

The Importance of Sputum Cytology in the Diagnosis of Lung Cancer

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Introduction: Worldwide lung cancer is the leading cause of death. The incidence of lung cancer is increasing in developing countries like Pakistan. Mortality is more than 90 % in diagnosed cases and it is directly related to the stage of disease so it is important to diagnose at an early stage. Sputum cytology is a definite way to diagnose lung cancer. It is cost effective, non-invasive, does not need any instrumentation and free of investigating complications.

Objective: To study the role of sputum cytology in the diagnosis of lung cancer.

Study Setting: This study was conducted at the Institute of Chest Medicine, Mayo Hospital – A tertiary care hospital affiliated with King Edward Medical University, Lahore.

Study Design: Cross sectional evidence based study.

Materials and Methods: Ninety seven patients (80 males, 17 females) with radiological suspicion of malignancy were included in the study. Three Consecutive morning sputum samples were collected after deep coughing. Two smears were made of each specimen and stained with Haematoxylin and Eosin and papanicolaou. All the specimens were examined by a consultant cytohistopathologist.

Results: A total of 97 patients (80 males and 17 females) with clinical and radiological suspicion of lung cancer were included in the study. The patient's ages ranged between 50 – 83 years with mean age of 66.5 ± 14.5 years. Sputum cytology was positive in 46 (45.3%) patients. Amongst males 41 (51.25%) have positive cytology, while in females 5 (29.41%) have positive sputum cytology. Out of 46 patients with positive cytology 37 (80.43%) patients (33 males and 04 females) have non small cell carcinomas while 09 (19.56%) patients (08 males and 01 female) have small cell carcinoma.

Conclusion: Sputum cytology is a definite way of lung cancer detection. It is cost effective, non invasive and free of investigating complications.

Key Words: Lung cancer, Sputum, Cytology, Non small cell carcinoma, Small cell carcinoma, Staining, H and E (Haematoxylin and Eosin), papanicolaou.

Introduction

Lung cancer is the leading cause of death in the world. Almost one million people died every year because of this fatal disease.¹ The incidence of lung cancer is growing. Lung cancer is the most common malignancy in male population of Pakistan. The only way to decrease the mortality of this disease remains in diagnosing the lung cancer at the earlier stage before the lesion is visible.² Lung cancer is fatal in more than 90% of diagnosed cases. The reason of such a high mortality is so because most of the cases are diagnosed at a very late stage when the disease is incurable. Mortality is directly related to the stage of disease at the time of diagnosis, ranging from 30% for stage I disease to more than 95% for stage IV disease.³ Seventy-five percent of patients with lung cancer when diagnosed they have symptoms of local or distant metastasis. So, early detection is the only way when disease can be cured with resection of the part of the lung which is involved before the local or distant metastasis occurred. There has been a lot of interest in tests for detection of early lung cancer. There are many screening tests like sputum cytology, chest X-Ray and fiberoptic bronchoscopy which are commonly used for the early diagnosis of lung cancer.⁴

Sputum cytology has been successful in a large number of cases in the diagnosis of bronchogenic carcinoma. Sputum can be collected spontaneously or it can be induced. A sputum sample is considered adequate if alveolar macrophages or bronchial epithelial cells are present because this shows that the samples originate from deep within the lung and just not the salivary secretions. There should be at least 5 – 150 macrophages in the specimen to label it adequate sample.⁵ Usually a small portion of the sputum sample is processed and examined under microscope for the presence of atypical cells and in the sputum sample only about 1% cell are atypical. There are different studies of sputum cytology showing an the average sensitivity of 65% with a wide range of 22 – 98%. This wide variability is because of the location of the lesion. Centrally located lesions like small cell carcinoma and squamous cell carcinoma are more likely to be detected than the peripheral lesions like large cell carcinoma and adenocarcinoma.⁶ There are a number of factors which are involved in the success of screening but most important of which is to obtain a suitable specimen. Other factors that are involved are very small specimen, dried specimen, only saliva or nasal secretions. All these can interfere with the results. Many years ago, Saccomanno et al⁷ defined

the cytological changes occurring during the development of lung cancer. They described the transition from mild, moderate and marked atypia to carcinoma in situ and then to invasive carcinoma. The time needed for this transition varies in different patients but average time is five years from mild to marked atypia and another five years from marked atypia to invasive carcinoma. The transition time is shorter in small cell carcinoma as compared to non small cell carcinomas and it is maximum for adenocarcinoma.⁷

The sensitivity of this procedure varies in different studies and in single adequate sample it is about 41% but the sensitivity increases to 85% if the number of specimens increases to four or more than that. However increasing the number of specimens causes a significant burden on the cytopathologist because an experienced cytopathologist requires 10-20 minutes to examine a single slide.⁸

In the process of diagnosing lung cancer, patients having radiographs suggestive of lung cancer, usually undergo different diagnostic tests for the histopathological diagnosis like bronchoscopy, fine needle aspiration, thoracoscopy, thoracotomy and less commonly sputum cytology.⁹ Before 1960s, sputum cytology was considered the best initial test in the diagnostic evaluation of patients with chest radiographs suggestive of lung cancer.¹⁰ Sputum cytology is now less commonly used because of the availability of more sophisticated investigations like fiberoptic bronchoscopy and computerized tomography. They are known to have a better diagnostic yield. However, there are many patients, who have contraindication to bronchoscopy or bronchoscopy facility is not readily available.¹¹ In developing countries like Pakistan where facilities of bronchoscopy, CT chest and thoracoscopy are available at tertiary care centers only and with limited resources sputum cytology is a very good tool for the diagnosis of lung cancer because of very low cost and having no morbidity and mortality.

Objective

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Study Design

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Materials and Methods

Sample Size

Ninety seven patients (80 males, 17 females) with radiological suspicion of malignancy were included in the study.

Sampling Technique

Convenient randomized sampling.

Sample Collection

Patients were provided three sterile sputum containers. Each container has fixative liquid (70 – 90% ethyl alcohol) in it with the proportion of 1 : 3 of the specimen. The difference between sputum and spit was explained to the patient. Patients were advised to rinse their mouth with water and after deep coughing; the sputum was directly collected in the container, screwed the lid back on the container and checked for any leak. Consecutive 3 morning sputum samples were collected. Each specimen was labeled and transported immediately to the pathology laboratory.

Sputum Specimen Processing and Interpretation

Two smears were made of each specimen by the cytotechnician. Smear stained with H and E (Haematoxylin and Eosin) and papanicolaou. Samples regarded as satisfactory if alveolar macrophages were present. All the specimens were examined by a consultant cytohistopathologist.

Results

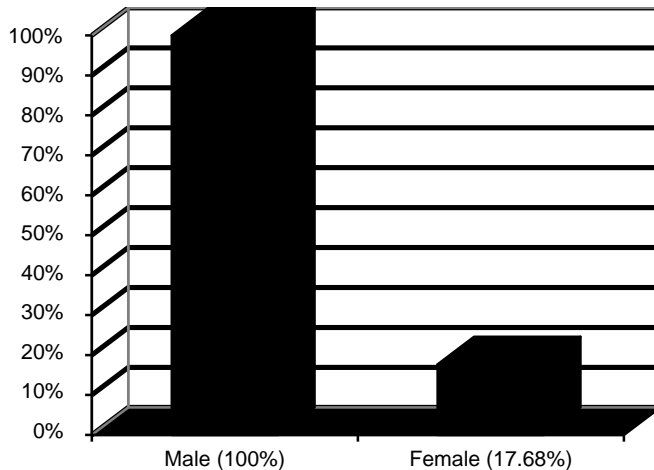
A total of 97 patients (80 males and 17 females) with radiological suspicion of lung cancer were included in the study (Tab 1). Age ranged between 50-83 years with mean age of 66.5 ± 14.5 years. Thirty seven patients (30 males and 07 females) were between the ages of 50 – 59 years, 40 patients (35 males and 05 females) were between the ages of 60 – 69 years, 17 patients (13 males and 04 females) were between the ages of 70 – 79 years and 3 patients (02 males and 01 female) were between the ages of 80-89 years (Tab 2). All the males (100%) were smokers while out of 17 females only 3 (17.68%) were smokers (Graph 1). Radiologically 60 (61.85%) patients (56 males and 4 females) having central lesion and 37 (38.14%) patients (24 males and 13 females) have peripheral lesion. Sputum cytology was positive in 46 (45.3%) patients out of 97 patients. Amongst males 41 (51.25%) have positive malignant cytology while in females 5 (29.41%) have positive sputum cytology. Out of 46 patients with positive cytology 37 (80.43%) patients (33 males and 04 females) were differentiated as non small cell carcinoma while 09 (19.56%) patients (08 males and 01 female) as small cell carcinoma. Amongst 46 patients of positive sputum cytology, 39 patients (37 males and 2 females) had centrally located lesions and remaining 07 patients (4 males and 3 females) had peripherally located lesions on chest radiographs (Graph 2). Out of 97 patients diagnosis of lung cancer was made in 78 (80.41%) patients with the help

Table 1: Gender Distribution (n= 97).

Sex	No. of Patients	Percentage
Male	80	82.47%
Female	17	17.52%
Total	97	100%

Table 2: Demographic Characteristics. (n= 97).

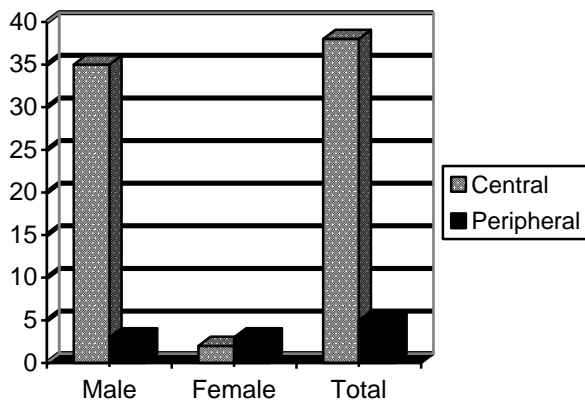
Age (Years)	No. of Patients	Males	Females
50 – 59	37	30	07
60 – 69	35	30	05
70 – 79	17	13	04
80 – 89	03	02	01



Graph 1: Smoking Habits.

Table 3: Sputum Cytopathology : (n = 46).

	Non small cell carcinoma	Small cell carcinoma
Male	33	08
Females	04	01
Total	37	09



Graph 2: Radiographic lesion location.

of bronchoscopic biopsy, brushing and bronchoalveolar lavage; fine needle aspiration and CT guided biopsy while in 19 (19.58%) patients diagnosis was not made because of inadequate tissue and refusal of the patients for repeating the procedure.

Discussion

Lung cancer is an epidemic disease. Increasing evidence suggests that screening and early detection may improve outcome in lung cancer.¹² Sputum cytology is a definite diagnostic test for lung cancer.¹³ A review of 22 articles revealed that malignant cells had been found in 28.6% to 88.9% of patients with histologically proven cancer.¹⁴ The variability of the reported sensitivity values is probably due to differences in tumour location and the number of sputum samples examined. Sensitivity increases with repeated examinations and is highest in tumours located in the main bronchus.^{15,16}

Recently sputum cytology atypia is being studied for the prediction of incidence of lung cancer, defining the latency and histological specificity of lung cancer. The association between sputum atypia and incident lung cancer is strong when the repeated samples for an individual are modeled as a time varying covariate as compared with a single sputum sample taken at the baseline enrollment.¹⁷ The cytological abnormalities of the sputum are usually classified as mild, moderate, marked atypia and positive identification of carcinoma cells.¹⁸ In our study, it was the definite positive malignant cytology identification.

Considering the results of our study, the study patients were between 50 – 83 years which is an elder age and lung cancer is predominantly a disease of elder age group. Smoking is a common etiological factor for the lung cancer. In our study all male patients (100%) were smokers while 17.8% of females were smokers. Sputum cytology is affected by smoking.¹⁹ Out of 97 patients, malignancy was diagnosed in 46 (45.3%) with male to female proportion of 8.2:1 (89.1: 10.8%) by sputum cytology.

Analyzing the type of malignancy it was 80.4% (37 out of 46) non small cell carcinoma and 19.6% (9 out of 46) small cell carcinoma. By using advanced techniques like bronchoscopy, CT guided biopsy and FNA, we were able to find malignancy in 78 (80.41%) patients. Remaining patients were not diagnosed either due to inadequate tissue sampling or they refused for repeating the procedure. Considering the positive yield of the sputum cytology that correlates the results achieved by the studies.¹⁴ There was significant difference in the positive yield of cytology in the centrally situated malignant lesions (84.7%) as compared to peripherally situated lesions (15.2%) on the chest radiographs. Presently advanced techniques like bronchoscopy, computerized tomography and FNA are used to diagnose lung cancer. These advanced techniques are costly, need expertise and instrumentations and have investigating complications. In our country, these facilities are available only at tertiary care hospitals. Sputum cytology is a definite way of

diagnosing lung cancer. Our findings indicate that there should be reconsideration of the appropriateness of the sputum cytology in the diagnostic evaluation of patients with suspected lung cancer because this is cost effective, free of complications, non-invasive technique of much use for the early detection of lung cancer.

Conclusion

Sputum cytology is a definite way of lung cancer detection. It is cost effective, non-invasive and free of investigating complications.

References

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