Histocytopathological Types of Lung Carcinoma and Its Correlation with Various Pathological Parameters

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ABSTRACT

Introduction: Lung cancer in Nepal is the most common cancer in men (18% of new cases diagnosed) and the third most common cancer in women (7.7%). Nine percent of total annual deaths are due to cancer. Carcinoma of lung is classified histologically into small-cell lung carcinoma (SCLC) and non-small-cell lung carcinoma (NSCLC). The objective of this study is to find histopathological types of lung carcinoma in adult Nepalese population and to find correlation of lung carcinoma with age, sex, smoking-behavior and SCLC versus NSCLC.

Methods: Age, sex and various histological parameters were noted in cases of lung specimens at Dhulikhel, Kathmandu University Hospital. Other clinical parameters were traced back. The reports were analyzed with cytology, Biopsy and Immunohistochemistry (IHC) in four cases.

Results: Among 122 cases, 74 were the specimens of biopsy and 48 of FNAC. Fifty-four of them were positive for malignancy with specific subcategorization of tumors. Among them 30 (55.5 %) were Squamous cell carcinoma (SCC), 8 (14.8%) were Adenocarcinoma, one (1.8%) adenosquamous carcinoma, nine (16.6%) NSCLC Not Otherwise Specified (NOS) and six (11.1%) were Small cell carcinoma. Mean age of the patients was 63.1 years, male to female ratio 1.5:1 and 79.6% of the patients having lung cancer were smokers.

Conclusion: SCC was found to be the most common subtype, instead of globally reported incidence of adenocarcinoma. Most cases are above 50 years old and have history of smoking.

Keywords: Adenocarcinoma; Immunohistochemistry; Lung carcinoma; Smoking; Small cell carcinoma; Squamous cell carcinoma

INTRODUCTION

Cancer a growing public health problem is expected to rise every year. According to GLOBOCAN, there were 19.3 million new cases and 10 million cancer deaths globally.[1] Lung cancer, accounts for an estimated 2 million diagnoses and 1.8 million deaths. It is the leading cause of cancer death among men and the second leading cause of cancer death among women worldwide.[2] In Nepal more than twenty-two thousand (22,008) new cases and fourteen thousand (14,704) deaths were estimated in 2022.[1] Lung cancer in Nepal is the most common cancer in men (18% of new cases diagnosed) and third most common cancer in women (7.7%).[3] The average age of diagnosis is 70 years old.[4]

Carcinoma of lung is classified histologically into small-cell lung carcinoma (SCLC) and non-small-cell lung carcinoma (NSCLC).[5] The predominant type is NSCLC, which accounts for 85% of all cases. Histological subtypes of NSCLC are squamous cell carcinoma (SCC), large cell carcinoma and adenocarcinoma.[6]

According to various studies, Adenocarcinoma is the most frequent subtype among patients with early onset lung carcinoma.[7] SCC is the most frequent type in older men.[8] Some studies suggest that the reduction of tar in smokes and the introduction of filtered cigarettes could have

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favored the development of adenocarcinoma at the expense of SCC.[9]

Based on Tumor Node, Metastasis (TNM) staging, 5-year survival estimates in NSCLC range from 73 % in stage IA disease to 13 % in stage IV disease. TNM stage followed by tumor histological grade, and patient age, sex remains the most important prognostic factor in predicting recurrence rates and survival.[10] Incidence of lung carcinoma gradually increase with age and the cases are more in males and people who smoke.[4] However, very few studies in Nepal have shown the relation of various histopathological subtypes of lung carcinomas with the age and sex of the patient. In this study, we have evaluated the histopathological types of lung carcinoma in Nepalese adult population, and have correlated with age, sex, smoking-behavior and small cell versus non-small cell types of carcinomas.

METHODS

It is retrospective, observational study of all the histopathological cases of lung biopsy and fine needle aspiration cytology (FNAC) cases available during the study period (1st January 2017 to 30th December 2023). Dhulikhel Hospital, Kathmandu University Hospital one of the tertiary health care centers of Nepal. The site of aspiration and biopsy includes lung, bronchus and pleura. Age, sex and various histological parameters like types of carcinomas were observed. Other clinical parameters like smoking history were traced back. Clinical and radiological suspicious cases were put in biopsy table. All cases of suspected lung carcinoma cases whose biopsy and cytological samples were sent to department of pathology is included. Inadequate samples and cases with incomplete diagnosis were excluded from the study. The cases in which biopsy could not be done were examined with Fine needle aspiration cytology (FNAC). We have performed per-cutaneous transthoracic CT (Computerized Tomography), USG (Ultrasonography) and endoscopic guided FNAC. Those FNAC samples were stained with Giemsa and Papanicolaou stain. Biopsy were processed and stained with Hematoxylin and eosin (H&E) stain. At least 3 pathologists were consulted for final diagnosis. The criteria for diagnosis were based on architecture of cells, cell types and Immunohistochemistry (IHC). The cells with features of neoplasm like pleomorphism, hyperchromatic nuclei, mitosis, necrosis, nuclear molding (for SCLC), acinar/lipidic pattern (for adenocarcinoma) were analyzed for diagnosis. Confusing cases were sent for IHC. WHO classification of tumors was used for classification of tumors.[11]

IHC for final diagnosis were performed in 4 cases. Because of the financial constraints we were not able to perform IHC in all cases. Microsoft Excel sheet 2007 was used to analyze the findings of cytology, biopsy and IHC.

RESULTS

Total number of cases analyzed was 122. Among 122 cases, 74 were the specimens of biopsy and 48 were of FNAC specimens. Five cases were performed both FNAC and Biopsy.

Table 1: Incidence of various carcinomas

NSCLC (Total 48)	SCC (Fig 1)	30	
	Adenocarcinoma (Fig 2)	8	
	Adenosquamous carcinoma (Fig 3)	1	54
	NSCC - NOS	9	
Small cell carcinoma(SCLC) (Fig 4)		6	
Poorly differentiated carcinoma, undifferentiated carcinoma (Fig 5)			2
Metastasis (breast or dermal origin)			1
Positive for malignancy			13
Total			70

Among 70 positive cases of total 122 examined, 48 were diagnosed as NSCLC out of which 30 were SCC (Fig 1), 8 were adenocarcinoma (Fig 2), 9 were not specified and were just diagnosed as NSCLC not otherwise specified. Six cases were SCLC (Fig 4).

Since, we could not further classify the type of tumor 13 cases were just diagnosed as positive for malignancy. (Table 1)

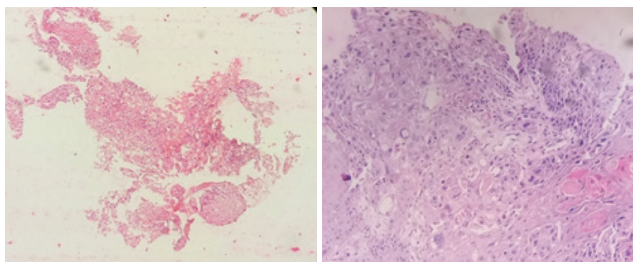**Fig 1: 100x and 400x H & E section slides Squamous cell carcinoma**

Fig 2: 100x and 400x H & E section slides, Adenocarcinoma of lung
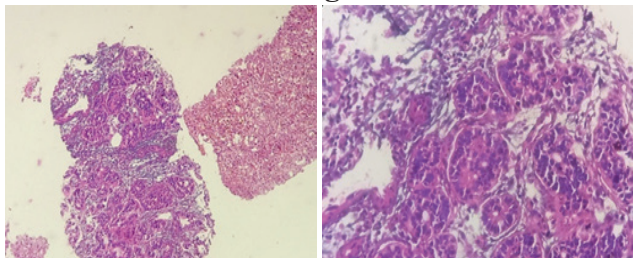

Fig 3: 100x and 400x H & E section slides, Adenosquamous carcinoma
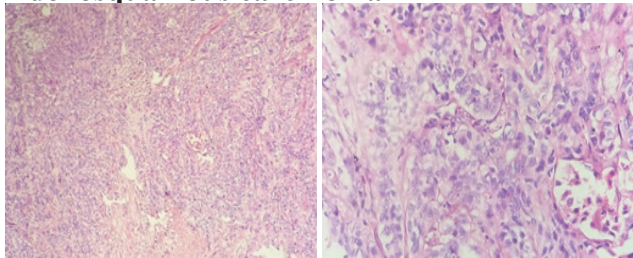

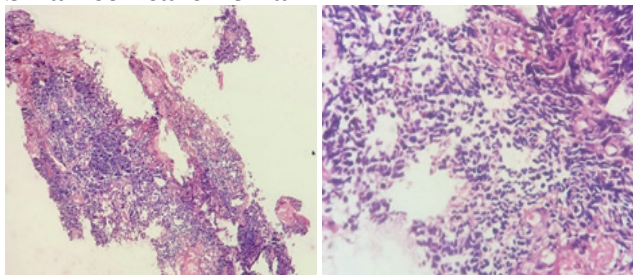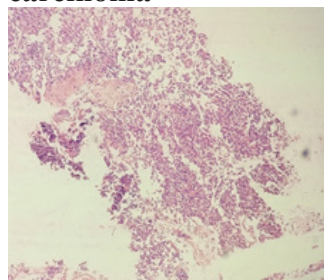**Fig 4: 100x and 400x H & E section slides, Small cell carcinoma**

Fig 5: 100x H & E section slide of undifferentiated carcinoma

Among the study samples, 7 were diagnosed suspicious of malignancy, 4 were dysplastic samples and 41 were benign cases.

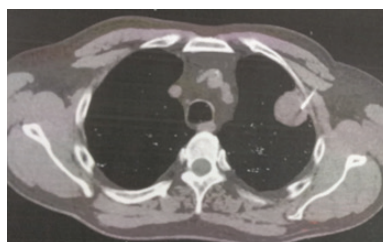Mean age of the patients was 63.1 years. Oldest case is of 86 years and 19 years was the youngest age of the patient.

Table 2: Age group of patients with lung carcinoma

Age group	Number of cases
less than 30 years	1 (1.4%)
30-39 years	1 (1.4%)
40-49 years	3 (4.2%)
50-59 years	17 (24.2%)
60-69 years	21 (30%)
70-79 years	25 (35.7%)
80 - 89 years	2 (2.8%)

Out of 70 positive cases, 36 were lesions of right lung and 20 were of left lung. In 18 cases, particular site of the tumor was not possible to diagnose. Those cases were samples from hilum, bronchus or from pleura.

Fig 6: CT image of Lung lesion (SCLC)

Among positive cases, 42 were males and 28 were females. Males have higher incidence of carcinoma with male to female ratio of 1.5:1 (Table 3)

Table 3: Sex distribution among carcinoma cases

Tumors	Male	Female	Total
NSCLC	31	17	48
SCLC	0	6	6
Poorly differentiated	0	2	2
Metastasis	1	0	1
Positive for malignancy	10	3	13
Total	42	28	70

Table 4: Smoking habits with sex distribution of lung carcinoma cases

	Smokers	Nonsmokers	Total
Male	36	6	42
Female	19	9	28
Total	55	15	70

DISCUSSION

Biopsy of lung tissue by means of bronchoscopy or transthoracic samplings is required for confirmation of lung carcinoma.[3] Among the 54 positive cases with specific subcategorization of carcinoma (diagnosed as NSCLC and SCLC), 30 (55.5 %) were SCC, 8 (14.8%) were Adenocarcinoma, one (1.8%) adenoquamous carcinoma, nine (16.6%) NSCLC-NOS, and six (11.1%) were SCLC. Similar to our study NSCLC represents approximately 84% of all worldwide lung cancers, whereas SCLC represents approximately 13% cases.[12]

The relative frequency of adenocarcinoma has shown a global rising trend.[13,14] Contrary to most recent worldwide studies, most of our study in Nepal are different. (Table 5)

The study of Pradhan S et al., Shrestha HG et al. and Chandrashekhar et al. are similar to our study.[15-17] The incidence of SCC is still much more common than Adenocarcinoma. However, study by Dhunagna et al show relative increase in number of adenocarcinomas.[18]

Similarly, in a study by Hashibe et al which included 209 patients with lung cancer; 38% had SCC whereas only 10% had adenocarcinoma.[19] In their study most of the patients were labeled as NSCLC NOS.

In these studies, only morphological characteristics were used for histological classification. Our study also includes mostly morphological classification. Only 4 cases were performed IHC.

IHC with antibodies p40 and Thyroid transcription factor-1 (TTF-1) are used to conform the type of NSCLC.[20] In our study Synaptophysin, Chromogranin are used to conform the cases of SCLC. Cytokeratin (CK), TTF1 and Napsin A are positive in Adenocarcinoma. P40 is positive in SCC. One case was conformed to be metastatic carcinoma in which Cytokeratin 7 (Ck7) and GATA transcription factor GATA3 were positive.

The reason for the rise in incidence of adenocarcinoma are due to advances in IHC based diagnosis which decreased reporting of NSCLC-NOS.[17-19] The relative low frequency of adenocarcinoma in our study may be due to the lack of IHC studies and the high incidence of first- and second-hand smokers in Nepal.

In the present study, 60-79 age groups was found to be the most common age group (65.7%) whereas 35.7% were in age group of 70-79 years and 30.0% in the age group of 60-69 years. The average age group was 63.1 years. Similarly, Pradhan S et al and Shrestha HG et al also found the maximum number of cases in their sixth and seventh decade of life.[15,16]

Out of lung carcinoma cases studied by Pradhan S et al, 60% patients were male and 40% were female with Male: Female ratio of 1.5:1.[15] In the similar study of Shrestha HG et al, the ratio was 2.2:1.[16] In another study of Radzikowska et al, it was 6.2:1.[21] The ratio was much higher than our study (1.5:1). In the present study, the increased incidence of lung carcinoma in female could be due to increasing incidence of first- and second-hand smoking in females. Then again, more females are seeking medical treatment. This also might be the reason for higher incidence of lung carcinoma among females.[15]

Study by North et al showed 41.4% of women with adenocarcinoma compared to 34.1% in men. In women, the incidence of adenocarcinoma is slowly increasing, while that of SCC is slowly decreasing.[22] However, in our study, out of 8 adenocarcinoma cases only one (12.5%) was female. Adenocarcinoma is found to be more common in males (87.5%). This might be because of the higher incidence of first- and second-hand female smokers. While smoking is the main risk factor for lung cancer, other risk factors including genetic alterations also play a major role.Since, males have more exposure to harmful substances and irradiation, the risk of adenocarcinoma in males are more frequent than females.[23] 17 out of 30 (56.6%) SCC cases were males.

The incidence of SCLC has remained relatively stable.[22] Incidence rates for SCLC are higher among males than females.[24] However, in our case, all 6 SCLC were females.(Table 3) The reason might be the result of smoking in females.

Table 5: Various studies showing types of lung carcinoma

	Pradhan S et al.[15]	Shrestha HG et al.[16]	Chandrasekhar TS et al.[17]	Dhungana A et al.[18]	Our study
SCC	63.6%	60.9%	52%	35.9%	55.5%
Adenocarcinoma	29.0%	8.0%	18%	37.8%	14.8%
SCLC	7.2%	19.5%	8%	24.5%	11.1%

In our study, 74 were biopsy specimens and 48 were FNAC specimens. The FNAC were performed with CT, USG or endoscopy guided procedures. Pradhan S et al has used CT guided FNAC, biopsy, pleural fluid, bronchial brush, sputum cytology and alveolar lavage for the diagnosis.[15] Similar to our study, they have also used both FNAC and Biopsy as final diagnosis. We received a total of 14 Sputum and pleural fluid cytology specimens with inconclusive results so they were not included in the study. However, their findings were traced with FNAC or biopsy findings (which were included).

Out of 70 cases 15, (21.4%) were nonsmokers. The rate of smoking is more than the study of Pradhan S et al. In their study, 52.7% were found to be either smoker or Ex-smoker and 47.2% of cases were nonsmoker.[15] Our study has included patients with current smokers, ex-smokers and second-hand smokers (spouse as smokers) as the criteria in smoking. This might be the reason for increase in number of smokers. However, WHO has estimated that 25% of lung cancer worldwide occurs in never smokers.[25] This data is more or less similar to our findings.

Pradhan S et al also showed most of the nonsmokers were female comprising 76.92% of cases. Out of total 15 nonsmokers our study showed 9 (60%) females in a study done by Shrestha HG et al., like our study (78.6%) most of the patients having lung cancer were smokers (85.71%) but all nonsmokers developing lung cancer were females.[15]

Since, only one case was a female with adenocarcinoma the relation of adenocarcinoma and smoking could not be associated.

CONCLUSION

SCC is found to be the most common subtype of lung carcinoma. Adenocarcinoma cases are not found to be rising in number. Findings in this study do not concur with the global trend of rising incidence of adenocarcinoma. Most cases are above 50 years old and have history of smoking.

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