Section: Pathology

Original Research Article

ETIOLOGICAL SPECTRUM OF PLEURAL FLUID SAMPLES IN A TERTIARY CARE HOSPITAL OF NORTH INDIA

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ABSTRACT

Background: Pleural effusion is a common clinical presentation resulting from diverse pulmonary and systemic conditions. Accurate characterization of the etiological spectrum is essential for timely diagnostic evaluation and therapeutic planning. The objective is to evaluate the etiological pattern, clinicopathological profiles, and biochemical characteristics of pleural fluid samples in a tertiary care teaching hospital in North India. **Materials and Methods:** A retrospective observational study was conducted analyzing 742 consecutive pleural fluid samples submitted for cytological, biochemical, and microbiological evaluation. Data regarding demographic characteristics, clinical presentation, radiological effusion grade, gross appearance, fluid chemistry (protein and sugar content), and final diagnoses were extracted and categorized into granulomatous/tuberculous (G), infective non-tubercular (I), malignant (M), transudative/benign systemic (B), synovial/special (S), and undetermined (U) etiologies. **Result:** Among 742 patients, 533 (71.8%) were male and 209 (28.2%) were female (male-to-female ratio 2.55:1), with a mean age of 48.36 ± 18.54 years (range: 9–91 years). Exudates accounted for 82.1% (n = 609) of cases, whereas transudates comprised 17.9% (n = 133). The predominant etiology was tuberculous pleural effusion (Category G, n = 463, 62.4%), followed by non-tubercular infective etiologies (Category I, n = 80, 10.8%; including parapneumonic effusion n = 59, empyema n = 21), malignant effusions (Category M, n = 67, 9.0%), undetermined (Category U, n = 62, 8.4%), benign systemic/transudative conditions (Category B, n = 54, 7.3%), and synovial/special (Category S, n = 16, 2.2%). Primary pulmonary adenocarcinoma was the most common malignant cause (n = 33, 49.3% of malignancies). Mean fluid protein levels were significantly higher in exudates (5.11 ± 1.05 g/dL) than transudates (1.65 ± 0.98 g/dL). **Conclusion:** Tuberculous pleurisy remains the leading cause of pleural effusion in North India, predominantly affecting younger to middle-aged males. Cytological and biochemical profiling, integrated with clinical correlation, provides a reliable diagnostic strategy in resource-limited tertiary settings.

INTRODUCTION

Pleural effusion is an abnormal accumulation of fluid in the pleural space, resulting from an imbalance between fluid production and lymphatic resorption. It represents a manifestation of local pleuropulmonary infections, systemic illnesses, underlying malignancies, or organ failure. Globally, the etiology of pleural effusion varies according to geographic location, socio-economic factors, endemic disease prevalence, and demographic trends.[1-3]

In developing nations, particularly in India, infectious diseases—most notably tuberculosis and acute bacterial infections—remain major drivers of pleural pathology. Conversely, developed nations report a higher incidence of congestive heart failure and malignant pleural effusions. Accurate differentiation between exudative and transudative effusions using Light's criteria forms the crucial initial step in diagnostic algorithms.[4-6]

While diagnostic modalities such as closed pleural biopsy, thoracoscopy, and advanced imaging have enhanced diagnostic yield, cytological evaluation and fluid chemistry remain indispensable, cost-effective primary diagnostic tools in tertiary care facilities. This study aims to evaluate the etiological spectrum, clinical manifestations, biochemical parameters, and diagnostic distribution of 742 pleural fluid samples managed at a tertiary care institution in North India.

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MATERIALS AND METHODS

Study Design and Patient Selection: This retrospective observational study evaluated 742 consecutive pleural fluid samples received for routine cytological, biochemical, and microbiological examination over a period from September 2016 to December 2017 in the department of Pathology, Pt. B D Sharma PGIMS, Rohtak, a tertiary care teaching hospital in North India.

Inclusion and Exclusion Criteria

Inclusion Criteria

All patients of all age groups presenting with clinical or radiological evidence of pleural effusion who underwent therapeutic or diagnostic thoracentesis.

Exclusion Criteria

Inadequate samples, clotted fluid specimens preventing standard processing, and duplicate serial diagnostic taps from the same hospital admission.

Laboratory Processing & Diagnostic Procedures

Gross Examination: Fluid color, clarity, and physical appearance (yellow clear, hemorrhagic, turbid/purulent, milk-like) were documented immediately upon reception.

Biochemical Analysis: Fluid protein (g/dL) and glucose/sugar (mg/dL) levels were quantified using automated biochemical analyzers. Fluid samples were classified as exudates or transudates based on standard biochemical criteria (fluid protein cut-off ≥ 3.0 g/dL or Light's criteria).

Cytological Examination: Fresh samples were centrifuged at 2000 RPM for 10 minutes. Smears prepared from the sediment were fixed in 95% ethyl alcohol and stained with Papanicolaou (PAP) and Hematoxylin & Eosin (H&E) stains for cytomorphological assessment. Air-dried smears were stained with Giemsa stain for differential cell counting.

Microbiological Testing: Acid-Fast Bacilli (AFB) staining (Ziehl-Neelsen stain) and microbiological cultures were performed where clinically indicated.

Histopathological Correlation: Where available, cytological findings were correlated with closed pleural biopsy or tissue immunohistochemistry.

Statistical Analysis: Data extracted from the master chart were categorized, tabulated, and analyzed using statistical software (Python pandas and scipy.stats). Quantitative data were expressed as mean ± standard deviation (SD) or median (IQR), and qualitative categorical variables were presented as absolute frequencies (n) and percentages (%).

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

Baseline Demographic and Clinical Characteristics: The study evaluated 742 patients. The mean overall age was 48.36 ± 18.54 years (range: 9 to 91 years). Males constituted 71.8% (n = 533) of the cohort, while females accounted for 28.2% (n = 209), yielding a male-to-female ratio of 2.55:1.

Shortness of breath (SOB) was the most frequent presenting clinical symptom (n = 707, 95.3%), followed by cough (n = 370, 49.9%), chest pain (n = 116, 15.6%), fever (n = 81, 10.9%), and weight loss/loss of appetite (n = 15, 2.0%). Unilateral effusion was present in 96.0% of cases, with right-sided effusion (n = 400, 53.9%) being more frequent than left-sided (n = 312, 42.0%). Bilateral involvement was observed in 30 cases (4.0%). Radiological grading revealed Grade 2 effusion in 57.7% of cases (n = 428).

Table 1: Baseline Demographic and Clinical Profile of Patients (N = 742)

Parameter	Frequency (n)	Percentage (%)
Age (Years) [Mean ± SD]	48.36 ± 18.54	Range: 9–91
Gender - Male	533	71.8%
Gender - Female	209	28.2%
Effusion Side - Right (R)	400	53.9%
Effusion Side - Left (L)	312	42.0%
Effusion Side - Bilateral (B/L)	30	4.0%
Grade 1 (Mild Effusion)	149	20.1%
Grade 2 (Moderate Effusion)	428	57.7%
Grade 3 (Severe / Massive Effusion)	164	22.1%
Grade 4 Effusion	1	0.1%
Fluid Nature - Exudative (E)	609	82.1%
Fluid Nature - Transudative (T)	133	17.9%

Diagnostic Categorization: Exudative pleural effusions predominated (n = 609, 82.1%), whereas transudative effusions represented 17.9% (n = 133). The single largest diagnostic category was Granulomatous/Tuberculous effusion (Category G), comprising 463 cases (62.4%). Non-tubercular infective etiologies (Category I) were identified in 80 cases (10.8%), including Parapneumonic Effusion (PPE, n = 59) and Empyema (n = 21). Malignant pleural effusions (Category M) were detected in 67 cases (9.0%). Transudative effusions secondary to systemic benign organ dysfunction (Category B) were found in 54 cases (7.3%), comprising Congestive Heart Failure (CHF, n = 23), Liver

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Cirrhosis (n = 17), and chronic kidney disease (CKD, n = 14).

Table 2: Etiological Categorization across the Study Population (N = 742)

Code	Etiological Category	Cases (n)	Percentage (%)
G	Granulomatous (Tuberculous Pleural Effusion)	463	62.4%
I	Infective Non-Tubercular (Parapneumonic / Empyema)	80	10.8%
M	Malignant Pleural Effusion	67	9.0%
U	Undetermined / Unclassified	62	8.4%
B	Transudative / Benign Systemic (CHF, Cirrhosis, CKD)	54	7.3%
S	Synovial / Other Special Findings	16	2.2%

Biochemical and Physical Profile: Grossly, clear straw/yellow fluid was the most frequent appearance (n = 285, 38.4%), followed by hemorrhagic (n = 222, 29.9%), yellow turbid (n = 133, 17.9%), yellow/clear (n = 44, 5.9%), purulent pus (n = 20, 2.7%), and yellow-turbid/clear (n = 18, 2.4%).

Biochemical evaluation demonstrated clear separation between exudates and transudates. Exudates had a mean pleural fluid protein of 5.11 ± 1.05 g/dL (median 5.1 g/dL) and mean sugar level of 83.34 ± 40.79 mg/dL. Transudates had a mean protein of 1.65 ± 0.98 g/dL (median 1.5 g/dL) and sugar level of 76.76 ± 52.90 mg/dL. Non-tubercular infective effusions displayed markedly depressed sugar levels (mean 54.13 ± 44.65 mg/dL).

Table 3: Biochemical Parameters Across Diagnostic Categories

Category	Fluid Protein (g/dL) [Mean ± SD]	Fluid Sugar (mg/dL) [Mean ± SD]
Granulomatous (G - TB)	5.18 ± 1.02	87.20 ± 39.58
Infective (I - PPE / Empyema)	5.16 ± 1.29	54.13 ± 44.65
Malignant (M)	4.08 ± 1.34	80.13 ± 37.73
Benign Systemic (B)	1.51 ± 0.59	79.79 ± 40.94
Synovial / Special (S)	4.56 ± 1.10	85.50 ± 23.82
Undetermined (U)	1.50 ± 0.69	82.79 ± 62.59

Spectrum of Malignant Pleural Effusions: Malignancy was confirmed in 67 cases. Adenocarcinoma [Figure 1 & 2]was the most frequent malignant diagnosis (n = 33, 49.3%), followed by poorly differentiated carcinoma (PDC, n = 10, 14.9%), squamous cell carcinoma (SCC, n = 7, 10.4%), poorly differentiated squamous cell carcinoma (PDSCC, n = 5, 7.5%), non-Hodgkin lymphoma (NHL, n = 3, 4.5%), sarcomatoid carcinoma (n = 2, 3.0%) [Figure 3], malignant mesothelioma (n = 2, 3.0%) [Figure 4], renal cell carcinoma metastasis (RCC, n = 1, 1.5%), invasive ductal carcinoma metastasis (IDC Mets, n = 1, 1.5%), acute leukemia (n = 1, 1.5%), and chronic myeloid leukemia (n = 1, 1.5%).

Table 4: Subtype Distribution of Malignant Pleural Effusions (n = 67)

Histological / Cytological Diagnosis	Cases (n)	Proportion (%)
Adenocarcinoma	33	49.3%
Poorly Differentiated Carcinoma (PDC)	10	14.9%
Squamous Cell Carcinoma (SCC)	7	10.4%
Poorly Differentiated SCC (PDSCC)	5	7.5%
Non-Hodgkin Lymphoma (NHL)	3	4.5%
Sarcomatoid Carcinoma	2	3.0%
Malignant Mesothelioma	2	3.0%
Renal Cell Carcinoma (RCC) Metastasis	1	1.5%
Invasive Ductal Carcinoma (IDC) Metastasis	1	1.5%
Acute Leukemia	1	1.5%
Chronic Myeloid Leukemia (CML)	1	1.5%

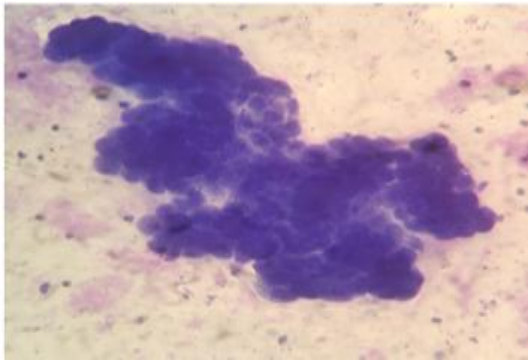

Figure 1: Photomicrograph showing papillary structures of adenocarcinoma on Leishman-stained conventional cytology smear of pleural fluid (400X).

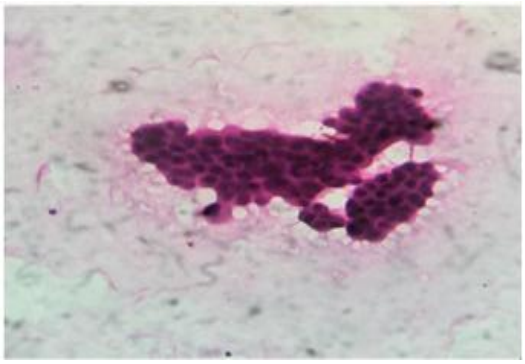

Figure 2: Photomicrograph showing papillary structures of adenocarcinoma on H&E-stained conventional cytology smears of pleural fluid (400X).

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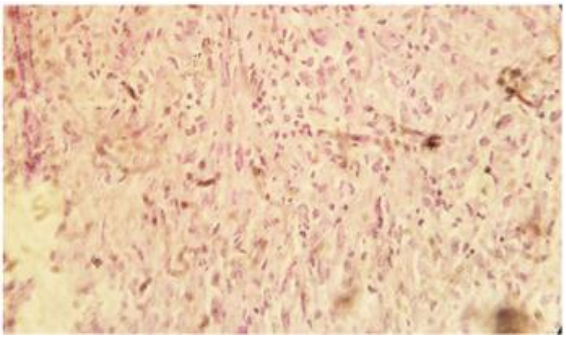

Figure 3: Photomicrograph showing sarcomatoid carcinoma on H&E-stained section of pleural biopsy (400X).

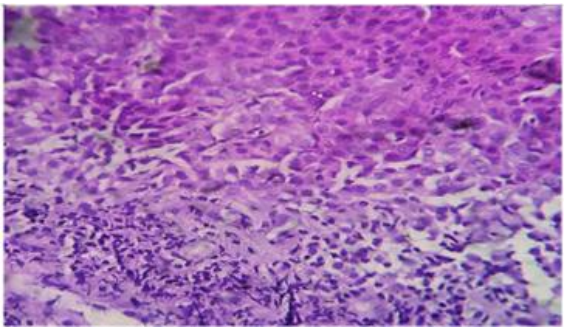

Figure 4: Photomicrograph showing malignant mesothelioma on H&E-stained sections of pleural biopsy (400X).

DISCUSSION

This study provides a comprehensive evaluation of 742 pleural fluid samples in a tertiary care teaching hospital in North India. The findings underscore the predominant burden of infectious disease, specifically tuberculosis, in this region.

Demographics and Clinical Presentation: Our study noted a marked male predominance (71.8%) with a male-to-female ratio of 2.55:1. The mean age of 48.36 years reflects the vulnerability of young to middle-aged adult populations to pulmonary tuberculosis in endemic zones, consistent with findings by Verma et al,[7] in similar Indian cohorts. Dyspnea and cough were the primary presenting features, aligning with standard clinical manifestations of pleural fluid collection compressing adjacent lung parenchyma.

Tuberculosis as the Leading Cause: Tuberculous pleural effusion accounted for 62.4% (n = 463) of all cases, confirming that tuberculosis remains the single largest etiology of pleural effusions in North India. Tuberculous effusions were characteristically exudative with elevated protein levels (mean 5.18 g/dL) and lymphocytic cytological predominance. These findings align with epidemiological data from Asian and African tertiary institutions where tuberculosis accounts for 50–70% of exudative effusions.[8]

Non-Tubercular Infections: Infective non-tubercular effusions constituted 10.8% (n = 80), represented by parapneumonic effusions and empyema. Notably, this group exhibited markedly decreased fluid sugar levels (mean 54.13 mg/dL). The drop in fluid glucose reflects high metabolic consumption by active bacterial pathogens and polymorphonuclear leukocytes during acute inflammatory reactions.

Malignant Pleural Effusions: Malignancies represented 9.0% (n = 67) of total cases, with adenocarcinoma emerging as the primary subtype (49.3% of malignancies). Primary lung adenocarcinoma, alongside metastatic lesions from breast and renal organs, represents the main etiology in malignant effusion series, consistent with findings by Light et al.[9] Cytological examination of pleural fluid serves as a rapid, minimally invasive technique for establishing diagnosis and guiding molecular subtype testing in neoplastic diseases.

Transudative Effusions: Transudates constituted 17.9% of total cases (n = 133), primarily caused by systemic organ failures including congestive heart failure, liver cirrhosis, and chronic renal disease. Mean fluid protein levels in transudates (1.65 ± 0.98 g/dL) were significantly lower than in exudative categories, supporting the utility of biochemical profiling for preliminary categorization. These findings are consistent with findings by Patel et al.[4]

CONCLUSION

Pleural effusion presents across a diverse etiological spectrum in North India, with tuberculous pleurisy remaining the predominant disease entity, followed by non-tubercular bacterial infections and malignant neoplasia. Routine pleural fluid cytomorphology combined with quantitative biochemical assessment (protein and sugar) offers a rapid, reliable, and cost-effective approach for guiding patient management in tertiary care centers.

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