Research Article

Role of sputum cytology in lung cancer

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Abstract

Background: Background: In individuals with lung cancer, sputum is a readily available lung material that contains exfoliated bronchial epithelial cells and several leukocyte kinds, including premalignant and malignant cells. Screening of lung cancer can be of great help in early detection as it can increase survival rate and reduce mortality. Aims: To assess the role of cytological examination of sputum in the diagnosis of individuals with suspected lung cancer. **Methods:** A cross-sectional study was held at Chest Department, Minia cardiothoracic university hospital in association with the Department of Pathology. Seventy-three patients were included in our study with suspected lung cancer. These patients underwent either bronchoscopy or CT-guided biopsy for histopathologic examination. Samples were collected, and the 'pick and smear' technique is used for sputum preparation. **Results:** the study was conducted on 73 patients, 46 cases proved to be malignant by biopsy either Bronchoscopic or CT-guided biopsy. The overall sensitivity of sputum samples was 58.8% in the detection of lung cancer. Squamous cell carcinoma was present in 6 cases (17 %) in cases diagnosed by sputum cytology. Adenocarcinoma represented 8 cases (23 %) of cases. Sputum cytology detected malignancy in most cases (91.7%) having tumor size ≥ 2 cm. **Conclusion:** The diagnostic yield of sputum cytology for the detection of lung cancer increased with lesion greater than 2 cm, and the overall sensitivity of our sputum samples was 58.8% in this regard.

Key words: sputum cytology, lung cancer, bronchoscopy

Introduction

In individuals with lung cancer, sputum is a readily available lung material that contains exfoliated bronchial epithelial cells and several leukocyte kinds (1), including premalignant and malignant cells (2). According to statistics, 1.8 million additional deaths and 2 million new lung cancer diagnoses were reported, that's why lung cancer is considered one of the main causes of mortality worldwide. Lung cancer comes in second place after breast and prostate cancer in women and men respectively.(3)

Uncontrolled cell proliferation in the lung tissues is a characteristic feature of a malignant lung tumor known as lung cancer. In the event that it is not treated, this tumor may eventually metastasize anywhere in the body or surrounding tissues. The majority of primary lung cancers, or tumors that first appear in the lungs, are epithelial cell carcinomas. Non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) are known to be the two most common types of lung cancer.(4)

Through screening, lung cancer could be detected early and it can also reduce morbidity and increase survival.(7-5)

The least intrusive option for detecting people who may have lung cancer is sputum cytology tests. Direct smears from suspicious particles in fresh sputum and paraffin embedding and processing as employed in histological diagnostics are the two most used techniques for diagnosing lung cancer in sputum.(8)

For a long time, sputum cytology was expected to be a screening or case-finding method for the early detection of lung cancer (9, 10).

Patients and Methods

A cross-sectional observational study was done at Chest Department, Minia Cardiothoracic University Hospital in association with Department of Pathology, from November 2021 to November 2022. Seventy-three patients were included in this study and have soft tissue mass in their CT chest.

Inclusion criteria:
1.   Adult age (More than 16 years old).
2.   Any sex.
3.   Any patient with clinical and radiological finding suggesting lung cancer.

Exclusion criteria:
1.   Patient age less than 16 years old.
2.   Pregnant females.
3.   Patients with high risk of bleeding.
4.   Untreatable life threating arrhythmias.
5.   Patients with raised intracranial tension.
6.   Patients with COVID 19 infection .
7.   Patients with positive sputum for acid fast bacilli.
8.   Patient with Contraindications to bronchoscopy

All Patients were subjected to:
1.   Complete medical history: focusing on smoking history, history of TB, and occupational history.
2.   Thorough clinical examination: both local and general examination.
3.   Lab investigations: including CBC, ESR, liver enzymes, serum albumin, RFT, INR & PC to assess the case's general condition and fitness for either bronchoscopy or CT-guided biopsy.
4.   Conventional chest radiography, Chest computed tomography (CT).
5.   Sputum cytology analysis: A non-invasive test for detecting lung cancer is sputum cytology. Multiple sputum samples are collected over several days to optimize sensitivity. For sputum cytology, deep cough specimens collected in the early morning are preferred. Expectoration was induced by having the patient breathe in nebulized water or saline if the patient was unable to expectorate sufficiently. This technique increases lung cancer detection. The 'pick and smear' technique is used for sputum preparation. Areas with blood, tissue fragments, or both are used to prepare smears. Smears are fixed immediately in 95% ethanol, then sputum is processed using thin layer method. All slides were stained using the Papnicolaou method. By identifying numerous pulmonary macrophages, which suggest that the sample was obtained from the lower respiratory tract, the sputum sample is deemed adequate. Squamous cell, bacterial, and candida organism-containing specimens are inadequate because they represent oral contents. Negative sputum cytology does not guarantee the absence of malignancy. Then slides are examined using light microscope (Olympus, BX50, Tokyo, Japan,1998).

6.   Fiber optic bronchoscopy (FOB) (PENTAX, EB-1970(2.8), Japan): biopsy of visible lesion and BAL fluid was collected and sent for histopathological examination.

Ethical consent:

Every patient received an explanation of the purpose of the current study. There were no ethical dilemmas with the laboratory or radiological techniques because they were normal practice. Every patient consent to take part in the research. Approval No. 147:2021 was acquired with the consent of the Minia Faculty of Medicine Research Ethics Committee. The Declaration of Helsinki, the World Medical Association's code of ethics for human subjects research, has been followed in the conduct of this work.

Statistical analysis

Data were collected, and analyzed via SPSS program (Statistical Package for Social Sciences) version 24. Mean and standard deviation were used to express quantitative data, while percentage and number were used to express the categorical data .

Independent t-test was used to describe the parametric quantitative data between the groups. Chi square test was used for analyzing the quantitative data and Fisher's Exact test was used; (if more than 20% of cells have expected count less than 5). A P value of less than 0.05 was deemed significant.

Results

Most of the studied cases were in their 5th and 6th decade of life ranging between 20–82 years old. Male sex representing 75.3 % and most of them were heavy smokers (52%), as shown in table.(1)

Squamous cell carcinoma was present in 28 % in cases diagnosed by bronchoscpic biopsy and represented 17 % in cases diagnosed by sputum cytology. Adenocarcinoma represented 33 %, 23 %, in cases diagnosed by bronchoscopic biopsy, sputum cytology respectively .

And p-value shows statistically significant difference as regard cancer type between bronchoscopic biopsy, sputum cytology and BAL. as shown in table.(2)

As shown in table, (3). The overall sensitivity of sputum 58.8 %, specificity 85.7 %, negative predictive value 38 % and positive predictive value 83.3 %. With P-value = 0.004.

In table (4): Chi square test was done to show association between tumor site & size, and positive sputum cytology. It showed that sputum cytology detected malignancy in most cases (91.7%) having tumor size ≥ 2 cm, whereas only 22.7 % of cases with size < 2 cm were positive by sputum cytology.

Table (1): Demographic data of studied cases

Variables	Descriptive statistics
Age: mean ±SD (range)	57.4±11.8 (20-82)
Sex: n (%) Males Females	35(75.3%) 11 (24.7%)
Occupation: n (%) No (housewife/ student) Manual Clerk Professional	14 (30.1%) 26 (56.1%) 2 (4.1%) 4 (9.6%)
Smoking: n (%) Smoker Ex-smoker Nonsmoker	21 (46.6%) 10(21.9%) 15 (31.5%)
Smoking index: n (%) Mild Moderate Heavy	2(6%) 13 (42%) 16 (52%)

SD: standard deviation, n (%): number

**Table (2): histopathological types according to different diagnostic procedures**

Cancer type	diagnostic procedures	
	Bronchoscopic biopsies No (46)	Sputum cytology No (20)
Squamous cell carcinoma	13 (28%)	6 (17%)
Adenocarcinoma	15 (33%)	8 (23%)
Small cell carcinoma	12 (26%)	5 (14%)
NHL	1 (2%)	1 (2 %)
Others	5 (11%)	0 (0%)
Total	46 (100%)	20 (100%)
P value	< 0.001	

Table (3): Association between tumor site, size and sputum cytology:

	Patient number	Positive sputum cytology
	46 (100%)	**27 (58.7%)**
Tumor site		
Central	35 (76%)	20 (57.1%)
Peripheral	11 (23.9%)	7 (63.6%)
Tumor size		
$\geq$2cm	24 (52.2%)	22 (91.7%)
<2cm	22 (47.8%)	5 (22.7%)

Table (4): Diagnostic efficacy of sputum cytology

AUC	sensitivity	Specificity	PPV	NPV	p-value	95% CI
0.694	58.8%	85.7%	83.3%	38%	0.004	0.570-0.817
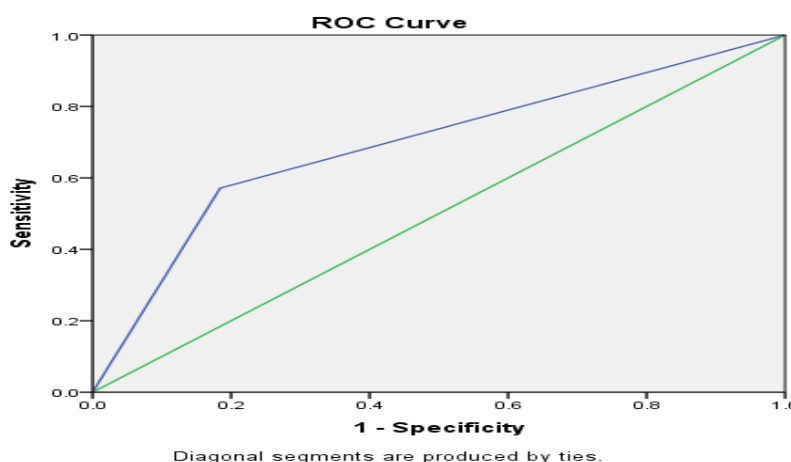
Figure 1: ROC of Diagnostic efficacy of sputum cytology

Discussion

The severe acute respiratory syndrome the least uncomfortable approach to making a diagnosis in patients with suspected lung cancer is still the cytological analysis of sputum. Sputum is a readily available lung material that contains exfoliated bronchial epithelial cells and a variety of leukocytes (1), including premalignant and malignant cells in patients with lung cancer (2). Sputum cytology is still used in clinical practise as a reliable and affordable diagnostic method, even though in industrialized nations tumor biopsies and tumor cytology have superseded it as the gold standard for lung cancer diagnosis.

Exfoliative cytology, which is based on the spontaneous shedding of cells originating from the mucosal lining of the respiratory tract were

they can be eliminated by non-invasive techniques, is an example of sputum cytology. For premalignant and malignant disorders, it is a quick, precise, trustworthy, economical, and non-invasive technique.(13-11)

In the current study most of the studied clinically suspected lung cancer cases were in their 5th and 6th decade of life with mean age (57.4). Male sex representing 75.3 %. This was similar to studied populations of Bandyopadhyay et al. (14) as male sex represents 79%, also with Ammanagi et al. (15), male patients were 75% and female 25% .

As Smoking is a common etiological factor for the lung cancer, In the current study most of our patients had history of smoking either current or ex-smoker. They were heavy smokers representing 52%, this came in accordance with

Ammanagi et al. (15), as most of their patients were smokers for long duration.

In the study in our hands the overall sensitivity of our sputum samples was 58.8%, specificity 85.7%, positive predictive value 83.3 % and negative predictive value 38%, p-value <0.004.

In a study conducted by Ammanagi et al. (15), it was discovered that 60% of the cases were malignancy-positive on sputum cytology. However, another study by Thunnissen, et al. (16) made the assumption that only 11 of the 39 individuals evaluated (28%) had malignant cells in their sputum .

According to Böcking et al. (17), sputum cytology detected lung cancer at a rate of 59.5%. According to Risse, et al. (18), the detection rate for lung cancer was 60.1%. Hinson and Kuper's (19), in another investigation, found that 59.8% of the subjects they examined had malignancy-positive sputum. Sputum cytology is a reliable method for the early detection of malignant lung tumors, according to Sumitani et al.(20) .

In the study of Bandyopadhyay et al., (14), the overall sensitivity of their post-bronchoscopy sputum sample was 7.9%, specificity 100%, positive predictive value 100%, and negative predictive value 25.53%.

In the study of Wongsurakiat et al., (21), the sensitivity of post-bronchoscopy sputum was 7.7% and BAL cytology was 46.7%. In another study done by Yüksekol et al., (22), the sensitivity of post bronchoscopy sputum was 31.8% for visible endobronchial lesion under FOB. It increases to 42.9% when the lesion is not visible, that is, for peripheral lesion .

This variation in the sensitivity of sputum cytology in diagnosis of lung cancer may be due to the difference in the studied population and the number of sputum samples collected. The incidence of diagnostic cells in sputum depends on the histological type of the tumor.

Histopathology of biopsies taken from malignant specimens (46 cases) indicated that all cancer types shed diagnostic cells into sputum, and revealed that number of cases which showed squamous cell carcinoma regarding taken biopsy were 13 cases (28%) from which 8 cases were positive by sputum cytology, and number of cases that showed adenocarcinoma were 15 case (33%) from which 8 cases were diagnosed positive by sputum cytology, while small cell lung cancer were 12 cases (26%) from which 8 cases were

positive by sputum cytology, 1 case (2%) showed non-Hodgkin's lymphoma and 5 cases (11%) showed other types (spindle cell tumors and, Poorly differentiated carcinomas), from which there were no patients diagnosed positive by sputum cytology

Acharya et al., (23) revealed that squamous cell carcinomas constituted 40.6% of the lesions while 30.1% of lesions were adenocarcinomas. But Sputum cytology confirmed diagnosis in 9 patients (6.29%) of whom 3 were squamous cell carcinoma, 2 adenocarcinoma, 1 small cell carcinoma and 2 reported as atypical cells. Also, Cao et al., (24) stated that among patients with lung cancer, the majority of them had squamous cell carcinoma followed by adenocarcinoma. 77 (66.4%) patients and 39 (33.6%) patients were in stage I–II and III–IV, respectively. Discussion 74 Furthermore, the study of Bandyopadhyay et al., (14), reported that Squamous cell carcinoma was found to be the most common lung cancer (47.4%), followed by adenocarcinoma (23.7%), small-cell carcinoma (15.8%), large cell neuroendocrine (5.2%), and large cell anaplastic carcinoma. A study by Byers et al (25) found that dysplastic cells in the sputum were correlated more directly with squamous cell carcinomas than with adenocarcinomas

Our results showed that 57.1% of central tumors were malignant by sputum cytology. Whereas 63.6 % of peripheral tumors were malignant by sputum cytology, and this may be due to small sample size and difference in the studied population.

The study by Ammanagi et al. (15) central lesions were found to be malignancy-positive on sputum cytology, with a detection rate of 72.7% for central tumors as opposed to 44.4% (four to nine instances) for peripheral lesions. Our findings were in line with their findings. The 81% for central and 42% for peripheral tumor pick-up rates reported by Duguid and Huish (26) are comparable to these pick-up rates. On the chest radiographs, the centrally located malignant lesions (84.7%) had a much higher positive yield of cytology than the peripherally located lesions (15.2%), according to Chaudhary et al., (27). Our findings also contradicted Elsawy's study (28), which asserted that bronchial lesions and their lobar locations had a higher yield for diagnosis.

As regarding tumor size in our study, larger tumors (≥ 2 cm) were associated more

frequently with positive sputum for cancer cells. As 91.7 % of cases having tumor size ≥ 2 cm were malignant by sputum cytology.

Our findings are corroborated by those of a study conducted by Neumann et al (2), which showed that when comparing tumor sizes, larger tumors (>2 cm) were more frequently related with sputum that was positive for cancer cells .

Matsuda et al., (29) observed that the diagnostic performance of sputum cytology and tumor sizes did not differ significantly.

Conclusion: The overall sensitivity of our sputum samples was 58.8% in detection of lung cancer, the diagnostic yield of sputum cytology for detection of lung cancer increased with lesion more than 2 cm.

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