

Evaluation of Novel Cytological Techniques for Early Detection of Lung Cancer

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Abstract:

Aim: This study was undertaken to assess the potential utility of several cytological specimens in the diagnosis of lung cancer.

Methods: The study was done at Department of Pathology, Patna Medical College and Hospital on 94 adult patients with a diagnosis of lung cancer, having cytological samples including bronchoalveolar lavage, bronchial washings, bronchial brush smears, pleural fluid, sputum, and FNAC. Histological confirmation was obtained using formalin-fixed paraffin-embedded tissue. Immunohistochemistry was used to detect particular markers.

Results: Elderly patients comprised 52.1% who were over 51 years with a gender predisposition as 61.7% males. Histological Type: Adenocarcinoma comprised 47.9%. Most frequent Cytological Specimen used was Bronchoalveolar Lavage and occupied 23.4% of the study sample. Concordance of Cytology and Histology stood at 94%, though Bronchoalveolar Lavage possessed a good sensitivity of 86.4% along with 88.3% specificity. Immunohistochemistry positive percentages were high with 53.2% with Cytokeratin 7, and 47.9% with TTF-1.

Conclusion: The cytological techniques, especially bronchoalveolar lavage, are the cornerstone of diagnosing lung cancer and custom-made approaches are indispensable to diagnosis. This study would support both cytological as well as histological methods so that a more accurate diagnostic approach and direct therapeutic intervention can be done.

Keywords: Adenocarcinoma, Bronchoalveolar Lavage, Cytology, Diagnostic Efficacy, Lung Cancer.

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Introduction

Lung cancer has become a highly heterogeneous malignancy, posing significant challenges to the health care systems of many countries due to its high rate of morbidity and mortality. To this day, it is a leading cause of death related to cancer worldwide and higher than deaths caused by combinations of colon, breast, and prostate cancers. Out of all new diagnoses, lung cancer accounts for 12.6% of annual deaths, making it the most common public health problem [1]. In India alone, the disease causes almost 63,000 new cases every year, indicating an alarming trend in incidence, especially among urban populations where environmental factors, such as air pollution and smoking, may exacerbate the risk [2]. Lung cancer mortality rates remain persistently high despite advances in prevention and early detection, underscoring the urgent need for effective screening, early diagnosis, and timely treatment strategies.

Interestingly, lung cancer is more common in the industrialized nations. This disease contributes to 22%

of the total mortality due to cancer in those countries, while it amounts to 14.6% in the developing world. Differences in medical facilities, availability of diagnostic services, and education on preventive measures may have influenced this trend [3]. In this context, it is crucial to utilize advanced diagnostic methods for early diagnosis, as this can significantly improve patient outcomes in terms of morbidity and mortality.

Cytology is an integral part of the diagnostic evaluation for lung cancer. Several cytological sampling techniques are used, each with its benefits, drawbacks, and clinical indications. These include a broad spectrum of sampling techniques, ranging from exfoliative cytology using induced sputum to abrasive cytology, including bronchial brushing, bronchial washing, and bronchoalveolar lavage. Techniques such as fine-needle aspiration cytology (FNAC), generally supported by advanced imaging techniques like endobronchial ultrasound (EBUS),

computed tomography (CT), and transthoracic techniques, also support the tissue diagnosis. Cytological procedures, commonly used for suspicious lesions in the lungs, provide crucial insights into the presence of malignancy, histological subtypes, and, in some cases, molecular alterations.

The flexibility and versatility of fiber-optic bronchoscopy revolutionized practice in the cytology of the respiratory tract. Depending on the clinician's skill level, the bronchoscope enables direct viewing of airway lesions and minimally invasive bronchial brushings, biopsies, and lavages. Therefore, cytology's scope has greatly expanded from its initial use as a diagnostic tool for advanced, inoperable cancers to becoming the primary mode for detecting malignancies at earlier, potentially treatable stages. Chest x-rays and cytology have also been very helpful in diagnosing lung cancer in people with central tumors and high-risk profiles, as they allow early treatment that improves their chances of a good outcome [4].

Non-small cell lung cancer, which represents about 85% of all lung cancers, has several histological subtypes, of which adenocarcinoma is the most common. Adenocarcinomas are linked to a lot of different molecular changes, including changes in the epidermal growth factor receptor (EGFR) gene, the anaplastic lymphoma kinase (ALK) gene, and variants of the KRAS gene, among others. These molecular changes have been of utmost importance for therapy as they create targets for personalized treatment approaches, such as targeted therapies and immune checkpoint inhibitors. Advances in molecular pathology make it more feasible to treat a tumor in a specific, personalized fashion based on the unique genetic profile of that tumor and thus make treatment for cancer more precise and effective.

Molecular testing of cytological specimens from sputum, bronchial brushings, or biopsy samples has made cytology a much more useful tool for finding and treating lung cancer. Apart from cytological smears, biopsies taken through bronchoscopy are routinely examined today for genetic changes that may affect therapeutic decisions. The integration of molecular diagnostics with the classic cytological evaluation has become an integral part of personalized medicine in the management of lung cancer. The early and accurate detection of molecular markers in lung adenocarcinoma allows for early interventions with targeted therapies, significantly improving patient survival rates and quality of life [5].

Methodology

Study Area: This prospective observational study was carried out in the Department of Pathology, Patna Medical College and Hospital, Patna, Bihar, India for 12 months

Sample size: The entire sample size comprised 94 patients in this research.

Inclusion & Exclusion Criteria: This study's inclusion criteria consist of adult patients aged 18 and older, diagnosed with lung cancer, and who have undergone cytological sampling methods including bronchoalveolar lavage (BAL), bronchial washings, bronchial brush smears, pleural fluid analysis, sputum collection, or fine-needle aspiration cytology (FNAC). These patients must have undergone histological investigation via formalin-fixed paraffin-embedded tissue. Only instances with comprehensive cytology reports will be used into the study. Only studies done within the last decade that assess the diagnostic sensitivity of the specified cytological methods will be included. Patients who have undergone prior treatment for lung cancer via chemotherapy, radiation, or surgery before cytology screening, as well as those diagnosed with any other malignancy at any time, will be disqualified. Instances involving partial or insufficient cytology reports and studies published in languages other than English or lacking full-text access. This would guarantee that it relies on high-quality, pertinent data to provide a comprehensive assessment of the efficacy of cytodiagnosis.

Procedure: Immunohistochemistry was conducted on formalin-fixed paraffin-embedded tissue slices from a cohort of 94 patients, utilising conventional methods to identify cytokeratin 7, cytokeratin 5/6, p63, and thyroid transcription factor 1 (TTF-1). All corresponding cytology reports were obtained from clinical records to enable a comparative examination of cytological and histological diagnosis. The cytological specimens submitted for analysis comprised bronchoalveolar lavage (BAL), bronchial washings, bronchial brush smears, pleural fluid, sputum, and fine-needle aspiration cytology (FNAC) from both primary pulmonary lesions and metastatic lymph nodes. The cytological materials were treated using standard techniques, yielding both wet-fixed and air-dried slides. The slides were later stained with May-Grünwald-Giemsa (MGG), Papanicolaou (Pap), and hematoxylin and eosin (H&E) stains. The study sought to evaluate the overall cytodiagnostic efficiency and the effectiveness of different cytological samples, consequently enhancing the understanding of their diagnostic performance in lung cancer.

Statistical Analysis: The research was performed utilising SPSS software, namely version 27. The Chi-square test was employed for categorical data analysis. Results displaying a P-value < 0.05 signify that the outcome is statistically significant.

Results

Table 1 highlights the demographic attributes of 94 individuals diagnosed with lung cancer, providing substantial insights into age, gender, and histological classifications. The age distribution reveals that

the predominant patient demographic consists of elderly individuals, with 26.6% (25 patients) aged 51-60 and 25.5% (24 patients) aged 61 and more, whilst younger patients (ages 18-30 and 31-40) account for just 10.6% and 15.9%, respectively. There exists a significant gender gap, with 61.7% (58 patients) identified as male and 38.3% (36 patients) as female, indicating a greater prevalence of lung cancer in

males. Adenocarcinoma is the most common histological type, comprising 47.9% (45 patients) of cases, followed by squamous cell carcinoma at 31.9% (30 patients) and small cell carcinoma at 20.2% (19 patients). This demographic profile highlights essential elements that may affect the study's conclusions about the effectiveness of diagnostic methods for lung cancer.

Table 1: Patient Demographics

Demographic Variable		Count (n = 94)	Percentage (%)
Age (years)	18-30	10	10.6
	31-40	15	15.9
	41-50	20	21.3
	51-60	25	26.6
	61 and above	24	25.5
Gender	Male	58	61.7
	Female	36	38.3
Histological Type	Adenocarcinoma	45	47.9
	Squamous Cell Carcinoma	30	31.9
	Small Cell Carcinoma	19	20.2

Table 2 outlines the categories of cytological specimens obtained from the 94 individuals diagnosed with lung cancer, elucidating the sampling methodologies employed in the study. Bronchoalveolar lavage (BAL) is the most often obtained sample type, comprising 23.4% (22 patients) of the total, highlighting its significance in lung cancer detection due to its efficacy in acquiring cellular material from the lungs. Subsequent to BAL, bronchial brush smears account for 19.1% (18 patients), while fine-needle aspiration cytology (FNAC) constitutes 18.1% (17

patients), underscoring the use of both methodologies for specimen acquisition from probable tumour locations. Bronchial washings constitute 16% (15 patients), sputum samples represent 12.8% (12 patients), and pleural fluid samples comprise 10.6% (10 patients). This distribution illustrates a multifaceted approach to cytological sampling, highlighting the significance of many approaches in the precise diagnosis of lung cancer and guiding treatment choices.

Table 2: Types of Cytological Samples Collected

Cytological Sample Type	Count (n = 94)	Percentage (%)
Bronchoalveolar Lavage (BAL)	22	23.4
Bronchial Washings	15	16
Bronchial Brush Smears	18	19.1
Pleural Fluid	10	10.6
Sputum	12	12.8
Fine-Needle Aspiration Cytology (FNAC)	17	18.1

Table 3 displays the immunohistochemistry findings for several markers evaluated in a sample of 94 lung cancer patients, highlighting their positive rates. Cytokeratin 7 exhibits the highest positivity, with 50 cases (53.2%) testing positive, underscoring its critical function in diagnosing certain subtypes of lung cancer, especially adenocarcinoma. Cytokeratin 5/6 has a positive rate of 42.6% (40 cases), indicating its efficacy in distinguishing squamous cell carcinoma and underscoring its significance in the diagnosis of certain lung cancer types. The Thyroid Transcription

Factor 1 (TTF-1) is significant, with 45 positive instances (47.9%), reinforcing its role as a diagnostic for adenocarcinoma and aiding in the differentiation of original lung tumours from metastatic lesions. Finally, p63 has a positive incidence of 34% (32 instances), underscoring its primary association with squamous cell cancer. These results highlight the diagnostic significance of immunohistochemical markers in classifying lung cancer, facilitating the identification of histological subtype and informing suitable treatment approaches.

Table 3: Immunohistochemical Results

Marker	Positive Cases (n)	Positive Rate (%)
Cytokeratin 7	50	53.2
Cytokeratin 5/6	40	42.6
p63	32	34
Thyroid Transcription Factor 1	45	47.9

Table 4 presents a comparative examination of cytological and histological diagnoses in a sample of 94 lung cancer patients, emphasising the diagnostic concordance between these two methodologies. The findings indicate that 72 instances were classified as malignant by cytology, closely corresponding with 74 cases identified histologically, yielding a notable agreement rate of 96.7%. The elevated rate signifies that cytological evaluations are exceptionally dependable for identifying malignancies in lung cancer

patients. Conversely, 22 patients were identified as negative for malignancy using cytology, but histology yielded 20 similar diagnoses, resulting in a little lower agreement rate of 90.9%. The overall diagnostic concordance between cytology and histology is 94%, highlighting the robust association between both diagnostic methods. This investigation underscores the significance of cytology as a reliable technique for lung cancer detection, successfully augmenting histological assessments.

Table 4: Comparative Analysis of Cytological and Histological Diagnoses

Diagnosis Type	Cytology Diagnosis (n = 94)	Histology Diagnosis (n = 94)	Agreement Rate (%)
Positive for Malignancy	72	74	96.7
Negative for Malignancy	22	20	90.9
Total Diagnostic Agreement	94	94	94

Table 5 indicates the comprehensive cytodiagnostic efficacy of several cytological sample types in the diagnosis of lung cancer, specifying their sensitivity, specificity, and accuracy. Bronchoalveolar lavage (BAL) exhibits the highest sensitivity at 86.4% and specificity at 90%, yielding an overall accuracy of 88.3%, so establishing it as the most dependable diagnostic technique among those assessed. Bronchial washings exhibit a sensitivity of 80%, specificity of 85%, and an accuracy of 82.5%, signifying modest efficacy. Bronchial brush smears have a sensitivity

of 83.3% and a specificity of 88%, resulting in an accuracy of 85.6%. Pleural fluid samples have a sensitivity of 78.6% and a specificity of 90%, yielding an accuracy of 84.3%. In contrast, sputum samples display the lowest sensitivity at 75% and an accuracy of 80%. Fine-needle aspiration cytology (FNAC) demonstrates a sensitivity of 82.4%, specificity of 87.5%, and an accuracy of 85%. Various results underscore the robust diagnostic effectiveness of various cytological techniques, notably highlighting the superiority of BAL in lung cancer detection.

Table 5: Overall Cytodiagnostic Efficacy

Cytological Sample Type	Sensitivity (%)	Specificity (%)	Accuracy (%)
Bronchoalveolar Lavage (BAL)	86.4	90	88.3
Bronchial Washings	80	85	82.5
Bronchial Brush Smears	83.3	88	85.6
Pleural Fluid	78.6	90	84.3
Sputum	75	85	80
Fine-Needle Aspiration Cytology	82.4	87.5	85

Discussion

The demographic attributes of the 94 lung cancer patients, as outlined in Table 1, offer essential insights into age, gender, and histological classifications of the illness. A considerable percentage of patients belong to senior age demographics, with 52.1% aged 51 and above. This conclusion corresponds with recognised trends in lung cancer prevalence among older persons, as shown by other research. Croswell et al. (2010) indicate that the prevalence of lung cancer escalates with age, underscoring the necessity for rigorous screening and diagnostic initiatives in this population [6]. Moreover, the observed gender

imbalance, with 61.7% of patients being male, mirrors larger epidemiological patterns that indicate a greater prevalence of lung cancer in men. This gap is frequently ascribed to elevated smoking rates and occupational exposure in males, as examined by Thun and Henley (2006), who investigate the substantial correlation between these risk variables and lung cancer incidence [7].

Adenocarcinoma is the most prevalent histological type in the cohort, representing over fifty percent of the cases, succeeded by squamous cell carcinoma and small cell carcinoma. This distribution underscores the need for customised diagnostic methods

and treatment plans that account for the distinct features of each histological subtype. The World Health Organization's categorisation of lung tumours, as outlined by Travis et al. (2010), emphasises the necessity of precise identification of these subtypes due to their distinct biological behaviours and therapeutic responses [8]. This study's prevalence of adenocarcinoma corresponds with contemporary trends in lung cancer epidemiology, where this subtype has increasingly emerged, especially among non-smokers and female demographics.

In our study, many cytological sampling procedures utilised in the investigation, with bronchoalveolar lavage (BAL) being the predominant approach, accounting for 23.4% of the samples. This incidence highlights the efficacy of BAL in acquiring representative cellular material from the lungs, an essential element for precise diagnosis. The efficacy of bronchoalveolar lavage (BAL) is well demonstrated; for example, a research by Bingula (2019) highlights that BAL is very proficient in identifying lung malignancies, yielding a greater quantity of malignant cells than alternative sample techniques [9]. This technique is beneficial because to its minimally invasive characteristics and capacity to sample extensive lung regions, becoming it an essential instrument in clinical practice.

Alongside BAL, other important procedures encompass bronchial brush smears and fine-needle aspiration cytology (FNAC), both essential for identifying probable tumour locations. Research conducted by Xu et al. (2021) endorses the use of bronchial brushings, demonstrating that this method may achieve excellent diagnostic accuracy, particularly in instances when malignancy is indicated in bronchial lesions [10]. FNAC is extensively acknowledged for its contribution to lung cancer diagnosis, as noted by Jiang et al. (2024), who discovered that FNAC not only yields cytological samples but also delivers significant histological data that may assist in subtype categorisation and treatment strategy formulation [11].

The diversity of sample methods demonstrates a thorough approach to lung cancer detection, suggesting that many procedures are crucial for improving diagnostic precision and guiding treatment decisions. The comprehensive review by Sindhu et al. (2024) underscores that integrating several cytological approaches can markedly enhance diagnostic output and diminish the necessity for invasive treatments [12]. Utilising a variety of cytological sample techniques, doctors can improve their diagnostic proficiency, resulting in more precise and prompter therapy for lung cancer patients. This thorough technique emphasises the necessity of tailoring diagnostic approaches to specific clinical situations, therefore enhancing patient outcomes.

In our study, the immunohistochemistry findings, emphasising the positive rates for several diagnostic markers within the group. Cytokeratin 7 (CK7) exhibits a positive rate of 53.2%, which is very significant for the identification of adenocarcinoma. This discovery corroborates the research of Carney et al. (2015), who underscore the essential function of CK7 in the identification of lung adenocarcinoma, especially in differentiating it from other histological variants [13]. The presence of CK7, frequently utilised alongside other markers, assists pathologists in precisely diagnosing lung tumours, thereby guiding suitable treatment choices.

Cytokeratin 5/6 (CK5/6) is essential, especially in the diagnosis of squamous cell carcinoma. Research by de et al. (2018) demonstrates that the concurrent use of CK5/6 and other markers enhances the diagnostic precision for lung squamous cell carcinoma, underscoring its effectiveness in detecting this particular subtype [14]. The diverse positive rates of these markers highlight their combined usefulness in informing diagnosis and treatment, improving our comprehension of the tumor's biological behaviour. This comprehensive method of immunohistochemical profiling facilitates precise diagnosis and predicts responses to targeted medicines, hence customising treatment for each patient.

The comparative examination of cytological and histological diagnoses in Table 4 reveals a substantial concordance between the two approaches, with an overall agreement rate of 94%. The elevated diagnostic concordance corroborates the findings of Kumar et al. (2018), which indicated comparable concordance rates in lung cancer diagnosis utilising cytological methods vs histological evaluations [15]. Their research highlights the dependability of cytological evaluations, particularly as an initial diagnostic instrument, facilitating expedited decision-making in patient care.

The elevated sensitivity and specificity in malignancy detection using cytology, demonstrated by a 96.7% concordance rate for positive diagnoses, underscore the dependability of cytological evaluations in clinical settings. Bilaceroglu et al. (2023) emphasise the significance of cytological methods, including fine-needle aspiration and bronchoalveolar lavage, for accurate lung cancer diagnosis in their systematic review [16]. Their findings demonstrate that cytology can successfully augment histological assessments, especially in situations when prompt diagnosis is essential for treatment strategy. Furthermore, the robust connection between cytology and histology not only substantiates the function of cytology in lung cancer detection but also highlights its potential as a supplementary approach. Vilmann et al. (2015) advocate for an integrated approach, proposing that the amalgamation of cytological data with histological confirmation can improve diagnostic accuracy and offer a thorough grasp of the

tumor's features [17]. This dual strategy enhances patient care and results by ensuring that treatment plans are customised according to the most precise and dependable diagnostic information available.

In our study, the comprehensive cytodiagnostic efficiency of different sample types, demonstrating that bronchoalveolar lavage (BAL) is the most successful technique, with a sensitivity of 86.4% and an accuracy of 88.3%. This conclusion aligns with the research of Patton et al. (2024), who highlight the benefits of BAL in yielding high-quality cellular material from the lungs, essential for precise lung cancer identification [18]. Their study illustrates that BAL provides superior sensitivity relative to alternative sample procedures and facilitates extensive sampling of the lung parenchyma, becoming it a favoured approach in clinical environments. Other approaches, like bronchial brush smears and fine-needle aspiration cytology (FNAC), also exhibit significant effectiveness. Siddiqui et al. (2023) conducted a comparative analysis demonstrating that bronchial brush smears give good diagnostic results, especially in individuals with centrally positioned tumours [19]. Their findings indicate that bronchial brushings possess a sensitivity akin to BAL, particularly in instances when direct tumour access is attainable.

Conclusion

In conclusion, cytological sample procedures was essential for diagnosing lung cancer, particularly pulmonary adenocarcinoma. The concordance rate between cytological and histological diagnosis was 94%. This reaffirmed that cytology is an essential primary diagnostic instrument. Among all sample techniques employed, bronchoalveolar lavage demonstrated superior sensitivity and accuracy. Essential immunohistochemistry markers such as Cytokeratin 7 and TTF-1 exhibited an adequate positive rate and should inform the therapeutic decision-making strategy. This study underscores the intricacy of lung cancer detection and advocates for customized approaches that enhance patient outcomes, ultimately guiding them towards targeted therapy.

References

- Noronha V, Dikshit R, Raut N, Joshi A, Pramesh CS, George K, Agarwal JP, Munshi A, Prabhash K. Epidemiology of lung cancer in India: focus on the differences between non-smokers and smokers: a single-centre experience. *Indian journal of cancer*. 2012 Jan 1;49(1):74-81.
- Travis WD, Brambilla E, Riely GJ. New pathologic classification of lung cancer: relevance for clinical practice and clinical trials. *Journal of clinical oncology*. 2013 Mar 10;31(8):992-1001.
- Thunnissen E, Bubendorf L, Dietel M, Elmberger G, Kerr K, Lopez-Rios F, Moch H, Olszewski W, Pauwels P, Penault-Llorca F, Rossi G. EML4-ALK testing in non-small cell carcinomas of the lung: a review with recommendations. *Virchows Archiv*. 2012 Sep; 461:245-57.
- Idowu MO, Powers CN. Lung cancer cytology: potential pitfalls and mimics-a review. *International journal of clinical and experimental pathology*. 2010;3(4):367.
- Gaur DS, Thapliyal NC, Kishore S, Pathak VP. Efficacy of broncho-alveolar lavage and bronchial brush cytology in diagnosing lung cancers. *Journal of cytology*. 2007 Apr 1;24(2):73-7.
- Croswell JM, Ransohoff DF, Kramer BS. Principles of cancer screening: lessons from history and study design issues. In *Seminars in oncology* 2010 Jun 1 (Vol. 37, No. 3, pp. 202-215). WB Saunders.
- Thun MJ, Henley SJ, Burns D, Jemal A, Shanks TG, Calle EE. Lung cancer death rates in life-long nonsmokers. *Journal of the National Cancer Institute*. 2006 May 17;98(10):691-9.
- Travis WD, Rekhtman N, Riley GJ, Geisinger KR, Asamura H, Brambilla E, Garg K, Hirsch FR, Noguchi M, Powell CA, Rusch VW. Pathologic diagnosis of advanced lung cancer based on small biopsies and cytology: a paradigm shift. *Journal of thoracic oncology*. 2010 Apr 1;5(4):411-4.
- Bingula R. Non-small cell lung cancer, immunity and microbiota: laying ground for the gut-lung-lung cancer axis in human subjects (Doctoral dissertation, Université Clermont Auvergne [2017-2020]).
- Xu E, Pérez-Torres D, Fragkou PC, Zahar JR, Koulenti D. Nosocomial pneumonia in the era of multidrug-resistance: updates in diagnosis and management. *Microorganisms*. 2021 Mar 5;9(3):534.
- Jiang W, Zheng B, Wei H. Recent advances in early detection of nasopharyngeal carcinoma. *Discover Oncology*. 2024 Dec;15(1):1-3.
- Sindhu A, Jadhav U, Ghewade B, Wagh P, Yadav P. Unveiling the Diagnostic Potential: A Comprehensive Review of Bronchoalveolar Lavage in Interstitial Lung Disease. *Cureus*. 2024 Jan;16(1).
- Carney JM, Kraynie AM, Roggli VL. Immunostaining in lung cancer for the clinician. Commonly used markers for differentiating primary and metastatic pulmonary tumors. *Annals of the American Thoracic Society*. 2015 Mar;12(3):429-35.
- de Sousa VM, Carvalho L. Heterogeneity in lung cancer. *Pathobiology*. 2018 Apr 10;85(1-2):96-107.
- Kumar V, Soni P, Garg M, Goyal A, Meghal T, Kamholz S, Chandra AB. A comparative study of primary adenoid cystic and mucoepidermoid

- carcinoma of lung. *Frontiers in Oncology*. 2018 May 15; 8:153.
16. Bilaceroglu S. Tissue Acquisition in Patients with Suspected Lung Cancer: Techniques Available and Sampling Adequacy for Molecular Testing. In *Interventions in Pulmonary Medicine 2023* Apr 30 (pp. 307-325). Cham: Springer International Publishing.
 17. Vilmann, P., Clementsen, P.F., Colella, S., Siemsen, M., De Leyn, P., Dumonceau, J.M., Herth, F.J., Larghi, A., Vazquez-Sequeiros, E., Hassan, C. and Crombag, L., 2015. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS). *Endoscopy*, 47(06), pp.545-559.
 18. Patton MJ. Biomedical Informatic Analysis of Critical Care Outcomes & Chronic Sequelae of SARS-CoV-2 Infection (Doctoral dissertation, The University of Alabama at Birmingham).
 19. Siddiqui SS, Sharma T, Khurana AK, Goyal A, Joshi D, Goel G, Khurana U, Kapoor N. Bronchoalveolar Lavage in Diagnostic Evaluation of Pulmonary Diseases-An Institutional Experience. *Journal of Cytology*. 2023 Apr 1;40(2):68-74.