

A Study of Different Cytological Typing of Primary Bronchogenic Carcinoma and their Different Diagnostic Methods with Special Reference to Ultrasonography-guided Fine-needle Aspiration Cytology

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Abstract

Introduction: Lung cancer is a leading cause of cancer-related deaths worldwide and one of the most common cancers in both men and women. Despite its increasing incidence, knowledge about its morbidity and mortality in our country remains limited. **Materials and Methods:** This study analyzed 142 patients with confirmed primary lung cancer, focusing on demographic, clinical, and radiological parameters. Various diagnostic methods were employed to obtain histological or cytological diagnoses, with special emphasis on Ultrasonography (USG)-guided fine-needle aspiration cytology (FNAC) for peripheral lung lesions. **Results:** The male-to-female ratio was 4.68:1, with most patients aged 51–60 years (31.69%). Common symptoms included cough, chest pain, and breathlessness, while superior vena cava obstruction was seen in 10.56% of cases. Squamous cell carcinoma (SCC) was the most frequent histological type (46.48%). Clubbing, pallor, and pleural effusion were common clinical findings. Radiologically, mass lesions (74.65%) were the most common presentation, with central lesions in 53.52% and mediastinal lymphadenopathy in 61.97%. Diagnostic modalities included fiber-optic bronchoscopy, lymph node FNAC, image-guided FNAC, tru-cut biopsy, and pleural biopsy. **Conclusion:** Men aged 51–60 years are at higher risk for lung cancer, with SCC being the predominant type. Mass lesions with mediastinal lymphadenopathy, cough, chest pain, and breathlessness are common presentations, often accompanied by clubbing, pallor, or pleural effusion. USG-guided FNAC is a safe, cost-effective, and accurate diagnostic technique for peripheral lung cancers, providing reliable results without radiation exposure.

Keywords: Lung cancer, squamous cell carcinoma, USG-guided fine-needle aspiration cytology

INTRODUCTION

The World Health Organization reports cancer to be the leading cause of death worldwide, accounting for nearly 10 million deaths in 2020.^[1,2] The projected annual incidence of lung cancer in 2020 in India was around 98,000, indicating that almost 1 person among every 100 will have lung cancer.^[3]

However, similar data in Eastern India are lacking. Moreover, it is extremely important to reach a conclusive diagnosis in the shortest possible time, minimal cost and least morbidity. Hence, in our study, we have studied the

trends of lung carcinoma in a tertiary care hospital in Eastern India and compared various diagnostic procedures for the same.

The present study aimed to evaluate patients of lung carcinoma with relation to their demographic profile and personal history such as smoking habits, clinical and radiological profile,

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dyspnea (61.97%), hemoptysis (39.44%), weight loss (35.21%), and anorexia (35.92%) [Table 1], while clubbing (47.89%), pallor (50%), pleural effusion (30.28%), and palpable lymph nodes (28.17%) were the common clinical manifestations. 80.28% patients were smokers (bidi – 90.35%, cigarette – 9.65%) and approximately 78% smoked more than 10 cigarettes/bidis per day and 50.88% people smoked for more than 30 years [Table 2].

Chest X-ray was abnormal in all our patients. In CT thorax, both central and peripheral lesions were seen (53.52% vs. 46.48% respectively) with bilateral lesion in 13.38% cases. Mass lesion was the commonest presentation (74.65%) followed by mediastinal lymphadenopathy (61.97%), pleural effusion (30.28%), collapse (25.35%), and cavitory lesions (8.45%).

The most common histopathological type of cancer was squamous cell carcinoma (SCC, 46.48%), followed by adenocarcinoma (24.65%), and small cell carcinoma (SLCC, 22.54%) [Table 3]. SCC and SLCC had a higher mean age of presentation (around 60 years) as compared to undifferentiated non-small cell lung carcinoma (NSCLC) (40.8 years, $P=0.004$) [Figure 2]. Histopathology slides with descriptions for the same are given in Figures 3-6.

Overall, adenocarcinoma was almost five times more common in females ($P=0.0008$), whereas SCC and SLCC (OR = 8.65 [95% confidence interval (CI): 1.12–66.67]) were more common in males ($P = 0.137$ and 0.0077 , respectively). SCC presented predominantly as a central lesion ($P = 0.0047$) and adenocarcinoma as a peripheral lesion ($P = 0.0001$) [Table 4].

Young females (30–50 years), presented with SCC and adenocarcinoma more than the males ($P = 0.003$ and 0.03 , respectively), whereas elderly males (50–70 years) presented with adenocarcinoma and SCC, which was however statistically significant only for adenocarcinoma ($P = 0.035$) [Figure 2].

SCC and SLCC were more common among smokers, which was however statistically significant only for the latter ($P = 0.153$ and $P = 0.003$, OR = 10.08 (95% CI: 1.31–77.41), while adenocarcinoma was more common among nonsmokers ($P = 0.003$) [Figure 7].

Among the diagnostic modalities, sputum cytology was positive only in 24.65% of patients, whereas bronchial lavage cytology was positive in 52.63% cases. Bronchial biopsy was taken in 76 cases, out of which 86.84% had a positive yield.

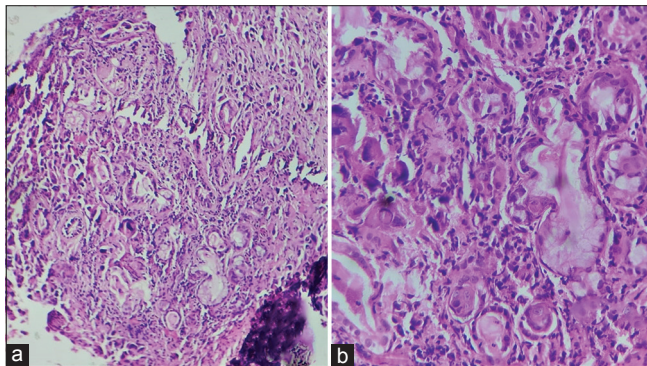


Figure 3: Histopathological images showing well-differentiated adenocarcinoma. (a) At $\times 100$, glandular structures are well-formed with clear cell borders. (b) At $\times 400$, the tumor cells exhibit minimal pleomorphism, with abundant mucin production

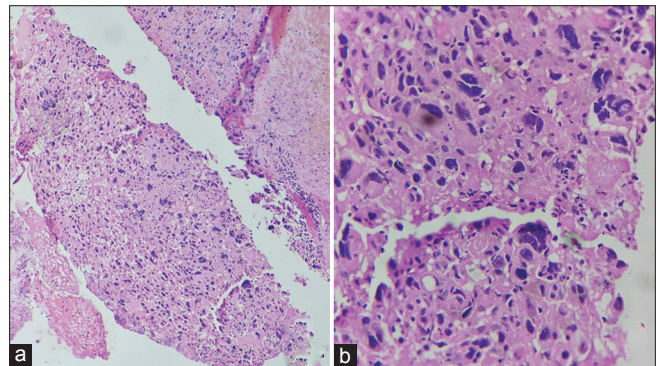


Figure 4: Histological images of poorly differentiated non-small cell lung carcinoma. (a) At $\times 100$, the tumor appears as solid sheets of cells with indistinct borders. (b) At $\times 400$, there is marked cellular pleomorphism, with high mitotic activity and irregular nuclei

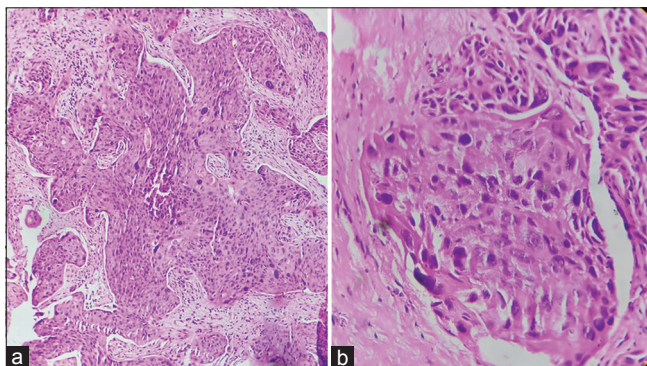


Figure 5: Histopathological images of moderately differentiated keratinizing squamous cell carcinoma. (a) At $\times 100$, atypical squamous cells with keratin pearls are visible. (b) At $\times 400$, the cells show moderate pleomorphism with increased keratinization and intercellular bridges

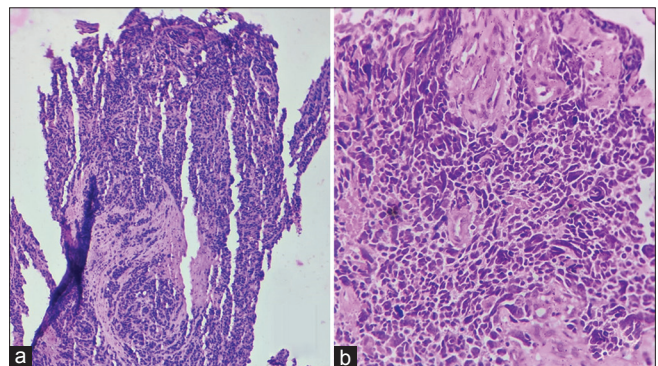


Figure 6: Histological images of small cell carcinoma. (a) At $\times 100$, the tumor is composed of small, round cells arranged in sheets with a high nuclear-to-cytoplasmic ratio. (b) At $\times 400$, the cells exhibit dense, hyperchromatic nuclei and scant cytoplasm with high mitotic activity

Table 1: Demographic and clinical characteristics of lung cancer patients (n=142)

Baseline parameters	n (%)
Age (years), mean±SD	58.92±12.33
Gender (male:female)	117:25 (4.68:1)
Occupation	
Farmers	53 (37.32)
Housewife	23 (16.20)
Labourers	16 (11.27)
Clerk	13 (9.15)
Businessman/shopkeepers	13 (9.15)
Professor/school teacher	12 (8.45)
Officer	5 (3.52)
Drivers	4 (2.82)
Service	3 (2.11)
Symptoms	
Cough	117 (82.39)
Chest pain	92 (64.79)
Shortness of breath	88 (61.97)
Fever	66 (46.48)
Hoarseness of voice	56 (39.44)
Loss of appetite	51 (35.92)
Loss of weight	50 (35.21)
Expectoration	46 (32.39)
Haemoptysis	11 (7.75)
Dysphagia	4 (2.82)

SD: Standard deviation

Table 2: History and clinicroadiological features of lung cancer patients (n=142)

Clinico-radiological parameters	n (%)
Comorbidities	
Hypertension	10 (7.04)
Diabetes mellitus	11 (7.75)
Tuberculosis	22 (15.49)
Smoker:nonsmoker	114:28 (4.07:1)
Metastatic and nonmetastatic features	
Pallor	71 (50.00)
Clubbing	68 (47.89)
Pleural effusion	43 (30.28)
Horner’s syndrome	40 (28.17)
Superior vena cava obstruction	15 (10.56)
Radiological features	
Unilateral lesion	123 (86.62)
Lymphadenopathy	88 (61.97)
Central lung mass	76 (53.52)
Pleural effusion with lung mass	43 (30.28)
Pleural effusion	43 (30.28)
Collapse	36 (25.35)
Hilar mass	21 (14.79)
Cavitary lesion	12 (8.45)
Sputum study	
PAP stain positive	35 (24.65)
Acid-fast bacilli positive	3 (2.11)

PAP: Papanicolaou

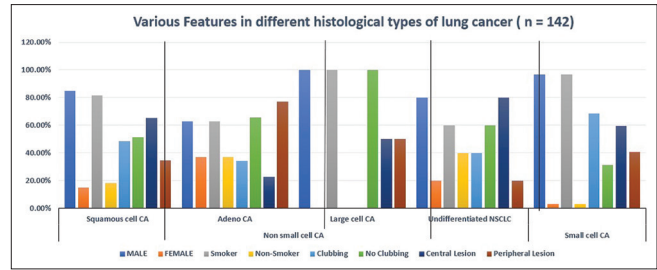


Figure 7: Gender: Males have 8.65 times more chances to have small cell carcinoma, and females 5 times more prone to develop adenocarcinoma ($P = 0.0008$). Smoking status: Adenocarcinoma is 4 times more common in non-smokers and small cell carcinoma 10 times more common in smokers ($P = 0.003$). Clubbing: Clubbing was found more in small cell carcinoma than in adenocarcinoma but the findings were not statistically significant. Central Lesion: Central lesions are 2.4 times more common in squamous cell carcinoma and peripheral lesions are 6 times more common in adenocarcinoma ($P = 0.004$). (By Chi-square test) CA: Carcinoma, NSCLC: Non-small cell lung carcinoma

Pleural fluid cytology was positive in 44.2% cases whereas pleural biopsy only had a yield of 33.3%. This discrepancy is probably because biopsy was done in only those patients whose pleural fluid cytology for malignant cell was negative.

CT or USG-guided FNAC was positive in 92.1%, with 91.67% and 92.86% sensitivity, respectively. USG-guided FNAC was done only in peripherally located lung mass attached to pleura or chest wall without any complications, while CT-guided FNAC had 18.75% complication rate. Tru-cut biopsy was done in 6 patients with peripheral mass lesions and had a yield of 100%. However, complications were more in the form of pneumothorax found in 16.67% (compared to 10.4% in CT-guided FNAC and 12.5% in pleural biopsy). Lymph node (LN) FNAC was done when feasible and had a positive yield in 82.5% of cases. However, LN excision biopsy was not done in inconclusive cases because final diagnosis was already confirmed by other methods [Table 5].

DISCUSSION

Lung cancer was initially thought to be infrequent in India.^[4] There has been a formidable rise in the mortality from bronchogenic carcinoma. In India according to annual reports of the National Cancer Registry of Indian Council (1984),^[5,6] carcinoma of lung ranks third amongst all cancer mortality (in females, it ranks next to breast cancer). As of July 1, 2002, a total of 41,000 cases of lung cancer were diagnosed for that year in India as per the ICMR data from its cancer registry.^[6] Lung cancer constituted 14.4% of all cancers in a review of 9210 consecutive autopsies by Nagrath *et al.*^[7] Sirsat reported that lung cancer formed one per cent of all cancers in Tata Cancer Hospital.^[8] In Viswanathan *et al.*,^[9] they collected information from different hospitals of the country and found that the incidence of lung cancer in hospital population was 27.4 per million in 340 and in 78.6 per million in 1959. They also found an increase in the incidence of bronchogenic carcinoma (16.1 in 340–11.9 in 391 per 1000 malignancies), following analysis

of the records of 15 teaching institution in India over a period of 10 years. According to Wig et al.,^[10] lung carcinoma was a frequent diagnosis among all types of chest diseases. The survey conducted in Uttar Pradesh in 1966 by Misra and Chakravarty showed that the incidence was 4.2 per 10,000 hospital admissions and 2.1 per cent of all malignancies.^[11]

In the present study, 142 cases of pathologically proven lung cancer were studied in relation to clinical and radiological features. Different procedures such as bronchoscopy, LN FNAC, CT or USG-guided FNAC, and tru-cut lung biopsy were done in relevant

cases. Mediastinoscopy could not be done due to nonavailability of the procedure. In all patients with pleural effusion, pleural fluid cytology was done and pleural biopsy was done in those patients in whom pleural fluid cytology was negative.

Age, gender, occupation, and symptoms

In our study, the prevalence of lung carcinoma was found to be the most common in the 6th and 7th decade (51–70 years) with a male predominance (M: F–4.68:1).

The mean age of presentation of lung cancers was lower in females than the males ($P = 0.01$). Adenocarcinoma was more common in females and SLCC in males ($P = 0.0008$). Hence, young females in the age group of 30–50 years were more prone to develop lung cancer, while the same may be said for males in the 50–70 years of age group.

Ji-Min et al.^[12] found that adenocarcinoma was the most frequent type (39.7%) in women. Dey et al.^[13] found that in women adenocarcinoma was common (40%).

Cough (82.39%) was the most common presenting symptom followed by chest pain (64.79%), dyspnea (61.97%), hemoptysis (39.44%), weight loss (35.21%), and anorexia (35.92%). Superior vena cava obstruction occurred in 15 (10.56%) of patients and hoarseness of voice in 11 (7.75%) of patients. Dysphagia was also found in 4 (2.82%) of patients which was similar to the findings of Jha et al.^[14] and Jindal et al.^[15]

Farmers were found to be the occupation group that was maximally affected in this study population. This finding is also supported by various other Indian studies.^[16]

Smoking history

The prevalence of lung carcinoma was more among smokers and furthermore in bidi smokers with increased duration of smoking. Most males were smokers and most females were nonsmokers ($P = 0.001$). Behera and Balamugesh^[16] found that the risk of lung cancer was higher in bidi smokers than cigarette smokers, which was also supported by this study.

Smokers and males were more prone to SCC and SLCC whereas adenocarcinoma was found mostly in nonsmokers and females

Table 3: Gross, histological findings and distant metastasis in lung cancer patients (n=142)

Tumor features	n (%)
FOB macroscopic findings	
Cauliflower-like growth	22 (28.95)
External compression	16 (21.05)
Growth with distortion of bronchus	16 (21.05)
Exophytic mass	14 (18.42)
Distorted carina with mucosal irregularity	6 (7.89)
Necrotic mass	2 (2.63)
Histological diagnosis	
Squamous cell carcinoma	66 (46.48)
Adenocarcinoma	35 (24.65)
Large cell carcinoma	4 (2.82)
Undifferentiated non-small cell lung carcinoma	5 (3.52)
Small cell carcinoma	32 (22.54)
Distant metastasis	
Lung	19 (13.38)
Liver	11 (7.75)
Supraclavicular lymph node	10 (7.04)
Adrenals	4 (2.82)
Ribs	3 (2.11)
Vertebrae	2 (1.41)
Bone (other than ribs/vertebrae)	2 (1.41)
Kidney	1 (0.70)
Chest wall	1 (0.70)
Pericardial effusion	6 (4.22)

FOB: Fiber-optic bronchoscopy

Table 4: Subgroup analysis and comparison of various cancer types in the population (n=142)

Subgroups	Adenocarcinoma		Squamous cell lung Ca		Small cell cancer	
	n	P, OR	n	P, OR	n	P, OR
Gender						
Male	22	0.0008, 0.21 (0.09–0.53)	56	0.137 ^a , 1.38 (0.57–3.32)	31	0.0077 ^b , 8.65 (1.12–66.67)
Female	13		10		1	
Smoking status						
Smoker	22	0.003 ^a , 0.28 (0.12–0.66)	54	0.153 ^a , 1.20 (0.52–2.76)	31	0.003 ^b , 10.08 (1.31–77.41)
Nonsmoker	13		12		1	
Site of lesion						
Central	8	2.2E-05 ^a , 0.17 (0.07–0.41)	43	0.005 ^a , 2.44 (1.23–4.81)	19	0.121 ^a , 1.36 (0.61–3.02)
Peripheral	27		23		13	
Age (years), mean±SD		58.26±12.5		60.49±11.7		59.72±12.3

^aChi-square test, ^bFisher’s exact test. OR, 95% CI in brackets. SD: Standard deviation, CI: Confidence interval, OR: Odds ratio

Table 5: Diagnostic modalities, their yield, and complications in lung cancer patients (n=142)

Diagnostic modalities	Performed in	Positive results	Yield (%)	Complications		
				Pneumothorax	Haemoptysis	Bronchospasm
Pleural fluid PAP stain	43	19	44.19	3	0	0
Pleural biopsy	24	8	33.33	3	0	0
LN FNAC	40	33	82.50	0	0	0
LN biopsy	40	37	92.50	2	2	0
FNAC of lung mass						
TTNA (unguided)	0	NA	NA	NA	NA	NA
CT-guided	48	44	91.67	2	1	0
USG-guided	28	26	92.86	1	1	0
Tru-cut biopsy	10	10	100	1	0	0
Bronchoscopy	76	72	94.74	0	8	6

PAP: Papanicolaou, FNAC: Fine-needle aspiration cytology, LN: Lymph node, TTNA: Transthoracic needle aspiration, CT: Computed tomography, USG: Ultrasonography, NA: Not applicable

similar to the studies done by Rawat *et al.*,^[17] Prasad *et al.*^[18]

Metastatic, nonmetastatic manifestations, and associated diseases

Clubbing (47.89%), pallor (50%), palpable lymph node (28.17%), and signs of pleural effusion (30.28%) were the common presentations. SVC syndrome was found in 15 cases (10.56%).

Prasad *et al.*^[18] showed that clubbing was found in 25% cases; lymphadenopathy found in 37% cases; SVC syndrome in 6.5% of cases. Pallor was found in 55% of cases.

Sridhar *et al.*^[19] found clubbing was present in 32 (29%) cases among the 111 patients with lung cancer. In that study, clubbing was more commonly found in women (40%) than in men (19%) and was more commonly found in patients with NSCLC (35%) than those with SCLC (4%).

In our study, tuberculosis was found in 15.5% of our cases and 7.04% patients also had hypertension and 7.75% patients had diabetes. Hamilton *et al.*,^[20] also found that hemoptysis, dyspnea, and abnormal spirometry were independently associated with lung cancer after exclusion of signs and symptoms reported in the final 180 days before diagnosis.

Campbell (1970)^[21] and Berroga reported co-existing pulmonary tuberculosis and lung carcinoma. Jindal and Behera^[22] found only 1.2% patients with lung cancer had clinical evidence of tuberculosis and 3.8% had radiological evidence of tuberculosis.

Radiological profile

In the present study, mass lesion was the commonest presentation (68.2%), where SCC had central lesions and adenocarcinoma had predominantly peripheral lesions.

Overall, central lesions were seen in 53.52% and peripheral lesions in 46.48% cases, whereas bilateral lesion was seen in 13.38% patients. Other prominent radiological findings were mediastinal lymphadenopathy (61.97%), pleural effusion (30.28%), collapse (25.35%), and cavity (8.45%).

Prasad *et al.*^[18] also showed that mass lesion (68.2%) was common radiological findings with pleural Effusion was found in 41.7% cases, collapse in 18.7% cases, and cavitations were found in 3.7% cases.

Fontana and Miller^[23] found unilateral hilar enlargement in all his 50 patients before onset of symptoms.

Upper lobe involvement is more common than lower lobe involvement and middle lobe is involved the least. Sharma *et al.*^[24] found that mass with or without collapse was the commonest radiological finding in lung cancer. Pleural effusion was observed in 25.1% of lung cancer cases, rib erosion in 4.8%, and lymphangitis in 2.8%, with normal chest X-rays in 0.4%. Upper zones were most affected. Adenocarcinoma mostly appeared as peripheral masses (61%), SCC as central lesions (72.2%), and SLCC predominantly central (83.6%). Isolated pleural effusion was the most common in adenocarcinoma (22%).

Sputum test positivity

In our study, sputum positivity for malignant cells by Pap's stain method was found only in 35 patients (24.65%) which is very low as compared with other studies.

However, Prasad *et al.*^[18] also showed that sputum for malignant cell was positive only in 10% cases.

Andrews *et al.*^[25] after examining 736 patients failed to prove sputum cytology as a simple screening method in determination of carcinoma of the lung. Sputum cytology is known to be 98% accurate in skilled hands. Umiker^[26] found 62.5% sputum positivity in central radiological lesion.

Yield of various diagnostic procedures

The yield for LN FNAC was 82.5% in our study as compared to 70% as reported by Jamplis *et al.*,^[27] and 20% as reported by Umiker.^[26]

Out of 43 patients with pleural effusion, 44.2% were diagnosed by cytology, while pleural biopsy was positive in 33.3%. Pleural biopsy has a lower yield than pleural fluid cytology as the costal parietal pleura is uninvolved in about 50% of

malignant pleural disease cases. Closed pleural biopsy has a diagnostic yield of 38%–47%.

Bronchoscopy was performed in 76 patients with central lesions. Bronchoscopic aspirates showed malignancy in 52.63% of cases, while bronchoscopic biopsy revealed an 86.84% diagnostic yield. Biopsy yield increases with lesion size: 10%–40% for 1–2 cm lesions, 60% for 2–3 cm, and 80% for >3 cm lesions. Tumors >2 cm had an 87% yield, and bronchoscopy's overall sensitivity for diagnosing lung cancer was 88%.

FNAC was done in 66 patients with peripheral lesions. USG-guided FNAC was performed in 28 patients with pleural or chest wall-attached lesions or for financial constraints, yielding 92.86% sensitivity. CT-guided FNAC was done in 38 peripheral lesions and 10 central lesions (total 48 cases), achieving 91.67% sensitivity and yielding malignancy in 44 cases. Tru-cut biopsy confirmed the diagnosis in 4 remaining cases. Among 28 USG-guided FNAC cases, 11 were positive for malignancy, and 2 were confirmed by Tru-cut biopsy.

Percutaneous approaches had higher yields than bronchoscopy, with FNAC providing reliable diagnosis, especially for lesions <2 cm, yielding positive results in >60% of malignant cases. CT-guided FNAC was preferred for precise lesion targeting, while Tru-cut biopsy showed 100% sensitivity. These techniques demonstrated higher diagnostic reliability compared to bronchoscopic methods, especially for smaller or peripheral lesions. These findings are similar to other studies.^[14,28,29]

Histological types of lung cancer

In this study, we came across with the following percentage of lung cancer

- Adenocarcinoma – 24.65%
- SCC – 46.48%
- SLCC – 22.53%
- Large cell carcinoma – 2.82%
- Undifferentiated NSCLC – 3.52%.

SCC was still the most common histological type in India in contrast to the Western countries, although adenocarcinoma is becoming more common.^[16]

Complications of various procedures

In this study, hemoptysis occurred in 10.51% of cases after FOB and 8.33% after CT-guided FNAC, with no massive cases, all managed conservatively. Zavala and Schoell^[30] reported 4%–8% hemorrhage in lung after transthoracic needle aspiration. Pneumothorax was noted in 16.67% of tru-cut biopsy cases, 10.4% of CT-guided FNAC, and 12.51% of pleural biopsies, consistent with reported rates (11%–32% for tru-cut and 20%–30% for FNAC). Using Abram's needle, pneumothorax was seen in 12.51% of pleural biopsies and 6.98% of pleural fluid aspiration cases. Bronchospasm occurred in 7.9% during bronchoscopy, higher due to Chronic obstructive pulmonary disease prevalence, and was managed conservatively.

Metastasis to other organs

Thirty-three (23.24%) patients had distant metastasis, most

commonly to opposite lung (13.4%), followed by liver (7.04%). Sixty-two patients (43.66%) have Stage IV disease, as these patients have pleural effusions or distant metastasis to other organs.

Malik *et al.*^[31] found that 56.75% patients were of Stage IV. They also found that liver, bone and adrenal were the most common site of distant metastasis. Mandal *et al.*^[32] found that the distant metastasis at presentation was seen in 32.5% patients with most common site as brain (23.8%), followed by a positive malignant cell in pleural effusion (23.1%), bone (18.4%), liver (15.7%), contralateral lung (9.5%), and adrenal gland (1.3%).

Strengths and limitations

Our study provides valuable insights into the demographic and clinical profile of the lung carcinoma patients in Eastern India, a region where such data is scarce. The inclusion of a variety of diagnostic modalities, including USG-guided FNAC, allows for a comprehensive evaluation of their sensitivity and safety, thereby contributing to the optimization of diagnostic strategies in resource-limited settings. However, the study has several limitations. This is a single-center study with a limited sample size and may not be fully generalizable. The lack of molecular profiling limits insights into genetic mutations, and economic constraints restricted advanced imaging and complete staging. Despite subgroup analyses, potential biases inherent to observational studies remain.

CONCLUSION

This study confirms USG-guided FNAC's diagnostic accuracy for lung lesions, aligning with prior research while highlighting its value in specific subgroups. It supports USG as a safer, cost-effective alternative to CT-guided procedures, especially in resource-limited settings. Further research should focus on optimizing techniques, refining patient selection, and integrating adjunct imaging to improve yield. Controversies persist around operator dependency and efficacy compared to emerging biopsy methods. Multicenter studies with larger cohorts and molecular data are needed to validate and expand these findings, ensuring broader applicability and improved diagnostic strategies.

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Conflicts of interest

There are no conflicts of interest.

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