"A CLINICO-MORPHOLOGICAL STUDY OF SMALL LUNG BIOPSIES"

Pathology

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ABSTRACT

Background: Small lung biopsies have become the primary method of diagnosis when a radiological abnormality is detected and tissue diagnosis is required. Lung carcinoma, being the most common cause of cancer mortality in India and worldwide, kills more people than breast and prostate cancers combined. Histopathological characterization of lung cancers by small lung biopsy techniques have helped in guiding therapeutic modalities and genomic classification of lung carcinoma. The highest diagnostic success will be achieved by the multidisciplinary work up between the pathologist, radiologist and clinician altogether.
Objectives Of The Study:
1. To evaluate the utility of cytology and histopathology in diagnosing small lung biopsies.
2. To study and tabulate the clinicopathological profile of patients diagnosed by small lung biopsies.
Materials And Methods The present prospective study was conducted in the central diagnostic laboratory of a tertiary care teaching hospital in Dakshina Kannada District. This was a 2-year study of 87 small lung biopsy specimens. The histopathological, cytological, radiological and clinical records of the patients were studied for small lung biopsies between September 2020 to august 2022. All the examination findings and relevant results were noted. **Results:** A total of 87 small lung biopsy specimens (67 males and 20 females) were studied for a period of 2-years. The average age of the study population was 62.8+/- 9.85 years. Majority of the patients presented with loss of weight. The benign(non-neoplastic) lesions constituted 13(14.9%) of the total number of biopsies (87) while the malignant cases were 74(85.1%). Maximum number of cases 39(44.8%) were reported in the age group of 61-70 years with male preponderance. In all the age groups, malignant lesions were more common in which Adenocarcinoma (Mucinous and Non-mucinous) is the most predominant with 23 cases (31.08%) followed by Squamous Cell Carcinoma of lung with 22 cases (29.7%) and metastasis in lung with 10 cases (13.5%). **Conclusion:** To conclude, the present study explored the usefulness of cytology, histopathology and immunohistochemistry in the diagnosis of various lung lesions from materials obtained as a part of small lung biopsies.

KEYWORDS

Small lung biopsy, Cytology, Histopathology, Lung carcinoma.

1. INTRODUCTION

Small lung biopsies have become the initial method of diagnosis when a radiological abnormality is detected and when histopathological diagnosis is required.[1] In a developing country like India, many patients present in a locally advanced or advanced stage of lung morbidity, where small lung biopsy becomes an important source of tissue diagnosis.[2]

The various methods of obtaining a small lung biopsy specimens are as follows:
a) Transbronchial and endobronchial biopsy using forceps.
b) Endobronchial biopsy, Cryo-biopsy and navigational bronchoscopic biopsy.
c) Transthoracic core needle biopsy – USG or CT guided biopsy.[3]

Amongst these techniques, CT guided biopsy has an advantage for obtaining more tissues to perform cytological, histopathological, IHC and/or molecular studies.[4][5][6]

If bronchoscopy is performed alone, the diagnostic yield is only 60% but increases up to 90% when combined with interventional radiological techniques like CT/ USG guided to confirm the location.[7][8][9] Small lung biopsy is deemed as a boon in establishing diagnosis of lung lesions.[10]

Histopathological characterization of lung cancers by small lung biopsy techniques have helped in genomic classification and treatment modalities of lung malignancies.[11,12] EGFR mutations revealed by small lung biopsy explained the therapeutic importance of molecular classification.[13] Poorly differentiated NSCL carcinoma can be subclassified using small lung biopsies or cytology specimens. The highest diagnostic success will be achieved by the multidisciplinary work up between the pathologist, radiologist and clinician altogether.

The present study intends to explore the usefulness of cytology, histopathology and immunohistochemistry in the diagnosis of various lung lesions from materials obtained as a part of small lung biopsies.

2. AIMS AND OBJECTIVES OF THE STUDY
1. To evaluate the utility of cytology and histopathology in diagnosing small lung biopsies.
2. To study and tabulate the clinicopathological profile of patients diagnosed by small lung biopsies.

3. MATERIALS AND METHODS
The present study was conducted in the Central Diagnostic Laboratory of a tertiary care teaching hospital in Dakshina Kannada District from September 2020 to august 2022(2 years). A cross-sectional study design was used. The sampling technique followed was purposive sampling for the selection

3.1 Inclusion Criteria
1. All the small lung biopsies received were included in this study, irrespective of them being non neoplastic and neoplastic, including primary and metastasis.
2. USG guided/CT guided, per cutaneous transthoracic biopsies and endobronchial biopsy samples.
3. All age groups and both sexes.

3.2 Exclusion Criteria
1. Pleural and mediastinal biopsies.
2. Lobectomies and pneumonectomies.
3. Inadequate material/ haemorrhage/necrotic material.

Sample Size:
- Based on the study conducted by Fei Yang et al, assuming
- $P=0.118$, $n=4pq/l^2$ with 95% Confidence interval and 10% allowable error, the sample
- size estimated for the study = **87.**
- The specimens of the patients were sent to the central diagnostic laboratory in a formalin filled bottle and were given for processing on the same day.

4. RESULTS
The study consisted of 87 patients with an average of 62.80+/- 9.85 years. The youngest patient in this study was 23 years old while the oldest patient was 81 years old. The below figure depicts majority of the study population is between 61-70 years and constituted 44.8%. The next frequency is between the age group of 51-60 years and constituted 22.9%. 1.1% which include the age group between 31-40 years were with least number of cases involved in this study. [Fig 1]
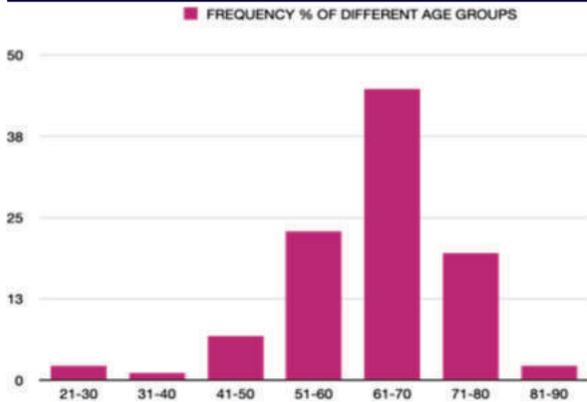
Figure 1: Frequency Percentage Of Different Age Groups

Table 1: Types Of Small Lung Biopsies

TYPES	NUMBER	PERCENTAGE (%)
CT GUIDED BIOPSY	78	89.6
USG GUIDED BIOPSY	2	2.2
BRONCHOSCOPIC BIOPSY	8	9.2
TOTAL	87	100

This study showed majority (89.6%) of the patients had undergone CT guided lung biopsy, followed by bronchoscopic biopsy (9.2%) and the remaining 2.2% had USG guided biopsy. [Table 1]

Table 2: Clinical Presentation

SYMPTOMS	FREQUENCY	PERCENTAGE %
COUGH	32	36.8
BREATHLESSNESS	4	4.6
FEVER	4	4.6
WEIGHT LOSS	44	50.6
HEMOPTYSIS	1	1.1
PAROTID SWELLING	1	1.1
PAIN ABDOMEN	1	1.1
TOTAL	87	100.0

The above table shows majority 44(50.6%) of the patients had weight loss followed by 32(36.8%) of the patients with cough, 4(4.6%) each had breathlessness and fever and 1(1.1%) each had haemoptysis, parotid swelling and pain abdomen.

Table 3: Distribution Of Cect Findings

CECT FINDINGS	NUMBER	PERCENTAGE %
HILAR MASS	2	2.2
RIGHT LUNG MASS	35	40.2
LEFT LUNG MASS	38	43.6
COLLAPSE/CONSOLIDATION	6	6.8
PLEURAL EFFUSION	2	2.2
MEDIASTINAL LAP	2	2.2
METASTASIS	2	2.2

Among the 87 patients, 38(43.6%) presented with CECT findings of mass in the left lung, followed by 35(40.2%) with mass in the right lung. Rest of the patients showed collapse/consolidation in 6(6.8%) and 2(2.2%) each showed hilar mass, pleural effusion, mediastinal lymphadenopathy and metastasis.

Table 4: Distribution Of Fiberoptic Bronchoscopy Findings

Bronchoscopic Findings	Number	Percentage %
Endobronchial Mass Lesion	12	13.7
Narrowing Of Bronchus	4	4.5
Vocal Cord Paralysis	4	4.5
No Eb Lesion	67	77
Total	87	100.0

Out of 87 patients, 12(13.7%) patients had endobronchial mass lesion detected on bronchoscopy, followed by 4(4.5%) patients with narrowing of bronchus and vocal cord paralysis. Majority of the patients 67(77%) showed no endobronchial lesion.
Out of the total 32 patients with an imprint cytology report, 28(87.5%) were malignant and 4(12.5%) were benign. [Table 5]

Table 5: Distribution Of Benign And Malignant Cases Based On

Cytology(imprint)

NATURE	FREQUENCY	PERCENTAGE %
BENIGN	4	12.5
MALIGNANT	28	87.5
TOTAL	32	100.0

Out of the 13 non-neoplastic cases, most common being Granulomatous inflammation (7), followed by pneumonia (3) and pulmonary hamartoma (1), bronchopulmonary candidiasis (1) and acute inflammation(1). [Table 6]

Table 6: Non-neoplastic Lesions Of Small Lung Biopsies

Diagnosis	Number Of Cases
Pulmonary Hamartoma	1
Granulomatous Inflammation (including Tb)	7
Pneumonia	3
Bronchopulmonary Candidiasis	1
Acute Inflammation	1
Total	13

Out of the 74 malignant lesions, Adenocarcinoma [Fig 2] was the most common, followed by Squamous cell carcinoma. [Table 7] [Fig 3]

Table 7: Malignancies In Small Lung Biopsies

| Neoplasms	Number And Percentage
Adenocarcinoma	1(1.35%)
- Mucin Secreting	22(29.7%)
- Non-mucinous	
Squamous Cell Carcinoma	22(29.7%)
Small Cell Carcinoma	7(9.45%)
Undifferentiated/poorly Differentiated Carcinoma	5(6.75%)
Metastasis/secondaries	10(13.5%)
Sarcomatoid Carcinoma	1(1.35%)
Adenosquamous Carcinoma	1(1.35%)
Neuroendocrine Carcinoma	3(4.05%)
Hodgkin Lymphoma	1(1.35%)
Adenoid Cystic Carcinoma	1(1.35%)
Total	74(100%)
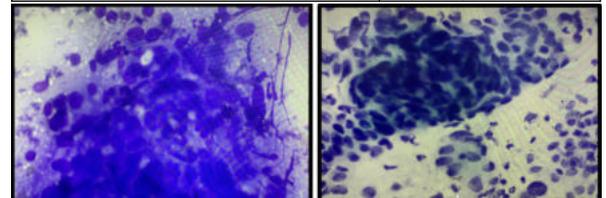
Mgg Stain   **Pap Stain**
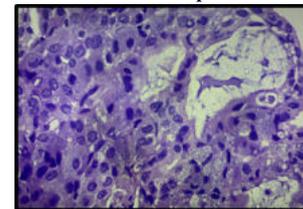
High Power[40x]

Figure 2: Imprint And Histopathology Of Adenocarcinoma Lung

Mgg Stain   **Pap Stain**
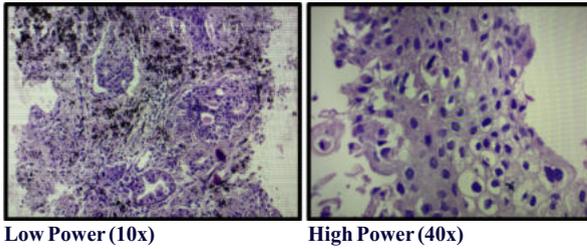
Low Power (10x)   High Power (40x)
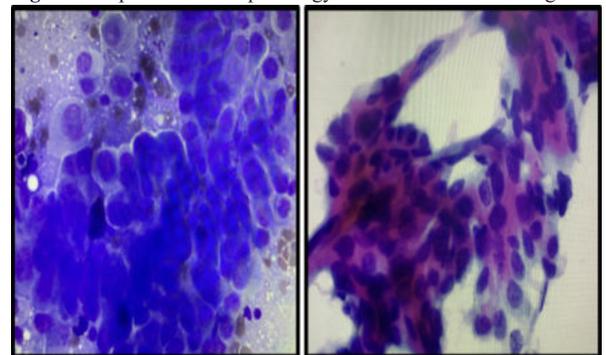
Figure 3: Imprint And Histopathology Of Squamous Cell Carcinoma Lung

Kappa coefficient was used to find the agreement between imprint cytology and histopathology. The Kappa coefficient was 0.404 with p<0.001 .This indicates a significant agreement between imprint cytology and histopathology.

Table 8: Measure Of Agreement

		Value	P value
Measure of Agreement	Kappa	.404	P<0.001

Table 9: Sensitivity, Specificity, Ppv, Npv And Accuracy Of Small Lung Biopsy

Sensitivity	Specificity	PPV	NPV	Accuracy(type-wise)
100%	100%	100%	100%	100%

The overall sensitivity, specificity, PPV, NPV and accuracy of small lung biopsy to diagnose malignant lesions were 100%.

5.DISCUSSION

In today's era, cancer diagnostics has drastically improved with the advent of newer methodologies and techniques by incorporating radiological findings, cytology, histopathology and ancillary studies like immunohistochemical markers and molecular analysis.

According to the study done by Abdulkhader M et.al,[14] out of 139 cases of lung tumors, the majority were seen in the age group of 60-69 years and is similar to our present study. In our study also, majority of the lung tumors 64.8% belong to the age group of 60-69 years. [Table 10]

Table 10: Comparision Of Malignant Cases And Age Group

Study	Present Study	Abdulkhader M et.al
Site	Lung	Lung
Number of malignant cases	74	139
Maximum age group	55-69	60-69
Percentage	64.8%	31.8%

According to the study conducted by **B. Garima et.al[15]**out of 89 cases of lung biopsies, male patients constituted the majority of cases with 74.1% and female patients constituted 25.9% of cases and are similar to our study. In another study conducted by **Nirali Lad et.al[16]** out of 65 cases of lung biopsy, majority 79.27% were male patients and remaining 20.73% of cases were female patients which is similar to the current study.[Table 11]

Table 11: Gender Distribution

Study	Site	No. Of Cases	Male	Female
Present Study	Lung	87	77%	23%
B. Garima et.al	Lung	89	74.1%	25.9%
Nirali Lad et.al	Lung	65	79.27%	20.73%

Table 12: Histological Subtypes Of Lung Tumors In Various Study

Study	Present study	Nirali Lad et.al
Cases	74	52
Adenocarcinoma	31.1%	36.54%
Squamous Cell Carcinoma	29.7%	30.77%
Neuroendocrine Carcinoma	4.05%	1.92%
Others	35.1%	30.77%

According to the study conducted by Nirali Lad et.al, out of 52 cases of lung malignancies, majority of the cases (36.54%) was adenocarcinoma, 30.77% cases showed squamous cell carcinoma, 1.92% cases were neuroendocrine carcinoma which is similar to the current study with 31.1% showed adenocarcinoma, 29.7% cases showed squamous cell carcinoma and 4.05% showed neuroendocrine carcinoma .[Table 12] Thus, analysing different studies,

adenocarcinoma appears to be the most common malignancy followed by squamous cell carcinoma.

6.CONCLUSION

Small Lung biopsy is a widely accepted procedure for diagnosing pulmonary disorders by obtaining samples of lung tissue and it can be used to diagnose a variety of pulmonary conditions, in addition to lung nodules and masses, such as ILD, hypersensitivity pneumonitis, granulomatous disorders like sarcoidosis and infections like tuberculosis.

In this study, we have evaluated and found correlation between imprint cytology and histopathology and found the relationship between clinical presentations, radiological findings with the final histopathological diagnosis of small lung biopsy specimens.

Imprint cytology gives us a fast result and help us differentiate between benign and malignant tumors and gives an idea to the surgeon on deciding the extent of surgery and providing a good surgical margin. It also gives an idea about the adequacy of the sample. The only drawback of imprint cytology is its propensity to incorrectly classify lesions as malignant. Hence, histopathology in adjunct with IHC analysis is the gold standard in diagnosing lung lesions as benign or malignant.

Different studies were analyzed, and, in this study, it was found that the accuracy rate, the positive predictive value, negative predictive value, sensitivity and specificity were high with 100%. This study showed a statistically significant association between imprint cytology and histopathology. The Kappa coefficient was 0.404 with p<0.001 which indicates a significant agreement between imprint cytology and histopathology.

From the present study it may be concluded that there is a humungous role of small lung biopsy in the diagnosis of various lung lesions and malignancies. The procedure is done as a routine outpatient procedure in a much less complicated settings than the operating room. Imprint cytology, histopathology, ancillary studies like special stains and immunohistochemical analysis can be done in a small biopsy sample. Also, various molecular studies for further analysis may be performed.

7. Conflict Of Interest
There is no potential conflict of interests related to this study.

8. Source Of Funding
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