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Original Research Article

Study of Bronchoalveolar Lavage Fluid with Conventional Method and Liquid Based Cytology in Lung Cancer Diagnosis

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Conflict of interest: Nil

Abstract:

Background: Lung cancer is the most significant worldwide health problem and contributes to 30% of male and 26% of female cancer related deaths. The sensitivity of bronchoalveolar lavage cytology has been variably reported. The liquid based monolayer cytological preparation is an automated cytopreparatory technique that has been designed to improve sample collection and cytopreparation.

Material and Methodology: The study was conducted at Gujarat cancer and research institute, Ahmedabad. A total of 280 patients of suspected lung cancers who came to our hospital were included in the study. The present study was a prospective study conducted during September 2016 to August 2018. Every case will be investigated under both conventional cytology and liquid based cytology followed by histological examination.

Results: A total of 280 cases were evaluated. Mean age was 58 years. There were 53 male patients and 27 female patients suggesting male predominance in lung cancer. The positive detection rate of malignancy in BAL fluid was 31.2% in the conventional group whereas it was 54.4 % in the LBC group. The negative rate was higher (66%) in the conventional and comparatively lower (45.3%) in LBC. A chi-square test was applied which gave significant result. (p value < 0.005).

Conclusion: LBC was found to be superior to conventional preparation in terms of cellularity and cytomorphology which translated into a reduction in unsatisfactory rate and increased diagnostic rates and sensitivity, the potential for ancillary tests including immunocytochemical staining and DNA analysis makes this technique a promising candidate for more widespread usage.

Keywords: Lung cancer, Bronchial cytology, Lavage fluid.

Introduction

Lung cancer is the most significant worldwide health problem and contributes to 30% of male and 26% of female cancer related deaths and approximately 1.38 million people die of lung cancer each year. [1,2] According to the GLOBOCAN 2012 report, the estimated incidence of lung cancer in India was 0,275 in all ages and both sexes. One million of the current 5 million deaths in world are contributed by India. [3]. Most lung cancer patients are diagnosed at advanced stage of disease making curable surgery not an option. Thus, early diagnosis and effective treatment are key to prolong the survival of lung cancers patients. Cytology has been widely used for the diagnosis of lung malignancy.

There are a variety of sample preparation techniques available for cytological evaluation and detection of lung cancer [4] including exfoliative and abrasive cytology (bronchoalveolar lavage, bronchial brushing, bronchial washing) and fine needle aspiration cytology. [5,6]. Bronchial cytology specimens are of considerable diagnostic value in the evaluation of lung cancer especially in cases where it is difficult to obtain bronchoscopic biopsy material for histological evaluation as well as in peripheral lesion.

The sensitivity of bronchoalveolar lavage (BAL) cytology has been variably reported to be 39.4% to

80.4 % [7,8]. BAL performed using fiberoptic bronchoscopy is a safe technique with a diagnostic accuracy. It is valuable for detection of opportunistic infections and since it samples multiple bronchi, it is also suitable for sampling diffuse lesions. The overall reported diagnostic yield of BAL for malignancy is about 50%. Conventional smears suffer from problem related to preparation and fixation artifacts, obscuring elements, and thickness. As an alternative to conventional cytology, LBC was introduced in mid 1990s. The liquid based monolayer cytological preparation is an automated cytopreparatory technique that has been designed to improve sample collection and cytopreparation [9]. The utility of LBC has been widely accepted as a major diagnostic method in various clinical settings and has been proven to have great association with tissue histological diagnosis [10,11]. The advantages of this method include improved visualization of diagnostic cells, uniform thickness of cytology slides, better cellular preparation, removal of air-drying artifacts and elimination of obscuring blood and inflammatory exudates. [12].

Aims and Objective

1. To introduce Liquid Based Cytology test for Cytopathological diagnosis of lung cancer.
2. To compare sensitivity and specificity between Conventional cytology and Liquid Based Cytology.
3. To compare diagnostic significance of Liquid Based cytology and Conventional cytology in Bronchoalveolar Lavage fluid in Lung Cancer Patients.

Material and Methodology

The study was conducted at Gujarat cancer and research institute (GCRI), Ahmedabad. A total of 280 patients of suspected lung cancers who came to our hospital were included in the study. The present study was a prospective study conducted on the 280 patients during a period of 2 years ranging from September 2016 to August 2018. Every case will be investigated under both conventional cytology and liquid based cytology.

Inclusion criteria: Cases included are clinically and radiologically suspected lung cancer patients in our hospital.

Exclusion criteria: Low cellular smear / unsatisfactory smears in both preparations are excluded.

Procedure: The samples were collected via bronchoscope using standard guidelines. Bronchoalveolar Fluid samples were then collected in EDTA tube and collected fluid forwarded to cytology laboratory. 2 tubes were taken for each patient, one tube for conventional preparation and one tube for LBC. For conventional cytology (CC) preparation, sample is centrifuged at 2000 rpm for 10 minutes. The supernatant is decanted and a minimum of 2 smears are made from the sediment, fixed immediately and stained by PAP (Papanicolaou) stain. For processing by LBC Sure Path system, equal volume of Cytorich Red solution was added to the fluid, vortexed and kept for fixation. After fixation, specimen was processed and stained according to the Sure Path manual protocol in fully automated LBC machine.

For histology, tissue was put into 10% formalin and proceeds for fixation and for routine Haematoxilin & Eosin stain. Immunohistochemistry was performed by standard procedure on formalin fixed paraffin embedded tissue material.

Based on cytomorphology, cases in both the groups were divided into four diagnostic categories as follows:

Positive: included cases with definite malignant cells in adequate cellularity.

Suspicious for malignancy: included cases with few atypical cells highly suggestive of malignancy.

Negative: included cases with normal cellular components (alveolar macrophages, ciliated columnar cells) and/or inflammatory cells without any atypical cells.

Unsatisfactory: included cases with few/no epithelial cells and alveolar macrophages, excessive background obscuration with inflammation, blood, and mucus.

Follow-up: The cytology results were correlated with the results of subsequent bronchial biopsy. Immunohistochemistry was also applied for the cases where morphology was not adequate for diagnosis.

Statistical analysis: A chi-square test was performed to assess the significance of comparison between CC and LBC. The level of significance was set at 0.05. Comparison of cytology results using CC and LBC was done with respect to sensitivity, specificity, positive predictive value, negative predictive value, positive and negative diagnostic rates and unsatisfactory rates.

Observations and Results

A total of 280 cases were evaluated. After performing data analysis, following observations were made.

Table 1: Demographics of patients (N=280). Mean age of the study group was 58 years. The age of patients diagnosed with lung cancer ranges between 22 to 88 years. Highest number of patients 111 out of 280 (39.6%) were between 61-70 years of age followed by 84(30.0%) between 51-60 years. Fig 1: - Comparison of diagnostic rates in

conventional cytology and Liquid Based Cytology. (N=280) Figure gives the diagnostic rates of BAL as processed by both the methods. The positive cases were 54(19.2%) by the conventional method while it was 130 (46.4%) in the LBC. The cases negative on conventional method were 182(65.0%) while 122(43.6%) cases were negative by LBC. Unsatisfactory rates showed reduction from 2.9% in conventional method to 0.4% in the LBC group.

Table 2: - Comparison of cytological tumor sub typing in conventional and liquid based cytology. Table 2 illustrates a comparison of cytological subtyping of tumors in BAL specimens with both techniques. 52 cases were diagnosed as adenocarcinoma on LBC out of which 21 cases were subtyped as adenocarcinoma on conventional and others are diagnosed as NSCLC (7 cases), suspicious for carcinoma (7 cases) and negative (17 cases).

There were 37 cases diagnosed as SCC on LBC. On conventional cytology, only 8 cases could be subtyped as SCC, 19 cases were negative, 5 cases were suspicious, and 2 cases were diagnosed as NSCLC.

18 cases were diagnosed as small cell carcinoma on LBC as compared to conventional method in which 8 cases could be subtyped as small cell carcinoma.

Table 3: - Detection of different type of lung cancer on bronchoscopic biopsy. (N=280)

Table 3 shows that out of 280 cases, 88 cases (31.4%) were subtyped as adenocarcinoma, 80 cases (28.6%) were diagnosed as squamous cell carcinoma and 43 cases (15.4%) as small cell carcinoma.

Table 4: - Comparison of cytological tumor subtyping with follow-up on histology. Table 4 presents a comparison of cytological subtyping of tumors in BAL specimens with follow-up data. Out of 37 cases diagnosed as SCC on LBC, 35 cases were subtyped correctly when compared with subsequent biopsy. 1 case diagnosed as SCC on LBC was typed as adenocarcinoma on biopsy. 18 cases were diagnosed as small cell carcinoma on LBC, from which 16 cases were correctly typed when compared with biopsy. 52 cases were diagnosed as adenocarcinoma on LBC. Out of these, 33 cases diagnosed as adenocarcinoma and 14 cases as NSCLC. Out of these 14 cases, Immunohistochemistry was done in 10 cases and 9 cases were diagnosed as adenocarcinoma.

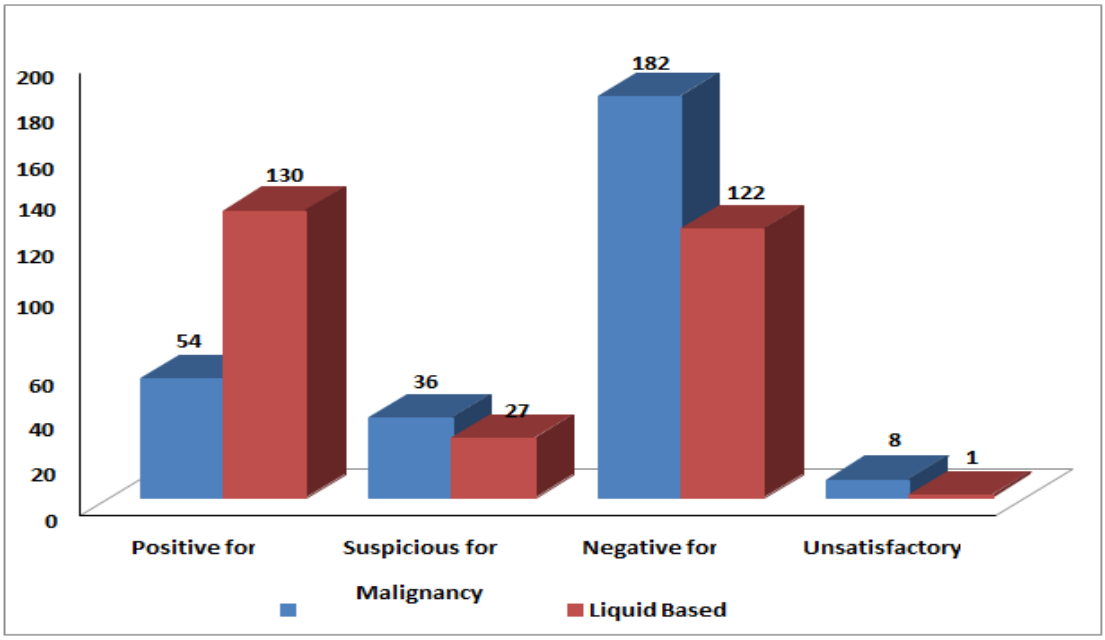

Figure 1: Comparison of diagnostic rates in conventional cytology and Liquid Based Cytology. (N=280)

Figure gives the diagnostic rates of BAL as processed by both the methods.

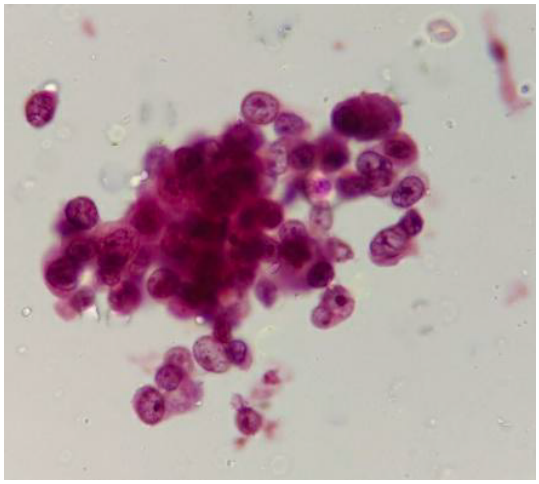

Figure 2(A): LBC preparation showing preserve three-dimensional clusters with clear background

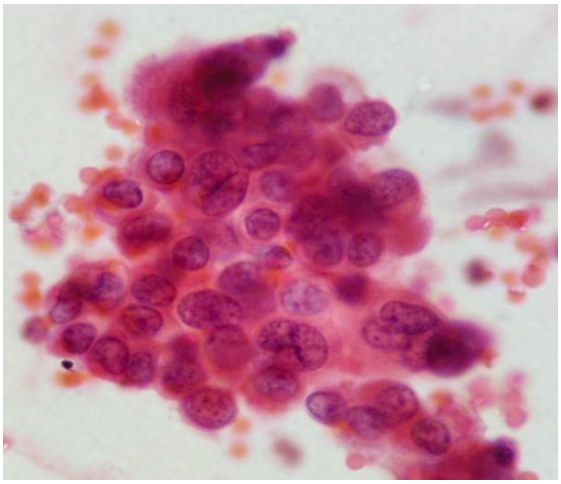

Figure 2(B): Same slide on conventional preparation showing clusters of adenocarcinoma in hemorrhagic background (Pap stain, 40x)

Figure 2: Cytomorphology of Adenocarcinoma:

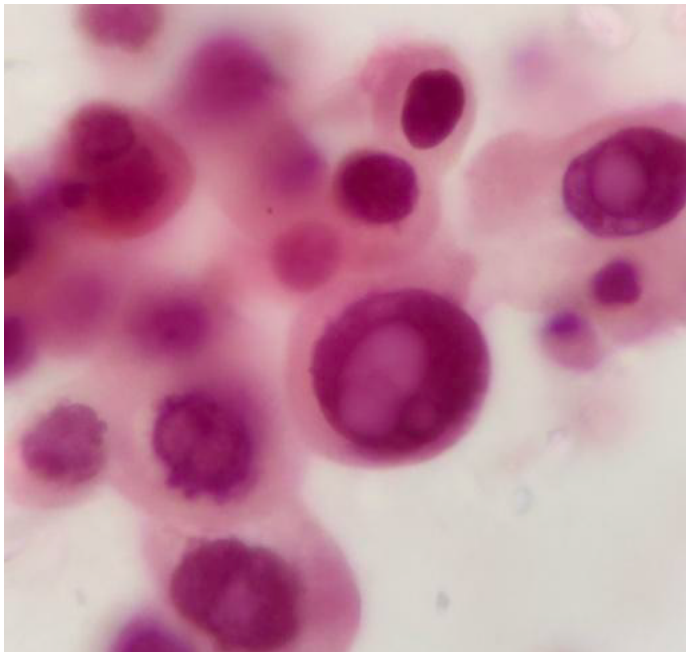

Figure 3: adenocarcinoma on LBC preparation showing high N/C ratio, intranuclear inclusions, pale eosinophilic cytoplasm (Pap stain 100x).

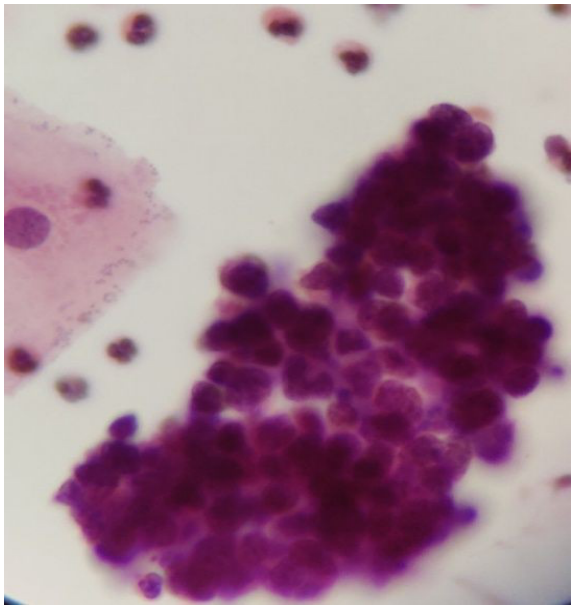

Figure 4(A): LBC preparation showing atypical squamous cells with well-defined cell borders, dense eosinophilic cytoplasm, high N/C ratio (see inset)

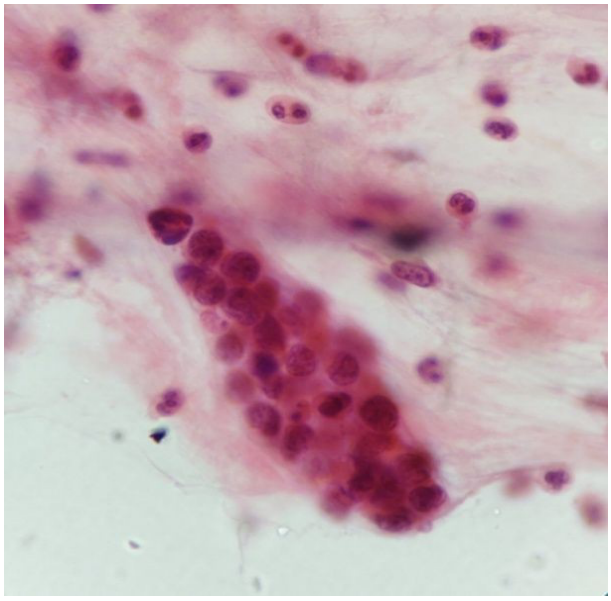

Figure 4(B): (B) conventional preparation showing atypical squamous cells entrapped in inflammatory exudates. (Pap stain 100x)

Figure 4: Cytomorphology of squamous cell carcinoma

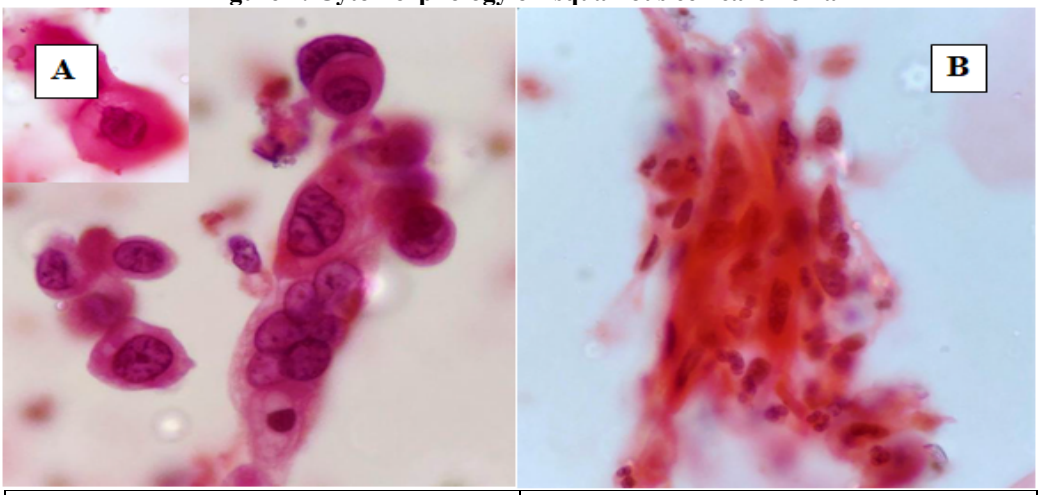

Figure 5(A): LBC preparation shows small tumor cells with scanty cytoplasm, hyperchromatic nuclei, salt and pepper like chromatin, nuclear molding

Figure 5(B): conventional cytology showing small cell carcinoma with inflammatory background.

Figure 5: Cytomorphology of small cell carcinoma

Table 1: Demographics of patients (N=280)

Age Group (In years)	Frequency	Percentage
20-30	1	0.40%
31-40	12	4.30%
41-50	42	15.00%
51-60	84	30.00%
61-70	111	39.60%
71-80	28	10.00%
≥81	2	0.70%
Total	280	#####

Mean age of the study group was 58 years. The age of patients diagnosed with lung cancer ranges between 22 to 88 years. Highest number of patients 111 out of 280 (39.6%) were between 61-70 years of age followed by 84(30.0%) between 51-60 years.

Table 2: Comparison of cytological tumor sub typing in conventional and liquid based cytology

Diagnosis on conventional l cytology	Cytological diagnosis on LBC						
	Adenocarcinoma (52)	SCC - 37	Small cell (18)	NSC LC (21)	Suspicious (27)	Negative -122	Unsatisfactory (01)
Adeno carcinoma	**21**						
SCC		**8**					
Small cell			**8**				
NSCLC	**7**	**2**		**6**			
Suspicious	**7**	**5**	**8**	**5**	**11**		**1**
Negative	**17**	**19**	**2**	**9**	**13**	**122**	
Unsatisfactory		**3**		**1**	**3**		

*SCC= Squamous cell carcinoma, NSCLC=Non-Small Cell Lung Carcinoma

Table 2 illustrates a comparison of cytological subtyping of tumors in BAL. specimens with both techniques. 52 cases were diagnosed as adenocarcinoma on LBC out of which 21 cases were subtyped as adenocarcinoma on conventional and others are diagnosed as NSCLC (7 cases), suspicious for carcinoma (7 cases) and negative (17 cases). There were 37 cases diagnosed as SCC on LBC. On conventional cytology, only 8 cases could be subtyped as SCC, 19 cases were negative, 5 cases were suspicious, and 2 cases were diagnosed as NSCLC.

18 cases were diagnosed as small cell carcinoma on LBC as compared to conventional. Methods in which 8 cases could be subtyped as small cell carcinoma.

Table 3: Detection of different type of lung cancer on bronchoscopic biopsy (N=280)

Diagnosis	Frequency	Percentage
Adenocarcinoma	88	31.40%
Squamous cell Carcinoma	80	28.60%
Small Cell Carcinoma	43	15.40%
NSCLC	49	17.50%
poorly diffentiated carcinoma	13	4.60%
Negative	7	2.50%
Total	280	100%

Table 3 shows that out of 280 cases, 88 cases (31.4%) were subtyped as adenocarcinoma, 80 cases (28.6%) were diagnosed as squamous cell carcinoma and 43 cases (15.4%) as small cell carcinoma.

Table 4: Comparison of cytological tumor subtyping with follow-up on histology

Diagnosis on Histology	Cytological diagnosis on LBC				
	Adeno Carcinoma (52)	SCC (37)	Small cell Carcinoma (18)	NSCLC (21)	Negative (122)
Adenocarcinoma	33	01		03	42
SCC		35		07	34
Small cell	01		16	01	17
NSCLC	14	01	01	9	29
Negative	04		01	01	

*SCC: squamous cell carcinoma, NSCLC: non-small cell lung carcinoma.

Table 4 presents a comparison of cytological subtyping of tumors in BAL specimens with follow-up data. Out of 37 cases diagnosed as SCC on LBC, 35 cases were subtyped correctly when compared with subsequent biopsy. 1 case diagnosed as SCC on LBC was typed as adenocarcinoma on biopsy. 18 cases were diagnosed as small cell carcinoma on LBC, from which 16 cases were correctly typed when compared with biopsy. 52 cases were diagnosed as adenocarcinoma on LBC.

Out of these, 33 cases diagnosed as adenocarcinoma and 14 cases as NSCLC. Out of these 14 cases, Immunohistochemistry was done in 10 cases and 9 cases were diagnosed as adenocarcinoma.

Table 5: Comparison of positive detection rate of malignancy between conventional method and LBC reported by different authors

Authors	Years	Positive detection rate on CS (%)	Positive detection rate on LBC (%)
D.N.Rana et al(19)	2001	16.4	17.8
E. Astall et al (18)	2003	29.9	37.9
Yang Yang et al (16)	2013	11.5	35.8
Kathiresan et al (20)	2013	38	68
Abha Thakur et al (17)	2017	28.6	32.9
Present study	2018	31.2	54.4

CS: conventional smear, LBC: liquid based cytology.

Table 6: Comparison of unsatisfactory rate between conventional method and LBC

Authors	Years	Sensitivity for CS (%)	Sensitivity for LBC (%)
Yi-Bo Fan et al (22)	2010	57.8	71.5
Abha Thakur et al (17)	2017	50.7	55.8
Dan Gong et al (23)	2017	86.7	87.3
Present study	2018	30.4	54.9

Table 7: Comparison of sensitivity between conventional method and LBC reported by different authors

Authors	Years	Conventional (%)	LBC (%)
D.F.Fischler et al(21)	1996	17	1
Abha Thakur et al (17)	2017	4.4	0.6
Present study	2018	2.8	0.3

Table 8: Comparison of statistical values

Author	True negative (%)	True positive (%)	False positive (%)	False negative (%)
Abha Thakur et al (17) (CS)	58.2	100.0	0.0	41.8
Abha Thakur et al (17) (LBC)	59.4	100.0	0.0	40.6
Present Study (CS)	11.1	26.3	2.2	57.7
Present Study (LBC)	11.1	47.6	2.2	38.7

Discussion

BAL cytology is a widely accepted, safe, simple, minimally invasive technique to evaluate lung pathologies. In this study I assess the diagnostic value of Liquid based BAL cytology in comparison to the conventional BAL cytology and corresponding histological diagnosis in each of 280 patients with lung cancer. LBC is an alternative automated cytopreparatory technique which is now widely used for both gynecological and non-gynecological specimens.

In the present study maximum number of cases was noted between 61 to 70 years which is consistent with data in the study done by Chaoying Liu et al, [13]. De Groot P. et al; [14] and Dela Cruz et al; [15]. Age of patients ranges between 22 to 88 years. There were 53 (90.4%) male patients and 27 (9.6%) female patients suggesting male predominance in lung cancer which is comparable to study done by Yang Yang et at; [16] showing 80% male and 20% female patients. The average age was 58 years in this study thus bronchial cytology may apply to this age group for screening lung cancer. CT scan was performed in 267 cases out of 280 cases.

About 65% cases of adenocarcinoma are located peripherally. The present study justifies this as 82 cases (30.7%) of adenocarcinoma were located peripherally. Most cases of squamous cell carcinoma are centered in segmental bronchi and therefore present as hilar or perihilar mass in chest radiographs and CT scans. In this study, 49 cases (18.3%) of squamous cell carcinoma were centrally located and 41 cases (15.3%) were peripherally located. Small cell carcinoma is typically a lesion of the central portions of the lung, but occasionally it is found in a peripheral location. In present study, 33 cases (12.3%) of small cell carcinoma were located centrally and 15 cases (4.11%) were located peripherally. So, overall BAL procedure showed higher diagnostic sensitivity for detection of peripheral lesions. The positive detection rate of malignancy in BAL fluid was 31.2% in the conventional group whereas it was 54.4 % in the LBC group. The negative rate was higher (66%) in the conventional and comparatively lower (45.3%) in LBC. In our study the positive diagnostic rate of LBC was higher than that of conventional method which indicated statistically significant difference. A chi-square test was applied which gave significant result. (p value < 0.005).

The LBC provided a higher diagnostic yield of pulmonary malignancy in BAL specimens. Our finding was in concordance with the studies of Abha Thakur et al;[17] E. Astall et al;[18] Yang Yang et al;[16] D.N.Rana et al;[19] Kathiresan et al.[20] They also reported increased positive detection rate of malignancy on LBC than conventional smears, which was statistically significant. Table: 5 Comparison of positive detection rate of malignancy between conventional method and LBC reported by different authors within this study, sample producing an inconclusive diagnosis were reported as suspicious for malignancy.

The number of suspicious cases was higher within the conventional smear technique with 27 cases in the LBC technique in comparison with 37 cases in the conventional method. Out of these 37 suspicious cases on conventional smear, 25 cases could be further subtyped on LBC which included 7 cases of adenocarcinoma, 5 cases of squamous cell carcinoma, 8 cases of small cell carcinoma, and 5 cases diagnosed as NSCLC. The reduction in cases noted to be suspicious may relate to the improved morphological appearances of the preparation. In particular the nuclear detail was defined better using LBC, possibly as a result of virtual instant fixation and reduced amount of obscuring blood, mucus and debris. This correlates with one study done by E. Astall et al; [18]. Which also shows number of suspicious cases much higher on conventional, 23 cases compared to only 12 cases in LBC Cyto- SED technique.

LBC technique reduced the number of cases classified as unsatisfactory. In this study there were 8 cases diagnosed as unsatisfactory on conventional cytology which reduced to only 1 case on LBC so unsatisfactory rate decrease from 2.8 % to 0.3%. Few studies were also carried out in the past which showed reduced unsatisfactory rates on LBC compared to conventional method. Table: 6 Comparison of unsatisfactory rate between conventional method and LBC. The advantages of this method include improved visualization of diagnostic cells, uniform thickness of cytology slides, enhanced cellular and nuclear morphology, better cellular preparation, removal of air-drying artifacts an elimination of obscuring blood and inflammatory exudates.

Fig 2 (A) and (B) shows comparison between LBC and conventional smear in case of Adenocarcinoma. Fig 3 shows nuclear features of adenocarcinoma on LBC. Fig 4 shows cytomorphology of squamous cell carcinoma on conventional smear and LBC. Fig 5 shows cytomorphology of squamous cell carcinoma on conventional smear [and LBC.

The sensitivity of BAL in the detection of lung cancer using LBC was 54.95% as compared to 30.40% by conventional method. Therefore, there was a significant improvement in sensitivity with the introduction of LBC. Different studies by Abha Thakur et al;[17] Yi-Bo Fan et al;[22] Dan Gong et al; [23] were carried out to compare sensitivities between two methods.

Table:7 Comparison of sensitivity between conventional method and LBC reported by different authors. The specificity of BAL in detection of malignancy was 83.33% with the use of both the techniques. Abha Thakur et al;[17] reported 100% specificity with the use of both techniques. Similar high specificity of BAL has been reported in literature i.e., 80% to 96.6% [8]. Chaoying Liu et al;[13] detected the specificity 62.93% using LBC thinprep cytology. The results shows that LBC technique identified more number of malignancies than conventional preparation. In particular, a definitive diagnosis of malignancy could be made rather than suspicious for malignancy. In the broad category of a small cell carcinoma v/s non-small cell carcinoma there was a good correlation; using LBC more cases identified as non-small cell carcinoma grouped with squamous cell carcinoma and adenocarcinoma. False negatives were 57.7% and 38.7% in conventional cytology and LBC group respectively. Thus, false negative rate significantly reduced with LBC technique. Table 8: Comparison of statistical values on biopsy, 88 cases (31.4%) were diagnosed as adenocarcinoma, 80 cases (28.6%) as squamous cell carcinoma, 43 cases (15.4%) as small cell carcinoma and 62 cases (22.1%) were diagnosed as NSCLC or poorly differentiated carcinoma. Immunohistochemistry (IHC) was performed in 48 cases where morphology could not help to diagnose definite subtype. The panel of adenocarcinoma markers- TTF1, CK7, napsinA; panel of squamous cell carcinoma- p63, CK5/6; chromogranin, synaptophysin for small cell carcinoma

Conclusion

Bronchoalveolar lavage specimens are often used as a part of primary investigation of suspected pulmonary disease, including malignancy of either primary or secondary origin. The sensitivity of BAL in the detection of lung cancer using LBC (SurePath) was 54.95% as compared to 30.40% by the conventional technique and specificity was 83.33% for both the techniques. LBC was found to be superior to conventional preparation in terms of cellularity and cytomorphology which translated into a reduction in unsatisfactory rate and increased diagnostic rates and sensitivity. Furthermore, the potential for ancillary tests including immunocytochemical staining and DNA analysis

makes this technique a promising candidate for more widespread usage.

References

1. Ferlay J, Parkin DM, Steliarova- Foucher E. Estimates of cancer incidence and mortality in Europe in 2008. Eur J Cancer 2010; 46: 765–781.
2. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2000; 127: 2893–2917.
3. Dutt N, Singh AK. Sputum cytology for lung cancer: Not just part of the past. Lung India 2012; 29: 199.
4. Idowu MO, Powers CN. Lung cancer cytology: potential pitfalls and mimics a review. Int J Clin Exp Pathol 2010; 3:367–385.
5. Wright PK, Thiryayi SA, Rana DN Fine needle aspiration cytology diagnosis of extramedullary haematopoiesis presenting as a pre-sacral mass: a pitfall avoided. Cytopathology 2012; 23: 133–134.
6. Yang Y, Pan QJ, Teng MF, Li ZL, Zhao LL, et al. Application of protein markers in combination with Thin Prep bronchial brush cytology in classification of lung cancer subtypes. 2008; 30: 616–619.
7. Gaur DS, Thapliyal NC, Kishore S, Pathak VP. Efficacy of Broncho-Alveolar Lavage and Bronchial Brush Cytology in Diagnosing Lung Cancers. J Cytol 2007; 24:73-7.
8. Ahmad M, Afzal S, Saeed W, Mubarik A, Saleem N, Khan SA, et al. Efficacy of bronchial wash cytology and its correlation with biopsy in lung tumours. J Pak Med Assoc 2004; 54:13-6.
9. Hutchinson ML, Cassin CM, Ball HG 3rd. The efficacy of an automated preparation device for cervical cytology. Am J Clin Pathol 1991; 96: 300–305.
10. Choi YD, Han CW, Kim JH, Oh IJ, Lee JS, et al. Effectiveness of sputum cytology using ThinPrep method for evaluation of lung cancer. Diagn Cytopathol 2008; 36: 167–171.
11. Elsheikh TM, Kirkpatrick JL, Wu HH Comparison of ThinPrep and cytospin preparations in the evaluation of exfoliative cytology specimens. Cancer 2006;108: 144–149
12. Michael CW, Hunter B. Interpretation of fine-needle aspirates processed by the ThinPrep technique: cytologic artifacts and diagnostic pitfalls. Diagn Cytopathol.2000; 23: 6–13.
13. Chaoying Liu, Zhongmei Wen, Yang Li, Liping Peng, Application of ThinPrep Bronchial Brushing Cytology in the Early Diagnosis of Lung Cancer: A Retrospective Study.April 2014; 9(4):1-7
14. De Groot P, Munden RF, Lung cancer epidemiology, risk factors, and prevention. Radiol Clin North Am.2012; 50: 863–876.
15. Dela Cruz CS, Tanoue LT, Matthay RA. Lung cancer: epidemiology, etiology, and prevention. Clin Chest Med.2011; 32: 605–644.
16. Yang Yang, Xiuwei Zhang, Jianbao Lu, Paul Zarogoulidis, Xin'an Wang & Haidong Huang, Application of liquid-based cytology test of bronchial lavage fluid in lung cancer diagnosis, Thoracic Cancer.2013;4:318-322.
17. Abha Thakur, Pooja Bakshi, Gagandeep Kaur, Kusum Verma, Liquid-based and conventional cytology for bronchial washings/ bronchoalveolar lavages in the diagnosis of malignancy – An institutional experience, Journal of Cytology. July-September 2017; 34(3):127-132.
18. E. Astall, C. Atkinson, N. Morton and M. J. Goddard, The evaluation of liquid-based 'Cyto-SEDTM' cytology of bronchioalveolar lavage specimens in the diagnosis of pulmonary neoplasia against conventional direct smears, Cytopathology 2003;14:143–149
19. D. N. Rana, M. O'donnell, A. Malkin And M. Griffin, A comparative study: conventional preparation and Thin Prep 2000 in respiratory cytology, Blackwell Science Ltd, Cytopathology, 2001; 12: 390-398.
20. Kathiresan B, Iles S, Glinski L. Conventional cytology VS liquid-based cytology in preparation of bronchial wash, does the later have potential advantages? Eur Respir J 2013; 42(Suppl 57):5091.
21. Fischler D F, Toddy S M. Non gynecologic cytology utilizing the Thinprep Processor, Acta Cytol, AU 1996;40:669-675.
22. Yi-Bo Fan, Qing-Shan Wang, Lin Ye, Tian-Yu Wang, and Guang-Ping Wu, Clinical application of the SurePath liquid-based Pap test in cytological screening of bronchial brushing for the diagnosis of lung cancer, Cytotechnology. Jan 2010; 62(1): 53–59.
23. Dan Gong, Tao Chen, Qiyuan Li, Nian Liu, Xueying Su, Surepath liquid- based cytology combined with conventional bronchial brushing smears in the diagnosis of primary and secondary pulmonary malignant tumors, Int J Clin Exp Pathol 2017; 10(4):4115-4122.