ISSN: 0975-3583,0976-2833 VOL13, ISSUE 01, 2022

Diagnostic Value of Bronchoalveolar Lavage in Lung Malignancies and Its Correlation with Bronchial Biopsy

Sunita Haobam[1], Urvashi Chongtham[2], Khaidem Mani Singh[3], Urmila Thiyam[4]

[1]Associate Professor, Department of Pathology, JNIMS, Imphal, Manipur, India
[2]Associate Professor, Department of Microbiology, JNIMS, Imphal, Manipur, India
[3]Associate Professor, Department of Radiodiagnosis, JNIMS, Imphal, Manipur, India
[4]Associate Professor, Department of Pathology, JNIMS, Imphal, Manipur, India.

Abstract

Background: Lung cancer is the most common diagnosed cancer in the world and one of the leading causes of death due to cancer in both men and women. Early diagnosis of cancer has a pivotal role in reducing death rate due to lung cancer. Majority of the lung cancers are diagnosed in small biopsies or cytologic samples.**Aims:** The objectives of this study were (1). To determine the diagnostic reliability of bronchoalveolar lavage (BAL) cytology in the diagnosis of lung cancer. (2) To assess the cytological and histopathological correlation of lung tumours.**Material and Methods:**The study was done in the department of pathology, JNIMS, Imphal. All patients who were clinically and radiologically suspected of lung malignancies and underwent BAL and transbronchial biopsy between the period March 2016 and October 2018 were included in the study.**Results:**Out of a total of 100 clinically suspected lung cancer patients, tumor was found in 15 cases by biopsy and in 11 cases by BAL. Sensitivity of BAL was found to be 66.66% and specificity of 97.43%.BAL had a positive predictive value of 90.90% and a diagnostic accuracy of 88.88%.**Conclusion:**BAL is a reliable diagnostic tool in detecting neoplastic and non neoplastic lesion in central as well as in accessible lesions. A high diagnostic accuracy is achieved by a combination of BAL and bronchial biopsy.

Keywords: Bronchoalveolar lavage cytology, histology, lung cancer.

Corresponding Author: Dr. Urmila Thiyam, Associate professor, Department of Pathology, JNIMS, Imphal, Manipur, India.Email ID: urmilath2014@gmail.com

Introduction

Lung cancer is the most common cancer in the world and one of the leading cause of cancer mortality in both men and women.[1]It constitutes about 17% of the total new cancer cases in males and 23% of the total death due to cancer.[2] Flexible fibreoptic bronchoscope revolutionized respiratory cytology as procedures such as bronchial brushing (BB), bronchoalveolar lavage (BAL), and bronchial biopsy became more easy, accessible and popular.[3]Bronchoalveolar lavage (BAL) is a method to recover sample of cells that line the airways and alveoli.[4] Around 70% of lung malignancies are diagnosed in small biopsies or cytologic samples.[5] Particularly in patients with advanced-stage disease, the subtyping of NSCLC in cytologic samples and small biopsies is of increasing significance due to new therapeutic options and strategies.[5,6] The aim of our study was to determine the diagnostic reliability of bronchoalveolar lavage cytology(BAL) using histopathological examination of transbronchial biopsy as gold standard in the diagnosis of lung carcinoma and also to assess the cytological and histopathological correlation of lung tumors.

Material and Methods

The study was carried out in the department of pathology at Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India. All patients who were clinically and

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 01, 2022

radiologically suspected of lung malignancy or infectious pathology and underwent BAL were included in the study. Simultaneous BAL and Transbronchial biopsy were obtained in patients with strong suspicion of malignancy. A total of 100 cases were evaluated in our institute between the period of March 2016 to Oct 2018. Patients with heart complications (recent MI), unstable angina or dysrhythmias or patients with respiratory distress, coagulation disorders and un-cooperative were excluded from the study.

Bronchoalveolar lavage samples were received as 20 ml aliquots of normal saline in sterile vials. It was centrifuged at 1500 rpm for 10 minutes. 4 slides were prepared from the cell concentrate. 2 slides were stained with May-Grunwald Giemsa. Two alcohol fixed slides were stained with papanicolaou stain and additional slides stained with Ziehl Neelsen -stain when clinically suspected. The bronchial biopsies size and number of bits were noted. The tissues were processed and sections cut at 4 – 5 micron thickness and stained with hematoxylin and eosin. The cytologic smears were grouped into inflammatory smear, dysplastic /a typical, suspicious and malignant cells. The sensitivity, specificity, positive predictive value and negative predictive value and diagnostic accuracy of BAL were obtained using histopathology of bronchial biopsy as gold standard.

Results

The study group comprised of 100 patients in which lung cancer was found in 15 cases. Male to female ratio was 1:2. The maximum number of malignancy were seen in the age between 61-71 years and the mean age of primary lung cancer was 66.83 years. [Table 1]

Majority cytological diagnosis comprised of non-specific inflammation (69%) with malignancy accounting for 11 % [Table 2]. Diagnosis of malignancy or suspicious cases through BAL and bronchial biopsy were available in 54 /100 cases. In our study BAL cytology had a 73.3% correlation with histology for malignant lesions [Table 3]. Histologically there was an equal distribution of squamous cell carcinoma and adenocarcinoma of 40% each followed by small cell carcinoma of 13.3%and poorly differentiated carcinoma of 6.6% [Figure 1].

In comparision with bronchial biopsy, the statistical evaluation of BAL cytology are as follows:

1. Sensitivity – 66.66%
2. Specificity – 97.43%
3. False positive rate -1(2.56%)
4. False negative rate -5(33.33%)
5. Positive predictive value 90.90%
6. Negative predictive value 88.37%
7. Diagnostic accuracy of BAL -88.88%

The diagnostic accuracy for cytologic typing of tumor for Squamous cell carcinoma and adenocarcinoma [Figure 2] were 66.66% each. For small cell lung cancer [Figure 3] there was 100 % concordance with histology.

Table 1: Age and sex distribution of malignant cases.

Age group	Male	Female	Total	Percentage
31-40	1	0	1	6.67%
41-50	0	0	0	0
51-60	0	2	2	13.33%
61-70	1	6	7	46.67%
71-80	1	2	3	20%
81-90	2	0	2	13.33%
Total	5	10	15	100%

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 01, 2022

Table 2: Distribution of lesion on cytological basis.

Cytomorphological diagnosis	No.of cases	Percentage
Malignant	11	11%
Suspicious	1	1%
Dysplasia	8	8%
Tuberculosis	5	5%
Non specific inflammation	69	69%
No pathological change	6	6%
Total	100	100%

Table 3: Correlation of BAL cytology with histopathology for malignancy.

Tumour subtype	BAL No.	Percentage	Biopsy No.	Percentage
Small cell carcinoma	3	27.27%	2	13.33%
Squamous cell carcinoma	4	36.36%	6	40%
Adenocarcinoma	4	36.36%	6	40%
Poorly differentiatedcarcinoma	-	-	1	6.67%
Total	11		15	

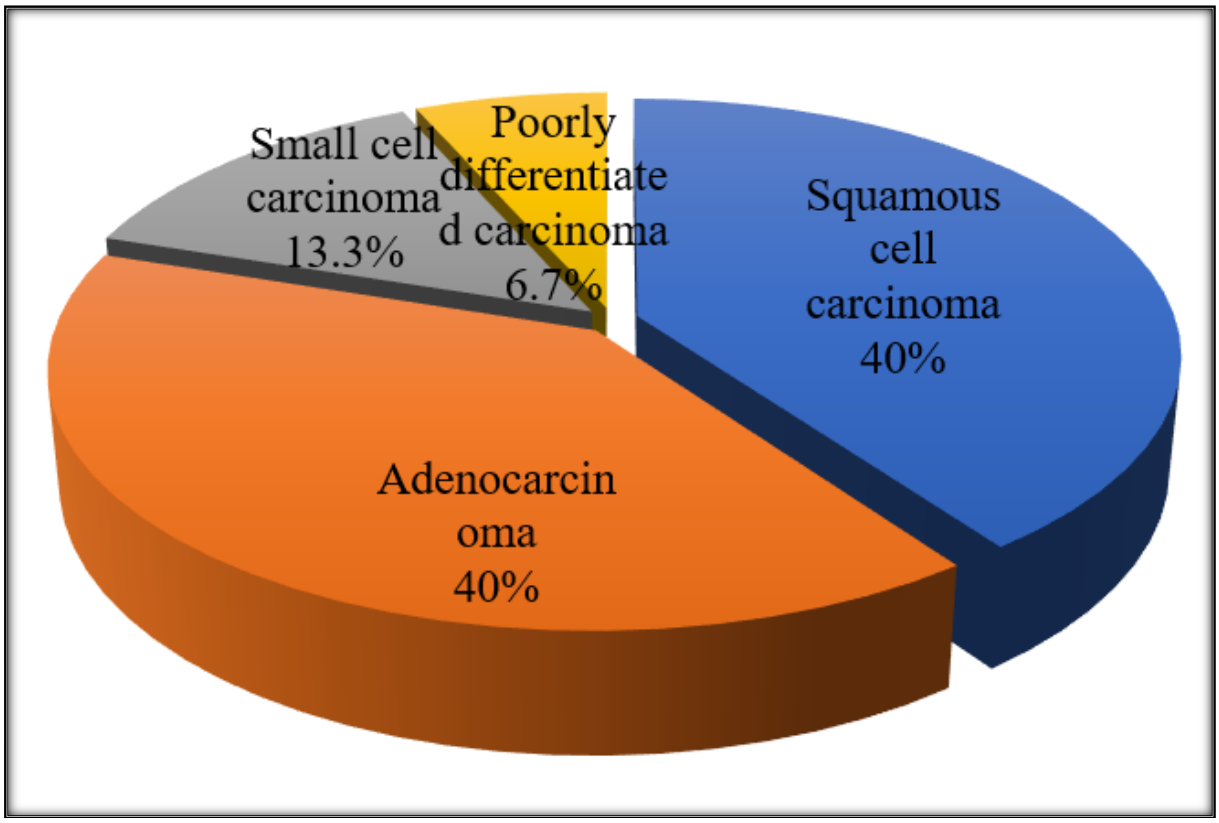

Figure 1: Frequency of lung carcinoma according to histological subtype.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 01, 2022

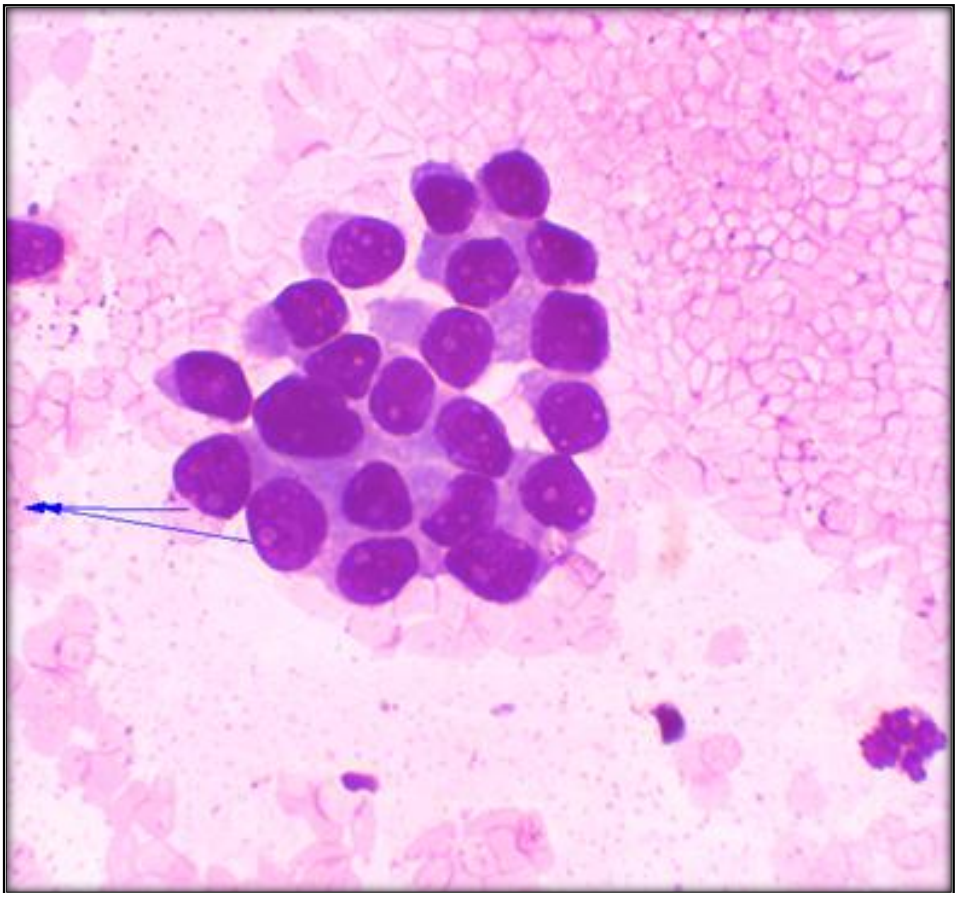

Figure 2: Cluster of tumour cells with prominent nucleoli in adenocarcinoma (MGGX 400)

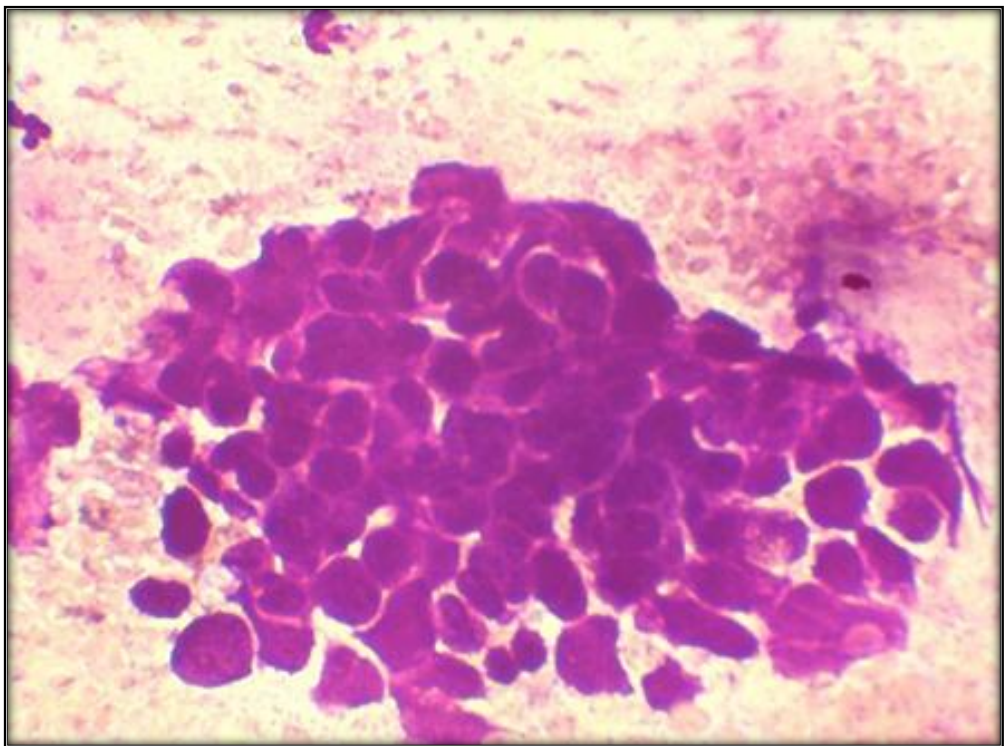

Figure 3: Tumour cells with speckled chromatin and nuclear moulding in small cell carcinoma (MGGX400).

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 01, 2022

Discussion

Pathological diagnosis of bronchial carcinoma has become more challenging with new developments in the field of oncology.[5,7] Travis et al,[5] stated that vast majority of clinically suspected lung cancer are diagnosed based on small biopsy and cytology specimens.

BAL and bronchial biopsy are valuable methods for diagnosis of bronchogenic carcinoma but the literature reports a low sensitivity for washing procedure. With flexible bronchoscopy, for centrally located bronchogenic carcinoma the sensitivities of BAL range from 31 To 78%, while that of peripherally located tumor ranged from 12 to 65%.[8] Renard SI observed that BAL specimens could detect malignancy in 69%.[9]

In our study the overall sensitivity for both centrally and peripherally located lung tumor was 66.66%which is concordant with the findings of Troung et al.[10] However, Annette Zimper et al,[11] reported a high sensitivity rate of 83%. They stated that the diagnostic yield of BAL was statistically significantly higher in the second cytological specimen, when BAL was performed both before and after forceps biopsy. The reason being the biopsy procedure led to the detachment of the tumor cells in the second BAL specimen. A Fernandez et al,[12] stated that diagnostic yield of bronchial washing can be profoundly increased by combining the findings of cytological samples both before and after biopsy with the only drawback of excessive blood in the second bronchial biopsy specimen. The diagnostic sensitivity of bronchial biopsy in diagnosing lung cancer ranges from 65 to 83%.[13,14] Although histopathological diagnosis of bronchial biopsy is considered the gold standard, it has certain drawbacks, it is an invasive technique and requires more expertise. The yield of tumor tissue is higher in patients with endoscopically visible tumor as compared to those that are not visible.[15]Diagnostic ratio of bronchoscopies is lower for peripheral tumors.

Cytological methods as bronchial brushing, washing or BAL samples obtained from relevant lobar segments has played a crucial role in diagnosing more peripheral lesions that cannot be visualized. BAL is a valuable diagnostic tool in detecting peripheral primary malignant neoplasm.[16]

The accuracy of cytological tumor typing in our study was highest for small cell carcinoma (100%) followed by 66.66% for Squamous cell carcinoma and adenocarcinoma. Difficulties in cytological tumor typing are particularly seen in poorly differentiated carcinomas. Various reasons accounting for low accuracy of cytological tumor typing were, paucity of cells in BAL specimens, low quality of preservation of material and inflammatory background.[17,18]

In our study there was a false negativity of 33.33%, which was almost similar to another study by Fariba et al,[19] who had reported a false negative rate of 33.8%. The reason for a high percentage of false negative cases in our study were due to superadded inflammation, on representative material and paucity of cells in the lavage fluid. Gaur DS et al,[20] on the other hand reported a significantly high rate of false negative index of 60.60%.

As the cytological yield through BAL depends predominantly on the cells exfoliated from the malignant tumor, the sample adequacy depends on certain vital factors.

1. The degree of differentiation of the malignant tumor.
2. Preservation of morphology of the cytological material acquired
3. Technical skill of the pulmonologist, who is collecting the lavage fluid from the bronchus.

Usually the poorly differentiated, anaplastic lesions have more dyscohesive cells as compared to the well differentiated lesions and therefore exfoliate larger number of cells into the bronchial cavity.[21] Further these exfoliated cells start developing degenerative changes while they are lying in the bronchus, thus causing them to lose their morphological details which are important for differentiating them from non malignant cells shed off by the normal bronchial epithelial lining.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 01, 2022

If the technique of the pulmonologist is improper the sample retrieved might be less in amount and may have inadequate cytological material than expected, thus again increasing the chances of false negative results.[3,10]

We had a low false positive rate of 2.56%. False positive results could be chiefly due to misinterpretation of smears due to cellular changes associated with chronic inflammatory disorders such as pneumonia, TB, bronchiectasis (misinterpretation of cuboidal epithelial cells as small cell carcinoma) squamous metaplasia and alveolar atypia in the background of lung fibrosis.

False positive reporting has a very unfortunate consequences for patients, therefore it is advised by some to give "under reporting" instead of "over reporting" of suspicious cases.[22]

If cytology is suspicious for malignant cells, a repeat biopsy along with clinical, radiological and bronchoscopic findings, correlation is necessary for ruling out malignancy.

Wongsurakiat et al,[23]observed that the diagnostic yield of BAL was affected by the size and segmental location of the tumor. While in the study of Pirozynski the diagnostic yield of BAL for peripheral,[24] primary lung cancer was influenced by the type of cancer and size of tumor. Highest yields were seen in adenocarcinoma (59.2%) and bronchioloalveolar carcinoma (80%). He stated that average size of tumor in the group with accurate cell typing was 4.9+1.8 cm while in patients with non-diagnostic BAL, the average size was 2.6+1.2 cm.

BAL is regarded as a very safe procedure. Side effects are more or less comparable to regular fibrebronchoscopy unless invasive procedure like transbronchial lung biopsy is performed. The overall complication rate with BAL is reported to be 0.3% as compared to 7% with transbronchial lung biopsy and 13% when using open lung biopsy.[25]Minor side effects of BAL include coughing during lavage, fever and chills some hours after lavage which is usually treated with simple antipyretics.

Conclusion

BAL is a reliable tool in detecting neoplastic and non-neoplastic lesions in central as well as peripheral sites. A combination of both BAL and bronchial biopsy significantly increases the diagnostic accuracy. However, it may be unavoidable to get a high false negative diagnosis due to superadded inflammation, paucity of material in the BAL or due to improper technique of the pulmonologist.

References

1. M. Parkin, J.E. Tyezynski, P. Boffelta et al," Tumours of the lung", in: WD Travis, E Brambill, H.K. Muller-Hermelink and C.C Harris, Eds, World health organization Classification of Tumours. Pathology and genetics of Tumors of lung. Pleura, Thymus and Heart, IARC Press Lyon,2004:.9-124.
2. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D, Global cancer statistics.CA cancer J Clin,2011;61(2):69-90
3. Johnston WW, Elson CE, Respiratory tract. In Bibbo M editor. Comprehensive cytopathology.2nd ed. Philadelphia: W.B. Saunders company;1997:325-401.
4. A.M. Hoffman AM, Bronchoalveolar lavage technique and cytological diagnosis of small airway inflammatory disease, Vet Clin North AM Equine Pract.2008;24(2):423-35
5. W.D. Travis, E Brambill, M. Noguchi et al," International association for the study of lung cancer/American Thoracic Society /European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma" Journal of Thoracic Oncology. Vol 6 No.2,2011: 244-85.
6. G.V. Seagliotti, P. Parikh, J. Von Pawel et al," Phase III study comparing cisplatin plus Gemcitabine with cisplatin plus pemetrexed in chemotherapy – Naive patients with

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 01, 2022

advanced –stage Non Small Lung Cancer". Journal of clinical oncology, Vol 26, No21, 2008:3543-3551.

7. K.M. Kerr," Pulmonary Adenocarcinomas: Classification and reporting "Histopathology, Vol.54, No1, 2009:12-27.
8. G. Schreiber and D.C McCroy," Performance characteristics of different modalities of suspected lung cancer: Summary of published evidence", Chest, Vol 123 No 1, 2003:115-28.
9. S.I Rennard," Bronchoalveolar lavage in the diagnosis of Cancer", Lung, Vol 168, Supp.1,1990:1035-40.
10. L.D. Truong, R.D. Underwood, S. D Greenberg and J.W. Mclarty," Diagnosis and Typing of Lung Carcinomas by cytopathologic methods" A review of 108 cases, Acta Cytologica, Vol 29. No 3,1985:379-84.
11. Annette Zimper, Antonia Park, Andrea Bier, Kundt, Sana Kolbel, Friedrich Prall, Johan C. Virchow, Andreas erbersdobler, Assessment of Diagnostic accuracy of Bronchoalveolar lavage cytology in the diagnosis of lung Tumors and contribution to the classification of Non –Small Cell Lung Cancer Entities: A retrospective clinicopathological study. Open Journal of Pathology,2013,3:107-12.
12. A Fernandez-Villar, A Gonzalez, V. Leiro, et al," Effect of different Bronchial Washing sequences on Diagnostic yield in Endoscopically visible Lung Cancer", Archives de Bronchoneumologia, Vol 42, No 6,2006:278-82.
13. Naryshkin S, Daniels J, Youung NA. Diagnostic correlation of fiberoptic bronchoscopic biopsy and bronchoscopic cytology performed simultaneously. Diagn Cytopatho.1992;8:119-23.
14. Govert JA, Dodd LG, Kussin PS, Samelson WM. A prospective comparison of fiberoptic transbronchial needle aspiration and bronchial biopsy for bronchoscopically visible lung carcinoma. Cancer 1999;(87):121-34.
15. Lam WK, So SY, Hsu C, Yu DY, Fiberoptic bronchoscopy in the diagnosis of bronchial cancer: comparison of washings, brushings and biopsies in central and peripheral tumours. Clin Onco.1983;(9):35-4 .
16. Rennard SI. Bronchoalveolar lavage in the assessment of primary and metastatic lung cancer. Respiration.1992;59(1):41-3.
17. RS Saad and JF. Silverman" Respiratory cytology Differential diagnosis and pitfalls". Diagnostic cytopathology vol38,No.4;2010:297-307.
18. J.P Crapanzano and A Saqi," Pitfalls in pulmonary cyto-pathology", Diagnostic cytopathology vol39, No.2,2011:144-154.
19. Fariba Binesh, Azarr Pirdehghan, Mohammed Reza Mirjalili, Mohammed Samet, Zahra Amini Majomerd, Ali Akhavan: Comparative Assessment of the Diagnostic value of Transbronchial lung biopsy and Bronchoalveolar lavage fluid cytology in lung cancer. Asian Pacific Journal of cancer prevention.2015, vol 16(1):201-04.
20. Gaur DS, Thapliyal NC, Kishore S. Pathak VP. Efficacy of broncho-alveolar lavage and bronchial brush cytology in diagnosing lung cancer. Journal of cytology.2007;24(2):73-7
21. Husain AN. The lung. In Kumar V, Abbas AK, Fausto N, editors. Robbins and Cotran pathologic basis of disease. 7thed. India: Sauunders: 2004:711-72
22. Ahmed A, Ahmed S. Comparison of Bronchoalveolar lavage cytology and transbronchial biopsy in the diagnosis of carcinoma of lung. J Ayub Med Cott Abbottabad 2004:16:29-33.
23. Wongsurakiat P. Wongbunnate S, Dejsomritrutai W. Diagnostic value of bronchoalveolar lavage and post bronchoscopic sputum cytology in peripheral lung cancer. Respiratory 1998,3:131-7

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 01, 2022

24. Pirozynski M. Bronchoalveolar lavage in diagnosis of peripheral primary lung cancer. Chest. 1992;102:372-4
25. H. Klech and C. Hutter. Introduction, side effects and safety of BAL. European Respiratory Journal ,1990:939.