Section: Pathology

Original Research Article

ETIOLOGICAL SPECTRUM OF INTRATHORACIC LESIONS EVALUATED VIA CONVENTIONAL TRANSBRONCHIAL NEEDLE ASPIRATION (C-TBNA) IN A TERTIARY CARE HOSPITAL OF NORTH INDIA.

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ABSTRACT

Background: Intrathoracic lymphadenopathy and lung masses present a diagnostic challenge in developing nations. While Endobronchial Ultrasound-guided Transbronchial Needle Aspiration (EBUS-TBNA) is the gold standard for nodal evaluation, financial and infrastructure constraints severely limit its availability. Conventional transbronchial needle aspiration (c-TBNA) remains an affordable, minimally invasive alternative. The objective is to evaluate the diagnostic yield and characterize the etiological spectrum of intrathoracic (mediastinal, hilar, and pulmonary) lesions diagnosed via c-TBNA in a tertiary care center in North India. **Materials and Methods:** A cross-sectional observational study was conducted on 100 adult patients with radiological evidence of mediastinal/hilar lymphadenopathy or submucosal/peri-bronchial lung masses over a one-year period (January 1, 2017 to December 31, 2017). c-TBNA was performed using a 21-gauge cytology needle guided by pre-procedural computed tomography (CT) and the Wang nodal map, combined with Rapid On-Site Evaluation (ROSE) using toluidine blue stain. Definitive reference histopathology was available for 81 patients (analyzed per-protocol). Statistical analyses included Chi-square and Fisher's exact tests ($p < 0.05$ considered statistically significant). **Result:** Among 81 analyzed patients (mean age: 54.6 years; 64 males, 17 females; M:F ratio 3.7:1), 52 were smokers. The subcarinal (Station 7; 48%) and lower paratracheal (Station 4; 22%) nodes were the primary sampling targets. The overall diagnostic yield of c-TBNA was 75.3% (61/81). Sensitivity was 46.0% (23/50) for malignant conditions and 63.6% (7/11) for granulomatous diseases, with 100% specificity and positive predictive value for both. Among c-TBNA confirmed malignancies (n=23), small cell lung carcinoma (SCLC) was the predominant subtype (34.7%, 8/23), followed by squamous cell carcinoma (21.7%, 5/23). All 23 confirmed malignant cases occurred in smokers ($p < 0.001$), with a significant male predominance ($p = 0.031$). **Conclusion:** c-TBNA with ROSE is a safe, economical, and rapid diagnostic modality. In resource-constrained healthcare systems where EBUS-TBNA is inaccessible, c-TBNA remains vital for defining the etiological spectrum of intrathoracic lesions during routine initial diagnostic bronchoscopy.

INTRODUCTION

Intrathoracic lesions—encompassing mediastinal and hilar lymphadenopathy alongside parenchymal and peri-bronchial lung masses—represent a substantial burden of disease globally and in low- and middle-income countries (LMICs). Establishing a rapid, accurate diagnostic and etiological profile is crucial for initiating appropriate therapeutic strategies, whether for infectious etiologies such as tuberculosis or malignant conditions like bronchogenic carcinoma.[1,2]

Determining nodal status and tissue histology remains a major diagnostic hurdle. Diagnostic options range from non-invasive imaging (computed tomography [CT] and positron emission tomography [PET]) to surgical techniques (mediastinoscopy, video-assisted thoracoscopic surgery [VATS]), standard transbronchial lung biopsy, and endobronchial ultrasound-guided fine-needle aspiration (EBUS-FNA/TBNA).[3,4] Although EBUS-TBNA has emerged as the modern gold standard due to real-time sonographic guidance, its widespread clinical implementation in developing countries is hindered by high hardware acquisition

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costs, maintenance expenses, disposable supply costs, and a lack of trained interventional pulmonologists.[5]

Conventional transbronchial needle aspiration (c-TBNA), first introduced in flexible bronchoscopy by Wang et al. in 1981, provides a minimally invasive, highly specific, and cost-effective approach for sampling intrathoracic lesions. Utilizing pre-procedural CT imaging, anatomic landmarks, and rapid on-site evaluation (ROSE), c-TBNA can yield reliable diagnostic material without substantial capital expenditure.[6-9]

This study was undertaken at a tertiary care facility in North India to evaluate the diagnostic yield and characterize the etiological spectrum of intrathoracic disease using c-TBNA, highlighting its pragmatic utility in resource-limited public healthcare settings.

MATERIALS AND METHODS

Study Design and Setting: A hospital-based retrospective cross-sectional observational study was conducted at the Department of Pathology in collaboration with Pulmonary Medicine at Pt. B.D. Sharma PGIMS, Rohtak, from January 1, 2017 to December 31, 2017.

Study Population: A convenience sample of 100 adult patients presenting with documented mediastinal/hilar lymphadenopathy or peri-bronchial/submucosal lung masses requiring diagnostic confirmation or lung cancer staging was retrospectively enrolled.

Inclusion Criteria

Patients aged ≥ 18 years with radiologically documented mediastinal/hilar lymphadenopathy or peribronchial/submucosal lung masses clinically indicated for diagnostic evaluation.

Exclusion Criteria

Patients with high bleeding risk (uncorrected coagulopathy), severe cardiovascular instability, severe baseline hypoxia, an already established histopathological/microbiological diagnosis, or severe anatomical distortions obstructing upper airway access.

c-TBNA Procedure and Rapid On-Site Evaluation (ROSE)

Pre-procedure CT scans were reviewed to locate lesions according to the Wang lymph node map. Procedures were performed under local anesthesia (topical lidocaine) in the supine position. A flexible bronchoscope fitted with a 21-gauge, 13-mm long cytology needle was passed into the tracheobronchial tree. Standard needle puncture techniques (e.g., piggy-back method) were executed by an experienced pulmonologist.[10]

Aspirated material was extruded onto glass slides. Rapid On-Site Evaluation (ROSE) was performed immediately by an attending cytopathologist using 1% toluidine blue stain (air-dried smear, stained for 1 minute, rinsed under gentle tap water, and reviewed under light microscopy within 2 minutes). Sample adequacy was defined by the presence of at least 5 clusters of 6–8 intact epithelial cells and/or lymphoid cells. If specimens contained only blood, mucus, or necrotic debris, immediate re-aspiration was performed. Formal cytological evaluation was subsequently completed on air-dried (May-Grünwald-Giemsa) and alcohol-fixed (Papanicolaou) smears.[11]

Reference Standard: Biopsy tissue was obtained in parallel or sequentially (endobronchial biopsy, transbronchial lung biopsy, or surgical excision) and subjected to paraffin embedding and hematoxylin and eosin (H&E) histopathological evaluation, which served as the gold standard diagnostic reference.

Statistical Analysis: Data were processed using IBM SPSS Statistics version 20.0. A per-protocol diagnostic efficacy analysis was conducted on 81 cases with full histopathological correlation. Continuous variables were expressed as mean ± standard deviation, while categorical variables were reported as proportions and percentages. Diagnostic accuracy metrics (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) were calculated using standard 2 × 2 contingency formulas. Association between categorical parameters (e.g., smoking status, sex vs. malignancy) was evaluated using Fisher's exact test. A p-value < 0.05 was considered statistically significant.

Ethics: This study was a retrospective cross-sectional 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: Of 100 initially enrolled patients, 81 cases had definitive reference histopathology and completed the study protocol (19 cases were excluded due to missing reference tissue or loss to follow-up). The mean age of the analyzed cohort was 54.6 years. Male patients predominated (n = 64, 79.0%) over females (n = 17, 21.0%), giving a male-to-female ratio of 3.7:1. Over half of the study population (n = 52, 64.2%) were smokers, with 51 of 52 smokers being male.

Sampling distribution showed that subcarinal lymph nodes (Station 7) were the primary site targeted (48.0%), followed by lower paratracheal nodes (Station 4; 22.0%). Adequate cytological material was obtained on a single needle pass in 80.0% of cases, while 16.0% required two passes.

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Table 1: Baseline Demographic and Radiological Characteristics of the Study Cohort (N = 81).

Parameter	Subgroup	Count (n)	Percentage (%)
Gender	Male	64	79.0%
	Female	17	21.0%
Smoking Status	Smokers (Male / Female)	52 (51 / 1)	64.2%
	Non-smokers (Male / Female)	29 (13 / 16)	35.8%
Primary Anatomical Target Site	Station 7 (Subcarinal)	39	48.0%
	Station 4 (Lower Paratracheal)	18	22.0%
	Other Nodal / Parenchymal Sites	24	30.0%
Needle Passes Required	Single Pass	65	80.0%
	Two Passes	13	16.0%
	≥ Three Passes	3	4.0%

Diagnostic Performance and Etiological Spectrum c-TBNA provided a conclusive diagnostic result in 61 out of 81 cases, yielding an overall diagnostic yield of 75.3%. Histopathologically, 50 cases were diagnosed as malignant, 11 as granulomatous inflammation, and 20 cases presented with non-specific benign/normal tissue changes. The overall diagnostic performance of c-TBNA across diagnostic categories is summarized in [Table 2 & Figure: 1-8]

Table 2: Diagnostic Efficacy Metrics of c-TBNA by Etiological Category.

Diagnostic Category	Reference Gold Standard (n)	c-TBNA Positive (n)	Sensitivity	Specificity	PPV	NPV
Malignant Disease (n=70)*	50	23	46.0% (23/50)	100.0% (20/20)	100.0%	42.6%
Granulomatous Disease (n=31)*	11	7	63.6% (7/11)	100.0% (20/20)	100.0%	83.3%

*Sub-cohort calculations for diagnostic metrics isolate target entity against true negative benign cases (n=20) per standard diagnostic calculation protocols.

Distribution of Malignancies: Among the 23 malignant cases diagnosed by c-TBNA, Small Cell Lung Carcinoma (SCLC) was the dominant subtype, accounting for 34.7% (n = 8) of cases. Squamous cell carcinoma represented 21.7% (n = 5), metastatic deposits accounted for 17.3% (n = 4), non-specific malignancies comprised 17.3% (n = 4), and adenocarcinoma represented 8.6% (n = 2) [Table 3].

Table 3: Etiological Breakdown of Malignancies Diagnosed via c-TBNA (n = 23).

Malignant Histotype	Number of Cases (n)	Percentage (%)
Small Cell Lung Carcinoma (SCLC)	8	34.7%
Squamous Cell Carcinoma	5	21.7%
Metastatic Carcinoma	4	17.3%
Non-Specific Malignancy	4	17.3%
Adenocarcinoma	2	8.6%
Total	23	100.0%

Statistical Associations: All 23 patients diagnosed with malignancy on c-TBNA had a history of smoking, whereas no non-smokers (0/29) were diagnosed with malignant disease via c-TBNA ($p < 0.001$, Fisher's exact test). In addition, males demonstrated a significantly higher malignancy detection rate on c-TBNA compared to females (22/64 vs. 1/17; $p = 0.031$, Fisher's exact test) [Table 4].

Table 4: Association of Malignancy Detection via c-TBNA with Smoking and Gender.

Variable	Subgroup	c-TBNA Malignant (n)	c-TBNA Non-Malignant (n)	Total (N)	Statistical Significance
Smoking Status	Smoker	23	29	52	Fisher's Exact Test
	Non-Smoker	0	29	29	$p < 0.001$
Gender	Male	22	42	64	Fisher's Exact Test
	Female	1	16	17	$p = 0.031$

Microscopic Cytomorphological and Histopathological Findings: Representative photomicrographs demonstrating key diagnostic cytological and matching histopathological features are detailed below:

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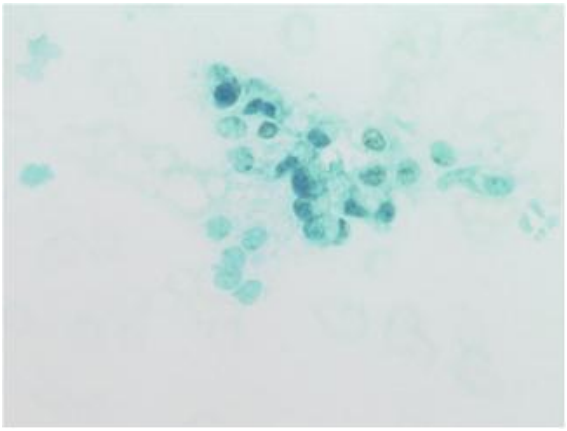

Figure 1: Toluidine-stained photomicrograph of adenocarcinoma. (400X)

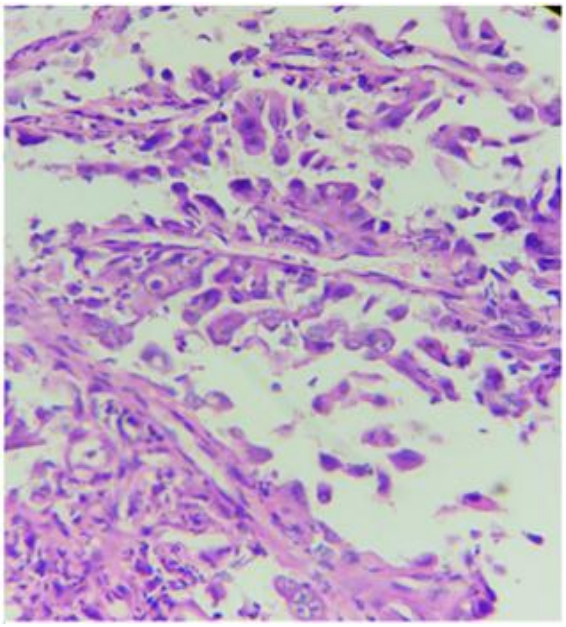

Figure 2: H&E-stained photomicrograph of adenocarcinoma. (400X)

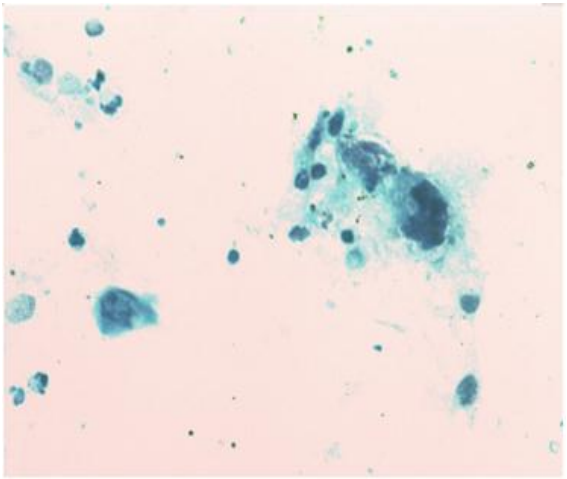

Figure 3: Toluidine-stained photomicrograph of squamous cell carcinoma. (400X)

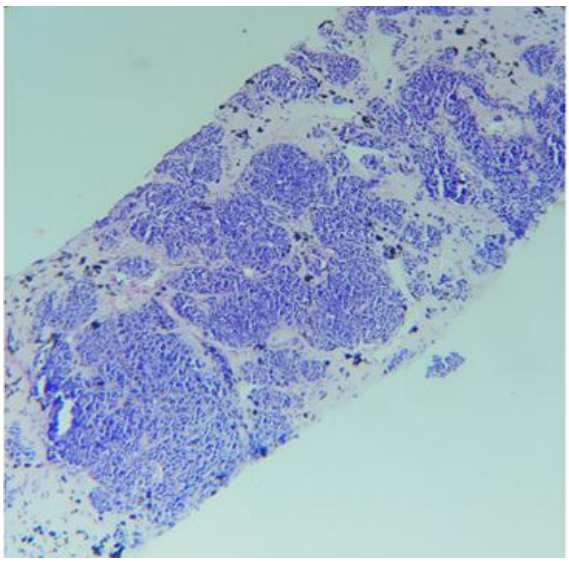

Figure 4: H&E- stained photomicrograph of squamous cell carcinoma. (400X)

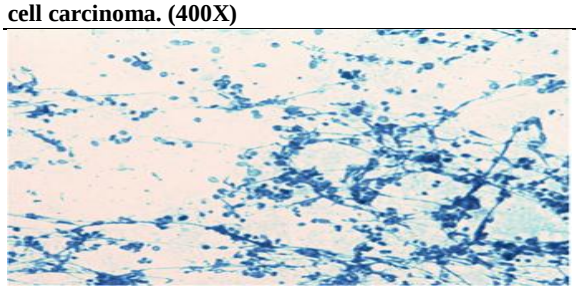

Figure 5: Toluidine-stained photomicrograph of small cell carcinoma lung. (200X)

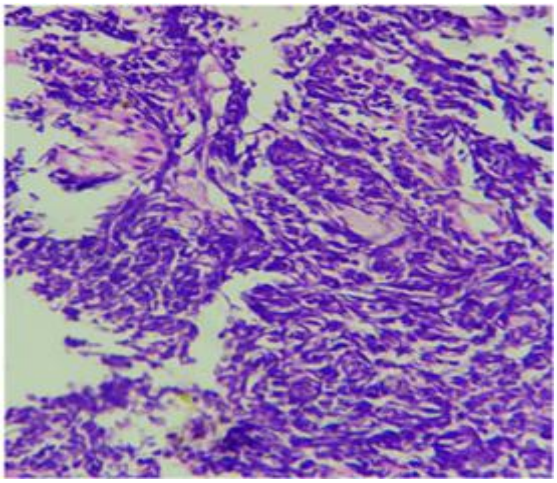

Figure 6: H&E- stained photomicrograph of small cell carcinoma lung. (400X)

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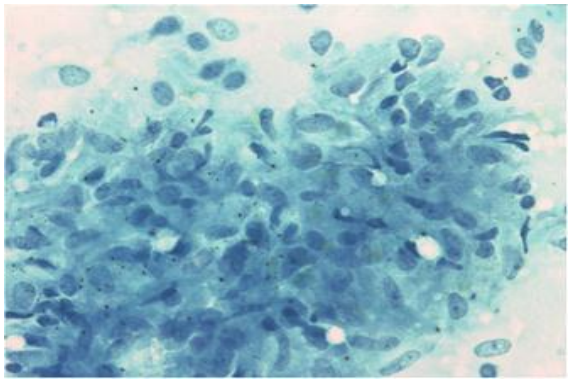

Figure 7: Toluidine-stained photomicrograph of epithelioid cell granuloma. (400X)

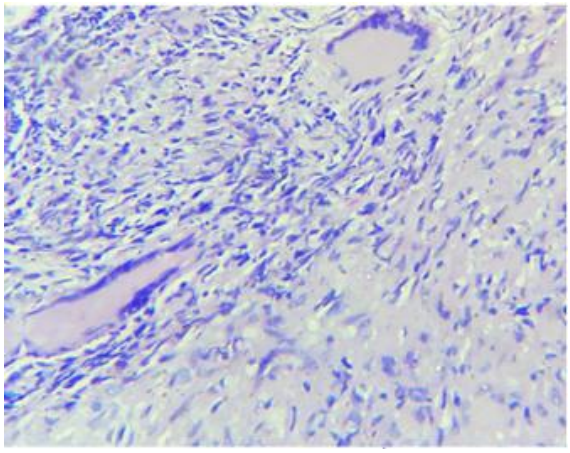

Figure 8: H&E-stained photomicrograph of epithelioid cell granuloma. (400X)

DISCUSSION

In resource-constrained public healthcare systems, implementing costly technological solutions like EBUS-TBNA for every patient with mediastinal lymphadenopathy is often unfeasible. This study demonstrates that conventional TBNA (c-TBNA), when supplemented by pre-procedural CT guidance and Rapid On-Site Evaluation (ROSE), remains an effective, highly specific, and accessible diagnostic procedure.

Our observed overall diagnostic yield of 75.3% falls well within the range of 60%–85% reported in international literature and aligns closely with regional studies such as Walia et al,[12] (73.3%) and Khoo et al,[13] (65.0%). Variations in diagnostic yield across published series are primarily driven by target node diameter, operator experience, pre-procedural imaging protocols, and the presence of specialized core-biopsy needles (19-gauge vs. 21/22-gauge).

In our study, c-TBNA achieved moderate diagnostic sensitivity for malignant conditions (46.0%) and granulomatous lesions (63.6%), paired with 100% specificity and PPV. The 27 false-negative malignant cases consisted of adequate cytological samples containing predominant lymphoid populations without atypical cells, reflecting the non-real-time nature of conventional aspirates, where sampling off-target reactive lymphoid tissue remains a known limitation.

Interestingly, Small Cell Lung Carcinoma (SCLC) was the single most frequent malignant entity identified on c-TBNA (34.7%), followed by squamous cell carcinoma (21.7%). SCLC frequently presents with central submucosal infiltration and massive subcarinal/paratracheal nodal involvement. This central anatomical propensity makes SCLC especially suitable for c-TBNA sampling, consistent with findings reported by Darjani et al.[14]

Statistical analysis demonstrated a strong positive association between smoking and malignancy ($p < 0.001$), as well as a significant male predominance ($p = 0.031$). These findings reflect regional epidemiology in North India, where high smoking rates among males contribute significantly to the burden of centrally located bronchogenic carcinomas.

CONCLUSION

Conventional transbronchial needle aspiration (c-TBNA) combined with ROSE is a safe, rapid, specific, and highly cost-effective diagnostic tool. In healthcare environments where EBUS-TBNA is unfeasible due to high capital costs, c-TBNA should be systematically integrated into routine initial diagnostic bronchoscopy protocols for evaluating mediastinal lymphadenopathy and central pulmonary masses.

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