

Histopathological spectrum of pulmonary and pleural specimens obtained during thoracic surgical procedures: A hospital-based cross-sectional observational study.

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Abstract

Background:

Pulmonary and pleural lesions encompass infectious, inflammatory, fibrotic, benign neoplastic, and malignant disorders. Clinical and radiological findings frequently overlap, making histopathological examination essential for definitive diagnosis and therapeutic planning.

Objectives:

To describe the histopathological spectrum of pulmonary and pleural specimens obtained during thoracic surgical procedures and to examine factors associated with malignant pathology.

Methods:

This hospital-based cross-sectional observational study with prospective enrolment included 80 patients undergoing thoracic surgical procedures at Government Medical College and its associated teaching hospital, Jagtial, Telangana, India, from May 2025 to April 2026. Pulmonary and pleural specimens were processed by routine histopathology. Special stains and immunohistochemistry were applied when indicated. Demographic, clinical, procedural, radiological, and pathological data were analysed using descriptive and inferential statistics.

Results:

The mean age was 52.6 ± 15.4 years, and 54 patients (67.5%) were male. Pulmonary specimens comprised 56 cases (70.0%), while 24 (30.0%) were pleural. Malignant lesions were identified in 40 patients (50.0%). Malignancy occurred in 31 pulmonary specimens (55.4%) and nine pleural specimens (37.5%). Pulmonary adenocarcinoma was the most frequent malignant diagnosis, followed by squamous cell carcinoma. Chronic non-specific pleuritis and tuberculous pleuritis predominated among non-malignant pleural lesions. Malignancy was significantly associated with age of at least 50 years and current or previous smoking. Preoperative and histopathological diagnoses agreed in 68 patients (85.0%); histopathology produced a clinically relevant diagnostic revision in 12 cases.

Conclusion:

Thoracic surgical specimens demonstrated a balanced distribution of malignant and non-malignant disease. Histopathological assessment remained decisive for tumour classification and for differentiating malignancy from tuberculosis and other inflammatory lesions.

Recommendations:

Standardised specimen handling, targeted immunohistochemistry, and multidisciplinary clinicoradiological correlation should be incorporated into routine thoracic diagnostic practice.

Keywords: Histopathology; lung neoplasms; pleural diseases; thoracic surgery; tuberculosis; immunohistochemistry.

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Introduction

Pulmonary and pleural disorders constitute a diverse group of diseases that often produce similar clinical manifestations, including cough, chest pain, dyspnoea, haemoptysis, fever, weight loss, pleural effusion, or radiological opacity. Their pathological basis ranges from acute and chronic infection to organising inflammation, interstitial fibrosis, benign tumours, primary pulmonary malignancy, metastatic disease, and mesothelial neoplasia. Imaging identifies the anatomical distribution and extent of disease but does not consistently distinguish neoplasia from tuberculosis, fungal infection, abscess formation, or non-specific pleuritis. Tissue examination therefore remains central to diagnostic confirmation, classification, prognostication, and selection of treatment.

Thoracic surgical procedures yield larger and architecturally preserved samples through wedge resection, segmentectomy, lobectomy, pneumonectomy, surgical lung biopsy, pleural biopsy, decortication, and pleurectomy. Such specimens permit assessment of tumour growth pattern, differentiation, stromal invasion, pleural involvement, necrosis, vascular invasion, and associated parenchymal changes. Contemporary World Health Organization classifications emphasise integrated morphological evaluation supported by immunohistochemistry and, where clinically relevant, molecular testing.^{1,2} The revised frameworks provide defined criteria for pulmonary adenocarcinoma, squamous cell carcinoma, neuroendocrine neoplasms, mesothelioma, and uncommon thoracic tumours, while encouraging conservative use of tissue for ancillary investigations.¹⁻⁴

Adenocarcinoma has emerged as a frequent histological subtype of primary lung carcinoma, whereas squamous cell carcinoma remains closely linked to tobacco exposure. Poorly differentiated non-small-cell carcinomas can show overlapping morphology; panels incorporating thyroid transcription factor-1, Napsin A, p40, and related markers improve lineage assignment and reduce unclassified diagnoses.^{5,6} Pulmonary neuroendocrine neoplasms also require careful integration of architecture, mitotic activity, necrosis, and neuroendocrine marker expression because their biological behaviour ranges from indolent typical carcinoid to aggressive large-cell neuroendocrine carcinoma.⁷

Pleural specimens create a distinct diagnostic challenge. Reactive mesothelial proliferation, chronic pleuritis, metastatic adenocarcinoma, and mesothelioma can display overlapping epithelioid features, especially in limited tissue. Demonstration of invasion, appropriate positive and negative immunohistochemical markers, and clinicroadiological correlation are consequently

important.^{2,8,9} In tuberculosis-endemic regions, granulomatous inflammation and caseous necrosis remain common and can clinically resemble malignant pleural disease. Histopathological assessment of pleural and pulmonary tissue therefore contributes not only to cancer diagnosis but also to recognition of treatable infectious conditions.¹⁰

The present study was undertaken to characterise the histopathological spectrum encountered in pulmonary and pleural specimens obtained during thoracic surgical procedures at a government teaching hospital. The objectives were to determine the relative frequencies of malignant, infectious, inflammatory, fibrotic, and other benign lesions; describe the distribution of specific pulmonary and pleural diagnoses; assess demographic and specimen-related factors associated with malignant histopathology; and evaluate agreement between the preoperative clinicroadiological impression and the final tissue diagnosis.

Materials and methods

Study design and setting

This hospital-based cross-sectional observational study with prospective enrolment was conducted from May 2025 to April 2026 in the Department of Pathology, Government Medical College and its associated Government General/teaching hospital, Jagtial, Telangana, India, in collaboration with the Departments of Surgery, Respiratory Medicine, and Radiodiagnosis. The institution functions as a government teaching and district-referral facility and provides outpatient, emergency, inpatient, surgical, respiratory, radiological, laboratory, operating-theatre, and supportive critical-care services. It serves patients from Jagtial town and the surrounding rural and semi-urban communities, including referrals from peripheral government health facilities across Jagtial district. Consecutive patients undergoing thoracic surgical procedures that yielded pulmonary or pleural tissue were screened.

Study population

Patients of either sex and all eligible adult age groups were included when a pulmonary resection, surgical lung biopsy, pleural biopsy, decortication, or pleurectomy specimen was submitted for histopathological examination. Specimens obtained through lobectomy, wedge resection, pneumonectomy, segmentectomy, and related procedures were eligible. Patients were excluded when the tissue was insufficient for a definitive opinion, essential clinical information was unavailable, or neoadjuvant treatment had

been administered before tissue sampling because therapy-related alteration could obscure the primary morphology. Eighty-six patients were assessed; 80 fulfilled the eligibility criteria and formed the final study cohort.

Sample size determination

The required sample size was estimated using the single-population proportion formula $n = Z^2 p(1-p)/d^2$. In the absence of a reliable local estimate for the proportion of malignant histopathology among surgically obtained pulmonary and pleural specimens, a conservative expected proportion of 50% was used, with a 95% confidence level ($Z = 1.96$) and 11% absolute precision. The calculated minimum sample size was 79.4 and was rounded to 80 participants. To accommodate exclusions during eligibility assessment, 86 patients were screened; 80 fulfilled the eligibility criteria and were included in the final analysis.

Specimen processing and histopathological evaluation

Fresh surgical specimens were transferred promptly to the pathology laboratory and fixed in 10% neutral buffered formalin. Gross examination documented specimen type, dimensions, pleural thickening, nodules, consolidation, cavitation, necrosis, tumour size, cut-surface appearance, resection margins, and lymph nodes when supplied. Representative sections were processed routinely, embedded in paraffin, cut at approximately 3-5 μ m, and stained with haematoxylin and eosin. Ziehl-Neelsen, periodic acid-Schiff, and Grocott methenamine silver stains were used when mycobacterial or fungal infection was suspected. Tumours were classified using contemporary WHO thoracic tumour criteria.^{1,2}

Ancillary testing

Immunohistochemistry was selected according to the morphological differential diagnosis. Pulmonary carcinomas were assessed, where required, with markers such as thyroid transcription factor-1, Napsin A, p40, cytokeratin 5/6, synaptophysin, chromogranin, and leukocyte common antigen.⁵⁻⁷ Pleural malignancies were evaluated with complementary mesothelial and epithelial panels, including calretinin, WT1, D2-40, broad-spectrum cytokeratin, epithelial membrane antigen, Ber-EP4 or MOC-31, and organ-directed markers when metastatic disease was considered.^{2,8,9} Final diagnoses were issued

after integrating microscopy, ancillary findings, operative observations, and available radiological information.

Bias minimization

Potential bias was reduced by enrolling consecutive eligible patients rather than using convenience selection and by applying the stated inclusion and exclusion criteria uniformly. All specimens underwent standardized fixation, gross examination, tissue processing, sectioning, and haematoxylin-and-eosin staining, with special stains and immunohistochemistry used according to the morphological differential diagnosis. Tumours were classified using contemporary WHO criteria to reduce diagnostic misclassification. A structured data-collection form was used to limit information bias, and the same predefined statistical approach was applied to all cases. Complete blinding of pathologists to clinical and radiological information was not feasible because clinicoradiological correlation formed part of the final diagnostic assessment; therefore, standardized morphological criteria and focused ancillary panels were used to limit interpretive bias.

Data collection and statistical analysis

Age, sex, tobacco exposure, specimen site, operative procedure, preoperative clinicoradiological diagnosis, histopathological category, specific diagnosis, and use of immunohistochemistry were recorded on a structured form. Continuous variables were summarised as mean $\pm$ standard deviation, and categorical variables as frequencies and percentages. The 95% confidence interval for the overall malignancy proportion was calculated. The independent-samples t-test compared mean age between malignant and non-malignant groups. Pearson's chi-square test assessed associations between malignancy and age category, sex, smoking status, and specimen site; Fisher's exact test was reserved for sparse cells. Two-sided p-values below 0.05 were considered statistically significant. Analysis was performed using a standard statistical software package.

Ethical considerations

Ethical committee approval was obtained from Government Medical College Jagtial, Telangana, India. Written informed consent was obtained before enrolment, and patient identifiers were removed from the analytical dataset.

Results

Participant recruitment and baseline characteristics

During the study period, 86 patients undergoing thoracic surgical procedures were assessed for eligibility. Six

patients were excluded: three had inadequate tissue for definitive histopathological evaluation, two had incomplete clinical records, and one had received neoadjuvant therapy before tissue sampling. The remaining 80 patients were included in the final analysis.

The mean age of the study population was 52.6 ± 15.4 years, with a range of 18-79 years. Fifty-four patients (67.5%) were male, and 26 (32.5%) were female, giving a male-to-

female ratio of 2.1:1. Most patients were aged 50-69 years. Current or previous tobacco smoking was documented in 45 patients (56.3%). Pulmonary specimens accounted for 56 cases (70.0%), whereas 24 specimens (30.0%) originated from the pleura. Lobectomy was the most frequent procedure, followed by wedge resection and pleural decortication or pleurectomy (Table 1).

Table 1: Demographic and specimen characteristics of the study population

Characteristic	Value
Total patients	80
Age, years	52.6 ± 15.4
Age range, years	18-79
Age <30 years	7 (8.8%)
Age 30-49 years	19 (23.8%)
Age 50-69 years	39 (48.8%)
Age ≥ 70 years	15 (18.8%)
Male	54 (67.5%)
Female	26 (32.5%)
Current or former smoker	45 (56.3%)
Never-smoker	35 (43.8%)
Specimen site	
Pulmonary specimen	56 (70.0%)
Pleural specimen	24 (30.0%)
Thoracic surgical procedure	
Lobectomy	24 (30.0%)
Wedge resection	16 (20.0%)
Decortication or pleurectomy	15 (18.8%)
Pleural biopsy	9 (11.3%)
Pneumonectomy	6 (7.5%)
Segmentectomy	5 (6.3%)
Surgical lung biopsy	5 (6.3%)

Note. Values are presented as mean $\pm$ standard deviation, range, or number (percentage).

Overall histopathological spectrum

Malignant lesions were identified in 40 patients, producing an overall malignancy rate of 50.0% (95% confidence

interval: 39.3-60.7%). The remaining 40 specimens (50.0%) showed benign, inflammatory, infectious, or fibrotic pathology. Among the 56 pulmonary specimens, 31 (55.4%)

were malignant, and 25 (44.6%) were non-malignant. Of the 24 pleural specimens, nine (37.5%) demonstrated malignancy and 15 (62.5%) showed non-malignant

pathology. The difference in malignancy frequency between pulmonary and pleural specimens was not statistically significant ($p=0.143$) (Table 2).

Table 2: Broad histopathological categories according to specimen site

Histopathological category	Pulmonary specimens, n=56	Pleural specimens, n=24	Total, n=80
Malignant lesions	31 (55.4%)	9 (37.5%)	40 (50.0%)
Infectious lesions	13 (23.2%)	7 (29.2%)	20 (25.0%)
Non-specific inflammatory lesions	7 (12.5%)	7 (29.2%)	14 (17.5%)
Fibrotic or interstitial lesions	2 (3.6%)	1 (4.2%)	3 (3.8%)
Other benign lesions	3 (5.4%)	0	3 (3.8%)

Note. Values are expressed as numbers (percentages within the specimen site).

Histopathological findings in pulmonary specimens

Primary malignant epithelial tumours constituted the predominant pulmonary pathology. Adenocarcinoma was the most frequent malignant lung tumour, identified in 13 specimens, followed by squamous cell carcinoma in eight. Neuroendocrine tumours were found in three cases, comprising two typical carcinoid tumours and one large-cell neuroendocrine carcinoma. Metastatic deposits were identified in three pulmonary specimens; the primary sites

were the breast, colon, and kidney in one patient each. Less frequent malignant diagnoses included adenosquamous carcinoma, sarcomatoid carcinoma, and primary pulmonary lymphoma.

Among non-malignant pulmonary lesions, pulmonary tuberculosis was the most common diagnosis, observed in eight cases. Bronchiectasis, organising pneumonia, lung abscess, fungal infection, interstitial lung disease, and pulmonary hamartoma constituted the remaining non-malignant conditions (Table 3).

Table 3: Histopathological diagnoses in pulmonary specimens

Pulmonary histopathological diagnosis	Number	Percentage of pulmonary specimens
Malignant lesions	31	55.4%
Adenocarcinoma	13	23.2%
Squamous cell carcinoma	8	14.3%
Metastatic tumour	3	5.4%
Neuroendocrine tumour	3	5.4%
Adenosquamous carcinoma	2	3.6%
Sarcomatoid carcinoma	1	1.8%
Pulmonary lymphoma	1	1.8%
Non-malignant lesions	25	44.6%
Pulmonary tuberculosis	8	14.3%
Bronchiectasis	5	8.9%

Pulmonary histopathological diagnosis	Number	Percentage of pulmonary specimens
Organising pneumonia	4	7.1%
Lung abscess	3	5.4%
Fungal infection	2	3.6%
Interstitial lung disease	2	3.6%
Pulmonary hamartoma	1	1.8%
Total	56	100.0%

Histopathological findings in pleural specimens

Chronic non-specific pleuritis was the most common pleural diagnosis, accounting for seven cases. Tuberculous pleuritis was detected in five specimens and was characterised by granulomatous inflammation with caseous necrosis. Fibrinopurulent inflammation consistent with empyema was

observed in two cases, while dense pleural fibrosis was identified in one.

Malignant pleural disease was present in nine patients. Mesothelioma and metastatic adenocarcinoma were identified in four cases each. One patient had pleural involvement by lymphoma. Immunohistochemical examination was used for tumour classification in seven of the nine malignant pleural lesions (Table 4).

Table 4: Histopathological diagnoses in pleural specimens

Pleural histopathological diagnosis	Number	Percentage of pleural specimens
Chronic non-specific pleuritis	7	29.2%
Tuberculous pleuritis	5	20.8%
Mesothelioma	4	16.7%
Metastatic adenocarcinoma	4	16.7%
Fibrinopurulent pleuritis or empyema	2	8.3%
Pleural fibrosis	1	4.2%
Pleural lymphoma	1	4.2%
Total	24	100.0%

Factors associated with malignant histopathology

Patients with malignant lesions were significantly older than those with non-malignant lesions (60.1 ± 10.7 versus 45.1 ± 16.0 years; $p < 0.001$). Malignancy was identified in 33 of 54 patients aged 50 years or older (61.1%), compared with

seven of 26 patients younger than 50 years (26.9%; $p = 0.004$). Malignant pathology was also more frequent among current or former smokers than among never-smokers (62.2% versus 34.3%; $p = 0.013$). Although the proportion of malignant lesions was higher among males than females, the difference was not statistically significant (Table 5).

Table 5: Association of selected variables with malignant histopathology

Variable	Malignant, n=40	Non-malignant, n=40	p-value
Age ≥50 years	33 (82.5%)	21 (52.5%)	0.004
Age <50 years	7 (17.5%)	19 (47.5%)	
Male	29 (72.5%)	25 (62.5%)	0.340
Female	11 (27.5%)	15 (37.5%)	
Current or former smoker	28 (70.0%)	17 (42.5%)	0.013
Never-smoker	12 (30.0%)	23 (57.5%)	
Pulmonary specimen	31 (77.5%)	25 (62.5%)	0.143
Pleural specimen	9 (22.5%)	15 (37.5%)	

Clinicopathological correlation

The preoperative clinical and radiological diagnosis agreed with the final histopathological diagnosis in 68 patients (85.0%). Histopathological evaluation resulted in a clinically relevant diagnostic revision in 12 patients (15.0%). These included eight malignancies initially considered inflammatory or infective lesions and four radiologically suspected malignant lesions that were subsequently diagnosed as benign inflammatory conditions. Among the unexpected malignancies, adenocarcinoma was identified in three patients, squamous cell carcinoma in two, metastatic carcinoma in two, and mesothelioma in one. Histopathological examination therefore provided definitive tumour typing, identified unsuspected malignant disease, and distinguished neoplastic lesions from infections and non-specific inflammatory processes.

Discussion

This study demonstrates the broad diagnostic range represented in thoracic surgical pathology. Half of the specimens were malignant, while the remainder comprised infectious, inflammatory, fibrotic, and benign lesions. Pulmonary samples constituted 70.0% of the material and showed a higher, though statistically non-significant, proportion of malignancy than pleural samples. The balanced distribution highlights a central practical issue: radiological suspicion alone cannot reliably separate cancer from tuberculosis, organising inflammation, abscess, or chronic pleuritis. Tissue architecture and ancillary testing remain decisive when treatment pathways differ substantially.

Adenocarcinoma was the leading primary pulmonary malignancy, followed by squamous cell carcinoma. This

pattern is compatible with the contemporary prominence of adenocarcinoma and with classification systems that integrate growth pattern, immunophenotype, and molecular relevance.^{1,3,4} The significant association between malignancy and smoking supports the established link between tobacco exposure and pulmonary carcinoma, although adenocarcinoma also occurred in patients without documented smoking. Distinction between poorly differentiated adenocarcinoma and squamous carcinoma is clinically important, and focused panels using thyroid transcription factor-1 or Napsin A with p40 or cytokeratin 5/6 improve reproducibility while preserving tissue for predictive testing.^{5,6} The three neuroendocrine tumours in the series further illustrate the heterogeneous grades and behaviour within this diagnostic group.⁷

Pleural lesions were more frequently non-malignant. Chronic non-specific pleuritis and tuberculous pleuritis together accounted for half of all pleural specimens, reflecting the continuing importance of inflammatory and mycobacterial disease in Indian practice. Pleural tuberculosis can remain microbiologically difficult to confirm, whereas granulomatous inflammation with caseous necrosis provides strong pathological evidence in an appropriate clinical setting.^{10,11} Conversely, metastatic adenocarcinoma and mesothelioma require adequate tissue to demonstrate invasion and apply complementary immunohistochemical panels. The pleural neoplasm spectrum reported by Venkatachala and colleagues similarly emphasised the value of morphology combined with immunohistochemistry for separating primary from metastatic disease.⁸ Thoracoscopic or surgical biopsy also provides a higher diagnostic yield than pleural fluid cell block alone in selected malignant effusions.^{12,13}

Clinicoradiological and histopathological diagnoses agreed in 85.0% of patients, yet tissue evaluation changed the clinically relevant diagnosis in 15.0%. Eight occult malignancies had initially resembled inflammatory or infectious disease, while four presumed cancers were benign. This bidirectional reclassification is clinically important because both delayed oncological treatment and unnecessary cancer-directed therapy carry substantial consequences. Surgical lung biopsy also retains high diagnostic yield in selected diffuse parenchymal disorders when non-invasive assessment remains inconclusive, although procedural risks require multidisciplinary selection.¹⁴

Generalizability: The findings are most applicable to government teaching hospitals and regional referral centres serving populations with simultaneous burdens of tobacco-related malignancy and pulmonary tuberculosis. Consecutive inclusion and analysis of several operative specimen types support relevance to routine thoracic pathology practice. Nevertheless, case mix depends on referral patterns, surgical availability, local infection prevalence, and thresholds for resection or biopsy. Multicentre studies with larger cohorts and molecular correlation are required before extrapolating exact diagnostic proportions to other settings.

Conclusion

Histopathological examination of pulmonary and pleural specimens obtained during thoracic surgery revealed an equal distribution of malignant and non-malignant disease. Adenocarcinoma was the predominant pulmonary malignancy, while chronic non-specific pleuritis and tuberculous pleuritis were frequent pleural diagnoses. Older age and current or previous smoking were significantly associated with malignant pathology. Importantly, histopathology revised the clinicoradiological diagnosis in 15.0% of patients by identifying unsuspected cancers and confirming benign inflammatory lesions in radiologically suspicious cases. Adequate tissue sampling, systematic morphological assessment, targeted special stains, and judicious immunohistochemistry are therefore essential for accurate classification, timely multidisciplinary decision-making, and appropriate clinical management of thoracic lesions in routine hospital practice and regional referral centres.

Limitations

This study was conducted at a single institution with a modest sample size and a one-year enrolment period. Selection was restricted to surgically obtained specimens, excluding lesions diagnosed through cytology, needle

biopsy, or clinical follow-up. Molecular testing was not routinely available, and survival or treatment outcomes were not assessed. Referral patterns and surgical selection could have influenced the observed proportions of malignant and non-malignant disease.

Recommendations

Thoracic specimens should be transported promptly, fixed adequately, and sampled according to standard grossing protocols. Pathologists should apply WHO-based morphological criteria and use focused immunohistochemical panels rather than broad indiscriminate testing. Special stains and microbiological correlation should be prioritised when granulomatous or suppurative inflammation is present. Complex pulmonary and pleural lesions should be reviewed through multidisciplinary meetings involving pathologists, radiologists, pulmonologists, surgeons, and oncologists. Hospitals should establish prospective thoracic pathology registries containing clinical, radiological, operative, histological, immunohistochemical, molecular, treatment, and outcome data. Larger multicentre studies are recommended to validate regional disease patterns and identify clinically relevant predictors of diagnostic discordance.

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Abbreviations

ADA- adenosine deaminase
CI-confidence interval
H&E- haematoxylin and eosin
IHC- immunohistochemistry
PAS-periodic acid-Schiff
TTF-1-thyroid transcription factor-1
WHO-World Health Organization
WT1- Wilms tumour 1

Conflict of Interest

The authors declare no conflict of interest.

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Author contributions

Dr. Kontham Praveen: Conceptualization, study design, methodology, data interpretation, literature review, manuscript drafting, critical revision, supervision, and final approval of the manuscript.

Dr. Mikkili Reetu Jones: Data collection, histopathological evaluation, literature review, data analysis, preparation of tables, manuscript review, and approval of the final version.

Dr. Narsipuram Roja Rani: Histopathological assessment, data validation, interpretation of findings, literature search, manuscript editing, critical intellectual revision, and approval of the final manuscript.

Data availability

Data available on request

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