Original Article

Pathology Section

Histopathological Patterns of Lung and Pleural Diseases: A Cross-sectional Study

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ABSTRACT

Introduction: Lung diseases, including lung cancers, are prevalent and deadly worldwide, especially in India. Lung biopsies are crucial for diagnosing pulmonary conditions when non invasive methods are inconclusive. Histopathological examination of biopsy samples provides vital insights for accurate diagnosis and effective treatment planning.

Aim: To evaluate the frequency of various histopathological lung lesions detected through biopsy and to assess the demographic and clinical characteristics of patients with lung pathologies.

Materials and Methods: This cross-sectional, retrospective study was conducted over a period of 12 months (August 2023 to July 2024) at a tertiary care hospital in Ahmedabad, Gujarat, India. It included 50 patients who underwent lung or pleural biopsies. Patient demographics (age and gender) and clinical features were recorded. The anatomical location (topography) and types of biopsies performed were also evaluated. Histopathological evaluation was done to determine the frequency of neoplastic and non neoplastic lesions. Data were analysed using Microsoft Excel (version 2021). Descriptive statistics and Chi-square tests were applied as appropriate.

Results: The cohort consisted of 50 cases who underwent lung biopsy consisted of 32 males and 18 females, with a mean age of 55.18 years. The most common symptoms were cough in 40 (80%), expectoration in 36 (72%) and breathlessness in 30 (60%). A smoking history was noted in 26 (80%) males. Most biopsies were lung-based, predominantly transbronchial in 30 (60%). Histopathologically, 25 (50%) had non neoplastic lesions, including non specific inflammation 16 (64%), granulomatous inflammation indicative of tuberculosis 4 (16%), fungal infection in 2 (8%), reactive mesothelial hyperplasia in 2 (8%), and interstitial fibrosis in 1 (4%). Neoplastic lesions were found in 24 (48%) cases, with Squamous Cell Carcinoma (SCC) being the most frequent in 8 (33%), followed by non small cell lung carcinoma in 5 (21%), adenocarcinoma in 3 (12.5%), small cell carcinoma 3 (12.5%) and solitary fibrous tumour in 1 (4%). Other findings included atypical cells suspicious of malignancy, high-grade bronchial dysplasia, and metastatic carcinoma. Gender differences were statistically significant in both non neoplastic (p-value=0.037) and neoplastic lesions (p-value=0.016).

Conclusion: Histopathological examination of lung biopsy specimens plays a crucial role in the accurate diagnosis of various lung diseases, including infections, inflammation, and cancers. Minimally invasive techniques like transbronchial and imaging-guided needle biopsies provide essential tissue samples, enabling early and precise diagnosis. This facilitates tailored treatment plans, ultimately improving patient outcomes and prognosis.

INTRODUCTION

Lung diseases are some of the most common medical conditions, affecting millions of people worldwide, including in India [1]. Lung cancer is a leading cause of cancer-related deaths in India. In 2022, there were 54,220 deaths due to lung cancer deaths in the country, accounting for 7.8% of all cancer-related deaths [2]. Lung biopsy is a crucial diagnostic procedure for evaluating a wide range of pulmonary diseases, especially when non invasive methods such as imaging or sputum analysis fail to provide a definitive diagnosis. Histopathological study provides invaluable insights into the nature of these diseases, helping clinicians to determine the most appropriate treatment and prognostic outcomes. While transbronchial biopsy is the least invasive and commonly used for central or diffuse lung diseases, percutaneous needle biopsy provides a viable option for peripheral lesions that are inaccessible by bronchoscopy. Surgical biopsy, though more invasive, is reserved for cases requiring larger samples or when other methods fail to provide sufficient tissue. Each biopsy technique offers unique advantages depending on the clinical scenario.

Histopathological examination of lung biopsy specimens is essential for evaluating various lung conditions, including infections, malignancies, interstitial lung diseases, and autoimmune disorders. Thus, histopathology plays not only diagnostic role but also instrumental in guiding therapeutic approaches, including

immunosuppressive therapies and targeted treatments in oncology. The present study aimed to evaluate the frequencies of various lung lesions detected through lung biopsies and to assess the diagnostic utility of different types of lung biopsies in diagnosing pulmonary diseases. The study also aimed to assess patients' demographics and clinical features with various lung pathology.

MATERIALS AND METHODS

This study was a cross-sectional, retrospective analysis of lung biopsy samples obtained from patients diagnosed with various pulmonary diseases. The biopsies were collected over a 12-month period, from August 2023 to July 2024, at a tertiary care center in Ahmedabad, Gujarat, India. A total of 50 hospital-based patients were included in the study. All patients' data were anonymised to maintain confidentiality.

Inclusion criteria: All patients who underwent lung biopsy, including biopsies from the pleura (transbronchial bronchoscopic biopsies and percutaneous imaging-guided biopsies) were included in the study.

Exclusion criteria: Patients with incomplete clinical data and biopsy specimens deemed inadequate for histopathological analysis were excluded from the study.
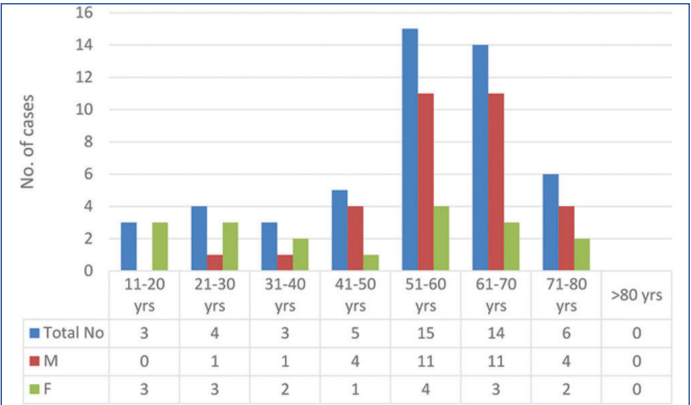
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Study Procedure

All biopsy specimens were fixed in 10% formalin and embedded in paraffin. The tissues were then sectioned and stained with Haematoxylin and Eosin (H&E) for general examination. Special stains, including Periodic Acid-Schiff (PAS), Gomori's Methenamine Silver (GMS), and Ziehl-Neelsen (ZN), were used to identify specific microorganisms in cases of suspected infection. Histopathological evaluation was performed, and lung and pleural lesions were categorised in neoplastic and non neoplastic lesions. Lung tumours were classified according to the WHO Classification (4th Edition, 2015) [3].

STATISTICAL ANALYSIS

Descriptive statistics were used to summarise patient demographics, clinical characteristics, biopsy topography and types, and histopathological findings. The diagnostic yield of each biopsy method was calculated as the proportion of samples that provided a definitive diagnosis. Data were analysed using Microsoft Excel (version 2021). Chi-square tests were applied to assess associations between categorical variables, with statistical significance defined as a p-value <0.05.

RESULTS

A total of 50 lung biopsy cases were included in the present study. The age of the patients ranged from 13 to 80 years, with a mean age of 55.18 years (standard deviation: 16.5 years) and a median age of 60 years [Table/Fig-1]. The majority of patients were in the 6th to 7th decades of life. The study cohort comprised 32 male and 18 female patients (M:F ratio=1.78:1). Although a slight male preponderance was observed, the number of male and female participants was consistent with what would be expected by chance, and no statistically significant difference was found between the genders in this cohort (p-value=1.0).

[Table/Fig-1]: Age and genderwise distribution of patients.

The clinical presentation of the patients varied, with several common symptoms observed in the cohort. Cough was the most frequently reported symptom, 40 cases (80%). This was followed by expectoration in 36 cases (72%), breathlessness in 30 cases (60%), fever in 25 cases (50%), weight loss in 22 cases (44%), and haemoptysis in 20 cases (40%). Pleural effusion was noted in 10 cases (20%). Other symptoms, such as chest pain and fatigue, were reported in a smaller proportion of cases.

An important clinical finding in this study was the notable prevalence of smoking among male patients as a history of smoking (H/O smoking) was elicited in 80% of male patients.

A total of 50 biopsy procedures were performed, with the majority focusing on the lung (42 procedures) and a smaller proportion targeting the pleura (8 procedures). [Table/Fig-2] Among the lung biopsies, most were transbronchial (30 procedures), while the remaining 12 were percutaneous. All pleural biopsies were performed using image-guided percutaneous needle biopsy. The distribution of lung biopsies between the right and left lungs was fairly even, with

Biopsy site-lung		Biopsy site pleura			Type of biopsy		
Side/Laterality	No.	Side/Laterality	No.	Total	Trans-bronchial biopsy	Percu-taneous needle biopsy	Total
Rt.	20	Rt.	4	24			
Lt.	19	Lt.	4	23			
Bilateral	1	Bilateral	0	01	30	20	50
Carina	2			02			
Total	42		8	50			

[Table/Fig-2]: Sites and types of biopsies.

a small number of bilateral and carinal biopsies. Pleural biopsies were equally distributed between the right and left sides. The choice of biopsy technique played a crucial role in achieving optimal diagnostic yield and tissue adequacy. Transbronchial biopsy was effective for diagnosing central and diffuse lung diseases, providing adequate tissue with minimal invasiveness. For peripheral lesions inaccessible by bronchoscopy, CT-guided percutaneous needle biopsy served as a reliable alternative, yielding sufficient material for histopathological evaluation.

Histopathological findings: The lung biopsies were categorised into two major groups based on histopathological evaluation: non neoplastic lesions and neoplastic lesions.

[Table/Fig-3] shows roughly equal distribution of non neoplastic and neoplastic lesions in the present study, with slight female preponderance among non neoplastic lesions and clear male preponderance among neoplastic lesions. The gender differences observed in both non neoplastic and neoplastic lesions were statistically significant, with p-value=0.037 for non neoplastic lesions and p-value=0.016 for neoplastic lesions. This indicates that the gender distribution was unlikely to have occurred by chance.

Type of lesion	No.	Male	Female
Non neoplastic (n=25)			
Granulomatous inflammation indicative of TB	4	0	4
Non specific inflammation	16	9	7
Fungal infection (Aspergilloma)	2	0	2
Reactive mesothelial hyperplasia with pleuritis	2	1	1
Interstitial fibrosis	1	1	0
Total non neoplastic lesions	25	11	14
Gender differences of patients for non neoplastic lesions (p-value=0.037)			
Neoplastic (n=24)			
Squamous Cell Carcinoma (SCC)	8	7	1
Adenocarcinoma	3	1	2
Small cell carcinoma	3	3	0
Undifferentiated non small cell carcinoma	5	5	0
Atypical cells suspicious of malignancy	2	2	0
Solitary fibrous tumour of pleura	1	1	0
High grade bronchial dysplasia	1	1	0
Metastatic carcinoma	1	1	0
Total neoplastic lesions	24	21	3
Gender differences of patients for neoplastic lesions (p-value=0.016)			
Inconclusive/Normal tissue	01		

[Table/Fig-3]: Histopathological types of lesions and association with gender distribution.
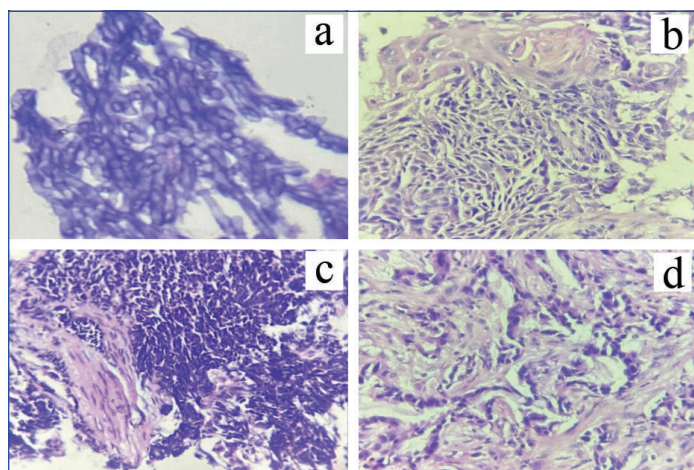
Non neoplastic lesions: A total of 25 cases (50%) were diagnosed with non neoplastic lesions. The most common finding was non specific inflammation, observed in 16 cases (64%) of the non neoplastic group. This category included inflammatory changes in the lung tissue that did not fit the specific diagnostic criteria for other conditions and may have been associated with chronic irritation or

infection. Granulomatous lesions, indicative of TB, were found in four cases (16%). Granulomatous inflammation is a hallmark of TB and other infectious processes, and these cases were consistent with a prior clinical diagnosis or suspicion of TB.

Fungal infections were diagnosed in two cases (8%), suggesting the presence of fungal pathogens contributing to pulmonary pathology, though less frequent than other causes in this cohort. The two cases of aspergillosis were diagnosed based on histopathological features, which included the presence of septate hyphae with characteristic 45-degree branching [Table/Fig-4a]. Reactive mesothelial hyperplasia of pleura was noted in two cases (8%) a condition is often associated with pleural inflammation or injury and may represent a reactive process secondary to chronic disease or irritation. Interstitial fibrosis was found in one case (4%), indicating scarring or fibrosis of the lung interstitium, which can occur due to long-standing inflammatory or fibrotic lung diseases.

Neoplastic lesions: A total of 24 cases (48%) exhibited neoplastic lesions. Among the neoplastic lesions, the most common malignancy was SCC, observed in eight cases (33% of neoplastic lesions) [Table/Fig-4b]. The second most common neoplastic lesion was Non Small Cell Lung Carcinoma (NSCLC), observed in five cases (21%). These tumours comprised a diverse group of lung cancers. NSCLC was diagnosed in cases where the lesions could not be categorised into specific subtypes—such as SCC, adenocarcinoma, or large cell undifferentiated carcinoma—using routine histopathological techniques and H&E staining. According to the WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart (4th Edition), the diagnosis of large cell carcinoma cannot be made based on small biopsy specimens.

Adenocarcinoma was diagnosed in three cases (12.5%), while small cell carcinoma, a more aggressive and fast-growing form of lung cancer, was seen in three cases (12.5%) [Table/Fig-4c,d]. Atypical cells suspicious of malignancy were noted in two cases (8%), indicating the presence of cells with irregular features that raised concern for malignancy, although definitive diagnosis could not be made. This might be due to limited sampling in a small biopsy specimens.

[Table/Fig-4]: a) Aspergillosis - Collection of uniform, septate fungal hyphae exhibiting acute-angled branching (H&E; 40x); b) Moderately differentiated Squamous Cell Carcinoma (SCC) - Nests of infiltrative neoplastic squamous cells exhibiting nuclear atypia and focal keratinisation (H&E; 40x); c) Small cell carcinoma - Infiltrative sheets of small round to oval blue cells with hyperchromatic nuclei, scant cytoplasm and nuclear molding (H&E ; 40x); d) Moderately differentiated adenocarcinoma - Infiltrative neoplastic glands and strands of tumour cells showing pleomorphic, hyperchromatic nuclei and mitoses (H&E; 40x).

Additionally, one case (4%) of solitary fibrous tumour of the pleura, one case (4%) of high-grade bronchial dysplasia (a precancerous lesion), and one case (4%) of metastatic carcinoma were identified.

DISCUSSION

This study provides valuable insights into the histopathological spectrum of lung biopsies and its correlation with patient's demographics and clinical findings.

Age and gender differences in lung pathology: The findings from 50 lung biopsy cases contribute to a better understanding of lung diseases and malignancies across a diverse patient population. A male preponderance was observed, with a male-to-female (M:F) ratio of 1.78:1, consistent with established trends, especially in lung cancer, where smoking is a major risk factor. Male patients showed a higher prevalence of neoplastic lesions, particularly SCC and small cell carcinoma, aligning with global data that indicates men are more likely to develop lung cancer due to higher smoking rates. A slight female preponderance was noted in non neoplastic lesions, which may reflect different underlying conditions including chronic inflammatory and infectious diseases not directly linked to smoking. The higher prevalence of non specific inflammation and granulomatous lesions in women suggests distinct aetiologies compared to the male cohort.

Statistically significant p-values (0.037 for non neoplastic lesions and 0.016 for neoplastic lesions) indicate that these gender differences are unlikely to be due to chance. These findings are in line with other studies [Table/Fig-5] [4-16], except for one study by Mittal AR et al., which showed a female preponderance—likely due to a higher incidence of adenocarcinoma (72%) compared to SCC (12.7%) in their study, as adenocarcinoma is more common among women, especially non smokers [14].

The majority of cases in the present study occurred in the 6th and 7th decades in present study, indicating that lung pathology predominantly affects older adults, with a substantial proportion in the elderly age group. This age distribution aligns with other studies [4-16]. These findings highlight the increased risk of lung diseases with advancing age, reinforcing established epidemiological trends.

Clinical features and smoking association: The clinical symptoms in this study—including cough, expectoration, breathlessness, fever, weight loss, and haemoptysis—align with those observed by Sorde D et al., and Nasreen K et al., emphasising the need for careful evaluation in patients presenting with these symptoms [13,17]. Smoking was highly prevalent among male patients (80%), consistent with other studies [5-8,10,11], where smoking was associated with 60-80% of cases. The higher frequency of SCC and small cell carcinoma in males further reinforces the central role of smoking in the pathogenesis of lung cancer.

Histopathological findings: The study highlights a nearly equal distribution of non neoplastic and neoplastic lesions, with non specific inflammation being the most common non neoplastic lesion (64%). This suggests a high prevalence of chronic inflammatory processes or infections. Similar findings were observed by Garima B et al., Shah HS et al., and Lad N and Daveshwar M [4,15,16], where non specific inflammation was the predominant non-neoplastic lesion.

Granulomatous lesions (16%) were commonly linked to (TB), consistent with findings by Sorde D et al., [13], who identified granulomatous lesions as the dominant type among non neoplastic cases. Aspergillus-related fungal infections (8%) underscore the importance of considering fungal aetiology in lung pathology, especially in immunocompromised individuals. Additionally, interstitial fibrosis (4%) and reactive mesothelial hyperplasia (8%) indicate chronic conditions, highlighting the need for long-term follow-up and management. Overall, the study underscores the diverse nature of non neoplastic lesions and their relevance to chronic conditions, infections, and the necessity for tailored therapeutic approaches.

Among neoplastic lesions (48%), SCC was the most prevalent malignancy (33%), followed by NSCLC at 21%, adenocarcinoma at 12.5%, and small cell carcinoma at 12.5%. These findings are consistent with some other studies [10-13], where SCC was the most common malignancy. In contrast, some studies showed adenocarcinoma as the predominant type [4-9,14,16], highlighting a shift towards adenocarcinoma, particularly in non smokers.

NSCLC includes several histological subtypes, such as SCC, adenocarcinoma, and large cell undifferentiated carcinoma. In some

Study	Adeno Ca (%)	Squamous Cell Ca (%)	Small Cell Ca (%)	Undiff. NSCLC* (%)	Metastasis (%)	Peak age (yrs)	M:F Ratio	Smoking (%)
Present study (2026)	12.5	33	12.5	21	4	51-60	1.78	80
Garima B et al., (2020) [4]	71	17	4.5	1.5	-	41-60	2.86	-
Agarwal A et al., (2018) [5]	29.3	21.88	12.8	24	6.4	50-60	4.7	76
Malik PS et al., (2013) [6]	37.3	32.1	16.1	2.8	-	51-60	4.6	69.7
Krishnamurthy A et al., (2012) [7]	42.6	15.8	13.2	2.3	-	40-60	3.5	60.4
Sundaram V and Sanyal N (2014) [8]	43.33	31.67	10	3.33	-	61-70	4.2	71.67
Li Liang et al., (2014) [9]	30.3	18.9	8.33	16.66	-	66 (Mean age)	1.35	-
Sarfraz S et al., (2018) [10]	3.75	50	15	-	-	59.9 (Mean age)	5.15	88.75
Mandal SK et al., (2013) [11]	30.8	49.1	14.8	3.7	-	>60	1.09	78.7
Kulshrestha R et al., (2012) [12]	12.8	60.5	12.8	10.1	-	49 (Mean age)	1.17	-
Sorde D et al., (2024) [13]	24.48	36.73	8.16	4.08	-	61-70	1.55	-
Mittal AR et al., (2021) [14]	72	12.7	2.1	2.1	-	61-70	0.9	-
Shah HS et al., (2020) [15]	34.09	32.95	10.23	18.18	2.27	51-60	2.8	-
Lad N and Daveshwar M (2019) [16]	38.46	32.69	7.69	9.63	-	51-60	3	-

[Table/Fig-5]: Comparison of various studies in lung malignancies [4-16].

cases—especially when only small biopsies, it may not be possible to definitively classify the tumour definitively into a specific subtype by routine histopathology. In such instances, the broad diagnosis of NSCLC is made for therapeutic purposes, as treatment strategies for NSCLC differ from those for small cell lung carcinoma.

The variability in the frequency of NSCLC across studies is a multifactorial, influenced by demographic, geographic, epidemiological, diagnostic, and methodological factors. The use of ancillary studies can reduce the frequency of NSCLC diagnoses, highlighting the importance of comprehensive diagnostic approaches. Understanding these variables is crucial for accurately interpreting study results. The recognition of NSCLC in 21% of cases underscores the diagnostic challenges associated with small biopsies and emphasising the need for precise diagnosis to guide appropriate treatment planning.

The frequency of small cell carcinoma varies across studies [4-16], with reported incidences ranging from 2.1-16.1%. Small cell carcinoma has distinct therapeutic implications compared to other lung cancer types. It is often treated with chemotherapy and radiotherapy, whereas NSCLC may involve surgical resection, targeted therapy, or immunotherapy, depending on the subtype and molecular profile. Accurate diagnosis ensures that patients receive the most appropriate and effective treatment for their specific condition.

Selecting the appropriate biopsy technique based on lesion location is a key to optimising diagnostic yield. Transbronchial biopsy is effective for central and diffuse lung diseases, while its limitations in peripheral access are addressed by image-guided percutaneous needle biopsy. The complementary use of both methods enhances diagnostic accuracy and guides targeted clinical management.

Implications for clinical practice: The strong association between smoking and lung cancer underscores the need for smoking cessation programs and early screening in high-risk populations. Clinicians should also consider differential diagnoses such as TB and fungal infections, which may mimic malignancies. Early diagnosis through lung biopsy is essential for detecting cancer at a potentially treatable stage. Tailored treatment based on histopathological findings—whether chemotherapy, surgery, or targeted therapy—improves survival and overall outcomes. Accurate histopathological evaluation remains critical for guiding appropriate treatment plans and reducing mortality.

Limitation(s)

Given the small sample size of 50 cases, larger multicentre studies are needed to validate these findings. Additionally, small biopsies may not fully represent the entire lung lesion, leading to potentially false-negative results, especially in diseases with patchy involvement (e.g., interstitial lung disease).

CONCLUSION(S)

This study offers valuable histopathological insights into the spectrum of lung and pleural lesions, underscoring the heterogeneity of pulmonary pathology. It highlights the pivotal role of small biopsy techniques—such as transbronchial and image-guided needle biopsies—in enabling early and accurate diagnosis. These minimally invasive methods facilitate timely and appropriate treatment strategies, ultimately enhancing patient outcome. Early histopathological evaluation remains critical for effective disease management and prognosis.

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