

## Original Research Article

# FNAC, cell block and core needle biopsy in diagnosis of lung masses: a necessity or choice?

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### ABSTRACT

**Background:** Lung cancer is the commonest cancer mortality in the world. In targeted therapy era, precise cytohistological diagnosis is offered traditionally by FNAC, Cell Block (CB) and Core Needle Biopsy (CNB). However, little is known whether one technique is superior to other or all the three techniques complement each another. Therefore, this is a unique study as no other study has compared these techniques together till date. The objective of the study was to evaluate performance of FNAC, Cell block (CB) and Core Needle Biopsy (CNB) individually and comparing them with each other.

**Methods:** This was a prospective study of 50 cases who underwent two passes-1<sup>st</sup> for FNAC smears and Cell Block and 2<sup>nd</sup> for CNB.

**Results:** Material was Inadequate in 8 cases by FNAC 16 with Cell Block and 02 with CNB. When adequate, diagnosis and typing was possible by Cell Block (32) and CNB (48). In 08 FNAC cases having adequate material, cytological typing wasn't possible. These 08 cases were typed by cell block as 07 malignant and 01 pre-malignant. The combined inadequate cases with cyto-technique (FNAC and Cell Block) were 04 compared to 02 cases on CNB. Combined sensitivity of Cyto-techniques was 95.4% compared to 97% on CNB. The specificity was 100% for both Cyto-techniques and CNB.

**Conclusions:** Diagnostic adequacy and test parameters improved and approached CNB when both cyto-techniques are combined. So, we strongly recommend that Cell Block be made routine diagnostic procedure in all the government institutions especially for guided FNAC.

**Keywords:** Cell block, Core needle biopsy, FNAC, Lung masses

### INTRODUCTION

Lung cancer is the most common cause of cancer-related mortality in the world. Its early and accurate diagnosis is the key for the optimal treatment.<sup>1,2</sup> In this era of targeted therapy, precise cytological and histological diagnosis is required.<sup>3</sup> This can be offered traditionally by FNAC, another cytology technique Cell Block (CB) and thirdly Core Needle Biopsy (CNB) which is competing these days with both the cytological techniques. Cell Block has an added advantage over FNAC of providing tissue

architecture and use of ancillary techniques.<sup>4</sup> CNB on the other hand is a gold standard.

However, very little is known whether one technique is superior to other or all the three techniques complement each another.

A thorough search was done using 'FNAC', 'Cell Block', 'CNB', 'comparison' and 'Lung' as key words, but no study was found comparing all the three techniques together. Instead study comparing FNAC with Cell Block

or FNAC with CNB were found. Therefore, this is a unique study of its own kind as no study is performed comparing all the three techniques together till date.

This study was conducted with the objective to evaluate performances of

- FNAC, Cell Block and CNB techniques in the diagnosis of lung masses,
- To compare the findings of cytology (FNAC and Cell Block) with Core Needle Biopsies,
- To establish technique of Cell Clock as a routine diagnostic procedure in the institute.

**METHODS**

The present study “Comparative Study of FNAC, Cell Block and Core Needle Biopsy in Lung Masses” is a Cross sectional prospective diagnostic test study and was carried out in Department of Pathology over two years with total 50 number of cases. Patients above 18 years of age with lung mass detected on X-ray or CT thorax and having normal coagulation profile were included in the study.

All the three procedures were performed on each patient under CT guidance with two dedicated passes. First pass was used to make FNAC smears and the left-over material was used for Cell Blocks. From second pass CNB was performed.

After taking consent and detail history of the patient, the mass was localized and an appropriate position was given to the patient. Prone position was preferred as interference of respiratory movements are minimal in this position. The area of interest was cleaned with Betadine and spirit. Local anaesthesia was given only for CNB.

CT guided FNAC of lung lesions was done using disposable 22G, 90mm long lumbar puncture needle with trocar. The needle is sufficiently rigid and trocar prevents contamination during the passage through surrounding tissue. The aspirate is obtained by to and fro movements of the needle within the lesions and four smears were prepared. CT guidance gave advantage of precise location of needle, angle of entry and route of entry of needle. Immediately after aspiration, two smears were wet fixed in 95% alcohol and were subsequently stained by H&E and papanicolau. Two smears were dried for MGG and AFB stain.

The left-over material after FNAC smears was used for Cell Block. The material left in needle hub was rinsed with normal saline and taken into glass test tubes. It was centrifuged at 4000 rpm for 10 minutes. After discarding supernatant, equal volume of control plasma and thrombin was added to the sediment. When the sediment was completely clotted, it was detached from the bottom of the test tube, fixed in formalin and processed for histology. CNB was performed using 18G Cook semi-

automated biopsy gun (Figure 1). This gun is 15cm long with 20mm throw length. After infiltration of 2% lignocaine, skin incision of 0.5mm was given. First a coaxial guide needle was inserted to guide the biopsy gun. Coaxial needle has a cannula and trocar (Figure 1). Coaxial needle helped taking multiple cores from the same point but from different directions. Total 05 cores were taken, fixed in formalin and processed. Tincture Iodine was applied at the site of skin incision. Post procedural CT scan was performed to check for pneumothorax and patient was observed for at least 6 hours for post procedural complications.



**Figure 1: 18-gauge semi-automated cook biopsy gun with trocar and cannula.**

All the FNAC smears and Cell Block diagnosed or reported were confirmed on histology i.e. CNB. CNB here is taken as gold standard.

**RESULTS**

Present study comprised of total 50 cases fulfilling the eligibility criteria. All the patients were recruited from chest OPD from December 2013 to September 2015. Out of total 50 cases, 78% were males. Table 1 shows gender wise distribution of total 50 cases.

**Table 1: Gender wise distribution of cases.**

Sex	No. of cases	%
Male	39	78
Female	11	22
<b>Total</b>	<b>50</b>	<b>100</b>

**Table 2: Age wise distribution of cases.**

Age (years)	No. of cases	%
20 – 30	03	06
31 – 40	03	06
41 – 50	05	10
51 – 60	13	26
61 – 70	20	40
71 – 80	04	08
81 – 90	02	04
<b>Total</b>	<b>50</b>	<b>100</b>

The age group ranged from 20 to 90 years. Most common age group encountered was between 61-70 years (40%) i.e. between 6<sup>th</sup> to 7<sup>th</sup> decades as shown in Table 2. Out of total 50 cases, 64% were smokers. Table 3 shows distribution of cases according to the smoking habit.

**Table 3: Distribution of cases according to smoking habit.**

Category	No. of cases	%
Smokers	32	64
Non-smokers	18	36
Total	50	100

In our study, we encountered maximum masses in left lower lobe (22%) followed by right lower lobe (16%) as shown in Table 4.

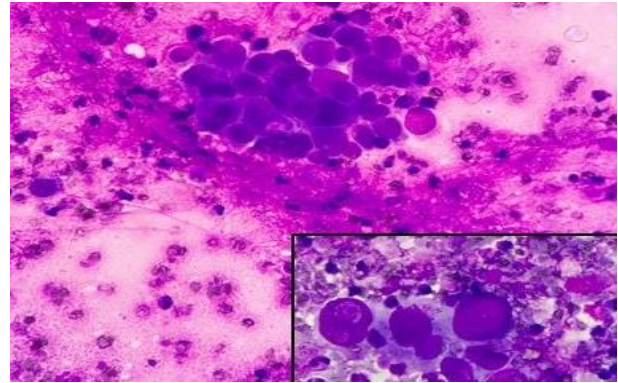
**Table 4: Distribution of cases according to the location of masses.**

Site of lesion	No. of cases	%
<b>Right lung</b>		
Ul	05	10
Ml	05	10
Ph	03	06
Ll	08	16
More than one lobe	06	12
<b>Left lung</b>		
Ul	06	12
Ph	02	04
<b>Ll</b>	<b>11</b>	<b>22</b>
More than one lobe	01	02
<b>Both lungs</b>		
Ul	01	02
Ml	00	00
Ph	00	00
Ll	01	02
More than one lobe	01	02
Total	50	100

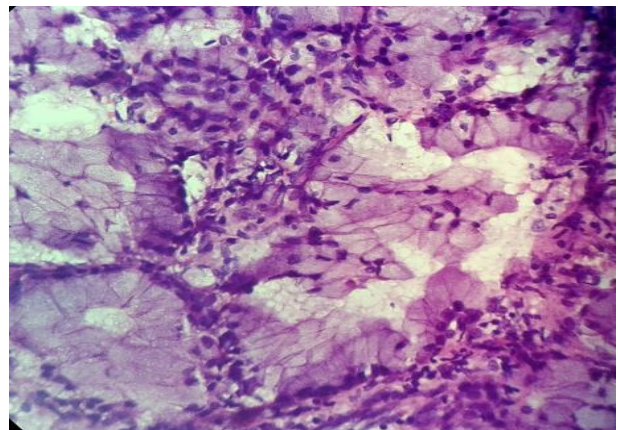
**Table 5: Conditions encountered in the study.**

Conditions	No. of cases	%
<b>Non – neoplastic</b>		
Granulomatous	02	04
Pneumonitis	01	02
Acute inflammatory lesion	01	02
<b>Neoplastic</b>		
Squamous cell carcinoma	14	28
Adenocarcinoma	13	26
Bronchioalveolar carcinoma (bac)	07	14
Small cell carcinoma (smcc)	06	12
Large cell anaplastic carcinoma (lcac)	02	04
Non – hodgkin’s lymphoma (nhl)	02	04
Metastasis	01	02
Dysplasia	01	02
Total	50	100

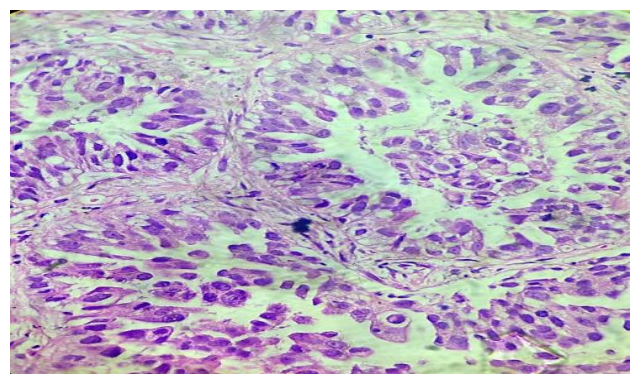
Various conditions encountered in our study are listed in Table 5. Most common condition encountered was Adenocarcinoma Lung. Rare and interesting cases like large cell anaplastic carcinoma, metastatic deposits of Osteosarcoma have also been encountered. Images of various conditions have been shown from Figure 2 to 5.



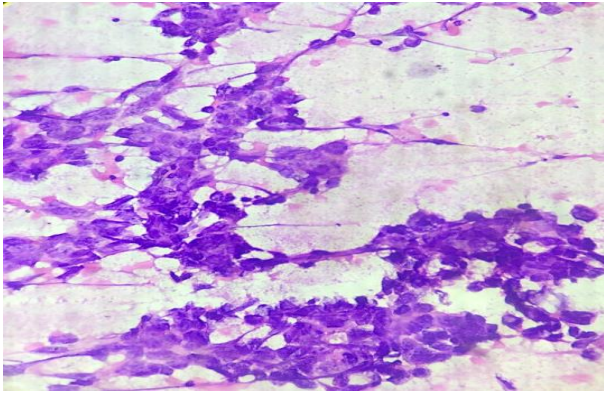
**Figure 2A: BAC (cytology smear) showing an ill-defined cluster of glandular cells with intranuclear cytoplasmic inclusion (inset) (MGG, 10x).**



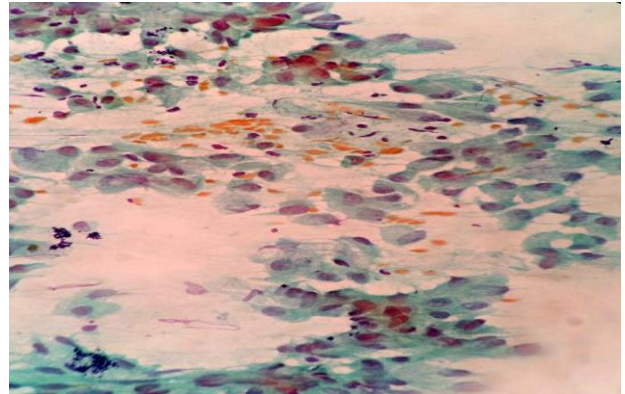
**Figure 2B: BAC (CB) showing mucus secreting columnar cells lining the respiratory spaces in a lepidic fashion without invading stroma. (H and E, 40x).**



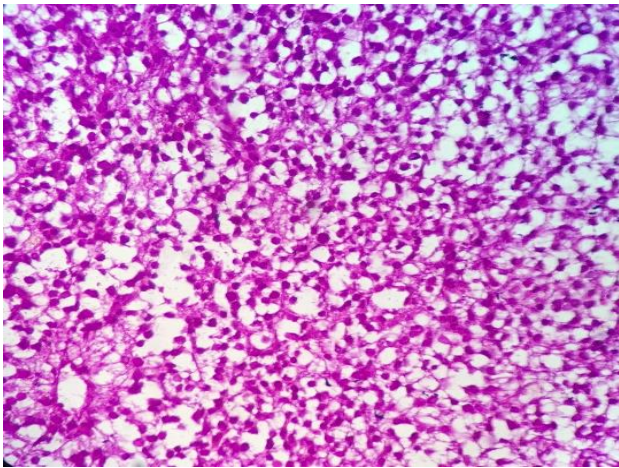
**Figure 2C: BAC (CNB) showing columnar cells lining the respiratory spaces in a lepidic fashion without invading stroma. (H and E, 40x).**



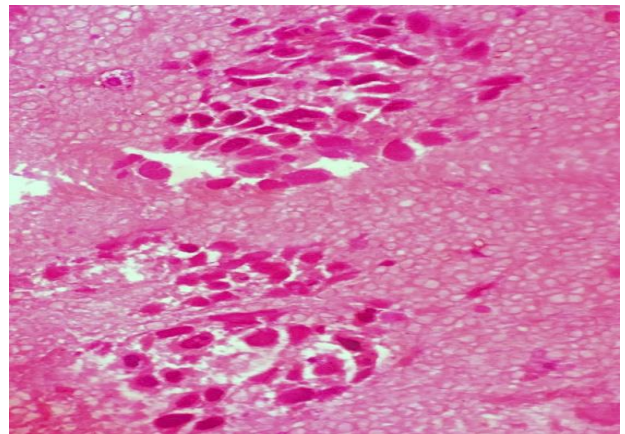
**Figure 3A: SMCC (cytology smear) showing small loose clusters with some dispersal, absence of cytoplasm, finely granular chromatin, inconspicuous nucleoli and smearing artefact (MGG, 40x).**



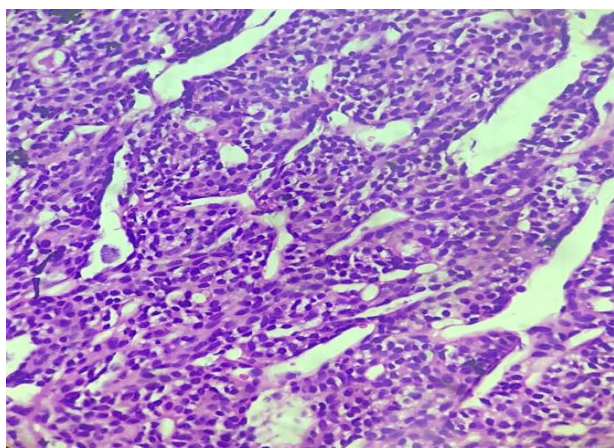
**Figure 4A: LCAC (cytology smear) showing discrete malignant cells having abundant cytoplasm with ill-defined margins, eccentric pleomorphic nuclei and coarse chromatin. There is no Squamoid or glandular differentiation (Pap, 40x).**



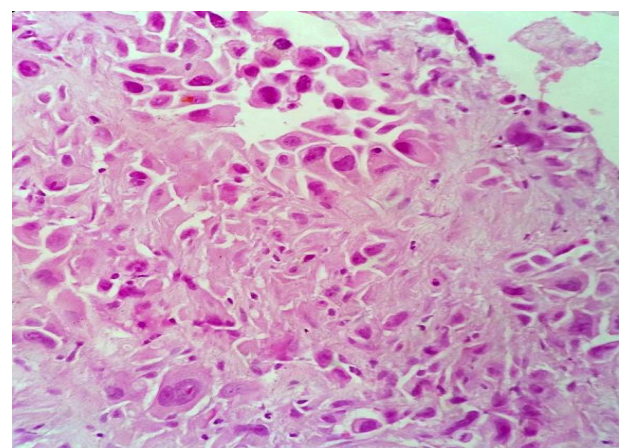
**Figure 3B: SMCC (CB) showing cells with darkly staining oval nuclei and extremely scanty cytoplasm. (H and E, 40x).**



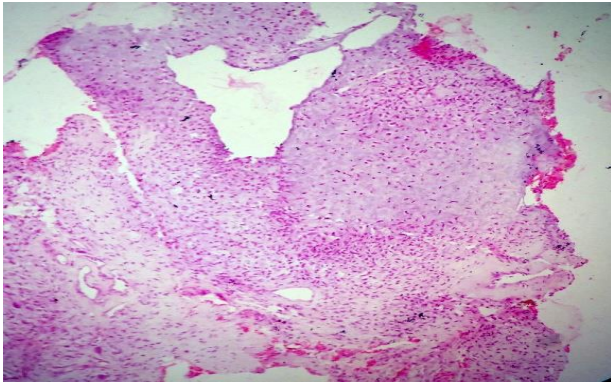
**Figure 4B: LCAC (CB) showing large pleomorphic cells with abundant cytoplasm, eccentric hyperchromatic nuclei. (H and E, 40x).**



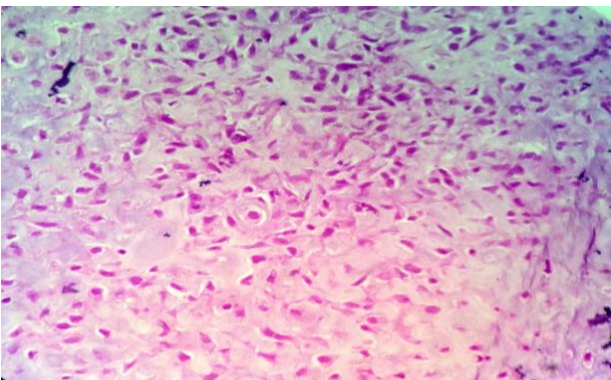
**Figure 3C: SMCC (CNB) showing cells with darkly staining oval to spindle nuclei and extremely scanty cytoplasm. (H and E, 40x).**



**Figure 4C: LCAC (CNB) showing large pleomorphic cells with abundant cytoplasm, eccentric pleomorphic, hyperchromatic nuclei. Binucleate cell seen at left lower corner. Prominent nucleoli seen at places. There is no squamoid or glandular differentiation. (H and E, 40x).**



**Figure 5A: Metastatic deposit of osteosarcoma (CNB) showing malignant osteoid intermittently mixed with spindle shaped tumour cells (H and E, 10x).**



**Figure 5B: Same (H and E, 40x).**

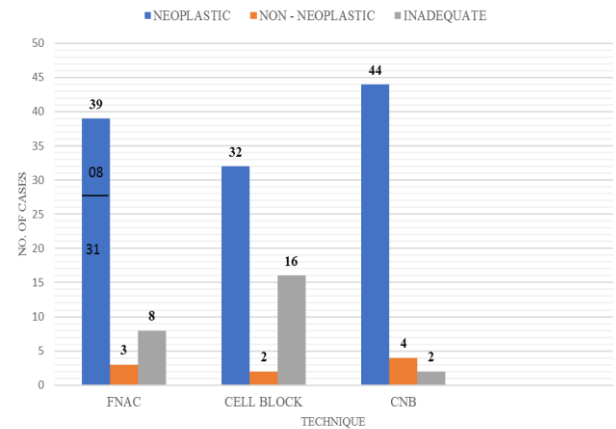
Distribution of cases on individual techniques is shown in Figure 6.

Inadequate cases on FNAC were 08, 16 on cell block and 02 on CNB. Out of 42 adequate cases on FNAC, 39 were neoplastic and 03 were non- neoplastic. Out of 39 neoplastic cases on FNAC it could accurately type the malignancy in 31 cases but in remaining 08 cases it could not type the malignancy and reported as poorly differentiated epithelial malignancy (as shown in Figure 6).

On Cell block, 32 cases were neoplastic and 02 were non-neoplastic and all these cases (32 + 02) were diagnosed and accurately typed. The gold standard CNB showed 44 neoplastic cases and 04 non- neoplastic.

The cell block having the advantage of tissue architecture could accurately type the malignancy in 08 cases where FNAC could not (reported as poorly differentiated epithelial malignancy).

The 08 cases of poorly differentiated epithelial malignancy on FNAC, cell block typed them into malignant (07) and as pre-malignant (01, severe dysplasia).

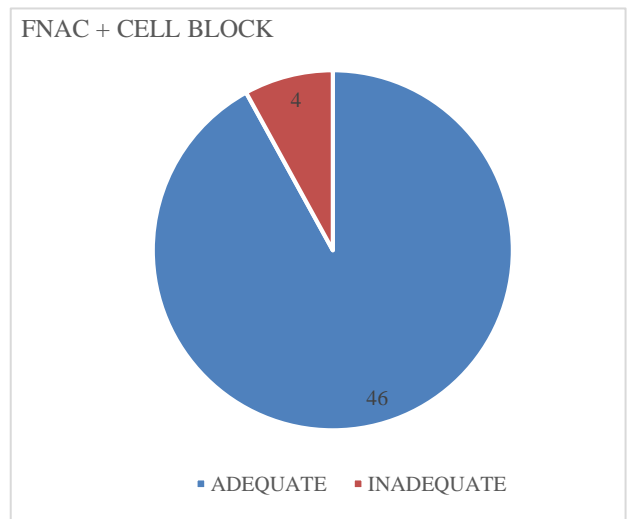


**Figure 6: Technique wise distribution of cases.**

On comparing the number of inadequate cases, as mentioned above, 08 were of FNAC and 16 were of CB. Out of 08 inadequate cases on FNAC, 06 cases were accurately diagnosed on CB whereas out of 16 inadequate cases on CB, FNAC was able to make diagnosis of 14 cases only. So, the combined inadequate cases on cytology techniques (FNAC and Cell Block) have reduced to 04 than the individual test alone (Table 6 and Figure 7) i.e. total 04 cases were still undiagnosed on both the cytology techniques.

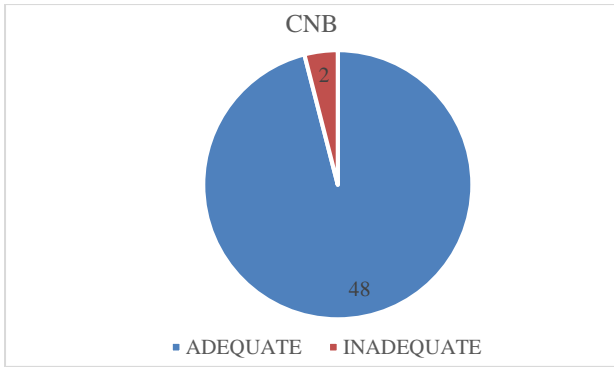
**Table 6: Inadequate cases on cytology techniques.**

Cytology techniques	Inadequate cases	Accurately typed (FNAC/ CB)	Still undiagnosed
FNAC	08	06 (on CB)	02
CB	16	14 (on FNAC)	02
FNAC+ CB	24	20	04



**Figure 7: Adequacy criteria on combined cytology techniques.**

Figure 8 shows that there were only 02 inadequate cases on CNB as mentioned above.



**Figure 8: Adequacy criteria on core needle biopsy.**

So, on comparing both cytology and histology, the difference of inadequate cases have reduced. The difference is of only 02 cases. Table 7 shows comparison of cytology techniques and Core Needle Biopsy.

**Table 7: Inadequate cases on both cytology and core needle biopsy.**

Techniques	Inadequate cases
FNAC+ CB	04
CNB	02
Difference	02

Studying the diagnostic parameters of all the three techniques, sensitivity and specificity of FNAC were 89% and 75% respectively, for Cell Block it was 73% and 100% respectively. The test parameters of gold standard CNB were 97% and 100% respectively. However, the combined sensitivity of both the Cyto-technique was much higher i.e. 95.4% than the individual techniques alone and was much closer to gold standard i.e. CNB whereas specificity was same i.e. 100%. Test parameters of all the three techniques are shown in Table 8.

**Table 8: Comparison of the test parameters of all the three techniques.**

Procedure	Sensitivity	Specificity
FNAC	89%	75%
Cell Clock	73%	100%
FNAC + cell block	95.4%	100%
CNB	97%	100%

**DISCUSSION**

CT guided transthoracic FNAC is a relatively simple, low cost, quick, safe, well tolerated and minimally invasive procedure.<sup>5</sup> The cell block technique employs the retrieval of small tissue fragments from a FNA specimen which are processed to form a paraffin block.<sup>6</sup> It is widely accepted that cell block technique increases the cellular yield and improves diagnostic accuracy. Cell Block is easy, inexpensive and does not require a special team or instruments.<sup>7</sup> With this method, cellularity is increased,

the morphological details are better observed, special histo-chemical staining and immune histo-chemical studies can be done.<sup>4</sup> Cell Block sections offer advantages over conventional cytological smears with respect to cellular architecture and archival storage. They also provide several sections, which can be utilized to perform special stains, immune-phenotypic analysis, ultra-structural studies and molecular tests, including cytogenetic and polymerase chain reaction (PCR) based techniques.<sup>8</sup> In our study Cell blocks were prepared simultaneously from residual material after FNAC smear preparation. There is sparse corroborative study in the literature on the routine use of cell blocks, probably because of differing emphasis placed on them in various institutions.<sup>6</sup>

Core needle biopsy (CNB) is a safe rapid method used to achieve definitive diagnosis for most thoracic lesions, whether the lesion is located in the pleura, the lung parenchyma, or the mediastinum. Diffuse disease and solitary lesions are equally approachable.

The peak age of incidence (60-69 years) was the same as that documented in the study of Wallace et al.<sup>9</sup> The reason may be due to increased incidence of malignancy in this age group. There was male preponderance (78%) in our study compared to female. This was well correlated with studies of Tan KB et al where males were 71%, Bandyopadhyay A et al with 80.6% of males and Saha A et al having 78.9% males.<sup>10-12</sup>

In this study, lung tumors were located more on the left side than on the right in contrast to the study of Santosh et al where in tumors were located more on right side. In our study, 64% were smokers and it's an established fact that smoking is strongly associated with lung cancer. Muhammad Furrukh also showed that smoking is strongly associated with lung cancer.<sup>13</sup> The most common condition encountered in our work was Adenocarcinoma lung which was very well correlated with studies of Santosh Kumar Mondal et al, Tan et al and Madan et al who also reported Adenocarcinoma as most common condition.<sup>5,10,14</sup>

In our series total neoplastic cases on FNAC were 39, out of which it could accurately type the malignancy in 31 cases but in 08 cases further subtyping was not possible. In these 08 cases, Cell Block was able to accurately type the lesions as 07 specific malignancy and 01 as severe dysplasia. All the adequate cases on Cell Block and CNB were accurately diagnosed and typed. So, cell block provided diagnostic architectural information which complemented FNA smears.<sup>15</sup> Zito and others observed that FNAC sometimes does not yield information for precise diagnosis, and the risk of false-positive diagnosis and indeterminate diagnosis is always present.<sup>16</sup>

However, the inadequacy with Cell Block was much higher than the FNAC in our study and it was because it was a split sample study where in left over material was

used for Cell Block. This was limitation of our study and it was unavoidable because one pass for each FNAC and Cell Block would do more harm than good to the patient. Study by Shehnaz Khan et al also reported to have inadequacy with Cell Block, they reported 8.5% of inadequacy with cell block which was quite low when compared with our study.<sup>6</sup> Their study included 47 cases of which separate pass for cell block was done in 30 cases. A separate dedicated pass for the cell block was not performed in our study and this was the limitation of our study.

The success or failure of obtaining adequate cell block samples is largely dependant on the skill of the aspirator and high cellularity of the aspirate.<sup>17,18</sup>

Though we did not require IHC, it can be performed on Cell Block whenever needed which is an added advantage to tissue architecture by same.

When we compared combined inadequate cases of both FNAC and Cell Block (cytology techniques) together with CNB the difference was of only 02 cases. In view of this, both FNAC and Cell Block complemented each other. Study by Shehnaz Khan et al and Akalin A et al also concluded that both the methods complement each other.<sup>6,15</sup> Nathan et al in their study found that Cell Block supported diagnosis where FNAC smears were insufficient.<sup>19</sup>

The combined sensitivity and specificity of both the cytology techniques (FNAC and CB) were 95.4% and 100% respectively. This result was very well co-related with the study of Salah Abobaker Ali, which concluded that combined sensitivity and specificity of both FNAC and CB were 97% and 97.5% respectively.<sup>20</sup> Also, study by Raafat Awad Hegazy et al showed combined sensitivity and specificity of 94% and 98% respectively.<sup>21</sup> Similarly when we compared the combined sensitivity and specificity of both FNAC and CB together (95.4% and 100%) with that of CNB (95.6% and 100%), it was very close and comparable. This finding was agreed with the study by Salah Abobaker Ali, who also compared the combined sensitivity of both FNAC and CB together with that of CNB but on intra-abdominal tumours. They found that sensitivity and specificity of both FNAC and CB together were 97% and 97.7% respectively and for CNB it was 75% and 91% respectively.<sup>20</sup>

On the other hand, CNB offers the advantage of making multiple cores available for different studies-Immunohistochemistry and cultures. However, it required wide gauge needle (18G) compared to FNAC (22G), also it's a painful and invasive procedure requiring Local anaesthesia and skin incision (0.5mm). Unlike FNAC, CNB is a time consuming skilled procedure and a costly affair which in government setup is not feasible for low socioeconomic strata patients. Moreover, both the cytology techniques provide faster results than CNB.

## CONCLUSION

Cell block offered the advantage of accurate subtyping of malignancy and specificity equal to CNB.

Diagnostic adequacy and test parameters are improved and closer to CNB when both the Cyto-techniques are combined together.

Direct FNA smears and cell blocks complement each other and our results indicate that both are NECESSARY in the diagnostic work-up of patients whereas core needle biopsy is a choice of clinicians.

So, we strongly recommend that Cell Block be made routine diagnostic procedure in all the government institutions especially for guided FNAC.

Implication: Combining both cytology techniques is cost effective strategy to achieve early and accurate diagnosis and will help avoid the need for repeat attempts.

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