"CYTOMORPHOLOGICAL STUDY OF BREAST LESIONS WITH HISTOPATHOLOGICAL CORRELATION"

BY

Dr. SUPRIYA R. KOKANAY

DISSERTATION SUBMITTED TO THE
SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

M.D

IN

PATHOLOGY

UNDER THE GUIDANCE OF

Dr. UDAYA KUMAR M, M.D
Professor of Pathology

DEPARTMENT OF PATHOLOGY
SRI DEVARAJ URS MEDICAL COLLEGE
KOLAR-563101

APRIL 2011

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH,

TAMAKA, KOLAR, KARNATAKA.

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation/thesis entitled

"CYTOMORPHOLOGICAL STUDY OF BREAST LESIONS WITH HISTOPATHOLOGICAL CORRELATION"

is a bonafide and genuine research work carried out by me under the guidance of

Dr. UDAYA KUMAR M, M.D

Professor,

Department Of Pathology,

Sri Devaraj Urs Medical College, Tamaka, Kolar.

Dr.SUPRIYA.R.KOKANAY

Date:

Place : Kolar .

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH,

TAMAKA, KOLAR, KARNATAKA.

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled

"CYTOMORPHOLOGICAL STUDY OF BREAST LESIONS WITH HISTOPATHOLOGICAL CORRELATION"

is a bonafide research work done by

Dr. SUPRIYA R. KOKANAY

in partial fulfilment of the requirement for the degree of

M.D in PATHOLOGY.

Dr. UDAYA KUMAR M, M.D

Professor,

Department Of Pathology,

Sri Devaraj Urs Medical College,

Tamaka, Kolar.

Date :

Place : Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH,

TAMAKA, KOLAR, KARNATAKA.

ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled

"CYTOMORPHOLOGICAL STUDY OF BREAST LESIONS WITH HISTOPATHOLOGICAL CORRELATION"

is a bonafide research work done by

Dr. SUPRIYA R. KOKANAY

under the guidance of

Dr. UDAYA KUMAR M, M.D

Professor,

Department of Pathology.

Dr. M. L. HARENDRA KUMAR,
Professor and HOD,
Department Of Pathology,
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:
Place: Kolar

Dr. M. B. SANIKOP,
Principal,
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:
Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH,

TAMAKA, KOLAR, KARNATAKA.

ETHICAL COMMITTEE CERTIFICATE

This is to certify that the Ethical committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has unanimously approved

Dr. SUPRIYA R. KOKANAY

Post-Graduate student in the subject of

PATHOLOGY at

Sri Devaraj Urs Medical College, Kolar

to take up the Dissertation work entitled

"CYTOMORPHOLOGICAL STUDY OF BREAST LESIONS WITH HISTOPATHOLOGICAL CORRELATION"

to be submitted to the

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH,

TAMAKA, KOLAR, KARNATAKA.

Member Secretary
Sri Devaraj Urs Medical College,
Kolar–563101

Date :

Place : Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH,

TAMAKA, KOLAR, KARNATAKA.

COPY RIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the Sri Devaraj Urs Academy Of Higher Education And Research, Kolar ,Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic /research purpose.

Dr. SUPRIYA R. KOKANAY

Date :

Place : Kolar

To,

My father, Late. Mr. RAMANATH KOKANAY,

my role model

My mother, Mrs. GAYATHRI R.KOKANAY,

my constant source of encouragement

ACKNOWLEDGEMENT

My continued reverence and acknowledgement to my beloved teacher and guide ***Dr. UDAYA KUMAR M,*** *professor who graced my study officially and at the same time informally by his constant support, encouragement and expert advice, thus enabling me to successfully complete the assignment. I dedicate the good part of the work to him.*

I convey my deepest regards and earnest gratitude to ***Dr. M. L. HARENDRA KUMAR,*** *professor and HOD, for his support, advice and constant encouragement in preparing this dissertation.*

I express my deep sense of gratitude to ***Dr. R. RUPNARAYAN*** *and* ***Dr. KALYANI R****, professors, for their advice and invaluable inputs for this study.*

I sincerely thank ***Dr. T. N .SURESH, Dr. C. S. B. R.PRASAD, Dr. SUBHASHIS DAS, Dr. APARNA NARASIMHA****, Associate professors for their thought provoking guidance and encouragement in preparing this dissertation.*

I express my gratitude to ***Dr. VIDYAVATHI K, Dr. MANJULA K, Dr. HEMALATHA A, Dr. GAYATHRI B. N and Dr. PRATHIMA S****, Assistant professors for their moral support and co-operation.*

I would like to thank my seniors ***Dr. CHETANA MANNEM*** *and* ***Dr. MANDEEP SINGH BINDRA*** *for keeping me on my toes by asking me thought provoking questions throughout my study.*

I would like to thank my colleagues ***Dr. SAPNA M, Dr. THOMAS ALEX KODIATTE, Dr. THEJ M.J, Dr. SHRUTHI P.S, Dr. VASAVI B, Dr. GOMATI N*** *and* ***Dr. SURAKSHA RAO B*** *for their whole hearted help and constant support.*

*I am thankful to the **technical staff** of department of Pathology for their kind co-operation during the period of this study.*

*I express my gratitude to **Dr. ANIL N.S**, Assistant professor, department of Community Medicine, for his invaluable help during this study.*

*My special thanks to my husband **Dr. SANDEEP H.S**, my mother **MRS. GAYATHRI R. KOKANAY**, my brother **Mr. SWAROOP R. KOKANAY**, my in-laws **Mr. SHANKARAPPA H. B** and **Mrs. GAYATHRIDEVI** for their valuable moral support in completing this study.*

*My thanks to all my **friends** for their help during this study.*

*I would also like to thank all the **patients** without whom; this study would not have been possible.*

*Above all I express my gratitude to the **Almighty** for His blessing.*

Dr. Supriya R. Kokanay

Date:

Place: Kolar

LIST OF ABBREVIATIONS

ADH – Atypical Ductal Hyperplasia

AFB – Acid fast bacilli

DCIS – Intraductal Carcinoma in situ

FNAC – Fine Needle Aspiration Cytology

HE - Hematoxylin and Eosin

HP – Histopathology

LCIS - Lobular Carcinoma-in-situ

LN – Lymph Node

NOS – Not Otherwise Specified

PAS – Per-iodic Acid Schiff

PASH – Pseudo Angiomatous Stromal Hyperplasia

TB - Tuberculosis

Z N - Ziehl- Neelson

ABSTRACT

Background :

Lump in the breast is the common presentation to surgical OPD. The breast lesions are spectrum of diseases ranging from non- neoplastic to neoplastic lesions. Fine Needle Aspiration Cytology(FNAC) is an important tool in the diagnosis of breast lesions.

Objectives of study :

The purpose of the present study was to study the cytological patterns of breast lesions, to test the diagnostic utility of FNAC of breast lesions by correlation with histopathology and to compare cytologic grading of breast carcinoma by Simplified Black grading system with histologic grading by Nottingham modification of Bloom-Richardson grading system.

Methods :

The present study is undertaken in the Department of Pathology, Sri Devaraj Urs Medical College, Kolar, during the period of 01-12-2008 to 30-11-2009. The study included smears from 50 cases presenting with breast lump. All 50 cases were correlated with histopathology. Sensitivity, specificity, positive predictive value, negative predictive value, false positive rate and false negative rate were used to calculate the diagnostic accuracy of FNAC to detect malignancy in 47 cases, 2 cases were of unsatisfactory cell yield and 1 case was suspicious for malignancy, were excluded.

Out of 47 cases the diagnosis of malignancy was offered in 26 cases. Nottingham modification of Bloom Richardson grading can be applied to ductal

carcinoma, special types of ductal carcinoma and lobular carcinoma. Hence 1 case of pleomorphic liposarcoma with myxoid change was excluded from analysis. 1 case of ductal carcinoma NOS misinterpreted as fibroadenoma on FNAC, was retrospectively included for grading.

Cytologic grading by Simplified Black system and histologic grading by Nottingham modification of Bloom Richardson was done in 25 cases of breast carcinoma. The statistical test used was Chi – square test.

Results :

In the present study, the results of diagnostic accuracy of FNAC to detect malignancy was sensitivity – 96.15%, specificity – 100%, positive predictive value – 100% and negative predictive value – 95.45%, false positive rate - 0% and false negative rate - 3.84%.

Cytologic grading by Simplified Black system and histologic grading by Nottingham modification of Bloom - Richardson done in 25 cases of breast carcinoma had good correlation (p value < 0.05).

Conclusion :

Fine needle aspiration cytology is a safe, rapid and minimally invasive procedure for the diagnosis of breast lesions. It has high sensitivity and specificity. It is effective replacement for open biopsy. Cytologic grading by Simplified Black system correlates well with histologic grading by Nottingham modification of Bloom Richardson. Hence it must be included in the cytology report of breast carcinoma whenever possible as it helps in determining the tumour aggressiveness and further treatment plan.

Key words : Breast lump; Fine Needle Aspiration Cytology; Grading.

.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

A palpable breast lump is a common diagnostic problem. It is important not only to diagnose breast lesion as benign or malignant, but also to to assay the prognosis of both. The pathologist must be able to distinguish the benign lesions with varying risks of subsequent development of breast carcinoma. In the past, excision biopsy was advised but now FNAC is an important diagnostic tool which lessens economic burden and time consumed by doing a open tissue biopsy.[1,2]

FNAC is cheaper, less traumatic, requires no local anaesthesia, can generate rapid diagnosis. It plays major role in the diagnosis of small lesions or lesions located just under the skin, close to the chest wall or in periclavicular area. It is the most convenient method of sampling multiple lesions.[3]

AIMS AND OBJECTIVES

1. To study the cytological patterns of breast lesions.
2. To test the diagnostic utility of FNAC by correlation with histopathology.
3. To compare cytologic grading of breast carcinoma by Simplified Black grading system with histologic grading by Nottingham modification of Bloom-Richardson grading system.

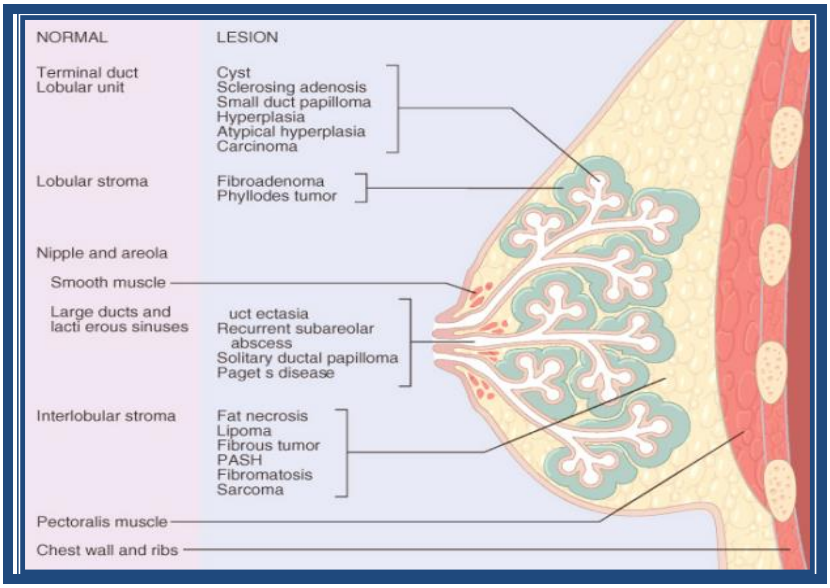
REVIEW OF LITERATURE

HISTORICAL ASPECTS

First report on needle biopsy dates back to 11th century, when Arab doctor Abdulcasis had mentioned in his book about performing needle biopsy on thyroid gland.[4] Needle aspiration cytology was also employed to diagnose cancer in mid nineteenth century by Kun (1847), Lebert (1851) and Menetrier (1886). Leyden also used this method to isolate pneumonic microorganisms. In United Kingdom, in 1927, Dudgeon and patrick and at about the same time in United States of America, Martin and Ellis proposed needling of tumours for rapid diagnosis. In 1950s and 1960s FNAC flourished in Europe and was practised by Soderstrom and Franzen in Sweden, Lopes Cardozo in Holland, Zajdela in France.[1]

In 1851 Skey performed needle biopsy for breast cysts. In 1853 needle biopsy was used to diagnose breast tumours by Sir James Paget and Erichsen. In 1863 to puncture breast lesions Pritchard used grooved needle. In 1950 Piaggio-Blanco and Paregro published their observation on FNAC in breast lesions.[4]

ANATOMY AND HISTOLOGY OF BREAST



The paired mammary glands rest on the pectoralis muscle on the upper chest wall. The epithelium is arranged in 10 to 15 segments each consisting of branching structure. The lobules contain blind ended ductules called acini which drain into ducts which in turn drain to collecting ducts, which further expands below the nipple to form lactiferous sinus which open onto the surface of nipple.

The lobule with terminal duct is called “terminal duct lobular unit”. The overlying skin is lined by keratinised squamous epithelium which continues into ducts and then changes into double layered epithelium which rests on a continuous basement membrane. The luminal cuboidal or columnar cells which produce milk rest on the flattened discontinuous myoepithelials cell which help in milk ejection.

The interlobular stroma consists of dense fibrous connective tissue with adipose tissue and the intralobular stroma consists of myxomatous stroma with scattered lymphocytes.

The areola contains sebaceous glands which open via lactiferous ducts or directly onto epidermis. During pregnancy these sebaceous glands become prominent to form surface elevations called Montgomery tubercles. Smooth muscle bundles are

present in the subareolar region. Intramammary lymph nodes are also found in the breast.[5,6,7]

The prepubertal breast, consisting terminal ducts with minimal lobule formation at puberty give rise to lobules with increase in interlobular stroma. In the follicular phase of menstrual cycle the lobules are relatively quiescent but after ovulation the cells proliferate, number of acini per lobule increases with vacuolization of epithelial cells and edematous intralobular stroma. During pregnancy the lobules increase in number and size and all the cells show high level of proliferative activity.[5,7]

As the age advances the radio dense fibrous interlobular stroma is replaced by radiolucent adipose tissue. The normal ductal system in some can extend into subcutaneous tissue of chest wall or axilla which can give rise to tumour.[5]

CYTOLOGY

The normal breast aspirate consists of bimodal population of cells – cohesive epithelial cells and single bare bipolar nuclei. The ductular epithelial cells are cohesive can be monolayered or multilayered. The cells have indistinct cell borders with scanty pale cytoplasm which can have blue granulation. The nuclei are small, round or oval with granular chromatin with no or micro nucleoli. The bare nuclei in the background are of same size as epithelial cells or slightly smaller than them. They have bipolar shape with smooth nuclear outline and dense homogeneous chromatin with no nucleoli. Similar nuclei are also seen amidst the epithelial cell fragments. The bare nuclei are derived from myoepithelial cells or specialised intralobular connective tissue. Small fragments of adipose tissue and collagen are also present.[1,8]

THE WORLD HEALTH ORGANIZATION (WHO) CLASSIFICATION OF TUMORS OF THE BREAST (2003).[9]

Invasive breast carcinomas

- Invasive ductal carcinoma
    - Most are "not otherwise specified(NOS)"
    - The remainder are given subtypes:
        - Mixed type carcinoma
        - Pleomorphic carcinoma
        - Carcinoma with osteoclastic giant cells
        - Carcinoma with Choriocarcinomatous features
        - Carcinoma with melanotic features
- Invasive lobular carcinoma
- Tubular carcinoma
- Invasive cribriform carcinoma
- Medullary carcinoma
- Mucinous carcinoma and other tumours with abundant mucin
    - Mucinous carcinoma
    - Cystadenocarcinoma and columnar cell mucinous carcinoma
    - Signet ring cell carcinoma
- Neuroendocrine tumours
    - Solid neuroendocrine carcinoma (carcinoid of the breast)
    - Atypical carcinoid tumour
    - Small cell / oat cell carcinoma
    - Large cell neuroendocrine carcinoma

- Invasive papillary carcinoma
- Invasive micropapillary carcinoma
- Apocrine carcinoma
- Metaplastic carcinomas
    - Pure epithelial metaplastic carcinomas
        - Squamous cell carcinoma
        - Adenocarcinoma with spindle cell metaplasia
        - Adenosquamous carcinoma
        - Mucoepidermoid carcinoma
    - Mixed epithelial/mesenchymal metaplastic carcinomas
- Lipid-rich carcinoma
- Secretory carcinoma
- Oncocytic carcinoma
- Adenoid cystic carcinoma
- Acinic cell carcinoma
- Glycogen-rich clear cell carcinoma
- Sebaceous carcinoma
- Inflammatory carcinoma
- Bilateral breast carcinoma

Mesenchymal tumors (including sarcoma)

- Haemangioma
- Angiomatosis
- Haemangiopericytoma
- Pseudoangiomatous stromal hyperplasia(PASH)
- Myofibroblastoma

- Fibromatosis (aggressive)
- Inflammatory myofibroblastic tumour
- Lipoma
    - Angiolipoma
- Granular cell tumour
- Neurofibroma
- Schwannoma
- Angiosarcoma
- Liposarcoma
- Rhabdomyosarcoma
- Osteosarcoma
- Leiomyoma
- Leiomysarcoma

Precursor lesions

- Lobular neoplasia
    - Lobular Carcinoma In Situ(LCIS)
- Intraductal proliferative lesions
    - Usual ductal hyperplasia
    - Flat epithelial hyperplasia
    - Atypical ductal hyperplasia
    - Ductal carcinoma in situ
- Microinvasive carcinoma
- Intraductal papillary neoplasms
    - Central papilloma
    - Peripheral papilloma

    - Atypical papilloma
    - Intraductal papillary carcinoma
    - Intracystic papillary carcinoma

Benign epithelial lesions

- Adenosis, including variants
    - Sclerosing adenosis
    - Apocrine adenosis
    - Blunt duct adenosis
    - Microglandular adenosis
    - Adenomyoepithelial adenosis
- Radial scar / complex sclerosing lesion
- Adenomas
    - Tubular adenoma
    - Lactating adenoma
    - Apocrine adenoma
    - Pleomorphic adenoma
    - Ductal adenoma

Myoepithelial lesions

- Myoepitheliosis
- Adenomyoepithelial adenosis
- Adenomyoepithelioma
- Malignant myoepithelioma

Fibroepithelial tumours

- Fibroadenoma
- Phyllodes tumour
    - Benign
    - Borderline
    - Malignant
- Periductal stromal sarcoma, low grade
- Mammary hamartoma

Tumours of the nipple

- Nipple adenoma
- Syringomatous adenoma
- Paget's disease of the nipple

Malignant lymphoma

- Diffuse large B cell lymphoma
- Burkitt lymphoma
- Extranodal marginal-zone-B-cell lymphoma of MALT type
- Follicular lymphoma

Metastatic tumours

Tumours of the male breast

- Gynecomastia
- Carcinoma
    - In situ
    - Invasive

STAGING. [9]

- Tx - Primary tumour cannot be assessed.
- T0 - No evidence of primary tumour.
- Tis - Carcinoma in situ.
    - Tis(DCIS) - Intraductal Carcinoma in situ.
    - Tis(LCIS) - Lobular Carcinoma in situ.
    - Tis(Paget's) - Paget's disease of the nipple with no tumour.
- T1 - Tumor 2 cm or less in its greatest dimension.
    - T1mic - Microinvasion 0.1 cm or less in greatest dimension.
    - T1a - Tumour more than 0.1 cm but not more than 0.5 cm in its greatest dimension.
    - T1b - Tumour more than 0.5 cm but not more than 1.0 cm in its greatest dimension.
    - T1c - Tumour more than 1.0 cm but not more than 2.0 cm in its greatest dimension.
- T2 - Tumour more than 2.0 cm but not more than 5.0 cm in its greatest dimension.
- T3 - Tumour more than 5 cm in its greatest dimension.
- T4 - Tumour of any size with direct extension to (a) chest wall or (b) skin as described below:
    - T4a - Extension to chest wall.
    - T4b - Edema (including peau d'orange) or ulceration of the breast skin, or satellite skin nodules confined to the same breast.
    - T4c - Both T4a and T4b.
    - T4d - Inflammatory breast cancer.

Lymph **N**ode - There are four lymph node classification values (N0, N1, N2 or N3) which depend on the number, size and location of breast cancer cell deposits in lymph nodes.

- Nx - Regional lymph nodes cannot be assessed. Perhaps due to previous removal.
- N0 - No regional lymph node metastasis.
- N1 - Metastasis to movable regional axillary lymph nodes on the same side as the affected breast.
- N2 - Metastasis to fixed regional axillary lymph nodes or metastasis to the internal mammary lymph nodes, on the same side as the affected breast.
- N3 - Metastasis to supraclavicular lymph nodes or infraclavicular lymph nodes or metastasis to the internal mammary lymph nodes with metastasis to the axillary lymph nodes.

Metastases - There are two metastatic classification values (M0 or M1) which depend on the presence or absence of breast cancer cells in locations other than the breast and lymph nodes (so-called distant metastases, e.g. to bone, brain, lung). But it includes supraclavicular lymph node.

INFLAMMATORY LESIONS

Acute Mastitis and Breast Abscess

Usually clinically diagnosed without need for FNAC or biopsy.[10] Breast abscess and acute mastitis occur usually in Pregnancy. Numerous neutrophils and histiocytes are seen. A benign bimodal component of breast tissue is seen. Sometimes these cells can show cytologic atypia. The background is necrotic.[1,2]

Fat necrosis

Fat necrosis of the breast can be due to radiotherapy and trauma or can be associated with carcinoma.[2] Aspirates are oily and contain foamy macrophages, multinucleated giant cells adipocytes with foamy cytoplasm, inflammatory cells and a paucity of epithelial elements. The dirty background contains fatty globules, fragments of adipose tissue calcified necrotic debris.[1]

Recurring Subareolar abscess/Zuska's disease /Lactiferous duct fistula

Subareolar abscess which is seen in nulliparous and young women beneath nipple is associated with recurrent bouts of inflammation and can form abscess and sinus tract.[1]

Cytologically the lesion consists of mature or anucleate squames with neutrophils, cholesterol crystals, keratinous debris and parakeratosis.[10,11]

Plasma cell mastitis/ Mammary duct ectasia

Plasma cell mastitis is a lesion of ageing breast which presents as a well defined lesion with nipple retraction, may mimic carcinoma. Aspirate is thick, creamy and homogeneous; much of the material dissolves in methanol fixative and leaves with amorphous debris with numerous plasma cells, foamy macrophages and other

inflammatory cells, occasionally multinucleated giant cells with small number of atypical epithelial cell.[2,10]

Granulomatous mastitis

Tuberculosis (TB) is the most common cause followed by sarcoidosis, amyloidosis, silicon breast prosthesis granulomatous angiopanniculitis, duct ectasia, high prolactin level in pregnancy or following phenothiazine therapy and actinomycosis.[1,10] Smears show epithelioid cells, multinucleated giant cells with necrotic debris and inflammatory cells.[10,12]

Fibrocystic Disease

Fibrocystic disease is the most common mass producing lesion in females over the age of 30 years. They are usually multifocal and may be bilateral.[7,13] Epithelial cells are generally arranged in tight, cohesive honey-comb like clusters with cells having round to oval nuclei, finely dispersed granular chromatin and imperceptible to small nucleoli. Apocrine cells are arranged in flat sheets or, singly with abundant granular cytoplasm and hyperchromatic nuclei with prominent nucleoli. Foam cells and stromal fragments can be present. An important component and indicator of benignity is presence of naked bipolar nuclei. Proliferative epithelial changes include duct papillomatosis, duct hyperplasia and atypical ductal hyperplasia.[13]

Fibrocystic change is not a cytological diagnosis. These changes are usually poorly circumscribed and the adjacent tissue may harbour hyperplasia, atypia or even malignancy. Malignancy cannot be ruled out in the tiny areas aspirated.[1]

Simple cyst

Breast cysts are easily diagnosed by ultrasound. However, aspiration helps in the diagnosis as well as relieving patient's anxiety as the lump disappears after aspiration. The aspirated fluid may be thin, clear or turbid, straw coloured, brown or

green. Smears may be partially cell free or may contain large number of cyst macrophages and more or less oxyphil/apocrine epithelial cells. Polymorphs may be variable. A carcinoma may be present adjacent to it which can be hidden by dominant cyst.[1]

Collagenous spherulosis

Collagenous spherulosis is stromal reaction encountered in areas of fibrocystic disease.[2] The cytological smears show regular hyperplasia with two cells types surrounding amorphous basement membrane material seen as translucent or metachromatic acellular spheres on Giemsa stain. In contrast to adenoid cystic carcinoma in collagenous spherulosis, benign bipolar bare nuclei are noted in the background.[14,15,16]

Fibrous mastopathy

Fibrous mastopathy aspiration usually yield less cells because of dense fibrous tissue.[10]

BENIGN EPITHELIAL LESIONS

Adenosis and Sclerosing Adenosis

FNAC alone cannot distinguish Sclerosing adenosis and other forms of adenosis. Epithelial cells can be arranged in microacinar pattern giving rise to differential diagnostic problems, especially with tubular carcinoma. Single bipolar nuclei are present, but there may be some loss of cohesion and mild nuclear atypia. Apocrine metaplasia can occur.[1]

Radial sclerosing lesion/ radial scar/ sclerosing ductal proliferation/ sclerosing papillary proliferation

The aspirates are poorly cellular but can be cellular with small uniform epithelial cell, dispersed stromal cells and few apocrine cells.[10] The picture is usually of epithelial hyperplasia with or without atypia. Suspected radial scars must be excised as cytological features overlap with tubular carcinoma and FNAC alone cannot arrive at a specific diagnosis.[1,17]

Adenomas

Tubular adenoma

Tubular adenomas are soft, yellowish, well circumscribed lesions which are clinically similar to fibroadenoma.[7,10,14] The smears are moderate to highly cellular with few bipolar stromal cells and occasional microacinar arrangements.[14,18,19]

Apocrine adenoma

They are well-circumscribed tumours with appearance resembling apocrine metaplasia commonly seen in fibrocystic change of the breast but with closely packed tubular and papillary structures. They are not distinctive by mammography or physical examination and should be managed as any other breast mass.[20]

MYOEPITHELIAL LESIONS

Adenomyoepithelioma

Adenomyoepithelioma is an uncommon tumour, whose aspirates are highly cellular with sheets of crowded clusters of uniform cells. The cells are round to oval and nuclei have fine chromatin. The cells are surrounded by many naked nuclei.

Stromal material is scanty. Positive immunostaining of tumour cells with keratin, S-100 and muscle specific actin is seen.[2]

Malignant myoepithelioma

The aspirates are cellular, consisting mainly of single spindle or polymorphic, polygonal cells with large nuclei, showing a distinct medium-sized nucleolus and granular chromatin. The nuclear outlines are irregular with buds and folds. The background shows abundant granular metachromatic ground substance and some metachromatic stromal fragments.[21]

FIBROEPITHELIAL LESIONS

Fibroadenoma

Fibroadenomas are most commonly occurring benign tumours, usually in young females 15- 35 years of age. Clinically it is a circumscribed, movable mass with firm, elastic consistency. Smears are cellular with biphasic pattern consisting of epithelial and stromal elements.[2] The epithelial cells are arranged in "antler horn" pattern with variable nuclear crowding and overlapping. The bare bipolar nuclei in background are probably of myoepithelial origin. There can be apocrine differentiation, foamy macrophages and fragments of fibromyxoid stroma. Epithelial atypia is common.[22] Pregnancy and lactational changes can increase cellularity and induce nuclear atypia and can have conspicuous nucleoli.[1,2] Chicken pox causing cytologic atypia and giant cell reaction in fibroadenoma has been reported.[23]

Juvenile fibroadenoma

It is rapidly growing, bilateral tumour of young patients. Smears are cellular with monomorphic uniform, bland, columnar cells in monolayered sheets and papillae. Foam cells and histiocytes can be seen.[2]

Phyllodes tumour

Because of leaf-like and fleshy gross appearance of this tumour it was named 'cystosarcoma phyllodes' by Muller. Smears are highly cellular with biphasic pattern. These uniform epithelial cells arranged in large folded sheets with numerous naked nuclei. The stromal component consists of spindle cells in acid mucopolysaccharide matrix which stains metachromatically.[2,24] Tumour often shows foam cells, occasional giant cells, squamous metaplastic cells, fat, bone, cartilage and skeletal muscle. Cytologic separation of benign from malignant phyllodes tumour is difficult**.**[10] However, malignant phyllodes should be considered when there is presence of mitosis, atypical stromal cells with increased cellularity in stromal component.[13]

Periductal stromal sarcoma

Few cases of periductal stromal sarcoma of breast have been reported.[25]

Mammary hamartoma

Clinically mammary hamartomas can be confused with fibroadenomas because they are discrete, well demarcated palpable or non-palpable masses; however they contain both lobules and ducts in addition to dense connective tissue. Cytological features are not well characterized but should be benign and heterogeneous.[2]

NONPROLIFERATIVE BREAST LESIONS

FNAC smears have variable cell yield with clusters of monotonous small epithelial cells in monolayered sheets with honeycomb pattern. The cells have regular nuclei with fine chromatin. Apocrine cells, foam cells, fragments of stromal cells and myoepithelial cells are seen.[2]

PROLIFERATIVE BREAST DISEASE WITHOUT ATYPIA

Cytological smears are moderate to highly cellular with ductal and myoepithelial cells arranged in tightly cohesive groups. Mild anisonucleosis, some loss of polarity and occasional overriding of nuclei can be seen but atypia is inconspicuous.[2]

PROLIFERATIVE BREAST DISEASE WITH ATYPIA

Atypical ductal hyperplasia(ADH)

Smears are highly cellular consisting of epithelial cells in sheets and aggregates. Like low-grade DCIS, cribriform pattern can be seen in ADH. Necrotic debris can be seen. The cytologic atypia is variable and can equal or sometimes even exceeds that of low-grade DCIS. There are no single features which can confidently separate ADH from low-grade DCIS.[1]

Atypical lobular hyperplasia

FNAC of Atypical lobular hyperplasia consists of small cells arranged in discretes and small groups. Cells may contain intracytoplasmic lumina which appear like ‘bulls eye’ with alcian blue stained microvillous membrane and PAS (per-iodic acid Schiff) stained mucin droplet in centre. Nuclear moulding is seen. With FNAC

alone it is difficult to distinguish atypical lobular hyperplasia, lobular carcinoma-in-situ and invasive lobular carcinoma.[14]

Intraductal carcinoma

Cytomorphology depends on whether the lesion is comedo or non-comedo type DCIS. Smears from non-comedo type show tumour cells arranged in three dimensional clusters in which occasional tumour cells border the central lumina. There are no myoepithelial cells. Nuclei have fine granular chromatin with some condensation along nuclear membrane with small nucleoli. Background shows no necrosis or haemorrhage.

Aspirates from comedo type DCIS are cellular with loose cohesive clusters showing significant nuclear atypia, mitotis and necrosis. But both lack increased number of atypical single cells in contrast to invasive ductal carcinoma.[13] Malignant cells with a tubular structure, cytoplasmic lumen formation in malignant cells, fibroblast proliferation and fragments of elastoid stroma are predictive of invasiveness when associated with a malignant cell pattern.[1]

Lobular carcinoma in situ

Cytologically the aspirates of LCIS are of low or rarely moderate cellularity. They are characterised by loosely cohesive small collections of uniform cells exhibiting eccentric nuclei, uniform nuclear chromatin and very little atypia. Some cells are discrete and show small nuclei with intracytoplasmic lumina . Differentiation from atypical lobular hyperplasia and lobular carcinoma in situ is not possible on cytological grounds alone, since the criteria are purely those of histological extent.[14]

Intraductal papilloma

Intraductal papilloma is benign papilliform proliferation of ductal epithelium. It can be solitary or multiple, in later case it is papillomatosis. It presents with serous

or bloody nipple discharge, small subareolar nodule or sometimes with nipple retraction. Cytologically smears are cellular with tall columnar epithelial cells in three dimensional papillary clusters. Cell ball with mild degree of atypia can be seen. The background is proteinaceous or haemorrhagic with large number of foamy macrophages, apocrine cells, and naked nuclei. Cytologically, differentiation between intraductal papilloma and well differentiated papillary carcinoma is difficult.[2]

Juvenile papillomatosis (Swiss cheese disease)

It is a localised breast tumour of young women, may carry increased risk of cancer in patients with family history hence, needs long term follow-up. The FNAC smears are highly cellular with epithelial cells in three dimensional clusters. This condition shows the features of fibrocystic change with apocrine metaplastic cells, bare nuclei and foamy macrophages. It needs long-term follow-up as it can be a marker for breast cancer for patient's family.[13,14]

MALIGNANT TUMOURS

Invasive Carcinomas

Infiltrating duct carcinoma NOS

Infiltrating duct carcinoma NOS is the most frequent type of breast carcinoma.[2] Aspirates are generally hypercellular, showing a 'classic' pattern with sheets and clusters of malignant cells, either individual cell predominance or cluster predominance.[14] The cellular pattern shows considerable variability, with tumour cells present in three - dimensional clusters, syncytial groupings or occasionally in acinar arrangement. The cell clusters show loss of polarity, nuclear moulding and variability in cell size. Individual tumour cells show increased nucleocytoplasmic ratio hyperchromatic coarsely granular chromatin and small-to-prominent nucleoli.[13] Other

features like multiple intracytoplasmic vacuoles, intracytoplasmic acini, cell cannibalism help in establishing the diagnosis of malignancy.[14] Poorly differentiated breast carcinomas show multinucleated tumour cells. Background shows cellular debris, fibrocalcific particles and red blood cells.[2] Tumours with fibroelastotic centres may have a low cellular yield. The probing sensation in this type of tumour is characteristically gritty and hard. The aspirated material is also minimal.[14]

Cytologic grade can determine the aggressiveness of invasive ductal carcinoma.[26] Histiocytoid breast carcinoma is an unusual morphologic pattern of apocrine change seen in ductal breast carcinoma. These cells show foamy and/or granular cytoplasm and must be differentiated from other benign tumours with foamy cells.[27]

Breast carcinoma with osteoclast-like giant cells

Multinucleated osteoclast-like giant cells can be found in ductal carcinoma, fibroadenoma and other benign lesions. Smears show features of invasive duct carcinoma along with multinucleated osteoclast-like giant cells not associated with stromal material. The giant cells are of histiocytic origin.[1] The giant cells have variable number of' nuclei which have active chromatin but are not malignant.[10,28]

Invasive Lobular Carcinoma

There is increased risk of synchronous or asynchronous bilaterality and multicentricity. Lobular carcinoma occurs chiefly in postmenopausalwomen.[7,29] Cytologically aspirates have low to moderate cell yield and consists of uniform population of small to medium sized cells. Tumour cells are well dispersed arranged in discrete, indian file pattern, cords and small groups.[2,30] Cytoplasm is scanty with some cells showing intracytoplasmic lumen. Nucleus is eccentric showing mild anisonucleosis with stippled chromatin and inconspicuous nucleolus. Differentiation

from atypical lobular hyperplasia or lobular carcinoma in situ is difficult cyiologically.[14]

Tubular carcinoma

Tubular carcinomas are a cytological challenge because of well-preserved cell cohesion and presence of bare bipolar nuclei, thus making the diagnosis of malignancy difficult.[1] The lesion can be multicentric and bilateral. Cytologically, aspirates are poorly or moderately cellular. Epithelial cells are in cohesive clusters and sheets with acinar structure and cell balls. Background is 'messy' with cell fragments and stromal elements. There is overlap in appearance with complex sclerosing lesions and radial scars mammographically, cytologically and histologically. This low grade variant of breast carcinoma is attended by a very good prognosis. [7,10,31,32]

Invasive cribriform carcinoma

The tumour is low grade and clinically behaves like a tubular carcinoma. Smears show sheets of regular cells with sieve-like holes but the prominent feature is dissociation and tiny cluster of small malignant cells.[14]

Medullary carcinoma

Medullary carcinoma comprises 5 to 10% of all breast carcinomas and presents as a well demarcated soft lesion.[13] Cytologically numerous malignant cells are arranged in clusters, syncytial groupings and in discretes. Tumours cells have scanty to abundant basophilic to finely granular or vacuolated cytoplasm, enlarged nuclei showing anisonucleosis, increased nuclear-cytoplasmic ratio with multiple macronucleoli. Occasionally, large stripped tumour nuclei may be seen.[14] Tumour giant cells are sometimes seen. Background shows small lymphocytes and plasma cells present either separately or intermingled among the tumour cells.[10]

Mucinous carcinoma

This type of carcinoma represents approximately 5% of all breast cancers, it is generally seen in older women.[13] Cytologically aspirated material has glistening appearance with abundant mucin which appears metachromatic in Diff-Quik and pale green to yellow in Papanicolaou stain.[2] The smear is usually cellular, the epithelial cells present as single cells, loose aggregates and in cohesive groups. The cells are small having uniform nuclei with smooth nuclear outlines, bland chromatin and inconspicuous nucleoli. Cells may be vacuolated and occasional signet ring cells are seen. Some smears show delicate vessels traversing the mucinous background which help to differentiate malignant mucinous aspirates from benign mucinous aspirates.[14,33,34]

Signet ring cell carcinoma

Cytologically smears are cellular with large cells having eccentrically placed, crescentic nuclei, often displaced by cytoplasmic mucin. There is marked anisonucleosis and moderate to marked hypcrchromasia.[10] Signet ring carcinoma of the breast should be distinguished from mucinous carcinomas which have much better prognosis.[14] The possibility of metastatic spread of a visceral signet ring carcinoma to the breast should be considered.[10]

Neuroendocrine carcinoma

Smears from this uncommon variant shows high cellularity with numerous small, uniform cells with coarse granular chromatin. These cells may or may not stain with neuroendocrine markers and contain dense core granules by electron microscopy.[1]

Papillary carcinoma

Many cytologically papillary breast lesions represents a gray zone in breast cytology and requires histologic confirmation.[35] Cytologically smears tend to be cellular with papillary arrangement containing fibrovascular core along with scattered columnar cells and haemosiderin laden macrophages. Sometimes eosinophillic bipolar cytoplasmic granules can be present.[36] The naked nuclei from papillary carcinoma are often larger and more elongated a feature which can differentiate it from fibroadenoma and benign papilloma.[13] Papillary carcinoma is larger than benign papilloma.[37]

Invasive micropapillary carcinoma

Smears show cells arranged in multilayered sheets, micropapillary fragments without stromal core but with discrete borders. The cells are columnar or rounded with moderate nuclear atypia.[1]

Apocrine carcinoma

Apocrine carcinoma is a rare entity although DCIS and invasive carcinomas NOS with apocrine change are common.[1,10] Smears from apocrine carcinomas are cellular with apocrine cells which have abundant acidophilic granular cytoplasm. The nucleus is also large but the high nuclear cytoplasmic ratio is not obvious. Nuclei contain coarse chromatin with single large nucleolus. Sometimes, multiple nucleoli can be seen in high grade tumours.[10]

Metaplastic carcinoma

Metaplastic carcinomas are defined as tumours which have two distinctly different components.[1] These tumours show features of both carcinoma and well differenciated sarcoma like osteosarcoma, liposarcoma, chondrosarcoma or

fibrosarcoma.[8] A case of metaplastic breast carcinoma metastasizing to thyroid has been reported.[38]

Squamous carcinoma of breast

These lesions, are rare and usually occur in elderly women. Squamous differentiation occurs in otherwise unremarkable ductal carcinoma.[2] Smears show mature and anucleate squames with obviously malignant cells. The cells are poorly cohesive with dense angular nuclei. Squamous carcinoma with a cystic centre may be mistaken clinically for fibrocystic change.[10]

Lipid rich carcinoma

On FNAC, smears are cellular showing loosely cohesive tumour cells with abundant foamy cytoplasm. Nuclei can show mild anisonucleosis but have distinct nuclear membranes, coarse chromatin and small nucleoli. Sometimes nuclear vacuoles and indentation can be seen.[2]

Secretory carcinoma

This rare neoplasm of breast was first described in children by McDivitt and Stervant. The other term is "juvenile carcinoma", because of its predilection for the young, although it can occur at all ages.[14,29] Smears show clusters of epithelial cells with ill defined cell borders, abundant, pale, multivacuolated, fragile cytoplasm and round nuclei and small nucleoli. Globules of condensed secretions can be found.[1,27]

Oncocytic carcinoma

Oncocytic carcinomas are composed mostly of cells with "low-grade" nuclei and abundant granular eosinophilic cytoplasm. Apocrine cells and oncocytes share similar morphologic features at the hematoxylin-eosin level; however, mitochondria in apocrine cells usually are in a perinuclear location and are not so numerous and diffusely dispersed as in oncocytes. In addition, apocrine cells display features of

active secretory elements: prominent microvilli, well developed golgi complex, and electron dense secretory granules polarized towards the luminal pole.[39]

Glycogen rich (clear cell) carcinoma

This lesion carries a significantly worse prognosis than ductal carcinoma of no special type. Smears are highly cellular, show branching loosely cohesive sheets of syncytial groups with abundant clear cytoplasm and centrally placed nucleus with obvious malignant nuclear features and apical cytoplasmic projections. The cytological appearance may resemble signet ring cell carcinoma but the prognosis is in any case is similar. Special stains demonstrate glycogen in cytoplasm.[10,27,40,41]

Sebaceous carcinoma

A reported case of sebaceous carcinoma showed aspirates with mostly uniform cells in singles and clusters with obvious clear cytoplasmic vacuolization and coarse nuclear chromatin.[42]

Inflammatory carcinoma

Clinically breast is swollen, erythematous with raised local temperature and mimics an inflammatory process. But this appearance is actually due to cancer cells infiltrating the lymphatics.[8] Cytologically smears show focal aggregates of tumour cells with malignant pleomorphism.[1]

Other malignant tumours that have been reported in breast are acinic cell carcinoma,[43] adenoid cystic carcinoma,[44,45]

CONNECTIVE TISSUE LESIONS

Pseudoangiomatous stromal hyperplasia

PASH is a benign mesenchymal lesion. FNAC is not specific or diagnostic and it can be misdiagnosed as fibroadenoma. Smears show few bipolar naked nuclei in background. These cells have spindle nuclei, some with intact cytoplasm as well as stromal fragments with marked crush artefact.[13]

Granular cell Tumour

Cytologically smears are adequate with cells showing abundant fragile granular cytoplasm. Stripped nuclei of varying size and shape and some with prominent nucleoli can be seen. This pattern can be mistaken for malignancy.[1]

Leiomyoma, lipoma, fibroma, osteoma, fibromatosis, pleomorphic adenoma,[46,47] nodular fasciitis,[48] schwanomma, adenolipoma, hamartoma, hemangioma, hemangiopericytoma,[49,50] myofibroblastoma,[1] angiosarcoma,[51] liposarcoma, malignant fibrous histiocytoma,[52] primary osteogenic sarcoma,[53] cystic hypersecretory duct carcinoma,[54] leiomyosarcoma, stromal sarcoma, have been reported and cytologically look similar like tumours occurring elsewhere in the body.[2,8,55]

BREAST CYTOLOGY IN PREGNANCY

Pregnancy related atypia

Aspirates taken from areas of fibroadenosis in pregnant or lactating breasts are moderate to markedly cellular with cells in singles which are large with abundant vacuolated cytoplasm, frequently stripping away leaving a naked nucleus. Nuclei are

round and uniform with granular or vesicular chromatin and single small nucleolus. Background is lipid rich or granular.[10]

Lactating adenoma

The term lactating adenoma refers to a breast mass presenting invariably in pregnant or lactating women.[7,14] On aspiration the material may be cloudy. Smears are moderately cellular with a proteinaceous foamy background. The majority of cells are discretely spread with some arranged in small clusters showing incomplete acini. The cytoplasm is vacuolated or whispy and stripped epithelial nuclei may be present. The nuclei are uniform and show fine stippled chromatin and prominent nucleolus.[10] Moderate degree of anisonucleosis and nuclear pleomorphism can be present.[14]

Galactocele

Galactocele is cystic degeneration of duct with secondary inflammation and necrosis occuring during lactation and women taking oral contraceptive pills. Smears consist of numerous foamy histiocytes, epithelial cells, and few inflammatory cells admixed with lipid micelles in a granular and proteinaceous background.[2] There is complete disappearance of the mass after aspiration. Galactocele may persist after lactation and may become thickwalled.[14]

Carcinoma in pregnancy

Carcinoma arising in pregnancy is not cytologically distinct but often tends to be high grade. The incidence is one cancer in 1000 pregnancies. Cytological features which, aid in diagnosis are high cellularity, nuclei having irregular nuclear contours, marked anisonucleosis, clumped chromatin and multiple irregular macronucleoli. Cytoplasm is vacuolated. Background is 'dirty' with nuclear debris.[14,56]

TUMOURS OF NIPPLE

Nipple adenoma/ Papillary adenoma/ Subareolar papillomatosis/ Florid papillomatosis

Nipple adenoma presents as a nodule beneath the nipple, misdiagnosed as carcinoma or Paget's disease. Aspirates are cellular with epithelial cells arranged in papillary pattern and discretes. The cells have uniform nuclei, finely dispersed chromatin and inconspicuous nucleoli. Naked nuclei and haemosiderin laden macrophages are seen. Background is inflammatory.[2]

Syringomatous adenoma

Infiltrating syringomatous adenomas are rare lesions of the nipple. The exact origin of these lesions is uncertain, although derivation from eccrine structures of the nipple has been postulated because the lesions are microscopically reminiscent of other tumours of eccrine origin, such as syringomatous carcinoma. The lesions are usually infiltrative, showing an expansile pattern of proliferation into adjacent tissues of the nipple and underlying breast. Involvement of the epidermis, however, has not been described. The lesions usually are benign, with no evidence of regional or distant metastasis.[57]

Paget's disease of the nipple

Paget's disease appears with an eczema like change of nipple and areola occasionally associated with underlying breast mass.[13,14] Smear consists of clusters of malignant cells which resembles those seen in high grade comedo ductal carcinoma-in- situ and show pleomorphism and are often vacuolated. Background may show plentiful epidermal cells and inflammatory cells.[14]

MALIGNANT LYMPHOMA

Primary malignant lymphomas of breast are rare. Large cell lymphomas show cells with basophilic cytoplasm, eccentrically placed nucleus with peri-nuclear halo with one or multiple nucleoli. They may closely resemble poorly differentiated breast carcinoma.[1]

METASTATIC TUMOURS

Metastatic malignancy must be considered, if cytological pattern does not fit in any of the subtypes of primary breast carcinoma. Malignant melanoma,[58] squamous cell carcinoma of cervix, bronchogenic small cell carcinoma, mucin secreting adenocarcinoma of stomach, ovarian adenocarcinoma, sarcomatoid renal cell carcinoma,[59] esthesioneuroblastoma[60] can metastasize to breast.[1] The knowledge of patient's clinical history and cytologic patterns of primary tumour is very important.[8]

TUMOURS OF MALE BREAST

Gynaecomastia

Gynaecomastia presents with well circumscribed breast nodule or diffuse enlargement of unilateral or bilateral breasts. Majority are idiopathic and can also results from altered endocrine function like hepatic cirrhosis, testicular neoplasms etc.[47] FNAC smears are variably cellular, with small uniform cells in monolayered sheets and bare nuclei. Presence of tall columnar cells can be misdiagnosed as papillary carcinoma. Macrophages, apocrine metaplasia, adipose tissue and tissue fragments can also be seen. Atypical proliferative changes can be seen which resemble non-comedo DCIS.[2]

Breast carcinoma in males

Most breast cancers in males are infiltrating duct carcinomas NOS which are identical to those in females.[1] Papillary carcinomas (both invasive and in situ) are more common and lobular carcinomas are less common. Carcinomas in men usually present as a palpable subareolar mass because breast epithelium is limited to large ducts near the nipple. Nipple discharge is a common symptom. Even small carcinomas can invade the overlying skin and underlying thoracic wall. Dissemination of cancer has similar pattern as that in women, and axillary lymph node involvement is present in about half of cases at the time of discovery of the lesion. Distant metastases can occur to the lungs, brain, bone, and liver. Although men present at higher stages, prognosis is similar in men and women when they are matched by stage. The same treatment guidelines are used for men and women, and response rates are similar.[5]

GRADING

The evaluation of the possible prognostic parameters in breast carcinoma like tumour histologic grading, cell proliferation index, estrogen receptor status and lymph node status is of growing interest.[61]

Grading of breast carcinoma as an independent factor has prognostic value.[62]

Histologic grade has been an important prognostic indicator that can predict overall and metastasis free survival for local and regionalized breast cancer.[63]

Apart from establishing the benign and malignant characters of a given lesion FNAC can provide additional information about intrinsic features of the tumour as well as its prognosis.[64]

There is much attraction in grading a tumour because neoadjuvant chemotherapy is becoming increasingly popular as primary medical treatment for breast cancer.[62] Attention must be focused on grading tumours on FNAC as it would allow assessment of the tumour and the morbidity associated with overtreatment of low grade tumours could be avoided.[65]

Histologic type of tumour and nuclear grade are two of the most important microscopically derived morphologic prognostic factors for breast carcinoma patients.[66] The value of histological grading of breast carcinoma is well established.[62] Hence assignment of a histologic grade has been recommended as a standard in all surgical pathology reports.[63]

Cytologic grading has shown a positive correlation with histologic grade, therefore cytological grade is useful in predicting histological grade preoperatively.[64]

Tumour grading based on cytology plays an important role in planning the treatment based on which pre-operative chemotherapy and/or radiation therapy is instituted.[67]

HISTOLOGIC GRADING

Several histologic grading systems were proposed, some consider ductoglandular differentiation or tumour secretory state. Some score only nuclear and nucleolar characteristics and others use both duct formation and nuclear abnormalities.[68]

There is always subjective element in the assessment of histological differentiation. Lack of strictly defined criteria is one of the fundamental problems with many of the systems used in previous studies.[69]

Greenough developed a histologic grading system for breast carcinoma which was simplified by Patey and Scarff. Bloom and Richardson made it more acceptable

by introducing a numerical scoring system to the method described by Patey and Scarff.[70]

Nottingham modification of Bloom Richardson grading combines measurement of differentiation (tubule formation) with details of cell morphology (nuclear pleomorphism) and an assessment of proliferation (mitotic frequency).[71]

TABLE 01 - NOTTINGHAM MODIFICATION OF BLOOM-RICHARDSON GRADING.[7]

FEATURE	SCORE
Tubule formation*	
> 75% of the tumour	1 point
10-75% of the tumour	2 points
< 10% of the tumour	3 points
Nuclear pleomorphism**	
Nuclei with minimal variation in size and shape	1 point
Nuclei with moderate variation in size and shape	2 points
Nuclei with marked variation in size and shape	3 points
Mitotic counts - per 10 HPF (40 x fields)***	
0 – 5	1 point
6 – 10	2 points
> 11	3 points

*The overall appearance of tumour has to be taken into consideration.

**the tumour areas having cells with greatest atypia should be evaluated.

***mitotic figures are to be counted only at the periphery of the tumour. Counting should begin in the most mitotically active area; 10 high power fields (HPF) are to be

counted in the same area (but not necessarily contiguous). The field should be filled with as much tumour as possible; poorly preserved areas are to be avoided. Cells in prophase are to be ignored.

Grade 1 (well differentiated) : 3 – 5 points

Grade 2 (moderately differentiated) : 6 – 7 points

Grade 3 (poorly differentiated) : 8 – 9 points

TABLE 02 - ASSIGNMENT OF POINTS FOR MITOTIC COUNTS ACCORDING TO THE FIELD AREA USING SEVERAL MICROSCOPES.[7]

	Microscope		
	Leitz Ortholux	**Nikon Labophot**	**Leitz Diaplan**
Objective	X25	X40	X40
Field diameter (mm)	0.59	0.44	0.63
Field area (mm^2)	0.274	0.152	0.312
Mitotic count			
1 point	0 – 9	0 – 5	0 – 11
2 points	0 – 19	6 – 10	12 – 22
3 points	> 20	> 11	> 23

CYTOLOGIC GRADING

The number of breast carcinomas diagnosed is increasing with the advent of FNAC. A cytologic tumour grading correlate well with histological grading and is highly reproducible.[67]

For practical purpose one pathologist's cytologic grade must be able to predict another's histologic grade, because in many practice situations the cytologic and histologic specimens will be signed out by different pathologists.[63]

Cytological grading systems of breast carcinoma :

1. Hunt's et al grading system.[72]
2. Mouriquand et al grading system.[72]
3. Modified Black grading system.[62]
4. Simplified Black grading system.[62]
5. Fisher's modification of Black's nuclear grading.[73]
6. Khan's grading system.[73]
7. Robinson grading system.[74]
8. Scarff-Bloom-Richardson grading system.[63]

According to a study done by Ohri A et al[62], cytological grading was done by Hunt's, Simplified Black and Modified Black grading systems. These systems were compared with modified Scarff Bloom-Richardson grading done on histologic sections. They concluded that among the three cytologic grading systems, the two-tier Simplified Black system has greater degree of correlation, well defined set of criteria, simple and objective.

TABLE 03 - SIMPLIFIED BLACK GRADING SYSTEM.[62]

LOW GRADE	HIGH GRADE
Nuclear uniformity	Anisonucleosis
Fine chromatin	Chromatin clumping
Absent nucleoli	Nucleoli easily seen at 100x
<3 mitosis per 10 HPF	>3 mitosis per 10 HPF
Small nucleus (<3x size of mature lymphocyte or RBC)	Large nucleus (>3x size of mature lymphocyte or RBC)

CYTOLOGIC AND HISTOLOGIC CORRELATION

FNAC report whenever possible should include nuclear grade because it has been found that nuclear grading of breast carcinoma is performed with ease, correlates well with tissue nuclear grade.[75]

The aim of comparing the cytological grading system with histological grading is to see whether the agreement is good enough for one to replace another.[62]

It is important to correlate because it is of clinical use and of prognostic value as it enables assessment of the biological aggressiveness of the malignancy. Thus cytological grading system which closely reflects the histological grade, biological behaviour of the tumour is assessed and systemic adjuvant treatment is instituted before surgery.[62]

ADVANTAGES OF FNAC

1. Easy procedure
2. Quick with rapid report unlike histopathology (HP)
3. Safe with minimal discomfort to patients
4. Outpatient procedure
5. Requires no anaesthesia
6. Cost effective
7. No wound is formed
8. Readily repeatable
9. Immediate diagnosis relieves patient anxiety
10. Definitive treatment can be planned in advance
11. Need for frozen section diagnosis is reduced

DISADVANTAGES OF FNAC

1. Practice and skill in aspiration technique is necessary
2. A percentage of aspirations are unsatisfactory
3. Experience is required for accurate interpretations
4. Diagnostic information is limited

MATERIALS AND METHODS

The present study emphasizes the role of fine needle aspiration cytology in the diagnosis of palpable breast lesions. This is a study undertaken in Department of Pathology, Sri Devaraj Urs Medical College, Kolar, during the period of 01-12-2008 to 30-11-2009.

Inclusion Criteria

All cases of FNAC of clinically palpable breast lesions along with its histopathology done at Sri R. L. Jalappa hospital and Research Centre attached to Sri Devaraj Urs Medical college, Tamaka, Kolar .

Exclusion Criteria

Radiologically detected breast lesions but clinically impalpable.

The referred patients were clinically examined and the procedure of aspiration biopsy was explained to the patient including reliability, limitations and complications. The patients were rested comfortably in supine position with arms raised over the head. An oblique or lateral position was needed for laterally located lesion. The overlying skin was cleaned with spirit. The lesion was localized between thumb and index finger of the left hand. The 22-23 gauge needle fitted to a 10 millilitre syringe was pierced into the lesion with firm and rapid movement making sure that the piston is in resting position. Plunger was then withdrawn and negative pressure was created in the syringe after entering the lesion, Then, maintaining the negative pressure the needle was moved up and down and at different direction to achieve multiple sampling from different sites of the lesion. Then the plunger was released and needle was removed from the lesion.

The needle containing the aspirated material was removed from syringe and air was drawn into the syringe and contents of needle were ejected on to the glass slides. At the site of aspiration little pressure was applied with sterile swab and the patients were then observed for 15-20 minutes after procedure for any complications. Naked eye examination of the aspirate was made and recorded, and then several smears were prepared. Caution was exercised to minimize cell damage and preserve the cell distribution.

Smears were promptly fixed in a fixative containing 95% ethyl alcohol, and they were stained by Papanicolaou stain and Hematoxylin and Eosin (HE). Air dried smears were also prepared and stained with Giemsa stain. ZN (Ziehl-Neelson) stain was done whenever necessary for demonstration of acid fast bacilli (AFB).

Whenever fluid was obtained, an attempt was always made to empty all the contents by applying gentle pressure over the lump. The fluid was centrifuged and smears were prepared from the sediment. Residual cystic swellings were re-aspirated from remaining solid areas.

FNAC results were compared with histopathological finding of the surgically resected specimen. These specimens were subjected to gross examination and fixed in 10% formalin for 24-48 hours. After fixation, representative areas were selected for paraffin embedding. Blocks were prepared by routine processing and sections of 5 microns thickness were cut and stained with HE. Special stains like ZN and PAS were used wherever required. Histopathological study was done separately and then results of cytological and histopathological study were correlated to evaluate the efficacy of the procedure.

INTERPRETATION OF ASPIRATE WAS DONE AS FOLLOWS

- Assess the adequacy of material in the smear.
- Cytomorphological features like cell pattern, cell population, individual cell morphology, background was studied and diagnosis was arrived.
- Breast lesions were categorized into –
    1. **Benign** – satisfactory sample with no evidence of malignancy
    2. **Atypical** – highly abnormal cellular findings probably reflecting malignancy
    3. **Suspicious** – small number of cells suggesting malignancy
    4. **Malignant** – irrefutable evidence of malignancy
    5. **Unsatisfactory** – scanty cellularity, air drying, distortion artefact or obscuring blood or inflammation.[61]

TABLE 04 - COMPARISON OF BENIGN AND LOW GRADE CARCINOMA IN FNAC SMEARS.[1]

Non-neoplastic breast tissue	**Low grade carcinoma NOS**
Low cell yield	Variable but high cell yield
Sheets and aggregates of cohesive, small, uniform cells	Irregular clusters of less cohesive, small, mildly irregular cells
Small rounded nuclei, bland chromatin, some overlapping	Slightly larger and darker nuclei
Myoepithelial cell nuclei among epithelial cells	Myoepithelial cell nuclei not seen
Variable numbers of single bare, bipolar nuclei scattered in background	No bare bipolar nuclei

For statistical analysis Statistical Package for Social Sciences, version 16 was used. Statistical analysis was done in all 50 cases where FNAC diagnosis was correlated with histopathological diagnosis. Chi-square test was used to calculate test of significance and p value < 0.05 was taken as statistically significant. For diagnostic accuracy of test- sensitivity, specificity and positive predictive value, negative predictive value, false positive rate and false negative rate were calculated.

Breast lesions diagnosed as malignant on cytology were graded by Simplified Black grading system on wet fixed Papanicolaou stained smears. Corresponding HE stained histologic sections were graded according to Nottingham modification of Bloom-Richardson grading system. The cytologic grading was correlated with histologic grading. Chi- square test was used to compare the results. p value < 0.05 was considered statistically significant.

Mitotic counts :

The microscope used was Olympus CX 21 with field of view number 18 (written on the eye piece) and high power field area of 0.152 mm^2. High power field area was calculated as

follows.

$$\text{Diameter of microscopic field}^{72} = \frac{\text{Field of view number}}{\text{Initial magnification of high power objective}}$$

$$= 18/40 = 0.45 \text{ mm}$$

$$\text{High power field area} = \Pi r^2$$

$$= 0.152 \text{ mm}^2$$

The total number of mitotic figures per 10 high power fields was recorded. Upto 5 mitosis/10 hpf was given 1 point, 6-10 scored 2 points and more than 11 scored 3 points. [7]

RESULTS

AGE DISTRIBUTION

FNAC was done in 50 patients who had breast lumps. The age of patients varied from 18 years to 72 years. Mean age of presentation was 44 years; median age of presentation was 41.5 years. The maximum number of cases (30%) was seen in the age group of 30-40 years.

TABLE 05 – DISTRIBUTION OF CASES IN DIFFERENT AGE GROUPS (FIG 01)

AGE GROUP	NO OF CASES	PERCENT
10-20	1	2.0
20-30	8	16.0
30-40	15	30.0
40-50	11	22.0
50-60	11	22.0
60-70	2	4.0
70-80	2	4.0
TOTAL	**50**	**100.0**

SEX DISTRIBUTION

Out of 50 patients 45 were females and 5 were males.

TABLE 06 – DISTRIBUTION CASES IN BOTH SEXES (FIG 02)

SEX	NO OF CASES	PERCENT
FEMALE	45	90
MALE	5	10
TOTAL	**50**	**100**

FIG 01

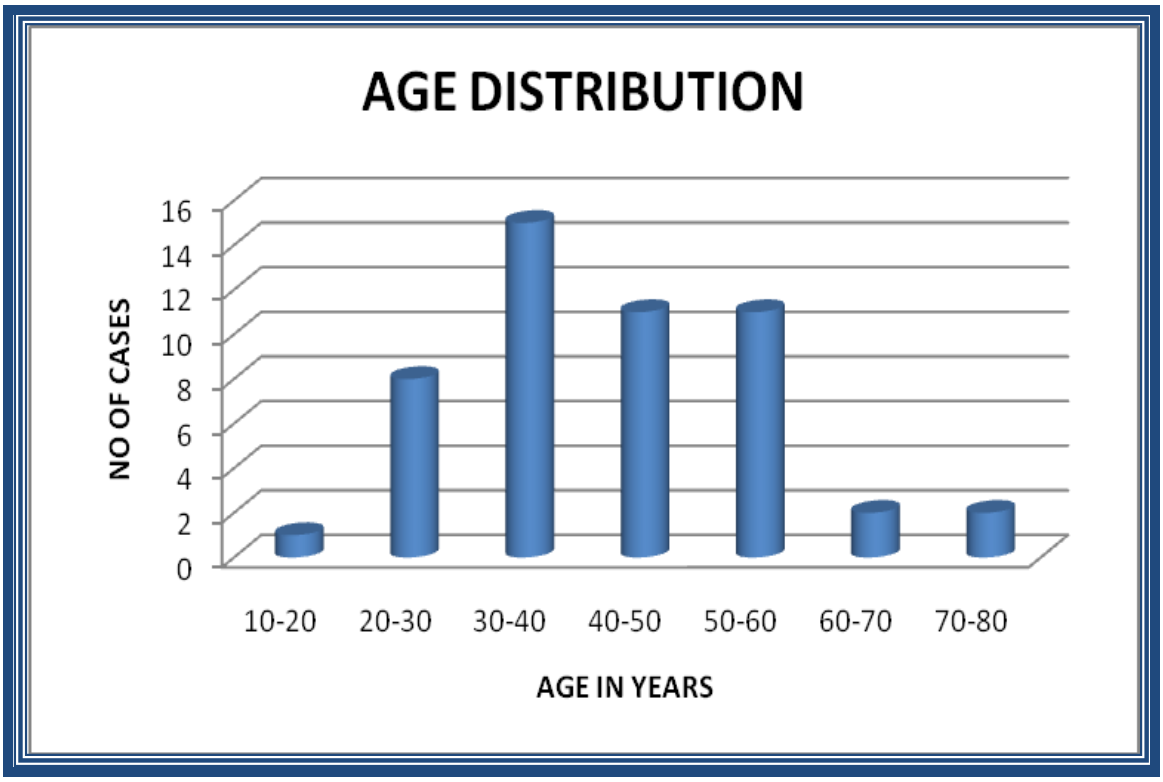
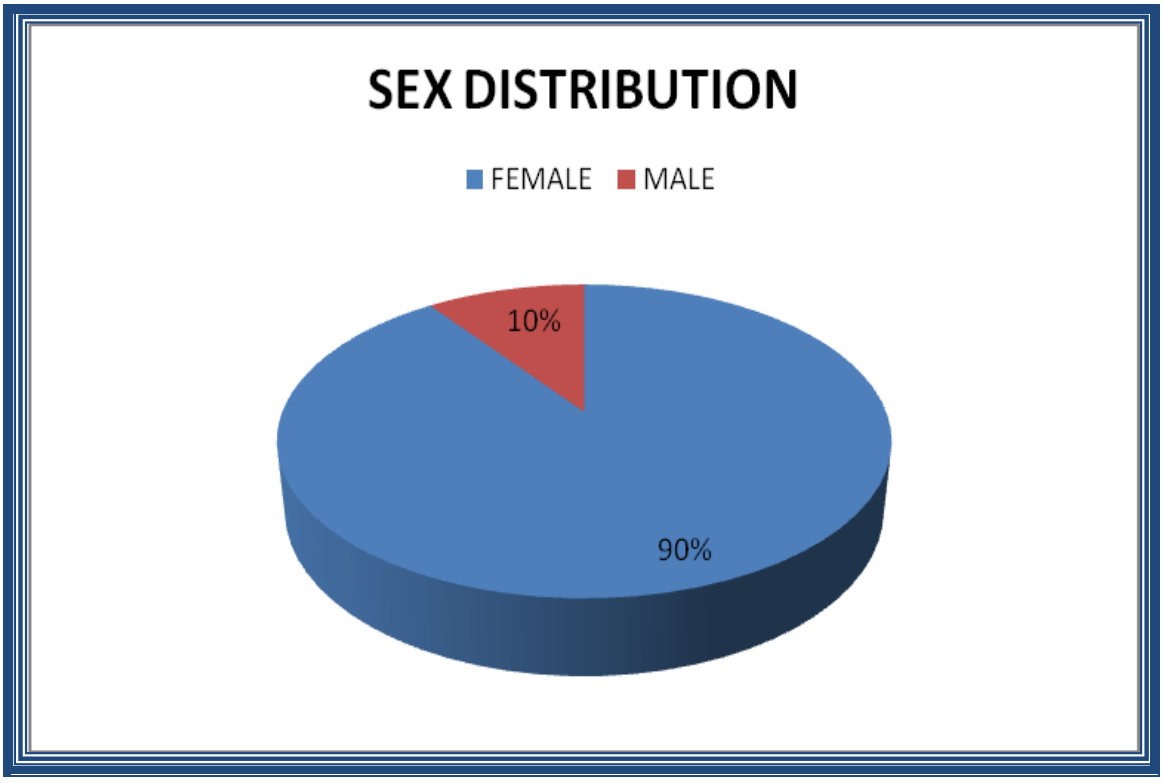

AGE DISTRIBUTION
NO OF CASES
16
14
12
10
8
6
4
2
0
10-20
20-30
30-40
40-50
50-60
60-70
70-80
AGE IN YEARS

FIG 02


SEX DISTRIBUTION
FEMALE
MALE
10%
90%

PRESENTING COMPLAINTS

The presenting complaint in all 50 (100%) patients was lump in the breast and 15 (30%) of 50 patients had pain associated with the lump.

MENARCHE AND MENOPAUSE

Out of 45 female patients 4 patients attained menarche at 10 years of age, 16 patients at 11 years of age, 15 patients at 12 years of age, 8 patients at 13 years of age and 2 patients at 14 years of age.

Out of 45 female patients, 15 patients had attained menopause. All 15 patients had attained menopause within 55 years.

PARITY IN FEMALES

Out of 45 female patients, 39 were parous and 6 females were nulliparous. The most common lesion in nulliparous females was fibroadenoma (4 cases) followed by Ductal carcinoma (2 Cases).

FAMILY HISTORY

Family history was present in only 1 case out of 50 cases. The patient was 65 year female with cytological diagnosis of Ductal carcinoma NOS. There was history of patient's sister with breast carcinoma.

LATERALITY OF BREAST LESIONS

Out of 50 cases, 31 cases presented with lump in right breast, 14 cases in left breast and 5 cases involved both breasts.

TABLE 07 – DISTRIBUTION OF LATERALITY OF BREAST LESIONS (FIG 03)

SIDE	FREQUENCY	PERCENT
BILATERAL	5	10.0
LEFT	14	28.0
RIGHT	31	62.0
TOTAL	**50**	**100.0**

SITE OF INVOLVEMENT

Upper outer quadrant (14 cases) was the most commonly involved region of breast among malignant lesions. Upper inner and lower outer quadrant (7 cases each) was most commonly involved in benign lesions. 1 malignant case showed diffuse involvement of breast. Sub-areolar involvement was seen in 1 malignant case.

TABLE 08 – DISTRIBUTION OF LESIONS IN DIFFERENT QUADRANTS OF BREAST (FIG 04)

QUADRANT	BENIGN	MALIGNANT	TOTAL
DIFFUSE	3	1	**4**
LOWER INNER	3	4	**7**
LOWER OUTER	7	0	**7**
SUB-AREOLAR	0	1	**1**
UPPER INNER	7	7	**14**
UPPER OUTER	3	14	**17**
TOTAL	**23**	**27**	**50**

χ^2 = 16.04, degree of freedom = 5, P value - 0.07 (p value was not significant)

FIG 03

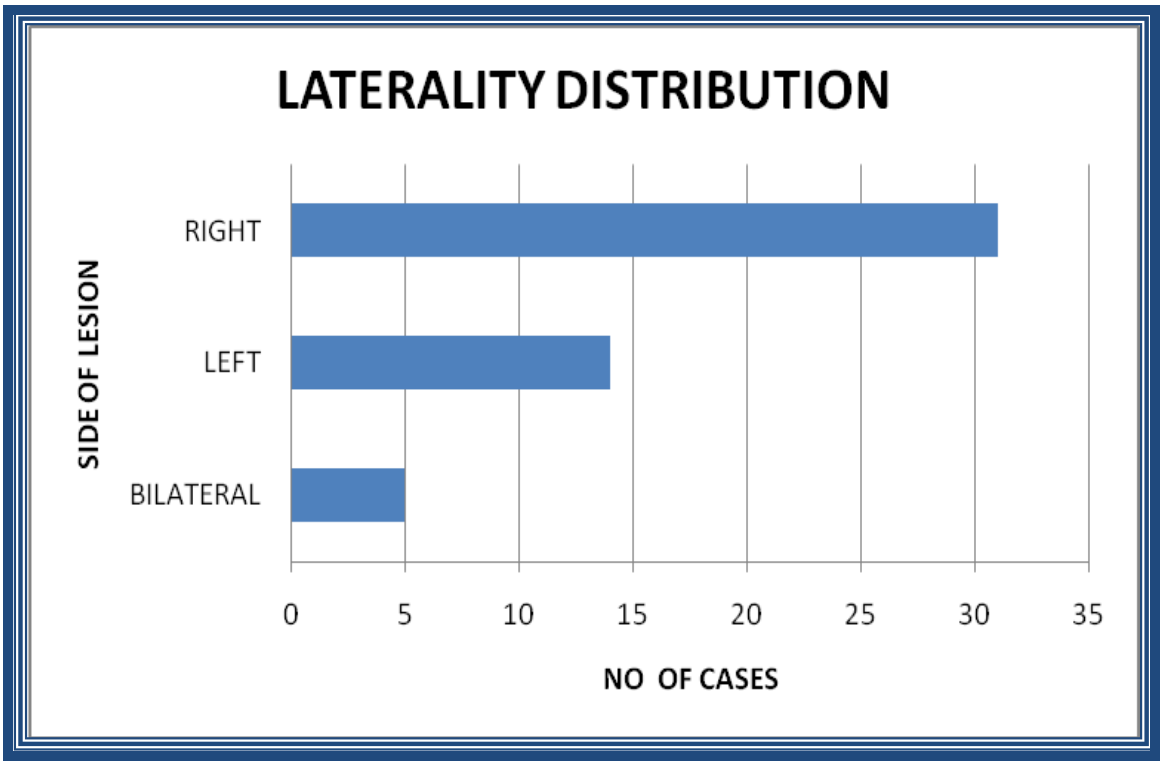
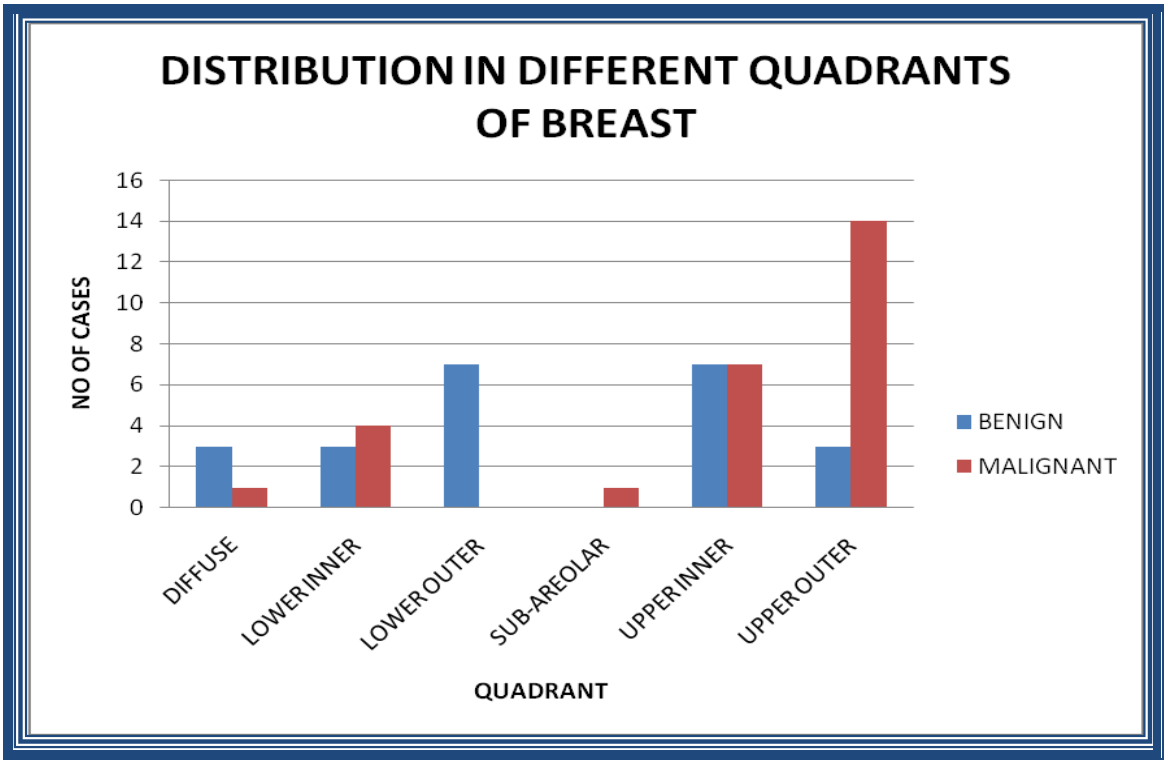

LATERALITY DISTRIBUTION
SIDE OF LESION
RIGHT
LEFT
BILATERAL
0
5
10
15
20
25
30
35
NO OF CASES

FIG 04


DISTRIBUTION IN DIFFERENT QUADRANTS OF BREAST
NO OF CASES
16
14
12
10
8
6
4
2
0
DIFFUSE
LOWER INNER
LOWER OUTER
SUB-AREOLAR
UPPER INNER
UPPER OUTER
QUADRANT
BENIGN
MALIGNANT

SIZE OF BREAST LESIONS

Most of the lesions (70%) were 2 to 5 centimetres in size. Smallest lump was 1.5x1 centimetres in a 42 year female diagnosed as fibroadenoma while largest was 11x14 centimetres in a 55 year male patient diagnosed as mixed ductal and lobular carcinoma.

TABLE 09 – SIZE WISE DISTRIBUTION OF BREAST LESIONS (FIG 05)

SIZE IN CENTIMETERS	NO OF CASES	PERCENT
<2	5	10.0
>5	10	20.0
2 TO 5	35	70.0
TOTAL	**50**	**100.0**

CONSISTENCY OF BREAST LESIONS

In 58% the lesions were firm in consistency and most of them were fibroadenoma. Hard consistency was seen in 17% of cases and most of them were malignant lesions. Soft consistency was seen in fibrocystic disease, fibroadenoma and TB mastitis.

TABLE 10 – DISTRIBUTION OF CONSISTENCY OF BREAST LESIONS (FIG 06)

CONSISTENCY	NO OF CASES	PERCENT
FIRM	29	58.0
HARD	17	34.0
SOFT	4	8.0
TOTAL	**50**	**100.0**

FIG 05

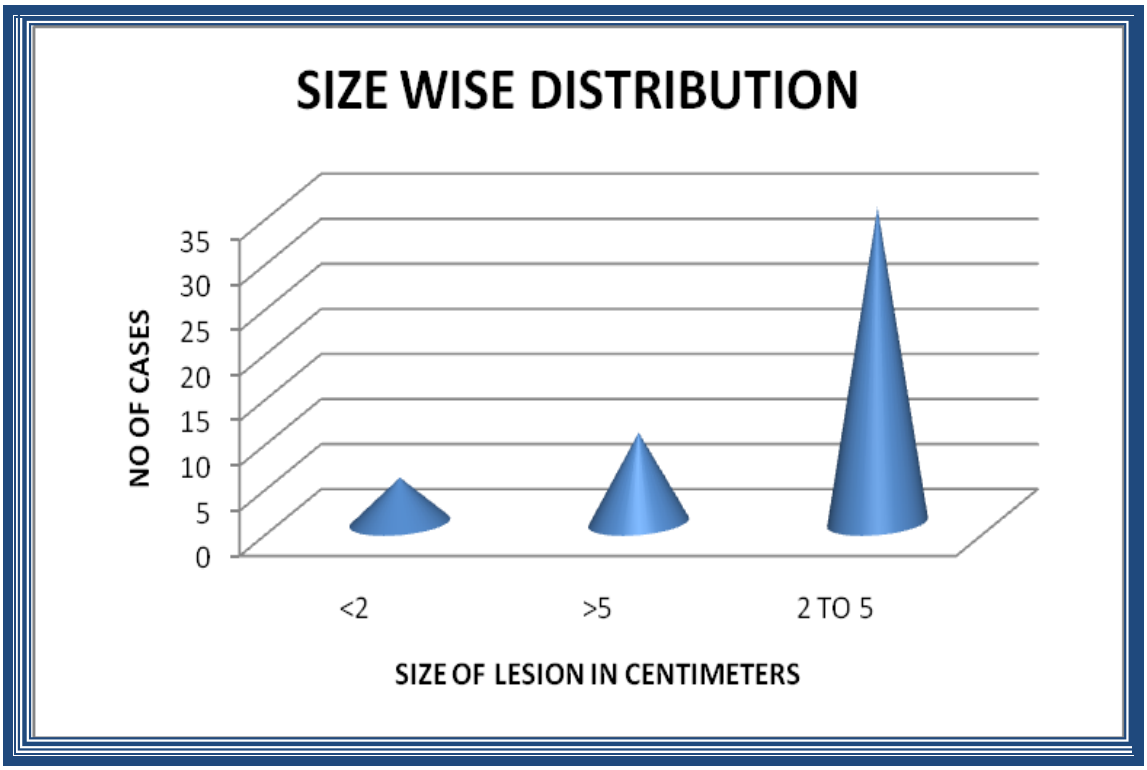
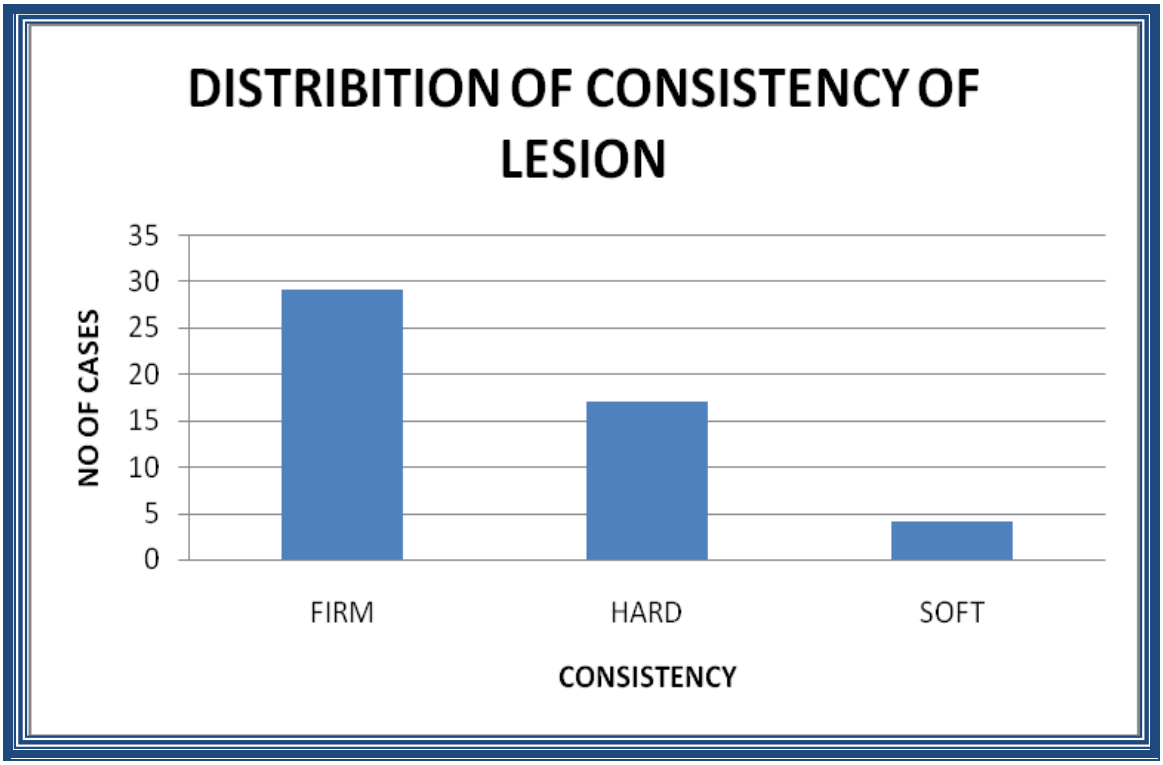

SIZE WISE DISTRIBUTION
NO OF CASES
35
30
25
20
15
10
5
0
<2
>5
2 TO 5
SIZE OF LESION IN CENTIMETERS

FIG 06


DISTRIBITION OF CONSISTENCY OF LESION
NO OF CASES
35
30
25
20
15
10
5
0
FIRM
HARD
SOFT
CONSISTENCY

BORDERS OF BREAST LESIONS

Most (18 of 27 cases) malignant lesions had ill-defined borders and most benign lesions (16 of 23 cases) had well-defined borders.

TABLE 11 – DISTRIBUTION OF BORDERS OF BREAST LESIONS (FIG 07)

BORDERS	BENIGN	MALIGNANT	TOTAL
BORDERS ILL-DEFINED	7	18	25
BORDERS WELL-DEFINED	16	9	25
TOTAL	**23**	**27**	**50**

χ^2 = 6.52, degree of freedom = 1, p value - 0.011 (p value was significant)

NATURE OF ASPIRATE

Grey white aspirate was obtained in 52% cases. Hemorrhagic aspirate was obtained in 46% of cases and most of them were malignant. 1 case of TB mastitis had purulent aspirate.

TABLE 12 – DISTRIBUTION OF NATURE OF ASPIRATE (FIG 08)

ASPIRATE	NO OF CASES	PERCENT
GREY WHITE	26	52.0
HEMORRHAGIC	23	46.0
PURULENT	1	2.0
TOTAL	**50**	**100.0**

FIG 07

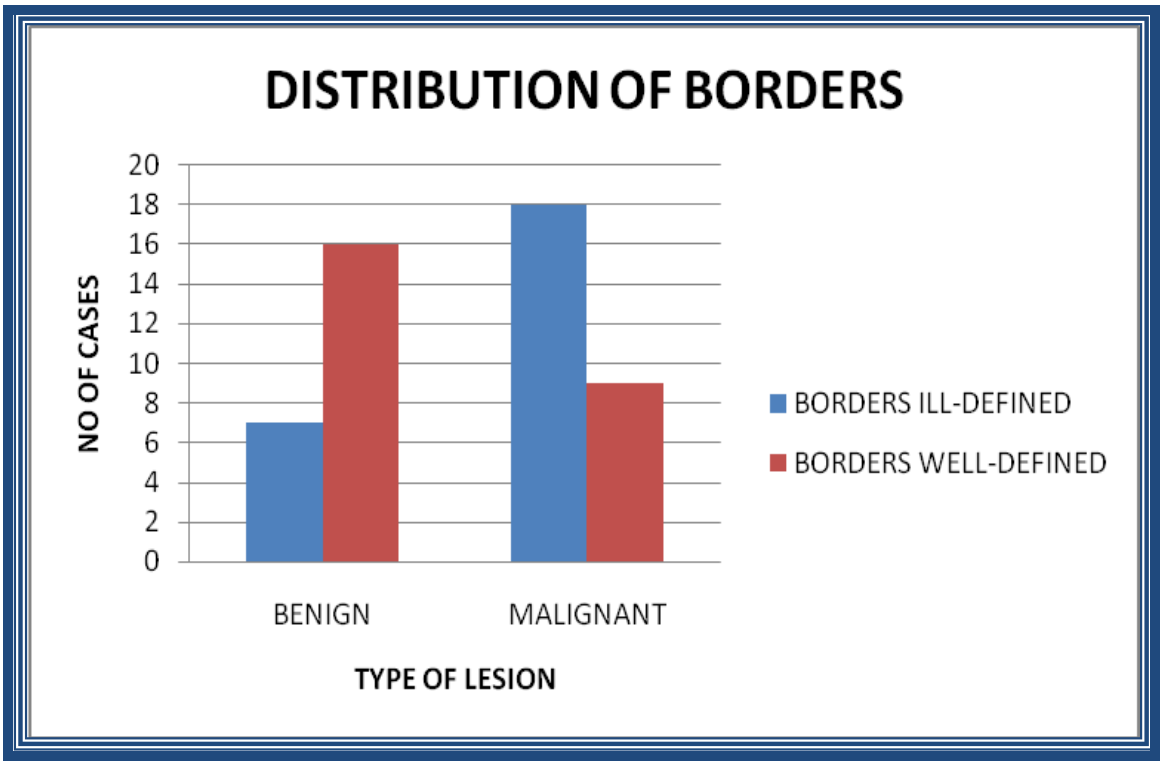
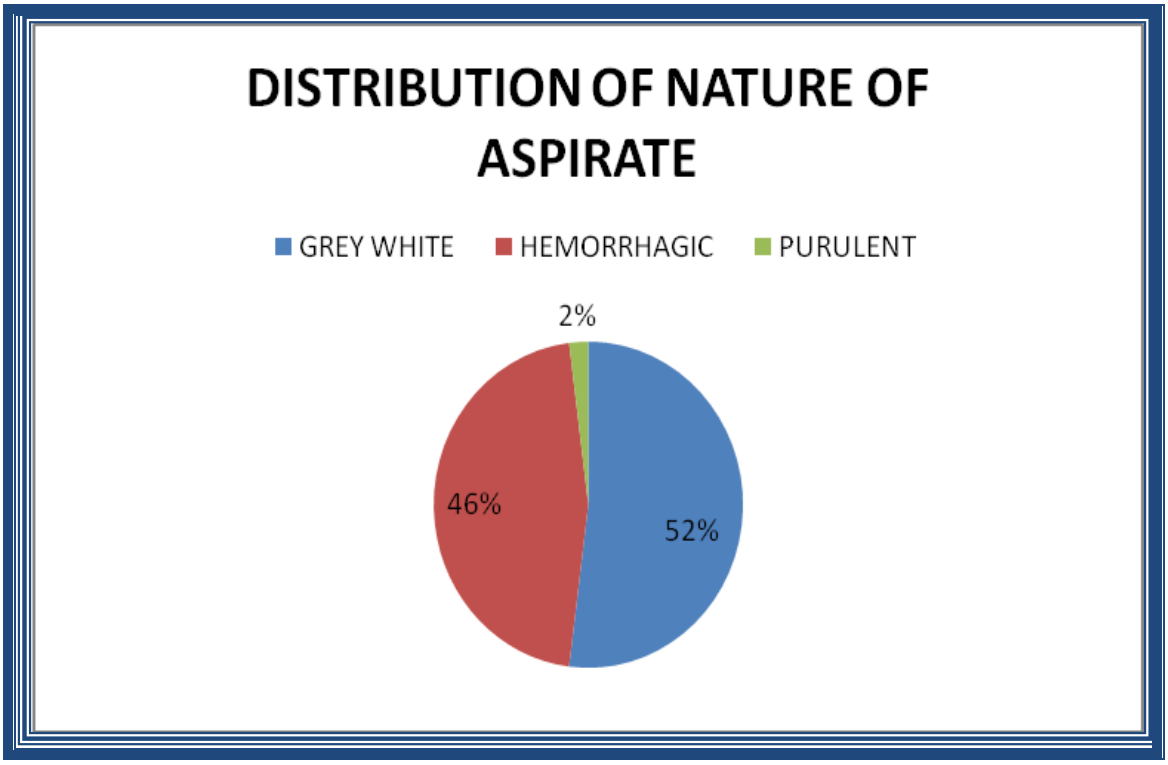

DISTRIBUTION OF BORDERS
NO OF CASES
20
18
16
14
12
10
8
6
4
2
0
BENIGN
MALIGNANT
TYPE OF LESION
BORDERS ILL-DEFINED
BORDERS WELL-DEFINED

FIG 08


DISTRIBUTION OF NATURE OF ASPIRATE
GREY WHITE
HEMORRHAGIC
PURULENT
2%
46%
52%

CYTOLOGICAL PATTERNS OF ARRANGEMENT OF CELLS

Various patterns of arrangement seen in present study were – antlerhorn, clusters, monolayered sheets, acinar, tubular, Indian file and singles. Arrangement of cells in clusters and singles was most common pattern of arrangement (20%). Antler horn pattern was seen in most of fibroadenomas.

TABLE 13 – DISTRIBUTION OF PATTERNS OF ARRANGEMENT (FIG 09)

PATTERN OF ARRANGEMENT	NO OF CASES	PERCENT
ANTLER HORN,CLUSTERS	4	8.0
ANTLER HORN,MONOLAYER,CLUSTERS	8	16.0
ANTLER HORN,MONOLAYER,CLUSTERS,SINGLES	1	2.0
CLUSTERS,SINGLES	10	20.0
MONOLAYER,CLUSTERS	7	14.0
CLUSTERS,ACINAR,SINGLES	2	4.0
MONOLAYER,CLUSTERS,ACINAR	3	6.0
MONOLAYER,CLUSTERS,TUBULAR	1	2.0
MONOLAYER,CLUSTERS,SINGLES	7	14.0
MONOLAYER,CLUSTERS,SINGLES,INDIAN FILE	1	2.0
MONOLAYER,CLUSTERS,SINGLES,ACINAR	5	10.0
MONOLAYER,CLUSTERS,SINGLES,CRIBRIFORM	1	2.0
TOTAL	**50**	**100.0**

CYTOLOGIC DIAGNOSIS

Ductal carcinoma NOS (20 cases) was most common lesion among which 1 case had chemotherapy induced changes and 2 cases had ipsilateral axillary lymph node metastasis. Other cases were fibroadenoma (16 cases), fibrocystic disease (2 cases), gynaecomastia (3 cases), lobular carcinoma (1 case), TB mastitis (1 case), tubular carcinoma (1 case), pleomorphic liposarcoma with myxoid change (1 case), metaplastic carcinoma (1 case) and medullary carcinoma (1 case). Because of inadequate cell yield, 2 cases were put under unsatisfactory category and in 1 case only few cells showed features of malignancy so was diagnosed as suspicious for malignancy.

TABLE 14 - DISTRIBUTION OF LESIONS ON CYTOLOGY (FIG 10)

DIAGNOSIS	NO OF CASES	PERCENT
UNSATISFACTORY	2	4.0
DUCTAL CARCINOMA NOS	17	34.0
DUCTAL CARCINOMA WITH CHEMO INDUCED CHANGES	1	2.0
DUCTAL CARCINOMA WITH LYMPH NODE METASTASIS	2	4.0
FIBROADENOMA	16	32.0
FIBROCYSTIC DISEASE	2	4.0
GYNAECOMASTIA	3	6.0
LOBULAR CARCINOMA	1	2.0
MEDULLARY CARCINOMA	1	2.0
METAPLASTIC CARCINOMA	1	2.0
PLEOMORPHIC LIPOSARCOMA WITH MYXOID CHANGE	1	2.0
SUSPICIOUS FOR MALIGNANCY	1	2.0
TB GRANULOMATOUS MASTITIS	1	2.0
TUBULAR CARCINOMA	1	2.0
TOTAL	**50**	**100.0**

FIG 09

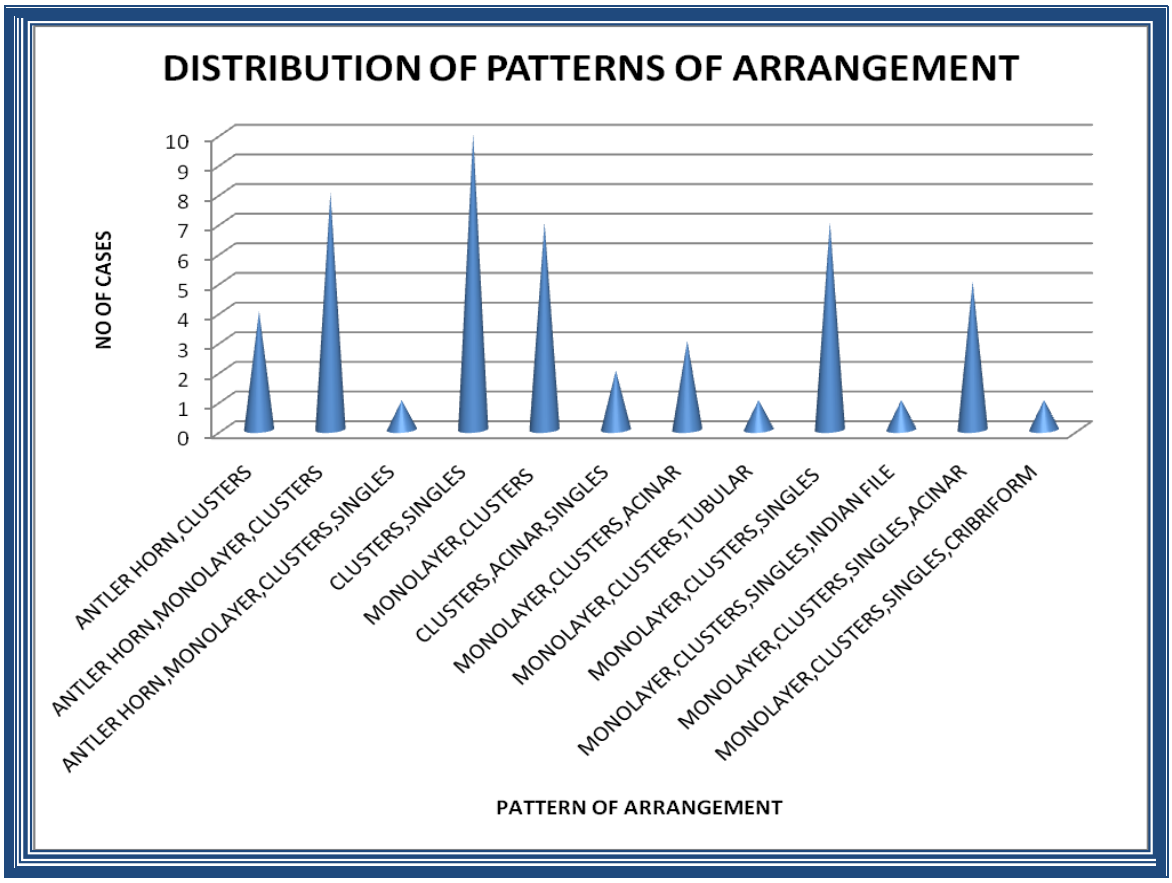
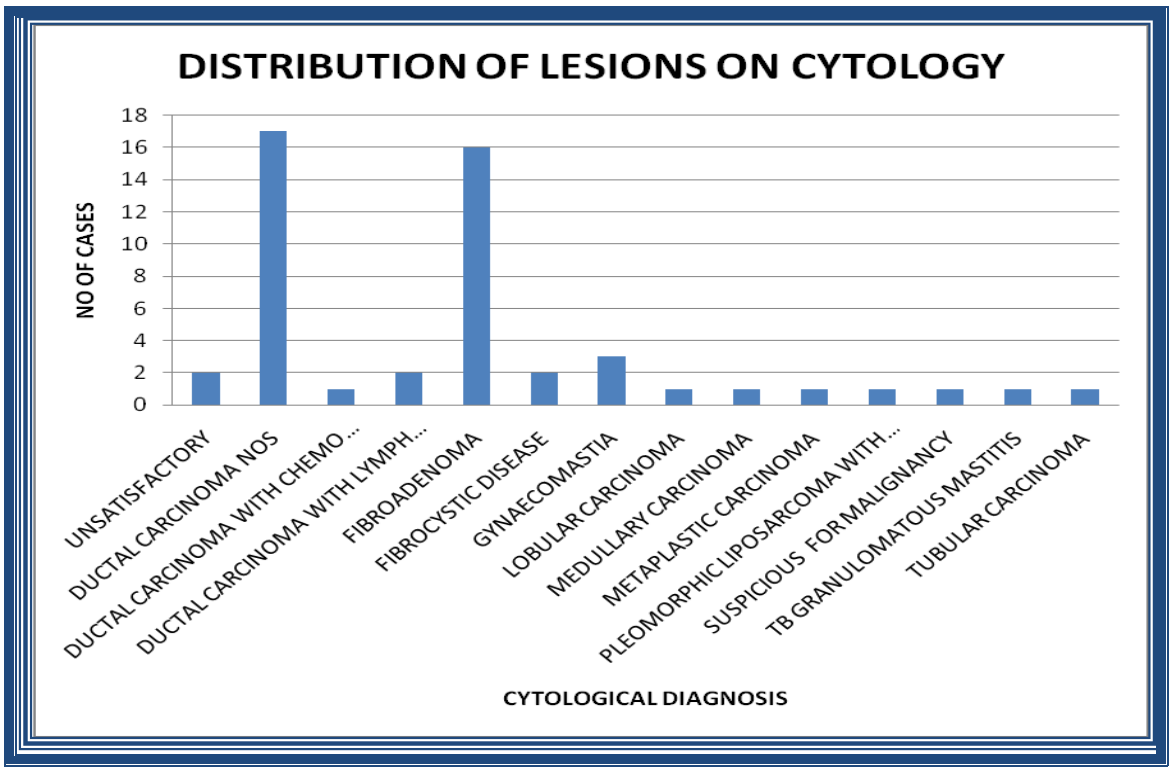

DISTRIBUTION OF PATTERNS OF ARRANGEMENT
NO OF CASES
10
9
8
7
6
5
4
3
2
1
0
ANTLER HORN,CLUSTERS
ANTLER HORN,MONOLAYER,CLUSTERS
ANTLER HORN,MONOLAYER,CLUSTERS,SINGLES
CLUSTERS,SINGLES
MONOLAYER,CLUSTERS
CLUSTERS,ACINAR,SINGLES
MONOLAYER,CLUSTERS,ACINAR
MONOLAYER,CLUSTERS,TUBULAR
MONOLAYER,CLUSTERS,SINGLES
MONOLAYER,CLUSTERS,SINGLES,INDIAN FILE
MONOLAYER,CLUSTERS,SINGLES,ACINAR
MONOLAYER,CLUSTERS,SINGLES,CRIBRIFORM
PATTERN OF ARRANGEMENT

FIG 10


DISTRIBUTION OF LESIONS ON CYTOLOGY
NO OF CASES
18
16
14
12
10
8
6
4
2
0
UNSATISFACTORY
DUCTAL CARCINOMA NOS
DUCTAL CARCINOMA WITH CHEMO ...
DUCTAL CARCINOMA WITH LYMPH...
FIBROADENOMA
FIBROCYSTIC DISEASE
GYNAECOMASTIA
LOBULAR CARCINOMA
MEDULLARY CARCINOMA
METAPLASTIC CARCINOMA
PLEOMORPHIC LIPOSARCOMA WITH...
SUSPICIOUS FOR MALIGNANCY
TB GRANULOMATOUS MASTITIS
TUBULAR CARCINOMA
CYTOLOGICAL DIAGNOSIS

CORELATION OF CYTOLOGIC AND HISTOPATHOLOGIC CATEGORIES

21 cases out of 23 benign cases were diagnosed as benign on FNAC and 25 out of 27 malignant cases were diagnosed as malignant on FNAC.

TABLE 15 - CORELATION OF CYTOLOGIC AND HISTOPATHOLOGIC CATEGORIES

CYTOLOGIC CATEGORIES	HISTOPATHOLOGIC CATEGORIES		
	BENIGN	**MALIGNANT**	**TOTAL**
BENIGN	21	1	**22**
MALIGNANT	0	25	**25**
SUSPICIOUS	0	1	**1**
UNSATISFACTORY	2	0	**2**
TOTAL	**23**	**27**	**50**

CORELATION OF CYTOLOGIC AND HISTOPATHOLOGIC DIAGNOSIS

2 unsatisfactory cases on FNAC turned out to be fibroadenoma on histopathology. 1 suspicious for malignancy case on FNAC was diagnosed as ductal carcinoma NOS on histopathology. 2 cases of fibrocystic disease were misinterpreted as fibroadenoma on FNAC and 1 case of mixed ductal and lobular carcinoma was misinterpreted as lobular carcinoma on FNAC. 1 case of ductal carcinoma was wrongly diagnosed as fibroadenoma.

TABLE 16 – CORELATION OF FNAC AND HISTOPATHOLOGY DIAGNOSIS

CYTO_DIAGNOSIS	**DUCTAL CA**	**DUCTAL CA WITH CHEMO INDUCED CHANGES**	**DUCTAL CA WITH LN METS**	**FIBROADENOMA**	**FIBROCYSTIC DISEASE**	**GYNAECOMASTIA**	**MEDULLARY CA**	**METAPLASTIC CA**	**MIXED DUCTAL AND LOBULAR CARCINOMA**	**PLEOMORPHIC LIPOSARCOMA WITH MYXOID CHANGE**	**TB GRANULOMATOUS MASTITIS**	**TUBULAR CA**	**TOTAL**
UNSATISFACTORY	-	-	-	2	-	-	-	-	-	-	-	-	**2**
DUCTAL CA	17	-	-	-	-	-	-	-	-	-	-	-	**17**
DUCTAL CA WITH CHEMO INDUCED CHANGES	-	1	-	-	-	-	-	-	-	-	-	-	**1**
DUCTAL CA WITH LN METS	-	-	2	-	-	-	-	-	-	-	-	-	**2**
FIBROADENOMA	1	-	-	13	2	-	-	-	-	-	-	-	**16**
FIBROCYSTIC DISEASE	-	-	-	-	2	-	-	-	-	-	-	-	**2**
GYNAECOMASTIA	-	-	-	-	-	3	-	-	-	-	-	-	**3**
LOBULAR CARCINOMA	-	-	-	-	-	-	-	-	1	-	-	-	**1**
MEDULLARY CA	-	-	-	-	-	-	1	-	-	-	-	-	**1**
METAPLASTIC CA	-	-	-	-	-	-	-	1	-	-	-	-	**1**
PLEOMORPHIC LIPOSARCOMA WITH MYXOID CHANGE	-	-	-	-	-	-	-	-	-	1	-	-	**1**
SUSPICIOUS FOR MALIGNANCY	1	-	-	-	-	-	-	-	-	-	-	-	**1**
TB GRANULOMATOUS MASTITIS	-	-	-	-	-	-	-	-	-	-	1	-	**1**
TUBULAR CA	-	-	-	-	-	-	-	-	-	-	-	1	**1**
TOTAL	**19**	**1**	**2**	**15**	**4**	**3**	**1**	**1**	**1**	**1**	**1**	**1**	**50**

STATISTICAL ANALYSIS

The statistical tests used in the interpretation of the results obtained in our study were the determination of:

Sensitivity, specificity, positive predictive value, negative predictive value, false positive rate and false negative rate of FNAC as a diagnostic procedure in detecting malignancy.

All 50 cases in the present study had histopathological correlation but to calculate the below mentioned parameters 47 cases were included. 3 cases (2 unsatisfactory and 1 suspicious for malignancy) were excluded from statistical assessment.

Out of 47 patients, the FNAC report of 43 patients matched with the final histopathology report. Out of the 4 patients, in which FNAC did not match, 3 showed fibroadenoma and 1 showed lobular carcinoma on FNAC. The histopathology of 2 cases of fibroadenoma on FNAC turned out to be fibrocystic disease, 1 case of fibroadenoma on cytology turned out to be ductal carcinoma and 1 case of lobular carcinoma on FNAC turned out to be mixed lobular and ductal carcinoma.

TABLE 17 - CYTOHISTOPATHOLOGICAL CORRELATION FOR MALIGNANT LESIONS

CYTOLOGY	**HISTOPATHOLOGY**		**TOTAL**
	MALIGNANT	BENIGN	
MALIGNANT	25	-	**25**
BENIGN	1	21	**22**
TOTAL	**26**	**21**	**47**

The results of diagnostic accuracy of FNAC to detect malignancy was

Sensitivity – 96.15%

Specificity – 100%

Positive predictive value – 100%

Negative predictive value – 95.45%

False positive rate – 0%

False negative rate – 3.84%

CORRELATION OF CYTOLOGIC AND HISTOLOGIC GRADES

Out of 47 cases the diagnosis of malignancy was offered in 26 cases. Nottingham modification of Bloom Richardson grading can be applied to ductal carcinoma, special types of ductal carcinoma and lobular carcinoma.[7] Hence 1 case of pleomorphic liposarcoma with myxoid change was excluded from analysis. 1 case of ductal carcinoma NOS misinterpreted as fibroadenoma on FNAC, was retrospectively included for grading.

The cytologic and histologic grading was performed on 25 cases which included ductal carcinoma NOS (21 cases), mixed ductal and lobular carcinoma (1 case), tubular carcinoma (1 case), metaplastic carcinoma (1 case) and medullary carcinoma (1 case).

On cytologic grading 9 cases (36%) were low grade and 16 cases (64%) cases were high grade. Low grade Simplified Black grade when correlated with Nottingham modification of Bloom - Richardson grade revealed six cases out of 9 cases to be grade 1. 16 cases of high grade Simplified Black grade when compared with Nottingham modification of Bloom Richardson grade revealed only two cases to be grade 1, five cases to be grade 2 and nine cases to be grade 3.

In the present study, by application of Chi – square test, p value was <0.05 which is statistically significant. This indicates that the cytologic grading by Simplified Black method correlated well with Nottingham modification of Bloom - Richardson histological grading.

TABLE 18 – CORRELATION OF SIMPLIFIED BLACK CYTOLOGIC GRADING WITH NOTTINGHAM MODIFICATION OF BLOOM RICHARDSON HISTOLOGICAL GRADING.

CYTOLOGICAL GRADE	**HISTOPATHOLOGICAL GRADE**			
	TOTAL NO OF CASES	GRADE 1	GRADE 2	GRADE 3
LOW GRADE	**9**	6	3	-
HIGH GRADE	**16**	2	5	9
TOTAL	**25**	**8**	**8**	**9**

Chi – square value : 10.35

Degree of freedom : 2

p value < 0.01

FIG 11 – Assembly for FNAC procedure

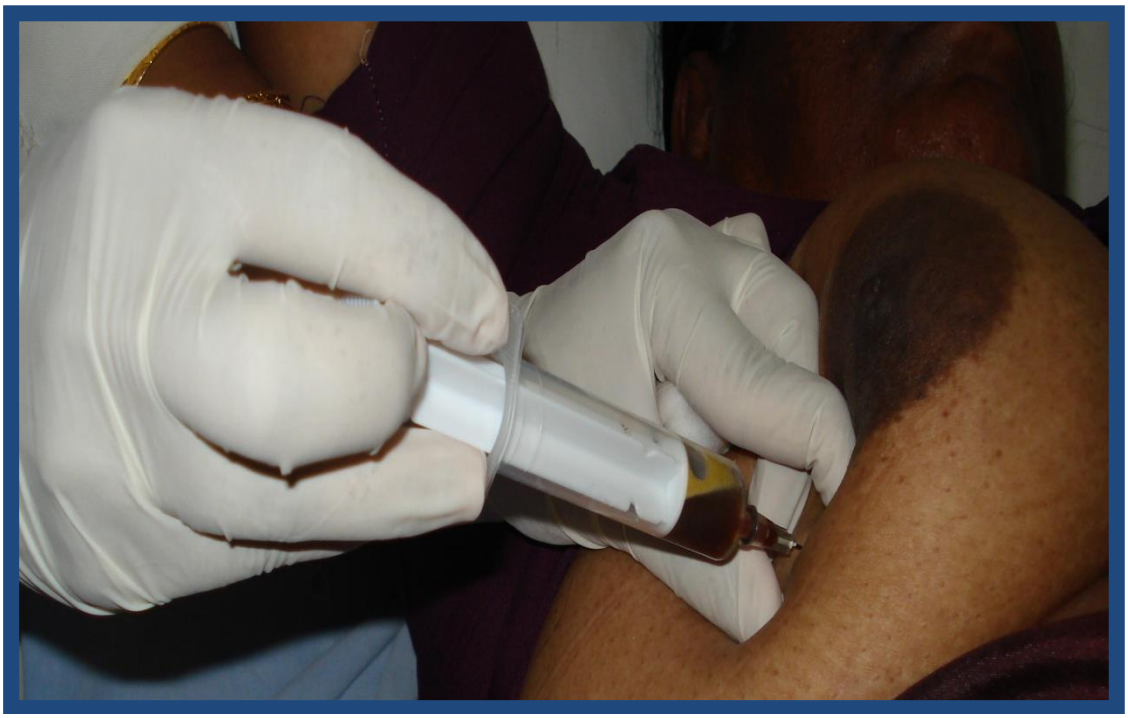


FIG 12 – Procedure of FNAC

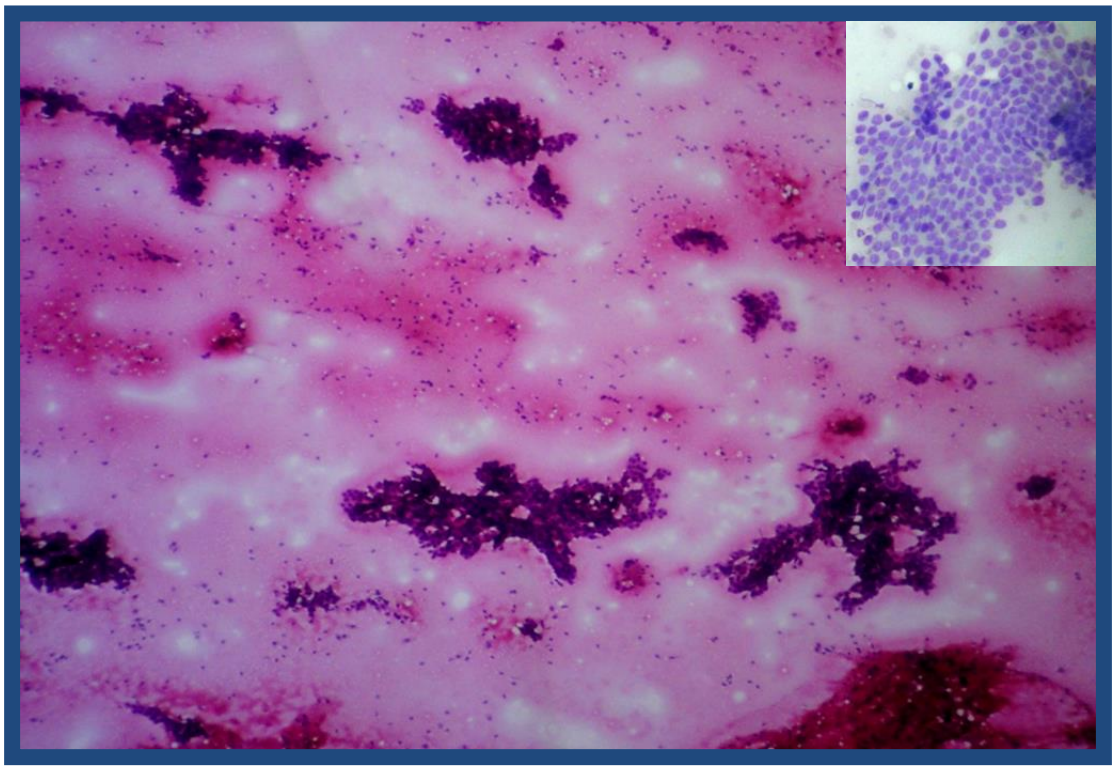


FIG 13 – FNAC of fibroadenoma showing ductal cells in antler horn pattern with numerous bare bipolar nuclei and a stromal fragment. HE X 100
Inset shows ductal cells with interspersed myoepithelial cells in monolayered sheets. MGG X 400

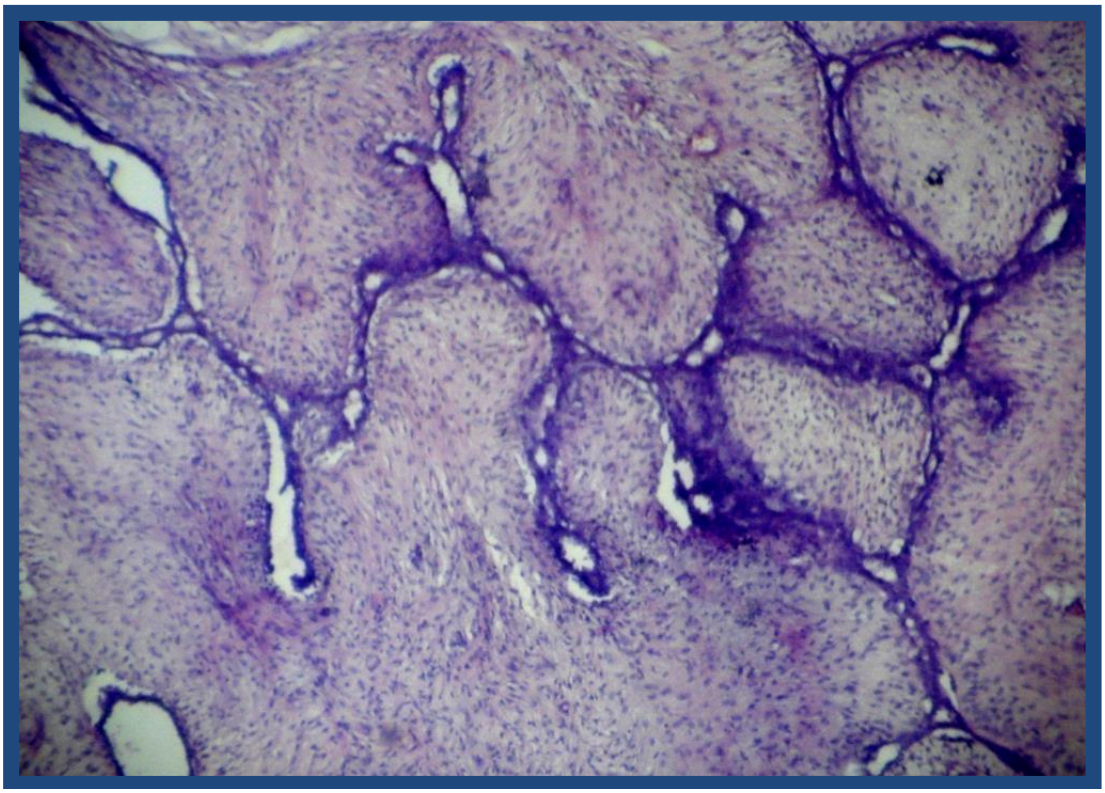


FIG 14 – HP of fibroadenoma showing intracanicular pattern. HE X 100

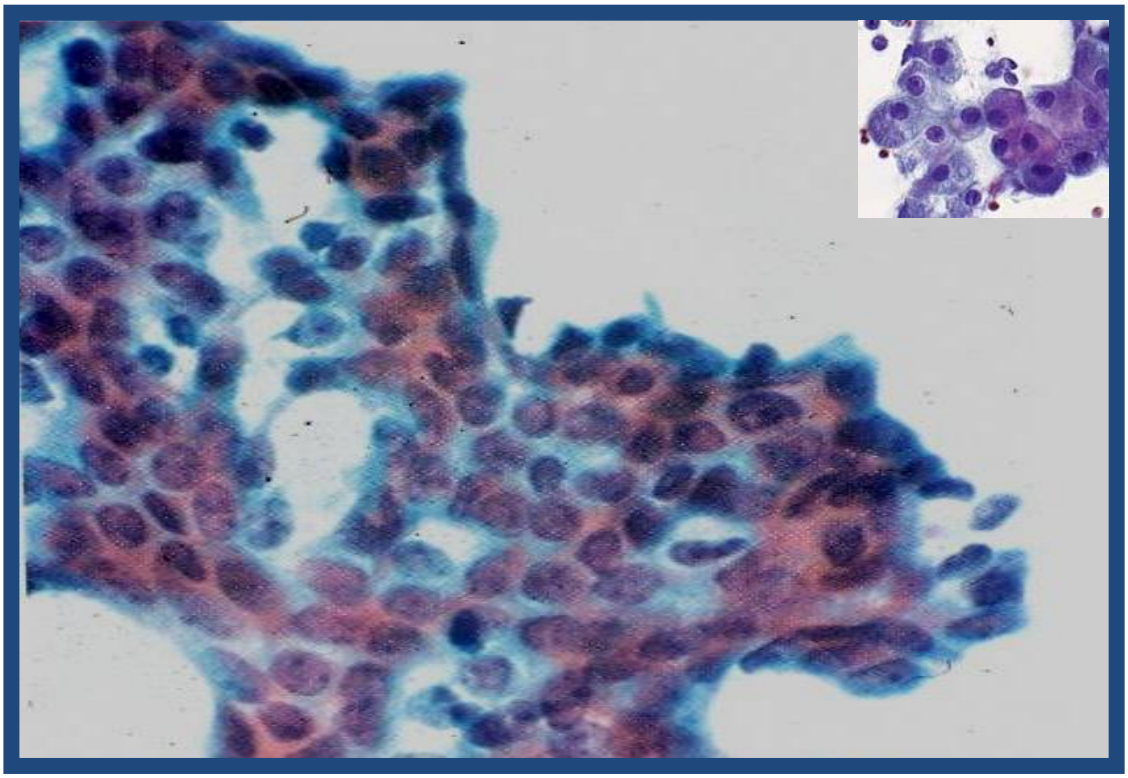


FIG 15 – FNAC of fibrocystic disease showing ductal cells in sheets. Pap X 400
Inset shows apocrine change. MGG X 400

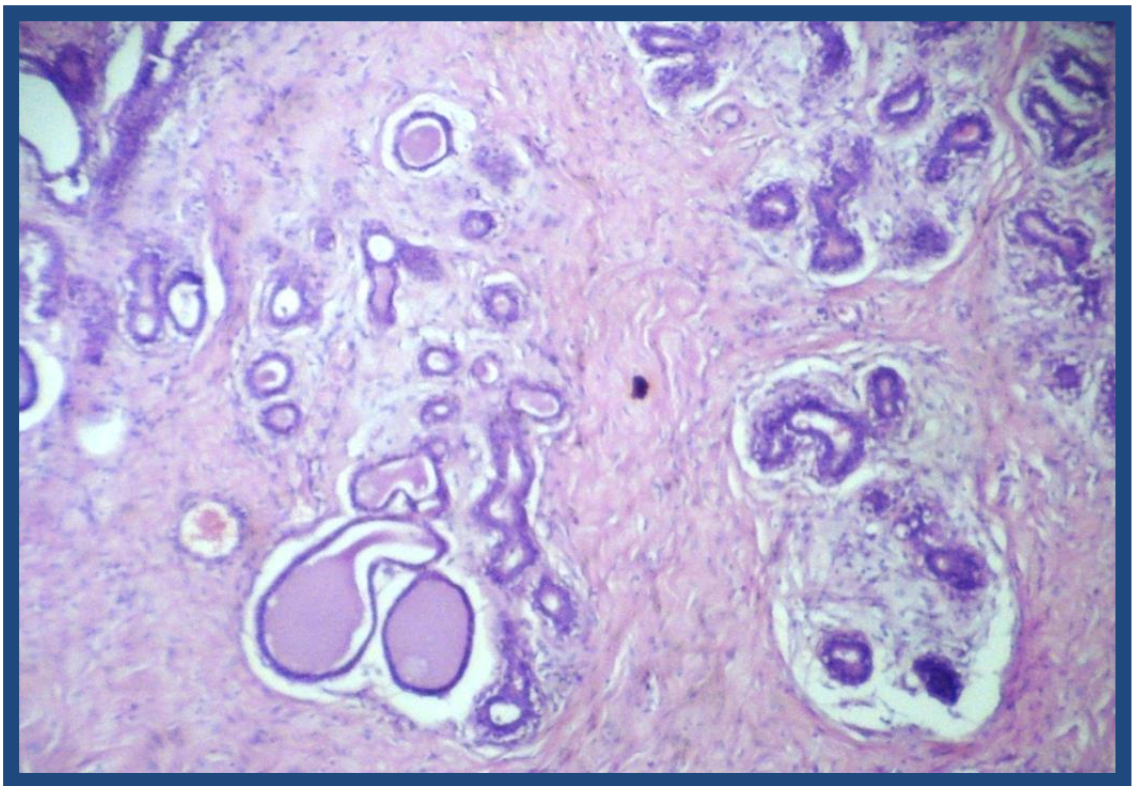


FIG 16 – HP of fibrocystic disease showing cystically dilated glands with surrounding stromal fibrosis. HE X 100

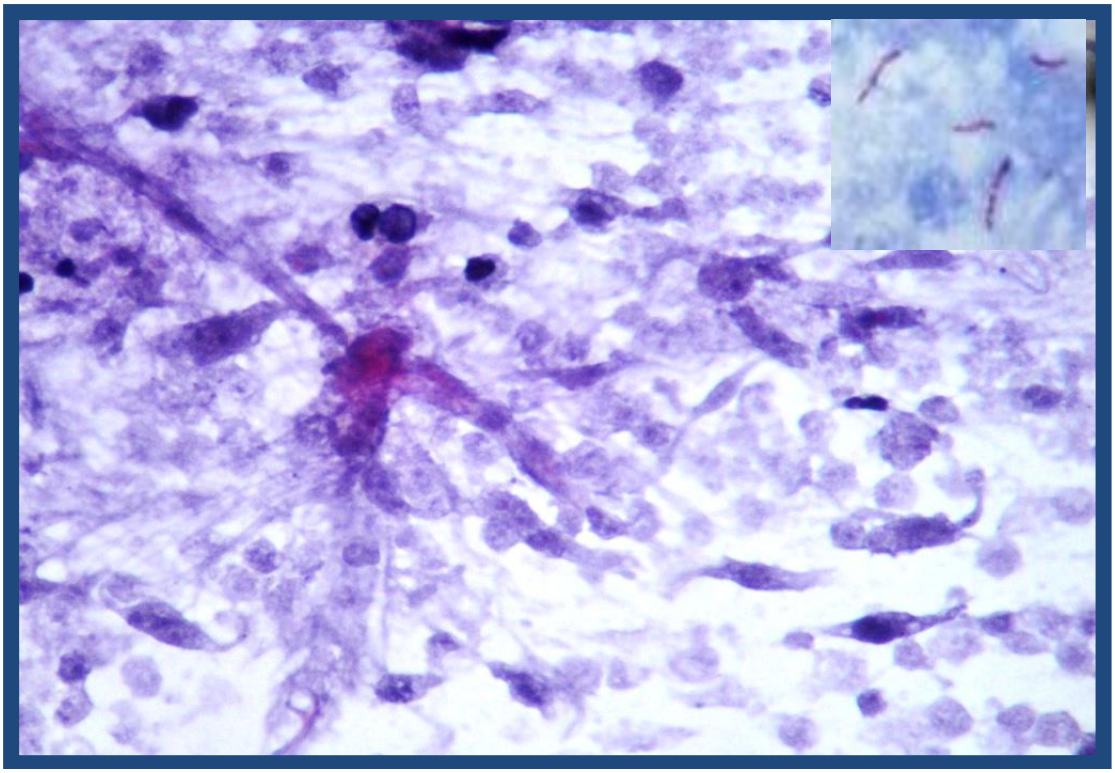


FIG 17 – FNAC of tuberculous mastitis showing cluster of epithelioid cells, few lymphocytes and necrosis. MGG X 400
Inset shows acid fast bacilli. ZN X 1000

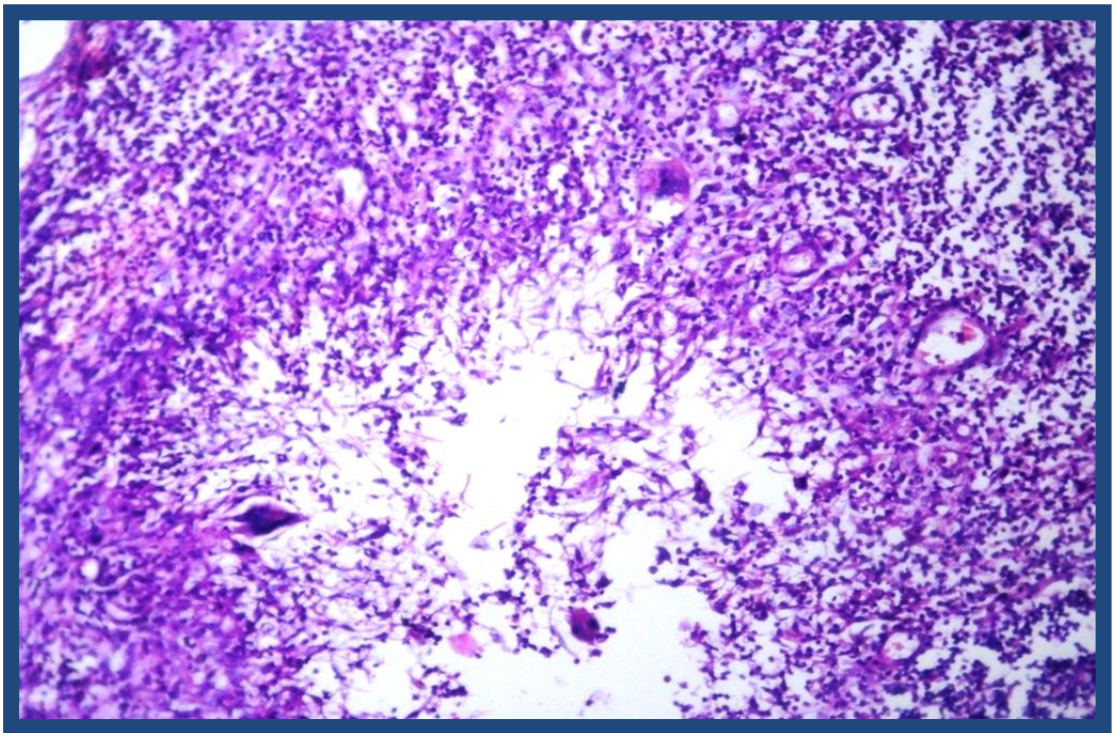


FIG 18 – HP of tuberculous mastitis showing granulomas consisting epithelioid cells, langhans giant cell and lymphocytes. HE X 100

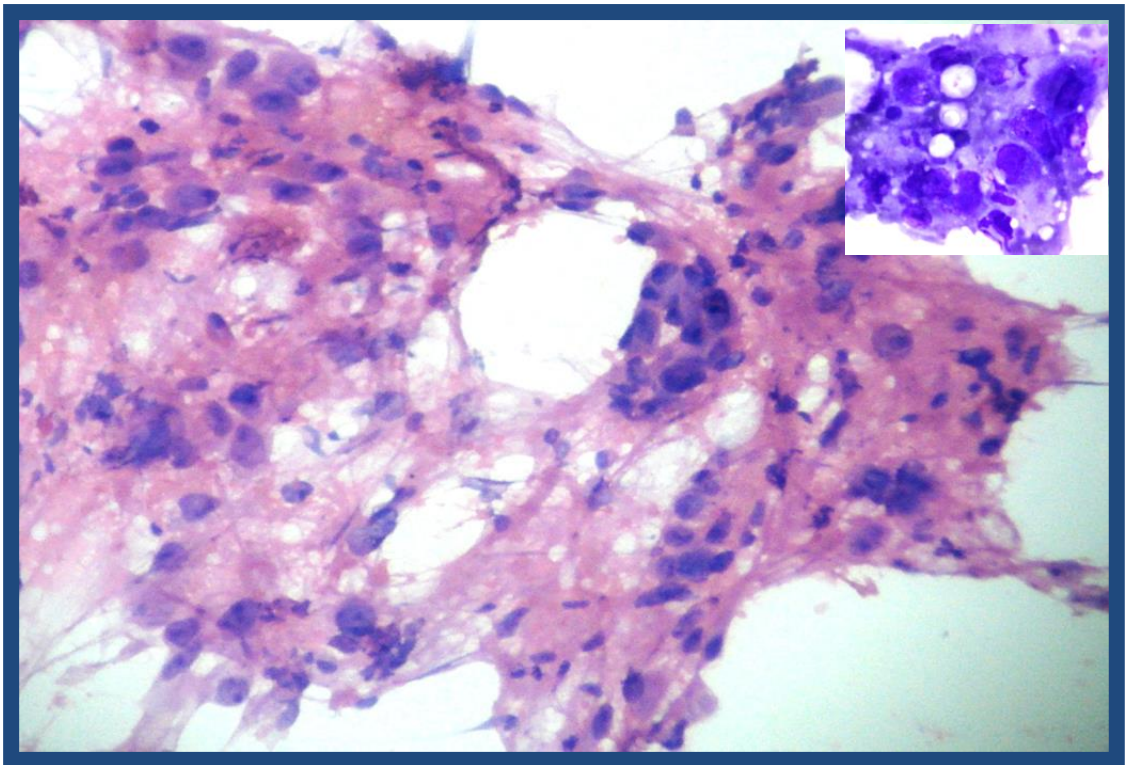


FIG 19 – FNAC of ductal carcinoma NOS showing cells in glandular pattern and discretes. HE X 100
Inset shows marked anisonucleosis and prominent nucleoli. MGG X 400

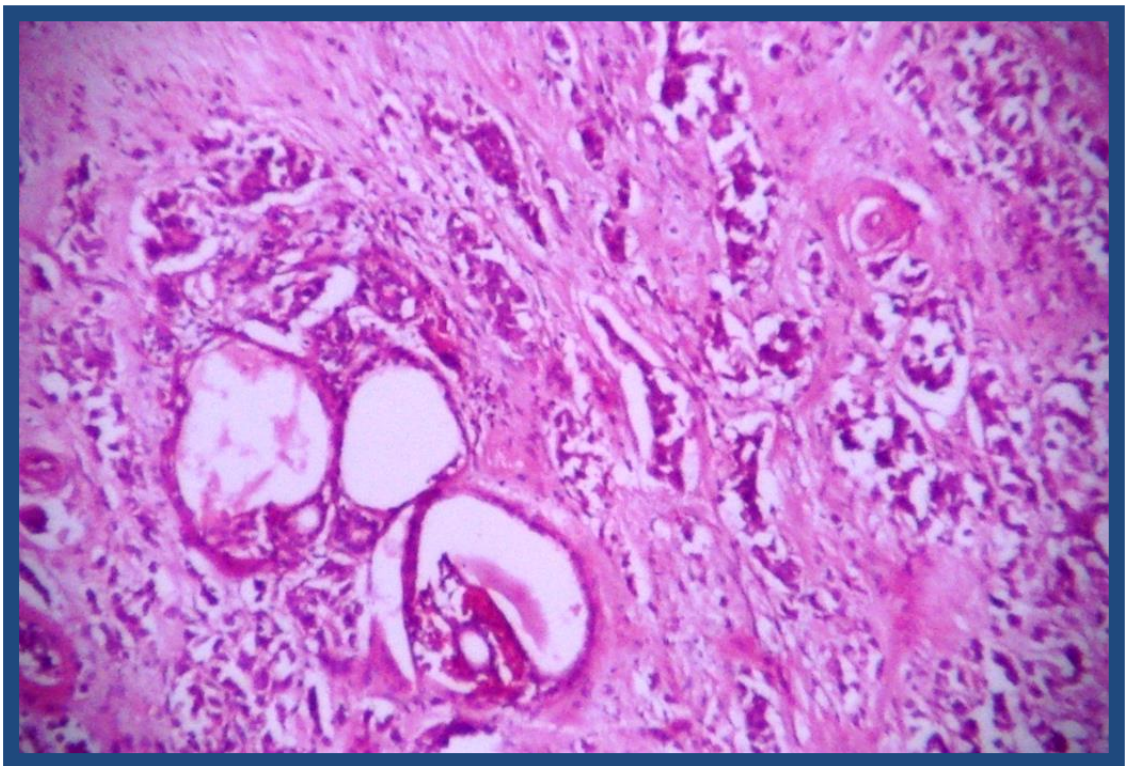


FIG 20 – HP of ductal carcinoma NOS showing pleomorphic cells in glandular pattern, cords and discretes. HE X 100

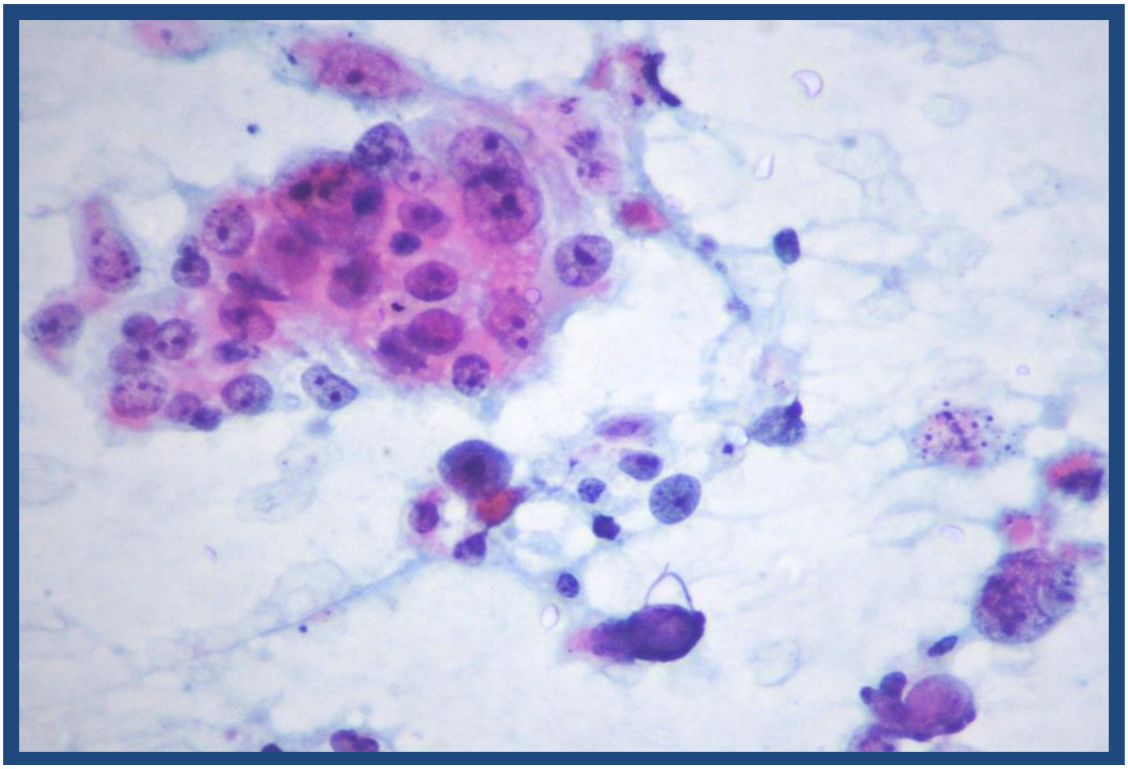


FIG 21 – FNAC of medullary carcinoma showing cells in clusters, marked anisonucleosis, stippled chromatin, prominent nucleoli and lymphocytes. PAP X 400

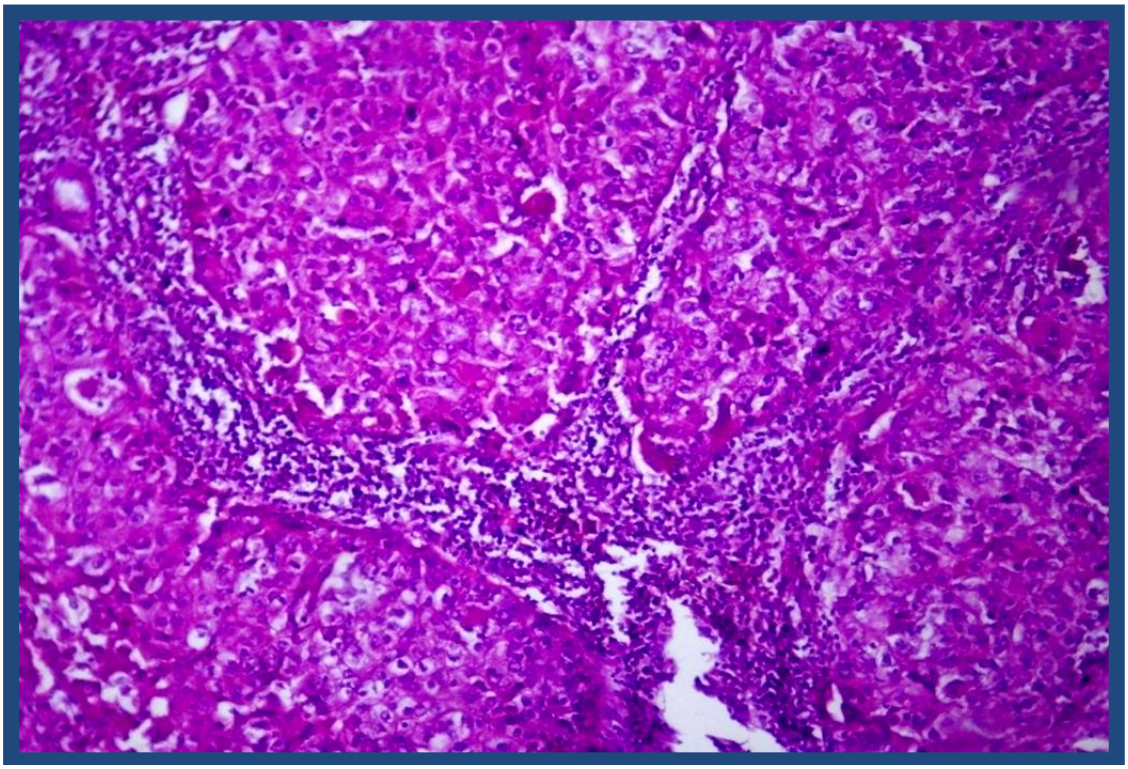


FIG 22 – HP of medullary carcinoma showing pushing borders, pleomorphic cells in sheets and lymphoplasmacytic infiltrate. HE X 100

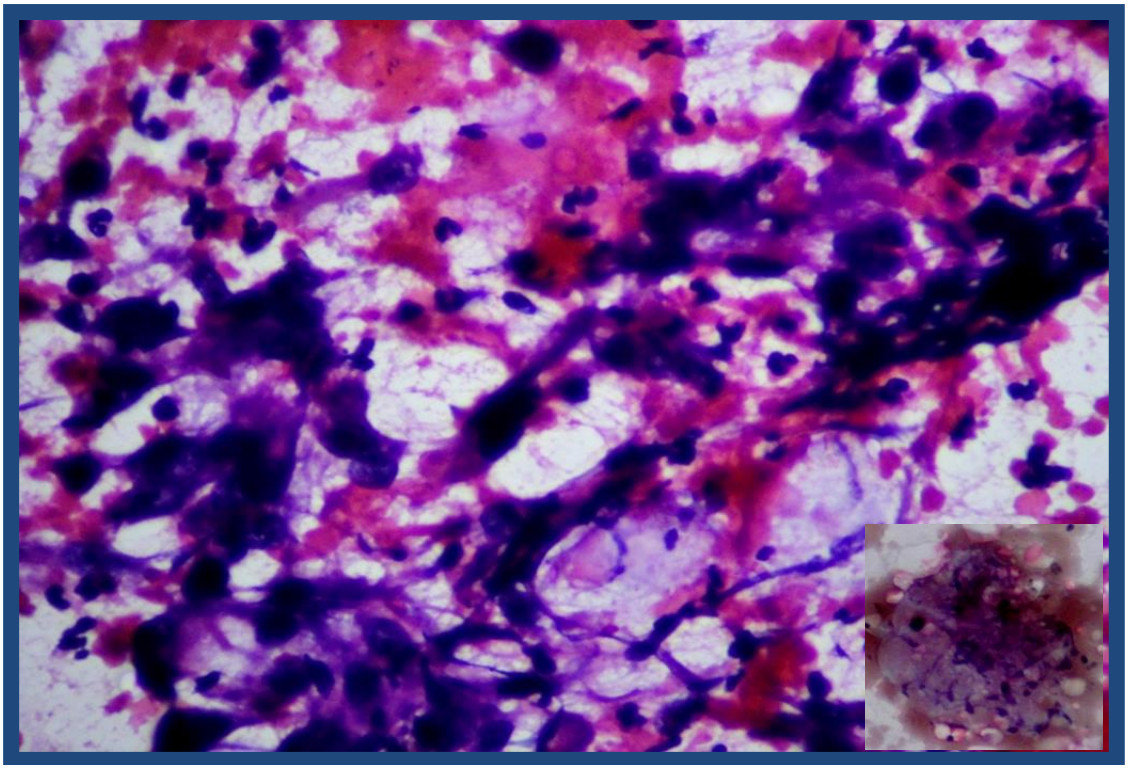


FIG 23 – FNAC of metaplastic carcinoma showing tumour cells in loosely cohesive clusters with hyperchromatic pleomorphic nuclei. HE X 400
Inset shows osteoid matrix. MGG X 400

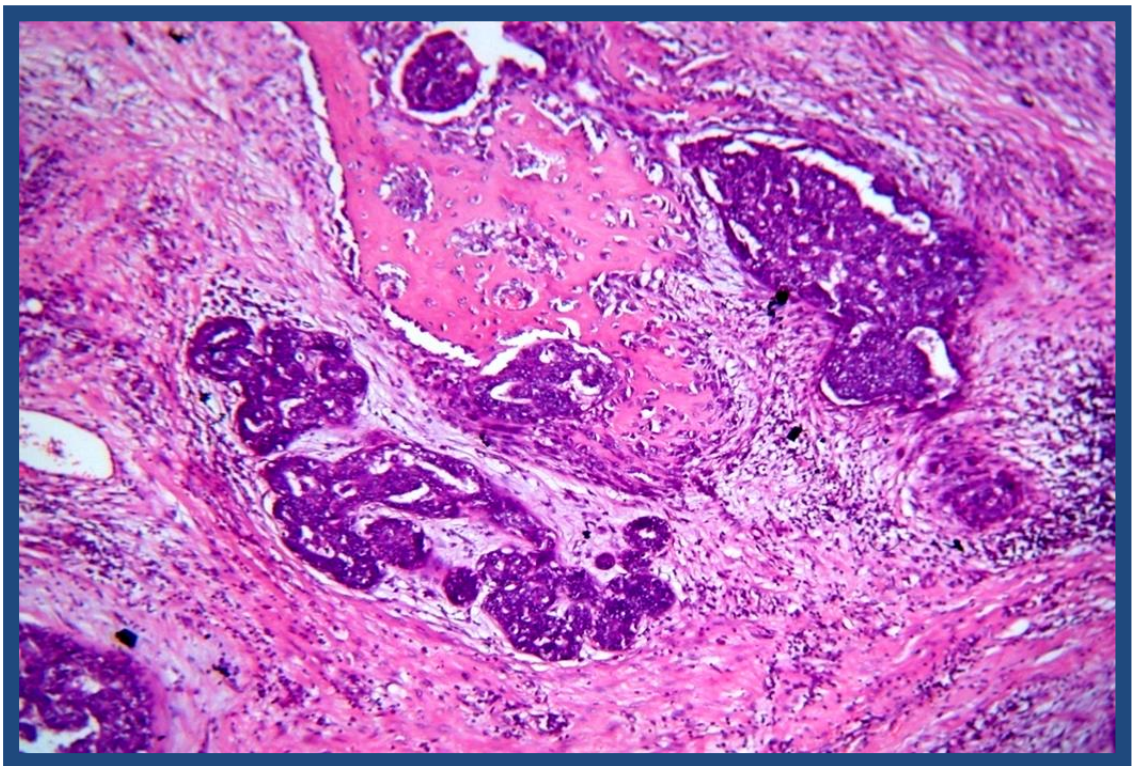


FIG 24 – HP of metaplastic carcinoma showing pleomorphic cells in glandular pattern, sheets, clusters with osteoid matrix. HE X 100

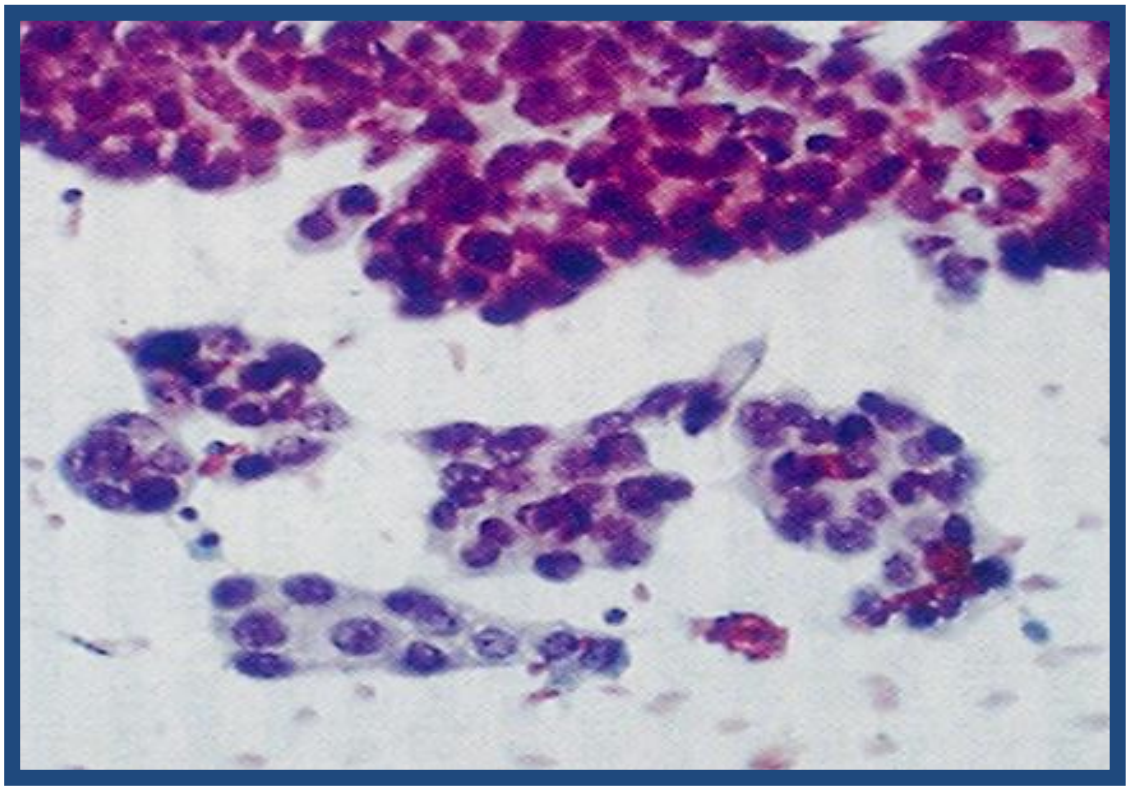


FIG 25 – FNAC of tubular carcinoma showing angulated tubules and isonucleosis. PAP X 400

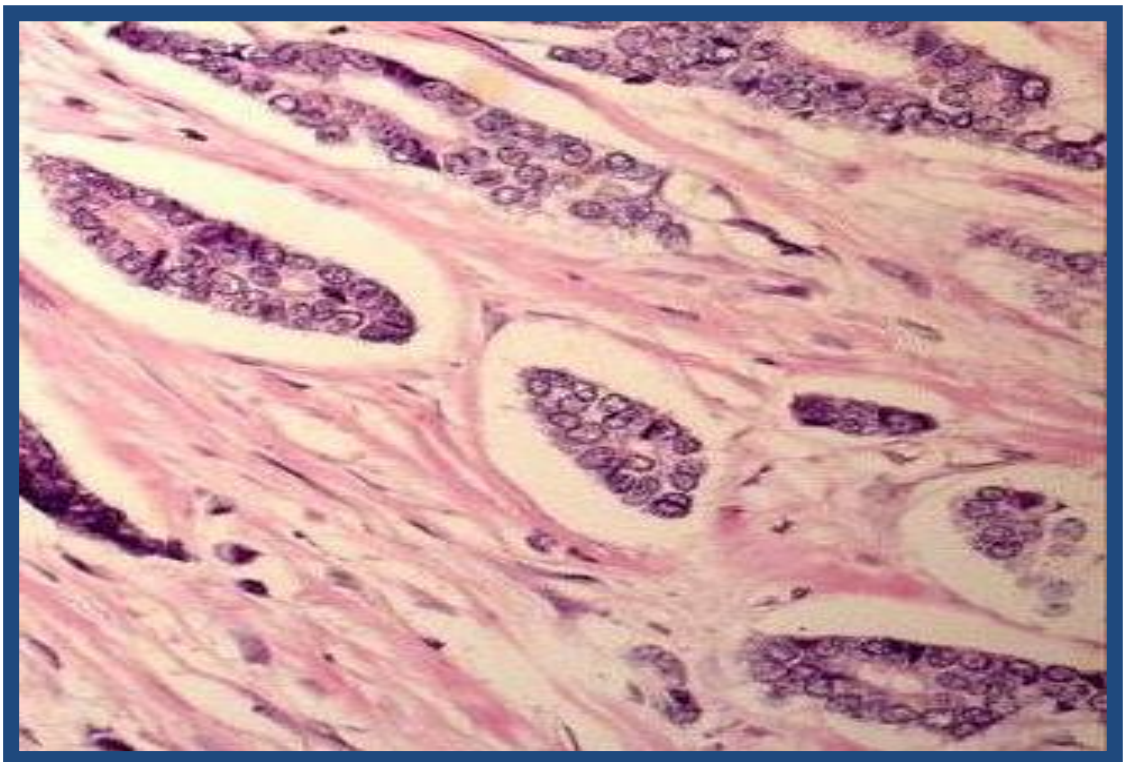


FIG 26 – HP of tubular carcinoma showing angulated tubules. HE X 400

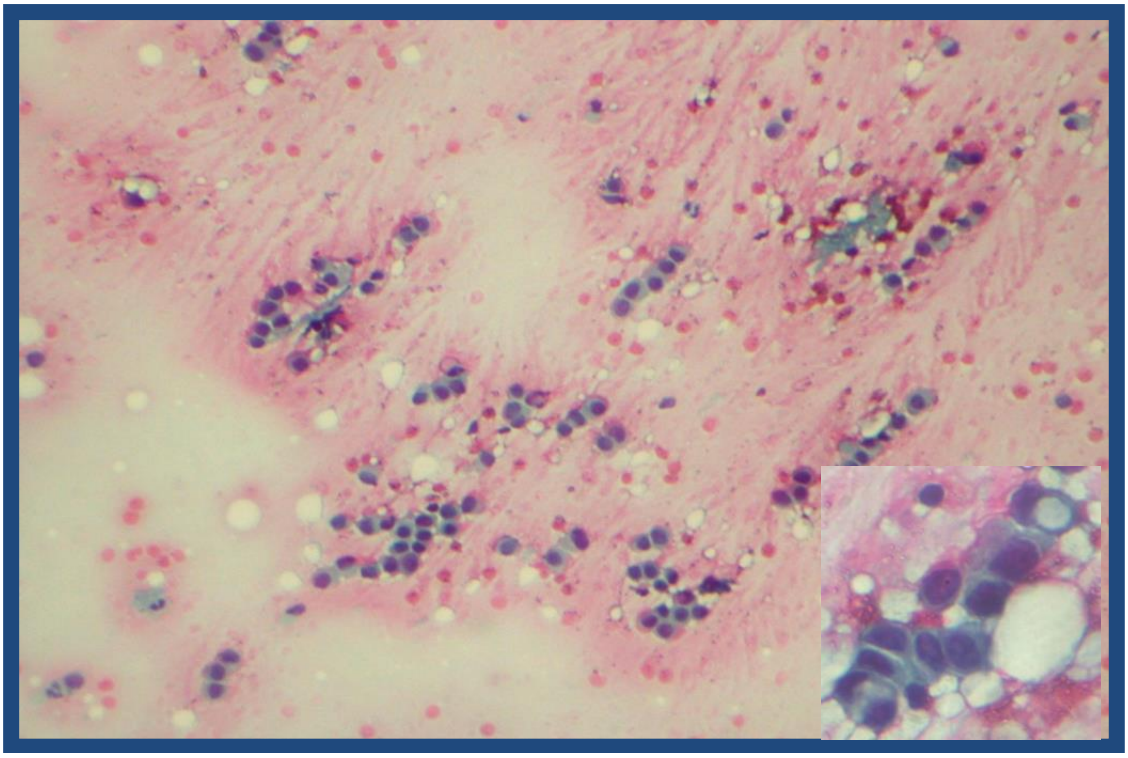


FIG 27 – FNAC of lobular carcinoma with small, uniform cell in “indian file” pattern. PAP X 100
Inset shows intracytoplasmic lumina. PAP X 100

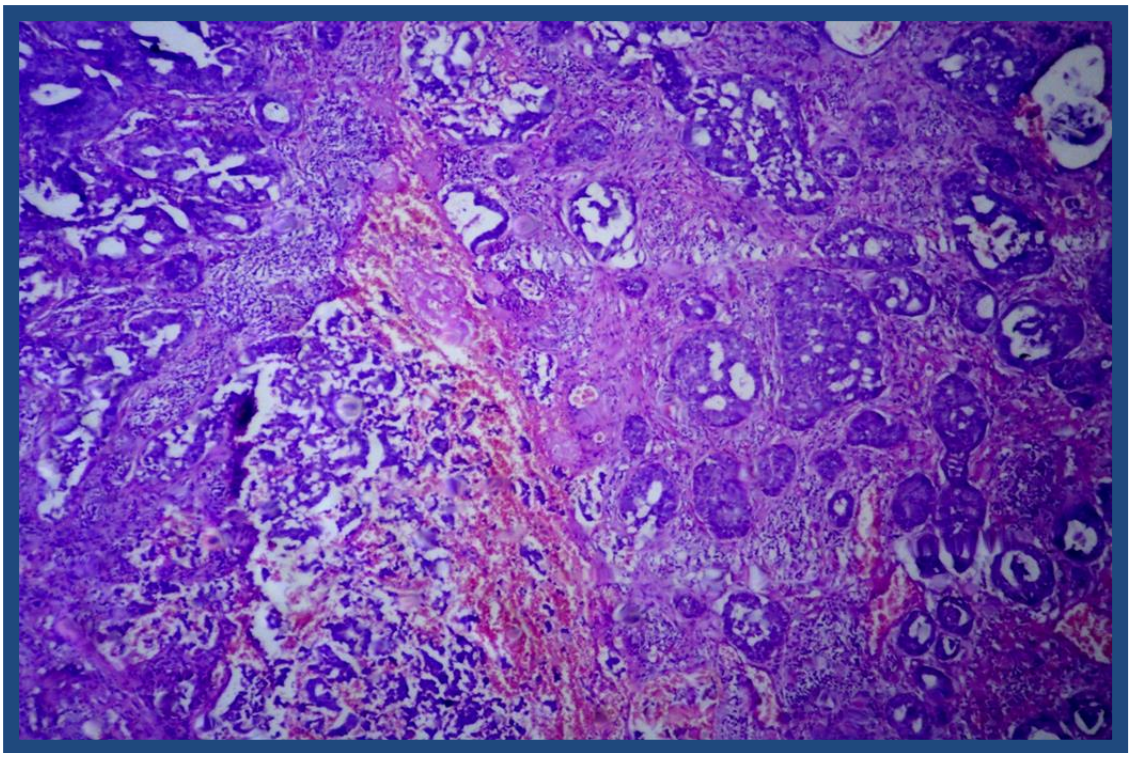


FIG 28 – HP of mixed ductal and lobular carcinoma with uniform lobular carcinoma cells on right and pleomorphic ductal carcinoma cells on left. HE X 100

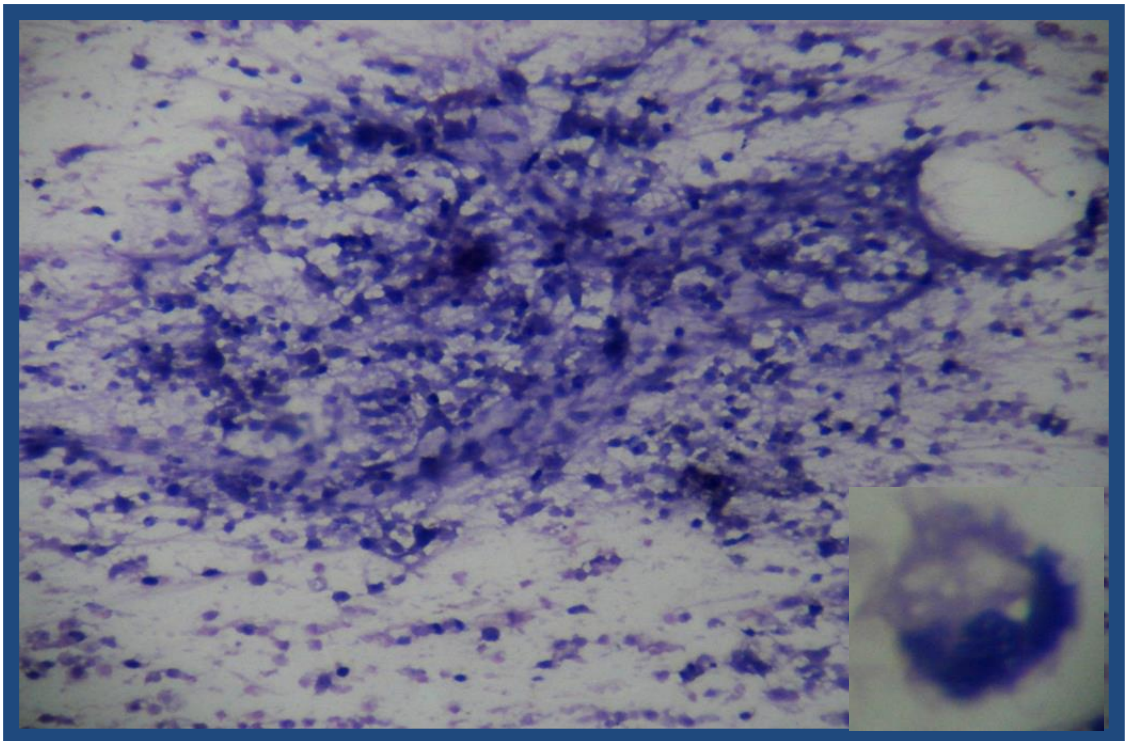


FIG 29 – FNAC of pleomorphic liposarcoma with myxoid change showing cells with abundant clear cytoplasm with peripherally pushed pleomorphic nucleus, myxoid background and necrotic debris. MGG X 100
Inset shows lipoblast. HE X 400

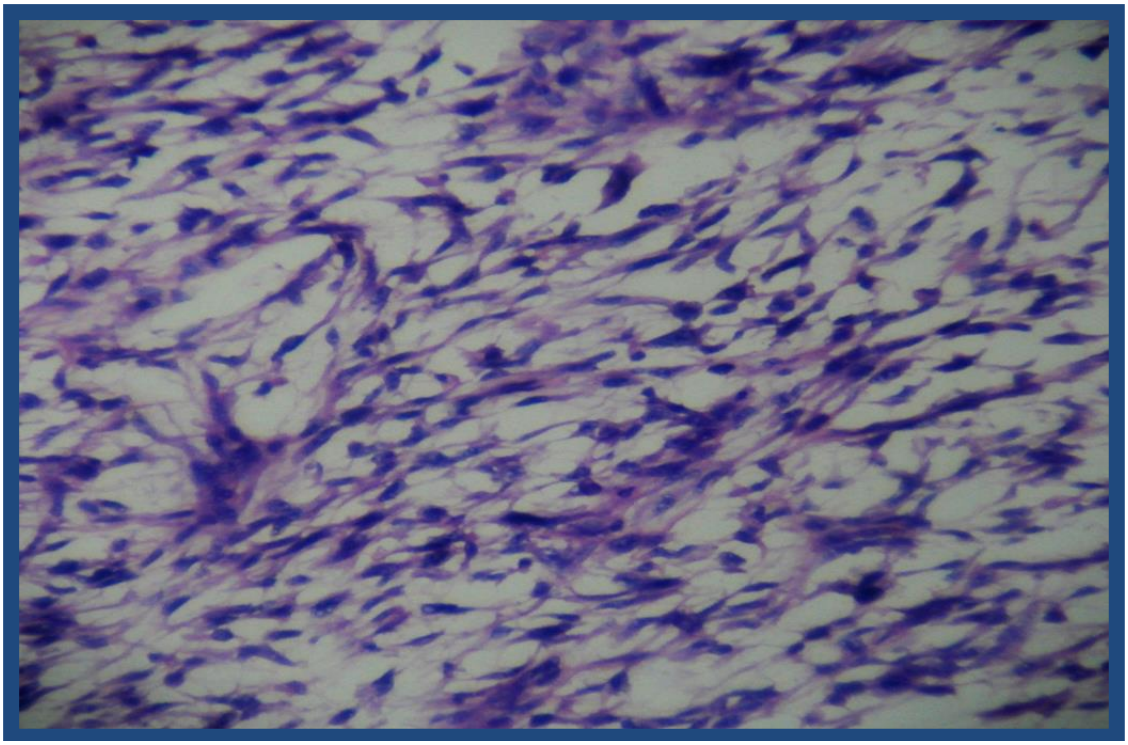


FIG 30 – HP of pleomorphic liposarcoma with myxoid change showing cells with abundant clear cytoplasm with peripherally pushed pleomorphic nucleus. HE X 100

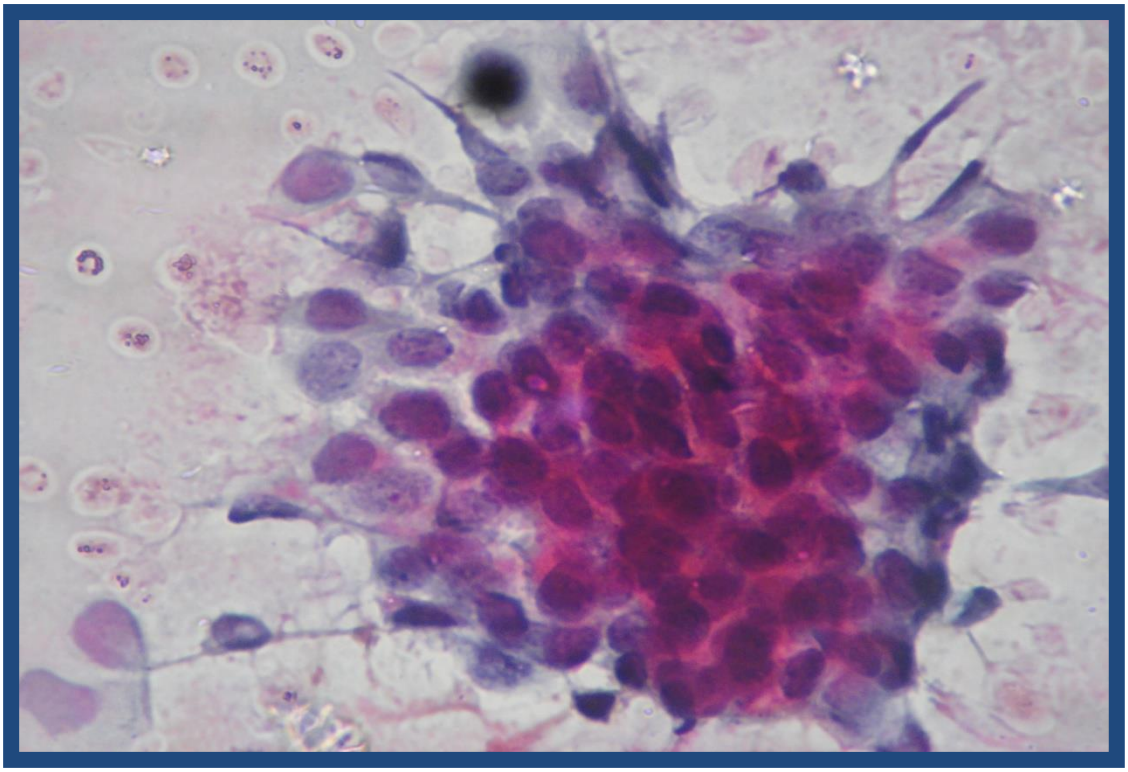


FIG 31 - FNAC of low grade Simplified Black system. PAP X 400

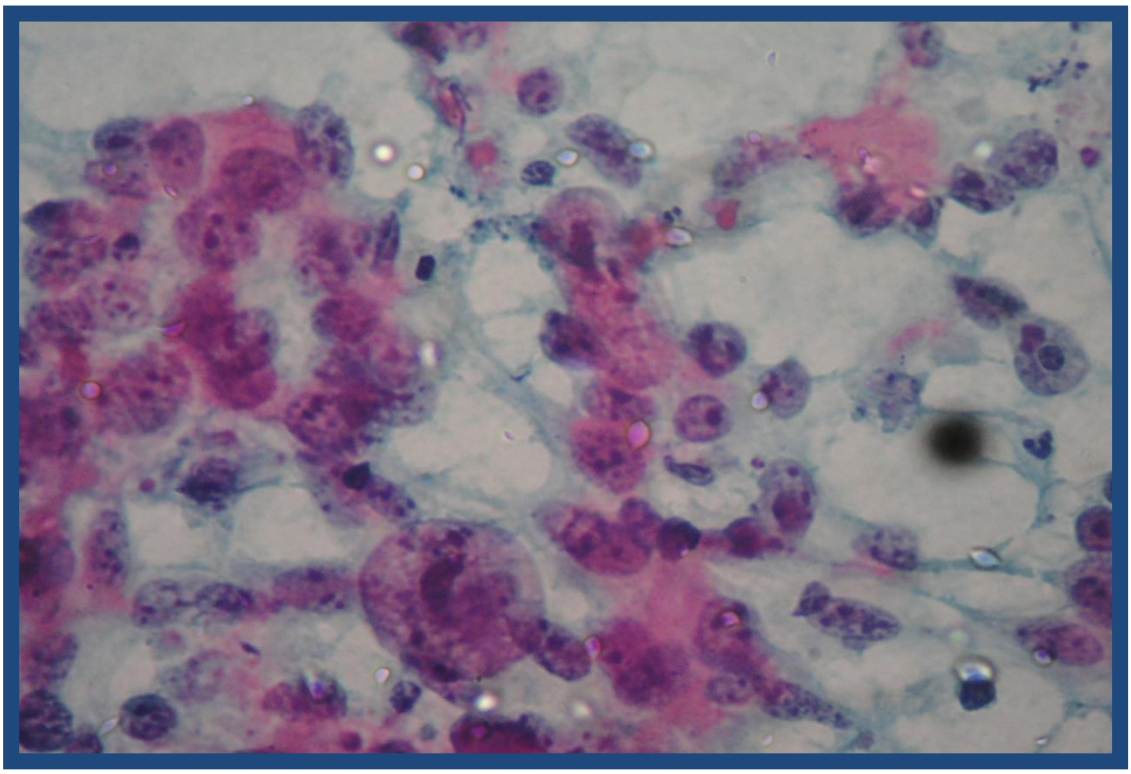


FIG 32 - FNAC of high grade Simplified Black system. PAP X 400.

DISCUSSION

FNAC is one of the routinely used diagnostic procedures in patients presenting with breast lump.

In our study 50 patients were subjected to FNAC of palpable breast lesions. The duration of study was 1 year. Cytology results were compared with histopathology in all 50 cases.

AGE DISTRIBUTION

In the present study the age of patients varied from 18 years to 72 years. Usually breast lesions occur during reproductive period and thereafter. Our study is in accordance with various other studies described in literature.[76,77,78]

TABLE 19 – AGE DISTRIBUTION IN DIFFERENT STUDIES

STUDIES	AGE DISTRIBUTION(in years)
Kim A et al[76]	15-78
Omoniyi-Esan G et al[77]	13-90
Ballo MS et al[78]	28-86
Present study	18-72

SEX DISTRIBUTION

Male breast lesions are rare as compared to female breast.[79] Like the female breast, the male breast is subject to hormonal influences.[5] In the present study out of 50 patients, 5 were males and 45 were females with a male to female ratio of 1:9, showing a distinctly high incidence of breast lesions in females.

The male to female ratio in different studies varied from 1:12.68 to 1:72.04.[79,80,81]

TABLE 20 - SEX DISTRIBUTION IN DIFFERENT STUDIES

STUDIES	MALE	FEMALE	TOTAL	RATIO
Joshi A et al[79]	507	12,668	13,175	1:24.98
Tiwari M[80]	2	89	91	1:44.5
Das DK et al[81]	188	2,385	2,573	1:12.68
Gupta et al[81]	99	7,132	7,231	1:72.04
Present study	5	45	50	1:9

SITE OF THE BREAST LESION

In present study out of 50 lesions, most common location was upper outer region of breast (17 cases) followed by upper inner region (14 cases). Kim A et al[76] also observed similar results. In their study out of 246 cases majority were located in upper outer quadrant (135) followed by upper inner quadrant (58 cases).

TABLE 21 - DISTRIBUTION OF LESIONS IN DIFFERENT QUADRANTS OF BREAST IN OTHER STUDY

STUDIES	UPPER OUTER	UPPER INNER	LOWER OUTER	LOWER NNER	SUB-AREOLAR	DIFFUSE	AXILLA	CHEST WALL	TOTAL
Kim A et al[76]	135	58	15	7	19	4	4	4	246
Present study	17	14	7	7	1	4	-	-	50

CATEGORISATION OF LESIONS ON FNAC

In the present study cytological diagnosis of benign lesions was made on 44% cases, suspicious for malignancy on 2% cases, malignancy on 50% cases and unsatisfactory on 4% cases. The smears were considered unsatisfactory in 4% cases because of scanty cellularity.

2 unsatisfactory cases on FNAC turned out to be fibroadenoma on histopathology. 1 suspicious for malignancy case on FNAC was diagnosed as ductal carcinoma on histopathology. 2 cases of fibrocystic disease were misinterpreted as fibroadenoma on FNAC and 1 case of mixed lobular and ductal carcinoma was misinterpreted as lobular carcinoma on FNAC. This limitation could be explained by sampling error i.e. the site the needle hits the lesion. 1 case of ductal carcinoma was wrongly diagnosed as fibroadenoma. This was due to interpretative error of lesion on cytology. In the study conducted by Park A et al[82] there was failure to recognize malignancy because of failure to aspirate the representative cells from the lesion rather than incorrect interpretation. Categorization of lesions on FNAC in other studies is shown in the following table.[76,82,83,84]

Kim A et al[77] concluded that higher proportion of unsatisfactory samples in their study was due to difficulty in cytologic diagnosis of large and diffuse tumours due to the presence of haemorrhage, necrosis or fibrosis in these tumours. They also stated that malignant cases can be misinterpreted as unsatisfactory, atypical or suspicious because of poor fixation of specimen.

Scopa et al[85] defined satisfactory specimens as “those containing epithelial cells on more than one slide and a minimum of 10 clusters composed of at least 10 cells: the background should be non-inflammatory and/or non-necrotic”.

Sneige et al[86] stated that unsatisfactory specimens were "those containing less than four to six well-visualized cell groups and/or specimens distorted or obscured by blood".

Hammond et al[87] stated that insufficient material was due to problem of technique and the diagnosis of atypical cells or cells suspected of being malignant may depend upon the expertise of the pathologist.

Kim A et al[76] indicated that there are few limitations in breast cytopathology. To distinguish high-risk, premalignant lesions from malignant lesions the definitive diagnostic criteria are not available due to overlapping features.

In study conducted by Kim A et al[76], atypical and suspicious category was derived partly due to author's lack of experience. But they stated that these categories along with suggested differential diagnosis are safer than misleading diagnosis.

TABLE 22 – COMPARISON OF CATEGORISATION OF LESIONS ON FNAC WITH OTHER STUDIES

STUDIES	BENIGN	ATYPICAL	SUSPICIOUS	MALIGNANT	UNSATISFACTORY	TOTAL
Kim A et al[76]	114	35	13	61	23	246
Park IA et al[82]	384	24	7	85	169	669
Takei H et al[83]	150	26	15	78	44	313
Choi YD et al[84]	981	-	38	182	96	1,297
Present study	22	-	1	25	2	50

Fibrocystic change comes to clinical attention when it produces palpable lump and mimics carcinoma. In our study, diagnosis of fibrocystic change was made in 2 cases on FNAC. Age group ranged from 35 to 40 years. Fibrocystic lesions are commonly tender and painful and giving convincing history of changes in breast lump and symptoms with menstrual cycle. In the present study both the cases gave history of pain associated with the lump. The smears showed ductal cells in clusters, bare nuclei, cyst macrophages and apocrine change. Features were similar to those mentioned in literature.[1] The diagnosis of fibrocystic change was confirmed on HP.

The diagnosis of fibroadenoma is based on the typical cytologic features, which to recognize these lesions as benign. The cytologic criteria include antler horn pattern, monolayered groups of cohesive ductal cells, stromal tissue fragments and numerous single naked nuclei.[22] In the present study the diagnosis of fibroadenoma on cytology was offered in 16 cases. One case was bilateral. The above mentioned cytological features were seen in our study. FNAC diagnosis matched in 13 cases. 2 cases were misinterpreted as fibroadenoma because lump was non-tender and firm in consistency and on cytology showed features of fibroadenoma without any features of fibrocystic change like apocrine change, cyst macrophages etc, and these two cases turned out to be fibrocystic disease on HP. 1 case of fibroadenoma on FNAC turned out to be ductal carcinoma on HP. In this case on cytology the cells showed high cellularity, mild anisokaryosis, some showing prominent nucleoli and few myoepithelial cells. Review of literature says such features can be present in fibroadenomas.[1] In Ferrer PL et al[22] study cytohistologic agreement was present in 287 out of 362 cases. The causes of diagnostic errors in fibroadenoma are presence of squamous metaplasia, adenosis, infarction, fibrocystic changes, stromal mucinous and myxoid changes, calcification, hyalinization, atypical multinucleated giant cells and

epithelial hyperplasia or atypia. Fibroadenoma is the most common cause of false suspicious and false positive diagnosis in breast FNAC.[1]

In the present study 1 case was diagnosed as pleomorphic liposarcoma on FNAC. Liposarcoma of breast can arise from the periductal- perilobular stroma in the form of phyllodes tumour or from the interlobular stroma as primary liposarcoma. Liposarcoma of breast can be seen at any age with mean age being 47 years. It is seen usually in females but two cases in males have been reported.[52] Our case was a 55 year male patient who came with lump of size 11x14 centimetres diffusely involving the left breast present since 10 months. In a case of primary pleomorphic liposarcoma reported by Demeria S et al[52] the cytological features were scant cellularity consisting of isolated, plump, spindle cells and polygonal cells with prominent nuclear pleomorphism. The lipoblasts have scant to abundant vacuolated cytoplasm causing nuclear scalloping. Similar features were observed in our case. The case was histologically confirmed.

Rare form of tuberculosis is breast tuberculosis. The lump is usually present in central or upper outer quadrant of breast probably due to extension of tuberculosis from axillary nodes.[88] Our case was 57 year female patient who presented with lump in lower outer quadrant of right breast. Clinically the lump was tender and skin over the lump was inflamed. Aspirate was purulent. Cytological features of tuberculous mastitis are epithelioid cell granulomas and necrosis.[88] Similar features were seen in our case. AFB were demonstrated by ZN stain. The diagnosis was confirmed on HP.

The diagnosis of lobular carcinoma of breast was made in 1 case. The patient was 72 year, male with an ulcerated lump of size 3x4 centimetres in the subareolar region of left breast. In a study by Choi YD et al[84], the cytologic features of lobular carcinoma were monomorphic population of small cells in discohesive pattern and

numerous single cells. The cells show intracytoplasmic lumina with irregular nuclear shape.[1] Similar features were seen in our case. HP of this case turned out to be a mixed lobular and ductal carcinoma. This could be explained by area sampled by the needle during FNAC.

Medullary carcinoma is a mammographically and well circumscribed lesion.[1] The diagnosis medullary carcinoma was done in 1 case. Our case was a 58 year female patient who presented with a lump with well defined borders in right breast. The cytologic features were high cellularity, large pleomorphic cells, high grade nuclei with stippled chromatin and background consisting of numerous lymphocytes and neutrophils. The features were similar to those present in literature.[1] The diagnosis was confirmed on HP.

On cytology tubular carcinoma was diagnosed in one case. A 51 year patient presented with hard lump in the lower inner quadrant of right breast since 2 months. The aspirate was hemorrhagic. Cytological features were epithelial cells arranged in angulated tubular arrangement. The cells showed mild pleomorphism and few cytoplasmic vacuoles. Background showed fibromyxoid stroma with few erythrocytes and proteinaceous material. Similar features were observed by Bondeson et al.[89] Cytohistopathologic agreement was present in this case.

On FNAC the diagnosis of Ductal carcinoma NOS was made in 20 cases. The age of the patients ranged from 35-65 years. Out of 20 cases, 2 cases showed LN metastasis. The cytological features were high cellularity, tumour cells in loosely cohesive clusters and ductular pattern, nucleus with marked pleomorphism, prominent nucleoli, mitotic figures and background with erythrocytes and necrosis. All 20 cases were confirmed on HP. Out of 20 cases, one case had received chemotherapy so this case showed features of Ductal carcinoma NOS along with chemotherapy induced

changes. The cytological features were those of Ductal carcinoma NOS along with vacuolization of both nuclei and cytoplasm of malignant cells and background with fibrotic stromal fragments, lymphocytes and necrosis. Chemotherapy induced changes were seen in HP sections also. Similar features of chemotherapy changes are mentioned in literature.[6]

The diagnosis of Metaplastic carcinoma was offered in 1 case. A 56 year female patient presented with lump in the right breast since 6 months. The lump was hard in consistency with ill defined cell borders measuring 3x4 centimetres. Aspiration yielded 0.5 millilitre grey white material. The cytological features were similar to those mentioned in literature.[1] The smears showed high cellularity, cells arranged in clusters, monolayered sheets and discrete, individual cells showed moderate cytoplasm, nucleus with marked pleomorphism, few binucleate, trinucleate and multinucleated giant cells were seen. The background showed basophilic osteoid material along with necrotic material. On HP similar pleomorphic tumour cells with osteoid matrix was present.

Gynaecomastia is defined as the enlargement of male breast due to proliferation of both glandular and stromal elements.[81] In the present study FNAC diagnosis of gynaecomastia was offered in 3 cases out of 5 male patients. Gynaecomastia was most common lesion in our study followed by pleomorphic liposarcoma with myxoid change and mixed lobular and ductal carcinoma among male patients. Gynaecomastia was most common lesion among males in a study done by Das DK et al also.[81] In the present study the age group ranged from 18 to 50 years. The cytological features were moderate cellularity, cohesive clusters of ductal epithelial cells, numerous single bare bipolar nuclei and background with fragments

of fibrous stroma. The cytological features were similar to those mentioned in literature.[1,81]

STATISTICAL VALUES

In the present study the results of diagnostic accuracy of FNAC to detect malignancy was sensitivity – 96.15%, specificity – 100%, positive predictive value – 100% and negative predictive value – 95.45%, false positive rate - 0% and false negative rate - 3.84%. The results were comparable with other studies.[90]

Park SM et al[91] concluded that the cause of false negative result was due to sampling error in all FNAC samples.

Park IA[82] arrived at a conclusion that "inadequate" cytologic diagnosis category offered to certain lesions even though they were discrete, obviously malignant masses clinically caused the higher than expected false negative rate in their study.

In the study done by Choi et al[84] interpretive error was the most common cause of high rate of false negative result.

In our study also interpretive error was the cause for false negative result.

TABLE 23 – COMPARISON OF STATISTICAL VALUES WITH OTHER STUDIES[90]

STUDIES	NO OF CASES	SENSITIVITY(%)	SPECIFICITY(%)	POSITIVE PREDICTIVE VALUE(%)	NEGATIVE PREDICTIVE VALUE(%)	FALSE POSITIVE RATE(%)	FALSE NEGATIVE RATE(%)
Atamdede et al	100	97.0	95.4	94.2	97.6	5.8	2.4
Barrows et al	1,283	92.2	86.0	91.1	87.5	8.9	12.5
Ciatto et al	534	97.4	99.3	98.6	98.7	1.4	1.3
Collaco et al	276	92.1	98.6	99.4	82.1	0.6	17.9
Gelabert et al	107	96.7	100	100	80.0	0.0	20.0
Kline et al	3,545	90.3	98.1	84.5	98.8	15.5	1.2
Lanin et al	100	92.8	100	100	96.9	0.0	3.1
Zajdela et al	2,772	96.1	95.3	97.2	93.5	2.8	6.5
Present study	47	96.15	100	100	95.45	0.0	3.84

CORRELATION OF CYTOLOGIC AND HISTOLOGIC GRADES

FNAC is now considered a diagnostic tool upon which definitive therapy, such as mastectomy is performed. Pathologist plays an important role in providing the diagnosis including the tumour grade.[67]

The value of histological grading of breast carcinoma is well established. Since diagnosis of breast carcinoma is often made by FNAC, it is important to

perform grading on aspirates which will provide valuable information to the treating oncologist for further management.[92]

In the present study the cytologic and histologic grading showed good correlation (p value <0.05).

In the study done by Ohri A et al[62], cytological grading was done by Hunt's, Simplified Black and Modified Black grading systems. These systems were compared with modified Scarff Bloom-Richardson grading done on histologic sections. They concluded that among the three cytologic grading systems, the two- tier Simplified Black system is simple, objective, has greater degree of correlation and has well defined set of criteria.

In the study done by Cajulis RS et al[93], they concluded that the Simplified Black nuclear grading (two-tier system) system not only showed high reproducibility and concordance with histopathology but also a high correlation with flow cytometry.

Another study done by Cajulis RS et al[94] also concluded similarly.

In the study done by Fisher B et al[95] using the two-tier system, the nuclear grade had an independent influence on outcome of breast cancer.

According to a study done by Dantas KAN et al[96] the classifications were divided according to criteria of tumoural grading (nuclear and architectural criteria - Mouriquand and Guilford systems) and nuclear criteria (Black modified by Fisher, simplified Black system and Hunt system). They were compared with histological grading using Scarff-Bloom-Richardson modified by Elston. Best agreement was seen with Black modified by Fisher and simplified Black system based on nuclear criteria. Among the cytological grading systems based on nuclear and architectural criteria (combined), Guilford's classification showed the best agreement, possibly due to the larger number of variables used, which permitted a smaller margin of error.

CONCLUSION

This study has been undertaken to study the cytological patterns of breast lesions and to test the diagnostic utility of FNAC by correlation with histopathology. FNAC diagnosis will help the clinician to confirm or exclude the differential diagnosis made by the clinician. The rapid diagnosis made by FNAC relieves the anxiety of patient and helps the clinician to plan the treatment.

In the present study cytologic diagnosis correlated well with histopathology. It was a sensitive and specific tool of diagnosis in our study. The sensitivity and specificity can be further increased by utilizing various available imaging modalities.

Histological grade has been shown to be a valuable prognostic parameter in patients with breast cancer. As simplified Black cytological nuclear grading correlates well with Nottingham modification of Bloom-Richardson histopathological grading system it should be included in the cytology report.

Along with cytological diagnosis, cytological grading provides valuable information to clinicians to plan the treatment. Cytologic nuclear grade provides important prognostic information.

Simplified Black grading system is simple, objective, takes little time and has better reproducibility with lesser degree of observer errors.

SUMMARY

1. A total of 50 cases were included in the present study
2. Maximum number of cases was in the age group of 30-40 years (30%)
3. Our study showed female predominance (90%).
4. Out of 50 cases, 31 cases presented with lump in right breast, 14 cases in left breast and 5 cases involved both breasts.
5. Upper outer quadrant (14 cases) was the most commonly involved quadrant of breast among malignant lesions. Upper inner and lower outer quadrant (7 cases each) was most commonly involved in benign lesions.
6. Most of the lesions (70%) were 2 to 5 centimetres in size.
7. Most (18 of 27 cases) malignant lesions had ill-defined borders and most benign lesions (16 of 23 cases) had well-defined borders.
8. Arrangement of cells in clusters and singles was most common pattern of arrangement (20%). Antler horn pattern was seen in most of fibroadenomas.
9. Ductal carcinoma NOS (20 cases) was most common lesion.
10. Out of 50 cases, 3 cases (2 unsatisfactory and 1 suspicious for malignancy) were excluded from calculation of the parameters. Out of 47 cases FNAC diagnosis matched with that of histopathology in 43 cases. 2 unsatisfactory cases on FNAC turned out to be fibroadenoma on histopathology. 1 suspicious for malignancy case on FNAC was diagnosed as ductal carcinoma on histopathology. 2 cases of fibrocystic disease were misinterpreted as fibroadenoma on FNAC, 1 case of ductal carcinoma was misdiagnosed as fibroadenoma on FNAC and 1 case of mixed lobular and ductal carcinoma was wrongly diagnosed as lobular carcinoma on FNAC. This was due to sampling error and misinterpretation.

11. The diagnostic accuracy of FNAC to detect malignancy was sensitivity 96.15%, specificity - 100%, positive predictive value – 100%, negative predictive value – 95.45%, false positive rate – 0%, false negative rate – 3.84%.
12. Out of 47 cases the diagnosis of malignancy was offered in 26 cases. 1 case of pleomorphic liposarcoma with myxoid change was excluded. 1 case of ductal carcinoma NOS misinterpreted as fibroadenoma on FNAC, was retrospectively included for grading. On 25 cases, cytologic grading by Simplified Black method and histological grading by Nottingham modification of Bloom Richardson system was performed. The cytologic grading by Simplified Black method correlated well with Nottingham modification of Bloom-Richardson histological grading ($p < 0.05$) .

BIBLIOGRAPHY

1. Lindholn K. Breast. In: Orell SR, Sterrett GF, Whitaker D, editors. Fine Needle Aspiration Cytology. (4th edition). NewDelhi: Churchill Livingstone, 2005: 165-225.
2. Silverberg SG, Masood S. The Breast. In: Silverberg SG, Delellis RA, Frable WJ, editors. Principles and Practice of Surgical Pathology and Cytopathology. Vol 1 (3rd edition). Singapore: Churchill Livingstone, 1997: 575-673.
3. Feoli F, Paesmans M, Eeckhout PV. Fine Needle Aspiration Cytology of Breast, Impact of Experience on Accuracy, using Standard Cytologic Criteria. Acta Cytol 2008; 52: 145-151.
4. Diamantis A, Magiorkinis E, Koutselini H. Fine Needle Aspiration(FNA) Biopsy: historical aspects. Folia Histochemica et Cytobiologica 2009; 47(2): 191-197.
5. Lester SC. The Breast. In: Kumar V, Abbas AK, Fausto N, editors. Robbins and Cotran Pathologic Basis of Disease. (7th edition). New Delhi: Elsevier, 2007: 1119-1154.
6. Schnitt SJ, Millis RR, Hanby AM, Oberman HA. The Breast. In: Mills SE, Carter D, Greenson JK, Obermann HA, Reuter R, Stoler MH, editors. Sternberg's Diagnostic Surgical Pathology. Vol 1(4th edition). Noida: Lippincott Williams and Wilkins, 2006: 323-395.
7. Rosai, Ackerman. Breast. In: Rosai, Ackerman, editors. Surgical Pathology. Vol 2 (9th edition). New Delhi: Mosby, 2004: 1763-1876.
8. Koss LG, Melamed MR. The Breast. In: Koss LG, Melamed MR, editors. Koss' Diagnostic Cytology And Its Histopathologic Bases. Vol 2 (5th edition). Philadelphia: Lippincott Williams And Wilkins, 2006: 1082-1084.

9. Tavassoli FA, Devilee P, editors. World Health Organisation Classification of Tumours, Pathology and Genetics of Tumours of the Breast and Female Genital organs. Lyon: IARC, 2003.
10. Cohghill SB. Breast. In: Gray W, editors. Diagnostic Cytopathology. Hongkong: Churchill Livingstone, 1995: 227-297.
11. Lopez-Rios F, Dhimes P, de Agustin PP. Subareolar abscess of the breast in a male. A report of two cases with fine needle aspiration cytology diagnosis. Acta Cytol 1997; 41(6): 1819-1822.
12. Kobayashi TK, Sugihara H, Kato M, Watanabe S. Cytologic Features of Granulomatous Mastitis. Report of a Case with Fine Needle Aspiration Cytology and Immunocytochemical Findings. Acta Cytol 1998; 42(3): 716-720.
13. Saad RS, Silvermann JF. Breast. In: Bibbo M, Wilbur DC, editors. Comprehensive Cytopathology. (3rd edition). China: Saunders Elsevier, 2008: 713-772.
14. Zakhour H, Wells C, editors. Diagnostic Cytopathology of the Breast. (1st edition). China: Churchill Livingstone, 1999.
15. Sola Perez J, Perez-Guillermo M, Bas Bernal A, Rodriguez Bermejo M. Diagnosis of Collagenous Spherulosis of the Breast by Fine Needle Aspiration Cytology. A Report of Two Cases. Acta Cytol 1993; 37(5): 725-728.
16. Jain M, Niveditha SR, Bajaj P, Rani S. Collagenous Spherulosis of Breast : Diagnosis by FNAB with Review of Literature. Indian J Pathol Microbiol 2000; 43(2): 131-134.
17. Orell SR. Radial Scar/Complex Sclerosing Lesion- a Problem in the Diagnostic Work-up of Screen-Detected Breast Lesions. Cytopathology 1999;10(4): 250-258.

18. Kumar N, Kapila K, Verma K. Characterization of Tubular Adenoma of Breast-Diagnostic Problem in Fine Needle Aspirates (FNAs). Cytopathology 1998; 9(5): 301-307.
19. Shet T.M, Rege JD. Aspiration Cytology of Tubular Adenomas of the Breast .An analysis of eight cases. Acta Cytol 1998; 42(3): 657-662.
20. Cashell AW. Apocrine Adenoma of the Breast. W V med j 2008; 104(2): 16-19.
21. Sauer T. Cytologic Findings in Malignant Myoepithelioma: a Case Report and Review of the Literature. Cytojournal 2007; 4: 3.
22. Ferrer PL, Hefferman JAJ, Vicandi B, Ortega L, Viguer JM. Fine Needle Aspiration Cytology of Breast Fibroadenoma. A Cytohistologic Correlation Study of 405 Cases. Acta Cytol 1999; 43(5): 579-586.
23. Das DK, Rifaat AA, George SS, Grover VK, Mathew TC. Morphologic Changes in Fibroadenoma of Breast Due to Chicken Pox. A Case Report with Suspicious Cytology in Fine Needle Aspiration Smears. Acta Cytol 2008; 52: 337-343.
24. Lee WY, Cheng L, Chang TW. Fine Needle Aspiration Cytology of Malignant Phyllodes Tumour with Liposarcomatous Stroma of Breast. A Case Report. Acta Cytol 1998; 42(2): 391-395.
25. Tomas D, Jankovic D, Marusic Z, Franceschi A, Mijic A, Kruslin B. Low-grade Periductal Stromal Sarcoma of the Breast with Myxoid Features: Immuno-histochemistry: Case Report. Pathology International 2009; 59(8): 588-591.
26. Frias AR, Campora RG, Parra DM, Frias MJR, Cerezuela TV, Salaveri CO et al. Robinson Cytologic Grading of Invasive Ductal Breast Carcinoma. Correlation with Histologic Grading and Regional Lymph Node Metastasis. Acta Cytol 2005; 49: 149-153.

27. Murali R, Salisbury E, Pathmanathan N. Histiocytoid Change in Breast Carcinoma. A Report of 3 Cases with an Unusual Cytomorphologic Pattern of Apocrine Change. Acta Cytol 2006; 50: 548-552.
28. Phillipson J, Ostrzega N. Fine Needle Aspiration of Invasive Cribriform Carcinoma with Benign Osteoclast-like Giant Cells of Histiocytic Origin. A Case Report. Acta Cytol 1994; 38(3): 479-482.
29. Kline TS, Kline Ik, Howell LP, editors. Guides to Clinical Aspiration Biopsy Breast. (2nd edition). USA: Lippincott Williams And Wilkins,1999.
30. Dey P, Luthra UK. False Negative Cytologic Diagnosis of Breast Carcinoma. Acta Cytol 1999; 43(5): 801-805.
31. De La Torre M, Lindholm K, Lindgren A. Fine Needle Aspiration Cytology of Tubular Breast Carcinoma and Radial Scar. Acta Cytol 1994; 38(6): 884-890.
32. Gupta RK, Dowle CS. Fine Needle Aspiration Cytology of Tubular Carcinoma of the Breast. Acta Cytol 1997;41(4):1139-1143.
33. Dawson AE, Mulford DK. Fine Needle Aspiration of Mucinous (Colloid) Breast carcinoma. Nuclear grading and Mammographic and Cytology Findings. Acta Cytol 1998; 42(3): 668-672.
34. Sohn JH, Kim LS, Chae SW, Shin HS. Fine Needle Aspiration Cytologic Findings of Breast Mucinous Neoplasms. Differential Diagnosis Between Mucocele like Tumour and Mucinous Carcinoma. Acta Cytol 2001; 45(5): 723-729.
35. Jayaram G, Elsayed EM, Yaccob RB. Papillary Breast Lesions Diagnosed on Cytology. Profile of 65 Cases. Acta Cytol 2007; 51: 3-8.
36. Kumar PV, Talei AR, Malekhusseini SA, Monabati A, Vasei M. Papillary Carcinoma of Breast. Cytologic Study of Nine Cases. Acta Cytol 1999; 43(5): 767-770.

37. Choi YD, Gong GY, Kim MJ, Lee JS, Nam JH, Juhng SW et al. Clinical and Cytologic Features of Papillary Neoplasms of Breast. Acta Cytol 2006; 50: 35-40.
38. Gong Y, Jalali M, Staerkel G. Fine Needle Aspiration Cytology of Thyroid Metastasis of Metaplastic Breast Carcinoma. A Case Report. Acta Cytol 2005; 49: 327-330.
39. Damiani S, Eusebi V, Losi L, D'Adda T, Rosai J. Oncocytic Carcinoma (malignant oncocytoma) of the Breast. Am j surg pathol 1998; 22(2): 221-230.
40. Satoh F, Umemura S, Itoh H, Miyajima Y, Tokuda Y, Tajima T et al. Fine Needle Aspiration Cytology of Glycogen-Rich Clear Cell Carcinoma of the Breast. A Case Report. Acta Cytol 1998; 42(2): 413-418.
41. Akbulut M, Zekioglu O, Kapkac M, Erhan Y, Ozdemir N. Fine Needle Aspiration Cytology of Glycogen-Rich Clear Cell Carcinoma of the Breast. Review of 37 cases with Histologic Correlation. Acta Cytol 2008; 52: 65-71.
42. Ramljak V, Sarcevic B, Vrdoljak DV, Kelcec IB, Agai M, Ostovi KT. Fine Needle Aspiration Cytology in Diagnosing Rare Breast Carcinoma – Two Case Reports. Coll. Antropol 2010; 1: 201–205.
43. Damiani S, Pasquinelli G, Lamovec J, Peterse JL, Eusebi V. Acinic cell Carcinoma of the Breast: an Immunohistochemical and Ultrastructural Study. Virchows Archiv 2000; 437(1): 74-81.
44. Stahlschmidt J, Liston J, Aslam MM, Carder PJ. Educational case report. Fine Needle Aspiration Cytology of Adenoid Cystic Carcinoma of the Breast. Cytopathology 2001; 12(4): 266-269.
45. Jain M, Gautam S, Logani KB, Thomas S. Cytological Diagnosis of Adenoid Cystic Carcinoma Breast- a Case Report. Indian J Pathol Microbiol 1999; 42(1): 113-116.

46. Parham DM, Evans A. Pleomorphic Adenoma of the Breast; a Potential for the Misdiagnosis of Malignancy on Fine Needle Aspiration (FNA). Cytopathology 1998; 9(5): 343-348.

47. Sharkey FE, Allred DC, Valente PT. Breast. In: Damjanov I, Linder J, editors. Anderson's Pathology. Vol 2(10th edition). Noida: Mosby Elsevier, 2009: 2354-2385.

48. Maly B, Maly A. Nodular Fasciitis of the Breast. Report of a Case Initially Diagnosed by Fine Needle Aspiration Cytology. Acta Cytol 2001; 45(5): 794-796.

49. Jimenez-Ayala M, Diez-Nau MD, Larrad A, Ferrer-Vergara L, Rodriguez-Costa J, Lacruz C et al. Hemangiopericytoma in a Male Breast. Report of a Case with Cytologic, Histologic and Immunochemical Studies. Acta Cytol 1991; 35(2): 234-238.

50. Chhieng D, Cohen JM, Waisman J, Fernandez G, Cangiarella J. Fine- Needle Aspiration Cytology of Hemangiopericytoma: A Report of Five Cases. Cancer 1999; 87(4): 190-195.

51. Kiyozuka Y, Koyama H, Nakata M, Matsuyama T, Nikaido Y, Shimano N et al. Diagnostic Cytopathology in Type II Angiosarcoma of the Breast. A Case Report. Acta Cytol 2005; 49: 560-566.

52. Demaria S, Yee HT, Cangiarella J, Cohen JM, Chhieng DC. Fine Needle Aspiration of Primary Pleomorphic liposarcoma of the Breast. A Case Report. Acta Cytol 1999; 43(6): 1131-1136.

53. Trihia H, Valavanis C, Markidou S, Condylis D, Poulianou E, Dadioti PA. Primary Osteogenic Sarcoma of Breast. Cytomorphologic Study of 3 Cases with Histologic Correlation. Acta Cytol 2007; 51: 443-450.

54. Lee WY, Cheng L, Chang TW. Diagnosing Invasive Cystic Hypersecretory Duct Carcinoma of the Breast with Fine Needle Aspiration Cytology. A Case Report. Acta Cytol 1999; 43(2): 273-276.

55. Cangiarella J, Waisman J, Cohen JM, Chhieng D, Symmans WF, Goldenberg A. Plasmacytoma of the Breast. A Report of Two Cases Diagnosed by Aspiration Biopsy. Acta cytol 2000; 44(1): 91-94.

56. Mitre BK, Kanbour AI, Mauser N. Fine Needle Aspiration Biopsy of Breast Carcinoma in Pregnancy and Lactation. Acta cytol 1997; 41(4): 1121-1130.

57. Carter E, Dyess DL. Infiltrating Syringomatous Adenoma of the Nipple: A Case Report and 20-Year Retrospective Review. The Breast Journal 2004; 10(5): 443-447.

58. Artal EM, Aracil VG, Alvira RM, Romeo JA, Arraiza A. Spindle Cell Malignant Melanoma Metastatic to the Breast from a Pigmented Lesion on the Back. A Case Report. Acta Cytol 2004; 48: 387-390.

59. Ding GTY, Hwang JSG, Tan PH. Sarcomatoid Renal Cell Crcinoma Metastatic to the Breast. A Report of Case with Diagnosis on Fine Needle Aspiration Cytology. Acta Cytol 2007; 51: 451-455.

60. Mrad K, Mansouri D, Driss M, Sassi S, Abbes I, Ayed Fb et al. Esthesioneuroblastoma Metastatic to Breast in a Young Woman. A Case Report. Acta Cytol 2005; 49: 427-430.

61. Taniguchi E, Yang Q, Tang W, Nakamura Y, Shan L, Nakamura M, et al. Cytologic grading of invasive breast carcinoma. Correlation with clinicopathologic variables and predictive value of nodal metastasis. Acta Cytol 2000; 44: 587-591.

62. Ohri A, Jetly D, Shukla K, Bansal R. Cytological Grading of Breast Neoplasia and its Correlation with Histological Grading. Indian J Pathol Microbiol 2006; 49(2): 208-213.

63. Howell LP, Gandour-Edwards R, O'Sullivan D. Application of the Scarff- Bloom-Richardson tumor grading system to Fine Needle Aspirates of the breast.Am J Clin Pathol 1994; 101: 262-265.

64. Robles-Frias A, Gonzalez-Campora R, Martinez-Parra D, Robles-Frias M, Vazquez-Cerezuda T, Otal-Salaverri C, et al. Robinson cytologic grading of invasive ductal breast carcinoma. Correlation with histologic grading and regional lymph node metastasis. Acta Cytol 2005; 49: 149-153.

65. Robinson IA, McKee G, Nicholson A, D'Arey J, Jackson PA, Cook MG, et al. Prognostic value of cytological grading of fine-needle aspirates from breast carcinomas. Lancet 1994; 343: 947-949.

66. Dabbs DJ, Silverman JF. Prognostic factors from the fine-needle aspirate: breast carcinoma nuclear grade. Diagn Cytopathol 1994; 10: 203-208.

67. Cajulis RS, Hessel RG, Frias-Hidvegi D, Yu GH. Cytologic grading of Fine Needle Aspirates of Breast Carcinoma by Private Practice Pathologists. Acta Cytol 1997; 41: 313-320.

68. Doussal VL, Tubiana-Hulin M, Friedman S, Hacene K, Spyratos F, Brunet M. Prognostic value of histologic grade nuclear components of Scarff-Bloom-Richardson (SBR). An improved score modification based on a multivariate analysis of 1262 invasive ductal breast carcinoma. Cancer 1989; 64: 1914-1921.

69. Page DL, Ellis IO. Histologic grading of breast cancer. Let's Do It. Am J Clin Pathol 1995; 103: 123-124.

70. Parham DM. Mitotic activity and histological grading of breast cancer. Pathol Annu 1995; 30: 189-207.
71. Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer : experience from a large study with long-term follow-up. Histopathology 1991; 19: 403-410.
72. Pandit AA, Parekh HJ. Cytologic grading of breast carcinoma. Comparison of four grading systems. Journal of Cytology 2000; 17: 39-44.
73. Howell LP, Lin-Chang L. Cytomorphology of common malignant tumors of the breast. Clin Lab Med 2005; 25: 733-760.
74. Das AK, Kapila K, Dinda AK, Verma K. Comparative evaluation of grading of breast carcinomas in fine needle aspirates by two methods. Indian J Med Res 2003; 118: 247-250.
75. Dalton LW, Page DL, Dupont WD. Histologic grading of breast carcinoma. A reproducibility study. Cancer 1994; 73: 2765-2770.
76. Kim A, Lee J, Choi JS, Won NH, Koo BH. Fine Needle Aspiration Cytology of Breast – Experience at an outpatient Breast Clinic. Acta Cytol 2000; 44: 361-367.
77. Omoniyi-Esan G, Osasan S, Titiloye N, Olasode B. Cytopathological Review of Breast Lesions In Ile-Ife Nigeria. The Internet Journal of Third World Medicine 2009; 8(1).
78. Ballo MS, Sneige N. Can Core Needle Biopsy Replace Fine-Needle Aspiration Cytology in the Diagnosis of Palpable Breast Carcinoma - A Comparative Study of 124 Women. Cancer 1996; 78: 773-777.
79. Joshi A, Kapila K, Verma K. Fine Needle Aspiration Cytology in the Management of Male Breast Masses. Nineteen Years of Experience. Acta Cytol 1999; 43: 334-338.

80. Tiwari M. Role of Fine Needle Aspiration Cytology in Diagnosis of Breast Lumps. Katmandu University Medical Journal 2007; 5(18): 215-217.
81. Das DK, Junaid TA, Mathews SB, Ajrawi TG, Ahmed MS, Madda JP et al. Fine Needle Aspiration Cytology of Male Breast Lesions. A study of 185 cases. Acta Cytol 1995; 39: 870-876.
82. Park IA, Ham EK. Fine Needle Aspiration Cytology of Palpable Breast Lesions – Histologic Subtype in False Negative Cases. Acta Cytol 1997; 41: 1131-1138.
83. Takei H, Ruiz B, Dancer J, Hicks J. Fine Needle Aspiration of Poorly Defined Indurated and Well-Defined Breast Lesions – A Cytopathologic Comparative Study. Acta Cytol 2007; 51: 692-698.
84. Choi YD, Choi YH, Lee JH, Nam JH, Juhng SW, Choi C. Analysis of Fine Needle Aspiration Cytology of the Breast – A Review of 1,297 cases and Correlation with Histologic Diagnosis. Acta Cytol 2004; 48: 801-806.
85. Scopa CD, Koukouras D, Androulakis J, Bonikos D. Sources of Diagnostic Discrepencies in Fine Needle Aspiration of Breast. Diagn Cytopathol 1991; 7: 546-548.
86. Sneige N, Staerkel GA, Caraway NP, Fanning TV, Katz RL. A Plea for Uniform Terminology and Reporting of Breast Fine Needle Aspirates. The M.D. Anderson Center Proposal. Acta Cytol 1994; 38: 971-972.
87. Hammond S, Keyhani-Rofagha S, O'Toole RV. Statistical Analysis of Fine Needle Aspiration Cytology of the Breast. A Review of 678 cases plus 4,265 cases from the literature. Acta Cytol 1987; 37: 276-280.
88. Tewari M, Shukla HS. Breast tuberculosis: diagnosis, clinical features and management. Indian J Med Res 2005; 122: 103-110.

89. Bondeson L, Lindholm K. Aspiration Cytology of Tubular Breast Carcinoma. Acta Cytol 1990; 34: 15-20.

90. Collaco LM, Lima RSD, Werner B, Torres LFB. Value of Fine Needle Aspiration in the Diagnosis of Breast Lesions. Acta Cytol 1999; 43: 587-592.

91. Park SM, Lee DW, Jin SY, Kim DW, Jeen YM, Choi IH. Fine-needle aspiration cytology as the first pathological diagnostic modality in breast lesions: A comparison with core needle biopsy. Basic and Applied Pathology 2010; 3: 1–6.

92. Meena SP, Hemrajani DK, Joshi N. A comparative and evaluative study of cytological and histological grading system profile in malignant neoplasm of breast – an important prognostic factor. Indian J Pathol Microbiol 2006; 49: 199-202.

93. Cajulis RS, Hessel RG, Hwang S, Haines K, Hidvegi DF, O'Gorman M: Simplified Nuclear Grading of Fine Needle Aspirates of Breast Carcinoma: Concordance with Corresponding Histologic Nuclear Grading and Flow Cytometric Data. Diagn Cytopathol 1994; 11: 124-130.

94. Cajulis RS, Sneige N, El-Naggar A: Cytologic Nuclear Grading of Fine Needle Aspirates of Breast Carcinoma: Concordance with Corresponding Histologic Nuclear Grading and Flow Cytometric Data. Mod Pathol 1990; 3: 14A.

95. Fisher B, Fisher ER, Redmond C, Brown A: Tumour Nuclear Grade, Estrogen Receptor, and Progesterone Receptor: Their Value Alone or in Combination as Indicators of Outcome Following Adjuvant Therapy for Breast Cancer. Breast Cancer Res Treat 1986; 7: 147-160.

96. Dantas KAN, Santos GDC, Filho OG. Grading Systems for Breast Carcinoma: Comparative Study of Cytohistological Agreement. RBGO 2003; 25 (2): 87-92.

PROFORMA

Name- Age- Sex- IP/OP No:

Clinical diagnosis-

COMPLAINTS:

1) Lump in the breast: Rt/Lt Duration-

2) Pain in the breast: Yes/No

3)) Nipple discharge: Yes/No Duration-

Colour of discharge-

4) Onset: Insidious/ Rapid

5) Others:

MENSTRUAL HISTORY: Age of menarche-

Menopause-

OBSTETRIC HISTORY:

PAST HISTORY: Similar illness: Yes/ No

FAMILY HISTORY: Similar illness: Yes/ No

LOCAL EXAMINATION OF BREAST:

Nipple: Normal/ Retracted/Discharge/ Ulcer/ Others

Lump: Number:

Quadrant:

Size:

Borders: well defined/ill defined

Temperature: Normal/ Raised

Tenderness: Yes/ No

Consistency: Soft/ Firm/ Hard

Skin over the swelling: Normal/ Inflamed/Ulcerated/Peu d orange

Lymph nodes: Number:

Group:

CYTOLOGICAL FINDINGS:

GROSS:

Amount of aspirate:

Nature of aspirate:

MICROSCOPY:

Adequacy of smear: Adequate/ Inadequate

Cellularity: Poor/ Moderate/ High

Cohesiveness: loose/tight

Pattern of arrangement:

Type of cells:

Other cells:

Cell size: Small/ Normal/ Large

Cytoplasm: Scanty/ Moderate/ Abundant

Nuclear features: Size: Small/ Normal/ Large

N/C Ratio: Normal/ Increased

Nuclear membrane: Regular/ Irregular

Nuclear overlapping: Yes/ No

Chromatin pattern: Fine/ Coarse/

Vesicular/Bland/Hyperchromatic

Mitosis: Present/ Absent

Nucleoli: present/absent

Back ground: Proteinacious/ Mucin/ Fat globules/ RBCs/ necrosis/Others

CYTOLOGICAL DIAGNOSIS:

HISTOPATHOLOGICAL DIAGNOSIS:

REMARKS:

KEY TO MASTER CHART

SI.No – Serial Number

Y – Yes

N - No

OI – Onset Insidious

OR – Onset Rapid

P – Parous

NP – Nulliparous

RE – Retracted

NO – Normal

UO – Upper Outer

UI – Upper Inner

LO – Lower Outer

LI – Lower Inner

DI – Diffuse

SA – Sub-Areolar

BW – Borders Well Defined

BI – Borders ill Defined

TN – Temperature Normal

TR – Temperature Raised

TP – Tenderness Present

TA – Tenderness Absent

S – Soft

F – Firm

H – Hard

SN – Skin Normal

SU – Skin Ulcerated

SP – Skin Peu de orange

SI – Skin Inflammed

GW – Grey White

HE – Hemorrhagic

PU – Purulent

AA – Aspirate Adequate

AI – Aspirate Inadequate

CP – Cellularity Poor

CM – Cellularity Moderate

CH – Cellularity High

CL – Cells Loosely Cohesive

CT – Cells Tightly Cohesive

MONO – Monolayered sheets

CLUS – Clusters

ANT – Antler-Horn

ACIN – Acinar

SING – Singles

CRI – Cribriform

DUCT – Ductal

MYO – Myoepithelial

APO – Apocrine

STF – Stromal Fragments

BIN – Binucleate cell

TRI – Trinucleate cell

GIA – Giant cell

MAC – Macrophage

PLA – Plasma cell

NEU – Neutrophil

LYM – Lymphocyte

PRO – Proteinaceous

FAT – Fat Globules

RBC – Red Blood Cell

NEC – Necrosis

NP – Nucleoli present

NA – Nucleoli absent

MN – No Mitosis

NS – Nuclear Size Small

NN – Nuclear Size Normal

NL – Nuclear Size Large

INTRODUCTION

AIMS AND OBJECTIVES

REVIEW OF LITERATURE

MATERIALS AND METHODS

RESULTS

DISCUSSION

CONCLUSION

SUMMARY

BIBLIOGRAPHY

ANNEXURES