



EFFICACY OF LUNG CYTOLOGY AND ITS CORRELATION WITH LUNG BIOPSY IN DIAGNOSIS OF LUNG LESIONS

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ABSTRACT **Background:** Respiratory cytology has assumed a primary diagnostic place in evaluation of any patient with suspected lung lesion in which morphological confirmation is indicated. Endoscopic examination of tracheobronchial tree is the most proven valuable method in diagnosing lung cancer. Its advent revolutionized respiratory cytology as techniques like bronchial brush cytology (BBC), bronchial wash (BW), bronchoalveolar lavage and bronchial biopsy became more easy, accessible and popular. **Methods:** This retrospective observational study conducted at the Department of Pathology in Jaipur National Institute of Medical Sciences and Research Center, Jaipur. All the specimens of bronchial cytology and lung biopsy specimens between January 1, 2021, and January 31, 2023 were included in the study. The study included 156 cases, with 117 males and 39 females. Samples were collected using a flexible fiberoptic bronchoscope, and various staining techniques were used for analysis. The study received approval from the Institutional Ethics Committee. Statistical analysis was performed using SPSS for calculating sensitivity, specificity, positive predictive value, negative predictive value, and p-value using Fisher's test. **Results :** The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of bronchial brush cytology were 78.95%, 64.29%, 85.71% and 52.94 %, 75.0% respectively. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of bronchoalveolar lavage were 22.5%, 91.30%, 81.82 % and 40.38 % , 47.62% respectively. The p value for BAL and bronchial brush cytology were 0.41 and <0.01 respectively. **Conclusion :** Bronchial brushing cytology (BBC) and Broncho-alveolar lavage (BAL) are quick, safe non invasive and economical diagnostic modality. Bronchial brushing cytology (BBC) is better than Broncho-alveolar lavage.

KEYWORDS : Bronchoalveolar lavage (BAL), Bronchial Brushing Cytology (BBC), Bronchial Biopsy (BB).

INTRODUCTION

Respiratory cytology has assumed a primary diagnostic place in evaluation of any patient with suspected lung lesion in which morphological confirmation is indicated. (1) Endoscopic examination of tracheobronchial tree is the most proven valuable method in diagnosing lung cancer. Its advent revolutionized respiratory cytology as techniques like bronchial brush (BB), bronchial wash (BW), bronchoalveolar lavage and bronchial biopsy became more easy, accessible and popular. (2)

Bronchoalveolar lavage (BAL), which was originally developed as therapeutic tool for pulmonary conditions like pulmonary alveolar proteinosis, cystic fibrosis and intractable asthma, also has gained acceptance and steady popularity as a tool for diagnosing lung cancer. Bronchial brushing (BBC) is a technique where surface of a suspected lesion, visualized through a bronchoscope, is scraped by brush that are specially designed to pass through bronchoscope in order to collect the cytological sample. Bronchial brushings can be used for exfoliative cytology or microbiological analysis. (3)

Though sputum cytology continues to be the most frequently examined specimen than bronchial washing, brushing, BAL and FNAB, which are gaining irreplaceable position in the use of cytology. Each technique has its own indication, limitation and frequently complements each other. Sputum examined as multiple specimens will show more central tumors, whereas bronchial brushings and FNAB will show more peripheral and subpleural lesions. (4) Of all methods, the cytological diagnostic yield of brush cytology is of great value and has been proved by various studies. (4)

Bronchoscopy-aided biopsy cannot visualize early malignancy nor can be performed in more peripheral sites. It cannot be done in patients with risk of hemorrhage and in tumors that have lepidic growth. So alternative methods for diagnosis are required. Hence, bronchial cytology will complement tissue biopsy in lung lesions. [1]

The aim of the present study was to determine the efficacy of bronchoalveolar lavage, bronchial brush cytology and their correlation with bronchial biopsy in diagnosing lung lesions.

METHOD AND MATERIAL:

This is a retrospective observational study conducted in Department of Pathology of Jaipur National Institute of Medical Sciences and Research Center, Jaipur during the period between 1 January 2021 to 31 January 2023. We have included all the cases of bronchial cytology and lung biopsy specimen received in the Central lab, Pathology department.

Total 156 cases are included in this study in which 117 were males and 39 were females.

The samples were collected by the pulmonologist with the use of flexible fiberoptic bronchoscope. BAL samples were received as 20 ml aliquots of normal saline in sterile vials. Samples were centrifuged in cytospin and air-dried and wet-fixed smears were prepared. BBC samples were received as air-dried and wet-fixed slides. The air-dried smears were stained with May Grunwald Geimsa and the wet-fixed slides with Papanicolaou and Hematoxylin and Eosin stains and examined under microscope by pathologist. Bronchial Biopsy specimen received in 10% formaline filled container and kept for fixation and processed. Slides were stained with H&E stain and studied under microscope by pathologist. We have received approval from Institutional ethical committee for the same study.

Data Collection And Tools For Statistical Analysis

All the samples received in Central lab Pathology Department for bronchial cytology and bronchial biopsy examination were included in this study.

For statistical analysis SPSS was used for calculation of sensitivity, specificity, positive predictive value (PP) and Negative predictive value (NP). P value was calculated by Fisher test.

RESULTS

In this study we included 156 cases, in which 117 were males and 39 were females. The male:female is 3:1. The age of the patients included in this study varies from 22 yrs to 96 yr and mean age was 60.1 yrs. Out of 156 cases, BAL cytology in 122 cases, brush cytology in 82 cases and biopsy in 92 cases were received. In 62 cases both BAL and biopsy were received. In 53 cases both BBC and biopsy were received. The sensitivity, specificity, positive predictive value, negative predictive value for BAL were respectively 22.5%, 91.30%, 81.82%

and 40.38% and for BBC 78.95%,64.29%,85.71% and 52.94%. p value for BAL was 0.33 and for BBC<0.01.

Table - 1 :Agewise distribution of cases

Age group Yrs	Male	Female	Total	Percentage
21-30	3	1	4	2.6%
31-40	7	2	9	5.8%
41-50	12	9	21	13.5%
51-60	34	8	42	26.9%
61-70	40	13	53	33.9%
71-80	17	5	22	14.1%
81-90	3	1	4	2.6%
91-100	1	-	1	0.01
Total	117	39	156	100%

Table - 2 : Morphological categorization of lung lesions on Biopsy

Type	Number	Percentage
Squamous cell carcinoma	26	23.9%
Adenocarcinoma	14	15.2%
Small cell carcinoma	14	15.2%
Large cell neuroendocrine tumour	2	2.2%
Non small cell carcinoma	2	2.2%
Undifferentiated carcinoma	2	2.2%
Malignant epithelial tumor	1	1.1%
Metastatic adenocarcinoma	1	1.1%
Solitary fibrous tumor	1	1.1%
Malignant myxoid sarcoma	1	1.1%
Suspicious for malignancy	2	2.2%
Negative for malignancy	21	22.8%
Inadequate	5	6.3 %
Total	92	100%

Table - 3 : Sensitivity , Specificity, PPV, NPV, Accuracy of BAL and BBC

	BAL	95%CI	BBC	95%CI
Sensitivity	22.50%	10.84% to 38.45%	78.95%	62.68% to 90.45%
Specificity	91.30%	71.96% to 98.93%	64.29%	35.14% to 87.24%
Positive predictive value	81.82%	48.22% to 97.72%	85.71%	69.74% to 95.19%
Negative predictive value	40.38%	27.01% to 54.09%	52.94%	27.81% to 77.02%
Positive likelihood ratio	2.59	0.61 to 10.96	2.21	1.07 to 4.55
Negative likelihood ratio	0.85	0.69 to 1.05	0.33	0.16 to 0.68
Accuracy	47.623%	34.88 % to 60.59%	75.00%	61.05% to 85.97%

Descriptive analysis of BAL

Quantitative variables

	mean (sd)	median [Q25-75]	min	max	n
AGE	59.9 (13.1)	61.0 [50.2; 69.0]	22.0	96.0	122

Qualitative variables

		n (%)
RESULTS OF BAL	NEGATIVE	88 (72%)
	INADEQUATE	19 (16%)
	POSITIVE	15 (12%)
RESULTS OF BB	POSITIVE	40 (65%)
	NEGATIVE	17 (27%)
	INADEQUATE	5 (8.1%)
SEXBR	M	91 (75%)
	F	31 (25%)

Univariable analysis

By RESULT OF BAL

		Result Negative (n = 88)	Result Inadequate (n = 19)	Result Positive (n = 15)	n	p	test
AGE, mean (standard deviation)		59.5 (14.4)	62.9 (8.72)	57.7 (9.01)	122	0.35	Kruskal-Wallis
RESULT BB, n	Positive	26 (62%)	5 (56%)	9 (82%)	40	0.41	Fisher

	Negative	13(31%)	2 (22%)	2 (18%)	17	-	-
	Inadequate	3 (7.1%)	2 (22%)	0 (0%)	5	-	-
SEXBR, n	M	63(72%)	15 (79%)	13(87%)	91	0.45	Fisher
	F	25(28%)	4 (21%)	2 (13%)	31	-	-

The average rank of AGE is not significantly different depending on RESULT (p = 0.35) by (Kruskal-Wallis test). The distribution of results of BB is not significantly different depending on results of BAL(p = 0.41) by ex Fisher test. The distribution of SEX is not significantly different depending on RESULTS of BAL (p = 0.45) by Fisher test.

Descriptive analysis

Quantitative variables

	mean (sd)	median [Q25-75]	min	max	n
AGE	60.5 (11.0)	61.0 [51.8; 69.0]	22.0	87.0	82

Qualitative variables

		n (%)
RESULTS OS BBC	POSITIVE	52 (63%)
	NEGATIVE	29 (35%)
	INADEQUATE	1 (1.2%)
RESULT OF BB	POSITIVE	37 (70%)
	NEGATIVE	12 (23%)
	INADEQUATE	4 (7.5%)
SEX	M	60 (73%)
	F	22 (27%)

Univariable analysis

By RESULT OF BBC

		Result Positive (n = 52)	Result Negative (n = 29)	Result Inadequate (n = 1)	n	p	test
AGE, mean (standard deviation)		63.0 (10.0)	55.4 (11.0)	76.0 (-)	82	<0.01	Kruskal-Wallis
RESULT OF BB, n	Positive	30 (81%)	7 (44%)	0 (-)	37	<0.01	Fisher
	Negative	4 (11%)	8 (50%)	0 (-)	12	-	-
	Inadequate	3 (8.1%)	1 (6.2%)	0 (-)	4	-	-
SEX, n	M	40(77%)	20 (69%)	0 (0%)	60	0.17	Fisher
	F	12(23%)	9 (31%)	1(100%)	22	-	-

The average rank of AGE is significantly different depending on RESULT of BBC (p = <0.01) by Kruskal-Wallis test. The distribution of RESULT OF BB is significantly different depending on RESULTS of BBC (p = <0.01) by Fisher test. The distribution of SEX is not significantly different depending on RESULTS of BBC(p = 0.17) by Fisher test.

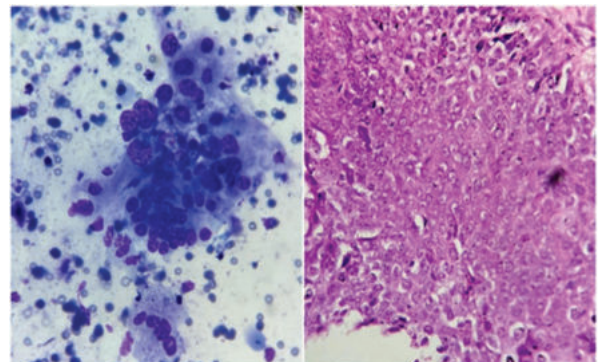


Figure showing Squamous Cell Carcinoma, Bronchial Brush Cytology showing atypical squamous cells with high N:C ratio and clumped chromatin(Giemsa stain 400X) and Bronchial Biopsy showing sheet of atypical squamous cells with high N:C ratio, clumped chromatin with atypical mitotic figures.(H &E 400X)

Figure showing Adenocarcinoma, Bronchial Brush Cytology showing tumor cells arranged in glandular pattern having highN:C ratio, coarse chromatin (Giemsa stain 400X) and Bronchial Biopsy showing acinar arrangement of tumor cells, cells having hyperchromatic nuclei with prominent nucleoli and presence of mucin. (H &E 400X)

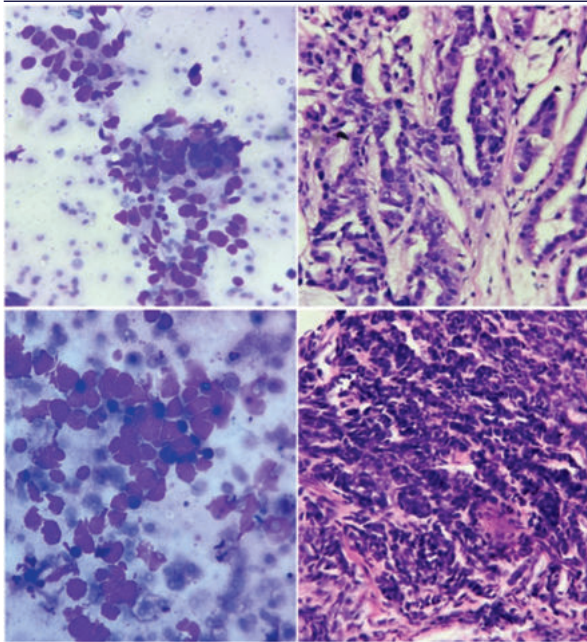


Figure showing small Cell Carcinoma, Bronchial Brush Cytology showing atypical cells with high N:C ratio, nuclear moulding and smudged chromatin (Giemsa stain 400X) and Bronchial Biopsy showing pleomorphic small round cells with high N:C ratio and scant cytoplasm. (H & E 400X)

DISCUSSION

Neoplastic and non-neoplastic pulmonary lesions have a high rate of morbidity and mortality. Lung cancer is the frequently diagnosed cause for cancer related deaths and tuberculosis is still the leading cause of death in developing countries. The increasing incidence of various lung lesions could be attributed to smoking, occupational hazards, increased environmental pollution. Early and accurate diagnosis is required to effectively manage these diseases.(5)

- Although conventional histopathology is the gold standard for their diagnosis, cytology is a useful adjunctive diagnostic test.(6) Cytologic techniques are safer, economical, and provide quick results. Bronchoscopic washing, brushing, and fine needle aspirations not only complement tissue biopsies in the diagnosis of lung cancer but are also comparable(7).

In our study Bronchioalveolar lavage was the most common type of cytological specimen which is similar to study of Rateesh Sareen et al and Dawan S et al.(7,8)

The most common age group of our study was between 51-70 years which was similar to Shreya Goel et al, Fadiya Zainudeen et al and Vijeta Tomar et al where most common age group were 5 th to 7 th decade.(1,2,9)

Our study showed male preponderance. The male to female ratio in our study was 3:1. This was similar to study done by Shreya Goel et al where ratio was 2.7:1, by Jofy George et al where ratio was 3.3:1 and study of Raiza D et al, where the male to female ratio was 6:1.(1,10,11) In our study there were 21 false negative and 2 False positive cases in BAL, the reason behind this may be that cytological sampling by BAL relies mainly on cells "exfoliated" from the malignant lesion. Exfoliated cells that are lying in the bronchus start developing degenerative changes, thus progressively losing their morphological details, which are important in differentiating them from nonmalignant cells that are shed off by the normal bronchial epithelial lining. With BAL, the bronchoscope is wedged into position as far as it goes, and the distal airways are flushed with several aliquots of sterile saline, usually approximately 20 mL. The first aliquot is more representative of the cellular material from larger airways, whereas subsequent aliquots reflect the alveolar compartment.(9)

In our study in BBC 6 false positive and 8 false negative cases were reported. False positives in cytology may be reported due to misinterpretation of smears due to cellular changes in chronic inflammatory disorders such as pneumonia (atypical histiocytes), TB,

bronchiectasis, (misinterpretation of cuboidal epithelial cells as small cell carcinoma), squamous metaplasia, and alveolar cell polymorphism in lung fibrosis. False positive have very unfortunate consequences for patients; therefore, some advice "underreporting" instead of "over reporting" of suspicious cases. The reasons of false negatives could have been superadded inflammation, nonrepresentative material, or hypocellular aspirate.(7)

Table 8 : Comparison with other studies

Study	Sensitivity		Specificity		Positive predictive value		Negative predictive value	
	BAL	BBC	BAL	BBC	BAL	BBC	BAL	BBC
Present study	22.5 0%	78.9 5%	91.3 0%	64.2 9%	81.82% %	85.71 %	40.38% %	52.94 %
Apar Agarwal et al	20.2 %	41.4 %	38% %	44% %	48.21% %	88.93 %	70.24% %	90.65 %
Vijeta Tomar et al	47.6 1%	65.0 7%	75% %	75% %	96.77% %	97.61 %	8.33% %	12% %
Rateesh Sareen et al	72.6 9%	77.7 8%	100 %	100 %	100% %	100% %	76.95% %	75% %
Bhat N et al.	35.5 %		78.1 6%.					
Jofy George et al	51% %	59.2 8%	100 %	100 %	100% %	100% %	43.18% %	47.62 %
Gaur DS et.al.	39.4 %	87.3 %	89.6 %	97.6 %				

On cytological examination we observed that cellularity was higher in BBC than BAL in most of the cases so sensitivity of BBC was more than BAL which is similar to the study of Apar Agarwal et al, Rateesh Sareen et al, Vijeta Tomar et al, Jofy George et al and Gaur DS et al.(3,7,9,10,13). PPV,NPV of Brush cytology were more than BAL which is similar to the study of, Apar Agarwal et al, Vijeta Tomar et al and Jofy George et al(3,9,10). The causes for varying sensitivity in other studies include the use of different techniques for the retrieval and processing of brushing specimens such as the type of brush used capped or uncapped and the inclusion of "suspicious" cases as positive for calculation of sensitivity. It is better than BAL due to less degeneration in brushing specimens in comparison to BAL(7)

In our study malignancy was more common in males, male : female was 4.5:1 and malignancy was more common in 61 -70 yrs age group. Same results were found in study of Fadiya Zainudeen et al, Vijeta Tomar et al(2,9).

According to WHO the most common type of lung malignancy is Adenocarcinoma but in our study most common type of malignancy on bronchial biopsy was Squamous cell carcinoma 23.9% followed by small cell carcinoma 15.2%, adenocarcinoma 15.2%, Large cell neuroendocrine tumour and undifferentiated tumor 2.2% each. The reasons behind this is that in our study most of the patients were males with smoking history as compared to females and on radiological findings tumours were centrally placed. Our results are similar to study of Apar Agarwal et al, Rateesh Sareen et al and Dawan S et al in which squamous cell carcinoma was most common followed by small cell carcinoma (3,7,8).

P value for BAL was 0.41 and for Brush cytology it was <0.01 which was same as Shreya Goel et al(1).

CONCLUSION

Bronchial brush cytology is better technique than BAL in diagnosis and morphological typing of lung cancer, as it demonstrates far better sensitivity and accuracy due to higher cellular yield. Specificity is higher for BAL so both the techniques are required simultaneously for better diagnostic yield. These techniques are better for centrally placed lesions than peripheral lesions and in patients where biopsy is contraindicated. Bronchial cytology is safe, quick and cost effective,

Conflicts Of Interest: There are no conflicts of interest.

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