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Original Article

Pathology Section

Comparison between Cytology and Histopathology of Lung Tumours: A Cross-sectional Study

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ABSTRACT

Introduction: Lung cancer is the leading cause of cancer deaths world-wide, predominantly Non-Small Cell Lung Cancers (NSCLC), consisting mainly of adenocarcinoma, followed by squamous cell carcinoma, Adenosquamous carcinoma, and large-cell anaplastic carcinoma. For early diagnosis, bronchoalveolar lavage plays a key role in diagnosis. Bronchoalveolar lavage is easier to perform, cost effective and yields good diagnostic value and is time saving.

Aim: To evaluate lung malignancies from bronchoalveolar lavage and to find the concordance between cytological diagnosis with the histopathological diagnosis.

Materials and Methods: The present cross-sectional study was conducted during the period of three years from December 2021 to December 2024 at the Stanley Medical College, Chennai, Tamil Nadu, India. A total of 60 lung carcinoma cases and 10 control cases, which received as bronchoalveolar lavage wash and brush were processed and reported along with their fibre optic bronchoscopic biopsy tissue blocks.

Results: In the present study, 60 cases of biopsy positive lung carcinoma and 10 control were taken and correlated with cytological studies. A total of 54 cases were positively reported as malignant in cytology, three smears had no cells and three showed no evidence of malignancy, giving 90% sensitivity-positive concordance between cytology and histopathology, yielding high positive predictive value (100%) with cytology smears. Data were analysed using IBM Statistical Package for the Social Sciences (SPSS) version 25 using descriptive statistics and the chi-square/Fisher's exact test, with $p<0.001$ was considered statistically significant.

Conclusion: Bronchoalveolar Lavage Wash and Brush specimens have excellent correlation with Fibre optic Bronchoscopic biopsy for Histopathology, thereby helping in early and quick diagnosis of lung carcinoma. Thus, an invasive procedure like biopsy can be avoided if cytology shows positive for malignancy.

Keywords: Bronchial wash, Brush, Cytology of lung, Fibre optic bronchoscopy, Lung carcinoma

INTRODUCTION

Lung cancer is the leading cause of cancer deaths worldwide. Approximately, 77% are predominantly NSCLC [1], consisting mainly of adenocarcinoma, followed by squamous cell carcinoma, adenosquamous carcinoma, and large-cell anaplastic carcinoma [1]. There has been a steady increase in lung carcinomas in the recent decades, more so among females and non-smokers [2]. The incidence of NSCLC in particularly adenocarcinomas is on the rise [3]. The diagnosis of early lung cancer plays a vital role in prognosis of the patient as earlier diagnosis with early intervention has better prognosis.

Bronchoalveolar lavage is a minimally invasive diagnostic procedure in pulmonary medicine used to sample the cellular and non cellular components of the lower respiratory tract [4]. Its diagnostic parameters include cellular analysis and differential counting [5], microbiological testing, cytopathology and malignancy and specialised diagnostic markers [6].

For early diagnosis, bronchoalveolar lavage plays a key role in diagnosis [7]. Bronchoalveolar lavage is easier to perform, cost-effective and yields good diagnostic value and time saving [8]. Studies have shown a high predictive value for bronchoalveolar lavage specimen in the diagnosis of lung tumours [9]. Wash and brush cytology is very accurate and almost in line with histopathological findings [10], thus helping in early diagnosis and thereby early intervention and increasing the life expectancy of the patients [11].

Thus, an invasive procedure like fibre optic bronchoscopic biopsy can be avoided, if bronchoalveolar lavage is done [12] and used effectively and novel ancillary studies like immunocytochemistry can be done in the bronchoalveolar lavage wash and brush [13], for the early and efficient diagnosis of lung carcinomas.

The objectives of the present study were to evaluate using broncho alveolar wash and brush specimens for diagnosing lung malignancy and to compare them with their respective biopsy specimen and evaluate the accuracy in small cytology samples, thereby helping in early diagnosis and quicker management of the patients and avoiding delay. Hence, the present study aimed to evaluate lung malignancies from bronchoalveolar lavage and to find the concordance between cytological diagnosis with the histopathological diagnosis.

MATERIALS AND METHODS

The present cross-sectional study was conducted during the period of three years from December 2021 to December 2024 at Stanley Medical college, Chennai, Tamil Nadu, India. The study was approved by the Ethical committee. (IEC No. ECR/131/Inst/TN/2013/RR19).

A total of 60 lung carcinoma cases and 10 negative cases (control), which we received bronchoalveolar lavage wash and brush were processed and reported along with 60 fibre optic bronchoscopic biopsy tissue blocks.

Sample size was calculated by the formula $n=\frac{Z^2\times p\times(1-p)/e^2}{(n=59.0)}$

where, z= 1.96, p= 0.04, e= 0.05

e- margin of error (0.05)

p- (0.04) prevalence calculated from statistical data of lung carcinomas in the Stanley Medical College Medical Record Data Department (Five years date: 2017-2022).

Inclusion criteria: All suspected cases of carcinomas of lung.

Exclusion criteria: Benign neoplasms of lung was not included in the present study.

Study Procedure

Method of tissue preparation: Broncho alveolar lavage-brush, wash and biopsy specimen are received and processed for cytology and histopathology respectively. Cytology slides are made on the same day and histopathological examination is done from paraffin embedded blocks of the biopsy specimen and cut in four micrometer sections.

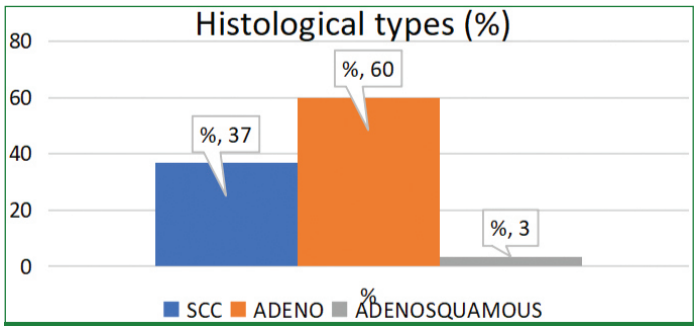
- Formalin fixed and paraffin embedded lung cancer tissue blocks were selected in our department of pathology.
- Sections of 4-5 µm thickness were cut from the paraffin block and taken on charged slides.
- Bronchoalveolar lavage specimen-wash and brush cytology was studied and Haematoxylin and Eosin (H&E) histopathology sections were studied to diagnose lung carcinoma and subtype the lung carcinomas in histopathology.

STATISTICAL ANALYSIS

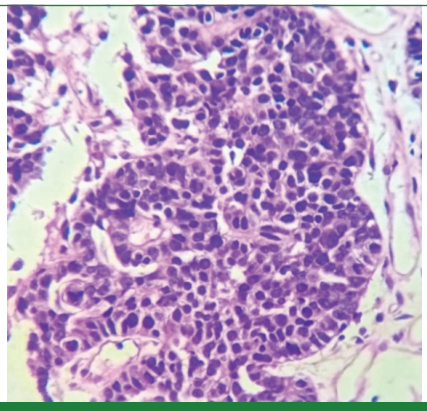
By using statistical methods, descriptive analysis of Age distribution, laterality, tumour site, cytology and histopathological correlation along with histopathological subtyping were done. Data were represented using appropriate diagram like bar diagram and tables. Chi square analysis and Fisher's exact p-value used. With degree of freedom=1 (2x2 table). The p-value of <0.001 considered statistically significant. IBM Statistical Package for the Social Sciences (SPSS) version 25 was used for statistical analysis. The values were compared and represented with appropriate tables and diagrams.

RESULTS

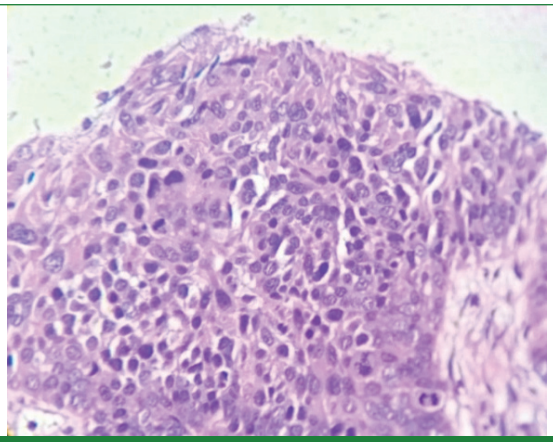
In the present study, out of 60 biopsy positive lung malignancies, 54 cases were reported positive in cytology specimens received, either in wash or brush cytology. Among 60 positive cases, 36 cases were adenocarcinoma of lung 36 (60%), 22 cases were squamous cell carcinoma of lung 22 (37%) and two cases were adenosquamous carcinoma of lung 2 (3%) [Table/Fig-1]. Out of 36 adenocarcinoma cases, 35 were positive in cytology specimen and one was negative. Among 22 Squamous cell carcinoma of lung, 17 were positive in cytology and five were negative. Both adenosquamous carcinoma of lung were positive in cytology [Table/Fig-2-6].



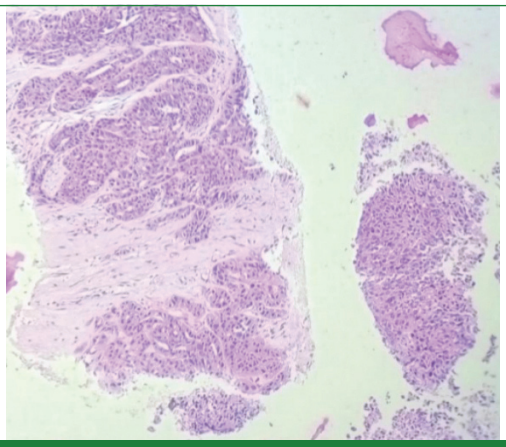
[Table/Fig-1]: Histological types of lung carcinoma in the study population (%).



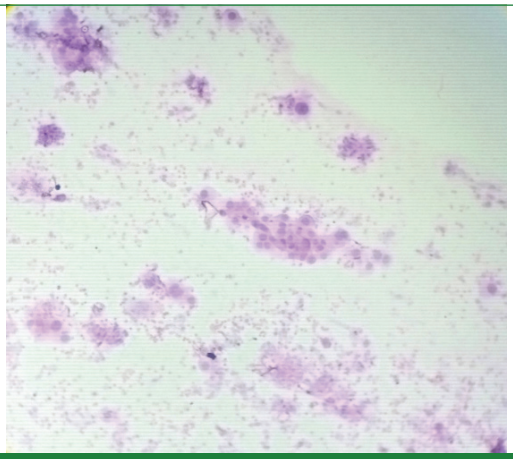
[Table/Fig-2]: Histopathology of adeno carcinoma of lung showing malignant glands, lined by cells exhibiting marked atypia (H&E, 40x).



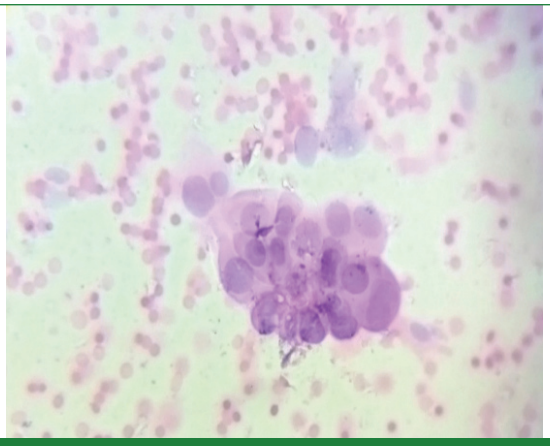
[Table/Fig-3]: Histopathology of squamous cell carcinoma of Lung, image showing squamous cells with marked pleomorphism (H&E, 40x).



[Table/Fig-4]: Histopathology of Adeno squamous carcinoma of lung, image showing both squamous and adenocarcinoma components (H&E, 10x).



[Table/Fig-5]: Cytology of bronchoalveolar wash showing clusters of malignant epithelial cells (H&E, 10x).



[Table/Fig-6]: Cytology of bronchoalveolar wash showing clusters of malignant cells with marked nuclear atypia (H&E, 40x).

Out of 60 positive cases, 47 were male and 13 were female [Table/Fig-7] with predominantly adenocarcinoma in both males and females with proportion of 51 % and 92%, respectively. With respect to adenocarcinoma of lung, females have a higher preponderance to adenocarcinaoma than squamous cell carcinoma, where females show 92% adenocarcinoma and 8% squamous cell carcinoma, in comparison with males, who show 51% adenocarcinoma and 45% squamous cell carcinoma [Table/Fig-8].

Age (years)	Male (n=47) (n)	Female (n=13) (n)	Total (n)
<40	1	2	3
40-60	25	9	34
>60	21	2	23
Total	47	13	60

[Table/Fig-7]: Age-wise distribution in study population (N=60).

Malignancy	Male (n=47) n (%)	Female (n=13) n (%)	Total n (%)
Squamous cell carcinoma	21 (45)	1 (8)	22 (37)
Adenocarcinoma	24 (51)	12 (92)	36 (60)
Adenosquamous	2 (4)	0	2 (3)
Total	47 (78)	13 (22)	60 (100)

[Table/Fig-8]: Frequency of histologic types of lung malignancies.

In the study population, 60% presented with adenocarcinoma of lung and 37% presented with squamous cell carcinoma of lung, with 3% of adenosquamous carcinoma of lung.

Commonest age group was between 40 to 60 years, 34 cases accounted for 57% of total study population. Three cases were young under 40 years of age giving rise to 5% of total study population. A total of 23 cases were above 60 years of age accounting for 38% of total population, and 78% were male and 22% were female, showing male preponderance from lung malignancies.

Among 60 cases, 31 patients had left sided lung malignancy accounting for 52 % of total population and 29 patients had right sided malignancy [Table/Fig-9], accounting for 48% of total study population.

Laterality	n (%)
Right	29 (48)
Left	31 (52)
Total	60 (100)

[Table/Fig-9]: Laterality distribution in study population (N=60).

Descriptive analysis of tumour site in study population (N=60): In this study, population of 60 cases, tumours were present in upper lobe, Lower lobe and hilar area in both right and left lungs.

It is observed that 67% of the lung malignancies occupy the upper lobe of both lungs in the study population, whereas, 25% occupies the lower lobe and only 8% were hilar [Table/Fig-10]. No middle lobe of right lung or multilobar tumours was there.

Laterality	Upper lobe (n)	Lower lobe (n)	Hilum (n)	Total n (%)
Right	22	6	1	29 (48)
Left	18	9	4	31 (52)
Total	40	15	5	60 (100)
%	67	25	8	

[Table/Fig-10]: Tumour site distribution in study population (N=60).

Descriptive analysis of Cytology histopathology in the study population: With respect to cytology of bronchoalveolar lavage washes and/or brush specimen when compared with the respective biopsy histopathology, 54 were positively correlated with 90% positive correlation and 10% were negatively correlated. There is no case that was cytology positive with negative biopsy [Table/Fig-11]. Among negative cases, three were found to have no material in cytology specimen received and three cases, no malignant cells were found.

Cytology/HP	Cytology positive	Cytology negative	Total
HP positive	54	6	60
HP negative	0	10	10
Total	54	16	70

[Table/Fig-11]: Contigency table of cytology and histopathology results.
HP: Histopath; True positive-54; True Negative-10; False positive- 0; False negative-6; Sensitivity of bronchoalveolar lavage (cytology) (True positive rate)- 90% Specificity of bronchoalveolar lavage (cytology) (True negative rate)-100%; Positive predictive value of cytology-100%; Negative predictive value of cytology-62.5%

Chi-square test results: Degree of freedom= 1;((2-1)x(2-1)) chi-square value=10.828 (Degree of Freedom 1 and p <0.001) Since the expected cell frequency for histopathology negative/cytology negative is (2.28)-which is less than 5, the Fisher's-exact Test p-value is used, which is p-value <0.001 (Statistically highly significant)

DISCUSSION

Lung cancer incidence is increasing and imparting major health problem worldwide including India. Older age group are affected most commonly [14]. However, nowadays there is a change in trend with increase in lung cancer incidence in young, middle aged people, females, non smoker. The changing trends in age of onset may be related to change in the life style, occupation, tobacco use and increasing pollution in the environment [15].

People with breathing difficulty often neglect the early symptoms and fail to come to hospitals until they present with some serious symptoms such as haemoptysis and severe breathlessness, later leading to airway obstruction. Lung masses can be easily screened with Chest X-rays and Chest Computed Tomography [16], following which the patients can undergo bronchoalveolar lavage as a diagnostic measure to visualise the tumour directly and to localise [17]. With the help of fibre optic bronchoscope, nowadays it's easier to perform bronchoalveolar lavage and the wash and brush specimen can be utilised as a vital diagnostic tool in evaluation of the lung tumours, along with fibre optic bronchoscopic biopsies to confirm the cytological diagnosis [18].

Out of 60 biopsy positive lung malignancies, 54 cases were reported positive in cytology specimens received, either in wash or brush cytology.

Among the 60 histopathologically positive cases, 36 cases were primary adenocarcinoma of lung, 22 cases were squamous cell carcinoma of lung and two cases were adenosquamous carcinoma of lung. Of 36 adenocarcinoma cases, 35 were positive in cytology specimen and one was negative.

Among 22 Squamous cell carcinoma of lung, 17 were positive in cytology and five were negative. Both adenosquamous carcinoma of lung were positive in cytology specimen.

A study conducted by Sackett MK et al., for cytology and histopathology correlation of lung tumours showed out of 231 biopsy positive cases [19], 225 were positive in cytology with a 97.4% concordance. In another study conducted by Sharma T et al., an overall cytology-biopsy concordance of 68% among 46 lung carcinoma cases was reported with 25 biopsy-positive and 17 cytology-positive cases [20]. The present study with 60 cases positive in histopathology 54 were positive in cytology 90% positive correlation, which shows cytology techniques aid in diagnosis of lung tumours with high positive predictive value and comparable with other studies [Table/Fig-12] [19,20]. The six negative cases were due to technical issues during procedure leading to non-availability of material or non representative sampling area.

Study	Total cases (all subtypes)	Positive concordance		Percentage
		Biopsy	Cytology	
Sackett MK et al., 2010 [19]	231	231	225	97.4%
Sharma T et al., 2021 [20]	46	25	17	68%
Present study	60	60	54	90%

[Table/Fig-12]: Comparison of concordance of cytology and biopsy in lung tumours with other studies [19,20].

Limitation(s)

Only biopsy positive cases were taken for the present study and biopsy negative cases are kept as control, so the specificity of the study may vary with the overall data, where negative cases are also included in the main study. Histological subtypes were based on the morphology and immunohistochemistry study of those cases was not included in the study, limiting the confirmation of the subtypes.

CONCLUSION(S)

Bronchoalveolar lavage wash and brush cytology with such high sensitivity and p-value high significance of the study, and in comparison with the histopathology, it gives the clinician, the significance of bronchoalveolar lavage cytology in early diagnosis of lung tumours, without performing an invasive procedure for positive cytology cases. This makes the diagnostic procedure patient friendly and also novel studies such as Immunocytochemistry can also be performed with bronchoalveolar lavage specimen, thus subtyping the tumours and an earlier targeted approach on treatment.

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