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A Study to Assess the Diagnostic Efficacy of Image Guided FNA in diagnosis of suspected lung cancers using cytology smears and cell block preparation.

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Abstract
Background: Lung cancer *is the leading cause of cancer-related death in both men and women. Cytology is a major, diagnostic modality used in the initial evaluation of patients with lung cancer because 70% of lung cancers are unresectable at the time of diagnosis.*
Material methods *: Purpose of the study was to evaluate diagnostic efficacy of image guided fine needle aspirations in cytological diagnosis of suspected lung cancer using cytosmears (CS) and cell block (CB) preparation, to evaluate their reliability in cytological diagnosis of lung cancer and to review the role of CB for additional diagnostic yield in cytodiagnosis.*
Result *: 85 cases included during the study. On CS, 91.25 % cases were diagnosed as positive for malignancy (PFM), 14.12% cases had atypical cells were reported as suspicious for malignancy (SFM), 34.12% cases were subcategorized on cytology, in 35.29% cases subtyping could not be achieved and were reported as NSCLC-NOS, 16.47% cases were classified as "malignant neoplasm". On CB, 98.75 % cases were diagnosed as PFM , 5.88% cases had atypical cells were reported as SFM, 71.76% cases were subtyped, in 8.24% cases subtyping could not be achieved, 12.94% cases were classified as "malignant neoplasm". Comparison of CS and CB showed that CB has provided additional pathologic information and improved diagnosis of CS in various groups such as PFM, SFM, subtyped carcinomas, NSCLC-NOS and malignant neoplasm. Additional diagnostic yield by CB for diagnosing the lung malignancy was improved by 7.06%.*
Conclusion *: In conclusion, lung FNAC is simple, fairly sensitive, relatively safe, minimally invasive and rapid reliable technique for detecting the lung malignancy. It can be regarded as an acceptable procedure for diagnosis and treatment planning, especially when other more invasive approaches are unfeasible. CB can be useful adjuncts to smears for establishing a more definitive cytopathologic diagnosis and without doubt of immense significance for improving overall diagnostic yield for detecting lung malignancy.*
Key words*: Cell Block, Cytosmears, Cytology, Lung Cancer, Image guided FNAC*

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I. Introduction

Lung cancer is the leading cause of cancer-related death in both men and women. **Several histotypes of lung cancer exist,** most common histotype being non-small cell lung cancer (NSCLC), which constitutes ~ 80 to 85% of lung cancers further classified into lung adenocarcinoma (LADC) (40%–50%), squamous cell carcinoma (SqCC) (20- 30%), and large cell carcinoma (9%).[1] The classic morphologic criteria for differentiating LADC versus SqCC may be focal or subtle in small specimens, particularly in poorly differentiated tumors.

The recent clinical studies have shown that patients with SqCC treated with bevacizumab are at increased risk for life-threatening hemorrhage.[2] LADC strongly associated with EGFR mutations and respond better to pemetrexed than SqCC.[2] Advanced NSCLC with EGFR mutations have a better outcome with tyrosine kinase inhibitors as a first therapy, whereas chemotherapy give better results in patients without EGFR mutations.[3] NSCLC harboring EML4-ALK translocations are responsive to ALK kinase inhibitors which almost exclusively in LADC.[3]As morphological subtype of lung cancer directly impact therapy, the precise distinction of sub types has become imperative**.**

Cytology is a major, diagnostic modality used in the initial evaluation of patients with lung cancer because 70% of lung cancers are unresectable as patients present in advanced stages.[3]Various types of cytology

specimens are available. Of these, FNAs offer the highest sensitivity (80–95%) and specificity (98–100%) in diagnosing malignancies, which is further improved by radiological techniques, such as USG and CT, which permit a better guidance and improve the modalities to limit complications.[4]

On comparison, FNAs & core biopsies are equivalent to classifying NSCLC and for molecular testing if sufficient material yielding recorded. For heterogeneous lesions, FNAs may outperform cores because of their strength to sample different aspects of the lesion with a single pass.[2]

One of the constraints of the FNA smear is the limited material for precise diagnosis and the risk of false negative or intermediate diagnosis always exists. In order to overcome these problems, CB technique has been resorted to make the best use of the available material for adjuvant investigations including IHC.[5] CB mimics as histology sections and support in further classifying various neoplastic lesions.

This study focused on the contribution of CB analysis to the diagnostic yield in lung cancer. The performance characteristics of CS and CB in lung cancer diagnosis and sub typing, particularly in reference to IHC stains is not well-established. This has made us to take this interesting study.

II. Material And Methods

This was a hospital based, cross sectional, observational study conducted over a period of 12 months, extending from May 2016 to May 2017. Chi square test and fisher exact test were used for nominal/categorical variables. 'Z' test for difference between two proportions were used to compare sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Sensitivity, specificity, PPV and NPV of CS and CB diagnosis were calculated as per standard formulae. P value<0.05 was considered statistically significant.

All the FNAC cases from lung masses diagnosed as "malignancy" or "suspicious for malignancy" on cytology smear preparation, irrespective of age and gender during study period, were included. Whereas the cases in which cell block preparation of aspirated material or biopsy from lung mass was not available were excluded from this study.

Study method:

After receiving the sample, all relevant clinical information regarding age, sex, smoking history and radiological findings of the patients has been recorded. Cytology samples were obtained by USG or CT scan guided procedure. Cytology smear (CS) were stained with May-Grünwald Giemsa stain (MGG), Hematoxylin & Eosin stain (H&E), Papanicolau stain and Cell block (CB) were stained with H&E stain. CS and CB were examined independently by different pathologists. The final diagnosis based on histopathology report (HPR)/IHC was considered the gold standard for determination of accuracy.

III. Results

During the study period a total of 85 cases were selected on the basis of CS- diagnosed as "lung malignancy" or "Suspicious for malignancy". The diagnosis based on CS and CB were categorized and evaluated in following groups:

a) Positive for malignancy (PFM);
b) Suspicious for malignancy(SFM)/Non-diagnostic(ND);
c) Subtyped carcinomas – LADC, SqCC, SCLC;
d) Unclassified carcinomas (NSCLC-NOS);
e) Malignant neoplasm.

On CS, 91.25 % cases were diagnosed as PFM, 14.12% cases were as SFM which would require further investigations for diagnosis. Among PFM cases 34.12% cases were subtyped, 35.29% cases subtyping could not be achieved and reported as NSCLC-NOS, 16.47% cases were classified as "malignant neoplasm". (Table no. 1)

Table 1: Distribution of 85 cases on basis of CS diagnosis

CS		**No.**	**%**
PFM 73(85.88%)	**NSCLC-NOS**	30	35.29
	LADC	18	21.18
	SqCC	08	9.41
	SCLC	03	3.53
	Malignant neoplasm	14	16.47
SFM		12	14.12
Total		85	100.00

SFM, Suspicious for malignancy*SFM cases were considered NFM (negative for malignancy) for purpose of calculation in study.

All 73 cases (100%) diagnosed as PFM on CS were confirmed PFM on final diagnosis. Out of 12 cases (100%) diagnosed as SFM on CS, 7 cases (58.33%) were diagnosed as PFM and remaining 5 cases (41.67%) were reported negative on final diagnosis. There was statistically significant association between CS and final diagnosis. (Table-2)

Table 2: Concordance of 85 cases between CS and Final diagnosis

CS	Final Diagnosis based on HPR+IHC				Total	
	NFM		PFM			
	No.	%	No.	%	No.	%
SFM	5	41.67	7	58.33	12	100.00
PFM	0	0.00	73	100.00	73	100.00
Total	5	5.88	80	94.12	85	100.00

Chi-square = 25.230 with 1 degree of freedom; P <0.001

Out of 43 cases of LADC, the CS alone could sub typed 18 (41.86%) cases as LADC. Out of 24 cases of SqCC, the CS alone could sub typed 8 (33.33%) cases as SqCC. Out of 7 cases of SCLC, the CS alone could sub typed 3 (42.86%) cases as SCLC. 1 case (100%) each of large cell lymphoma, malignant mesothelioma, adenosquamous carcinoma, poorly differentiated neoplasm and synovial sarcoma were classified as malignant neoplasm and could not be further sub classified on CS and 1 case of large cell lymphoma was reported as SFM. (Table-3, 11)

Table 3: Distribution of 85 cases on basis of concordance between CS and Final diagnosis

Final Diagnosis	CS													
	Malignant neoplasm		NSCLC-NOS		LADC		SqCC		SCLC		SFM		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
LADC	3	6.98	18	41.86	18	41.86	0	0	0	0.0	4	9.30	43	100.00
SqCC	2	8.33	12	50.00	0	0	8	33.33	0	0.0	2	8.33	24	100.00
SCLC	4	57.14	0	0.0	0	0	0	0	3	42.86	0	0.0	7	100.00
Large Cell Lymphoma	1	50.00	0	0.0	0	0	0	0	0	0.0	1	50.00	6	100.00
Adenosquamous carcinoma	1	100.00	0	0.0	0	0	0	0	0	0.0	0	0.0		
Malignant mesothelioma	1	100.00	0	0.0	0	0	0	0	0	0.0	0	0.0		
Poorly differentiated Neoplasm	1	100.00	0	0.0	0	0	0	0	0	0.0	0	0.0		
Synovial Sarcoma	1	100.00	0	0.0	0	0	0	0	0	0.0	0	0.0		
NFM	0	0.0	0	0.0	0	0	0	0	0	0.0	5	100.00	5	100.00
Total	14	16.47	30	35.29	18	21.18	8	9.41	3	3.53	12	14.12	85	100.0

On CB, 98.75 % cases were diagnosed as PFM, 5.88% cases had atypical cells were reported as SFM which would require further investigations for diagnosis. Among PFM 71.76% cases were subtyped, 8.24% cases subtyping could not be achieved and were reported as NSCLC-NOS, 12.94% cases were classified as "malignant neoplasm". (Table no. 4)

Table 4: Distribution of 85 cases on basis of CB diagnosis

CB		No.	%
PFM 79(92.94%)	**LADC**	38	44.72
	SqCC	18	21.18
	SCLC	5	5.88
	NSCLC-NOS	7	8.24
	Malignant neoplasm	11	12.94

SFM	5	5.88
Non diagnostic	1	1.17
Total	85	100.00

All 79 cases (100%) diagnosed as PFM on CB were confirmed PFM on final diagnosis. All 5 cases (100%) of SFM on CB were reported negative on final diagnosis. 1 case which was non diagnostic on CB was reported PFM. There was statistically significant association between CB and final diagnosis. (Table-5)

Table5: Concordance of 85 cases between CB and final diagnosis

CB	**Final Diagnosis**				**Total**	
	NFM		**PFM**			
	No.	**%**	**No.**	**%**	**No.**	**%**
SFM	5	100.00	0	0.00	5	100.00
ND	0	0.00	1	100.00	1	100.00
PFM	0	0.00	79	100.00	79	100.00
Total	5	5.88	80	94.12	85	100.00

Chi-square = 55.706 with 1 degree of freedom; P <0.001

Out of 43 cases of LADC, the CB alone could sub typed 38 (88.37%) cases as LADC. Out of 24 cases of SqCC, the CB alone could sub typed 18 (75%) cases as SqCC. Out of 7 cases of SCLC, the CB alone could sub typed 5 (71.43%) cases as SCLC. Each case of large cell lymphoma, adenosquamous carcinoma, malignant mesothelioma, poorly differentiated neoplasm and synovial sarcoma were classified as malignant neoplasm and could not be further sub classified on CB without IHC. (Table-6) Concordance of 85 cases between CS and CB were depicted. (Table-7)

Table 6: Distribution of 85 cases on basis of concordance between CB and Final diagnosis

Final Diagnosis	**CB**															
	LADC		**Malignant neoplasm**		**NSCLC-NOS**		**SCLC**		**SqCC**		**SFM**		**ND**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
LADC	38	88.37	2	4.65	2	4.65	0	0.0	0	0.0	0	0.0	1	2.33	43	100.0
SqCC	0	0.0	1	4.17	5	20.83	0	0.0	18	75.0	0	0.0	0	0.0	24	100.0
SCLC	0	0.0	2	28.57	0	0.0	5	71.43	0	0.0	0	0.0	0	0.0	7	100.0
Large Cell Lymphoma	0	0.0	2	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	6	100.0
Malignant Mesothelioma	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0		
Adenosquamous carcinoma	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0		
Poorly Differentiated Neoplasm	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0		
Synovial Sarcoma	0	0.0	1	100.0.	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0		
NFM	0	0.0	0	0.00	0	0.0	0	0.0	0	0.0	5	100.0	0	0.0	5	100.0
Total	38	44.70	11	12.94	7	8.23	5	5.88	18	21.18	5	5.88	1	1.18	85	100.0

Table 7: Concordance of 85 cases between CS and CB

CS	**CB**				**Total**	
	SFM		**PFM**			
	No.	**%**	**No.**	**%**	**No.**	**%**
SFM	5	41.67	7	58.33	12	100.00

PFM	1*	1.36	72	98.64	73	100.00
Total	6	7.06	79	92.94	85	100.00

In group of PFM on CS, 72 (98.64%) cases were PFM on both CB and CS. 1(1.36%) case was non diagnostic on CB which was reported as PFM on CS. In group of SFM on CS, 7 cases (58.33%) were diagnosed as PFM and remaining 5 cases (41.67%) were also reported as SFM on CB. There was statistically significant association between CS and CB.

The CS and CB showed sensitivity of diagnosing malignant lung lesions was 91.25% and 98.75%, specificity was 100% in each, positive predictive value was 100% in each, negative predictive value was 58.33% and 83.33% and overall diagnostic accuracy was 91.76% and 98.82% respectively.(table-8) In the assessment of agreement between two methods of sample preparation(CS and CB), CB served better than CS. However, this difference was not found statistically significant. (Table-8)

Table 8: Comparative analysis of CS and CB for the diagnosis of lung malignancy in relation to final Diagnosis

	CS		**CB**		**'p' Value***
	No.	**%**	**No.**	**%**	
Sensitivity	73/80	91.25	79/80	98.75	0.070
Specificity	5/5	100.00	5/5	100.00	NA
PPV	73/73	100.00	79/79	100.00	NA
NPV	7/12	58.33	5/6	83.33	0.596
Accuracy	78/85	91.76	84/85	98.82	0.070

*'Z' test for difference of two proportions

In the assessment of agreement between two methods of sample preparation(CS and CB), CB served better than CS. However, this difference was not found statistically significant.

Additional diagnostic yield by CB for diagnosing the lung malignancy was improved by 7.06%.
10 cases of NSCLC were evaluated for suitability of immunomarker (TTF-1, p63 and CK antibody) study on CB and showed 100% satisfactory results for positive and negative expression. (Table-9)

Table 9: Pilot study: Immunomarker study on CB and Biopsy. (Positive / negative expression)

Marker	**Diagnosis**	**CB**		**HPR**		**Total**
		Positive (%)	**Negative (%)**	**Positive (%)**	**Negative (%)**	
TTF-1	**LADC**	6 (100.0)	0 (0.00)	6 (100.0)	0 (0.00)	6 (100.0)
	SqCC	0 (0.00)	4 (100.0)	0 (0.00)	4 (100.0)	4 (100.0)
p63	**LADC**	0 (0.00)	6 (100.0)	0 (0.00)	6 (100.0)	6 (100.0)
	SqCC	4 (100.0)	0 (0.00)	4 (100.0)	0 (0.00)	4 (100.0)
CK	**LADC**	6 (100.0)	0 (0.00)	6 (100.0)	0 (0.00)	6 (100.0)
	SqCC	4 (100.0)	0 (0.00)	4 (100.0)	0 (0.00)	4 (100.0)

Out of 85 cases, LADC (50.59%) was the commonest primary lung cancer. 28.24% cases were diagnosed as SqCC, 8.24% cases were diagnosed as SCLC, 2.35% cases were diagnosed as large cell lymphoma and 1.18% case was diagnosed respectively each of adenosquamous carcinoma, malignant mesothelioma, synovial sarcoma and poorly differentiated neoplasm.

Maximum incidence of lung cancer including both sexes was seen in age group 61-70 years and 51-60 years being 28.75% and 27.50 % respectively. Maximum cases of LADC (54.55%) and SqCC (31.82 %) were diagnosed in >50 years of age.

Male predominance (80%) was seen with male/female ratio being 4:1. Most subtypes of lung cancer were prone to involve males. Among the female most frequent diagnosis was LADC (66.67%)

Among the positive for malignancy cases, 56.25 % cases were related to smoking, out of which LADC diagnosed in 51.11% cases and SqCC diagnosed in 37.78% cases. 70.83% case of SqCC cases were related to smoking.

In present study, 67.06% cases had peripherally located tumor, out of which most common tumor was LADC diagnosed in 68.42% cases. 32.94% cases had centrally located tumor, among which 100% cases of SCLC were centrally located.

The overall rate of complications (2.35%) encountered in our study was remarkably less. No fatalities were reported in our study.

IV. Discussion

Image guided lung FNAC (CS) is a simple, minimally invasive, relatively safe, and rapid reliable technique with diagnostic accuracy ranging from 70.8%[7] to 95.9%[6], sensitivity ranging from 92.2% to 97.7%[6,7,8,9,] specificity of 100%. [6,7,8,9]

CS group:

PFM - In present study, sensitivity of lung FNAC was 91.25% and specificity was 100%. Various other studies reported sensitivity of lung FNAC ranging from 84.2% to as high as 97.7% and specificity from 76% to as high as 100%.[6,8,9,10,11]

In present study, PPV for detecting lung malignancy was 100% and NPV was 58.33%. Konjengbam et al.[11] and Roy et al.[10] have reported PPV being 94.3% and 100% respectively and NPV being 91.3% and 47.62% respectively.

SFM - In present study, 14.12% were reported as SFM, which require further investigations (Biopsy/IHC/ Re-aspiration) for diagnosis. Sharma et al.[12], and Roy et al.[10] also reported 20.98% and 10% cases of SFM respectively while Konjengbam et al.[11] reported 3.5% cases of SFM.

Due to suboptimal preservation and fixation of smears; Poor spreading, presence of thick tissue fragments and air drying artifact despite aspiration of adequate material; Degenerated cells with hyper chromatic nuclei, reactive pneumocytes/ histiocytes may add to confusion in interpretation of cells.

Sub typed carcinomas- In present study, 34.12% cases were subtyped on CS alone which were further confirmed on biopsy and IHC. Sharma et al.[12] and Nizzzoli et al.[13] could achieve specific diagnosis of lung cancer in 71.60% cases and 85% cases respectively. L**ow percentage of sub typed carcinoma on CS in present study is assumed due to** paired specimens which may not be entirely representative of the individual (CS along with CB/biopsy), Rigid cytological criteria used for the various tumor types; poor diff erentiation of the tumor where distinguishing morphologic features are not apparent; Scant cellularity; Tumor heterogeneity.

41.86% cases of LADC, 33.33% cases of SqCC and 42.86% cases of SCLC could be sub typed on CS alone which were further confirmed on biopsy. Thus, there was 100% concordance between CS and biopsy for identifying LADC, SqCC and SCLC.

Hasanovic et al.[15] and Nandeesh et al.[14] have also reported high concordance between CS and resected specimens for identifying LADC of 93% and 91%, for SqCC of 97% and 100%, respectively. Roy et al.[10] also reported 83.3% of concordance between CS and histology for diagnosing SCLC.

Sharma et al.[12], Nizzoli et al.[13] and Roy et al.[10] were able to subtype LADC in 29.31%, 56% and 65.7% and SqCC in 62.06%, 44% and 46.6% cases respectively. Sharma et al.[12] could achieve sub typing in 40% cases of SCLC.

NSCLC-NOS - In 35.29% cases subtyping could not be achieved, out of which 60% cases were diagnosed as poorly differentiated LADC and 40% cases were diagnosed as poorly differentiated SqCC on biopsy and immunomarkers study.

The reported percentage of unclassified NSCLC varies significantly among prior studies, being unclassified NSCLC percentage of 34% in Edwards et al.[16], and 15% in Nizzoli et al. [13]

In present study, 16.47% cases were classified as "malignant neoplasm" which could not be further sub classified on CS. These groups includes poorly differentiated tumors and cases such as large cell lymphoma (2.35%), malignant mesothelioma (1.18%), adenosquamous carcinoma (1.18%) and synovial sarcoma (1.18%) which are known to have variable morphology and variable cellularity and usually require biopsy along with immunomarkers study for diagnosis.

In contrast to our study, other studies had also reported various tumors such as lymphoma, spindle cell neoplasm, thymoma, Fibrosarcoma, plasmacytoma, seminoma, melanocarcinoma.[8,9,10.]

In present study, there was a statistically significant agreement for detecting lung malignancy between cytologic and histologic diagnosis ($P < 0.001$) which was correlating with study done by Nandeesh et al.[14] and Nizzoli et al.[13] reported p<0.001.

CB group:

PFM -In Present study, 98.75% cases were diagnosed as PFM on CB alone which were further confirmed on biopsy and no false positive cases were noted. Kshatriya et al.[4], and Basnet et al [5] reported sensitivity of CB being 89% and 95.91% respectively.

SFM- 5.88% cases had atypical cells; require further investigations (Biopsy/IHC/ Re-aspiration) for diagnosis. Nair et al.[21], Yung et al.[18] and Thapar et al.[22] reported 2.56%, 28.6% and 11.4% cases of SFM respectively while in study done by Ugurluoglu et al.[58], none of the cases were reported as SFM on CB.

Non diagnostic (ND) 1.18% case was non diagnostic due to inadequacy of material which would require further investigations for diagnosis. Sanz- santos et al.[19] and Yung et al.[18] reported 10.3% and 14.3 % cases of non diagnostic material on CB.

Sub typed carcinoma- 88.37% cases of LADC , 75% cases of SqCC and 71.43% cases of SCLC could be sub typed on CB alone which were further confirmed on biopsy .Thus, there was 100% concordance between CB and biopsy.

Yung et al.[18], Ugurluoglu et al.[17] and Sanz-santos et al.[19] reported that additional pathologic information provided by CB being 57.1% ,21.7% and 26.4% cases respectively .But these studies have not mentioned individual subtyping of carcinomas on CB. So, comparison of our results with individual subtyped carcinomas on CB with these studies was not possible.

NSCLC-NOS - In 8.24% cases sub typing could not be achieved, out of which 28.57% cases were diagnosed as poorly differentiated LADC and 71.43% cases were diagnosed as poorly differentiated SqCC on biopsy and immunomarkers study.

Malignant neoplasm- 12.94% cases were classified as "malignant neoplasm" which could not be further sub classified on CB. These groups includes cases such as large cell lymphoma (2.35%), malignant mesothelioma (1.18%), adenosquamous carcinoma (1.18%) and synovial sarcoma (1.18%) which are known to have variable morphology and cellularity and usually require biopsy along with immunomarkers study for diagnosis.

In our study, CBs were instrumental in improving the overall positive results in 7 additional cases in comparison to CS and increasing the sensitivity for detecting malignancy from 91.25% to 98.75%. On the other hand, 1.18% case which was nondiagnostic on CB was subtyped on CS. **Thus, by combining CS and CB method, it is possible to reach comparable results with biopsy for detecting malignancy.**

Most of the other studies also showed that CB has an added advantage and increased sensitivity for diagnosis of lung malignancy from 9% to as high as 50%.[7,12]

While in contrast, few studies reported that CB has not an added advantage but in fact CS was superior to CB due to superior preservation of nuclear and cytoplasmic characteristics in PAP smears. [20]

In present study, CB has proved superior to CS in diagnosis of LADC by 46.51%, SqCC by 41.67% and SCLC by 28.57%. (Table-10)

Table 10: Comparison of CS and CB in sub typing of carcinomas

Final diagnosis(HPR+IHC)			CS		CB	
	No.	%	No.	%	No.	%
LADC	43	100	18	41.86	38	88.37
SqCC	24	100	08	33.33	18	75
SCLC	07	100	03	42.86	05	71.43

Comparison of CS and CB in various groups: CB proved superior to CS in group of "subtyped carcinoma", "NSCLC-NOS" and "SFM" by improving yield being 37.64%, 27.05% and 8.24% respectively. **In group of "malignant neoplasm", CB improved diagnostic yield by 3.53% only. But this group has special importance as with the application of IHC markers on CB, the diagnostic yield can also be achieved comparable to biopsy.** In 1.18% case, CB was inferior to CS due to inadequacy of material.

In present study, diagnostic yield improved on CB by 7.06% Most of the other studies also show that CB has achieved additional diagnostic yield from 5 % to as high as 35%.[4,19,21,22,23,24,25,26,27,31.] (Table-11)

Table 11: A comparative review of literature pertaining to additional diagnostic yield by CB for diagnosis of the lung malignancy

Sr. No.	Study	Year	Additional diagnostic yield by CB (%)
1	Thapar et al.[22]	2009	13
2	Sanz-Santos et al.[19]	2012	7.7
3	Shivkumarswamy et al.[23]	2012	15
4	Mutreja et al.[24]	2012	17
5	Köksal D et al.[25]	2013	10
6	Grandhi et al.[26]	2014	12
7	Nathani R et al.[27]	2014	05
8	Nair et al.[21]	2015	35

9	Kshatriya et al.[4]	2016	09
10	Pawar et al.[31]	2016	12
11	**Present study**	**2017**	**7.06**

Thus, histology can be easily correlates with cytologic findings by combining of CB with smears. However, some criteria of cytology not go together with histology and vice versa, so to avoid diagnostic pitfall cell blocks and smears studied together instead of using either cytology or histology alone.[5]

A Pilot study was conducted on randomly selected 10 cases of NSCLC. TTF-1, p63 and CK immunostaining has been successfully applied CB material which showed 100% cases of LADC with strong, diffuse, nuclear positivity for TTF-1 and 100% negativity for p 63. 100% cases of SqCC expressed strong, diffuse, nuclear positivity for p63 and 100% negativity for TTF-1. CK antibody expressed positivity in 100% cases with strong diffuse cytoplasmic and membranous expression.

All 10 cases were compared with IHC study on biopsy specimen and detected that CB preparation is suitable for IHC study and results were comparable to biopsy specimen.

Various other studies such as Kapila et al.[28], Kulshrestha et al.[29], Righi et al.[30] and Gupta et al.[3] evaluated CB for IHC markers (e.g.TTF-1, P63, CK-7) and observed that IHC has been successfully applied to CB to facilitate pathological differentiation.

V. Conclusion

Lung FNAC, in expert hands, is simple, fairly sensitive, relatively safe, minimally invasive and rapid reliable technique for detecting the lung malignancy. CB and smears together accompanied to arrive a more definitive cytopathologic diagnosis. A benefit of combining cell blocks with smears is possible to reach comparable results with biopsy for detecting malignancy. Only limitation when adequate material is not achieved which can be overcome by having dedicated pass for CB alone. Rapid on-site evaluation (ROSE)" for adequacy of material helps in reducing inconclusive diagnosis.

A limited panel of IHC immunomarkers can be used on CB as it is suitable for IHC study to further histotyping of originally diagnosed as NSCL–NOS in FNAC specimens. In today's era of personalized medicine, further studies on larger scale are necessary with an in depth analysis to determine suitability of CB material for other ancillary and molecular studies.

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