

# Immunohistochemical Evaluation of TTF-1 Expression in Lung Carcinomas: A Cross-sectional Study from a Tertiary Care Centre, Hyderabad, Telangana, India

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## ABSTRACT

**Introduction:** Lung cancer has been the most common cancer in the world for several decades. As a result of the identification of so many new therapeutic targets, the tissue samples are no longer managed for diagnosis alone, but also for immunohistochemical (IHC) staining and molecular testing. Thyroid Transcription Factor-1 (TTF-1) has been found in malignant tumours highly selectively in lung and thyroid cancers.

**Aim:** To evaluate the expression of TTF-1 in guided biopsies of primary lung carcinomas and assess its role in the histopathological diagnosis of various lung cancer subtypes.

**Materials and Methods:** This was an observational, cross-sectional, descriptive study conducted in the Department of Pathology, CMR Institute of Medical Sciences, Hyderabad, Telangana, India, over a period of two years and two months. A total of 50 {ultrasound-, Computed Tomography (CT)-, or bronchoscopy-guided} diagnosed as primary epithelial lung carcinomas were included. Autolysed, inadequate, benign, metastatic, and treated cases were excluded. All specimens were formalin-fixed, paraffin-embedded, and stained with Haematoxylin and Eosin (H&E). Confirmed malignant epithelial tumours were subjected to IHC for TTF-1. Data on age, gender, histological type of tumour, reaction with TTF-1 were analysed

using descriptive statistics and expressed as frequencies and percentages.

**Results:** A total of 50 lung carcinoma cases were studied. The most common histological type was adenocarcinoma 15 (30%), followed by small cell carcinoma 10 (20%), Squamous Cell Carcinoma (SCC) 9 (18%), Non Small Cell Lung Carcinoma (NSCLC) favour adenocarcinoma 7 (14%), NSCLC favour SCC 3 (6%), NSCLC- Not Otherwise Specified (NOS) 3 (6%), adenosquamous carcinoma 2 (4%), and carcinoid 1 (2%). Males constituted 36 (72%) cases and females 14 (28%). The highest incidence occurred in the 61-70 year age group, 20 (40%), followed by the 51-60 years age group, 14 (28%). TTF-1 positivity was observed in 36 (72%) cases overall. All adenocarcinomas 15 (100%), all NSCLC favour adenocarcinoma 7 (100%), both adenosquamous carcinomas 2 (100%), the carcinoid tumour 1 (100%), and 8/10 (80%) small cell carcinomas showed positivity. TTF-1 was negative in 8/9 (89%) SCCs and all 3 (100%) NSCLC favour SCC cases. Among NSCLC-NOS, 2/3 (67%) cases were positive.

**Conclusion:** One of the great advances in the past decade in lung cancer diagnosis and treatment was the concept of personalised medicine, where therapeutic decisions are based on the specific histologic and genetic characteristics of the patient's tumour.

**Keywords:** Adenocarcinoma lung, Immunohistochemistry, Lung cancer, Small cell carcinoma lung

## INTRODUCTION

Lung carcinoma is the most frequently diagnosed major cancer in the worldwide, especially in males and the most common cause of cancer mortality world [1]. The current male: female ratio is 1.5:1. More than 90% of the patients are over 40 years of age at the time of diagnosis, but cases have also been reported in young adults and adolescents [2].

The importance of differentiating between lung tumour subtypes cannot be overemphasised. For example, the treatment modalities for SCC and adenocarcinoma of the lung are very different. Some cases lack typical morphology and did not provide definitive histomorphological clues for diagnosis. This is where immunohistochemistry comes into the picture; it can give a great deal of clarity as to the nature of the lesion.

TTF-1 expression is employed widely as a marker of lung and thyroid tumours. Among all IHC markers, TTF-1 has emerged as one of the most sensitive and specific markers for pulmonary adenocarcinomas and small cell carcinomas. TTF-1 is a nuclear homeodomain-containing transcription factor involved in the embryogenesis and differentiation of the thyroid, lung, and diencephalon. Its expression is observed in approximately 70-80%

of pulmonary adenocarcinomas, 85-90% of small cell carcinomas, and is typically absent in SCCs and most extrapulmonary tumours. Because metastatic adenocarcinomas to the lung do not commonly express TTF-1, it serves as an invaluable tool in distinguishing primary lung tumours from metastatic lesions [3].

Beyond its diagnostic utility, TTF-1 expression has also been associated with prognostic significance. Several studies suggest that TTF-1-positive adenocarcinomas may have a better clinical outcome and may show distinct molecular profiles, including a higher frequency of EGFR mutations. Thus, accurate assessment of TTF-1 expression is not only essential for diagnosis but may also have implications for treatment planning in the era of personalised medicine.

The TTF-1 was identified as a sensitive marker for pulmonary and thyroid adenocarcinomas. TTF-1 also stains small cell carcinomas but is typically negative in metastatic lesions, nor does it stain SCCs [4].

There is limited regional data from South India, particularly Hyderabad, on the distribution of lung carcinoma subtypes and their TTF-1 expression patterns. With the increasing reliance on small biopsies for diagnosis and the rising incidence of adenocarcinoma

in India, assessing TTF-1 expression locally is important for accurate subtyping and improved diagnostic precision.

The present study offers updated regional evidence from a tertiary care centre in Hyderabad, evaluating TTF-1 expression across a broad spectrum of primary lung carcinomas using guided biopsies. Unlike earlier Indian studies that focused mainly on adenocarcinoma, it includes all major histological subtypes- NSCLC-NOS, adenosquamous carcinoma, and carcinoid tumours- providing a more comprehensive understanding of local disease patterns and enhancing diagnostic approaches in this region. Hence, the study aimed to evaluate the expression of TTF-1 in guided biopsies of primary lung carcinomas and assess its role in the histopathological diagnosis of various lung cancer subtypes. And the objectives were to perform IHC staining for TTF-1 on confirmed epithelial malignancies of the lung; to assess TTF-1 expression across different histological types of lung carcinomas and to analyse the distribution of lung carcinoma cases with respect to age, gender and tumour subtype.

## MATERIALS AND METHODS

This was an observational, cross-sectional, descriptive study conducted in the Department of Pathology at CMR Institute of Medical Sciences, Hyderabad, Telangana, India, over two years from June 2023 to July 2025. Institutional Ethics Committee approval (Ref No.: IEC/CMRIMS/2023/SI.NO.08) was obtained.

**Inclusion and Exclusion criteria:** All primary epithelial lung malignancies were included in the study, while autolysed and inadequate specimens, benign lesions, metastatic tumours, biopsies not conclusive for epithelial malignancy, patients already on treatment, and lobectomy specimens were excluded.

A total of 50 ultrasound-guided, computed tomography- (CT) guided, or bronchoscopy-guided biopsies diagnosed as primary epithelial lung carcinomas were included. The sample size was not derived using a statistical formula; instead, it comprised all eligible cases received during the study period, following a convenience sampling approach based on the availability of confirmed lung carcinoma biopsies.

### Study Procedure

The samples were fixed in 10% neutral buffered formalin, processed routinely, and 3-5 µm sections were stained with H&E for preliminary histopathological evaluation. All cases confirmed as epithelial malignancies were subsequently subjected to IHC staining using the TTF-1 marker to assess nuclear positivity and staining intensity.

The IHC staining for TTF-1 was performed on 3-5 µm thick sections prepared from formalin-fixed, paraffin-embedded lung biopsy tissue blocks. The sections were mounted on poly-L-lysine-coated slides and incubated overnight at 37°C. After deparaffinisation in xylene and rehydration through graded alcohols, antigen retrieval was carried out using Heat-Induced Epitope Retrieval (HIER) in citrate buffer (pH 6.0) for 20 minutes, followed by cooling at room temperature. The slides were then incubated with the primary antibody against TTF-1 using a rabbit monoclonal anti-TTF-1 antibody (clone HBPP/EP229; PathnSitu Biotechnologies Pvt. Ltd., for 30-60 minutes at room temperature. After washing with Phosphate-Buffered Saline (PBS), sections were incubated with a secondary antibody.

The TTF-1 staining was interpreted based on nuclear positivity, as cytoplasmic staining is considered non specific. The scoring was carried out using semi-quantitative methods described by Pelosi G et al., and Stenhouse G et al., [5,6].

Proportion score (PS) and intensity score (IS) were recorded, and a combined score (PS + IS) >2 was considered positive.

**Proportion Score (PS)- % of tumour nuclei stained:**

0 = 0% cells, 1 = <10%, 2= 10-50%, 3 = >50%

**Intensity Score (IS) – Strength of nuclear stain:**

0 = Negative, 1 = Weak, 2 = Moderate, 3 = Strong

Data regarding histological subtype, TTF-1 expression, age and gender distribution were recorded.

## STATISTICAL ANALYSIS

The data generated were input into the Statistical Package for Social Sciences (SPSS) software for Windows version 23.0 for analysis. Statistical analysis included descriptive methods, and results were expressed as frequencies and percentages.

## RESULTS

A total of 50 cases of primary lung carcinomas were included in the study. The distribution of cases following diagnosis on H&E is shown in [Table/Fig-1]. Based on H&E morphology, adenocarcinoma emerged as the most common subtype, accounting for 15 cases (30%). This was followed by Small Cell Carcinoma (SCC) (10 cases, 20%), SCC (9 cases, 18%), NSCLC favour adenocarcinoma (7 cases, 14%), NSCLC favour SCC (3 cases, 6%), NSCLC-NOS (3 cases, 6%), adenosquamous carcinoma (2 cases, 4%), and carcinoid tumour (1 case, 2%).

Cases	n (%)
Small cell carcinoma	10 (20%)
Squamous Cell Carcinoma (SCC)	09 (18%)
Adenocarcinoma	15 (30%)
NSCLC favour SCC	03 (06%)
NSCLC favour Adenocarcinoma	07 (14%)
NSCLC NOS	03 (06%)
Adenosquamous	02 (04%)
Carcinoid	01 (02%)
Total	50 (100%)

**[Table/Fig-1]:** Distribution of cases following preliminary diagnosis on H&E. Abbreviations: NSCLC: Non small cell lung carcinoma; NOS: Not otherwise specified; H&E: Haematoxylin and eosin.

Age distribution among different histological types of carcinomas is shown in [Table/Fig-2]. The patients ranged from 30 to over 70 years of age, with a mean age of 61.44 years. The highest number of cases occurred in the 61-70 year age group (20 cases, 40%), followed by the 51-60 year group (14 cases, 28%). Only 2 cases (4%) were seen in individuals below 40 years, indicating that lung carcinoma predominantly affects older adults.

Age (in years)	SCLC		SCC		ADC		NSCLC FAV SCC		NSCLC FAV ADC		NSCLC NOS		ADC SCC		CN	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
	8	2	8	1	8	7	2	1	7	0	2	1	1	1	0	1
30-40	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
41-50	1	0	2	0	0	0	0	0	0	0	1	1	1	0	0	0
51-60	2	2	6	0	3	0	0	3	0	3	0	0	1	0	0	0
61-70	6	3	5	3	2	1	0	2	1	0	1	0	0	0	0	0
>70	0	4	1	0	2	1	0	2	1	0	0	0	0	0	0	0
Total	10	09	15	03	07	07	03	07	03	02	03	02	01	01	01	01

**[Table/Fig-2]:** Age distribution among different histological types of carcinomas. Abbreviations: SCLC: Small cell lung cancer; ADC: Adenocarcinoma; SCC: Squamous cell carcinoma; NSCLC FAV SCC: Non small cell lung carcinoma favour squamous cell carcinoma; NSCLC FAV ADC: Non small cell lung carcinoma favour adenocarcinoma; NSCLC NOS: Non small cell lung carcinoma, not otherwise specified; ADC SCC: Adenosquamous carcinoma; CN: Carcinoid.

In terms of gender distribution, males constituted 36 cases (72%), whereas females accounted for 14 cases (28%), yielding a male-to-female ratio of 2.6:1. This male predominance was observed across most histological subtypes.

Results of TTF-1 staining among different histological types of lung carcinomas are shown in [Table/Fig-3]. It showed that 36 out of 50 cases (72%) were positive and 14 cases (28%) were negative. All adenocarcinomas (15/15, 100%) and all NSCLC favour adenocarcinoma cases (7/7, 100%) showed nuclear positivity for TTF-1. Among adenosquamous carcinomas, both cases (100%) were positive. The single carcinoid tumour included in the study also demonstrated TTF-1 positivity (1/1, 100%).

Cases	TTF-1 positive	TTF-1 negative	Total
Small cell carcinoma	08	02	10
Squamous Cell Carcinoma (SCC)	01	08	09
Adenocarcinoma	15	00	15
NSCLC favour SCC	00	03	03
NSCLC favour adenocarcinoma	07	00	07
NSCLC NOS	02	01	03
Adenosquamous	02	00	02
Carcinoid	01	00	01
Total	36	14	50

**[Table/Fig-3]:** Results of TTF-1 staining among different histological types of lung carcinomas.

Small cell carcinoma showed a high rate of TTF-1 expression, with 8 out of 10 cases (80%) staining positive. In contrast, TTF-1 expression was uncommon in SCC, with 8 out of 9 cases (88.9%) being negative and only 1 case (11.1%) demonstrating positivity. Similarly, all 3 cases of NSCLC favour SCC were TTF-1 negative (100%). Among the NSCLC-NOS group, 2 out of 3 cases (66.7%) showed positivity, assisting in further subtyping of these otherwise undifferentiated tumours.

The intensity of nuclear staining among different histological types of lung carcinomas positive for TTF-1 is shown in [Table/Fig-4]. Strong nuclear staining (3+) predominated in adenocarcinoma (13/15, 86.7%) and small cell carcinoma (5/8, 62.5%). NSCLC favouring adenocarcinoma and NSCLC NOS showed mainly moderate (2+) staining (5/6, 83.3%, 2/3, 66.6%). Weak positivity (1+) was seen in adenosquamous carcinoma, while one carcinoid showed moderate staining. SCC and NSCLC favouring SCC showed no TTF-1 expression.

Histological type	1+	2+	3+	Total
Small Cell Carcinoma (SMCC)	2	1	5	8
Squamous Cell Carcinoma (SCC)	0	0	0	0
Adenocarcinoma (ADC)	0	2	13	15
NSCLC - favouring SCC	0	0	0	0
NSCLC - favouring ADC	0	5	1	6
Adenosquamous carcinoma	2	0	0	2
Carcinoid	0	1	0	1
NSCLC - NOS	0	2	0	2

**[Table/Fig-4]:** Illustrating the intensity of nuclear staining among different histological types of lung carcinomas positive for TTF-1.

## DISCUSSION

Over the last century, lung cancer progressed from a rare disease to the leading cancer killer worldwide

and in some parts of the world, also of women (North America, East Asia, Northern Europe, Australia and New Zealand) [7]. The increase in the absolute number of lung cancer deaths in more developed countries is caused mostly by population aging and in less developed countries, predominantly by the evolving tobacco epidemic [7]. In the present study, the highest frequency of lung cancer occurred in the age group of 61-70 with 20 cases (40% of the cases), followed by the age group 51-60 with 14 cases (28% of the cases). Males accounted for 36 (72%) of the cases and females accounted for the remaining 14 (28%) in the present study. The lung

cancer distribution worldwide is 68% males and 32% in females, but in developing nations such as India, the percentage of males is higher than that of females [8].

In the present study, all NSCLC cases (excluding small cell carcinoma cases and the carcinoid case) account for 39 out of the 50 cases, of which adenocarcinoma is the most common histological type encountered. That is a percentage of 78%, which is in accordance with the worldwide average of 80% of all lung carcinoma cases being NSCLC cases [9].

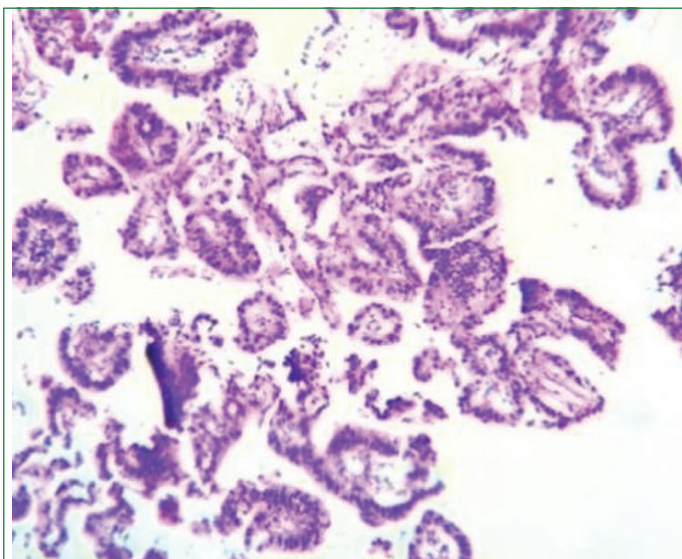
Epidemiological and pathological comparison between the current study and various Indian lung cancer series is shown in [Table/Fig-5] [10-15].

Author names, (place, year)	Total no. of cases	Mean age (in years)	M:F	SCLC (%)	SCC (%)	ADC (%)
Dey A et al., [10] (Kolkata, 2012)	607	57.9	4.1:1	16.5	35.1	30.8
Krishnamurthy A et al., [11] (Tamil Nadu, 2012)	258	56	3.5:1	13.2	15.8	42.6
Noronha V et al., [12] (Mumbai, 2012)	489	56	3.5:1	8	26.2	43.8
Mandal SK et al., [13] (Manipur, 2013)	466	58.5	1.1:1	14.8	49.1	30.8
Malik PS et al., [14] (New Delhi, 2013)	434	55	4.6:1	14.7	32.1	37.1
Mohan A et al., [15] (Delhi, 2016)	397	57.8	7.4:1	14.6	25.1	24.5
Present study	50	61.44	2.6:1	20	18	30

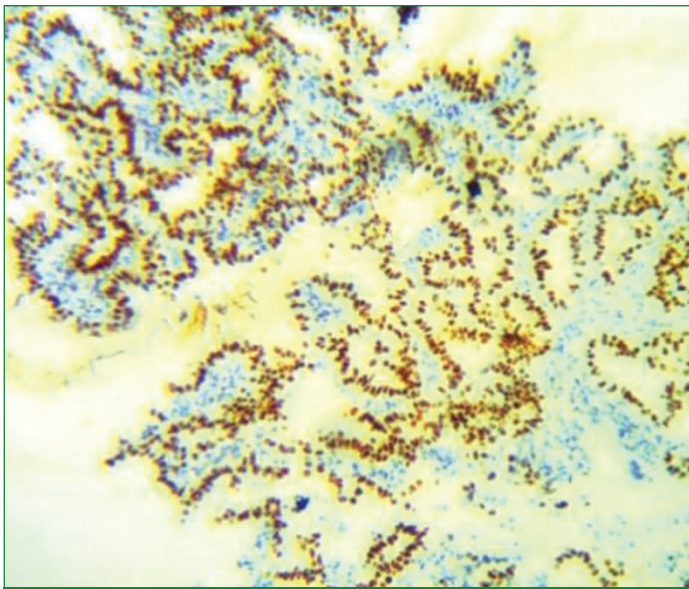
**[Table/Fig-5]:** Epidemiological and pathological comparison between current study and various Indian lung cancer series [10-15].

The TTF-1 was a tissue-specific homeodomain-containing transcription factor that plays an important role in the early differentiation and morphogenesis of the developing lung and thyroid gland. The expression of TTF-1 has also been found in malignant tumours highly selectively in lung and thyroid cancers. In lung cancer high frequency of TTF-1 expression has been observed in small cell carcinomas (85-90%) and in adenocarcinoma (75-80%), whereas squamous cell cancers and large cell carcinomas showed no expression, or at very low frequency [4]. Different histological types of lung carcinomas and their corresponding TTF-1 staining in the present study have been illustrated in [Table/Fig-6 (a-l)].

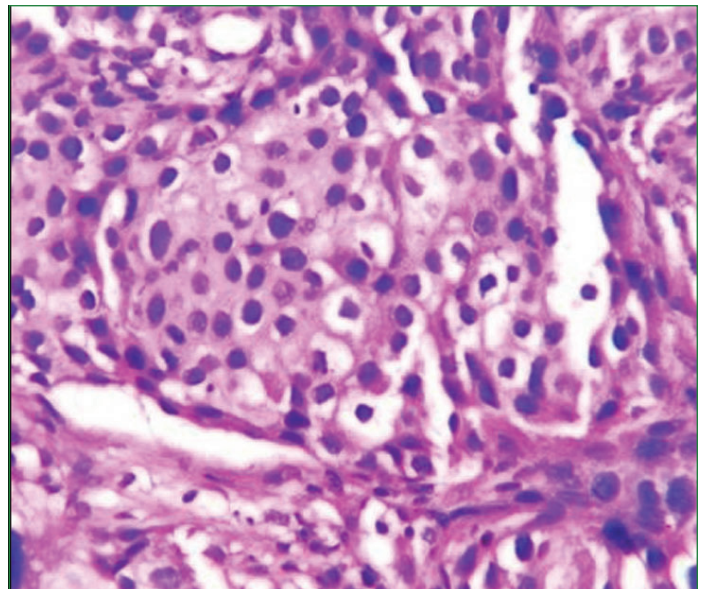
TTF-1 is a diagnostic IHC marker for primary pulmonary neoplasms. In a study by Pelosi G et al., six out of the 119 pulmonary SCC



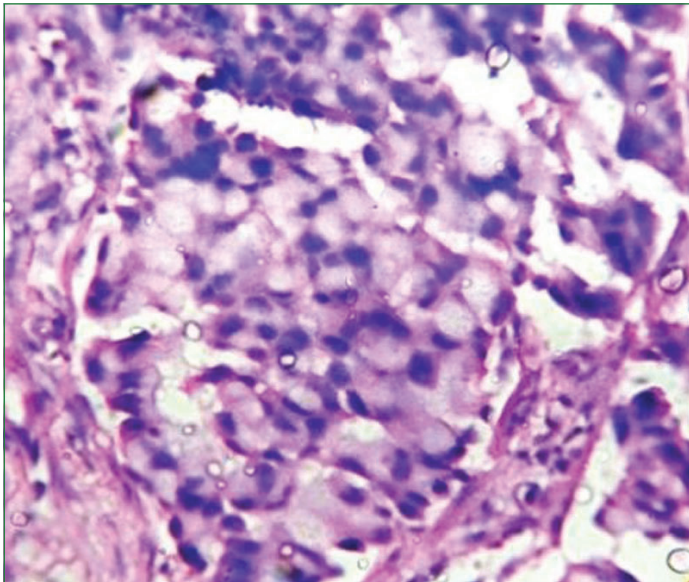
**[Table/Fig-6a]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph showing Adenocarcinoma with tumour cells arranged in papillary pattern (H&E, X100).



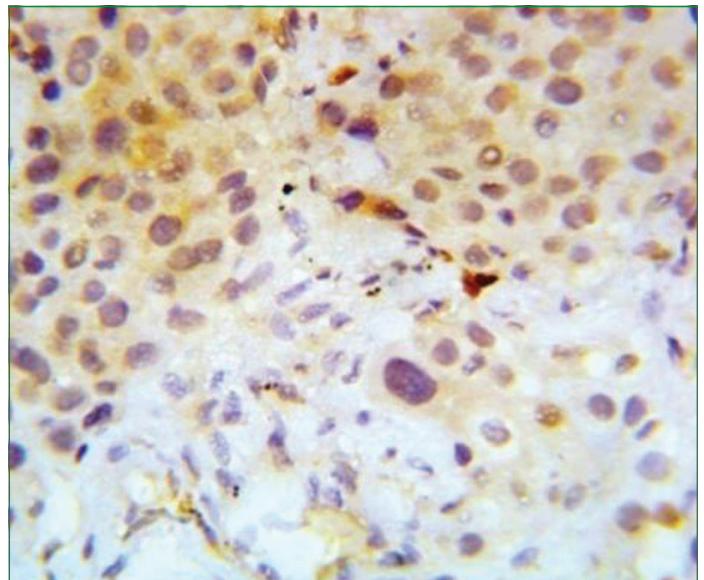
**[Table/Fig-6b]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of Papillary Adenocarcinoma showing positive staining with TTF-1 (IHC, X100).



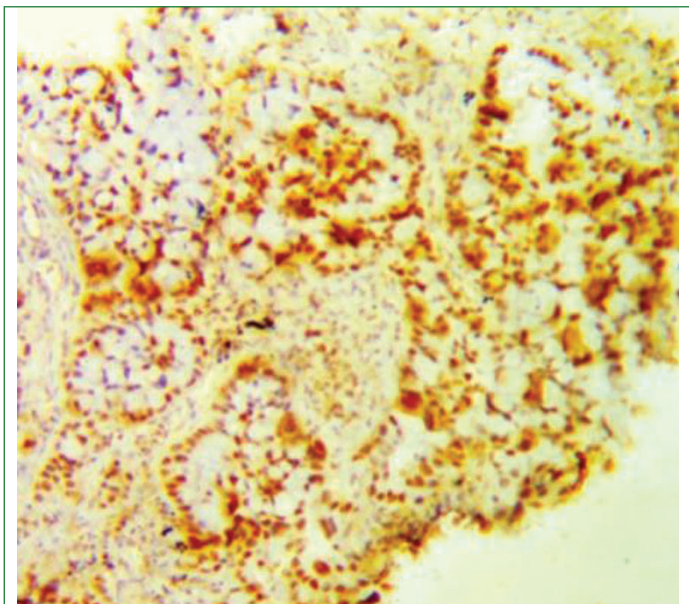
**[Table/Fig-6e]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of Squamous Cell Carcinoma (SCC) with polygonal shaped tumour cells having abundant eosinophilic cytoplasm (H&E, X400).



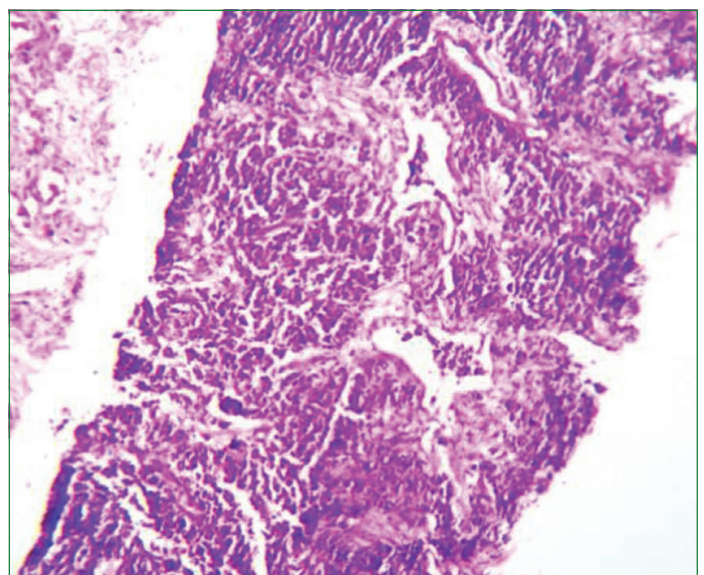
**[Table/Fig-6c]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of an Adenocarcinoma with evidence of mucin production. (H&E, X400).



**[Table/Fig-6f]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of Squamous Cell Carcinoma (SCC) showing negative staining of nucleus with TTF-1 (IHC, X400).



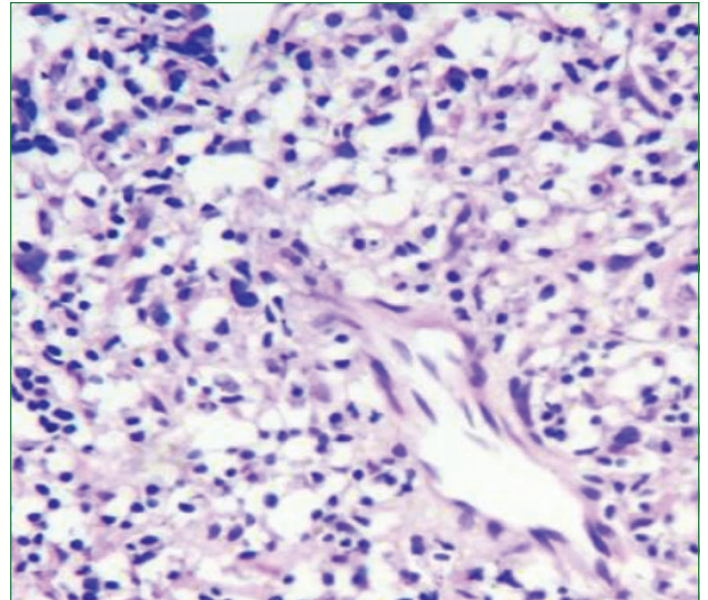
**[Table/Fig-6d]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of Mucinous Adenocarcinoma showing positive staining with TTF-1 (IHC, X100).



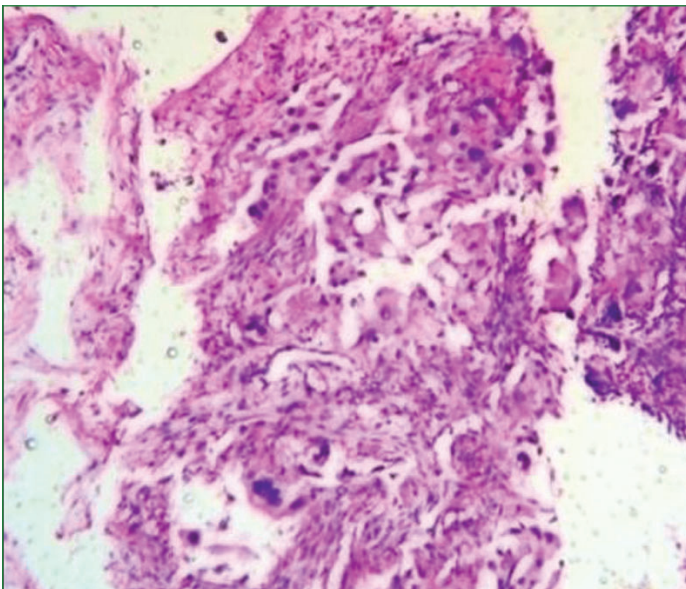
**[Table/Fig-6g]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of Small cell carcinoma with tumour cells arranged in sheets (H&E, X100).



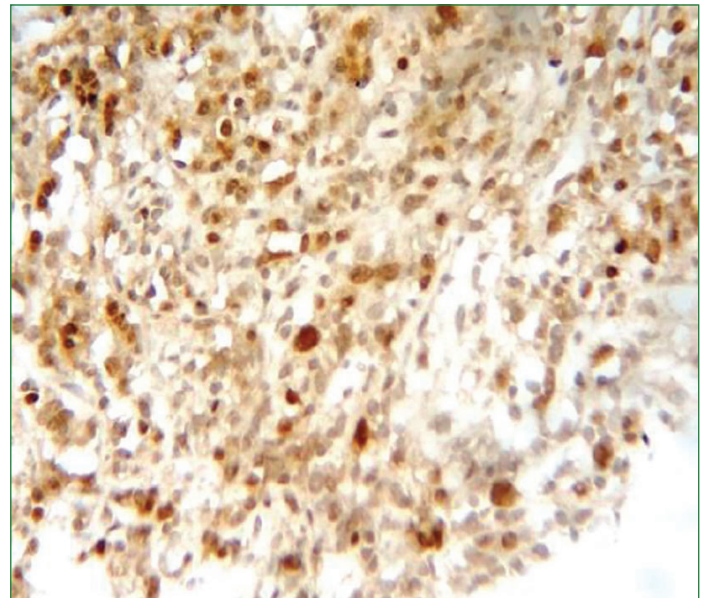
**[Table/Fig-6h]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of Small cell carcinoma showing positive staining with TTF-1 (IHC X 100).



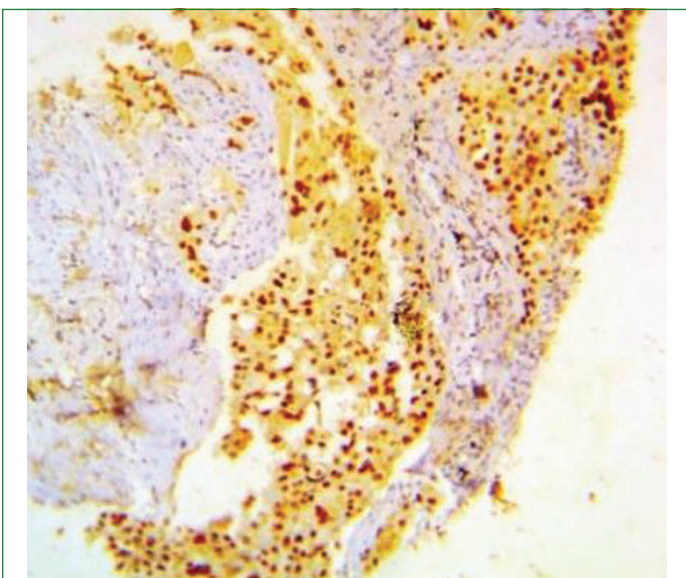
**[Table/Fig-6k]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of NSCLC NOS showing neither adenocarcinoma or Squamous Cell Carcinoma (SCC) differentiation (H&E, X 400).



**[Table/Fig-6i]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of NSCLC favours Adenocarcinoma (H&E X 100).



**[Table/Fig-6j]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of NSCLC NOS showing positive staining of nucleus with TTF-1 (IHC X 400).



**[Table/Fig-6l]:** Showing different lung carcinomas and their corresponding TTF-1 staining. Microphotograph of NSCLC favours Adenocarcinoma showing positive staining with TTF-1 (IHC, X100).

cases (5%) were positive for TTF-1 [5]. In the present study, all the 15 cases of primary pulmonary adenocarcinomas studied are TTF-1 positive, which is in accordance with Fabbro D et al.,'s study, in which all 11 cases (100%) of metastatic lesions from a lung primary stained positive for TTF-1 [16].

Whereas in other studies, like Saad RS et al., 100 cases of pulmonary adenocarcinoma were studied, including 50 cases of Conventional Adenocarcinoma (CA) and 50 cases of Bronchioloalveolar Adenocarcinoma (BAC) (32 non mucinous type and 18 mucinous type) [17]. Representative sections were immunostained for TTF-1. In the CA group, strong or moderate TTF-1 expression was seen in 30 of 50 (60%) patients, weak staining (7 cases; 14%) and negative staining (13 cases; 26%). In the BAC group, TTF-1 was strongly expressed in 34 of 50 cases (68%) and was negative in 16 of 50 cases (32%), including 14 mucinous BACs.

In Stenhouse G et al., study 128 primary lung adenocarcinomas, 106 primary non pulmonary adenocarcinomas, and 37 pulmonary non adenocarcinoma tumours were studied [6]. None of the 106 non pulmonary adenocarcinomas expressed TTF-1 and only three of the 37 non adenocarcinoma lung cancers, all neuroendocrine carcinomas, were positive. of the pulmonary adenocarcinomas,

75% were strongly positive for TTF-1. Mucinous (two of six) and poorly differentiated adenocarcinomas (four of 10) were less likely to stain. Of the peripheral adenocarcinomas, 33 of 37 were positive, whereas only seven of 14 of those of bronchial origin stained strongly. Atypical adenomatous hyperplasia strongly expressed TTF-1.

Amin MB et al., studied 35 cases of primary lung adenocarcinoma with a micropapillary component. TTF-1 immunostaining of tumour nuclei was seen in 12 of the 15 cases (80%) [18]. Immunostaining was seen in areas both with and without micropapillary differentiation.

Moldvay J et al., examined the expression of TTF-1 in 100 solitary pulmonary nodules. They included 50 stage I peripheral primary bronchial adenocarcinomas (30 men, 20 women, mean age: 60 years) and 50 metastatic pulmonary adenocarcinomas. In primary bronchial adenocarcinomas, they found immunopositivity in 46/50 cases, among them 30 cases showed strong nuclear immunostaining. In four primary adenocarcinoma cases, the observed immunopositivity was localised to the cytoplasm [4]. Whereas in the present study, 14/15 cases of primary lung adenocarcinomas showed strong nuclear immunostaining and one case showed moderate intensity of nuclear staining.

According to Fabbro D et al., TTF-1 was not expressed in neoplasms such as carcinoids but in the present study one case of carcinoid studied showed positivity for TTF-1 with grade 2 intensity and proportion score [18]. TTF-1 expression in Neuroendocrine Tumours (NETs) has not been studied as widely as that in non NETs, with the exception of small cell carcinomas, in which TTF-1 is highly sensitive but not specific for a primary lung tumour. The reported incidence of TTF-1 expression in pulmonary carcinoids has also been highly variable in the literature.

Based on published studies to date, anti-TTF-1 is a very useful reagent in distinguishing pulmonary adenocarcinoma from other primary carcinomas, identifying differentiated thyroid neoplasms, distinguishing mesothelioma from pulmonary adenocarcinoma, and distinguishing small cell carcinoma of the lung from Merkel cell carcinoma. It may also be useful in distinguishing NET of the lung from well-differentiated NET from other sites, such as the intestine [19].

In the present study, there were 22 cases of adenocarcinoma diagnosed on H&E. If we add the two groups, i.e., adenocarcinoma and NSCLC, then adenocarcinoma. All 22 were stained positively by TTF-1, which was a result of 100% positive stain for adenocarcinoma. Out of the three cases diagnosed as NSCLC NOS, two of them were reliably diagnosed as NSCLC favour adenocarcinoma, taking the tally of adenocarcinoma cases to 24, which was done based on the 2015 WHO classification of tumours of the lung and 2011 {International Association for the Study of Lung Cancer (IASLC), American Thoracic Society(ATS) and European Respiratory Society (ERS) (IASLC/ATS/ERS)} classification for lung biopsy specimens [20,21]. There were 10 cases of Small Cell Lung Cancer (SCLC), diagnosed in this study of 50 cases, which amounted to 20% of the cases. 8 out of the 10 cases were positive for TTF-1 and 2 were negative (80% positive).

In the study, conducted by Hecht JL et al., out of the four cases of SCLC, they had only one was positive for TTF-1 [22]. Other studies, such as those done by Cheuk W et al., and Yatabe Y et al., showed 83% and 92% positivity in 52 and 12 cases of small cell lung carcinomas studied, respectively [23,24].

The present study had a total of 12 cases diagnosed as SCC on H&E. If we were to consider both SCC and NSCLC favour SCC as one group, out of the 12 cases one case diagnosed as NSCLC, favour SCC was positive for TTF-1. Some of the other studies had similar results, for e.g., the study done by Hecht JL et al., gave the result that one out of their seven cases (14%) of their SCC cases were positive for TTF-1 [22]. A larger study of 43 cases by Tan D et

al., found that 9 cases out of the 43 cases (21%) diagnosed as SCC were positive for TTF-1 [25].

### Limitation(s)

A drawback in the present study is that other IHC markers like p40 or p63 for confirmation of squamous differentiation and for correct diagnosis of TTF-1 negative NSCLC NOS cases were not used.

### CONCLUSION(S)

Lung cancer remains a major cause of morbidity and mortality worldwide, accounting for more deaths than any other cancer. The clinicopathological profile of lung cancer has shown marked regional and geographical variation. This has given a new importance for pathologists to classify NSCLC further into specific pathologic subtypes (e.g., adenocarcinoma versus SCC) as this determines eligibility for certain types of molecular testing and therapeutic strategies. TTF-1 should be the first choice as a component of an antibody panel aiming to prove the histological type of lung carcinoma.

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