence of 16%.[1]

In the present study 90 Patients with suspected lung cancer were evaluated for the diagnostic yield of lung cancer on various Flexible Bronchoscopic modalities. In our study 84 (93%) were diagnosed as malignancy by various modalities which was higher than the study conducted by Khandelwal R et al and Tarun P Kotadia.[5,7] We observed that greatest prevalence of lung cancer was found in sixth followed by seventh decade which was similar in the study conducted by Khandelwal R et al.[5] Most of the other studies have reported 6 decades and 5 decades as commonest age group for lung cancer.[10,11]

In the study conducted by Neerav Tyagi found that out of 63 cases of lung cancer, 56 (88.88%) were males and 7 (11.12%) were females.[12] Also in most of the studies the M:F ratio in malignant cases was found to be 3.2:1 which was different from our study finding as out of 84 malignancy case 40 (44.44%) were male and 44 (48.88%) were females.[5,11,13] The different findings in our study may be generally attributed to differences in gendered smoking patterns or the women in our community of this age are mostly more exposed to firewood smoke previously or the frequency of patient presenting with suspected lung cancer were more female. As Lung cancer is often intimately linked to tobacco smoking and inflammation, in our study we found that among the total case of lung cancer 74% of the patients were smoker which was comparable to the study done by Siegel RL and Walser T et al. [14,15]

Squamous cell carcinoma was the most common malignancy in our study constituting 28 cases (32.94%), followed by adenocarcinoma 24 cases (28.23%), NSCLC 16 cases (18.82%) and small cell Carcinoma 11 cases (12.94%) which was similar to finding from the various studies[7,16,17,18] while some others have found small cell carcinoma more common than adenocarcinoma.[5,13,19] The sensitivity, specificity and accuracy rate of endobronchial biopsy was 83%, 100% and 83% respectively, which is quite comparable to the study conducted by Paulose et al, Tarun P Kotadia and also comparable to study done by Dhungana A.[20,7,21]

In our study, we observed 64.15% false negative cases on bronchial wash which was higher than the study done by Ruchee et al whereas we found 12.5% false negative cases on bronchial brush which was comparable to the finding shown by Tarun P Kotadia et al and lower than the findings shown by Ruchee et al.[7,5] The reason for missing the lesions on cytology could be due to several factors like secondary inflammation, non-representative material and suboptimal yield. We reported only 1 (2.08%) false positive case on bronchial brush and no false positive cases were found on BAL and EBB. Similar comparable finding was found in the study done by Ruchee et al, Ahmad et al and Sareen R.[5,10,22] In contrary higher false positive case 10 (5%) on brushing was observed by Bodh et al and Rao et al have also observed 4 (6.8%) false positive cases.[13,23] False positive cases may be due to reactive atypia secondary to inflammation, squamous metaplastic cells and basal cell hyperplasia.

In the present study, endobronchial biopsy was found to be false negative in 7 (17%) which was similar to findings conducted by Ruchee et al 5 (4.6%), Jones et al (17%), Bodh et al and Karahalli et al.[5,19,14,24] Bodh et al diagnosed 8 cases of adenocarcinoma on brush in biopsy negative cases, especially in compressive type

of lesions on bronchoscopy.[13] This could be due to rather small and shallow samples of tissue obtained with the small biopsy forceps used in this procedure. We reported 6 (5.6%) biopsies as inadequate. Jones et al have reported inadequate biopsy rate to be less than 1%.[19] The sensitivity, specificity and accuracy rate of Trans bronchial lung biopsy (TBLB) was 55%, 50% and 55 % respectively and false negative was in 13 (41.9%) and false positive in 1 (2.08%). In our study, we observed the diagnosed yield of TBLB was 55% which was comparable to the study finding shown by Jasna Tekavec et al and Hsiao CJ et al. [25,26] However, the study conducted by Ping Shi Zhu et al and Tang CC, Hsiao CJ, Chen H et al have shown that the diagnostic value can be increased up to 73.0% with BAL and TBLB together.[27,28] The sensitivity, positive predictive value (PPV) and accuracy rate of Transbronchial Needle Aspiration (TBNA) was 69%, 85% and 61% respectively in our study which was slightly higher than those reported by Robet chin et al who found the overall yield for malignancy was 57% and 46% yield seen in the study done by Diette and coworkers.[29,30] In contrast to this Piedonat Burno et al in their study on cytology on TBNA showed a positive predictive value of 1 and 78% diagnostic accuracy. Much of the literature regarding TBNA describes varying numbers of aspirations performed per patient. Most reports do not provide details regarding the number of aspirates in relationship to yield and have predominantly retrospective, rather than prospective designs.

LIMITATIONS

This is a single center-based study with moderate sample size and involvement of multiple centers with more patients would have improved the statistical power of the study.

CONCLUSION

Bronchoscopy guided brush cytology is a simple, safe and inexpensive procedure and is comparable to bronchial biopsy for diagnosis of lung carcinoma and in addition it reduces the time required for processing biopsy samples.

CONFLICT OF INTEREST:

No

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None

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