Section: Pathology

Original Research Article

ETIOLOGICAL SPECTRUM OF LUNG AND PLEURAL LESIONS IN 100 CONSECUTIVE BIOPSIES: A RETROSPECTIVE STUDY FROM A TERTIARY CARE CENTER IN NORTH INDIA

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Received : 16/07/2026
Received in revised form : 14/08/2026
Accepted : 27/08/2026

Keywords:
lung biopsy, pleural biopsy, adenocarcinoma, tuberculosis, histopathology, India.

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DOI: 10.47009/jamp.2026.8.5.14

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (5); 83-89

ABSTRACT

Background: Lung and pleural lesions in India often show an overlapping spectrum of infectious and malignant etiologies, making tissue diagnosis critical for appropriate management. This study aimed to describe the etiological spectrum and diagnostic yield of 100 consecutive lung and pleural biopsies received in the Department of Pathology, PGIMS Rohtak, with particular focus on the relative burden of tuberculosis and malignancy. **Materials and Methods:** This retrospective observational study included 100 consecutive core and tru‑cut biopsies from lung and pleura received from September 2016 to December 2017 in the Department of Pathology, PGIMS Rohtak. Demographic data, clinical features, radiological impression, and histopathological diagnosis, including special stains and immunohistochemistry (IHC) (CK, vimentin, TTF‑1, p63, calretinin, D2‑40, WT‑1, LCA, lymphoma panel and neuroendocrine markers), were retrieved from records and entered in a master chart. Lesions were categorized as malignant, specific benign (e.g. tuberculosis, granulomatous inflammation, interstitial fibrosis, suppurative inflammation), and non‑specific inflammation/inconclusive. **Result:** Of 100 biopsies, the majority were from males in the fifth to seventh decades, and right‑sided lesions were slightly more common. Non-specific biopsies constituted the largest subgroup despite adequate tissue, followed by malignant lesions which is followed by tuberculosis and other benign inflammatory conditions. Among malignancies, adenocarcinoma, including poorly differentiated and non‑small cell carcinoma favoring adenocarcinoma, was the most frequent subtype, followed by squamous cell carcinoma, small cell carcinoma, sarcomatoid carcinoma, papillary carcinoma with secondary pulmonary involvement, and malignant mesothelioma. IHC was pivotal in subtyping poorly differentiated tumors and distinguishing primary lung carcinoma from mesothelioma and metastatic deposits. Tuberculosis and other granulomatous lesions formed the major benign category, with a subset showing acid-fast bacilli on Ziehl–Neelsen stain. **Conclusion:** In this North Indian tertiary‑care setting, malignancy emerged as the leading etiology among patients undergoing lung and pleural biopsy, with adenocarcinoma predominating, while tuberculosis remained an important benign cause. Image‑guided biopsies with appropriate IHC significantly enhanced diagnostic precision, underscoring the role of histopathology in respiratory disease management in high TB and high cancer burden regions. Clinical significance: Tertiary care centers in high prevalence areas face high patient loads. By outlining the most common presentations in 100 consecutive cases, the study allows clinicians to prioritize specific diagnostic tests, depending upon the patient's demographic and macroscopic presentation.

INTRODUCTION

Lung diseases contribute significantly to morbidity and mortality worldwide, with lung carcinoma now among the leading causes of cancer‑related death, while tuberculosis (TB) continues as a major public health problem in developing countries such as India. In clinical practice, these etiologies frequently present with overlapping symptoms and radiologic features, making histopathological evaluation

essential to establish a definitive diagnosis and guide therapy.[1,2]

Image‐guided core biopsies from lung and pleura provide minimally invasive access to tissue, allowing both diagnosis and subtyping of neoplastic and non‐neoplastic lesions, including the use of immunohistochemistry (IHC) and special stains.[3-6] Several Indian studies have documented a shifting pattern toward adenocarcinoma as the predominant primary lung malignancy, alongside a persistent burden of TB and other infections. However, data from North Indian tertiary‐care centers, particularly describing the entire etiological spectrum in consecutive biopsy series, remain limited.

PGIMS Rohtak is a large teaching hospital catering to a predominantly rural population from Haryana and adjoining states, where TB, smoking‐related chronic lung disease, and environmental exposures co‐exist. Understanding the pattern of biopsy‐proven etiologies in this setting can help clinicians prioritize differential diagnoses, rationalize work‐up, and anticipate the need for ancillary tests.

Objective/Aim: The present study was undertaken to describe the etiological spectrum and diagnostic yield in 100 consecutive lung and pleural biopsies.

Need of the study: To establish the local epidemiological profile of lung and pleural diseases in North India, improve diagnostic accuracy for rising respiratory disorders, guide targeted clinical management, and provide regional data that addresses the under-representation of non-neoplastic and neoplastic chest pathologies in tertiary care literature.

Novelty of the study: Lies in highlighting the diagnostic limitations of non-specific biopsy results despite adequate tissue, coupled with demonstrating immunohistochemistry's (IHC) critical role in precisely subtyping challenging malignancies and resolving differential diagnoses like primary carcinoma versus mesothelioma in a high-tuberculosis demographic.

MATERIALS AND METHODS

Study design and setting: This was a retrospective, descriptive study conducted in the Department of Pathology, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India. The institute is a tertiary‐care teaching hospital receiving respiratory biopsies from internal medicine, pulmonary medicine, oncology, and thoracic surgery units.

Study period and case selection: All consecutive lung and pleural biopsies received from September 2016 to December 2017 were screened. From these, 100 biopsies with adequate tissue and complete histopathology reports were included in the analysis; repeat biopsies from the same lesion and cases with inadequate or autolyzed tissue were excluded. Both image‐guided core biopsies (CT or ultrasound‐guided) and thoracoscopic pleural biopsies were represented. Clinical suspicion at the time of procedure was recorded as "? TB", "? malignancy" or "? TB/? malignancy" where available.

Sampling method: Consecutive sampling method was used.

Data collection: Data were extracted from departmental registers and individual reports into a structured master chart that included: age, sex, symptom duration, major presenting complaints (cough, dyspnea, fever, chest pain, hemoptysis, loss of appetite/weight), presence and laterality of pleural effusion, radiologic impression, clinical diagnosis, and final pathological diagnosis. The chart also recorded whether the lesion was from lung parenchyma or pleura and whether there was a known primary cancer elsewhere in cases with suspected metastasis.

Inclusion criteria:

- **Study Period:** All consecutive patients whose lung or pleural biopsies were received between September 2016 and December 2017.
- **Tissue Adequacy:** Biopsies containing an adequate amount of tissue sample without significant autolysis (tissue degradation).
- **Data Completeness:** Cases with complete histopathology reports and accessible clinical/radiological records in the departmental registers.
- **Procedure Type:** Samples obtained via image-guided core biopsies (CT or ultrasound-guided) or thoracoscopic pleural biopsies.
- **Department:** Biopsies processed and reported within the Department of Pathology at PGIMS, Rohtak.

Exclusion criteria:

- **Inadequate Samples:** Biopsies with insufficient, crushed, or severely autolyzed tissue that prevents a definitive histopathological diagnosis.
- **Duplicate Data:** Repeat biopsies taken from the exact same lesion in the same patient.
- **Missing Information:** Cases with incomplete histopathology reports or missing critical clinical data in the registers.

Statistical analysis: Descriptive statistics (frequencies and percentages) were used to summarize the etiological spectrum; given the retrospective design and limited sample, no inferential statistics were performed.

Histopathology and ancillary techniques: All biopsies had been fixed in 10% neutral buffered formalin, processed routinely, and stained with hematoxylin and eosin (H&E). Ziehl–Neelsen (ZN) stain for acid‐fast bacilli (AFB) was performed in clinically suspected tuberculosis and in biopsies showing granulomatous inflammation. IHC panels were applied based on morphology and clinical suspicion and included cytokeratin (CK), vimentin, thyroid transcription factor‐1 (TTF‐1), p63, calretinin, D2‐40, WT‐1, Ber‐EP4, leukocyte common antigen (LCA), CD20, CD3/CD5/CD10, neuroendocrine markers (chromogranin,

ISSN (O): 2687-5365; ISSN (P): 2753-6556

synaptophysin, neuron‐specific enolase), mucin stains (PAS, mucicarmine) and others as indicated.[7-9]

Diagnostic categorization: Final histopathological diagnoses from the reports were reviewed and grouped into the following categories:

Malignant lesions: Primary lung carcinoma (adenocarcinoma, squamous cell carcinoma, small cell carcinoma, sarcomatoid carcinoma, poorly differentiated carcinoma/non‐small cell carcinoma favoring adenocarcinoma, papillary carcinoma)
Malignant mesothelioma (epithelioid)
Lymphoma (non‐Hodgkin, T‐cell)
Metastatic carcinomas to lung/pleura where a known primary (e.g. tongue, ovary) was recorded
Specific benign lesions
Tuberculosis (with or without AFB positivity)
Granulomatous inflammation (AFB negative)
Interstitial fibrosis, inflamed collagenous tissue, organizing/suppurative pneumonia
Non‐specific inflammation / non‐specific interstitial (NSI) and inconclusive biopsies

Ethics: This study was a retrospective clinical audit/evaluation. According to the policies of the ethical committee of our institution, formal ethical review and informed consent were not required for this type of observational, non-interventional study. All the patient data was fully anonymized and kept confidential prior to analysis. All the procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation and with the Helsinki Declaration of 1975, revised in 2008.

RESULTS

Demographic and clinical profile: Of the 100 biopsies, the majority were from male patients 72% (n=72) with male: female ratio of 2.57:1, reflecting a male predominance typical of hospital‐based lung biopsy series in India. Most patients were in the 5th to 7th decades, although the age range extended from the third to ninth decade, and a small number of young adults in their third decade were also represented. Common presenting complaints included chronic cough (78%) and dyspnea (72%), frequently associated with constitutional symptoms such as fever and weight loss; hemoptysis and pleuritic chest pain were variably documented. Pleural effusion, when recorded, showed a slight left‐side preponderance for malignant lesions and bilateral effusion in a subset of TB cases.

Radiologically, most lesions were described as mass lesions or areas of consolidation, with clinical impressions predominantly of "? TB" or "? malignancy". Many biopsies with a clinical suspicion of TB eventually turned out to be either non‐specific inflammation or malignancy, emphasizing the limitations of clinical‐radiologic assessment alone.

Overall etiological spectrum

When grouped by final diagnosis, non‐specific/inconclusive biopsies constituted the largest category (32%) in this series, followed by malignant lesions (27%). Other benign conditions account for 22% of cases & tuberculosis account for 19% of cases. This pattern is broadly comparable to contemporary Indian biopsy‐based series, where malignancy accounts for approximately two‐thirds of lung biopsies, with tuberculosis representing a substantial proportion of the remaining cases.

A schematic summary of the major categories is presented in [Table 1].

Table 1: Schematic summary of the major categories.

Category	Approximate share (n=100)	Key subtypes (examples)
Malignant lesions	27%	Adenocarcinoma, SCC, small cell, sarcomatoid, PDC, metastatic tumors, mesothelioma, lymphoma
Tuberculosis / granulomatous inflammation	19%	Classical TB with caseation, AFB-positive and AFB-negative granulomas
Other specific benign lesions	22%	Suppurative inflammation, organizing pneumonia, interstitial fibrosis, inflamed collagenous tissue
Non-specific inflammation / inconclusive	32%	NSI with or without radiologic correlation

Spectrum of malignant lesions: Adenocarcinoma, including poorly differentiated carcinoma and non‐small cell carcinoma favoring adenocarcinoma, emerged as the most frequent malignant diagnosis in this series. Many of these cases presented as peripheral masses, and TTF‐1 positivity, along with CK expression and absence of squamous markers, supported the diagnosis of primary lung adenocarcinoma. Mucin stains highlighted intracellular or extracellular mucin in mucin‐secreting variants, aiding subtyping.

Squamous cell carcinoma (SCC) was the next common subtype, characterized by keratinizing or non‐keratinizing squamous morphology and immunophenotype with p63 positivity and absence of TTF‐1. Some cases were labeled as poorly differentiated squamous carcinoma or non‐small cell carcinoma with squamous differentiation when classical features were limited but immunoprofile supported squamous lineage.

A smaller but important subset comprised small cell carcinoma and other neuroendocrine tumors, confirmed by positive staining for chromogranin, synaptophysin, and neuron‐specific enolase, along with high‐grade cytological features. Sarcomatoid carcinoma and undifferentiated pleomorphic carcinomas were identified in a few biopsies, showing spindle cell morphology, variable CK and

ISSN (O): 2687-5365; ISSN (P): 2753-6556

vimentin co‑expression, and negativity for mesothelial markers.

Pleural‑based malignant mesothelioma (epithelioid type) accounted for a distinct group, displaying diffuse positivity for calretinin, D2‑40, and WT‑1, with lack of Ber‑EP4 and TTF‑1, thus clearly separated from metastatic adenocarcinoma. Lymphoid neoplasms were represented by non‑Hodgkin lymphoma, including T‑cell lymphoma, confirmed by LCA positivity and appropriate T‑cell markers, in cases clinically suspected as "? TB" with mediastinal involvement.

Metastatic tumors to lung or pleura (e.g. tongue SCC, ovarian papillary carcinoma) were recognized when there was a known primary and histomorphology/IHC pattern matched the primary site. This underlines the need for careful clinical correlation and targeted IHC in biopsy interpretation. Percentage distribution of different types of malignancies along with IHC shown in [Table 2].

Table 2: Percentage distribution of different types of malignancies along with IHC.

Type of malignancy	Number (n=27)	IHC
Adenocarcinoma	41%	TTF-1 (+), CK (+)
SCC	20%	p63 (+), TTF-1 (-)
PDC	13%	
Small cell carcinoma	04%	Chromogranin, synaptophysin & neuron specific enolase (+)
Lymphoma	07%	LCA positivity & appropriate T & B cell markers
Mesothelioma	07%	Calretinin, D2‑40, and WT‑1 positivity, with lack of Ber‑EP4 and TTF‑1
Sarcomatoid carcinoma	04%	Variable CK & vimentin co- expression
Poorly differentiated papillary carcinoma	04%	

Benign and non‑neoplastic lesions: Tuberculosis and granulomatous inflammation formed the largest benign subgroup. Classical TB showed caseating granulomas with epithelioid histiocytes and Langhans giant cells, with a subset demonstrating AFB positivity on ZN stain, while others remained AFB‑negative but were interpreted as TB in conjunction with clinical and radiologic features. Non‑necrotizing granulomas without AFB were categorized as granulomatous inflammation, and infectious versus non‑infectious etiologies were suggested in the reports based on context.

Other specific benign conditions included suppurative inflammation, organizing pneumonia, interstitial fibrosis, and chronically inflamed collagenous tissue. These lesions often corresponded to cases with clinical suspicion of malignancy but radiology showing diffuse or patchy involvement; biopsy helped avoid unnecessary oncologic treatment and redirected management towards infection or chronic inflammatory lung disease.

A major proportion of biopsies were reported as non‑specific inflammation or "non‑specific interstitial" without definitive etiology, despite adequate tissue. These cases highlight the limitation of small biopsies in diffuse parenchymal lung disease and the need for clinico‑radiologic‑pathologic discussion and, in selected cases, repeat or surgical lung biopsies. [Figures 1 to 13]

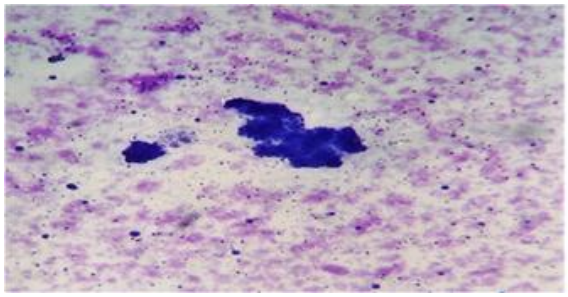

Figure 1: Photomicrograph showing papillary structures of adenocarcinoma on Leishman-stained conventional cytology smear (100X).

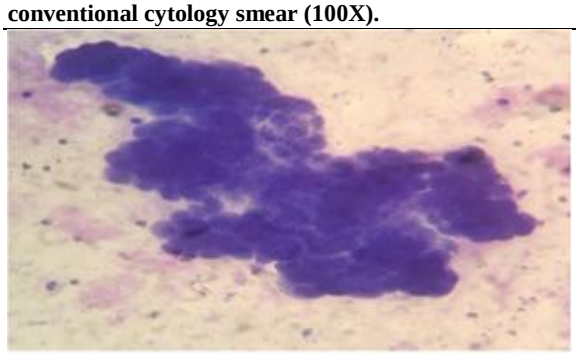

Figure 2: Photomicrograph showing papillary structures of adenocarcinoma on Leishman-stained conventional cytology smear (400X).

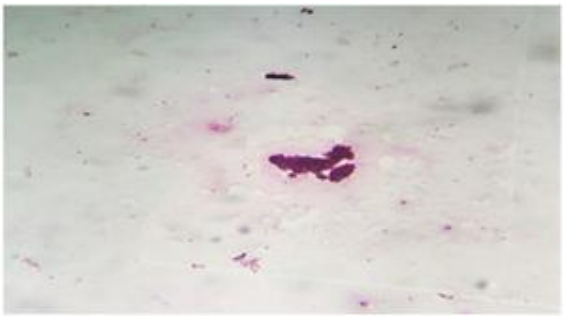

Figure 3: Photomicrograph showing papillary structures of adenocarcinoma on H & E-stained conventional cytology smears (100X).

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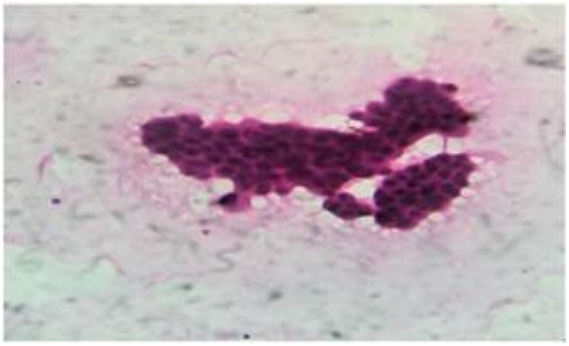

Figure 4: Photomicrograph showing papillary structures of adenocarcinoma on H&E-stained conventional cytology smears (400X).

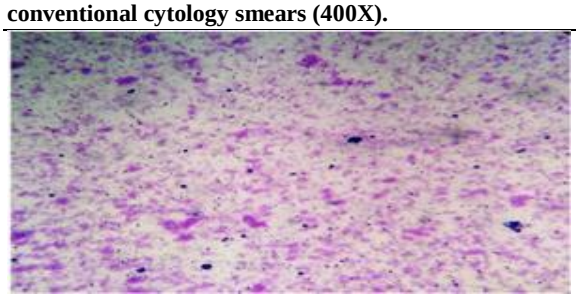

Figure 5: Photomicrograph showing predominantly lymphocytic infiltrates in pleural fluid on Leishman-stained smear (100X).

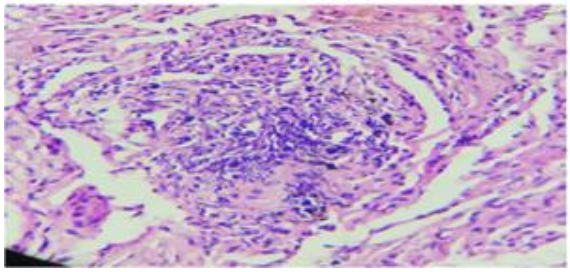

Figure 6: Photomicrograph showing granulomaa along with a giant cell on H&E stained sections of pleural biopsy (100X).

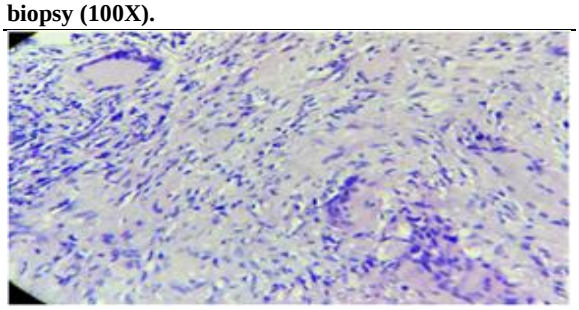

Figure 7: Photomicrograph showing granuloma along with a giant cell on H&E-stained sections of pleural biopsy (400X).

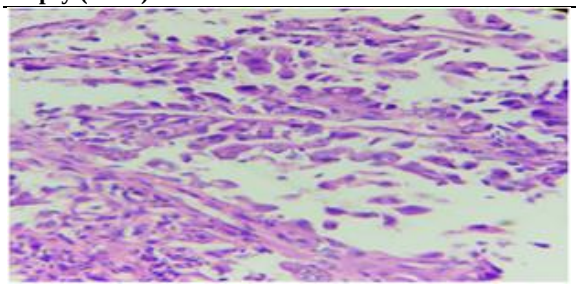

Figure 8: Photomicrograph showing papillary structures of adenocarcinoma on H&E-stained sections of pleural biopsy (400X)

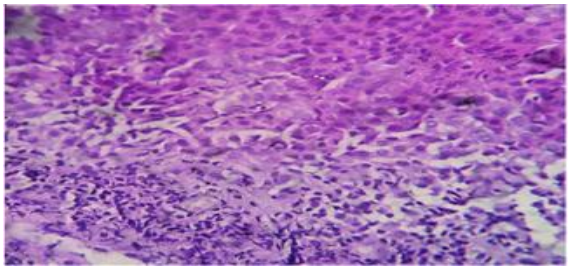

Figure 9: Photomicrograph showing malignant mesothelioma on H&E-stained sections of pleural biopsy (400X).

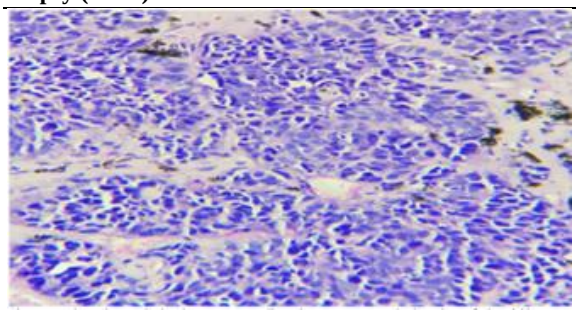

Figure 10: Photomicrograph showing squamous cell carcinoma on H&E-stained sections of pleural biopsy (400X).

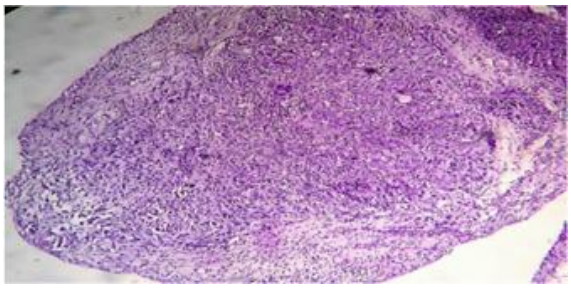

Figure 11: Photomicrograph showing poorly differentiated adenocarcinoma on H&E-stained section of pleural biopsy (100X).

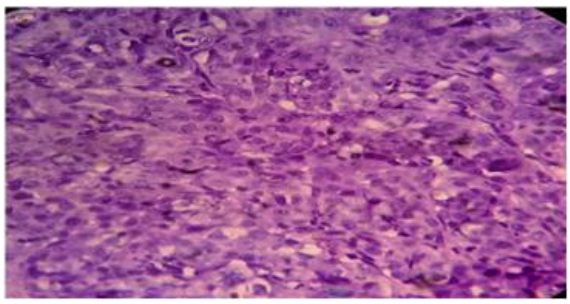

Figure 12: Photomicrograph showing poorly differentiated adenocarcinoma on H&E-stained section of pleural biopsy (400X).

ISSN (O): 2687-5365; ISSN (P): 2753-6556

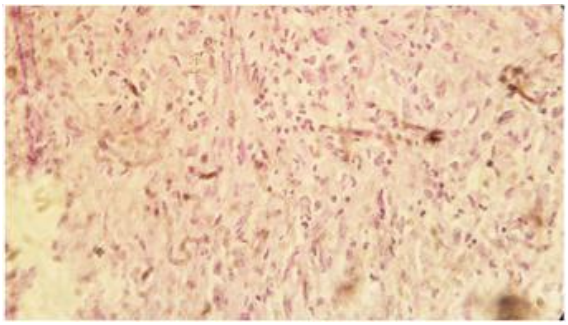

Figure 13: Photomicrograph showing sarcomatoid carcinoma on H&E-stained section of pleural biopsy (400X).

DISCUSSION

This retrospective study of 100 consecutive lung and pleural biopsies at a tertiary‐care center in North India demonstrates that malignancy is one of the most common histopathological - diagnosis among patients undergoing tissue sampling for suspected respiratory disease, with adenocarcinoma being the predominant subtype. This observation is in line with multiple Indian series that have reported a shift from squamous cell carcinoma to adenocarcinoma as the leading primary lung cancer, particularly in urban and semi‐urban populations.[10]

The high proportion of TB and granulomatous inflammation in the benign category confirms that, despite improved TB control strategies, tuberculosis remains an important differential diagnosis for mass‐like lung lesions in India. In the present series, many patients clinically suspected to have TB were ultimately diagnosed with malignancy, while others with suspected malignancy turned out to have TB or non‐specific inflammation, underlining the potential for misclassification when relying solely on clinical and radiologic findings.[11,12]

The pattern of malignancies in this study—adenocarcinoma followed by squamous cell carcinoma, small cell carcinoma, and less common entities such as sarcomatoid carcinoma and mesothelioma—parallels the spectrum reported in other biopsy‐based cohorts. The need for IHC in subtyping poorly differentiated tumors, confirming mesothelioma, and distinguishing metastatic from primary lung carcinoma is evident from the frequent use of markers such as TTF‐1, p63, calretinin, D2‐40, WT‐1, LCA, and neuroendocrine markers in this series. These tools not only refine diagnosis but also have therapeutic implications, especially in the era of histology‐driven chemotherapy and targeted therapy for lung cancer.[10]

The presence of lymphomas, metastatic carcinomas and papillary carcinoma involving the lung/pleura emphasizes that not all malignant lung lesions are primary, and underscores the importance of detailed clinical history and correlation with prior diagnoses. Similarly, recognition of benign entities such as interstitial fibrosis and organizing pneumonia highlights the value of biopsy in avoiding overtreatment and in steering patients toward appropriate medical management or follow‐up.

This study offers a pragmatic snapshot of the etiological spectrum encountered in routine lung and pleural biopsies in a large public sector teaching hospital in North India, and it reinforces the central role of histopathology with ancillary techniques in respiratory disease diagnosis.

Strength of the study: our study possesses several methodological and clinical strengths

- **Robust Sampling Framework:** The utilization of a consecutive sampling method over a defined 16-month period effectively eliminated selection bias, ensuring that the cohort truly represents the natural distribution of thoracic pathology at our center.
- **High Diagnostic Reliability:** By applying strict exclusion criteria for inadequate or autolyzed tissue, we ensured that all analyzed cases relied solely on high-quality, definitive histopathological diagnoses, enhancing the internal validity of our findings.
- **Comprehensive Thoracic Scope:** Unlike studies restricted to a single site, our inclusion of both lung parenchyma and pleural lesions provides a comprehensive, holistic overview of intrathoracic etiologies.
- **Multimodality Representation:** The data captures diverse advanced interventional modalities, including image-guided core needle biopsies (CT and ultrasound-guided) and thoracoscopic pleural biopsies, making the findings widely applicable across different diagnostic setups.
- **Clinical-Pathological Correlation:** By meticulously cross-tabulating baseline symptoms and initial clinical suspicions against final biopsy outcomes, this study provides high-utility data on diagnostic accuracy, directly addressing the frequent diagnostic overlap between tuberculosis and malignancy in North India.
- **Tertiary Referrals:** Conducted at a premier tertiary-care teaching hospital receiving complex referrals from pulmonology, internal medicine, oncology, and thoracic surgery units, the findings accurately reflect the true disease burden and diagnostic challenges of the region.

Limitation of the study: Despite these strengths, certain limitations must be acknowledged:

- **Retrospective Design:** Due to the retrospective nature of the study, data collection was dependent on existing institutional records, which inherently introduces the risk of missing or incomplete documentation for minor clinical variables.
- **Single-Center Setting:** Being a single-center study conducted at a specialized tertiary care referral hospital, the observed etiological spectrum may reflect a referral bias toward more complex or malignant cases, and may not fully generalize to primary or secondary healthcare settings.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

- **Sample Size:** While a sample size of 100 consecutive, biopsy-proven cases provides a valuable local snapshot, a larger multi-centric cohort would offer greater statistical power for sub-group analyses, particularly for rarer pulmonary pathologies.

CONCLUSION

In this series of 100 consecutive lung and pleural biopsies from a North Indian tertiary‐care center, malignancy, particularly adenocarcinoma, emerged as the leading etiology, followed by tuberculosis and other benign inflammatory conditions. The substantial overlap in clinical and radiologic presentations between malignant and non‐malignant lesions underscores the indispensability of histopathology, supported by appropriate IHC and special stains, for accurate diagnosis and optimal patient management in regions with high burdens of both TB and lung cancer.

Clinical significance: Major patient loads is faced by tertiary care centers. By summarizing the most common presentations in consecutive cases, this study allows physicians to prioritize specific diagnostic tests, depending upon the patient's data and gross appearance.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556