ORIGINAL ARTICLE

Correlation of Bronchoalveolar Lavage with Transbronchial and CT Guided Biopsy in Pulmonary Disease

Himil Parikh [1], Anupama Dayal [2], Himali Thakkar [2] and Deepak Joshi [2]
[1]Sterling Hospital, Ahmedabad, [2] Department of Pathology, GCS Medical College, Hospital and Research Centre, Ahmedabad -380025, Gujarat, India.

Abstract:
Background: Bronchoalveolar lavage (BAL) is usually done in patients where clinical, radiological and routine investigations are not helpful in diagnosis. BAL cytology with histopathology can give definitive diagnosis in various diseases of lung. *Aim:* The aim of this study was to evaluate the diagnostic accuracy of BAL in pulmonary diseases when compared with endobronchial and CT guided lung biopsy. *Material and Methods*: A prospective study of 100 BAL samples over a period of two years (June 2017 to June 2019) was done in a tertiary care centre in Ahmedabad. Cytohistological correlation was done in all the cases with histopathological examination as "Gold Standard". Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of BAL was calculated. *Results:* BAL cytology revealed that out of the 100 cases, 61 cases were non-neoplastic, 13 cases were suspicious for malignancy and 26 cases were malignant while on histopathology, 29 cases were non-neoplastic, 69 cases were malignant and 2 cases were negative for any pathological lesion. BAL was concordant in 39 out of total 69 cases of lung cancer. BAL had a sensitivity of 56.5% and a very high specificity of 100% in detecting malignancy with a diagnostic accuracy of 70%. *Conclusion:* BAL cytology shows a moderate sensitivity in diagnosing pulmonary diseases, but it provides a very good specificity for malignant lesions. Thus, patients with conclusive BAL reports could reliably be started with appropriate interventions at an early stage of disease.

Keywords: Bronchoalveolar lavage, Endobronchial Biopsy, CT guided Biopsy

Introduction:

The recent Global Burden of Disease (GBD) survey data has shown that both acute and chronic respiratory diseases are prevalent in substantial number in India [1]. In many pulmonary diseases, diagnosis is not possible despite consideration of radiological, clinical and laboratory investigations. In such situations cells or tissue for pathologic examination may be required, based on which a definitive diagnosis is possible in many instances [2]. Although transbronchial biopsy has remained the gold standard in diagnosing pulmonary diseases, BAL has recently gained its fame as an important diagnostic tool for pulmonary diseases [3]. BAL is also useful in lesions situated at peripheral sites or in patients at risk of haemorrhage where bronchial biopsies cannot be performed. Bronchoscopy with BAL when used appropriately can provide the patient and clinician with a safe and potentially excellent means for diagnosis and information to help with treatment [4]. The aim of this study was to evaluate the diagnostic accuracy of BAL in diagnosing pulmonary diseases by correlating them with histopathological diagnosis by transbronchial lung biopsy and CT guided lung biopsy.

Material and Methods:

A prospective study of 100 patients was done from July 2017 to June 2019 in Department of Pathology, of a tertiary care centre in Ahmedabad. Approval was taken from Institutional Ethical Committee before commencement of the present study. All specimens for BAL cytology, transbronchial lung biopsy and CT-guided lung biopsy obtained from clinically and radiologically suspected cases of pulmonary diseases and received in the histopathology section of pathology department were included in the present study.

Patients in whom only biopsy or BAL was performed or samples with inadequate BAL or biopsy tissue specimens were excluded. Chamberlain et al [5] criteria was followed to determine adequacy of BAL specimens which is as follows:

Paucity of alveolar macrophages<10/10 hpf, extensive epithelial cells, mucopurulent exudates, numerous red blood cells or degenerating changes.

BAL fluid smears were prepared using the Thermo Scientific Cytospin 4 machine, fixed in 99% isopropyl alcohol and stained with H&E & Pap.

Biopsies were fixed in formalin, then processed in automatic tissue processor (Electra by Yorco™), embedded in paraffin wax, sectioned into 3-4µm thick sections with Leica RM2125 RT microtome and stained with H&E. Special stains and immunohistochemistry were done whenever necessary. Most common IHC markers used were Cytokeratin (CK5/6), Ttf-1 and CD 56. BioGenex polymer kits and the standard operating protocols (SOPs) provided along with the kits were used for immunohistochemistry. Both BAL smears and histological sections were examined by two pathologists and were categorized into non-neoplastic or malignant with histological typing whenever possible.

Data was entered in Microsoft Office Excel-365 and then analyzed statistically. Histopathological examination was considered as 'Gold standard' and BAL cytology was considered the index test. For statistical analysis, suspicious of malignancy and malignant categories on cytology were considered malignant.

Definitions of terms:

True Positive (T.P.): Cases where BAL cytology was able to detect malignant lesions correctly.

True Negative (T.N.): Cases where both BAL cytology and histopathological examination were negative for malignancy.

False Positive (F.P.): Cases where BAL cytology results were positive but histopathological examination was negative for malignancy.

False Negative (F.N.): Cases where BAL cytology was not able to detect malignancy and was detected on histopathological examination.

Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of BAL were obtained by following formulas:

Sensitivity=TP/TP+FN x 100

Specificity=TN/TN+FP x 100

Positive predictive value (PPV) = TP/TP+FP x 100

Negative predictive value (NPV) = TN/TN+FN x 100

Accuracy = TP+TN/Total number of cases x100

Results:

Total 100 cases were evaluated. The overall male to female ratio was found to be 4:1 while for neoplastic lung lesions, it was 5:1 (Figure-1). Most common age-group at presentation of pulmonary diseases and neoplastic pulmonary disease was 51-70 years (Figure-2). The common presenting symptoms in patients undergoing bronchoscopy were cough with fever and/or dyspnoea. Non neoplastic lesions (61%) were more common on BAL cytology whereas malignant lesions were more common on histopathology (Table 1 and 2)

Amongst 29 non-neoplastic lesions reported on histopathology, inflammatory changes (72.5%) were the most common. Adenocarcinoma (49.3%) followed by squamous cell carcinoma (37.6%) were the most common malignant lesions on histopathology (Table-2). Table-3 shows comparison of BAL with transbronchial and CT-guided lung biopsy in cases of neoplastic pulmonary lesions. Thirty-nine out of a total 69 cases of lung cancer were identified by BAL cytology. Thus, the sensitivity of BAL in detecting malignancy was 56.5%. There was no false positive case on BAL cytology and hence its specificity was 100%. NPV& PPV of BAL in neoplastic pulmonary diseases was found to be 51% & 100% respectively. Overall diagnostic accuracy of BAL to detect malignancy was 70%. BAL was concordant in all the 22 cases of non-specific inflammation (i.e.,100% concordance) found on histopathological examination. It was concordant in 1 out of 2 cases of fungal infection (i.e., 50% concordance) &1 out of 5 cases of tuberculosis (Figure-3a,3b) (i.e., 20% concordance) found on histopathological examination. Although

BAL showed only inflammatory cells in a case of non-specific interstitial pneumonia diagnosed on histopathological examination, it was considered concordant as only inflammatory cells are expected in such cases in BAL. From the 2 lesions found negative for any pathology on histopathological examination, BAL was concordant in 1 case i.e., 50% concordance rate.

There were 22 cases of peripheral lung lesions where biopsy was obtained using a CT-guided approach. Out of these 22 cases, 17 cases were malignant and 4 cases were non neoplastic. Squamous cell carcinoma (Figure 3c, 3d) and adenocarcinoma (Figure 3e, 3f) were most common malignant lesions and were observed in equal frequency (31.8%). In 15 out of 22 cases, BAL cytology showed concordant findings.

Table No.1: Total distribution of pulmonary diseases on bronchoalveolar lavage

Disease	No. of patients
Non-neoplastic	61
Suspicious for malignancy	13
Malignant	26

Table No. 2: Spectrum of Pulmonary lesions on histopathological examination (n=100)

	Lesions	No. of cases
Non neoplastic Lesions (n=29)	Inflammatory changes	21
	Tuberculous inflammation	5
	Fungal infection	2
	Nonspecific interstitial pneumonia	1
Neoplastic lesions (n=69)	Adenocarcinoma	34
	Squamous cell carcinoma	26
	Small cell carcinoma	4
	NSCLC, NOS	2
	Adenosquamous carcinoma	1
	Spindle cell tumour	1
Negative for any pathological lesion		2
Total		100

Table No. 3: Comparative assessment of bronchoalveolar lavage with Transbronchial and CT guided lung biopsy in neoplastic pulmonary diseases

	Transbronchial lung biopsy				
		Malignant	Non Malignant	Total	
BAL	Malignant	39 (True positive) (TP)	0 (False Positive) (FP)	39	100% Positive predictive value (TP/TP+FP)
	Non malignant	30 (False negative) (FN)	31 (True negative) (TN)	61	50.8 % Negative predictive value (TN/TN+FN)
	Total	69	31	100	
		56.5 % Sensitivity (TP/TP+FN)	100% Specificity (TN/TN+FP)		

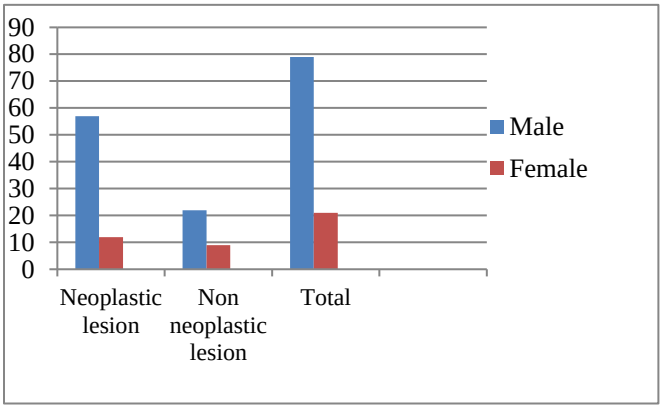

Figure 1: Gender Distribution

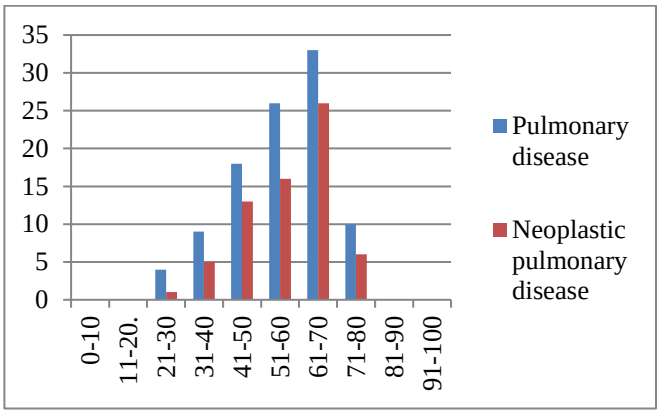

Figure 2: Distribution of age groups in pulmonary disease overall and neoplastic pulmonary disease

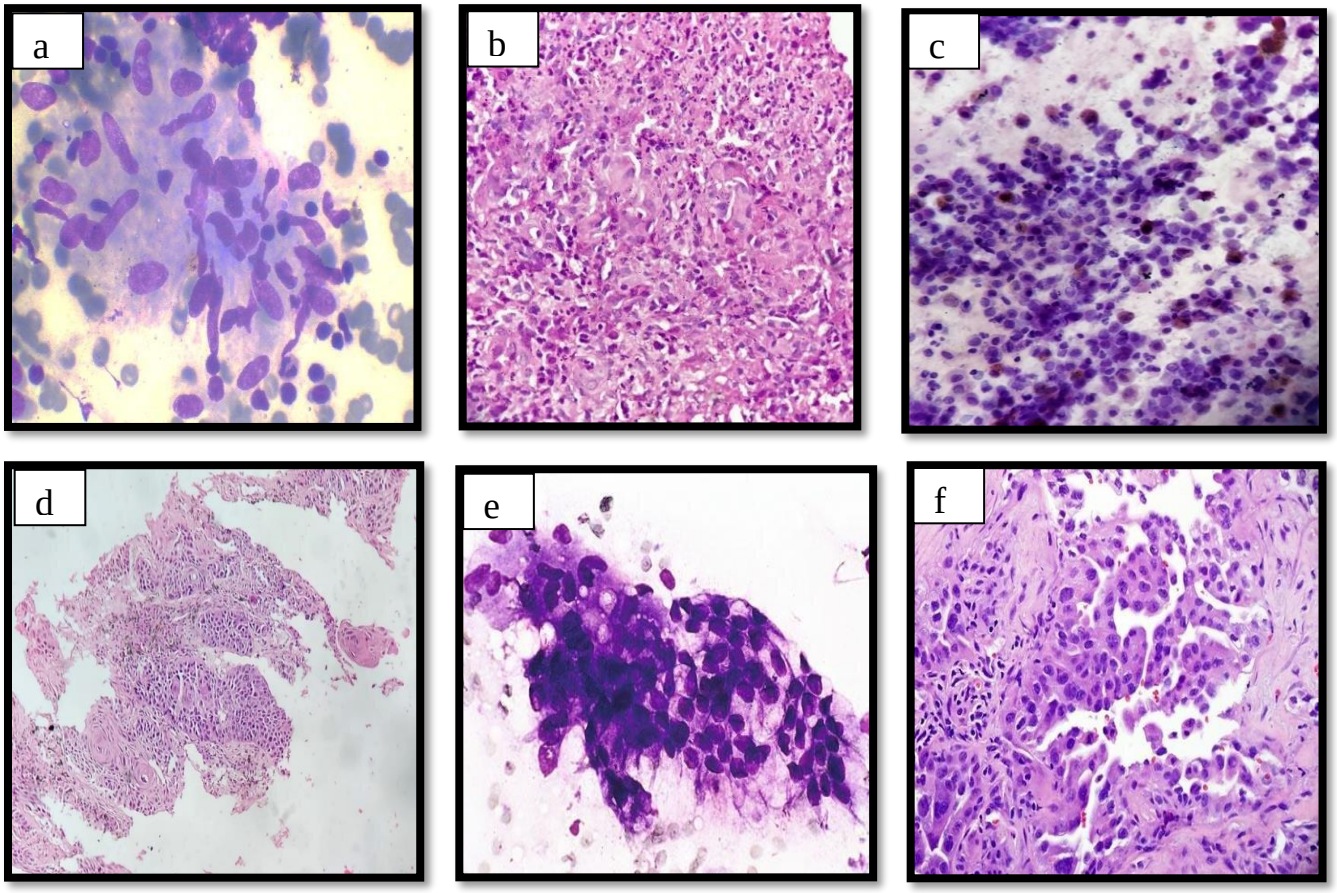

Figure 3:

(a) Granuloma containing epithelioid cells, in case of Tuberculosis, H&E, BAL, 40 x
(b) Tuberculous granuloma showing epithelioid cells and langhan's giant cells, biopsy, H&E, biopsy, 40 x.
(c) Clusters of atypical squamous cells, Squamous cell carcinoma, H&E, BAL, 40 x
(d) Squamous cell carcinoma, groups of atypical squamous cells with formation of keratin pearls, H&E, biopsy, 10 x
(e) Adenocarcinoma, Mucin producing cells are mixed with non-mucinous cells with high N:C ratio, Adenocarcinoma, H&E, BAL, 40 x
(f) Adenocarcinoma, projecting clusters of cells with small, abortive gland formation, H&E, biopsy, 40 x

Discussion:

This was a prospective study of 100 cases to find the diagnostic accuracy of BAL in patients with pulmonary diseases.

BAL plays an important role by showing good patient compliance and being useful in multiple investigations like cytology for detecting neoplastic cells in suspected cases of malignancies & microbiological tests like culture & sensitivity, Zeil-Nelson staining & Gene Xpert in suspected cases of tuberculosis. BAL is performed alongside endobronchial/CT-guided biopsy when radiologically a mass lesion is present in the lungs to confirm malignancy and is only rarely done for a suspected non-neoplastic lesion and hence the lack of literatures on the same.

In the present study, most common presenting symptoms were cough followed by fever and dyspnea. This was found to be similar to the study done by Girish M et al. [6] where majority of the patients presented with clinical symptom of cough (90%) followed by fever (45.3%), breathlessness (30.7%), hemoptysis (28%) and weight loss (15.3%).

Pulmonary neoplastic lesions:

In the present study, BAL showed a sensitivity of 56.5% in detecting neoplastic pulmonary lesions. Studies done by Farida Binesh et al. [7], Lam et al. [8] and Pradeep et al. [9] found the sensitivity of BAL to be 46.9%, 69% and 69.6% respectively which is comparable to the present study. Whereas Debeljak et al. [10] reported a lower sensitivity of 27.9% in detecting neoplastic pulmonary lesions which in their opinion was due to poor exfoliation. The frequency of smears suspicious for malignancy in this study was 13% which was comparable to the studies done by Ahmad et al. [11] and Spjut et al. [12] who found 12.6% and 10% smears suspicious for malignancy respectively. A study done by Raiza et al. [13] found only 3% of smears to be suspicious for malignancy which may be due to a smaller study population (i.e., 38 cases).

In the present study and the study done by Ahmad et al. [11], all the BAL fluid smears reported as suspicious for malignancy were found to be malignant on histopathological examination (100% concordance).

This concordance was slightly lower in the studies done by Spjut et al. [12] and Raiza et al. [13] who on histopathology found malignancy in 94 % & 80% of suspicious smears respectively.

In the studies done by Pradeep et al. [9], Rennard [14] and Linder et al. [15], there were no false positive cases making the specificity 100%. Present study also shows 100% specificity. Although the study done by Farida Binesh et al. [7] found 83.5% specificity, it was still considered significant. This shows that rare false positivity is a power of BAL and even when only suspicious cells are seen, it usually turns out to be a malignant lesion on biopsy.

Amongst the neoplastic lesions, adenocarcinoma followed by squamous cell carcinoma were found to be most common lesions. This finding was similar to the study done by Farida Binesh et al. [7] However, studies done by Raiza et al. [13]and Ahmad et al. [11] found more cases of Squamous cell carcinoma (i.e., 55.3% and 37.3% respectively) as compared to adenocarcinoma. Inclusion of CT-guided biopsies could account for this discrepancy as adenocarcinomas arise more commonly in the peripheral lung. Also, adenocarcinoma has been mentioned as the most common form of epithelial malignancy of lung in various literatures [16]. In the present study, 22 cases were of peripheral lung lesions were identified. Adenocarcinoma gave the highest yield on BAL i.e. 57.1% by detecting 4 out of 7 cases of adenocarcinoma. In a study of peripheral lung lesions, Pirozynski et al [17] found more cases of squamous cell carcinoma than adenocarcinoma (present study found same number of squamous cell carcinoma and adenocarcinoma-7 cases) but highest yield was obtained with adenocarcinoma i.e.59.29% which was similar to the present study. The diagnostic accuracy of BAL in detecting peripheral neoplastic lesions in this study i.e. 57.1%was comparable to the studies done by Pirozynski [17] and Wongsurakiat et al. [18] who found the diagnostic accuracy to be 58.3% and 46.7% respectively.

This concluded that bronchoalveolar lavage cytology is also useful for detecting peripheral neoplastic lung lesions as it can sample a wider area as opposed to endobronchial biopsy.

BAL is a type of exfoliative cytology and relies mainly on the sheded cells from malignant tumours for their detection. It is well-known that certain tumours show infrequent exfoliation & could be a reason for interpretive differences. Other plausible causes for discrepancies include sampling errors, false negativity in early stage of malignant disease with less or no exfoliations or the errors of interpretation.

Inflammatory lesion-

Tuberculosis: Cytopathology of BAL in the present study detected 1 case of tuberculous inflammation whereas on histopathology examination, 5 cases of tuberculous inflammation were detected. These 5 cases were confirmed by microbiological tests culture and Gene Xpert and out of these 5 tuberculous lesions, 3 were BAL-AFB smear positive and 2 were BAL-AFB smear negative. Study by Nikbaksh et al. [19] showed that BAL had a sensitivity and specificity of 60% & 91% respectively when a combined approach of AFB smears & culture of BAL in Lowenstein Jenson medium was implemented. Cytopathological examination of these cases were found to have chronic inflammatory cells only. The characteristic granulomas seen on histopathology are not usually visualized in BAL smears making the diagnosis difficult. Thus, in tuberculous inflammation, cytopathological examination alone is not very useful and a combined approach of cytopathology along with BAL fluid for AFB, culture & Gene Xpert might prove to be of diagnostic value in cases of negative sputum AFB and in patients who are immunocompromised [20].

The present study had only two cases of fungal infections out of which only one correlated with the histopathological examination and confirmed using PAS stain. Although BAL could be an important adjunct in diagnosis of invasive pulmonary fungal infections, a biopsy is almost always needed for confirmation. One case with inflammatory cells on BAL specimen showed non-specific interstitial pneumonia on biopsy. All these cases were so few that appropriate conclusions could not be made out of the results and a wider study targeted at inflammatory lesions is needed.

Conclusion:

Pulmonary diseases especially malignancies have shown a male predilection and this trend seems to be due to a higher rate of tobacco consumption amongst males. Although BAL cytology shows a moderate sensitivity in diagnosing pulmonary diseases, it does provide a very good specificity and thus patients with conclusive BAL reports could reliably be started with appropriate interventions at an early stage of the disease. BAL cytology provides a wider sampling as it can reach distal bronchioles and thus have better chances to sample peripheral lung lesions as compared to endobronchial biopsy.

Conflict of Interest - Nil

Sources of Support - Nil

References

1. Lalit Dondona, Rakhi Dandona, G Anil Kumar, D K Shukla, Vinod K Paul, Kalpana Balakrishnan et al. India State-Level Disease Burden Initiative Collaborators. Nations within a nation: Variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study. *Lancet* 2017; 390:2437-2460.
2. Fraser RS, Colman N, Müller NL, Pare PD. Methods of Pathologic Investigation. In: Fraser and Pare's Diagnosis of Diseases of the Chest. 4th ed. Vol. I, Philadelphia : WB Saunders Company : 1999.
3. Gray W. Normal respiratory tract and inflammatory conditions. In : Diagnostic Cytopathology. Gray W, McKee GT. Editors. 2nd ed. Edinburgh: Churchill Livingstone : 2003.
4. Goldstein RA, Rohatgi PK, Bergofsky EH, Block ER, Daniele RP, Dantzker DR, et al. Clinical role of bronchoalveolar lavage in adults with pulmonary disease. *The American Review of Respiratory Diseases* 1990; 142: 481-486.
5. Chamberlain DW, Braude AC, Rebuck AS. A critical evaluation of bronchoalveolar lavage. Criteria for identifying unsatisfactory specimens. *Acta Cytologica* 1987;31: 599-605.
6. Girish M. 2006. A cytodiagnostic study of pulmonary lesions by bronchoalveolar lavage. MD Pathology. Rajiv Gandhi University of Health Sciences. Karnataka.

7. Farida Binesh, Azar Pirdehghan, Mohammad Reza Mirjalili, Mohammad Samet, Zahra Amini Majomerd, Ali Akhavan et al. 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;16 (1),201-204.
8. Lam B, Wong MP, Ooi C, W K Lam, K N Chan, J C Ho, K W Tsang. Diagnostic yield of bronchoscopic sampling methods in bronchial carcinoma. *Respirology* 2000;5:265-270.
9. Pradeep Kumar L, Rudra Murthy K, Srinivasa Murthy G, Avanthi E. Comparison of effectiveness of BAL [bronchoalveolar lavage] with CT Guided FNAC in the diagnosis of lung cancer. *Journal of Evolution of Medical and Dental Science* 2014;11:2752-2756.
10. Debeljak A, Mermolja M, Sorli J, Zupancic M, Zorman M, Remskar J. et al Bronchoalveolar lavage in the diagnosis of peripheral primary and Secondary malignant lung tumors. *Respiration* 1993; 61(4): 226-230.
11. M. Ahmad, S. Afzal, W. Saeed, A. Mubarik, N. Saleem, S. A. Khan, S. Rafi. Efficacy of Bronchial Wash Cytology and its correlation with Biopsy in Lung Tumours. *Journal of Pakistan Medical Association* Jan 2004; 54(1): 13-16.
12. Ackerman LV, Spjut HJ. Exfoliative cytology and pulmonary cancer. *Acta: Unio Int Contra Cancrum* 1960;16:371-376.
13. Raiza D, Rout S, Reddy K P, Ramlaxmi P V, Prithvi B K, Harikishan K S et al., Efficacy of Bronchial Wash and Brush Cytology and its correlation with Biopsy in Lung Lesions. *International Journal of Health Research in Modern Integrated Medical Sciences* 2014;1 (1); 21-24.
14. Rennard SI. Bronochoalveolar lavage in the diagnosis of cancer. *Lungs* (Suppl):1035-40 1990; 168: 1035-1040.
15. James Linder, William P. Vaughan, James O. Armitage, Mo A. Ghafouri, Diane Hurkman, Elizabeth C. Mroczek, et al. Cytopathology of opportunistic infection in bronchoalveolar lavage. *American journal of clinical pathology* 1987; 88: 421-428.
16. Suster, S., & Moran, C. A. (2012). Biopsy interpretation of the lung. Wolters Kluwer Health Adis (ESP). 1st edition. 2013: p-255-268.
17. Pirozynski M. Bronchoalveolar lavage in the diagnosis of peripheral, primary lung cancer. *Chest* 1992 Aug;102 (2):331-332.
18. Wongsurakiat P, Wongbunnate S, Dejsomritrutai W, Charoenratanakul S, Tscheikuna J, Youngchaiyud P, Diagnostic value of bronchoalveolar lavage and postbronchoscopic sputum cytology in peripheral lung cancer. *Respirology*1998;3(2):131-137.
19. Novin Nikbakhsh, Masomeh Bayani, Sepideh Siadati et al The Value of Bronchoalveolar Lavage in the Diagnosis of Sputum Smear Negative Pulmonary Tuberculosis. *Iranian journal of Pathology* 2015;10 (1):33-40.
20. Khalil KF, Butt T. Diagnostic Yield of Bronchoalveolar Lavage gene Expert in Smear- Negative and Sputum Scarce Pulmonary Tuberculosis. *Journal of College of Physicians and Surgeons Pakistan* 2015:25(2); 115-118.

Address for correspondence: *Dr. Anupama I. Dayal. Associate Professor, Department of Pathology, GCS Medical College, Hospital & Research Centre, Ahmedabad -380025, Gujarat, India.*
Email: anupamadayal2019@gmail.com
Mobile: +91 9898264571.

How to cite this article: Himil Parikh, Anupama Dayal, Himali Thakkar and Deepak Joshi. Correlation of Bronchoalveolar Lavage with Transbronchial and CT Guided Biopsy in Pulmonary Disease. Walawalkar International Medical Journal 2021; 8(2):1-7. http://www.wimjournal.com.

Received date: 29/05/2021 Revised date: 21/09/2021 Accepted date: 22/09/2021