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Lung Cancer in a Tertiary Hospital in Nepal: Clinical-Radiological Profile and Histological Subtypes

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ABSTRACT

Background: Lung cancer is the most common cancer worldwide and in Nepal. Non small cell carcinoma is the commoner histological type. The incidence of adenocarcinoma subtype is increasing globally. This study aims to evaluate the clinical-radiological and histological profile and the diagnostic yield of various modalities in the diagnosis of lung cancer at a tertiary hospital in Nepal.

Methods: This is a prospective cross-sectional study conducted at National Academy of Medical Sciences, Kathmandu. Patients presenting with clinical and radiological features consistent with lung cancer and undergoing tissue sampling were included. The clinical and radiological characteristics, distribution of various histological subtypes and the diagnostic yield of various modalities were evaluated.

Results: Of the 253 patients screened, 77 meeting the inclusion criteria were enrolled into the study. Lung cancer was diagnosed in 53 patients. Forty (75.5%) patients had non small cell carcinoma and 13 (24.5%) had small cell carcinoma. Among the non small cell variants, 20 (37.7%) had adenocarcinoma and 19 (35.9%) had squamous cell carcinoma. Histopathological diagnosis of lung cancer was established in 39 of the 42 (92.9%) patients by bronchoscopy. Image guided biopsy and/or aspiration yielded the diagnosis in 13 (24.5%) patients. The diagnostic yields of endobronchial biopsy, needle aspiration, bronchial brush and bronchial wash cytology were 86.5%, 70%, 63% and 34.3% respectively.

Conclusions: The result of this study concurs with the global trend of rising incidence of adenocarcinoma subtype. Bronchoscopy remains the most commonly used tool for diagnosis of lung cancer and combination of procedures such as biopsy, bronchial brush, needle aspiration and bronchial wash provided the highest yield in our study.

Keywords: Bronchoscopy, Histological subtypes, Lung cancer, Tertiary hospital, Nepal.

INTRODUCTION

Lung cancer is the most common cancer and is the leading cause of cancer-related deaths worldwide.¹ Histologically it can be divided into two types: Non Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC). NSCLC is the most common and accounts for 85% of the cases. Adenocarcinoma, squamous cell carcinoma and large cell carcinoma are the major subtypes of NSCLC. The proportion of histological subtypes of NSCLC varies depending upon geographical distribution, ethnicity, smoking status, age and gender. Squamous cell carcinoma is the most common histological subtype of NSCLC reported by various studies including those from Nepal.^{2,3} Adenocarcinoma is more common in Asians, females and non-smokers. However, newer series have reported adenocarcinoma to be the commoner subtype even in males and smokers.^{4,6}

Flexible bronchoscopy and image guided biopsy are the most commonly used tool for histological diagnosis with yield of approximately 90%.⁷⁻⁹ Cytology has lower yields compared to histopathology.⁸ Only a few studies have explored into the relative incidence of lung cancer stage and histological subtypes in our country.^{2,3} The aim of this study was to evaluate the clinicoradiological profile and histological subtypes of lung cancer in a tertiary hospital in Nepal and to ascertain the diagnostic yield of various modalities.

METHODS

This prospective study was conducted in the Chest Unit of National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal from November 2017 to March 2018. Ethical clearance for the study was obtained from the Institutional Review Board.

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Patients presenting with clinical and radiological features consistent with malignancy and those undergoing tissue sampling with various modalities including bronchoscopy, image guided biopsy, FNAC and pleural fluid cytology were included into the study. Those who were unfit for obtaining tissue diagnosis and not willing for consent were excluded.

A written informed consent was obtained in all patients meeting the inclusion criteria and willing to participate in the study. Clinical data including age, gender, smoking status and symptoms were collected at the time of enrolment into the study. Computed tomography of the thorax was performed in all patients. The location of mass, presence of mediastinal nodes and associated effusion were noted. Patients with central mass underwent bronchoscopy and biopsy. Peripheral mass were sampled (FNAC or Biopsy) under image guidance and those with extrathoracic metastasis underwent biopsy/ FNAC from extrathoracic site if feasible. Pleural effusions, if present, were evaluated for malignant cells. The clinical and radiological characteristics, histological subtypes of lung cancer and the diagnostic yield of various modalities were evaluated. The data were presented as mean (\pm SD), frequency (percentage) and diagnostic yields ((Number of positive samples/Total number of samples) X100) and analyzed using Microsoft Excel Spreadsheet[®] 2019 16.0.6742.2048.

RESULTS

Among 253 patients screened, 77 were suspected to have lung cancer and were included in the study. Lung cancer was diagnosed in 53 patients by various modalities. Of the 24 patients with alternate diagnosis, 11 had tuberculosis, 6 had benign bronchial stenosis with collapse, 5 had post infective fibrosis and two Sarcoidosis. Of the 53 with lung cancer, 42 (79%) had Stage III / Stage IV disease at presentation. The flow of patients included in the study with modalities leading to diagnosis is depicted in Figure 1.

Of the 53 patients with lung cancer, 32 (60.4%) were males and 21(39.6%) were females. The mean age at diagnosis was 65 \pm 9.5 years; 49 (92%) patients were smokers. Cough was the most common symptom present in 40 (75%) patients followed by shortness of breath and hemoptysis. Four (7%) patients had superior vena cava obstruction (SVCO) at presentation. CT chest showed mass lesion in 36 (68%) patients. Effusion, cavitation and lobar collapse was present in 17 (32%), 16 (30%) and 15 (29%) patients respectively.

Thirteen (24.5%) had small cell carcinoma. Among

patients with NSCLC, adenocarcinoma was the commonest subtype present in 20 (37.7%).Nineteen (35.9%) had squamous cell carcinoma and 1 (1.9%). had large cell carcinoma. In 14 morphologically undifferentiated NSCLC biopsy samples were stained with TTF-1, CK5/6 and p63 immunohistochemical stains using Horseradish Peroxidase (HRP). Ten samples were positive for adenocarcinoma and four positive for squamous cell subtype. The gender wise distribution and the histological subtypes of lung cancer included in the study are depicted in Table 1.

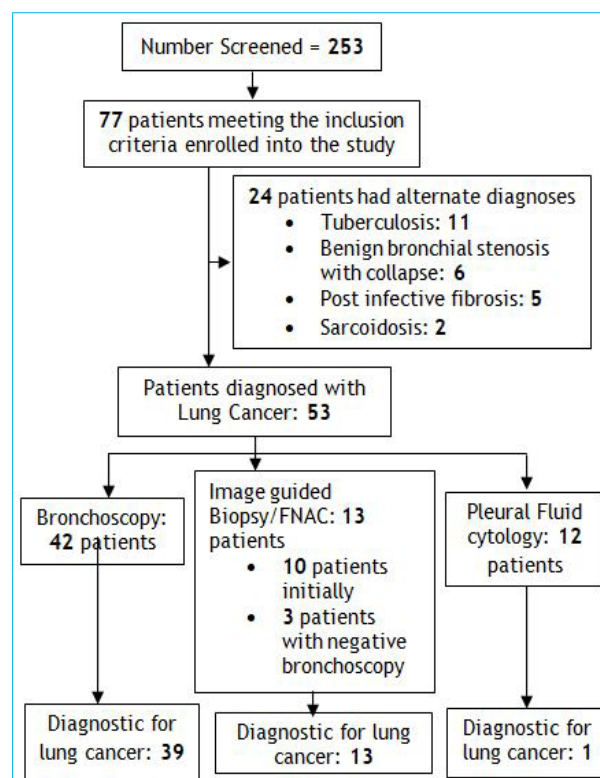


Figure 1. The flow of patients included in the study with modalities leading to diagnosis.

Table 1. Gender-wise distribution and histological subtypes of lung cancer in the study population.

	Gender		Total
	Male	Female	
Adenocarcinoma	14	6	20 (37.8%)
Squamous cell carcinoma	10	9	19 (35.9%)
Small cell carcinoma	7	6	13 (24.5%)
Large cell carcinoma	1	0	1 (1.9%)
Total	32	21	53

Of the 53 patients, 42 underwent flexible bronchoscopy for acquisition of tissue samples. Image guided samples were obtained in 11 patients. A total of 12 pleural fluid

aspirates were sent for cytology, of which one was positive for metastatic adenocarcinoma. Of the 42 patients undergoing bronchoscopy, following samples were obtained: 37 Endobronchial Biopsy (EBB), 32 Bronchial Wash (BW), 27 Bronchial Brush (BB), 7 Endobronchial Needle Aspiration (ENA), 2 conventional Transbronchial Needle Aspiration (TBNA) and 1 Endobronchial Ultrasound guided TBNA (EBUS-TBNA). Histopathological diagnosis of lung cancer was established in 39 (92.8%) patients undergoing bronchoscopy. The diagnostic yield of various bronchoscopic procedures is depicted in Table 2.

Table 2. Diagnostic Yield of various bronchoscopic procedures in lung cancer.

Procedure	Number	Positive	Diagnostic Yield
Endobronchial Biopsy	37	32	86.5%
Bronchial Brush	27	17	63.0%
Bronchial wash	32	11	34.3%
Needle Aspiration (ENA+TBNA+EBUS-TBNA)	10	7	70%
Endobronchial needle aspiration (ENA)	7	5	71.4%
Transbronchial needle aspiration (TBNA)	2	1	50%
Endobronchial Ultrasound guided TBNA (EBUS-TBNA)	1	1	100%

USG or CT guided biopsy and FNAC was done in 13 patients; 10 cases initially and 3 patients who had a negative bronchoscopic biopsy. Image guided biopsy yielded adenocarcinoma in 7 patients, small cell carcinoma in 3 patients and squamous cell carcinoma in 3 patients.

DISCUSSION

Since a population-based National Cancer Registry does not exist in Nepal, the data on relative proportion of cancer incidence by site is unreliable. Two of the largest studies report lung cancer to be the commonest malignancy not only in males but also in females.^{10,11} In a series of patients including 209 patients with lung cancer; 38% had squamous cell carcinoma whereas only 10% had adenocarcinoma.² However, only morphological characteristics were used for histological classification in their study and almost a fourth of the patients were labeled as NSCLC not otherwise specified (NSCLC-NOS). In another study including 136 patients with lung cancer, the relative incidence of squamous cell carcinoma,

adenocarcinoma and small cell carcinoma were reported to be 52%, 18% and 8% respectively.³

The clinicopathological profile of lung cancer has undergone noticeable changes over the last two decades. The relative frequency of adenocarcinoma has shown a global rising trend.^{4,12} The reason for this change can be attributed to the rising incidence of adenocarcinoma among smokers, advances in immunohistochemistry (IHC) based diagnosis and decreased reporting of NSCLC-NOS among many others. Squamous cell carcinoma is reported as the commonest subtype of NSCLC in studies from Nepal.^{2,3} However, newer studies from India report adenocarcinoma to be the commonest histological subtype of NSCLC.^{5,6} In our study, the frequency of adenocarcinoma and squamous cell carcinoma were similar concurring with the global and regional trends of rising incidence of adenocarcinoma. This finding can also be attributed to the use of IHC in undifferentiated NSCLC for histological classification. In our study, half of the adenocarcinoma diagnosis was established by IHC stains.

Bronchoscopy is the most commonly used tool for tissue diagnosis of lung cancer, especially in those with a central tumor and/or hemoptysis. Visible endobronchial mass or infiltrations can directly be biopsied and has a high yield. Other samples like endobronchial needle aspiration, bronchial brush and wash can also be obtained to increase the yield of the procedure. Even lesions that are not visualized during bronchoscopy and those that lie outside the tracheobronchial tree can be sampled by conventional TBNA and Endobronchial ultrasound. In this study, the overall yield of bronchoscopy was 92.8%. The reported yield of bronchoscopy in central lesions is 88-94% and in peripheral lesions is 69%.^{7,8} Although image guided biopsy has yield that are comparable to bronchoscopy the risk of pneumothorax and airway bleeding is higher.⁹ Image guided procedures may be preferred in peripheral lesions and those not accessible by bronchoscopy. Bronchoscopic techniques such as Radial probe EBUS and Electromagnetic Navigation Bronchoscopy have similar diagnostic yield but lesser complications for peripherally located lesions when compared to image guided techniques.^{9,13}

Among the bronchoscopic samples, bronchial biopsy has the highest yield for the diagnosis of lung cancer.⁷ In our study, bronchial biopsy was positive in 32 of the 37 patient with a yield of 86.5%. The diagnostic yield of bronchial wash and brush in suspected lung cancer is variable. The yield has been reported to be 28-76% for washing and 47-80% for brush.^{8,14,15} In our study the yields of bronchial wash and brush were 34.3% and 63%

respectively, which are comparable to earlier reports. The addition of bronchial washings and brushings to endobronchial biopsy increases the diagnostic yield. In our series, 7 additional cases of lung cancer were diagnosed by performing bronchial wash, brush and needle aspiration in addition to biopsy during bronchoscopy. Endobronchial needle aspiration is useful for lesions in the airway which are submucosal or likely to have torrential bleeding during biopsy. For lesions which lie outside the tracheobronchial tree conventional TBNA and EBUS-TBNA can be used to obtain samples during bronchoscopy. EBUS-TBNA, which has recently been introduced in Nepal is an excellent modality in diagnosis and staging of lung cancer with yield more than 90%.^{16,17}

Very few studies have evaluated the use of flexible bronchoscopy in the diagnosis of lung cancer in Nepal.¹⁸⁻¹⁹ Prospective studies on the diagnostic yields of various bronchoscopic and non bronchoscopic techniques for lung cancer diagnosis are lacking. The strengths of this study are its prospective nature and use of multiple modalities for diagnosis. We also used immunohistochemistry for subtyping the morphologically undifferentiated NSCLC. The limitations are relatively small sample size, lack of standard protocol for choice of diagnostic modality and lack of immunohistochemistry in all patients. We also did not perform cell block for cytological samples. Though this is a single centre pilot study with a relatively small sample size, it will pave a way for better designed larger studies in future on histological subtypes and the diagnostic modalities for lung cancer in Nepal.

CONCLUSIONS

The findings in this study concur with the global trend of rising incidence of adenocarcinoma subtype. Bronchoscopy remains the most commonly used tool and a combination of procedures such as biopsy, bronchial brush, needle aspiration and bronchial wash provided the highest yield in our study.

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