INTERPRETATION OF MICROBIOPSIES IN CYTOLOGICAL SMEARS AND HISTOPATHOLOGICAL CORRELATION

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ABSTRACT

BACKGROUND: Fine needle aspiration cytology (FNAC) is the first line of investigation in diagnosis of neoplastic processes of the body.The scope for diagnosis is often not met due to absence of recognizable tissue architecture. Hence this study is done to overcome these shortcomings by focusing on well preserved tissue fragments (microbiopsies) in cytological smears. These microbiopsies can provide additional information in terms of tissue architecture; thus aiding in diagnosis, tumor typing and also in predicting possible primary sites in metastatic tumors.

OBJECTIVES: To evaluate FNAC smears of malignant lesions for the presence of microbiopsies and theircyto-histopathological correlation.

MATERIALS AND METHODS : The study was conducted on FNAC smears obtained from clinically suspicious malignant lesions. The lesions were aspirated using 22-23 gauge disposable needles and 10 ml syringes. Deep seated lesions were aspirated under computed tomography or ultrasonography guidance. These smears were examined microscopically for the presence of well preserved tissue fragments, disregarding the loose tumour cells in the background. Subsequent histopathological correlation was done wherever possible.

RESULTS: A total of 80 FNA smears of clinically suspected malignant lesions were examined in the study from 1st December, 2014 to 30th July, 2016. Out of which 54 cases contained representative tissue fragments (microbiopsies) of the tumors. Majority of the cases were in the age group of 60 to 70 years accounting to 30% with slight female preponderance, male to female ratio being 1:1.16. Infiltrating ductal carcinoma (31.48%) was the most common malignancy in which the microbiopsies aided in the diagnosis. Other malignancies in which microbiopsies aided in diagnosis

were Squamous cell carcinoma (18.51%), Adeno carcinoma (11.11%), follicular neoplasm (9.25%), Hepatocellular carcinoma (7.4%), soft tissue sarcoma (7.4%), papillary carcinoma thyroid (5.56%) and others (9.25). In 37 casesHistopathological diagnosis wasavailable. In the present study, the cyto-hispathological concordance increased from 75% in absence of microbiopsies to 84% in their presence, thus an increase of 9% was noted.

CONCLUSION: In the current era, where "needle precedes the scalpel" and the biopsy material is getting limited, it would be useful to carefully evaluate smears with tissue fragments/microbiopsies. Microbiopsies are of ample help in diagnosis , typing of the tumour and indentifying the primary site in the metastatic lesions. Thus, enhancing the diagnostic accuracy of FNAC especially in resource poor setups.

KEY WORDS: FNAC, malignant lesions, microbiopsies.

LIST OF ABBREVIATIONS USED

FNAC	Fine Needle Aspiration Cytology
FNA	Fine Needle Aspiration
SCC	Squamous Cell Carcinoma
NHL	Non Hodgkin Lymphoma
HL	Hodgkin Lymphoma
STSs	Soft Tissue Sarcomas
DSFP	DermatofibrosarcomaProtuberans
FN	Follicular Neoplasm
SFN	Suspicious for Follicular Neoplasm
FV-PTC	Follicular Variant of Papillary Thyroid Carcinoma
PTC	Papillary Thyroid Carcinoma
MTC	Medullary Thyroid Carcinoma
MGG	May GrunwaldGiemsa
ATC	Anaplastic Thyroid Carcinoma
IDC	Infiltrating Ductal Carcinoma
HCC	Hepatocellular Carcinoma
N:C	Nuclear:Cytoplasmic
CT	Computed Tomography
USG	Ultrasonography
H&E	Hematoxylin and Eosin
PAP	Papanicolaou
PSA	Prostate Specific Antigen
GIT	Gastrointestinal tract

TABLE OF CONTENTS

Sl. No.	No. Contents	Page No.
1.	Introduction	1
2.	Objectives	3
3.	Review of literature	4
4.	Materials and Methods	23
5.	Results and observations	25
6.	Discussion	50
7.	Conclusion	60
8.	Summary	61
9.	Bibliography	63
10.	Annexure	67

LIST OF TABLES

Sl. No.	Tables.	Page No
1	Various patterns seen in soft tissue tumours	12
2	Cytological features of various breast malignancies	17
3.	Distribution of cases based on age groups	25
4.	Distribution of cases based on gender	26
5	Distribution of cases based on site of lesion	27
6.	Distribution of cases based on presence or absence of microbiopsies	28
7.	Comparison between primary and metastatic tumours diagnosed on microbiopsies (n=54)	29
8.	Distribution of cases based on predonimant pattern on microbiopsies	30
9.	Distribution of study subjects based on microbiopsies in lymph node	31
10.	Distribution of cases based on microbiopsies in breast	31
11.	Distribution of cases based on microbiopsies in thyroid	32
12.	Distribution of cases based on microbiopsies in soft tissue	32
13.	Distribution of cases based on microbiopsies in liver	33
14.	Distribution of cases based on microbiopsies in lung	33

15	Distribution of cases in which microbiopsies aided in diagnosis	34
16	Cyto-histopathological concordance.	35
17	Comparision of percentage of cases containing microbiopsies in different studies.	51
18	Comparision ofdistribution of cases according to type of malignancy diagnosed on the basis of microbiopsies	57
19	Comparison ofcyto-hispathological concordance	58

LIST OF FIGURES

Sl. No.	Figure	Page No.
1.	Fig 1- MGG 400X; photomicrograph of follicular neoplasm showingtumour cells arranged in follicular pattern on cytology.	36
2.	Fig 2 – H&E 400X; photomicrograph of follicular neoplasm showing follicular cells in repetitivemicrofollicular patternon cytology.	36
3.	Fig 3- MGG 400X; photomicrograph of papillary carcinoma thyroid showing tissue fragment with papillary pattern and anatomical borders oncytology.	37
4.	Fig 4- PAP 400X; photomicrograph of papillary carcinoma thyroid showing tissue fragment with well defined anatomical border on cytology.	37
5.	Fig 5- H&E 400X; photomicrograph of papillary carcinoma thyroid showing tumour cells arranged in papillary pattern on histopathology.	38
6.	Fig 6- MGG 400X; photomicrograph of metastatic adenocarcinoma showing tumour cells arranged in 3D clusters on cytology.	38
7.	Fig 7- H&E 100X; photomicrograph of metastatic adenocarcinoma of lymph node, showing acinar pattern on cytology.	39
8.	Fig 8- H&E 400X; photomicrograph of adenocarcinoma showing tumour cells arranged in glandular patternon histopathology.	39

9.	Fig 9- H&E 400X; photomicrograph of metastatic squamous cell carcinoma in lymph node showing sheets of tumour cells on cytology.	40
10.	Fig 10- H&E 400X; photomicrograph SCC showing individual cell keratinisationon histopathology.	40
11.	Fig 11- MGG 400 X; photomicrograph of metastatic melanoma showing cluster of neoplastic cells with intracytoplasmic melanin pigmenton cytology.	41
12.	Fig 12- H&E 400 X; photomicrograph of metastatic melanoma showing pleomorphic tumour cells with melanin pigmenton histopathology.	41
13.	Fig 13- MGG 400X; photomicrograph of HCC showing tissue fragment arranged in trabecular patternon cytology.	42
14.	Fig 14- MGG 400X; photomicrograph of HCC showing tissue fragment along with prominent endothelial cell transgressingon cytology.	42
15.	Fig 15-PAP 100X;Photomicrograph of metastatic embryonal carcinoma showing papillary fronds of tumour cellson cytology.	43
16.	Fig 16-PAP 400X; photomicrograph of metastatic embryonal carcinoma showing tumour cells arranged focally in acinar patternon cytology..	43
17.	Fig 17- H&E 100X; photomicrograph of embryonal carcinoma on histopathology.	44

18.	Fig 18- H&E 400X; photomicrograph of infiltrating ductal carcinoma showing dyscohesive clusters of tumour cells on cytology .	44
19.	Fig 19- PAP 400X; photomicrograph of infiltrating ductal carcinoma showing tubular epithelial fragment on cytology.	45
20.	Fig 20-H&E 100X; photomicrograph of infiltrating ductal carcinoma of breast on histopathology	45
21.	Fig 21- H&E 100X; photomicrograph of DFSP tissue fragment with tumour cells arranged in storiform pattern on cytology.	46
22.	Fig 22-H&E 400X; photomicrograph of DFSP showing tumour tissue arranged in storiform patternon histopathology.	46
23.	Fig 23- MGG 400X; photomicrograph of Ewing sarcoma showing small round blue cells arranged in rosetteson cytology..	47
24.	Fig 24- MGG 400X; photomicrograph of low to intermediate grade sarcoma showing cluster of elongated spindle cells on cytology.	47
25.	Fig 25- H&E 400 X; photomicrograph of high grade sarcoma showing multilayered sheet of pleomorphic tumour cells on cytology.	48
26.	Fig 26- H&E 400 X;photomicrograph of pleomorphic sarcoma showing pleomorphic cells on histopathology.	48
27.	Fig 27- PAP 400 X; photomicrograph of high grade sarcoma showing small cluster of tumour cells on cytology.	49
28.	Fig 28- H&E 400 X; photomicrograph of mesenchymalchondrosarcoma on histopathology.	49

INTRODUCTION

Fine Needle Aspiration Cytology(FNAC) is the first line of investigation in diagnosis of all kinds of neoplastic processes, benign or malignant, and for detecting local recurrences or metastasis in any organ or tissue of the body. It can also be used for diagnosis of inflammatory, infectious and degenerative conditions. The technique is minimally invasive, produces speedy results and is inexpensive.[1]

FNAC is a less demanding technique when compared to surgical biopsy, has a lower risk of complications and can be performed as an outpatient procedure. An early and preliminary tissue diagnosis can be provided within few hours, which aids in further investigation and management of the patient.[1,2]

The scope of FNAC is ever increasing, yet it is often not possible to come to a definitive diagnosis on FNAC alone.[3]This scope is often not met due to very small quantity of tissue material and absence of recognizable tissue architecture. In most of the cases FNAC can provide differential diagnosis rather than definitive diagnosis especially in undifferentiated tumors. Application of ancillary techniques like immunocytochemistry helps in arriving at definitive diagnosis in such cases. However, this is time consuming and expensive.[1,3]

Orell*et al*[1] are of the opinion that, if the treatment involves neoadjuvantpreoperative chemotherapy then cytological diagnosis must be equivalent to histopathological diagnosis, that is cytology must provide grade of malignancy and histogenetic type of tumour.

Hence in this study an attempt was made to make cytological diagnosis more effective by focusing on microbiopsies, which are defined as well preserved small tissue fragments or crowded group of cells in cytological smears. [4]

These microbiopsieswere assessed for the additional information provided by them in terms of tissue architecture; thus aiding in diagnosis, tumor typing and also in predicting possible primary sites in metastatic tumors.

OBJECTIVE OF THE STUDY

To evaluate FNAC smears of **malignant**lesions for the presence of microbiopsies and theircyto-histopathological correlation.

REVIEW OF LITERATURE

Technique of FNAC and historic perspective :

FNACis a technique used for obtaining cellular material for cytological examination and diagnosis by using 27–22-gauge needle which is30–50 mmlong. It is performedusing a 5, 10, or 20ml syringe either freehand or using special syringe holders.[1,5]

The technique of needling was first employed by Kun in 1847 to obtain material for microscopy. He described this as a "new instrument for the diagnosis of tumours".[6]This technique was used by many clinicians, toaspirate cells for isolation ofpneumonic microorganism.[5]

Later, Greig and Gray in the year 1904 aspirated nodes for identification of trypanosomes. Following this there was widespread use of similar technique to puncture and diagnose infected and malignant lymph nodes.[5]

In 1927, Dudgeon and Patrick diagnosed200 cases by FNAC and reported that diagnostic accuracy was 98.6%. They had proposed needle aspiration of tumors as a means of rapid microscopic diagnosis.[6]

In the late 20s and early 30s,two pathologists Steward and Ewing, a laboratory technologist Ellis, and one Head and Neck surgeon Martin form the Memorial Hospital, New York, started needle aspiration of deep seated palpable tumors.[6]

Steward in 1933, described 2500 tumours investigated by aspiration method for 3 years at the Memorial Hospital, New York.He used heat fixed smears stained by rapid Haemtoxylin and Eosin stain.In his report, he highlighted and specified points for optimal results which form the theoretical basis for FNAC. [6,7]The points he specified include:

i. Emphasis on the exact technique of aspiration and preparation of the smears.

ii. Importance of clinical correlation before interpretation of the smears.

iii. Comparison between cytology and histopathology.

iv. Combination of the pattern analysis along with cytologic details for appropriate interpretation.

v. Awareness about the limitation of the method.

During the 60s and 70s there was revival of the fine needle aspiration(FNA)technique again due the Swedish experience and the work of many pioneers who published numerous articles on aspiration cytology in many of the international journals .They concluded that FNAC had aided significantly to a timely diagnosis of neoplastic and non-neoplastic lesions. It has replaced or at least complemented tissue diagnosis in many clinical situations. [6]

INDICATIONS OF FNAC

The technique of FNAC can be applied to superficial lesions that can be easily palpated in the skin,subcutis and soft tissue; thyroid, breast, salivary glands and superficial lymph nodes. Ultrasound and computed tomography guidance makes percutaneous, transthoracic and transperitoneal FNAC of deeper structures like the mediastinal, abdominal, retroperitoneal and pelvic organs possible and safe. Guided FNAC can also be applied to deeper non palpable lesions of head and neck, breast and the soft tissues.[1,2]

The technique of FNAC can be used for

i. Diagnostic purposes.

ii. Therapeutic purposes e.g. evacuation of benign cystic lesion.[5]

The major indication for FNAC is to diagnose a lesion as either primary malignancy or metastatic disease.

As a diagnostic tool for evaluating potentially malignant conditions FNAC has the following indications:

i. Initial evaluation before treatment and in prognosis of a malignancy.
ii. Evaluation of recurrence of a malignancy following therapy.
iii. Evaluation of local and distant metastasis.[5]

ADVANTAGES OF FNAC

FNAC has now been widelyused as an initial diagnostic procedure for lesions.The advantages of FNAC include

i. It is a simple and cost effective procedure.
ii. It has lower risk of complications when compared to surgical biopsy.
iii. It is readily repeatable and is useful for multifocal lesions also.
iv. Minimal physical and psychological discomfort for the patient.
v. Provides rapid reports (within few hours) andbedside diagnosis of various neoplastic, and non- neoplastic conditions.
vi. Can be used as a therapeutic procedure for the evacuation ofnon neoplastic cystic lesions.
vii. Allows cases to be prioritized when there is a waiting time for surgery.
viii. Permits the diagnosis of some benign conditions for which there is no need for surgical intervention.
ix. Renders excision biopsy unnecessary in advanced disease, in elderly patients, or in cases where the treatment isnon-surgical, e.g. in neoadjuvant chemotherapy.

x. It is a rapid means of confirmation of recurrence of previously treated malignancy without surgery.[5,8]

LIMITATIONS

i. Sampling is scanty or inadequate and histological architecture may be lost thereby rendering diagnosis difficult.

ii. Inflammatory, metaplastic or degenerative lesions may sometimes mimic malignancy.

iii. Diagnosis is indefinite in some conditions such as follicular adenoma vs. carcinoma of the thyroid.

iv. Samples taken may not be representative of the lesion. e.g sampling of necrotic area in malignancy.[5]

OVERCOMING THE HURDLES:

After extensive search of literature the following ways and means stand out which have helped in overcoming the said limitations of FNAC.The first and foremost being careful searching for microbiopsies/intacttissue fragments/crowded group of cells.The next measure which can be of help is special stains/ immunocytochemistry.[3]Last but not the least is repeating the procedure with the help of imaging techniques even in case of superficial lesions.[3] The policy of involving two pathologists in the diagnostic process independent of each other also can be of help. Experience and nothing beats experience.[5]

After brief review of historical aspects of FNAC and addressing the indications, advantages, limitations and how to overcome these limitations; the review

tries to cover the same in context of frequently aspirated organs.The main focus is to discuss the lesions wherein microbiopsies play a role in the diagnosis.

FNAC OF MALIGNANTLYMPH NODES

Lymph node is the most common organ subjected to FNAC. Lymphadenopathy may be a sign of inflammation, infection,primary or secondary malignancy. In some patients it may be the first presenting clinical sign of non-hematologic malignancy as lymph nodes are common site of metastasis for various malignancies. Thus clinical recognition and urgent diagnosis of palpable lymphadenopathy is of great importance to differentiate between inflammatory lesions or malignant lesions (metastatic or primary).[9]

Although open biopsy with histopathological examination of excised tissue still remains the golden standard for diagnosis of lymph node neoplasms, yet FNAC has now become an integral part of the initial diagnosis and management of patients presenting with lymphadenopathy.[10]

Alam k *et al*[10] in their study mentioned that around 80.4% of the malignant lymph nodes were metastatic,15.3% were lymphomas and 4.4%of the clinically suspected cases turned out to be reactive lymph nodes. They also stated that FNAC results are comparable to those of tissue biopsies whenthe aspirates hadmicrobiopsy. Thus,FNAC can be an excellent first line method for investigating the nature of lesion, as it is economical andconvenient alternative to open biopsy.[11]

METASTATIC LYMPH NODES:

Rai NN *et al*[9] said that metastatic lesions reported on FNAC can give a clue to the nature and site of the primary lesion. The primary site can be better assessed in presence of thin tissue fragments or the microbiopsies.

Thus FNAC can be useful in detecting secondaries where primary tumour is evident as well as for detection of primary in carcinoma of unknown origin and for monitoring response to therapy.

Wilkinson AR *et al*[12] in their study stated that metastatic lymphadenopathy most commonly included squamous cell carcinoma, followed by adenocarcinoma.

Orell*et al*[13] has recommendeda stepwise approach to the investigation of nodal metastasis. The steps include

i. Age and sex of the patient.
ii. Anatomical site of the involved lymph node.
iii. Cytomorphology of the tumour.
iv. Cytochemical stains and immunocytochemistry.

The patients age is an important consideration whileassessing metastatic disease as certain tumours are morecommon in younger age groups while others in older individuals.

The anatomical site of the node may give some indicationto the possible site of the primary tumour. For example,the axillary lymphadenopathy may point towards metastatic deposits from thebreast, lungs or ovaries in middle-aged females. Enlarged nodes in theleft supraclavicular fossa may be the site of presentation ofpelvic malignancies, such as the prostate, testis orovaries as well as abdominal malignancies from the gastrointestinaltract.

The cytological patterns or the microbiopsies if keenly observed in routinely stained smears can often give clues to the site of the primary tumor. [13]

i. Columnar cells with elongated nuclei arranged in palisades along with stringy mucous and necrosis suggest a primary in the large bowel.

ii. Glandular cells arranged in a cribriform pattern,gland-in-gland or three-dimenstional (3D)clusters along with moderately pleomorphic cells suggest a prostatic carcinoma.

iii. Pulmonary and pancreatic adenocarcinoma can have a variety of patterns. They usually show glandular differentiation, prominent nuclear pleomorphism and variable amount of mucin secretion. As a rule, the presence of intracytoplasmicmucin excludes renal, adrenal, hepatocellular and thyroid carcinoma.

iv. Breast cancer usually displays poor glandular differentiation while cell clusters and single files of cells are more common. Cells with intracytoplasmicneolumina containing 'bulls-eye' inclusions are also suggestive of breast carcinoma.

Cytochemical stains and Immunohistochemistry can be offurther help in confirming the diagnosis in doubtful cases.[3]

LYMPHOMA:

The lymphomas are classified based on the combination of cytomorphology, immunophenotyping, genetic characteristics and clinical findings.[13]

Non Hodgkin Lymphoma(NHL): FNAC diagnosis is largely based on the presence of monomorphic population of neoplastic cells. Assessment of cell size and nuclear features help in subtyping NHL.[13]

Hodgkin lymphoma(HL): These account for 30% of all lymphomas. A confident cytological diagnosis of HL can be made by the presence of Reed Sternberg cells with a background of lymphocytes and reactive cells.[13]

FNAC OF SOFT TISSUE TUMOURS

Soft tissue can be defined as non epithelialextraskeletaltissue of the body exclusive of reticuloendothelial system, glia and supporting tissue of the parenchymal organs.[14] Soft tissue tumours can be either benign or malignant, can arise from these tissues and are named according to their apparent resemblance to mature tissues.[15]

Malignant soft tissue sarcomas(STSs)are rare; and account for less than 1% of total malignancies. Diagnosis of these tumours is a challenging job because of extreme histological diversity. It is difficult to interpret from a small biopsy sample as there may be variability in appearances in different parts of a single tumour.[15]

Although FNAC has been used as an initial diagnostic tool inSTSs it has certain diagnostic limitations which include:

i. Failure to obtain adequate sample particularly from deep seated or cystic or necrotic lesions.
ii. Misdiagnosis can occur if the specimens are drawn from the surrounding reactive zones.
iii. Failure to type specially the majority of the STSs.
iv. Difficulty to interpret rare variants.
v. Lack of adequate cytological diagnostic criteria of newly discovered/classified entities.

Rekha B *et al*[16] mentioned that a basic cytological approach towards STSs begins with familiarity to the normal structure along with myxoid or metachromatic stromal fragments and variety of dyscohesive cells which include spindle, round, pleomorphic or polygonal cells.

Cytological diagnosis of soft tissue tumours is challenging because most of the times single cells dominate the smears whether from benign tumours or sarcomas,

which makes diagnosis very difficult. Inherent in the aspiration technique is a dispersion of the individual cells that cause loss of recognizable tissue patterns.[17]Whilehistopathological diagnosis of soft tissue tumours is based mainly on the different growth patterns seen along with the cellular features which are not usually found in cytological smears.

Orell*et al*[17]was of the opinion that aggregates and bundles of cohesive cells or 'microbiopsies' if present in smears, can aid in diagnosis. Thus presence of microbiopsies can improve the diagnositic efficacy of FNAC in STSs.

The diagnosis of soft tissue tumours on histopathology is predominantly based on the growth pattern. If these patterns are seen on cytology smears then they will be useful in definitive diagnosis. The various patterns seen on histopathology issummarised below:[18]

TABLE 1: VARIOUS PATTERNS SEEN IN SOFT TISSUE TUMOURS

GROWTH PATTERN	TUMOUR TYPE
Alveolar	Alveolar soft part sarcoma, alveolar rhabdomyosarcoma
Fascicular	Fibromatosis, fibrosarcoma, malignant peripheral nervesheath tumor; synovial sarcoma
Palisading	Schwannoma, malignant peripheral nerve sheath tumor, leiomyosarcoma,extragastrointestinal stromal tumour, synovial sarcoma
Rosettes, pseudorosettes	Neuroblastoma, neuroepithelioma, malignant peripheral nerve sheath tumour (rare)
Storiform (cartwheel)	Dermatofibrosarcomaprotuberans(DFSP),malignant fibrous histiocytoma; neurofibroma;

FNAC OF MALIGNANT LESIONS OF THYROID GLAND

Thyroid lesions are a significant clinical problem in general population but majority are non neoplastic and less than 5% are neoplastic.[19,20] The initial screening procedures include FNAC, ultrasound and radionucleotide scan. Fine needle non-aspiration cytology is apreffered technique over aspiration because thyroid is a highly vascular organ.[20]

The cytology diagnoses of thyroid isclassified by the Bethesda system into:

- Nondiagnostic/unsatisfactory,
- Benign,
- Atypia of undetermined significance/follicular lesion of undeterminedsignificance,
- Follicular neoplasm/suspicious for a follicular neoplasm, (FN/SFN)
- Suspicious for malignancy
- Malignant.

FOLLICULAR NEOPLASM:

Architectural patterns: Predominantly 2 patterns are seen, follicular and microfollicular.Follicular pattern shows small or large flat sheets/groups of cells. Microfolliclesare microacinar clusters with central lumen that may contain a drop of colloid. Other patterns like trabecular and solid pattern may also be seen.[20,21]

CanberkS *et al*[21] in his article discussed that sampling from microfollicular or cellular areas of benignnodules may always trigger a diagnosis of FN/ SFN, thus leading to over diagnosis give rise to an unnecessary surgery.

Follicular variant papillary thyroid carcinoma (FV-PTC) is the biggest trap if diagnosis is made purely on pattern. Thus nuclear features are important to exclude this entity from FN/SFN category.[21]

Other cytologyical features of follicular neoplasm include:

- Moderate to high cellularity,
- Bloody, usually colloid-free background,
- Nuclear crowding and overlapping,
- Positive immunostaining for thyroglobulin and Thyroid Transcription Factor(TTF)-1.[20]

PAPILLARY THYROID CARCINOMA (PTC):

PTC is the most common thyroid malignancy. The cytological diagnosis of PTCis analyzed in two parts; firstly the pattern followed bynuclear features. [21]

- **Pattern**: Papillary tissue fragments with or without a fibrovascular core is the most common pattern seen in PTC. Syncytial aggregates and sheets focally with a distinct 'anatomical border' and three-dimensional tissue fragments may also be seen.[20,21]
- **Nuclear features**: Nuclear crowding and overlapping. Enlarged, ovoid, strikingly pale nuclei with finely granular powdery chromatin,intranuclear cytoplasmic inclusions and nuclear grooves.
- **Other features**:Scanty, viscous, stringy or chewing gum colloid and rarely psammoma bodies.[21]

The patterns mimicking PTC asformation of papillae have been described in theliterature. Pseudopapillary formation as an architecturalpitfall has been noted in hyperplastic nodular goitre and Graves disease.[21]

MEDULLARY THYROID CARCINOMA (MTC):

MTC is much more aggressive than follicular derivedneoplasms of the thyroid. It is characterized mainly by the presence of many single cells and loosetissue fragments. Follicular formation is usually not seenand papillary structures are very

rare to find in MTC. However, it maydisplay a nested, trabecular or a loose microfollicular pattern,which could be misleading as follicular neoplasm. [21]

The diagnosis of MTC is mainly based on the cellular features which include:

- Variable cell pattern like plasmacytoid, small cell or spindle cell. Moderate anisonucleosis, scattered very large nuclei andbinucleation may also be seen
- Uniform, stippled nuclear chromatin and coarse red cytoplasmic granularity which is usually found onMay GurnwaldGiemsa(MGG) stain.
- Amorphous pink/violet background material i.e amyloid can also be demonstrated.[20]

ANAPLASTIC THYROID CARCINOMA (ATC):

The diagnosis is predominantly based on the cellular features and tissue fragments are rare to find .[21]The cytological features of ATC include:

- Necrotic background with dissociated and/or clustered highly pleomorphic malignant cells,
- The tumour cells maybe multinucleate, bizarre giant cells and/or spindle cells showing marked atypia,
- Frequent and abnormal mitoses may be seen.[21]

FNAC OF MALIGNANT BREAST LESIONS

'Triple test'is multidisciplinary approach that centersaroundanalyzing clinical and radiologic findings in conjunction with the pathologic features to diagnose the lesion and determine the best treatment plan for the patient.[22]

The role of FNAC in the assessment of a breast lumpincludes.[23]

i. Diagnosis and evacuation of simple cysts,

ii. Investigation of suspected recurrence or metastasisin cases of previously diagnosed cancer

iii. Confirmation of inoperable, locally advanced breast cancer

iv. Preoperative confirmation of clinically suspectedcancer,

v. The tumour cellscan be obtained for special analysis andresearch, e.g. hormone receptor studies, DNA analysis,immunohistochemistry and molecularstudies.

Orell*et al*[23]said that approximately two-thirds of screen-detected cancers aregiven a definitive cancer diagnosis by FNAC as part of tripplediagnosis. The other one-third may further require investigationby core needle biopsy or open biopsy.

Howell LP *et al*[24] described six general cytologic criteria which are typically seen in the majority of carcinomas of the breast:

i. Cellularity: Malignant lesions are more cellular when compared to benign lesions.Malignant ductal epithelial cells do not have normal wellformeddesmosomes or other intercellular connections, and thereforethey are aspirated more easily than benign ductal cells.

ii. Dyshesion: Malignant ductal epithelial cells form a pattern of loosegroups rather than the tightly cohesive groups seen from aspirates of benignnodules. Dyshesion can be recognized by noting space between thecells in the clusters, by identifying cells that appear to be ‘‘falling off theedge’’ of a cluster, or appear as numerous single cells in the background.

iii. Monomorphism: A mixed polymorphic population of cells such as ductal epithelial cells, apocrine cells, fibroadipose tissue, and histiocytes are seen in the benign breast disease. While in malignancy a single population of cells representing the clonal proliferation of malignant cells from which a tumor originates are seen.

iv. Anisonucleosis: Nuclei of variable in size and shape.

v. Irregular nuclear membranes: Malignant nuclei exhibit nuclearfolds, notches, or grooves.

vi. Prominent nucleoli: Nucleoli are typically conspicuous, sometimeslarge enough to be considered macronucleoli.

TABLE2: CYTOLOGICAL FEATURES OF VARIOUS BREAST MALIGNANCIES

	Infiltrating Ductal Carcinoma(IDC)	**Lobular Carcinoma**	**Tubular carcinoma**	**Mucinous carcinoma**	**Medullary carcinoma**	**Papillary carcinoma**
Architectural Patterns	Tubular clusters	Single-file arrangement,	Angular epithelial clusters,	Small solid aggregates	Cohesive clusters syncytical sheets	Finger like 3-D papillae,
Cellularity	Moderate to high	Scant to moderate	Minimal to moderate	Moderate to high	High	Moderate to high
Dyshesion	Moderate to marked	Minimal to moderate	Minimal to moderate Variable	Variable;	variable	Variable;
Other features	Moderate to severe nuclear atypia,irregular nuclear membrane	Small hyperchromaticcells,irregularity in nuclear shape	Relatively uniform, mild to moderately atypical cells	Abundant mucin, branching capillaries	Large pleomorphic cells. Many plasma cells and lymphocytes are seen.	Nuclear atypia

[Modified from Howell *et al*[24] and Orell*et al*[23]]

FNAC OF MALIGNANT LIVERLESIONS :

With the advent of imaging techniques, FNAC of liver has been increasingly used for the diagnosis of focal liver lesions. [25]Liver is one of the most common organs for thelodgement of metastasis. Differentiation between benignand malignant primary or secondary tumours isextremely important from management point of view.Presence of metastases usually rules out surgerywhereas; if Hepatocellular carcinoma (HCC) is diagnosed at an early stage, surgicalresection is possible and may assure cure. The clinical andradiological presentations of both primary andmetastatic tumours can be similar. Here, FNAC plays a majordecisive diagnostic role.[25]

HEPATOCELLULAR CARCINOMA:

- **Architectural features** :Cohesive clusters, broad trabecular , pseudo acini and transgressing of endothelial cells.[26]
- **Cellular features**: Small, monotonous hepatocytes with nuclear crowding, increased N: C ratio, cytoplasmic hyaline inclusions, atypical naked nuclei and tumour giant cells. Well defined cytoplasmic borders, abundant thick and monotonous cytoplasm, eccentric nuclei, thick nuclear membranes, irregular nuclear contours, increased chromatin density, irregular chromatin distribution and macronucleoli are detectable in well differentiated HCC[27]

Three criteria differentiate HCC from metastatic tumor:

i. Polygonal cells with centrally placed nuclei.
ii. Malignant cells separated by sinusoidal capillaries
iii. Presence of bile.

Two additional criteria, namely, endothelial cellssurrounding tumour cell clusters and intranuclear inclusions were identified as being important secondarycriteria for HCC.The gold standard for the cytologicaldiagnosis of metastatic deposits remains the identificationof malignant cells of non-hepatocytic origin.[28]

CHOLANGIOCARCINOMA:

These tumours usually occur at the hilum and clinically present early due to obstructive jaundice.

Architectural patterns: Tumour cells are arranged in sheets,clusters and micro glandular pattern.

Cellular features: Individual tumour cells resemble bile duct epithelium and are small to medium sized cuboidal/columnar cells with variable nuclear enlargement, prominent nucleoli and delicate cytoplasm with fine vacuolization. Occasional stromal fragments may be seen.

METASTATIC LESIONS:

Localising the primary site is one of the mostchallenging problems in the field of aspiration cytology.Judicious use of supporting techniques such asimmunocytochemistry and electron microscopicexamination has been advocated strongly to help inascertaining the primary site or origin of tumour inFNAC. Few authors have made an attempt to identify the primary site on the basis of cell morphology andarchitectural pattern of aspirate.[25]

Swamy M C *et al*[28] mentioned in their study that adenocarcinoma was the commonest lesion metastasizing to the liver. The possible primary sitesof

adenocarcinoma according to their study were colon, rectum, ovary, breast, lung and unknown primary.They also mentioned that hypercellularity with tissue fragments(microbiopsies) showing columnar to cuboidal cells arranged in monolayered sheets,palisade forms, acinar pattern helped in the diagnosis.Thecells also showed altered N: C ratio, anisonucleosis with central or eccentrically placed nucleus with finecoarsedispersed chromatin and having vacuolated to granular eosinophilic cytoplasm.

The second commonest type was metastatic squamous cell carcinoma (SCC), smears of which showed sheets and scatteredsquamoid, tadpolelike and spindle shaped cells with well defined abundant keratinized cytoplasm and pleomorphic and hyperchromatic nuclei.

FNAC OF MALIGNANT LUNG LESIONS

Computed tomography(CT) guided FNAC is safe and reliable for the diagnosis of pulmonary lesions.[29]FNAC of lung has now been widely used as a first line of diagnostic. Procedure for evaluation of malignancy in inoperable cases and confirmation of metastasis.[30]

SQUAMOUS CELL CARCINOMA:

- Keratinizing: Scattered single cells are predominantly seen. Bizarre,spindle and caudate hyper chromatic cells with abundant eosinophilic cytoplasm are seen. Background may show necrosis and inflammation.[30]
- Non-keratinizing: Cells are usually more cohesive and presentas multilayered fragments. Their nuclei are usually spindleshaped or elongated with dense, irregularly distributed chromatin.There is often conspicuous variation in the

degree ofchromasia. Dense cytoplasm andwell-defined cell borders are indicators of squamous differentiation.[30]

ADENOCARCINOMA:

- Flat sheets,rosettes, acinar structures or cell clusters are seen. Cells are medium to large sized columnar cells with round to oval eccentric nuclei having large solitary nucleoli and abundant delicate cytoplasm.[30]

SMALL CELL CARCINOMA:

- Dispersed cell predominate and some small tight clusters may be seen. Individual cells are small or medium-sized cells with little or no cytoplasm. Nuclear molding and engulfment is seen along with irregular nuclei and uniform finely or coarsely granular nuclear chromatin and smallnucleoli. Numerous mitotic figures may also be seen.[30]

LARGE CELL CARCINOMA:

- Multilayered fragments of malignant tissue are seen. Individual cells are large, highly pleomorphic with abundant cytoplasm and a high N:C ratio, Tumor giant cells are also noted.[30]

CARCINOID TUMOURS:

- Typical carcinoid: Trabecular, palisading, small cell clusters and plexiform aggregates along with dispersed tumour cells are seen. Individual tumour cells are monomorphous small cells with round or oval nuclei having stippled nuclear chromatin, small nucleoli and scant cytoplasm.[30]
- Atypical carcinoid: In the spectrum of neuroendocrine carcinoma of the lung, these tumours lieinbetween carcinoid tumours and small cell carcinoma, in

terms of morphology and biological behaviour. These tumours show carcinoid growth pattern along with high mitotic activity and necrosis. Nuclear pleomorphism and atypia may also be associated.[30]

- Large cell neuroendocrine carcinoma: An organoid, trabecular or palisading pattern along with geographic necrosis is seen. Individual tumour cells are large with low N:C ratio with prominent nucleoli and a high mitotic rate.[29]

MATERIALS AND METHODS

Source of data

A study was carried out on FNA smears obtained from clinically suspicious malignant lesions containing tissue fragments obtained from the patients attending cytology laboratory of BLDEU ShriB.M.Patil Medical College, Hospital and Research centre, Vijayapur from 1st December, 2014 to 30th July, 2016.

Methods of collection of data

- The study was conducted on FNAC smears obtained fromlesions clinically suspicious of malignancy.
- The lesions were aspirated using 22-23 gauge disposable needles and 10 ml syringes.
- Deep seated lesions were aspirated under computed tomography (CT) or ultrasonography (USG) guidance.
- The smears prepared were fixed in 95% ethyl alcohol, stained with hematoxylin and eosin(H and E) and papanicolaou (PAP) stains, and air dried smears were stained with MayGurnwaldGiemsa(MGG).
- These smears were carefully examined microscopically for the presence of well preserved tissue fragments, disregarding the loose tumor cells in the background.
- Subsequent histopathological correlation was done whenever feasible.

Sample Size:

The study conducted by Sherwani RK*et al*[3]found that the concordance was raised from 81.2% to 93.2% in presence of microbiopsies.

Considering the common increase of cyto-histopathologic concordance was 91% at 95% confidence level and 80% power, the calculated sample size was 80.

Statistical formulan = $\frac{(Za + Zb)^2 \times 2 \times p \times (1-p)}{d^2}$

Za- Z value at a level =95%

Zb- Z value at b level=80%

p- common proportion value= 91%

d- difference between 2 groups.

Hence 80 malignant cases were included in the study.

Statistical analysis:

The data was entered in MS EXCEL and analysed by Epi INFO version 7.1. Qualitative data was expressed in percentages. Quantitative data was expressed in Mean ± Standard Deviation and ranges were specified.

Inclusion criteria: FNAC smears of malignant lesions were included in the study.These smears were screened for presence of viable tissue fragments which gave clues about the tissue architecture.

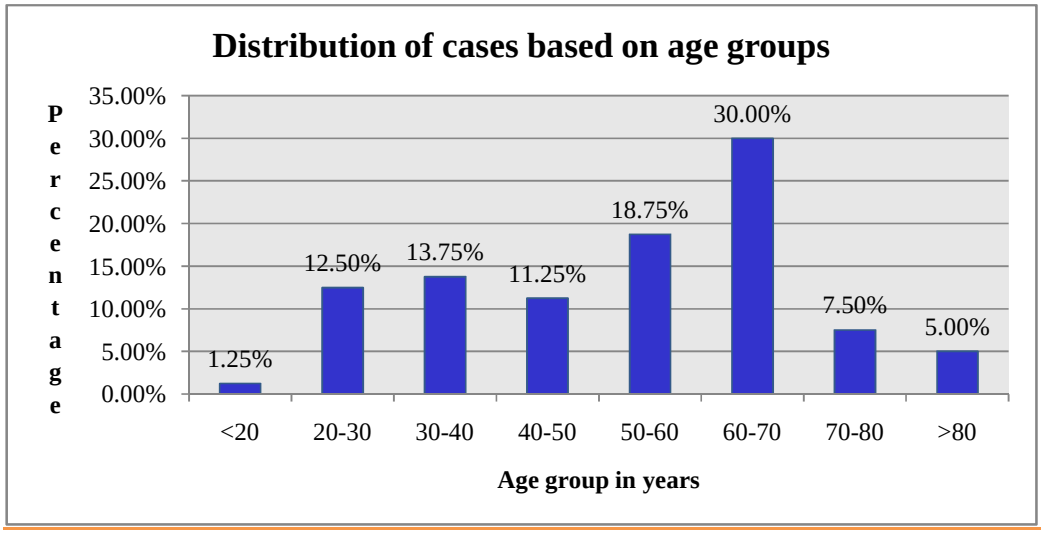
Exclusion criteria: FNAC smears not fulfilling the above mentioned criteria were excluded from the study.

RESULTS

A total of 80 FNA smears of clinically suspected malignant lesions were examined in the study from 1st December, 2014 to 30th July, 2016. Out of which 54 cases contained representative tissue fragments of the tumours (microbiopsies) and histopathology diagnosiswas available in 37 cases.

TABLE 3: DISTRIBUTION OF CASES BASED ON AGE GROUPS

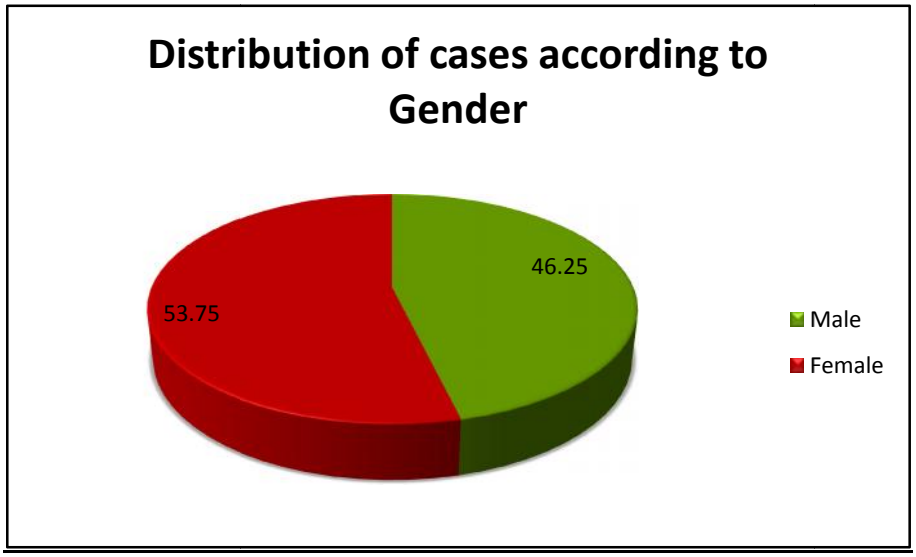
Age group (in years)	Frequency	Percentage
<20	1	1.25
20-30	10	12.50
30-40	11	13.75
40-50	9	11.25
50-60	15	18.75
60-70	24	30.00
70-80	6	7.50
>80	4	5



Majority of the cases were in the age group of 60 to 70 years (30%), followed by 50 to 60 years (18.75%) and 30 to 40 years (13.75%).

TABLE 4: DISTRIBUTION OF CASES BASED ON GENDER

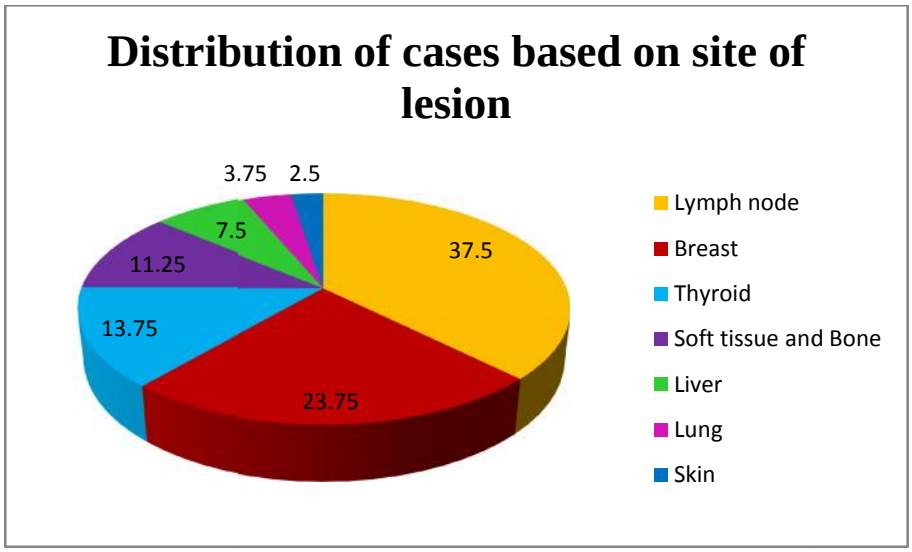
Gender	Frequency	Percentage
Male	37	46.25
Female	43	53.75
Total	80	100



Out of 80 cases, 53.75% were females and 46.25% were males.

TABLE 5: DISTRIBUTION OF CASES BASED ON SITE OF LESION

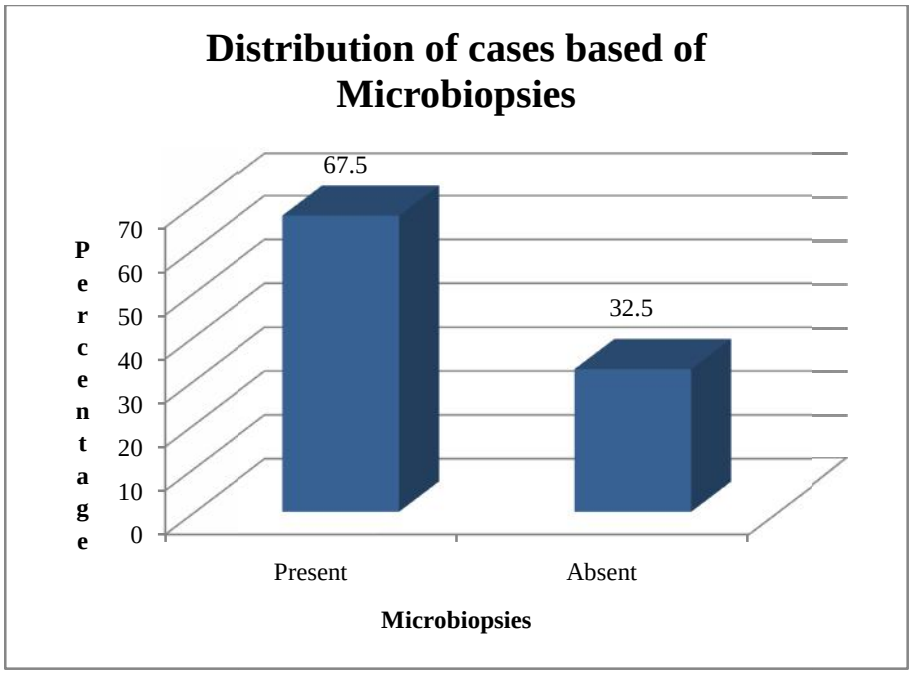
SITE OF LESION	FREQUENCY	PERCENTAGE
Lymph node	30	37.5
Breast	19	23.75
Thyroid	11	13.75
Soft tissue and Bone	9	11.25
Liver	6	7.50
Lung	3	3.75
Skin	2	2.50
Total	80	100



Most common site of lesion was lymph node (37.50%) followed by breast (23.75%) and thyroid (13.75%). A small proportion of cases were in soft tissue (11.25%), liver (7.5%), lung (3.75%) and skin (2.50%).

TABLE 6: DISTRIBUTION OF CASES BASED ON PRESENCE OR ABSENCE OF MICROBIOPSIES

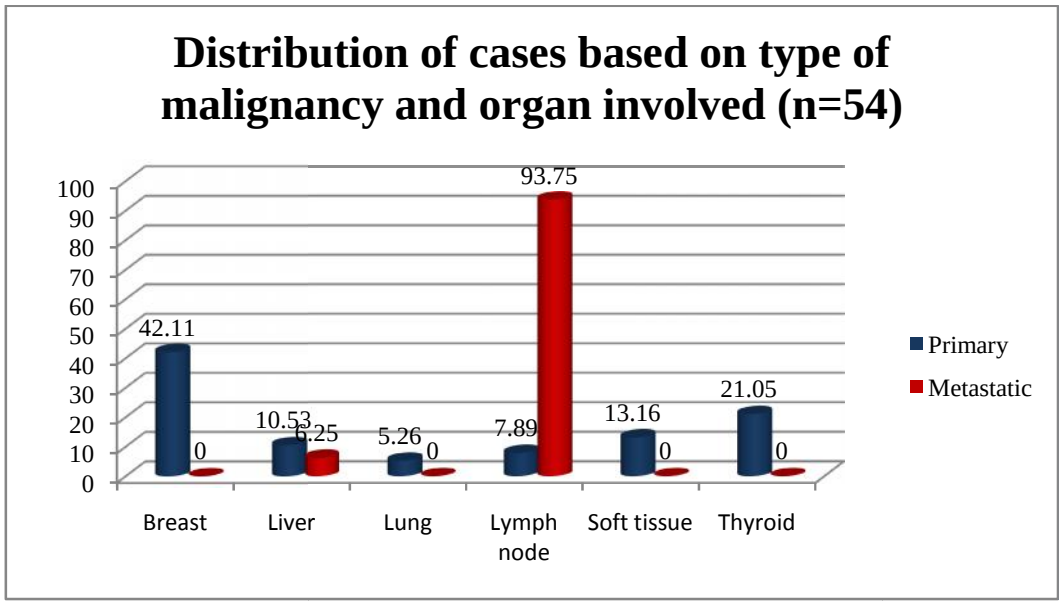
MICROBIOPSY	FREQUENCY	PERCENTAGE
Present	54	67.50
Absent	26	32.50
Total	80	100



In 80 cases screened, 67.5% of cases had microbiopsies and 32.5% did not have microbiopsies.

TABLE 7:COMPARISON BETWEEN PRIMARY AND METASTATIC TUMOURS DIAGNOSED ON MICROBIOPSIES (n=54)

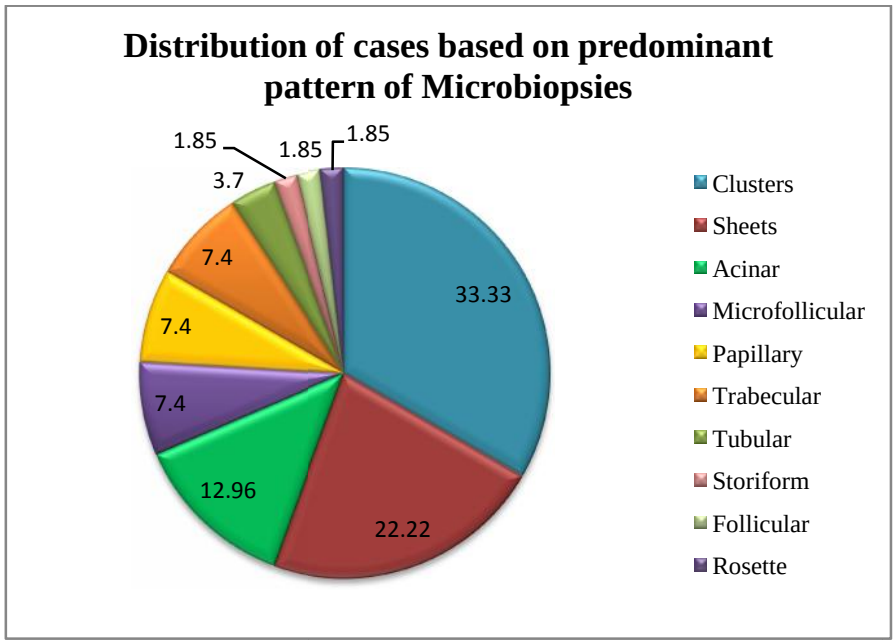
Organ	Primary		Metastasis	
	Number	Percentage	Number	Percentage
Breast	16	42.11	0	0
Liver	4	10.53	1	6.25
Lung	2	5.26	0	0
Lymph node	3	7.89	15	93.75
Soft tissue and bone	5	13.16	0	0
Thyroid	8	21.05	0	0
Total	38	100	16	100



Among 54 cases that had microbiopsies, 38 were primary lesions and 16 were metastatic lesions. Among the 38 cases, 42.11% were in breast, 21.05% were in thyroid, 13.16% were in soft tissues, 10.53% in liver, 7.89% in lymph node and 5.26% in lung. Among the 16 metastatic cases, majority of them were in lymph node (93.75%), followed by liver (6.25%).

TABLE 8: DISTRIBUTION OF CASES BASED ON <u>PREDOMINANT</u> PATTERN ON MICROBIOPSIES

Pattern on Microbiopsies	Frequency	Percentage
Clusters	18	33.33
Sheets	12	22.22
Acinar	7	12.96
Microfollicular	4	7.40
Papillary	4	7.40
Trabecular	4	7.40
Tubular	2	3.70
Storiform	1	1.85
Follicular	1	1.85
Rosette	1	1.85
Total	54	100



The predominant pattern seen on microbiopsies was clusters (33.33%), followed by sheets (22.22%) and acinar (12.96%). A small proportion of cases showed papillary pattern (7.4%), microfollicular pattern (7.4%), trabecular pattern (7.4%), tubular pattern (3.7%), storiform (1.85%), follicular (1.85%) and rosette (1.85%).

TABLE 9: DISTRIBUTION OF CASES BASED ON MICROBIOPSIES IN LYMPH NODE

MICROBIOPSIES	FREQUENCY	PERCENTAGE
Present	18	60.00
Absent	12	40.00
Total	30	100
Predominant pattern of microbiopsy		
Sheets	9	50.00
Acinar	5	27.77
Clusters	3	16.67
Papillary	1	5.55

A total of 30 cases of lymph node were included in the study, out of which 18 contained microbiopsies (60%) with the predominant pattern being sheets (50.00%) followed by acinar (27.77%).

TABLE 10: DISTRIBUTION OF CASES BASED ON MICROBIOPSIES IN BREAST

Microbiopsies	Frequency	Percentage
Present	16	84.22
Absent	3	15.78
Total	19	100
Predominant pattern of microbiopsy		
Clusters	13	68.42
Sheets	1	5.26
Tubular	2	10.52

Out of 18 cases in breast, 84.21% had microbiopsies. The most common pattern found in breast was clusters (68.42%) followed by tubular (10.52%) and sheets (5.26%).

TABLE 11: DISTRIBUTION OF CASES BASED ON MICROBIOPSIES IN THYROID

MICROBIOPSIES	FREQUENCY	PERCENTAGE
Present	8	72.72
Absent	3	27.27
Total	11	100
Predominant pattern of microbiopsy		
Follicular	1	12.50
Micro follicular	4	50.00
Papillary	3	37.50

Of 11 malignant thyroid lesions which were included in the study, 8 cases (72.72%) contained microbiopsies. The predominant pattern found was micro follicular (50.00%) followed by papillary (37.50%) and Follicular (12.50%).

TABLE 12: DISTRIBUTION OF CASES BASED ON MICROBIOPSIES IN SOFT TISSUE

MICROBIOPSIES	FREQUENCY	PERCENTAGE
Present	5	55.55
Absent	4	44.44
Total	9	100
Predominant pattern of microbiopsy		
Clusters	2	40.00
Sheets	1	20.00
Rosette	1	20.00
Storiform	1	20.00

Out of 9 cases of soft tissue sarcomas, 5(55.55%) cases had microbiopsies which aided in diagnosis. The patterns seen were sheets, clusters, rosette and storiform.

TABLE 13: DISTRIBUTION OF CASES BASED ON MICROBIOPSIES IN LIVER

MICROBIOPSY	FREQUENCY	PERCENTAGE
Present	5	83.33
Absent	1	16.67
Total	6	100
Predominant pattern of microbiopsy		
Trabecular	4	80
Acinar	1	20

In a total of 6 cases of malignant liver lesions, 5 (83.33%) had microbiopsies. Most common pattern seen was trabecular (80%), followed by acinar (20%).

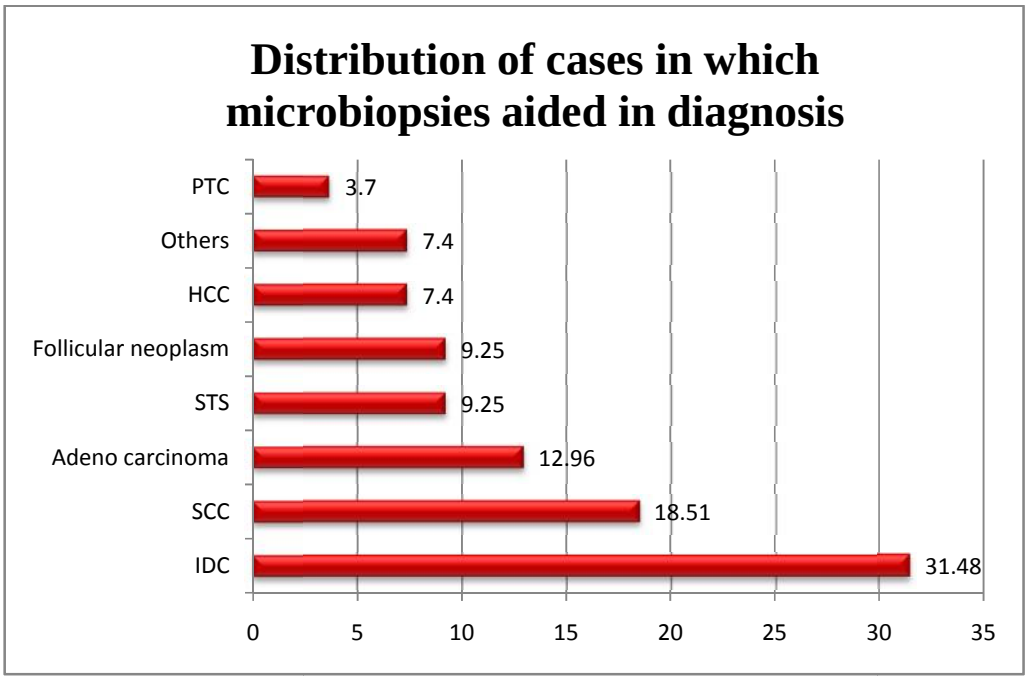
TABLE 14: DISTRIBUTION OF CASES BASED ON MICROBIOPSIES IN LUNG

Microbiopsies	Frequency	Percentage
Present	2	66.67
Absent	1	33.33
Total	3	100
Pattern of microbiopsy		
Sheets	1	50
Acinar	1	50

In lung, 2 out of 3 cases (66.67%) had microbiopsy which aided in the diagnosis. Sheets and acinar pattern were the common patterns found.

TABLE 15:DISTRIBUTION OF CASES IN WHICH MICROBIOPSIES AIDED IN DIAGNOSIS

MALIGNANCY	FREQUENCY	PERCENTAGE
IDC	17	31.48
SCC	10	18.51
Adeno carcinoma	7	12.96
STSs	5	9.25
Follicular neoplasm	5	9.25
HCC	4	7.40
Others	4	7.40
PTC	2	3.70
Total	54	100



Infiltrating ductal carcinoma (31.48%) was the most common malignancy in which the microbiopies aided in the diagnosis. Other malignancies in which microbiopies aided in diagnosis were Squamous cell carcinoma (18.51%), Adeno carcinoma (12.96%), Follicular Neoplasm (9.25%), Hepatocellular carcinoma (7.4%), Soft tissue sarcoma (9.25%), Papillary carcinoma thyroid (3.7%) and others (7.4%).

TABLE 16: CYTO-HISTOPATHOLOGICALCONCORDANCE

Microbiopsies	**Histopathological diagnosis**			
	Positive	**Negative**	**Total**	**Concordance**
Present	21	4	25	84%
Absent	9	3	12	75%
Total	30	7	37	

Total 37 cases had histopathological diagnosis available. In cases with microbiopsies, 21 cases out of 25 had concordance withhistopathological diagnosis (84%). In cases without microbiopsies, 9 cases out of 12 had concordance (75%).

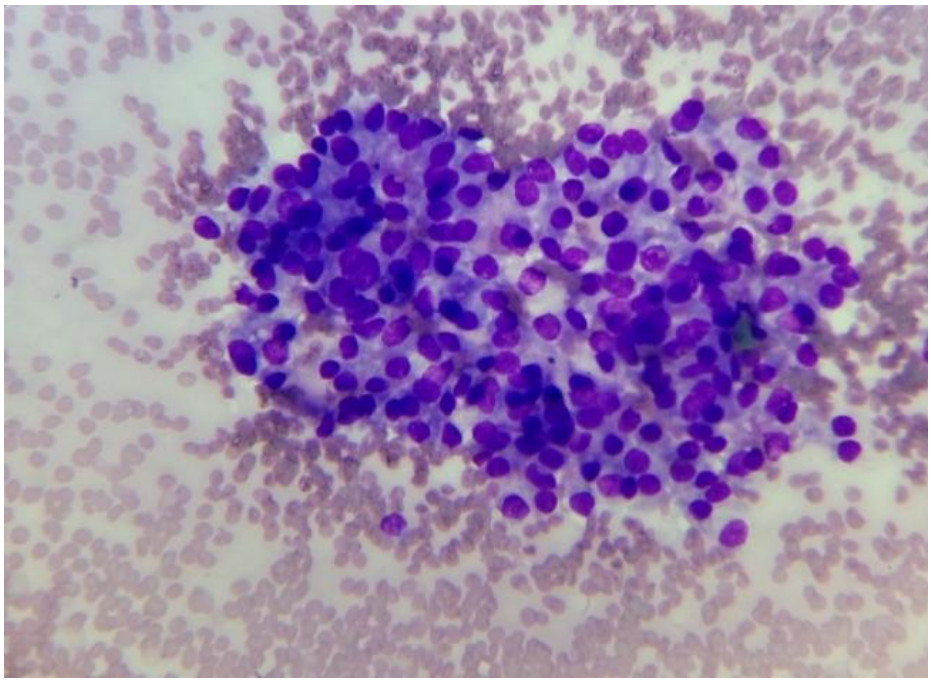


Fig 1- MGG stain 400X; Photomicrograph of follicular neoplasm showingtumour cells arranged in follicular pattern on cytology.

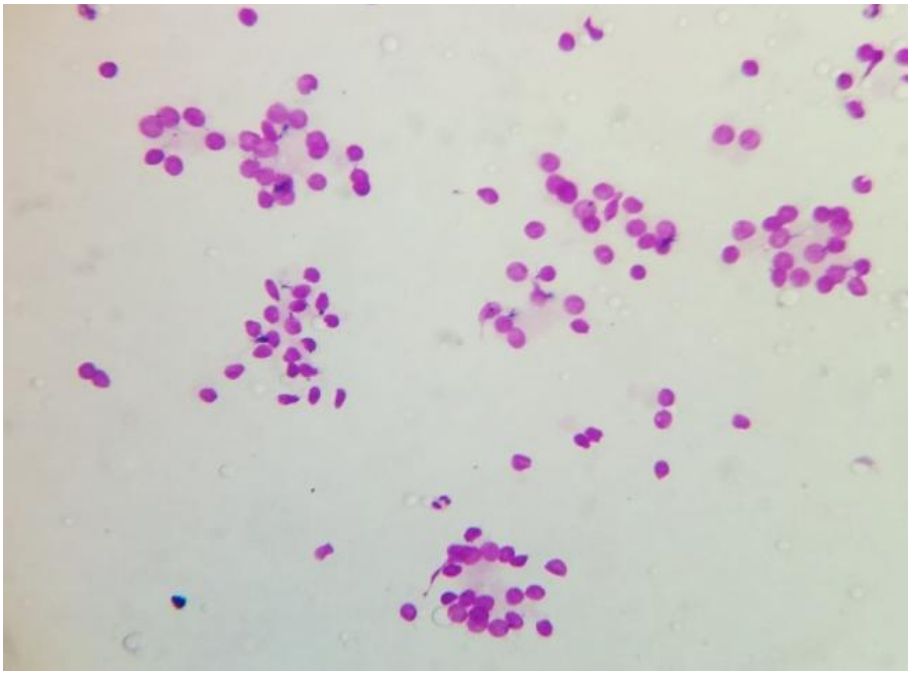


Fig 2 – H&E stain 400X; photomicrograph of follicular neoplasm showing follicular cells in repetitive microfollicular pattern on cytology

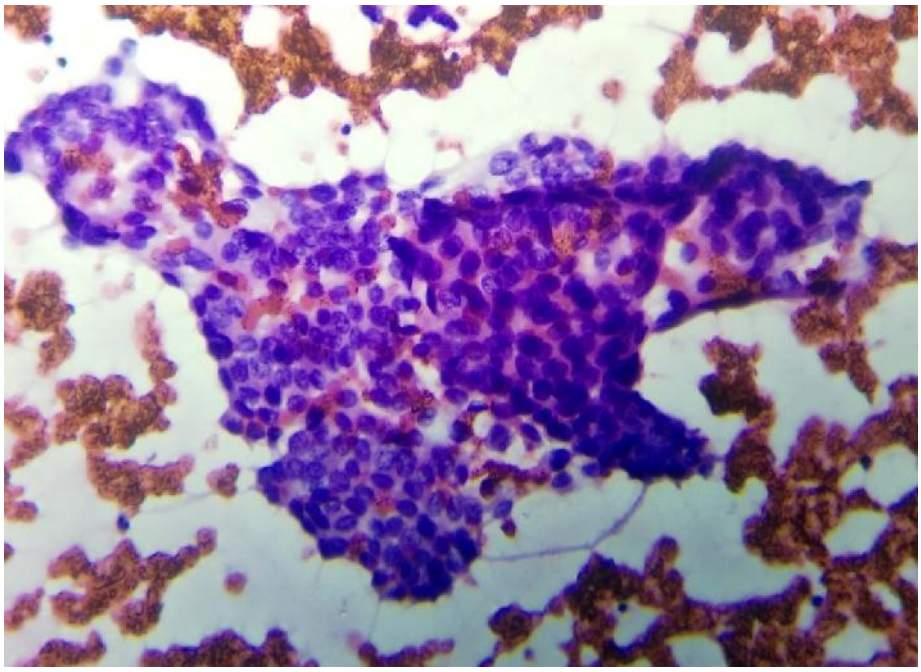


Fig 3- MGG 400X; photomicrograph of papillary carcinoma thyroid showing tissue fragment with papillary pattern and anatomical borders oncytology.

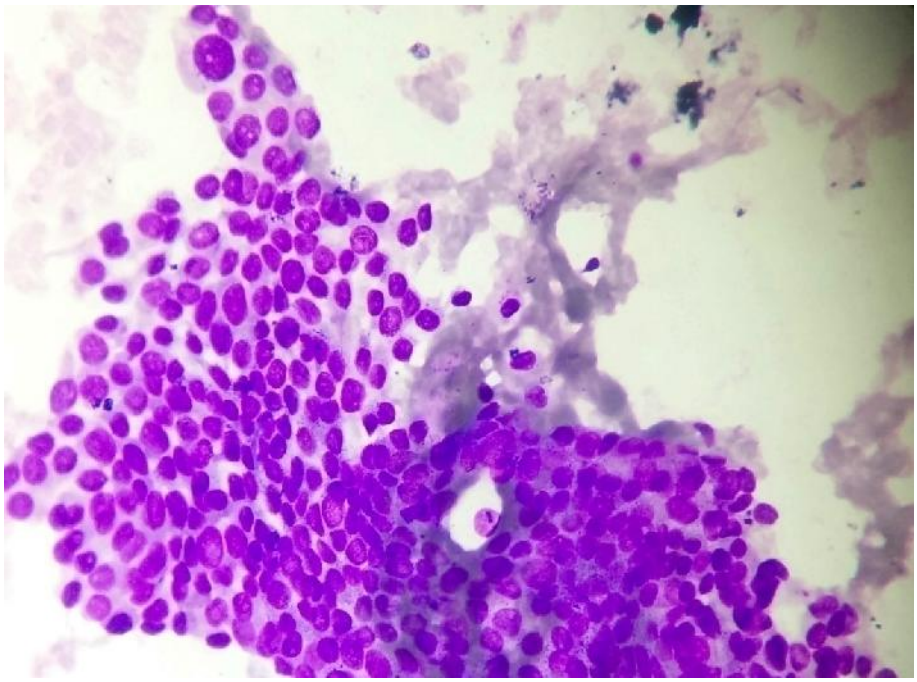


Fig 4- PAP 400X;photomicrograph of papillary carcinoma thyroid showing tissue fragment with well defined anatomical border on cytology.

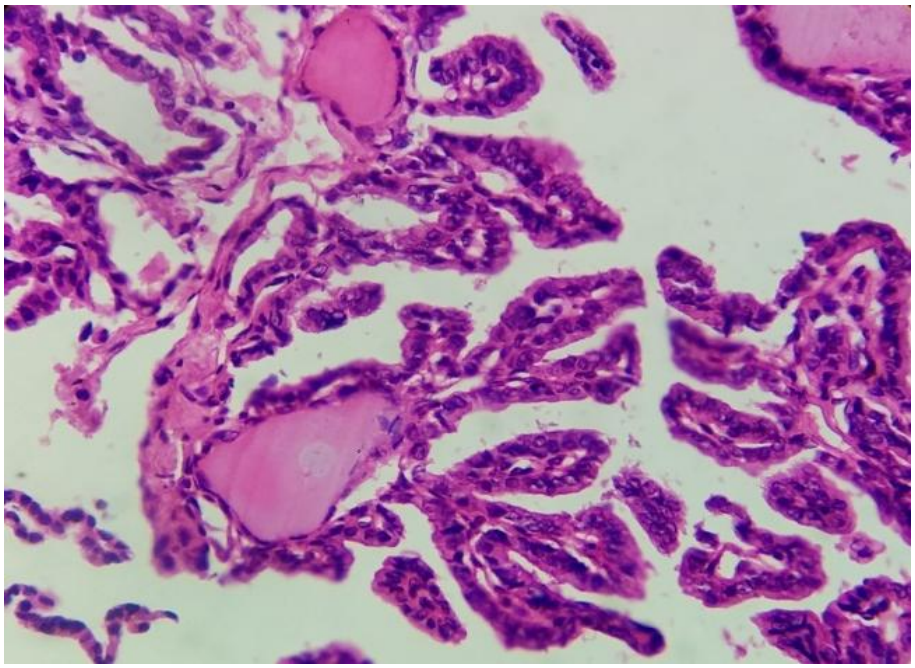


Fig 5- H&E 400X; Photomicrograph of papillary carcinoma thyroid showing tumour cells arranged in papillary pattern on histopathology.

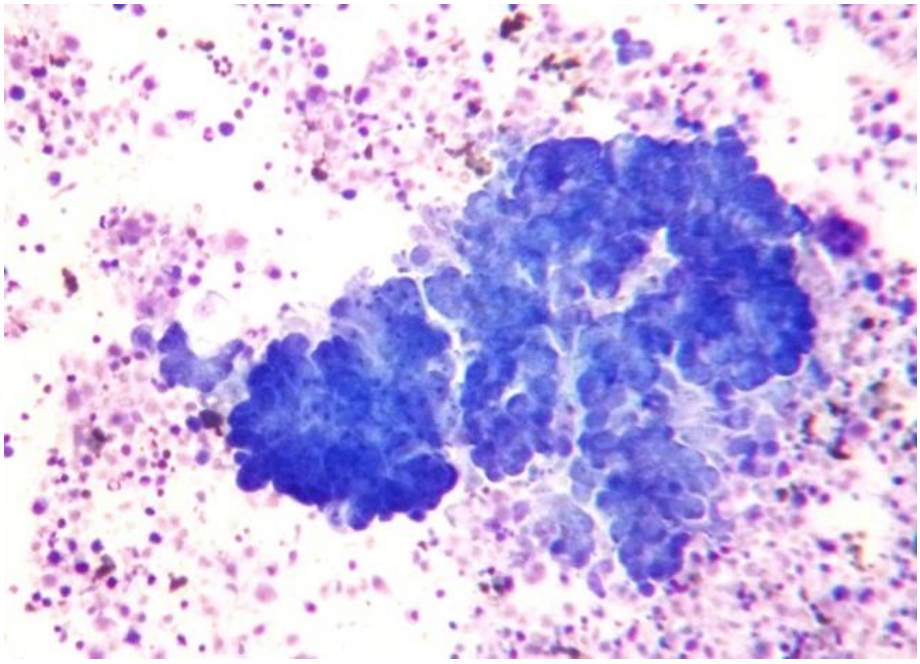


Fig 6- MGG 400X; photomicrograph of metastatic adenocarcinoma showing tumour cells arranged in 3D clusters on cytology.

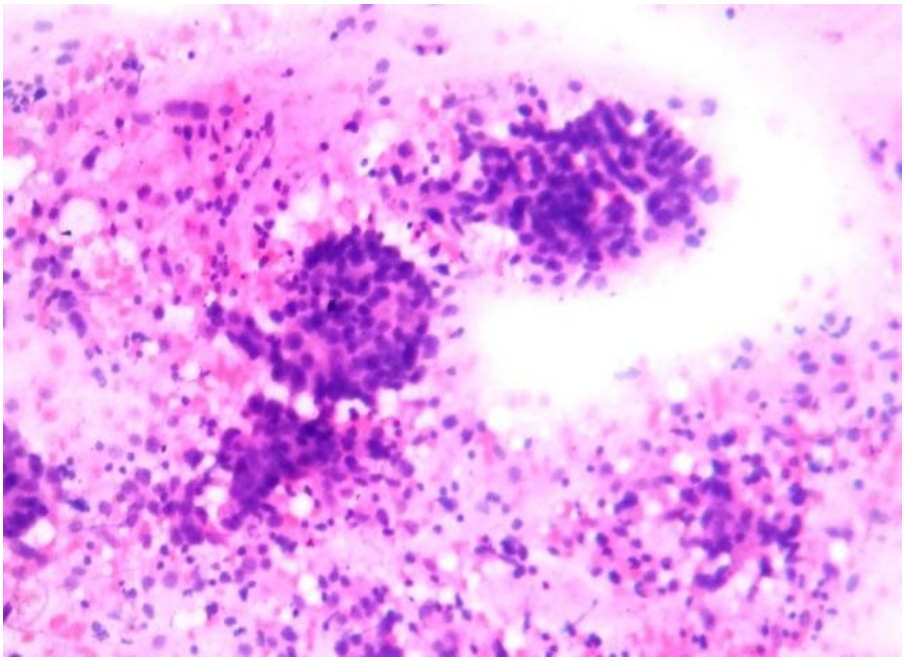


Fig 7- H&E 100X; photomicrograph of metastatic adenocarcinoma of lymph node, showing acinar pattern on cytology.

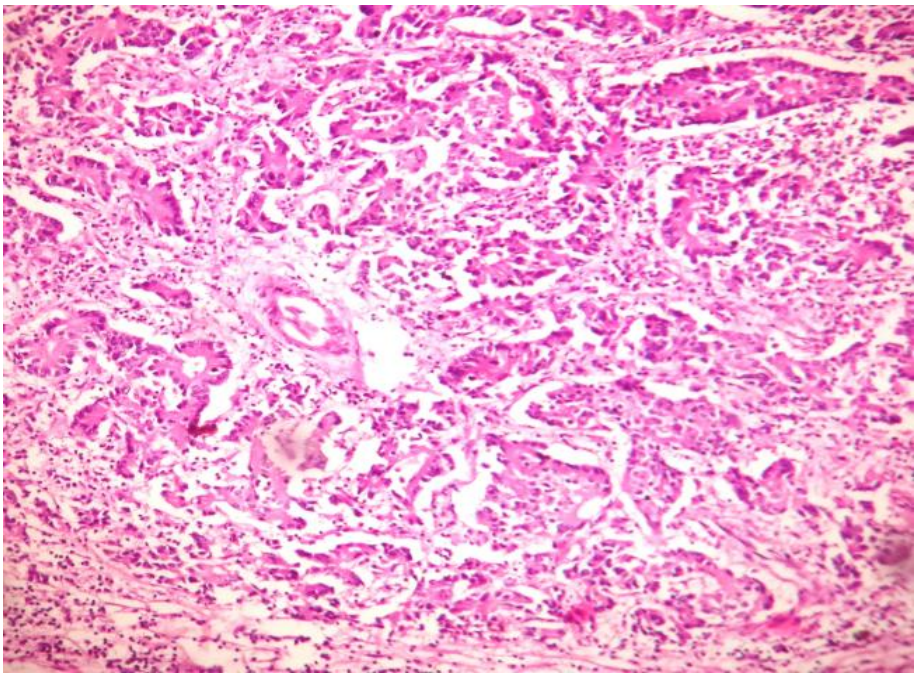


Fig 8- H&E 400X; photomicrograph of adenocarcinoma showing tumour cells arranged in glandular patternon histopathology.

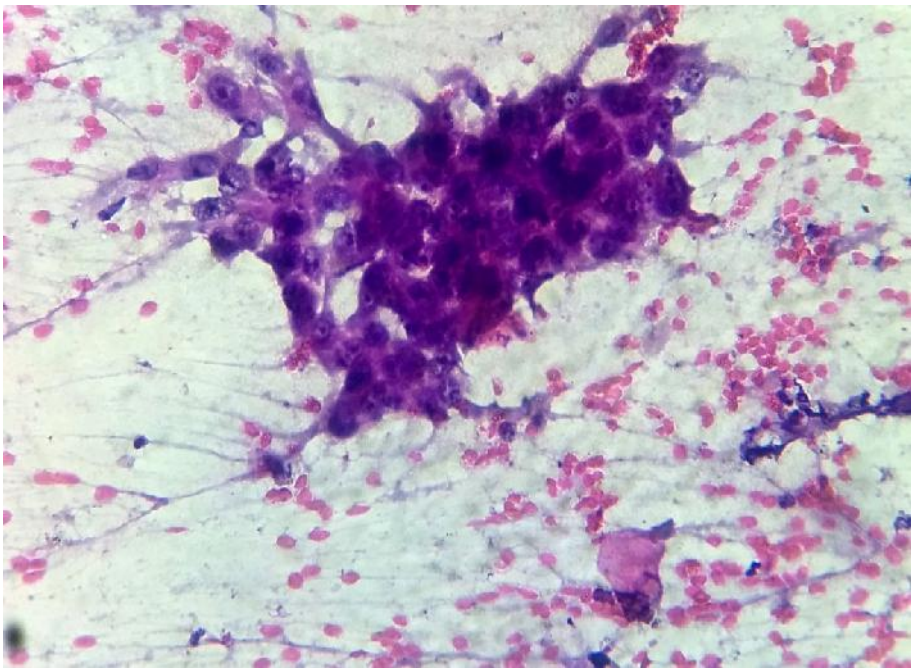


Fig 9- H&E 400X; photomicrograph of metastatic squamous cell carcinoma in lymph node showing sheets of tumour cells on cytology.

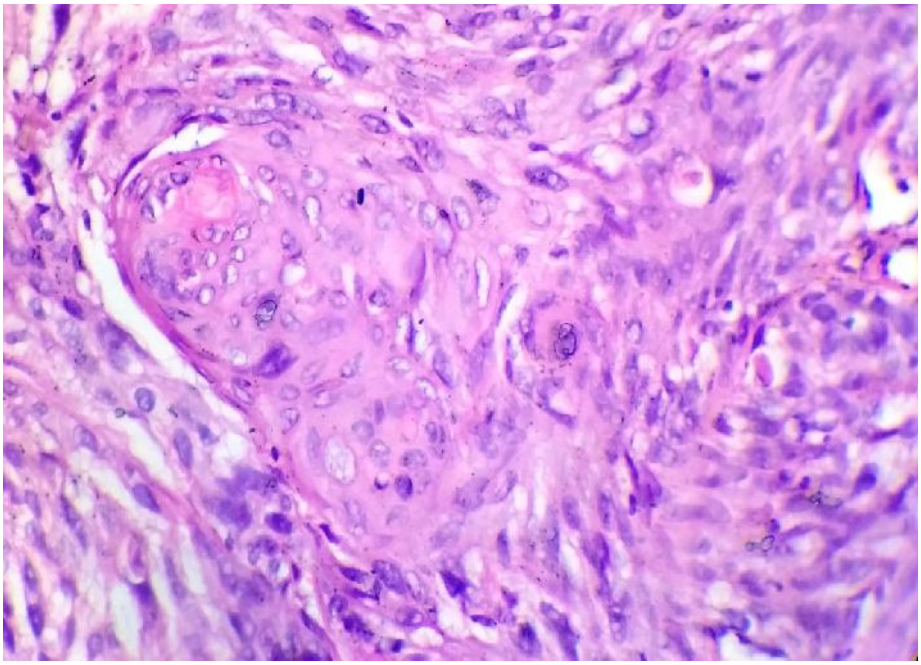


Fig 10- H&E stain 400X; photomicrograph SCC showing individual cell keratinisationon histopathology.

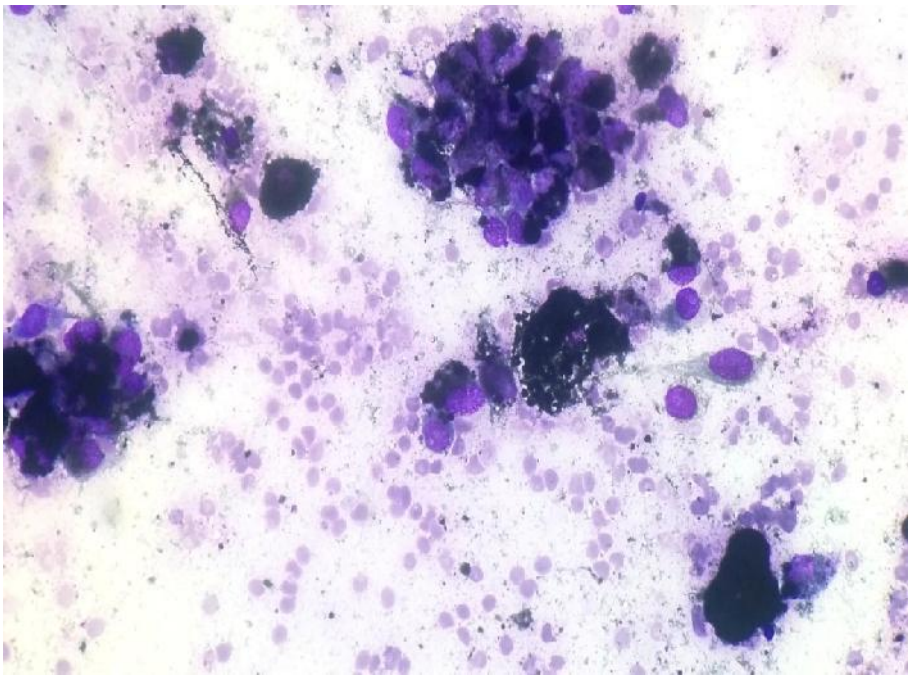


Fig 11- MGG 400X; photomicrograph of metastatic melanoma showing cluster of neoplastic cells with intracytoplasmic melanin pigment on cytology.

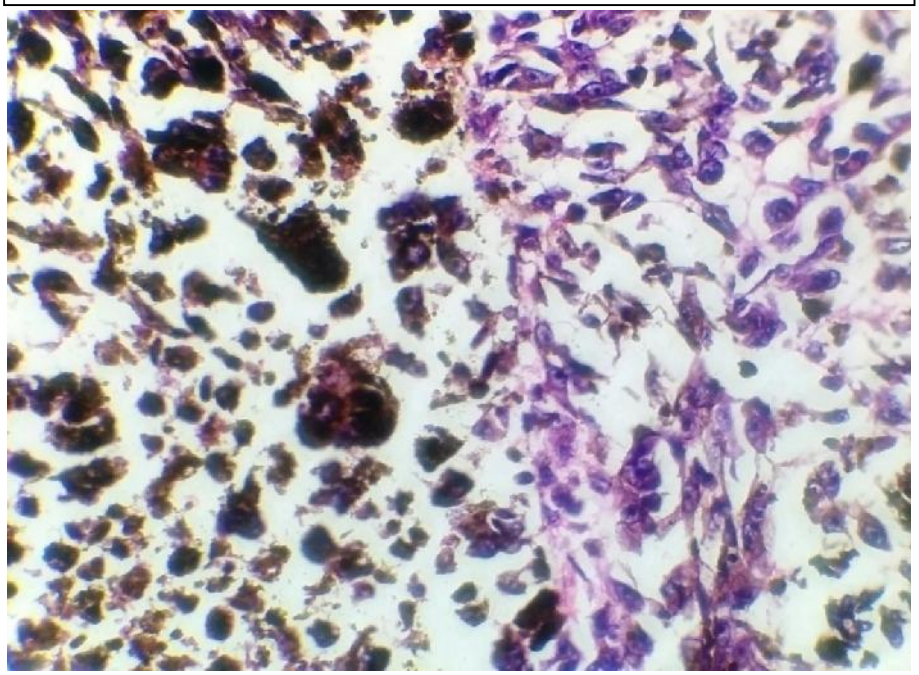


Fig 12- H&E 400X; photomicrograph of metastatic melanoma showing pleomorphic tumour cells with melanin pigment on histopathology.

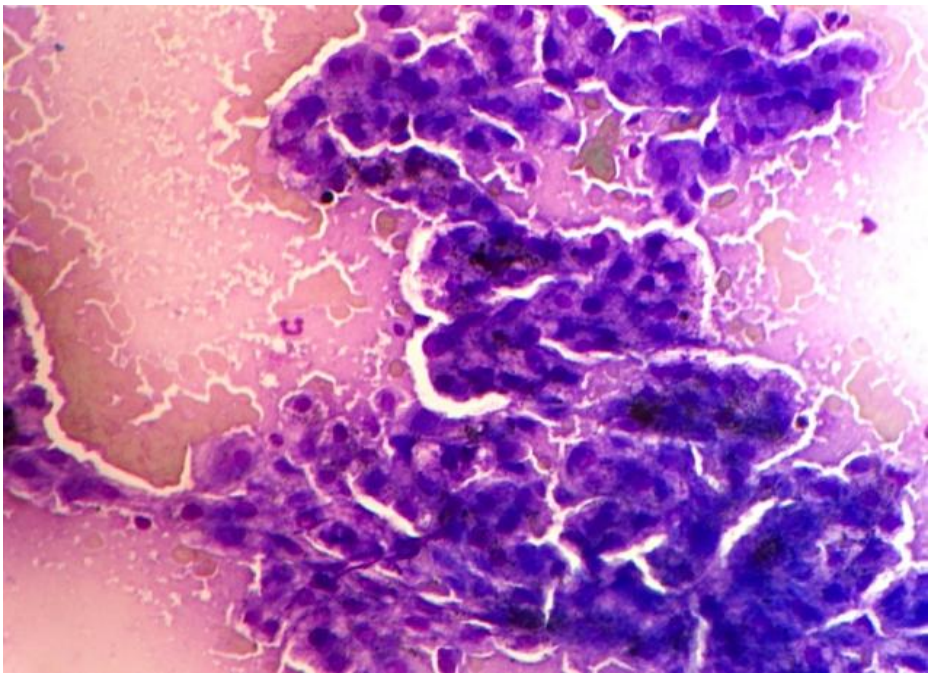


Fig 13- MGG 400X; photomicrograph of HCC showing tissue fragment arranged in trabecular pattern on cytology.

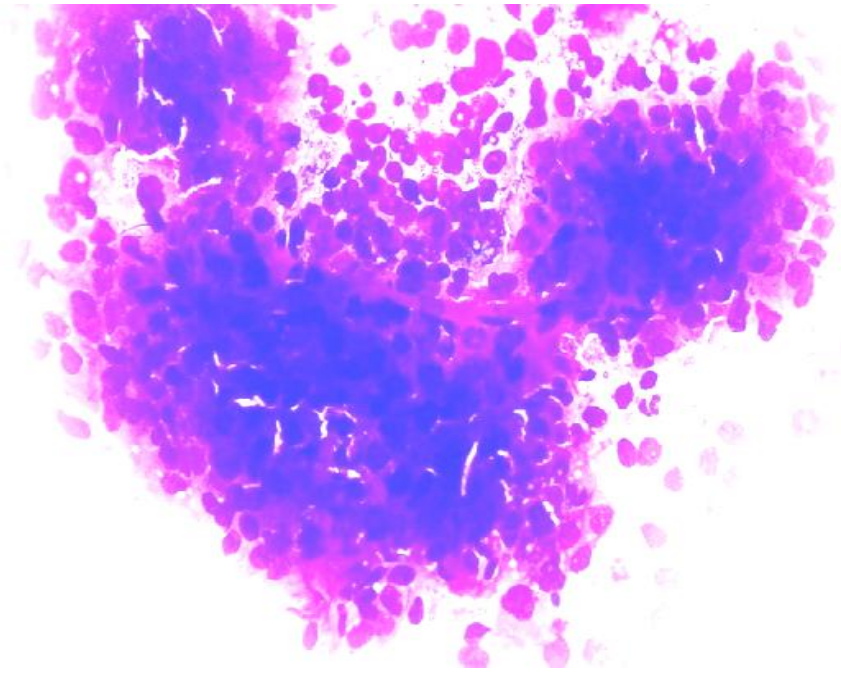


Fig 14- MGG 400X; photomicrograph of HCC showing tissue fragment along with prominent endothelial cell transgressing on cytology.

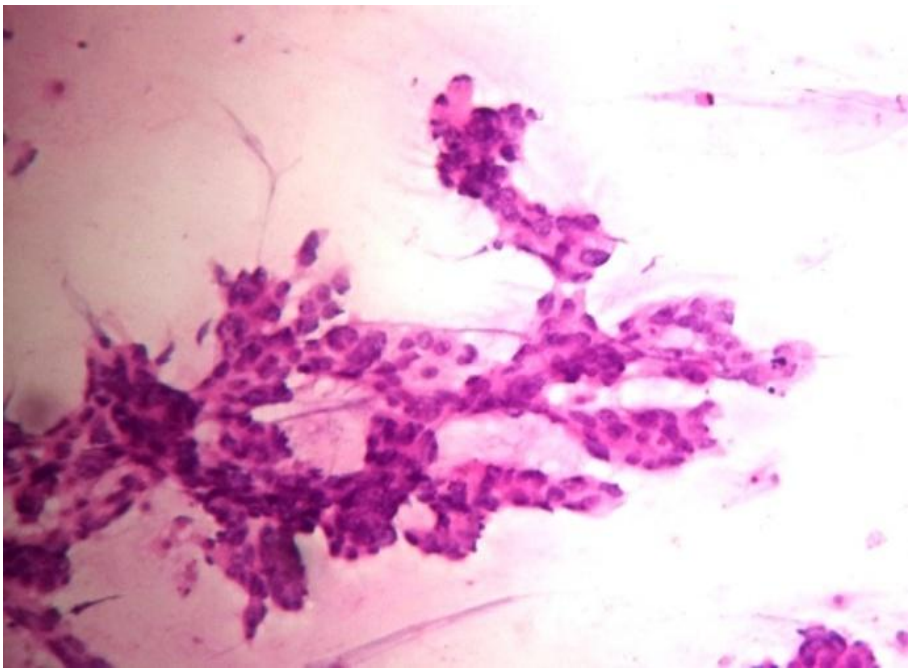


Fig 15-PAP 100X;photomicrograph of metastatic embryonal carcinoma showing papillary fronds of tumour cellson cytology.

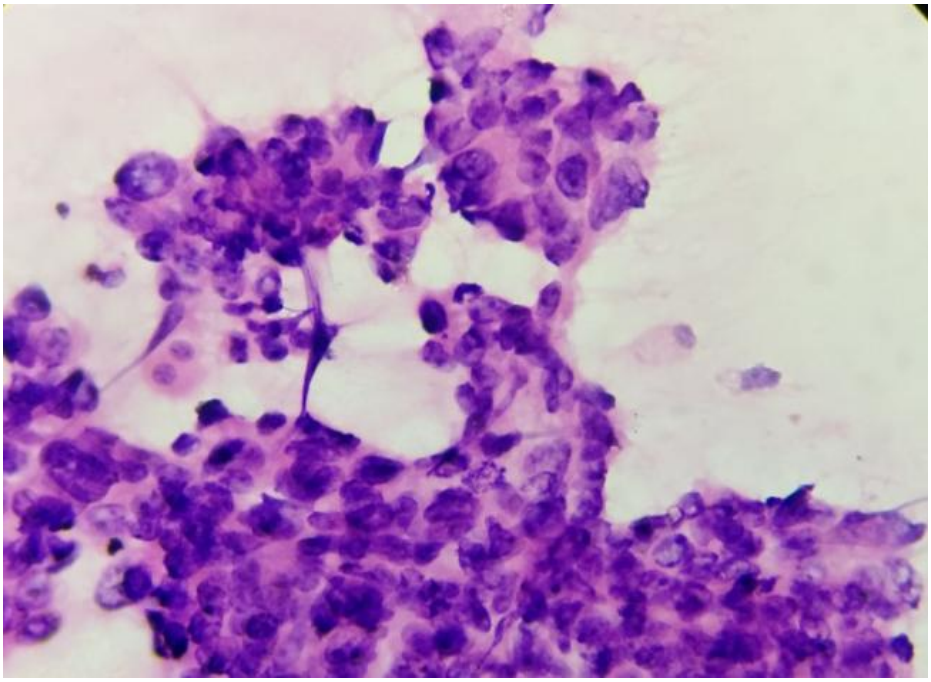


Fig 16-PAP 400X; photomicrograph of metastaticembryonal carcinoma showing tumour cells arranged focally in acinar pattern on cytology.

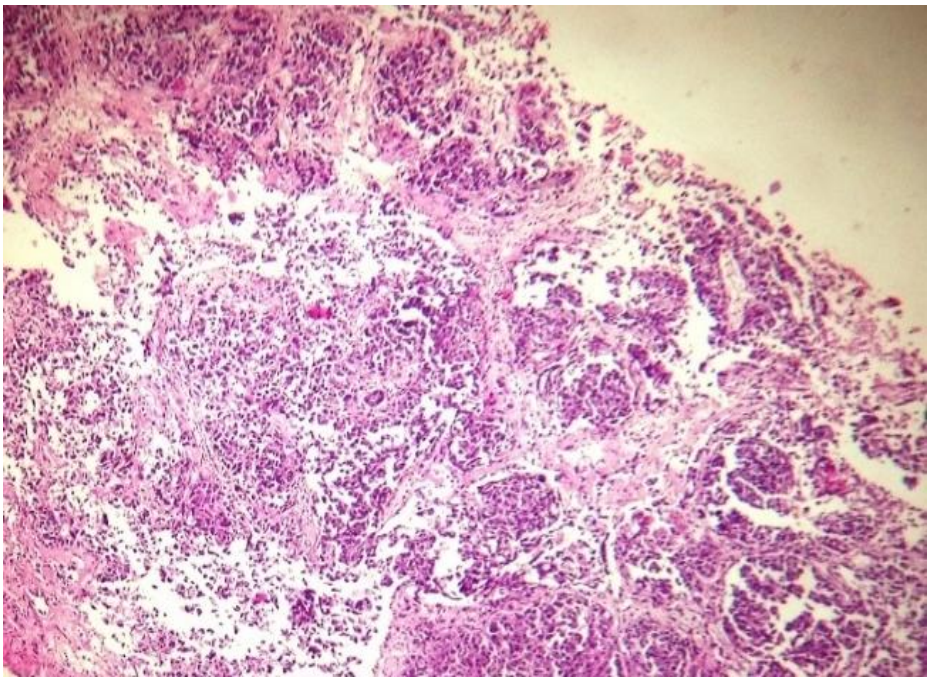


Fig 17- H&E 100X; photomicrograph of embryonal carcinoma on histopathology.

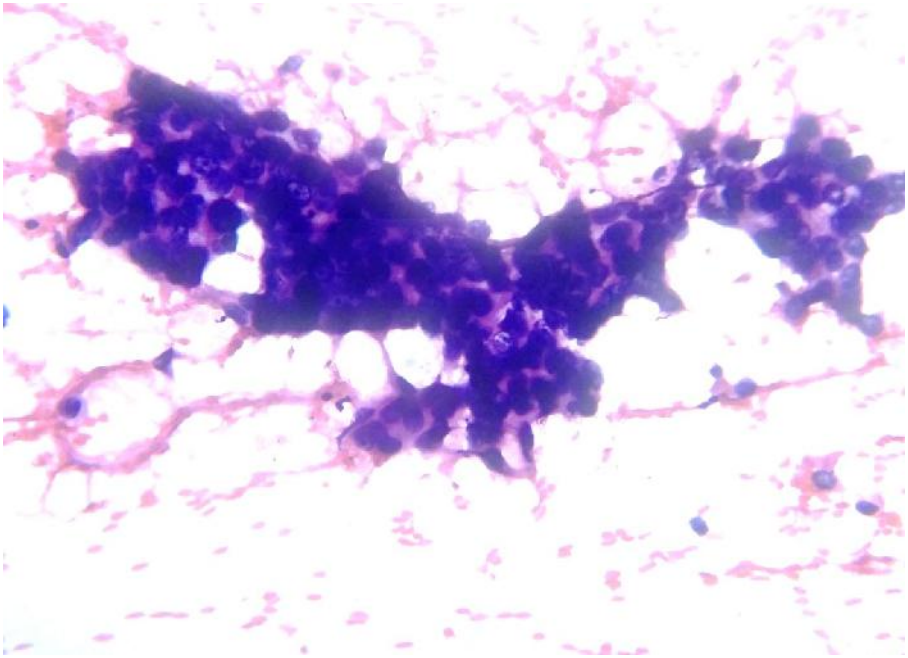


Fig 18- H&E 400X; photomicrograph of infiltrating ductal carcinoma showing dyscohesive clusters of tumour cells on cytology .

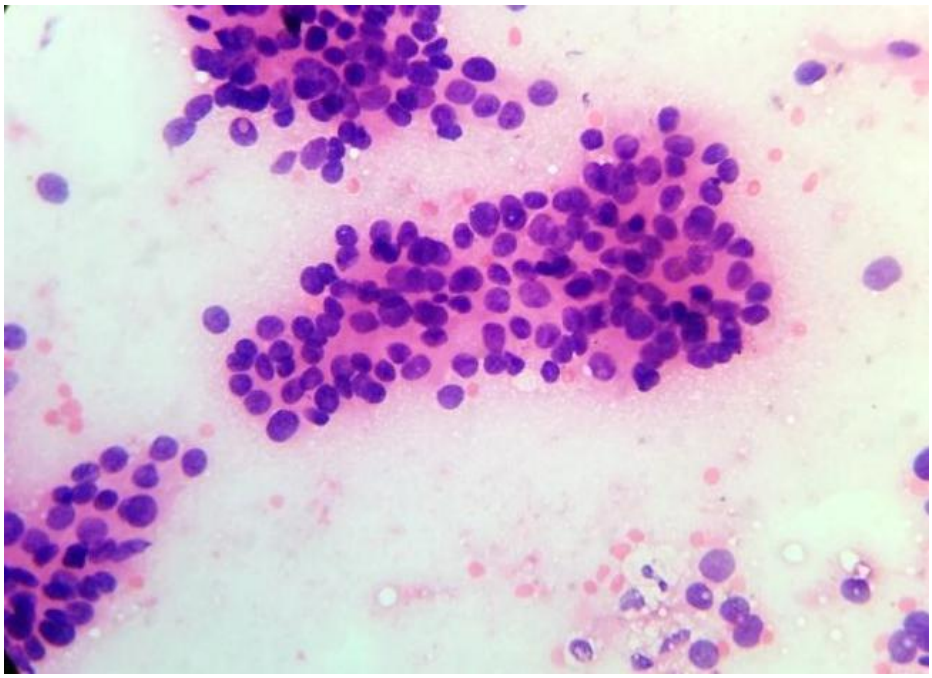


Fig 19- PAP 400X; photomicrograph of infiltrating ductal carcinoma showing tubular epithelial fragment on cytology.

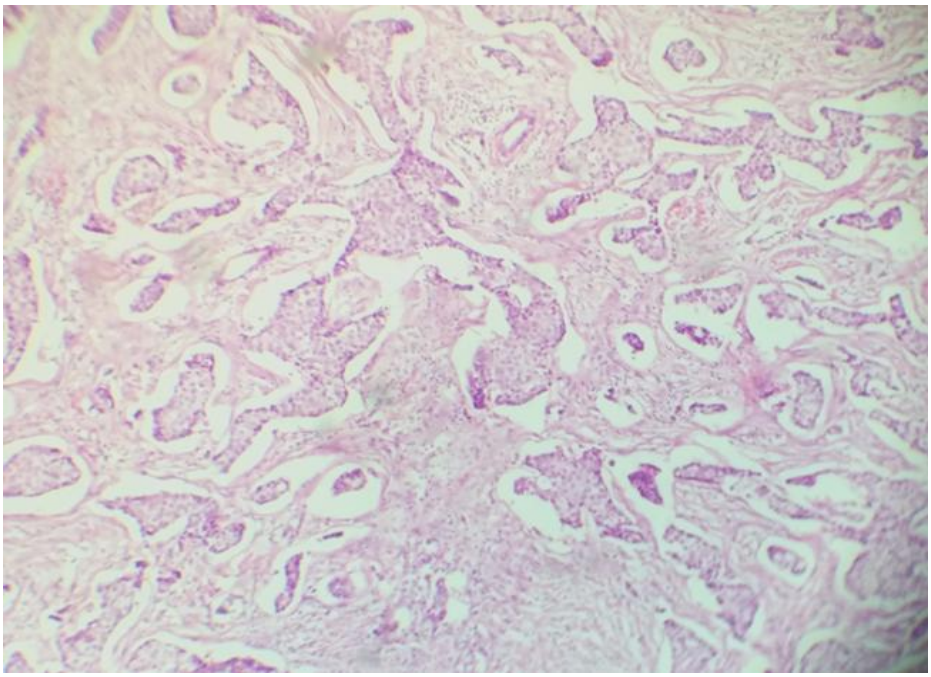


Fig 20-H&E 100X; photomicrograph of infiltrating ductal carcinoma of breast on histopathology.

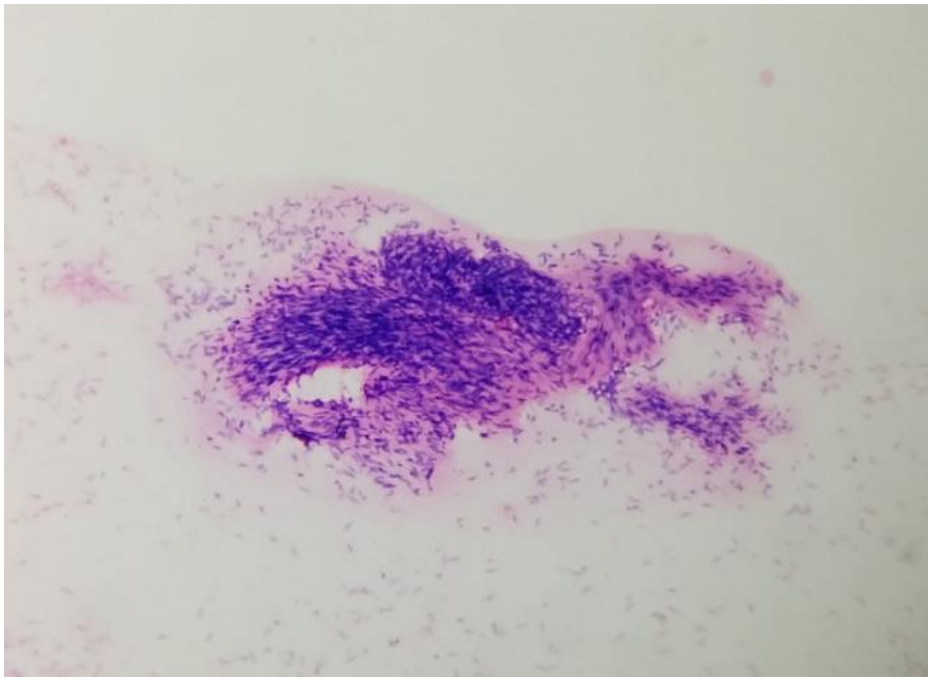


Fig 21- H&E 100X; photomicrograph of DFSP tissue fragment with tumour cells arranged in storiform pattern on cytology.

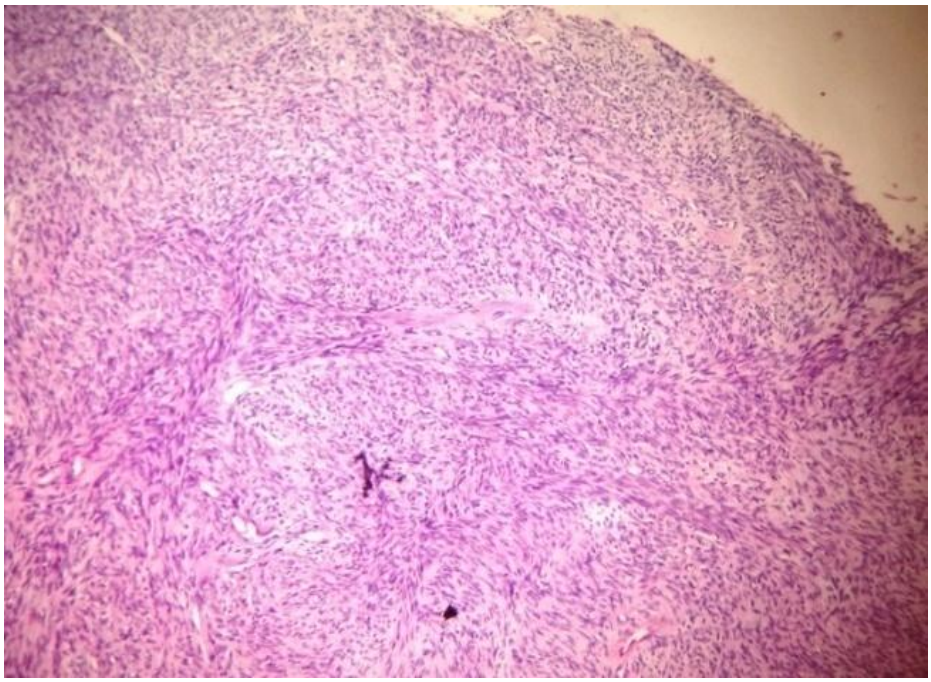


Fig 22-H&E 400X; photomicrograph of DFSP on histopathology showing tumour tissue arranged in storiform pattern.

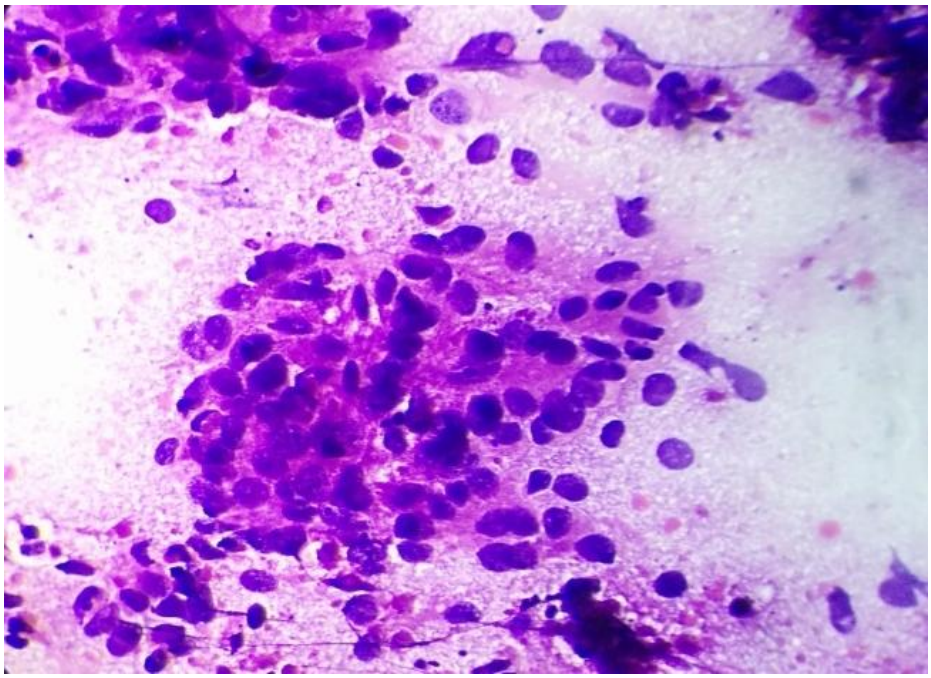


Fig 23- MGG 400X; photomicrograph of Ewing sarcoma showing small round blue cells arranged in rosettes on cytology.

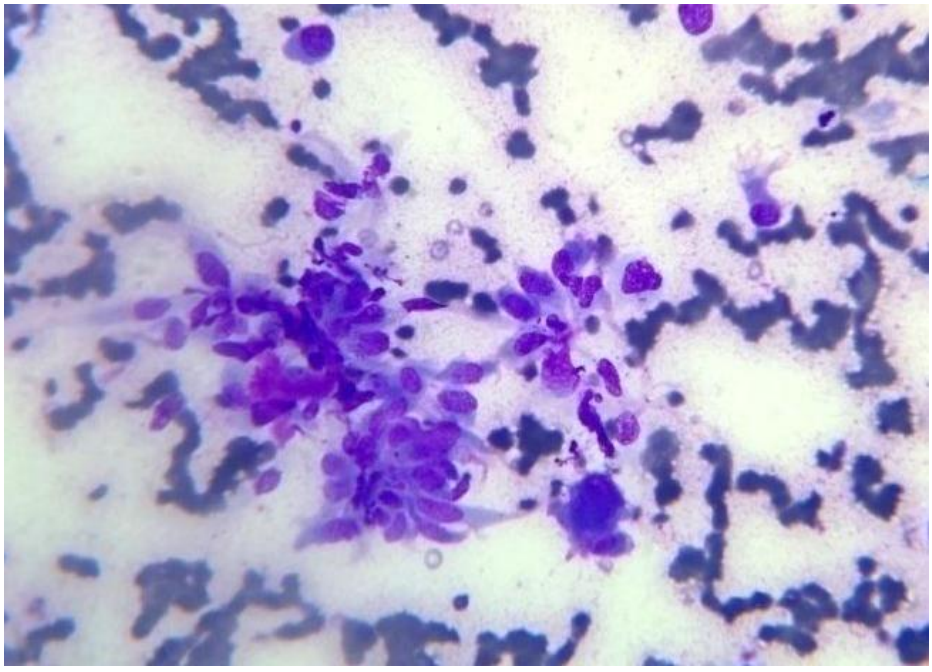


Fig 24- MGG 400X; photomicrograph of low to intermediate grade sarcoma showing cluster of elongated spindle cells on cytology.

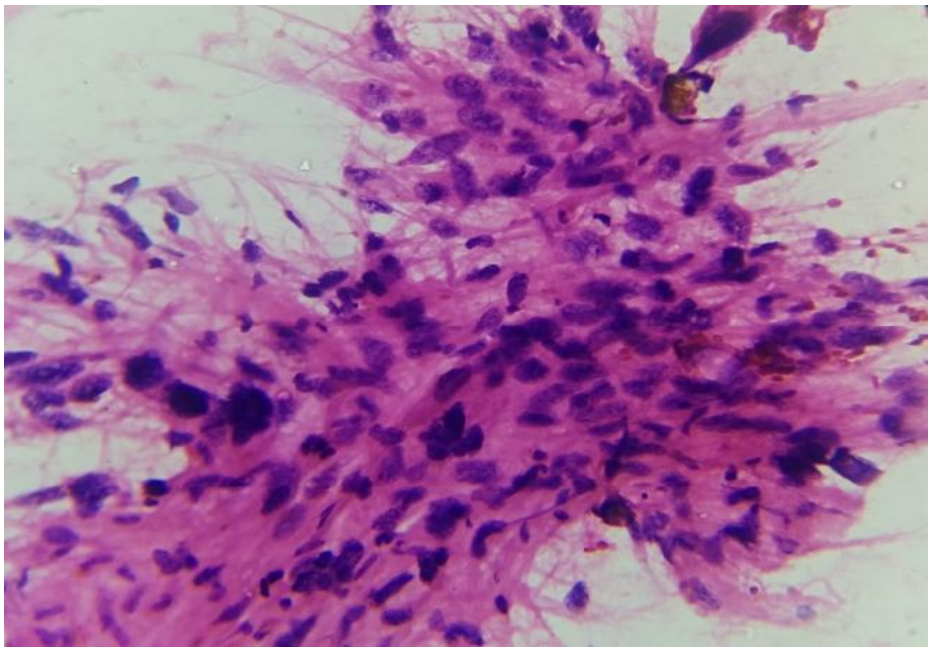


Fig 25- H&E 400X; photomicrograph of high grade sarcoma showing multilayered sheet of pleomorphic tumour cells on cytology

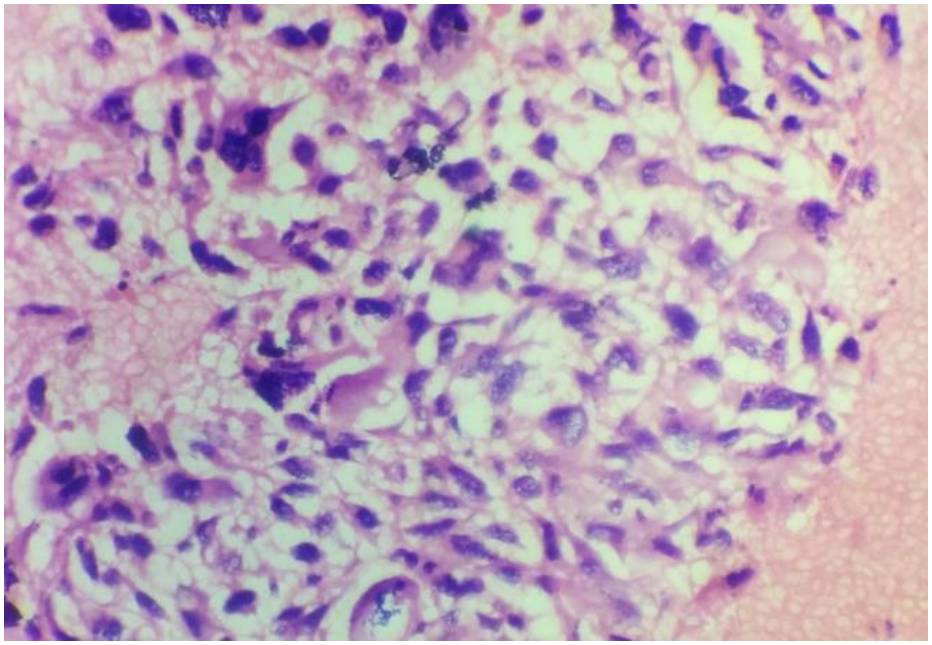


Fig 26- H&E 400X; photomicrograph of pleomorphic sarcoma showing pleomorphic cells on histopathology.

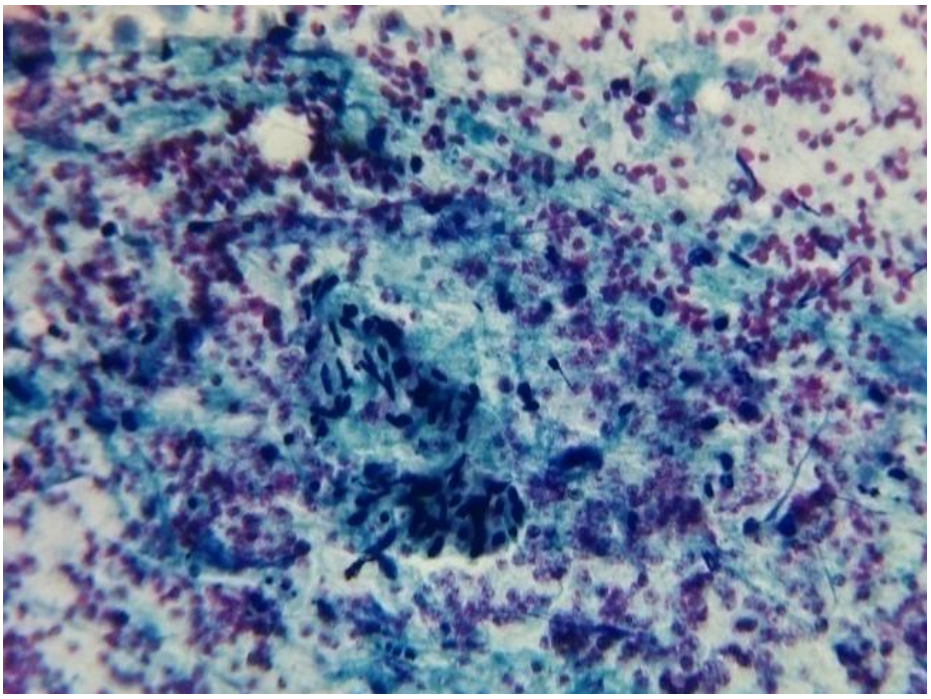


Fig 27- PAP 400X; photomicrograph of high grade sarcoma showing small cluster of tumour cells on cytology.

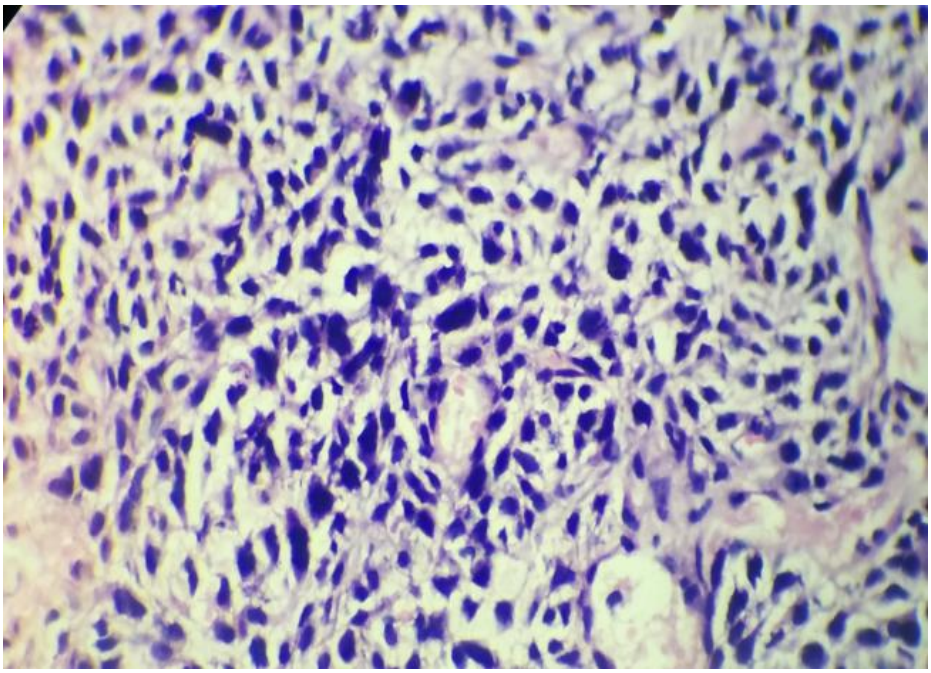


Fig 28- H&E 400X; photomicrograph of mesenchymalchondrosarcoma on histopathology.

DISCUSSION

FNA smears often contain tissue fragments which are identical to a needle biopsy[4]. These fragments or microbiopsies, have a considerable cell volume than the rest of cytology specimen. But these microbiopsies are often disregarded while evaluating cytological smears in favour of other areas where cells are dispersed for making a diagnosis.[3]

Sometimes these tissue fragments are too thick and interpreting them may be difficult.[4] Yet, periphery of these fragments where microbiopsies are thinner if examined carefully can provide invaluable clues to the microhistology of the lesions.[3,31] Analysis and interpretation of the smears with tissue fragments can provide both cytological and histological perspective in the same aspirate.[3] That is both cellular morphology and tissue architecture can be assessed on a single slide.

Few authours have described various techniques for processingmicrobiopsies from cytology smears.Mravunac M *et al*[4] and Verbeek DH*et al*[31] marked the location of microbiopsy on the underside of the slide using adiamond pen. Later a thick layer of Pertex synthetic mounting media was spread over the material from which the cover slip was removed. After solidification of Pertex, the biopsy along with a small margin of Pertexsurrounding the microbiopsy was cut using a scapel. The microbiopsy and surrounding Pertex were lifted off the slide with the knife and processed futher.

Nosanchuk J S [32]used another method for processing microbiopsies. He shaved offthe thick portion of the smear from the slide with a razor blade or scalpel blade. The shavings were collected in lens paper and processed as a tiny surgical specimen.However these methods increase the reporting time and are not cost

effective.[3]Further, these tissue fragments are small and are likely to be missed during processing.

Hence in this study an attempt was made to assesmicrobiopsies on the same cytology slide without processing them which was similar to the study done by Sherwani RK*et al*[3]. After extensive literature search this was the only study with almost similar objective throughout the study period.

A total of 80 cases were included in the study, out of which 54 cases contained microbiopsies accounting for 67.5%. Similar findings were noted by Sherwani RK*et al*[3] and Mravunac M*et al*[4] where microbiopsies were present in 70% and 71% of cases respectively.

TABLE 17- COMPARISION OF PERCENTAGE OF CASES CONTAINING MICROBIOPSIES IN DIFFERENT STUDIES.

MICROBIOPSIES	PRESENT STUDY	SHERWANI RK*et al*[3]	MRAVUNAC M*et al*[4]
PRESENT	67.5%(54 cases)	70%(81 cases)	71%(32 cases)
ABSENT	32.5%(26cases)	30%(35 cases)	29%(13cases)

The studypopulation in the present study was distributed over the age group of 9 years(youngest patient) to 86 years(oldest patient). Similar age distribution was noted by Sherwani RK*et al*[3] wherein the youngest patient was 13 years and oldest patient was 90years. The majority of cases(30%) in the present study were clustered in sixth decade of life, which was concordant with the study done by Sherwani RK*et al*[3] where 30.2% of the cases were seen in the sixth decade of life.

In the present study male: female ratio was 1:1.16 while in the study done by Sherwani RK *et al*[3] it was 1.9:1.

Among 54 cases that had microbiopsies, 38 were primary lesions and 16 were metastatic lesions. Among the 38 cases, 42.11% were in breast, 21.05% were in

thyroid, 13.16% were in soft tissues, 10.53% in liver, 7.89% in lymph node and 5.26% in lung. Among the 16 metastatic cases, majority of them were in lymph node (93.75%), followed by liver (6.25%).

While in the study done by SherwaniRK *et al*[3] lung was the most common primary site and lymph node was the most common secondary site.

Out of 30 cases of lymph node included in the present study, 18 contained microbiopsies. Sheets of largetumour cells with hyperchromatic nuclei and dense eosinophilic cytoplasm were seen in 9 cases which aided in diagnosis of metastatic SCC. Most of these lesions were seen in cervical group of lymph nodes and the search for the primary was made mainly in the head and neck region. In two cases primary could be identified in the oral cavity and in one case the patient presented with hoarseness of voice and a diagnosis of primary laryngeal carcinoma was made. In rest of the cases follow up was not available. Lung and larynx were the most common primary of metastatic SCC in the study by Sherwani RK*et al*.[3]

Acinar pattern was seen in 5 cases pointing towards the diagnosis of metastatic adenocarcinoma.In a case microbiopsies showed 3D clusters and acini of tumour cells having round to oval nucleus with prominent nucleoli and moderate cytoplasm ,favouring the diagnosis of metastatic adenocarcinoma , later it was found out that the patient had markedly elevated prostate specific antigen (PSA) levels and prostatomegaly. Thus in conjunction with clinical history and biochemical tests, microbiopsies aided in the diagnosis of metastatic prostatic adenocarcinoma in this patient. Rest of the cases, the search for the primary was made mainly in gastrointestinal tract(GIT).Similar findings were noted bySherwani RK *et al*.[3] In their study primary in cases of metastatic adenocarcinomas were mainly from upper GIT.

A patient presented with a pigmented ulcer over right foot along with right inguinal lymphadenopathy. FNAC was done from the lymph node which showed cluster of tumour cells which round to oval, having eccentric hyperchromatic nucleus and abundant cytoplasm with few cells showingintracytoplasmicmelanin pigment, suggesting a diagnosis of malignant melanoma. Subsequent excision biopsy of the ulcer and inguinal lymph node dissection was done. The diagnosis was confirmed on histopathological examination.

In two female patients who presented with axillary lymphadenopathy, FNAC was done which showed dyscohesive clusters of tumour cells which were pleomorphic, round to oval with high N:C ratio having coarse chromatin and moderate cytoplasm suggesting the diagnosis of metastatic IDC. In one case histopathological diagnosis was available which correlated with cytological diagnosis.

Another case of young male where USG guided FNAC of para- aortic lymph nodes was performed.Hehad a previous history of left testicular tumour for whichorchidectomy was done 6 months back. On routine follow uppara-arotic lymph nodes were found to be enlarged and guided FNAC was done. The FNAC smears containedmicrobiopsies with papillary fronds and focal acinar pattern. Individual tumour cells were large with large vesicular nuclei having coarse chromatin ,prominent nucleoli and pale to vacuolated cytoplasm. Thus, a diagnosis of metastaticembryonal carcinoma was made which was further confirmed on histopathology.

Out of 19 cases of breast malignancies, 16 cases containedmicrobiopsies. In 13 cases a diagnosis of IDC was made based on the presence ofdyscohesive clusters of tumour cells which were pleomorphic, round to oval with high N:C ratio, coarse chromatin and moderate cytoplasm. Also tubular epithelial fragments were noted in 2

cases and sheets of tumour cells in another. In 10 caseshistopathologicaldiagnosis was available and all the cases correlated with the cytology diagnosis.In the study by Sherwani RK *et al*[3] 5 cases of IDC with microbiopsies were mentioned.

Microbiopsies were present in 8 cases out of 10 cases of malignant thyroid lesions and histopathology correlation was available in 4 cases. Microfollicular and papillary pattern were the predominant pattern seen.

Presence of papillary pattern with fibrovascular core aided in the diagnosis of papillary carcinoma of thyroid in 2 cases. In a case presence of papillary pattern was reported as suspicious for malignancy but on histopathological examination it turned out to be a case of nodular goiter. Orell*et al*[20] mentioned that papillary foci may be seen in hyperplastic nodular goiter and Gravesdisease but these lesions lack nuclear features of PTC. Thus a careful look at the nuclear features is important. One case correlated with the histopathological diagnosis. One case was lost for follow up.

Follicular neoplasm was diagnosed in 5cases in which microbiopsies showed follicular and microfollicular patterns. In one of the cases wheretumour cells were predominantly arranged inmicrofollicular pattern a diagnosis of follicular neoplasm was made and on histopathological examination the case was diagnosed as follicular variant of papillary carcinoma. Canberk*et al*[21] in their article mentioned that if nuclear features are suspicious for papillary carcinoma then it should be reported as suspicious for malignancy regardless of prominent microfollicular pattern. He further added that FV-PTC do not show prominent nuclear features of PTC in 15-20% of the cases, thus these lesions are likely to be misdiagnosed as FN/SFN.

Soft tissue and bone lesions accounted for 9 cases. Out of whichmicrobiopsies were present in 5casesand histopathology diagnosis was available in 4 cases. In one of the cases, a 38 year old male presented with an anterior

abdominal mass, FNAC of which contained microbiopsies showing tumour cells arranged instoriform pattern. Individual tumour cells were spindle shaped having granular chromatin, small nucleoliand moderate cytoplasm. A diagnosis suggestive of DFSPwas made based on the site and cytological features.The diagnosis was further confirmed by histopathological examination.

Another case of a 24 year old male with mass over the left thigh ,which on radiological examination showed tumour arising from diaphysis of the left femur with soft tissue extension.FNAC showed small round blue cells arranged in rosettes,thus a diagnosis of small round blue cell tumoursuggestive of Ewing sarcoma was made.In anothercase adiagnosis of high grade sarcoma was made on cytologywhere in pleomorphic cells were arranged in multilayered sheets. Individual cells were spindle shaped having pleomorphic hyperchromatic nuclei and moderate eosinophilic cytoplasm. Foci of necrosis and atypical mitosis were also seen. The diagnosis was confirmed on hispathological examination.

In a case of a 28 year old male who presented with a swelling in the right groin; FNAC showed small clusters of spindle cells with elongated hyperchromatic nucleus and moderate cytoplasm and a diagnosis of soft tissue sarcoma was made. On histopthology thetumour cells were oval to spindle shaped with hyperchromatic nuclei, inconspicuous nucleoli and scant to moderate vacuolated cytoplasm. These tumour cells were embeded in a chondromyxoidstroma. Thus thecase was diagnosed as high grade sarcoma suggestive ofmesenchymalchondrosarcoma with the help of radiological findings which showed that the tumour was arising from the bone and extended into the soft tissue. In the study done bySherwani RK*et al*[3] 8 of the cases of soft tissue sarcoma werediagnosed based on microbiopsies.

Guided FNAC of the liver showed presence of tissue fragments in 5 out of 6 cases. The diagnosis of HCC was made in 4 cases. Microbiopsies in these cases showed tumour cells arranged predominantly in trabecular pattern and clusters with prominent endothelial cell transgressing . Individual tumour cells were polygonal having high N:C ratio, central nucleus with prominent macronucleoli and moderate to abundant granular cytoplasm . Extracellular bile plugs was also noted at places.

Another case contained microbiopsywith tumour cells arranged in acinar pattern. Individual tumour cells were round to oval with round to oval nucleus having prominent nucleoli and moderate cytoplasmfavouring the diagnosis of metastatic adenocarcinoma. While only 2 cases of HCC and a case of metastatic adenocarcinoma were mentioned in the study by Sherwani RK *et al*[3]

Wee A[26] in his article stressed that close attention must be paid to architectural patterns because these are essential for accurate distinction of HCC from metastasis.

Out of 3 cases of lung malignancies 2 cases contained microbiopsies. In one of the cases microbiopsies showed multilayered sheets of tumour cells suggesting a diagnosis of SCC and in another acinar pattern was noted favouring the diagnosis of adenocarcinoma. Thus microbiopsies not only helped in diagnosing the lung tumours but also aided in typing the lesions. In the study done by Sherwani RK*et al*[3] 14 cases of lung malignancies were included.

In thepresent study, guided FNAC was done 10 cases, which included 6 cases of liver malignancy, 3 cases of lung tumoursand a case ofpara aortic lymph node enlargement . It was found that these cases yielded higher cellularity and better tissue fragments as the lesion could be visualized and a larger bore needle (20 G lumbar puncture needle) was used for the procedure. Similar findings were reported

by SherwaniRK *et al*[3] where 14 cases of lung malignancies were aspirated under imaging guidance.

TABLE 18:COMPARISION OFDISTRIBUTION OF CASES ACCORDING TO TYPE OF MALIGNANCY DIAGNOSED ON THE BASIS OF MICROBIOPSIES

TYPE OF MALIGNANCY	PRESENT STUDY		SHERWANI RK *ET AL*[3]	
	No of cases	Percentage	No of cases	Percentage
Adenocarcinoma	07	12.96	17	20.9
Squamous cell carcinoma	10	18.51	11	13.6
Soft tissue sarcoma	05	9.25	08	9.9
Hepatocellular carcinoma	04	7.40	02	2.5
Infiltrating ductal carcinoma	17	31.48	08	6.2
Follicular neoplasm	05	9.25	04	4.9
Papillary carcinoma thyroid	02	3.70	00	00
Others	04	7.40	31	38.2
TOTAL	54	100%	81	100%

When assorted to the most common type of malignancy diagnosed on microbiopsies, infiltrating ductal carcinoma was the most common diagnosis followed by squamous cell carcinoma and adenocarcinoma in the present study, while adenocarcinoma was most common diagnosis in the study done by SherwaniRK *et al*[3].

TABLE 19:COMPARISON OFCYTO-HISPATHOLOGICAL CONCORDANCE

	PRESENT STUDY	SHERWANI RK*ET AL*[3]
Cyto-histopathological concordance in presence of microbiopsies	84%	93.2%
Cyto-histopathological concordance in absence of microbiopsies	75%	81.2%
Increase in concordance	9%	12%

In the present study, the cyto-hispathological concordance increased from 75% in absence of microbiopsies to 84% in their presence, thus an increase of 9% was noted. The present study is comparable to the study done by Sherwani RK *et al*[3] in which there was 12.1% increase.

THE FUTURE OF MICROBIOPSY

In the article titled “Five Top Stories in Cytopathology”, Fischer AH *et al*[33] mentioned that small core biopsies tend to become fragmented. Inspite of combined monolayer preparation and a cell block or direct histologic processing, the fragments smaller than 150micrometer cannot be retained. This is because the imate pore size of fliter bags and lens paper is approximately 150 micrometer. While a cytopathologist can make a diagnosis on a fragment which is smaller than 150micrometer. Many key diagnostic features usually present in material obtained with needle having diameter less than 23G needle.

Istvanic*et al*[34] in their study also mentioned that the actual volume of tissue obtained by one pass of FNAC is comparable to the volume of tissue sampled by core needle biopsies. Thus with careful observation ofmicrobiopsies in cytological smears and improvement in the FNAC needle design , the downward trend in the use of cytology as the primary diagnostic tool can be halted.

LIMITATIONS OF THE STUDY

Histopathology correlation was available in only 37 cases. Most of the patients with metastatic disease were subjected for neoadjuvant chemotherapy and excision biopsy was not done. Few patients were also lost for follow up.

CONCLUSION

In the current era, where "needle precedes the scalpel" and the biopsy material is getting limited, it would be useful to carefully evaluate cytological smears with tissue fragments/microbiopsies. Microbiopsies are of ample help in diagnosis , typing of the tumour and identifying the primary site in the metastatic lesions. Thus, enhancing the diagnostic accuracy of FNAC especially in resource poor setups.

SUMMARY

In the present study 80 FNA smears of clinically suspected malignant lesions received from1st December, 2014 to 30th July, 2016for cytological evaluation were included. These smears were evaluated for the presence of well preserved tissue fragments or microbiopsies.

Standard FNAC procedure was performed. Smears fixed in 95% alcohol were stained with Haematoxylin and Eosin (H&E) and Papanicoloau stains, while air dried smears were stained with May-GrunwaldGiemsa (MGG) stain.

Out of 80 cases, 54 cases contained representative tissue fragments of the tumors (microbiopsies).

Out of 30 cases of lymph node lesions, 18 cases contained microbiopsies, in 9 cases microbiopsies aided in diagnosis metastatic SCC. 6 cases were diagnosed as metastatic adenocarcinoma, one case of metastatic melanoma,a case as metastatic embryonal carcinoma and 2 cases of metastatic IDC.

Out of 19 cases in breast, 16had microbiopsies. The predominant pattern seen was dyscohesive clusters of tumour cells followed by tubular epithelial fragment and sheets of tumour cells which aided in the diagnosis of infiltrating ductal carcinoma.

Malignant thyroid lesions accounted for 10 cases. 8 cases had microbiopsies with tumour cells arranged in papillary pattern, microfollicular and follicular patterns. They aided in the diagnosis of papillary carcinoma and follicular neoplasm. While diagnosis of FV-PTC and adenomatoid nodule were misdiagnosed

as follicular neoplasm. And a case of MNG was misdiagnosed as suspicious of papillary carcinoma.

Out of 9 cases of soft tissueand bone tumours 5 cases had microbiopsies which aided in the diagnosis of DFSP, Ewing sarcoma, low to intermediate grade sarcoma and 2 cases of high grade sarcoma.

Guided FNAC of the liver showed presence of microbiopsies in 5 outof 6 cases. The diagnosis of HCC was made in 4 cases and another case was diagnosed as metastatic adenocarcinoma.

Out of 3 cases of lung malignancies 2 cases contained microbiopsies. One of them was diagnosed as SCC and another adenocarcinoma.

In the present study, the cyto-hispathological concordanceincreased from 75% in absence of microbiopsies to 84% in their presence, thus an increase of 9% was noted.

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ANNEXURE I

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 54/14
Date. 24/11/14
BLDE's Shri B.M. Patil Medical College,

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 22-11-2014 *at* 3-30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "Interpretation of Microbiopsies in cytological Smears and Histopathological correlation"

— x — x — x —

Name of P.G. student Dr. Namrata Balachandra Mestri.
Dept of Pathology.

Name of Guide/Co-investigator Dr. B.R. Yelikar, Prof & HOD.
Dept of Pathology.

for

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE II

B.L.D.E.UNIVERSITY , SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL

AND RESEARCH CENTER ,VIJAYAPUR-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

I, the undersigned, , S/O D/O W/O , aged years, ordinarily resident of do hereby state/declare that Dr of Hospital has examined me thoroughly on at (place) and it has been explained to me in my own language that I am suffering from disease (condition) and this disease/condition mimic following diseases . Further Doctor informed me that he/she is conducting dissertation/research titled under the guidance of Drrequesting my participation in the study. Apart from routine treatment procedure the pre-operative, operative, post-operative and follow-up observations will be utilized for the study as reference data.

Doctor has also informed me that during conduct of this procedurelike adverse results may be encountered. Among the above complications most of them are treatable but are not anticipated hence there is chance of aggravation of my condition and in rare circumstances it may prove fatal in spite of anticipated diagnosis and best treatment made available. Further Doctor has informed me that my participation in this study help in evaluation of the results of the study which is useful reference to treatment of other similar cases in near future, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator

will be kept secret and not accessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on information given by me, I can ask any clarification during the course of treatment / study related to diagnosis, procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Shri/Smt under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of patient:

Signature of doctor:

Witness: 1.

2.

Date:

Place

ANNEXURE III

PROFORMA

NAME	:	OP/IP No.	:
AGE	:		
SEX	:	D.O.A:	

RELIGION : D.O.D:

OCCUPATION :

RESIDENCE :

Presenting Complaints :

Past history :

Personal history :

Family history :

Treatment history :

General physical examination:

Pallor present/absent

Icterus present/absent

Clubbing present/absent

Lymphadenopathy present/absent

Edema present/absent

Built poor/average/well

VITALS: PR: RR:

BP: TEMPERATURE:

WEIGHT:

EXAMINATION OF LESIONS:

Inspection:

Number :

Site :

Size :

Margins :

Others :

Palpation:

SYSTEMIC EXAMINATION:

Cardiovascular system

Respiratory system:

Per Abdomen:

Central nervous system:

Examination of Breast, Thyroid, Genitourinary system:

Clinical Diagnosis:

INVESTIGATIONS:

Haematological investigations:

Biochemical Investigations:

Radiological Investigations:

Cytology: Site:

Adequacy:

Cellular features:

Interpretation of microbiopsies:

Impression on Cytology:

Histopathological Diagnosis:

Special investigations (wherever required):

Cytochemical Staining

Immunohistochemistry

Tumor marker assay

KEY TO MASTER CHART

IP	In Patient
OP	Out Patient
Rt	Right
Lt	Left

Ca	Carcinoma
USG	Ultrasound
CT	Computed tomography
HCC	Hepatocellular carcinoma
IDC	Infiltrating Ductal carcinoma
Mets	Metastatic
SCC	Squamous Cell Carcinoma
NHL	Non Hodgkin lymphoma
HL	Hodgkin lymphoma
DFSP	DermatofibrosarcomaProtuberans

MASTER CHART

Serial number	IP/OPNumber	Name	Age	Gender	Site of Lesion	Organ	FNAC diagnosis	METS/PRIMARY	Microbiopsies	Pattern on Microbiopsies	Histopathological Diagnosis
1	IP/2014/439903	Rajeshwari	24	Female	Rt lobe of thyroid	THYROID	papillary ca thyroid	Primary	YES	PAPILLARY	
2	IP/2015/1894	Sharanappa	80	Male	liver (USG guided)	LIVER	poorly differentiated HCC	Primary	NO		
3	IP/2015/2221	Shettavva	30	Female	Thyroid	THYROID	medullary ca thyroid	Primary	NO		Medullary ca thyroid
4	OP/2015/21560	Roopa	25	Female	Thyroid	THYROID	papillary ca thyroid	Primary	YES	PAPILLARY	paillary carcinoma thyroid
5	IP/2015/2520	Sheikhmehboob	50	Female	liver (USG guided)	LIVER	HCC	Primary	YES	TRABECULAR	
6	OP/2015/45485	Shreedevi	50	Female	Rt breast	BREAST	IDC	Primary	YES	SHEETS	IDC
7	OP/2015/65119	Shantabai	60	Female	Thyroid	THYROID	follicular neoplasm	Primary	YES	MICRO FOLLICULAR	
8	IP/2015/18347	Gollal	25	Male	Para aortic lymph node (USG guided)	LYMPH NODE	embroyonalca	Mets	YES	ACINAR	embroyonalca

9	IP/2015/20337	Pramod	35	Male	Rt cervical lymph node	LYMPH NODE	metsscc	Mets	YES	SHEETS	metastatic SCC
10	IP/2015/13646	Basvantrayagowda	60	Male	Lt supra clavicular lymph node	LYMPH NODE	metsadenoca	Mets	YES	ACINAR	
11	OP/2015/156879	Ramdev m	31	Male	ulnar aspect of handa	SOFT TISSUE	epitheloid sarcoma	Primary	NO		
12	OP/2015/244133	Sharanappa	24	Male	Thyroid	THYROID	follicular neoplasm	Primary	YES	MICRO FOLLICULAR	adenomatoid nodule
13	OP/2015/261091	ArjunChavan	32	Male	Lt submandibular swelling	LYMPH NODE	SCC	Mets	NO		
14	IP/2015/22365	Shekavva	45	Female	Rt breast	BREAST	IDC	Primary	YES	CLUSTERS	IDC
15	IP/2015/18581	Chandranappa	60	Male	Left cervical lymph node	LYMPH NODE	mets poorly differentiated SCC	Mets	NO		
16	IP/2015/91636	Appasab	21	Male	Skin	SKIN	cutaneous lymphoma	Primary	NO		cutaneous lymphoma

17	IP/2015/19378	Mallamma	26	Female	Multiple bilateral breast nodules	BREAST	NHL	Primary	NO		NHL
18	IP/2015/20107	Bheemappa	24	Male	Lt lower limb	SOFT TISSUE	Ewing sarcoma	Primary	YES	ROSETTE	
19	IP/2015/36708	Gurudevi	47	Female	Rt breast	BREAST	IDC	Primary	YES	CLUSTERS	
20	IP/2015/1204	Yadappa	35	Male	Rtjugulodiagastric node	LYMPH NODE	poorly differentiated ca	Primary	NO		
21	IP/2015/6653	Shridevi	55	female	Rt breast Lump	BREAST	IDC	Primary	YES	CLUSTERS	
22	OP/2015/82070	Siddaraud	70	Male	Rt cervical node	LYMPH NODE	metsSCC	Mets	YES	SHEETS	
23	OP/2015/100833	Mumtaz	38	Female	Rt breast Lump	BREAST	IDC	Primary	YES	CLUSTERS	
24	OP/2015/103642	Sahebgouda	48	Male	Lt cervical node	LYMPH NODE	metsca	Mets	NO		
25	OP/2015/25580	Irappa	66	Male	Lt supraclavicular lymh node	LYMPH NODE	mets poorly differentiatedca	Mets	NO		
26	OP/2015/306248	Gurushatappa	55	Male	Lt inguinal node	LYMPH NODE	metsadenoca	Mets	YES	ACINAR	
27	IP/2015/26542	Bhimanna	65	Male	liver (USG guided)	LIVER	HCC	Primary	YES	TRABECULAR	
28	IP/2015/28886	Basappa	70	Male	liver (USG guided)	LIVER	HCC	Primary	YES	TRABECULAR	
29	IP/2015/37425	Sharanavva	70	Female	Lt cervical lymph node	LYMPH NODE	metsSCC	Mets	YES	SHEETS	

30	IP/2015/38450	Yallamma	55	Female	Rt breast	BREAST	IDC	Primary	YES	CLUSTERS	IDC
31	OP/2015/364729	Gannapgouda	65	Male	Rt lung (ct guided)	LUNG	poorly differentiated SCC/ large cell carcinoma	Primary	NO		
32	IP/2015/33843	Somanabai	70	Female	Rt Axillary lymph node	LYMPH NODE	mets IDC	Mets	YES	CLUSTERS	
33	OP/2015/393833	Panchappa	55	Male	Rt cervical lymph node	LYMPH NODE	metsSCC	Mets	YES	SHEETS	
34	IP/2015/34830	Vinaykumar	37	Male	Lt cervical lymph node	LYMPH NODE	metsSCC	Mets	YES	SHEETS	
35	OP/2015/438771	Indirabai	30	Female	Rt breast	BREAST	IDC	Primary	YES	CLUSTERS	
36	OP/2015/447449	Gayatri	30	Female	Rt breast	BREAST	IDC	Primary	YES	CLUSTERS	
37	IP/2015/197193	Paravva	60	Female	Lt breast	BREAST	IDC	Primary	YES	CLUSTERS	IDC
38	OP/2015/474264	Neelamma	60	Female	Lt breast	BREAST	IDC	Primary	YES	CLUSTERS	IDC
39	IP/2015/10161	Meenakumari	23	Female	Thyroid	THYROID	follicular neoplasm	Primary	YES	FOLLICULAR	follicular varient of papillary carcinoma
40	IP/2016/257	Nandanabi	50	Female	Rt breast	BREAST	IDC	Primary	NO		IDC
41	IP/2016/7951	Meenakshi k	60	Female	liver (USG guided)	LIVER	metsadenoca	Mets	YES	ACINAR	

42	IP/2016/1374	Mahadevi	60	Female	Lt abdominal wall swelling	SOFT TISSUE	high grade sarcoma	Primary	YES	SHEETS	pleomorphic sarcoma
43	OP/2016/10437	Nangouda B	50	Male	Lt axillary lymph node	LYMPH NODE	mets poorly differentiated ca	Mets	NO		
44	IP/2016/2253	Ningamma	60	Female	Lt supra clavicularL lymph node	LYMPH NODE	metsSCC	Mets	NO		mets SCC
45	IP/2016/2076	Tayappa	60	Male	rt cervical lymph node	LYMPH NODE	metsSCC	Mets	YES	SHEETS	metsSCC
46	IP/2016/1654	Valu	65	Male	rt inguinal lymph node	LYMPH NODE	mets melanoma	Mets	YES	CLUSTERS	mets melanoma
47	OP/2016/42937	Kamala	50	Female	Lt breast	BREAST	IDC	Primary	YES	CLUSTERS	IDC
48	OP/2016/45814	Shivappa	76	Male	Bilateral cervical lymph node	LYMPH NODE	SCC	Primary	YES	SHEETS	
49	IP/2016/4166	Chandrashekar	45	Male	Rt cervical lymph node	LYMPH NODE	metsca	Mets	NO		
50	IP/2016/2390	Ningappa	68	Male	USG guided liver	LIVER	HCC	Primary	YES	TRABECULAR	HCC
51	IP/2016/8581	BirajasRasheed	68	Male	Rt groin	SOFT TISSUE	soft tissue sarcoma	Primary	YES	CLUSTERS	Mesenchymalchondrosarcoma
52	IP/2016/5041	Ratna	80	Female	Rt cervical lymph node	LYMPH NODE	mets poorly differentiated SCC	Mets	NO		

53	IP/2016/5185	Shakuntala	60	Female	Lt breast	BREAST	IDC	Primary	NO		IDC
54	IP/2016/5401	Basavva	25	Female	Thyroid	THYROID	follicular neoplasm	Primary	YES	MICRO FOLLICULAR	
55	IP/2016/11124	Neelamma	60	Female	ltsupraclavicular lymph node	LYMPH NODE	metsadenoca	Mets	YES	ACINAR	
56	IP/2016/12589	Parvati	70	Female	Swelling over lower abdomen	SOFT TISSUE	low to intermediate grade sarcoma	Primary	NO		
57	IP/2016/12889	Maligappa	80	Male	Rt lung(CT guided)	LUNG	SCC	Primary	YES	SHEETS	SCC
58	IP/2016/12493	Kantamma	33	Female	Rt inguinal lymph node	LYMPH NODE	metsadenoca	Mets	YES	ACINAR	
59	OP/2016/148840	Siddawwa	70	Female	Thyroid	THYROID	follicular neoplasm	Primary	YES	MICRO FOLLICULAR	
60	IP/2016/13045	Shridevi	40	Female	Thyroid	THYROID	suspicious for papillary ca	Primary	YES	PAPILLARY	MNG
61	IP/2016/14598	Gopal	59	Male	Swellling over rt shoulder	SOFT TISSUE	pleaomorphic sarcoma	Primary	NO		
62	IP/2016/14828	Shantamma	45	Female	Rt breast	BREAST	IDC	Primary	YES	TUBULAR	IDC
63	IP/2016/14820	Shankarappa	61	Male	Swelling over left anterior superior iliac spine	SOFT TISSUE	low to intermediate grade sarcoma	Primary	YES	CLUSTERS	
64	IP/2016/15503	Rudravva	65	Female	Rt breast	BREAST	IDC	Primary	YES	CLUSTERS	

65	IP/2016/15187	Mallikarjun	55	Male	Rt cervical lymph node	LYMPH NODE	SCC	Primary	YES	SHEETS	
66	IP/2016/15319	Ravatappa	56	Male	Lt supra clavicular	LYMPH NODE	metsadeno	Mets	YES	ACINAR	
67	IP/2016/16586	Ratnabai	55	Female	Rt axillary lymph node	LYMPH NODE	mets IDC	Mets	YES	CLUSTERS	mets IDC
68	IP/2016/20556	Shrishail	55	Male	Rtinguinal	LYMPH NODE	NHL	Primary	NO		NHL
69	IP/2016/21257	Ravi	40	Male	Rt cervical lymph node	LYMPH NODE	SCC	Primary	NO		
70	OP/2016/247174	Sidappa	65	Male	Rt cervical lymph node	LYMPH NODE	SCC	Primary	YES	SHEETS	
71	IP/2016/24205	Mavamma	9	Female	Rt axillary lymph node	LYMPH NODE	suspicious for malignancy	Primary	NO		HL-Nodular sclerosis
72	IP/2016/24927	Gomalabai	50	Female	Rt breast	BREAST	IDC	Primary	YES	CLUSTERS	IDC
73	IP/2016/27304	Sharanamma	60	Female	Lt breast	BREAST	IDC	Primary	YES	CLUSTERS	IDC
74	IP/2016/23189	Ningamma	35	Female	Thyroid	THYROID	colloid cyst	Primary	NO		papillary carcinoma thyroid
75	IP/2016/27159	Muhammad	65	male	(CT guided)lt lung mass	LUNG	adenocarcinoma	Primary	YES	ACINAR	Adenocarcinoma
76	OP/2016/242318	SonabaiKengar	86	Female	Rt leg	SKIN	SCC	Primary	NO		poorly differentiated SCC

77	IP/2016/22504	Indirabai	40	Female	Thyroid	THYROID	MNG	Primary	NO		multifocal papillary carcinoma
78	IP/2015/33539	Danamma	42	Female	Rt pelvic mass	SOFT TISSUE	NHL	Primary	NO		NHL
79	IP/2016/15503	Buddawwa	65	Female	Rt breast	BREAST	IDC	Primary	YES	TUBULAR	IDC
80	IP/2015/25107	Irappa	38	Male	Anterior abdominal wall	SOFT TISSUE	DFSP	Primary	YES	STORIFORM	DFSP