A QUANTITATIVE STUDY OF MYOEPITHELIAL CELLS IN FINE NEEDLE ASPIRATE FROM BREAST LUMPS.

By

DR. TOSHI AGARWAL

Dissertation submitted to the

BLDE (Deemed to be University), Vijayapura, Karnataka

In partial fulfilment of the requirements for the award of the degree of

DOCTOR OF MEDICINE

IN

PATHOLOGY

Under the Guidance of

DR. SUREKHA B. HIPPARGI M.D,

Professor

Department of Pathology

BLDE (Deemed to be University), SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA, KARNATAKA.

2021

BLDE (Deemed to be University)
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL
& RESEARCH CENTRE, VIJAYAPURA

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**A QUANTITATIVE STUDY OF MYOEPITHELIAL CELLS IN FINE NEEDLE ASPIRATE FROM BREAST LUMPS"** is a bonafide and genuine research work carried out by me under the guidance of **DR. SUREKHA B. HIPPARGI,** Professor, Department of Pathology, BLDE (Deemed to be University) Shri B. M. Patil Medical College, Hospital & Research Centre, Vijayapura, Karnataka.

Date: 29-09-2020 **DR. TOSHI AGARWAL**

Place: Vijayapura

BLDE (Deemed to be University)
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL
& RESEARCH CENTRE, VIJAYAPURA

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"A QUANTITATIVE STUDY OF MYOEPITHELIAL CELLS IN FINE NEEDLE ASPIRATE FROM BREAST LUMPS"** is a bonafide research work done by **DR. TOSHI AGARWAL** in partial fulfilment of the requirements for the degree of **Doctor of Medicine (Pathology).**

Date: 29-09-2020

Place: Vijayapura

DR. SUREKHA B. HIPPARGI

Professor
Department of Pathology,
BLDE (Deemed to be University), Shri B. M. Patil Medical College, Hospital & Research Centre, Vijayapura, Karnataka

BLDE (Deemed to be University)
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL
& RESEARCH CENTRE, VIJAYAPURA

ENDORSEMENT BY HEAD OF DEPARTMENT

This is to certify that the dissertation entitled **"A QUANTITATIVE STUDY OF MYOEPITHELIAL CELLS IN FINE NEEDLE ASPIRATE FROM BREAST LUMPS"** is a bona fide research work done by **DR. TOSHI AGARWAL** under the guidance of **DR. SUREKHA B. HIPPARGI,** Professor, Department of Pathology, Shri B. M. Patil Medical College, Hospital & Research Centre, Vijayapura, in partial fulfilment of the requirements for the degree of **Doctor of Medicine (Pathology).**

Date: 29-09-2020

Place: Vijayapura

DR. S. U. ARAKERI

Professor and H.O.D,
Department of Pathology,
BLDE (Deemed to be University), Shri B.M. Patil Medical College, Hospital & Research Centre,
Vijayapura,
Karnataka

BLDE (Deemed to be University)

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

ENDORSEMENT BY PRINCIPAL /HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"A QUANTITATIVE STUDY OF MYOEPITHELIAL CELLS IN FINE NEEDLE ASPIRATE FROM BREAST LUMPS"** is a bona fide research work done by **DR. TOSHI AGARWAL** under the guidance of **DR. SUREKHA B. HIPPARGI,** Professor, Department of Pathology, Shri B. M. Patil Medical College, Hospital & Research Centre, Vijayapura, in partial fulfillment of the requirements for the degree of **Doctor of Medicine (Pathology).**

Date: 29-09-2020

Place: Vijayapura

DR. ARAVIND V. PATIL

Principal,
BLDE (Deemed to be University), Shri B.M. Patil Medical College, Hospital & Research Centre, Vijayapura, Karnataka.

BLDE (Deemed to be University)
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL
& RESEARCH CENTRE, VIJAYAPURA

COPYRIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the BLDE (Deemed to be University), Karnataka shall have the rights to preserve, use and disseminate this dissertation / thesis in print or electronic format for academic / research purpose.

Date: 29-09-2020 **DR. TOSHI AGARWAL**

Place: Vijayapura

ACKNOWLEDGEMENT

It is most appropriate to begin by expressing my gratitude to the Almighty for all His blessings.

I would like to express my sincere and deepest gratitude to my teacher and guide **Dr. SUREKHA B. HIPPARGI, Professor, Department of Pathology**, for her time, patience, suggestions, encouragement and invaluable guidance throughout my study. I could not have envisaged a better advisor and mentor for my study.

I am equally obliged to **Dr. S. U. Arakeri, Professor and H.O.D, Department of Pathology** for her invaluable suggestions throughout this study. She has had a profound influence on both my personal growth and professional pursuits.

I am privileged to have such an approachable and supportive staff. I am thankful to **Dr. R.M. Potekar** Prof, **Dr. Prakash M. Patil** Assoc Prof, **Dr. Vijayalaxmi S. Patil** Assoc. Prof, **Dr. Savitri M. Nerune** Assoc prof, **Dr. Mamatha Kariyappa** Assoc prof, **Dr. Sneha Jawalkar** Asst Prof, **Dr. Satish Arakeri,** Asst Prof **Dr. Sai Kulkarni, Dr. Anil K. Reddy** and former faculty **Dr. B R Yelikar** Prof**, Dr. Mahesh H Karigoudar** Prof, for their advice, supervision, concern and feedback during this period.

I am deeply indebted to my parents **Dr. Anil Kumar Agarwal** and **Mrs. Neeru Agarwal** and my brother **Anirudh Agarwal** for their constant encouragement and moral support that helped me to complete my dissertation work.

Special thanks to my dearest friends **Dr. Silky Singh, Dr. Vartika Ratan Kothia, Dr. Prajwal Patil, Dr. Bithika Dey** and **Dr. Maitreyi Ojha Sharma** my seniors **Dr. Shilpa Gupta, Dr. Prashant Rajput** and **Dr. Afra Taqdees** and juniors who have helped me during my work.

I also express my sincere thanks to **Dr. Mohd Shahnawaz, Assistant Prof. Dept. of Community Medicine** for sharing her expertise at statistics and making it seem uncomplicated.

I am also extremely fortunate to have a caring, approachable and supportive department, who has advised and mentored me and made it possible for me to expedite this dissertation.

I am grateful to all the Technicians and non-teaching staff of the Department of Pathology.

Last but not the least**,** my sincere gratitude to all my study subjects for their contribution to this study.

Date: 29-09-2020 **DR. TOSHI AGARWAL**

Place: Vijayapura

LIST OF ABBREVATIONS

FNAC - Fine Needle Aspiration Cytology	**TDLU**-Terminal Duct Lobular Unit
ME Cells – Myoepithelial Cells	**MGG**- May Grunwald Geimsa
ROC – Receiving Operating Characteristics	**H & E** – Haematoxylin and eosin
DCIS – Ductal Carcinoma In Situ	**PAP**- Papanicolaou's and Pap
LCIS – Lobular Carcinoma In Situ	**N:C Ratio**- Nucleo- Cytoplasmic Ratio
IDC – Infiltrating Ductal Carcinoma	**IHC -** Immunohistochemistry
ILC - Infiltrating Lobular Carcinoma	**HPF** – High Power Field
ADH – Atypical Ductal Hyperplasia	**RT-PCR**- Reverse Transcriptase Polymerase
TP – True Positive	Chain Reaction
TN – True Negative	**DNA**- Deoxyribonucleic acid
FP – False Positive	**RNA**- Ribonucleic Acid
FN – False Negative	**SMA** – Smooth Muscle Actin
NPV – Negative Predictive Value	**HMW**- High Molecular Weight
PPV – Positive Predictive Value	**NST** – No Special Type

ABSTRACT

BACKGROUND

Fine needle aspiration cytology (FNAC) is a treasured tool in the evaluation of breast abnormalities. The main goal of breast FNA is to differentiate between benign or malignant lesions. Clinical and/or radiological findings are also correlated to avoid unnecessary surgery and to provide with a preoperative diagnosis of malignancy to allow proper patient counselling and definitive clinical management.

The bimodal pattern of aggregates of cohesive epithelial cells myoepithelial cells and scattered single, bare, bipolar nuclei are diagnostic of benign tumor and non-neoplastic breast lesion. Studies in regard with the quantification and differentiation among different benign lesions on the basis of quantification of ME cells are quite few. This aspect therefore merits further investigations.

OBJECTIVES OF THE STUDY

To quantify the myoepithelial cells (ME cells) and to know the diagnostic utility of myoepithelial cells in aspirates of various breast lesions.

MATERIALS AND METHODS

All patients with breast lumps referred to the cytology section of the department of the Pathology Shri B.M. Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be University) Vijayapura, for aspiration cytology were studied. A total of 124 cases were studied. A 22 or 23 gauge needle was used with 10 ml syringe for aspiration of material. Smears from aspirates were stained and mounted for microscopic evaluation.

Quantitative estimation of ME cells per 1000 ductal cells with at least 20hpf (x40) were scanned and areas with the least overlapping of cells were selected. Number of ME cells was correlated with the cytological diagnosis. ME cells were counted as the cell with same or smaller size than that of epithelial cells with bipolar shape, dense, homogeneous chromatin, smooth nuclear outline without any nucleoli, with definable cytoplasm, distributed within the epithelial clusters.

RESULTS

124 cases were included in the present study. The cases were between 04-84 years of age. The maximum number of cases were in 21-30 years age group (37.1%). The right breast was involved more than the left breast having 62 cases (50%) and 59 cases (47.6%) respectively, followed by 3 cases (2.4%) having bilateral involvement. Overall most common quadrant involved was superolateral (51 cases, 41.1%).

Out of 124 cases, 100 cases (80.6%) were benign and 24 cases (19.4%) were malignant. The mean of ME cells in benign lesions was 342.3 ± 130.7, whereas the mean of ME cells in malignant lesions was 3.1 ± 5.7. The difference in the number of ME cells in benign and malignant lesions was significant (<0.001).

Histopathology correlation was available for 30 cases (both benign and malignant), out of which 25 cases (83.3%) were concordant and 5 cases (16.7%) were discordant.

CONCLUSION

On quantification of ME cells, it was found that the mean of ME cells in benign lesions is greatly more when compared to malignant tumor and this difference was significant. Also it was found that there was a significant difference of mean of ME cells between benign non-neoplastic and benign neoplastic lesions. Hence, the quantification of ME cells helps to differentiate among various breast lesions.

KEYWORDS

Breast lumps, myoepithelial cells, benign, malignant, tumors.

Introduction

Breast lesions are one of the most common lesions in women. There is a high incidence of breast cancer in developed and developing countries.[1]

Fine needle aspiration cytology (FNAC) has most effective, simple, prompt, cost-effective and accurate diagnostic technique for diagnosis of breast lesions.[1] Sometimes there is difficulty in diagnosing lesions falling under a gray zones, so myoepithelial cells complement to distinguish between neoplastic and non- neoplastic as well as benign and malignant on cytological smears.[2]

Clinicians accept the requirement of acquiring prompt pathological correlation of any breast lump inferred to be benign or malignant. Type of disease is the most important prognostic factor at the time of presentation, so a reliable preoperative diagnosis is made for proper treatment and to reduce unnecessary surgical excision and proper management.[3]

Triple test includes FNAC along with the combination of clinical examination and mammography for diagnosing breast lesions like breast malignancies, which moreover highlights the importance of FNAC as a diagnostic and screening tool.[1]

The presence of myoepithelial cells has long been recognized as a prominent feature of benign breast disease which distinguishes it from malignant lesions. However, its quantification has rarely explored. So, the quantification of myoepithelial cells will aid our understanding in distinguishing various lesions of the breast.[2]

Objective of the study:

To quantify the myoepithelial cells (ME cells) and to know the diagnostic utility of myoepithelial cells in aspirates of various breast lesions.

Review of Literature

History -

In the UK Dudgeon and Patrick[4] in 1927 proposed the rapid microscopic diagnosis by needling of tumors. FNAC was first introduced in 1930's by Martin and Ellis[5.]

Masood et al[10] in 1995using immunocytochemistry (a monoclonal antibody against muscle specific actin) identified myoepithelial cells and demonstrated a significant difference of the number of myoepithelial cells in benign versus malignant tumors.

Olin PP et al[8] in 1998 told that the fetal breast epithelial cells that form the breast bud express transforming growth factor a (TGF-a), a mitogen and differentiation factor that may mediate the growth-promoting effect of estrogen on the developing breast.

Cowin and Wysolmersld[6] in 2010 and Van Keymeuelen et al[7] in 2011 reviewed molecular mechanisms guiding embryonic mammary gland development and the potential role of stem cells in normal mammary development and maintenance.

Hoda SA et al[9] in 2014 commented that myoepithelial cells appear to arise from basal cells between weeks 23 and 28 of gestation.

Education and examinations in FNAC techniques in breast have become an essential part of the skills of pathologists in today's practicing era.[11]

INDICATIONS OF FNAC IN BREAST LESIONS

1. It is useful for the diagnosis as well as evacuation of simple cyst.
2. The investigation of any palpable lump, clinically benign or malignant.
3. The preoperative confirmation of clinically suspected cancer.
4. The investigation of suspected recurrence or metastasis in previously diagnosed cancer.
5. To obtain cells for special analysis and research e.g. hormone receptor studies, D.N.A analysis, IHC, cell kinetics and molecular studies.[3]

ADVANTAGES OF FNAC

1. Immediate diagnosis relieves patient's anxiety[3].

2. Minimally invasive
3. Inexpensive/cost effective[11]
4. The definite treatment can be planned in advance with the consent of the patient.
5. The need for frozen section diagnosis is reduced.
6. It renders unnecessary need for excision biopsy in advanced cases, elderly patients or in cases where treatment is non- surgical.[3]

LIMITATIONS OF FNAC

1. Quality of samples and smears highly define the results and accuracy.
2. Proper training and experience is essential to get adequate material for diagnosis
3. Small samples obtained with a fine needle may not be representative even when image-guided aspiration is performed in case of heterogeneous pathological processes.
4. Multiple biopsies help, but a limited number of passes are advised to minimize trauma.
5. Cytological smears may not represent some lesions as they are recognized on some specific micro-architectural pattern
6. Exact typing of various hyperplastic and low-grade neoplastic lesions is sometimes not possible. [11]
7. Inability to distinguish DCIS from IDC &ADH from DCIS[12]
8. Precise cytological criteria are not defined in some rare conditions. Particularly in difficult areas of diagnosis, such as soft tissue tumors pediatric tumors, malignant lymphoma, etc., when patients are referred to higher centers.
9. Analysis of histological follow-up is recommended for a high level of diagnostic accuracy sufficient enough to form the basis for major therapeutic decisions. [11]

All FNAC should be diagnosed in light of the clinical picture and other investigations to minimize false negatives.

CONTRAINDICATIONS OF FNAC

1. There are no contraindications of FNAC
2. Even anticoagulation therapy is not a contraindication but it should be noted.[3]

Complications of FNAC

1. Complications are uncommon
2. Hemorrhage, infraction can be seen.
3. Rarely hematomas, pneumothorax is seen.
4. Very rarely tumor implantation is seen.[3]
5. FNB does cause some disruption of tissue, even with good technique. A range of changes including hemorrhage, infarction and epithelial implantation resembling invasion have been described.[13]
6. In patients with breast prostheses, accidental puncture of a breast prosthesis (silicone) can be avoided by careful positioning of the lesion, ultrasound guidance, and using the non-aspiration technique.[14]
7. The venous compression, dependence of the breast and inability to compress the site during stereotactic biopsy encourage bruising.[3]
8. Following FNAC, displaced epithelial fragments in tissue sections may potentially mimic stromal invasion giving a false diagnosis of invasive carcinoma in histological sections.[12]

DIAGNOSTIC ACCURACY

Due to the high sensitivity and specificity FNAC of the breast is a good diagnostic technique. The diagnostic accuracy is operator dependent to some extent. The sensitivity of the technique ranges from 68% to 99%.[1] The specificity of FNAC is as high as 99%.[15-17].The false-negative rate of FNAC is about 3–5%, and as high as 30%.[18]

False negatives can be avoided if the FNAC is done by trained cytologists and multiple sampling is performed. Clinical history should also be taken into account and any clinically suspicious mass that is negative on cytology, should be repeated. False-positive rate in breast is near about 4%.[16,19].

Cytology may not provide a definitive specific diagnosis but it helps in categorizing and giving a differential diagnosis for disease and suggest the appropriate further investigations, saving time and resources. Consequently, it has become as indispensable as surgical histopathology.[11]

ADEQUACY OF SMEAR

Zajdela et al[22] in 1987 in his study told that material on smear was considered inadequate for diagnosis when the

smear was acellular or when it contained only adipocytes. Also, he performed aspiration cytology on 7877 breast masses from 1954 to 1980> Cases with insufficient cellular material were 249 out of 3579 cases i.e. 6.9% for histologically benign and 226 out of 4293 case i.e. 5.2% for histologically malignant cases. The average score being 6%.

Layfield et al[20] in 1997 proposed of adequacy criterion "Six or more cell clusters (cumulative total) or the presence more than 10 intact bipolar cells per 10 medium-power fields (× 200)"

The National Cancer Institute (NCI) in 1997 sponsored conference in Bethesda on the uniform approach of breast did not recommend any specific number of cells for the adequacy of breast FNAC.[21]

Eckert R, Howell, LP et al[23] in 1999 concluded that quantitative parameters like overall cellularity (numbers of cell clusters), proportions of different-sized epithelial clusters (small, medium and large), and proportions of epithelial to fibro-fatty elements alone are insufficient measures for determining specimen adequacy in FNA of palpable breast lesions. Rather, adequacy remains based upon factors such as confidence of needle placement, cell preservations, correlation with clinical and mammographic findings.

NORMAL ANATOMY & HISTOLOGY

The breast or mammary gland is covered by skin and subcutaneous tissue and rests on the pectoralis muscle, from which it is separated by a fascia. The functional unit of the organ is the single gland, a complex branching structure that is arranged into lobes[24] and which is made up of two major components: the terminal duct–lobular unit (TDLU) and the large duct system. The TDLU is formed by the lobule and terminal ductule and represents the secretory portion of the gland. It connects with the subsegmental duct, which in turn leads to a segmental duct, and this to a collecting duct, which empties into the nipple. A fusiform dilation located beneath the nipple between the collecting and the segmental duct is known as the lactiferous sinus.[25]

NORMAL CYTOLOGY

Ductular epithelial cells:

- Small cohesive groups.
- Monolayer sheets.[26]

- Seen as epithelial fragments that represent cast of terminal ductules.
- Nucleus – irregularly distributed within the aggregates, generally crowded or multilayered.[3]
- Size - small, 8-10 micron[26]
- Shape - round to oval.
- Chromatin - dark, granular.
- Nucleoli - not visible or small.
- Minor variation in size or shape of nucleus may be seen.
- Cytoplasm- Visible but without distinct cell borders, Amount- scanty, Color - pale, may show blue granulation MGG.[3]

Acinar cells

Generally seen during lactation.

Poorly cohesive, mainly dispersed

Nucleus – round to vesicular, central, larger than ductular cells.

Nucleoli – central, small distinct.

Cytoplasm – fragile, vacuolated, finely granular. Amount- Abundant[3]

Myoepithelial cell

The breast ducts and acini are lined by two layers of cells. A luminal layer of epithelial cells and a basal layer of flattened ME cells. ME cells are scattered between the epithelial fragments.

- Size – small
- Shape – bipolar.
- Nucleus – dense, homogeneous darker staining.
- Nucleoli – not seen.
- Cytoplasm – scanty to absent.[3]

Single bare nuclei

Scattered in the background. Also known as stroma cell nuclei or stripped nuclei.[26]

- Size – same or smaller than those of the epithelial cells.

- Shape- bipolar shape, although most of the nuclei are truly naked, occasionally pale blue cytoplasm is seen on each pole.[23]
- Nucleus – very smooth nuclear outline.
- Chromatin – dense and homogeneous.
- Nucleoli – not seen[3].

Benign Pairs

Naked myoepithelial nuclei or 'bare bipolar nuclei' in the background, may occur as 'benign pairs' when the oval nuclei moderately touch each other on one extremity; also known as dyads.

- Size – Similar to ME cells/ bipolar nuclei
- Shape- Bipolar- ovoid
- Nuclei -oval
- Chromatin – fine
- Nucleoli – absent[27]

Smears characteristics of benign versus malignant breast lesions.[26]

Table 1 : Cytological findings of benign/malignant Breast lesions		
Features	**Benign Pattern**	**Malignant Pattern**
Cellularity	Low	Usually high
Cohesion	More cohesive	Less cohesive
Pattern of cells	Flat sheets	Overlapping, often 3D, irregular.
Cell Population	Mixture of cells, epithelial, myoepithelial cells	Uniform cell population
Background	Clean	Necrosis and macrophages.
Nucleus	Small round	Variable, often larger, pleomorphic
Nuclear membrane	Smooth	Irregular
Chromatin	Fine/Smooth	Irregular/Clumped
Nucleoli	Inconspicuous	Mostly conspicuous
Myoepithelial cell	Seen frequently	Not seen
Bare bipolar nuclei	Present	Absent

The nearest absolute criteria of benignancy is a biphasic pattern with stromal bipolar cells. Benign conditions are exceptions with few or no stromal cells. Sometimes aspirates will be poorly cellular. Difficulty arises in scanty aspirates. Sometimes aspirates of carcinomatous lesions contain a population of small naked nuclei, some of which may be ovoid and mistaken for bipolar cells. Careful examinations of the nature of chromatin and nucleoli avoid the pitfall. Some malignant aspirates will be contaminated with hyperplastic but benign tissue resulting in a population of bipolar cells that distract attention from the population of malignant cells.[26]

Nor Ashidi et al[28] evaluated cellularity, background information, cohesiveness, significant stromal component, clump thickness, nuclear membrane, bare nuclei, normal nuclei, mitosis, nucleus stain, uniformity of cell, fragility and number of cells in the cluster in 1300 reported breast pre-cancerous cases.

They developed a diagnosis system which produced excellent diagnosis performance with 100% accuracy, 100% sensitivity and 100% specificity.

Ohtani H et al[29] in 1980 told that ultrastructurally myoepithelial cells consist of bundles of microfilaments 50-70 A in diameter and associated with dense bodies being a common feature; Dense bundles of tonofilments, 80-100 A in diameter; Adjacent myoepithelial or carcinoma cells are connected by typical desmosomes.

Studies were done on the presence or absence of myoepithelial cells in different breast lesions.

In 1982 Barry A et al[30] told that for the detection of myoepithelial and epithelial cells by an

immunocytochemical method for fixed and paraffin-embedded human breast biopsies with the use of antibodies to myosin and keratin, respectively, and of basement membranes using antibodies to laminin and type IV collagen is reported. With the help of these markers, myoepithelial cells can be clearly distinguished in the normal breast and in benign breast diseases sclerosing adenosis, epitheliosis, and fibroadenoma. The major cellular component in sclerosing adenosis is formed by myoepithelial cells. They came to the conclusion that mature myoepithelial cells from a very minor component of the majority of infiltrating ductal carcinoma in contrast to benign breast diseases.

RB Nagle et al[31] in 1986 characterized breast carcinoma by two monoclonal antibodies distinguishing myoepithelial from luminal epithelial cells. KA 1 and KA 4, two monoclonal antibodies were raised against the human epidermis were biochemically and immunologically characterized to show reactivity with specific cytokeratin polypeptides. These antibodies could distinguish between myoepithelial and luminal epithelial cells. They found that cytokeratin 5 and KA 4 antibody cytokeratin 19 were recognized by KA 1 antibody. They also found out that KA 4 antibody reacted with the epithelial cells in normal mammary tissue. In contrast, only myoepithelial and basal epithelial cells of acini, duct, and sinus were decorated by KA 1 antibody. However, Luminal cells were stained by KA 1 in ductules. 73 invasive Lobular and ductal carcinoma were studied and it was concluded that all of them reacted with KA 4 antibody but only five of these were positive in the same tumor cells with KA in-situ carcinomas, KA 4 stained the tumor cells in a homogenous pattern. KA 1 antibody reacted only with the surrounding myoepithelium. In epithelial hyperplasia, the proliferating cells were decorated by KA 1 and KA 4 antibodies in a homogeneous pattern.

Thus it can again be concluded from this study that myoepithelial cells which are stained with KA 1 are more commonly found in benign conditions than in malignant ones.

Tsuchiya et al[32] in 1987 reported that most naked nuclei are derivative of stromal cells.

Gottileb C et al[33] in 1990 studied myoepithelial cells in the differential diagnosis of benign and malignant breast lesions, immunohistochemically. They said that the differentiation between non-invasive carcinomas, sclerosing adenosis, radial scars, occurring in sclerosing adenosis, and invasive carcinoma can be difficult. For diagnosis of complex benign breast proliferation as well as intraepithelial neoplasia in sclerosing adenosis, identification of

myoepithelial cell layer is helpful. They concluded that muscle actin was uniformly reliable in staining myoepithelial cells, as well as other actin-containing cells such as myofibroblasts and vascular smooth muscle.

Being poorly sensitive and less specific than muscle actin, HMW keratin was less reliable, for labeling of the myoepithelial cells. Myoepithelial cells were easily identified at the periphery of ductules in all complex benign breast lesions.

The presence of myoepithelial cells distinguished intraepithelial neoplasia involving scalloping adenosis from invasive carcinomas. Well-differentiated invasive carcinoma lacked a myoepithelial cell layer.

Tavassoli, Fattaneh A et al[34] in 1991 studied myoepithelial lesions of the breast:

31 breast lesions were studied for their clinical and pathological features which are composed of a prominent population of myoepithelial cells either along with epithelial cells or in pure form. The lesions were divided into three categories: Myoepitheliosis, Adenomyoepithelioma, and malignant mesothelioma (myoepithelial carcinoma) where purely ME cells are found in the latter lesion. Three multifocal, microscopic lesions located in the peripheral duct system were designated as Myoepitheliosis. Twenty-seven solitary, palpable grossly, predominantly centrally located lesions qualified as Adenomyoepithelioma. These were subdivided further into spindle cell, tubular and lobulated variants. Two lesions in the latter group had a carcinoma arising within them. Only one case, which was characterized by a solitary mass composed of an Infiltrating spindle cell proliferation, qualified as malignant mesothelioma (myoepithelial carcinoma).

McCluggage WG et al[35] in 1997 studied the FNAC features in two cases each of mammary adenoid cystic carcinoma and Adenomyoepithelioma. In both cases of adenoid cystic carcinoma, aspirants consisted of clusters that were tightly cohesive and cells arranged around spheres and interconnecting cylinders of cellular material. Both the aspirates of Adenomyoepithelioma were composed of large tightly cohesive clusters of cells with small amounts of stromal material. All four aspirates consisted of dual population of epithelial and myoepithelial cells and many bare nuclei were present. Histology showed the characteristic features of adenoid cystic carcinoma and Adenomyoepithelioma. Confirmation for the presence of large numbers of myoepithelial cells was done by IHC staining of histology sections for S-100 protein and alpha-smooth muscle actin within all four lesions, providing indirect evidence that bare nuclei in breast aspirates represent myoepithelial cells and many bare nuclei within a

breast aspirate which is generally indicative of a benign lesion. This is in contrast, as adenoid cystic carcinoma is a malignant tumor, and Adenomyoepithelioma, while generally exhibiting benign behavior, is capable of local recurrence and distant metastasis.

Moriki T et al[36] in 1999 reported that A fundamental feature of benign aspirate is the presence of a dual population of myoepithelial cells (naked, bipolar nuclei) and ductal epithelial cells which are variable within limits but cohesive and orderly.

Barbareschi, Mattia et al[37] in 2001 used p63, a p53 homolog which is a selective nuclear marker of myoepithelial cells of the human breast. They reported that p63 is a member of the p53 gene family, and its germline mutations are associated with severe mammary developmental defects.

Immunohistochemically 384 samples were investigated by Barbareschi et al of normal and diseased human breast, using four antibodies recognizing all p63 isoforms.

Furthermore, snap-frozen tissue samples from 3 fibroadenomas and 10 invasive ductal carcinomas with their paired non-neoplastic tissues and 3 corresponding lymph node metastases were evaluated for the expression of p63 mRNA by RT-PCR. They found that in all benign lesions, p63-immunoreactive cells formed a continuous basal rim along the epithelial structures. Stromal cells, and myofibroblasts, were consistently unreactive.

A peripheral rim of p63-immunoreactive cells was discontinuously present surrounding lobular and ductal carcinoma in situ, when compared to the normal structures.

Invasive breast carcinomas were consistently devoid of nuclear p63 staining, with the exception of the two adenoid-cystic carcinomas, of the two ductal carcinomas with squamous metaplasia, and of 11 (4.6%) ductal carcinomas not otherwise specified, showing p63 immunoreactive in a minor fraction (5-15%) of the neoplastic cells.

Thus it was concluded that in comparison with other myoepithelial markers, p63 was the most specific, sensitive and reliable marker being restricted exclusively to myoepithelial cell in both histological cytological preparations whereas antibodies to smooth muscle actin and, to a lesser extent, calponin also decorated stromal myofibroblasts. Thus they further conclude from this study that the number of myoepithelial cells are lesser in malignant conditions even when confirmed with nuclear markers.

However, a study done by Reis-Filho JS et al[38] in 2002 of P 63 immunosuppression in cells with naked nuclei concluded that the majority was of myoepithelial origin.

Bocker W et al[39] in 2002 Origin of myoepithelial cell – A committed stem cell in the terminal duct gives rise to luminal and myoepithelial cells.

Bofin AM et al[40] in 2004 studied 133 FNAC specimens from breast tumors and found that nuclear morphology, sign of invasion, myoepithelial cells and degree of cellular dissection are the most potent factors discriminating between benign epithelial proliferation, atypical intraductal hyperplasia, ductal carcinoma in-situ, and invasive carcinoma.

Bofin AM et al said that myoepithelial cells which are seen in the ductal fragments, appear as smaller, darker, and oval-shaped nuclei at the periphery of intact ductal structures, as opposed to naked nuclei. Such cells were present in non-proliferative/proliferative breast disease (87%), atypical intraductal hyperplasia, ducal carcinoma in situ (53%), and infiltrating ductal carcinoma (26%).

They found naked bipolar only in 5 of the 30 cases of DCIS and observed myoepithelial cells in fragments of ductal cells in 15 cases. In invasive carcinoma, either type of cells were rarely present.

Pattari SK et al[2] in 2008 conducted a study of 71 cases of FNAC of palpable breast lesion, which were histologically proven. There were 30 invasive carcinomas, 25 cases of benign lesions, 11 cases of proliferative breast lesions and 5 cases of carcinoma in situ. Quantitative estimation and analysis of myoepithelial cell were correlated with the final diagnosis.

The mean number of myoepithelial cells per 1000 ductal cells on cytology smears was 5.1 ± 5.5 in malignant, 30.8 ± 25 in carcinoma in situ, 28.3 ± 20.2 in proliferative breast disease and 38.4 ± 38.8 in benign breast lesions (Mean $\pm$ Standard Deviation)

In SMA stained histopathology sections, ME cells in benign were 741.12 ± 248, in proliferative breast disease were 238 ± 172, in carcinoma in situ were 121.6 ± 115 and in malignant cases 15.6 ± 25.1.

Thus he concluded that the number of ME cells in FNAC smear was significantly different between benign and malignant lesions as well as between proliferative breast disease and malignant lesions, but the difference was not significant between benign and proliferative breast disease on cytology smears.

But in histopathology sections stained for smooth muscle actin, a significant difference in the number of ME cells was found between benign and malignant conditions (p=0.000), benign group versus proliferative breast disease group was also found.(p=0.000) as well as between Proliferative breast disease and Invasive malignant lesion (p=0.000).

Agarwal P et al[41] in 2017 studied 50 cases in her study and found out that ME cells were maximum in cases of benign breast disease with non-specific descriptive (359.1) followed by fibroadenoma (161.1) and granulomatous mastitis (92). No. of ME cells were very less in ductal carcinoma with a mean of 5.8, and there was statistically significant difference between the mean of myoepithelial cells/1000 ductal cells in benign and malignant lesions.

Reported Cytohistological Correlation.

Jayaram et al[42] in 1996 performed FNAC on breast lumps and reported that out of 93 cytologically benign cases, 3 (3.22%) were malignant and out of 61 malignant cases, 1 case (1.66%) was benign on histology.

Kollur SM et al[43] in 2006 did a retrospective analysis of 110 cases of FNA smears, diagnosed as fibroadenoma of which surgical pathology follow-up was done in 33. The cytohistological correlation was obtained in 26 of 33 (79%) cases.

O Obaseki DE et al[44] in 2010 performed 103 FNA of breast masses during the study period. Following biopsies were done on 43 of these cases giving a biopsy rate of 41.8%. The absolute and complete sensitivities of this study were 84.6% and 97.4% respectively. The full specificity for biopsy cases was 75%. The PPV for malignancies came out to be 100% with a false positive rate of 0%; however, 2.6 was the false-negative rate with a suspicious rate of 9.7%. The inadequacy rate was 19.4%.

Common pitfalls in the interpretation of cytology of the breast.

Sneige, N.[45] in 1993 in his study found out that some cases like adenosis, duct hyperplasia, nipple adenoma, and fibroadenoma-shared some of the features seen in malignant tumors, such as hypercellularity, cell atypia, and loss of cell cohesion.

The conditions associated with false-positive diagnosis include:

Papillary lesions –Definite cytological diagnosis left to histology. Distinction between intraductal papilloma,

Papillary in-situ and well-differentiated invasive papillary carcinoma cannot be made on cytology.

Fibroadenoma with atypical features – This is the lesion most commonly mistaken for cancer. However, the presence of bare bipolar nuclei should prevent a diagnosis of Malignancy.

Mass or thickness associated with lactation – A clinical history is most important to prevent a false positive cytological diagnosis. During pregnancy, lactation, or post lactation, most of the cells are acinar and dispersed with prominent nucleoli. However, the presence of abundant cytoplasm, vacuolation and a lipo-proteinaceous background should prevent misdiagnosis, especially when used in conjunction with the triple test.

Radical scar with hyperplasia – Differentiation from a well-differentiated carcinoma can be difficult. Bare bipolar nuclei are usually a feature. It is important that a definite diagnosis of malignancy is not made if bare bipolar nuclei are present with the atypical cells.[46-48]

Foxcroft[49] in 2007 in his study found out that As phyllodes tumors mimic fibroadenomas, there diagnoses often becomes difficult and they only become evident when enlarged in size over a period of time significantly.

Classification of breast lesions[9]

Benign Non-Neoplastic

1. Mastitis
2. Granulomatous mastitis
3. Galactocele
4. Gynecomastia
5. Epithelial hyperplasia
    - Atypical ductal hyperplasia
    - Benign proliferative breast disease
    - Benign non proliferative breast disease
    - Benign proliferative breast lesion without atypia
    - Lactating adenoma

Benign Neoplastic

1. Fibroadenoma

2. Benign Phyllodes tumor
3. Papillary neoplasm

Malignant

1. Infiltrating ductal carcinoma (IDC)
2. Ductal carcinoma in situ (DCIS)
3. Papillary carcinoma

The various lesions in the breast are discussed as follows:

Mastitis[3]

- It shows a benign bimodal population.
- Regenerative epithelial atypia.
- Chronic/acute inflammatory cells.
- Population of epithelioid cells, plasma cells, multinucleated giant cells, histiocytes are associated in case of granulomatous pattern.
- Microorganisms seen in case of infectious mastitis.

Granulomatous mastitis[26]

- Ductal cells- reactive
- Nucleus- enlarged
- Nucleoli- distinct.
- Pattern of epithelioid cells- sheets/clusters
- Nuclei- elongated
- Cytoplasm- abundant
- Giant cells- multinucleated, Langhans type
- Other cells- inflammatory cells like lymphocytes, plasma cells, neutrophilic granulocytes

Galactocele[3]

Occasional dispersed cells in the background of granular and proteinaceous material are seen.

Cyst containing foamy histiocytes and inflammatory cell and lipid micelles are seen.[3]

According to Gray W et al[26] the aspirate is composed of milk with abundant granular secretory material along with foamy macrophages and calcified debris in "old" lesions.

Gynecomastia of male breast[3]

- Cellularity- variable, scant to markedly cellular
- Pattern of epithelial fragments- flat/ monolayered sheets, can be finger-like projections (like in fibroadenoma)
- Bare bipolar nuclei- present
- Nucleus- show atypia and moderate variation.
- Adipose tissue may be present.

Cibas et al[50] reported that gynecomastia resembles fibroadenoma and have a group of ductal cells having a small oval nucleus with scant cytoplasm.

Atypical Ductal Hyperplasia[26]

- Cellularity- High with crowding and overlapping 3D epithelial aggregates.
- Cohesion – Decreased.
- Nucleus- show anisonucleosis
- Nucleoli – prominent

Benign ductal proliferative lesion without atypia[50]

- Pattern – sheets or tight clusters without overlap of cells.
- Cellular spacing – regular
- Chromatin – finely granular.
- Nucleoli- inconspicuous/small

Fibroadenoma[3]

- Cellularity – high.
- Pattern – large branching sheets.
- Stroma – fibromyxoid.

- Cohesion – strong.
- Nucleus – overcrowding, overlapping.
- Size – may be mildly enlarged.
- Chromatin – bland, granular
- Nucleoli – 1 or 2 indistinct.
- Myoepithelial cell – frequently seen within aggregates
- Bare bipolar nuclei- more numerous than usual glandular breast tissue except for fibrotic and sclerosed fibroadenomas.

Importance of ME cell in fibroadenoma -Rogers and Lee in 1992 reported a series of 16 cases where low-grade invasive carcinomas have a loose fibromyxoid stroma and mimicked fibroadenoma. The presence or absence of single bipolar nuclei, typical of non-neoplastic breast tissue is of great importance in this context.[51]

Occasional fibroadenoma show decreased cohesion, nuclear enlargement with anisonucleosis and nuclear enlargement and prominent nucleoli which can be the common cause of false-positive diagnosis. The presence of bipolar nuclei becomes important in these cases.[26]

Phyllodes tumor

- Cellularity- high.
- Biphasic population of epithelial and stromal cells.
- Stromal cells – hypercellular, spindle-shaped cells
- Atypia of stromal cells- malignant phyllodes.
- Epithelial hyperplasia
- Bare bipolar nuclei- Numerous[12]

The clinical features along with cytological characteristics like cellularity of the stromal fragments and possible atypia of the stromal help in differentiating it from cellular fibroadenoma as both the conditions have very cellular smears which make the differentiation impossible.[26]

Shabb NS[52] in 1997 in his study found that bare bipolar nuclei are constantly present. The diagnosis of Phyllodes tumor was preferred over fibroadenoma when many Phyllode fragments were present.

Papillary Neoplasm[50]

- Cellularity- moderate to marked
- Pattern- papillary clusters, cribriform or tubular and also singly scattered
- Cells- uniform tall, columnar cells
- Nuclei- elongated, uniform
- Other cells – hemosiderin-laden macrophages.
- Myoepithelial cells- absent/few
- Bipolar cells – absent.

Infiltrating ductal carcinoma[3]

- Cellularity: Moderate to high
- Architecture: irregular clusters and single cells, crowding and overlapping noted
- Cohesion: poor.
- Nuclear atypia: Moderate to severe
- Nucleus: Large and pleomorphic.
- Pleomorphism: moderate to severe.
- Nuclear membrane: irregular.
- Nuclear chromatin: irregular distribution
- Nucleoli: prominent

Ductal carcinoma in situ (DCIS)

To distinguish between benign from malignant cells, one should not rely upon a single morphological feature. A complete cytological picture with "pattern of smear", nuclear and cytoplasmic details along with clinical and radiological findings leads to correct diagnosis[26]

Papillary carcinoma

- Cellularity- High
- Pattern – monotonous and appear clonal. Large papillary cell clusters forming arborizing arrays bearing

overlapping, palisaded cells on fibrovascular core.

- Nucleus –hyperchromatic, anisonucleosis
- Chromatin- coarse
- Nucleoli –prominent.
- Bipolar and myoepithelial cell – absent.[26]

Materials and methods

SOURCE OF DATA

The study was carried out at the department of Pathology, BLDE (Deemed to be University) Shri B.M Patil Medical College, Hospital and research center, Vijayapura from 1st December 2018 to 31st May 2020.

METHODS OF COLLECTION OF DATA.

All patients with breast lumps referred to the cytology section of the department of the Pathology Shri B.M. Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be University) Vijayapura, for aspiration cytology, were studied.

Quantification of myoepithelial cells was done unbiased with the final cytological diagnosis.

The cytohistological correlation was done whenever histopathology of the corresponding cases was available.

A total of 124 cases were studied. The breast lumps were palpated and the overlying skin was thoroughly cleaned with an antiseptic solution.

A 22 or 23 gauge needle was used with a 10 ml syringe for aspiration of material. Smears from aspirates were stained with May - Grunwald –Giemsa, Papanicolaou's stain and hematoxylin and eosin and were mounted with D.P.X. for microscopic evaluation.

Quantitative estimation of myoepithelial cells per 1000 ductal cells with at least 20hpf (x40) were scanned and areas with least overlapping of cells were selected. Number of myoepithelial cells was correlated with the cytological diagnosis.

Myoepithelial cells were counted as the cell with the same or smaller size than that of epithelial cells with bipolar shape, dense, homogeneous chromatin, smooth nuclear outline without any nucleoli, with definable cytoplasm, distributed within the epithelial clusters or scattered singly in the background.

SAMPLE SIZE

With 95% confidence level and margin of error of ±10%, a sample size of 65 subjects was allowed for the study

A Quantitative study of myoepithelial cells in fine needle aspirates from breast lumps with finite population

correction.[2]

By using the formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

where

Z= z statistic at 5% level of significance

d is the margin of error

p is the anticipated prevalence rate

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) were used. For categorical data, the number and percentage was used in the data summaries and data were analyzed by Chi-square test was used for the association, comparison of means using t-test, ANOVA and diagrammatic presentation.

The formula for the chi-square statistic used in the chi-square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The difference of the means of analysis variables between two independent groups was tested by unpaired t-test. The t statistic to test whether the means are different can be calculated as follows:

$$t = \frac{(\overline{x_1} - \overline{x_2}) - (\mu_1 - \mu_2)}{\sqrt{\frac{{s_1}^2}{n_1} + \frac{{s_2}^2}{n_2}}}$$

where $\bar{x}_1$ = mean of sample 1

$\bar{x}_2$ = mean of sample 2

n_1 = number of subjects in sample 1

n_2 = number of subjects in sample 2

$$s_1^2 = \text{variance of sample 1} = \frac{\Sigma(x_1 - \bar{x}_1)^2}{n_1}$$

$$s_2^2 = \text{variance of sample 2} = \frac{\Sigma(x_2 - \bar{x}_2)^2}{n_2}$$

ROC analysis was done and Sensitivity- specificity was calculated to check relative efficiency.

Type of study

Hospital-based, cross-sectional study.

INCLUSION CRITERIA:

All the patients with breast lump presented to the cytology section of the Department of Pathology in BLDE (Deemed to be University) Shri B.M. Patil Medical College, Hospital and Research center, Vijayapura.

EXCLUSION CRITERIA:

Nil

Results

1. Distribution of Cases according to Age

Table 2: Distribution of Cases according to Age		
Age(Years)	**N**	**%**
≤20	18	14.5
21-30	46	37.1
31-40	26	21
41-50	17	13.7
>50	17	13.7
Total	124	100

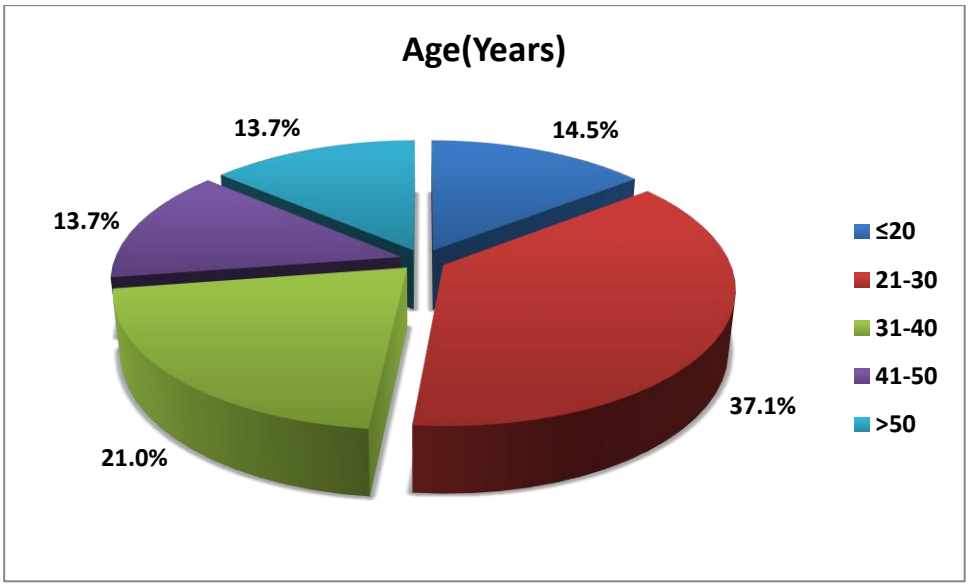

Chart 1: Distribution of Cases according to Age

124 cases were included in the present study. The cases were between 04-84 years of age. The youngest patient was 04 years old and the oldest patient was 84 years old. Maximum number of cases were in 21-30 years age group (37.1%). The details of which are mentioned in the Table 2 & Chart 1.

2. Distribution of Benign Cases according to Age

Table 3: Distribution of Benign Cases according to Age		
Age(Years)	**N**	**%**
≤20	17	17.0
21-30	46	46.0
31-40	22	22.0
41-50	10	10.0
>50	5	5.0
Total	100	100.0

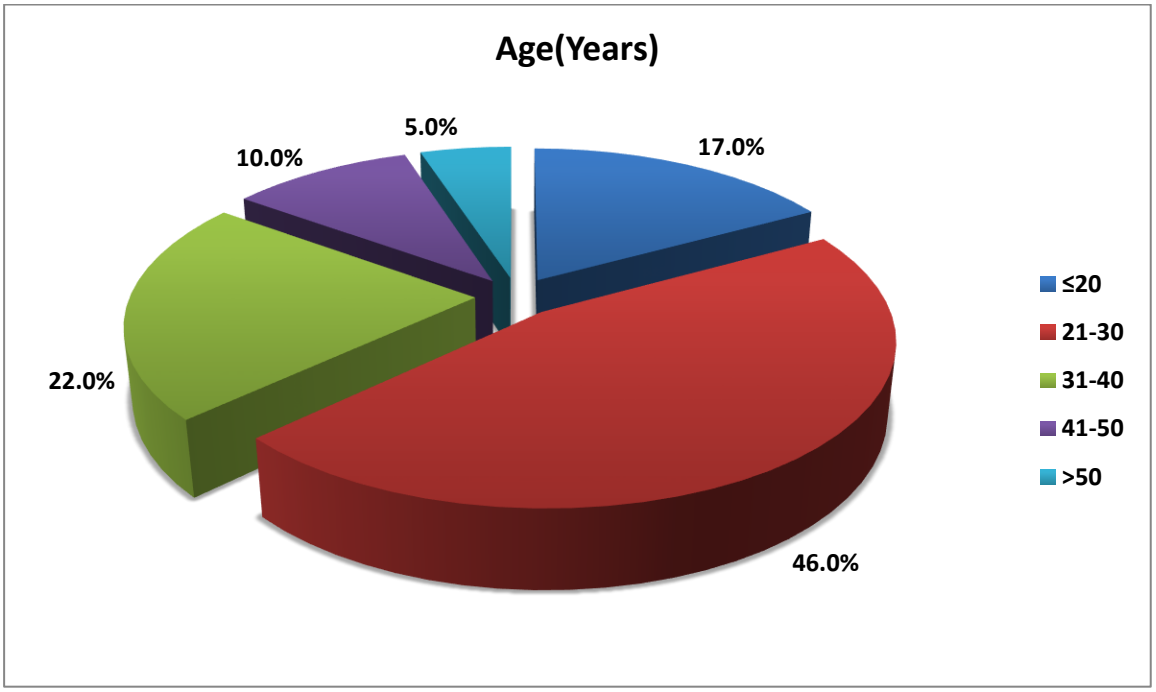

Chart 2: Distribution of Benign Cases according to Age

The age of all benign cases ranged from 12 to 80 years with majority of cases in between 21-30 years (46%) The details of which are mentioned in the Table 3 & Chart 2.

3. Distribution of Malignant Cases according to Age

Table 4: Distribution of Malignant Cases according to Age		
Age(Years)	**N**	**%**
≤20	1	4.2
21-30	0	0.0
31-40	4	16.7
41-50	7	29.2
>50	12	50.0
Total	24	100.0

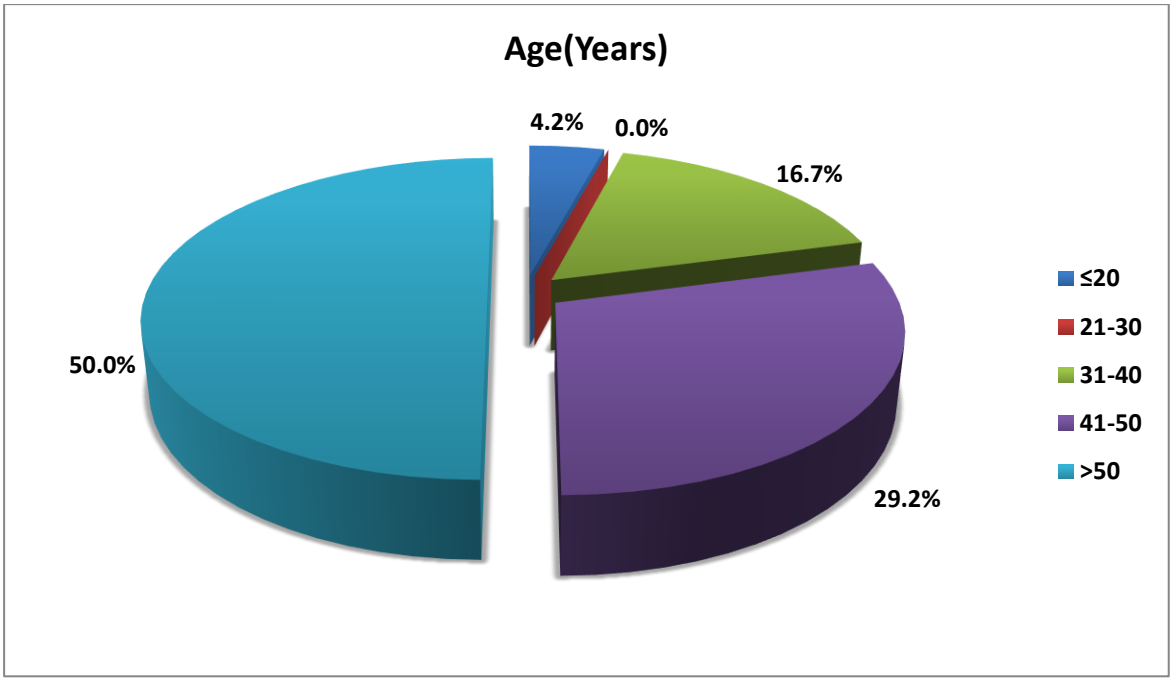

Chart 3: Distribution of Malignant Cases according to Age

The age of all malignant cases ranged from 04 to 84 years with majority of cases >50 years (50%) The details of which are mentioned in the Table 4 & Chart 3.

4. Distribution of cases according to Sex

Table 5: Distribution of cases according to Sex		
Sex	**N**	**%**
Male	10	8
Female	114	92
Total	124	100

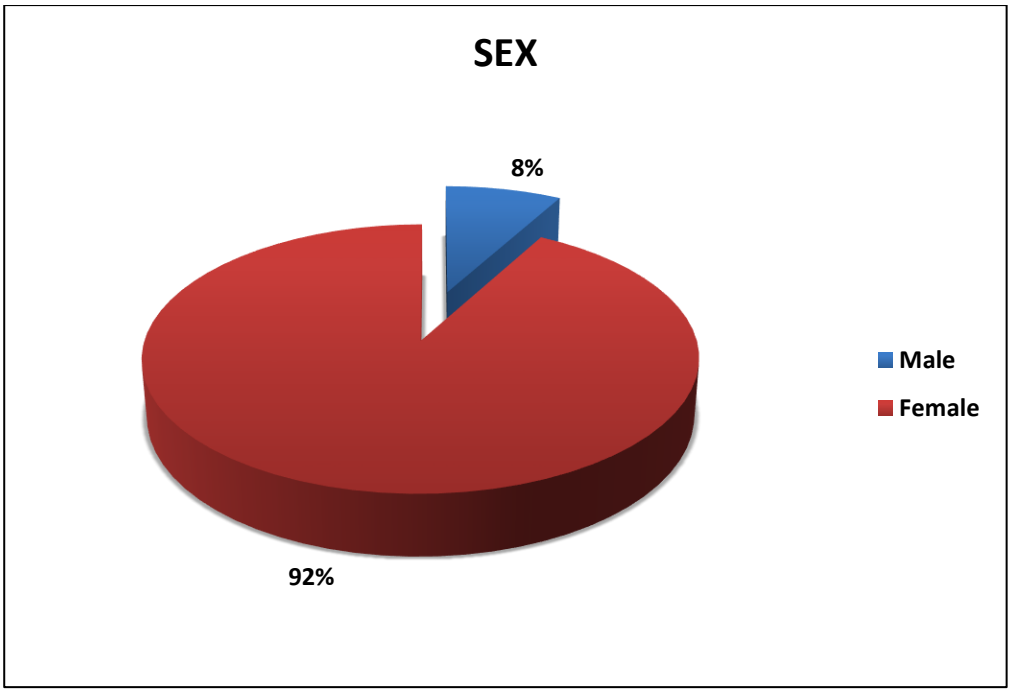

Chart 4: Distribution of cases according to Sex

Out of 124 cases, 114 patients (92%) were females and 10 patients (8%) were males. Table 5 & chart 4

5. Distribution of cases according to Laterality

Table 6: Distribution of cases according to Laterality		
Laterality	**N**	**%**
Left	59	47.6
Right	62	50
BL	3	2.4
Total	124	100

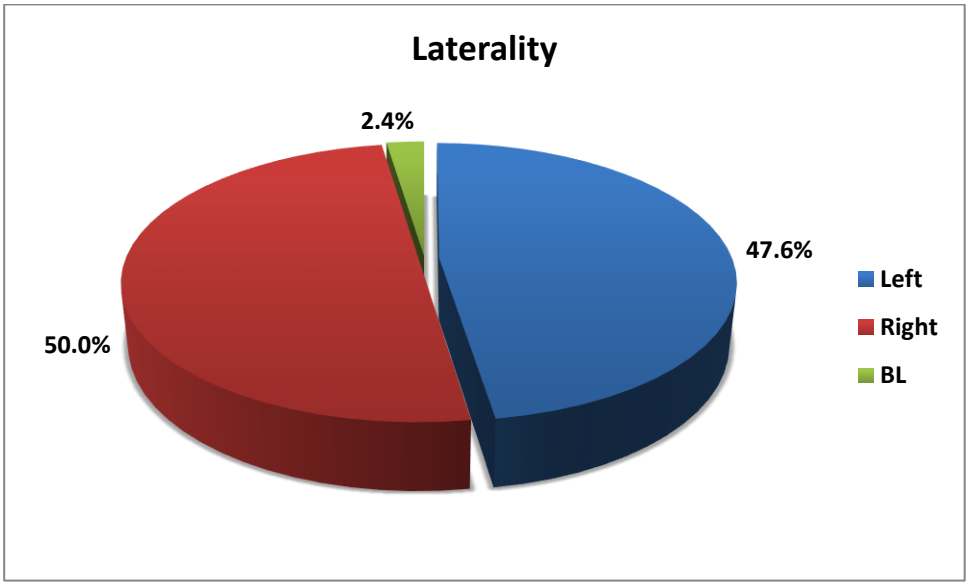

Chart 5: Distribution of cases according to Laterality

Right breast was involved more than the left breast having 62 cases (50%) and 59 cases (47.6%) respectively. Bilateral involvement of breast was noted in 3 cases (2.4%). The details of which are mentioned in the Table 6 & Chart 5.

6. Distribution of cases according to Quadrant

Table 7: Distribution of cases according to Quadrant									
Quadrant	Side						Total		p value
	Left		Right		BL				
	N	%	N	%	N	%	N	%	
All quadrants	3	5.1%	4	6.5%	0	0.0%	7	5.6%	0.002*
Central	4	6.8%	10	16.1%	3	100.0%	17	13.7%	
Inferolateral	8	13.6%	13	21.0%	0	0.0%	21	16.9%	
Inferomedial	5	8.5%	0	0.0%	0	0.0%	5	4.0%	
Superior	2	3.4%	1	1.6%	0	0.0%	3	2.4%	
Superolateral	24	40.7%	27	43.5%	0	0.0%	51	41.1%	
Superomedial	13	22.0%	7	11.3%	0	0.0%	20	16.1%	
Total	59	100.0%	62	100.0%	3	100.0%	124	100.0%	

Note: * significant at 5% level of significance (p<0.05)

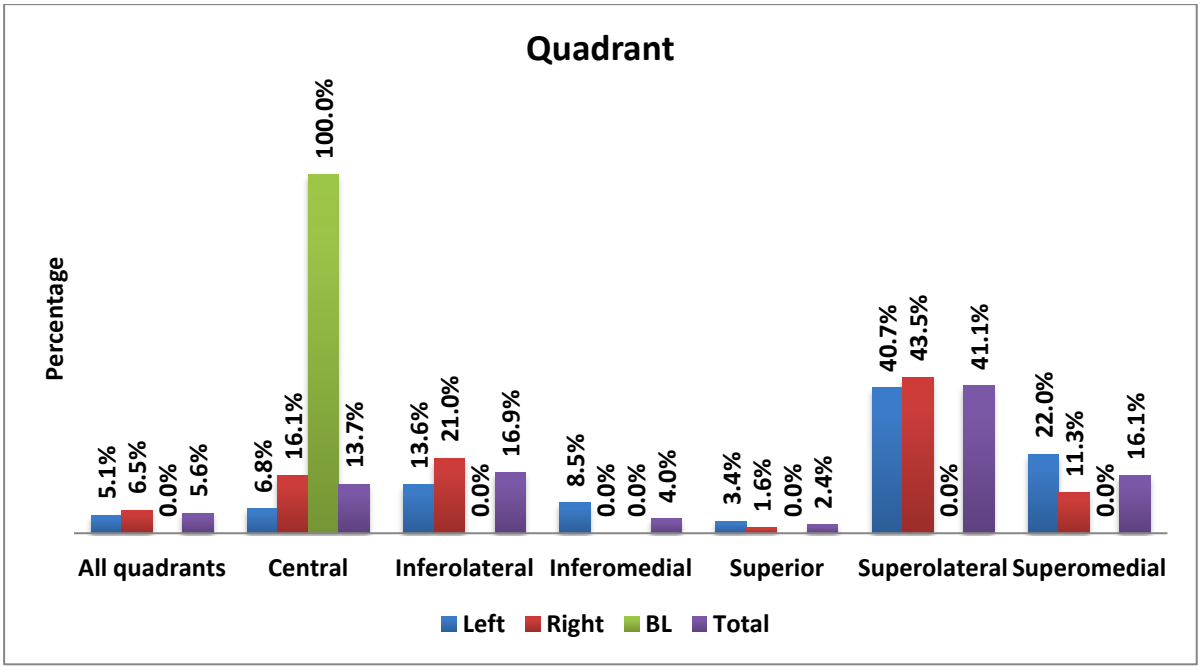

Chart 6: Distribution of cases according to Quadrant

Out of 59 cases of left breast lumps, majority were in superolateral quadrant (24 cases, 40.7%) followed by

superomedial (13 cases, 22.0%), Followed inferolateral (8 cases, 13.6%) and inferomedial (5 cases each, 8.5%). Out of 62 cases of right breast, the majority (27 cases, 43.5) were in superolateral quadrant, followed by inferolateral (13 cases, 21.0%), followed by central (10 cases, 16.1%), followed by superomedial quadrant (7 cases, 11.3%). Overall most common quadrant involved was superolateral (51 cases, 41.1%).

Out of 124 cases, 59 cases (47.58%) were in left breast, 62 cases (50%) were in right breast and 2.4% were central. Details of which are mentioned in Table 7 and Chart 6.

7. Distribution of cases according to Single/Multiple breast lumps

Table 8: Distribution of cases according to Single/Multiple breast lumps		
Single/Multiple	**N**	**%**
Multiple	6	4.8
Single	118	95.2
Total	124	100

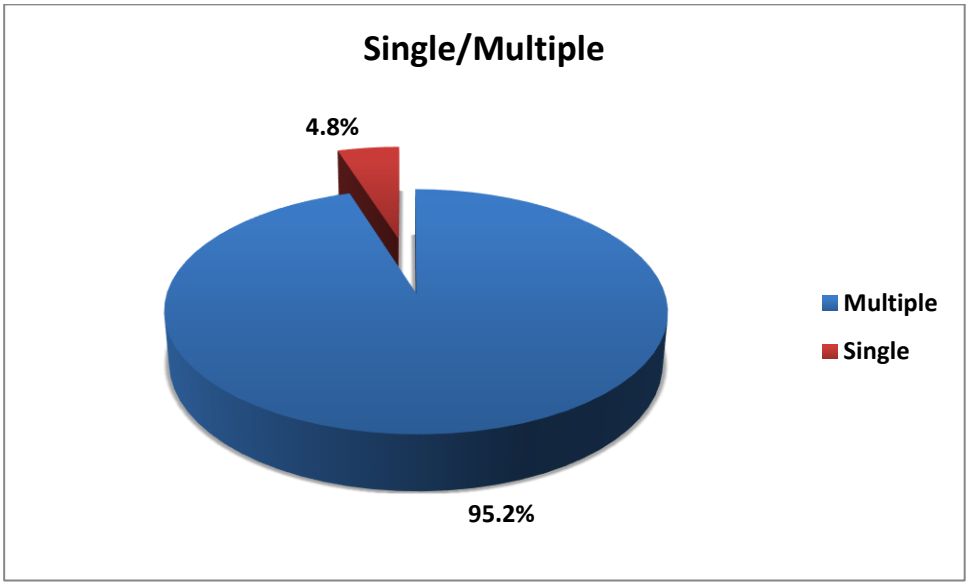

Chart 7: Distribution of Cases according to Single/Multiple breast lumps

Out of 124 cases, 118 cases (95.2%) had single lump in the breast and 6 cases (4.8%) has multiple (2) lumps in the affected breast. Table 8 & chart 7.

8. Distribution of cases according to Benign/Malignant

Table 9: Distribution of cases according to Benign/Malignant		
Benign/Malignant	**N**	**%**
Benign	100	80.6
Malignant	24	19.4
Total	124	100.0

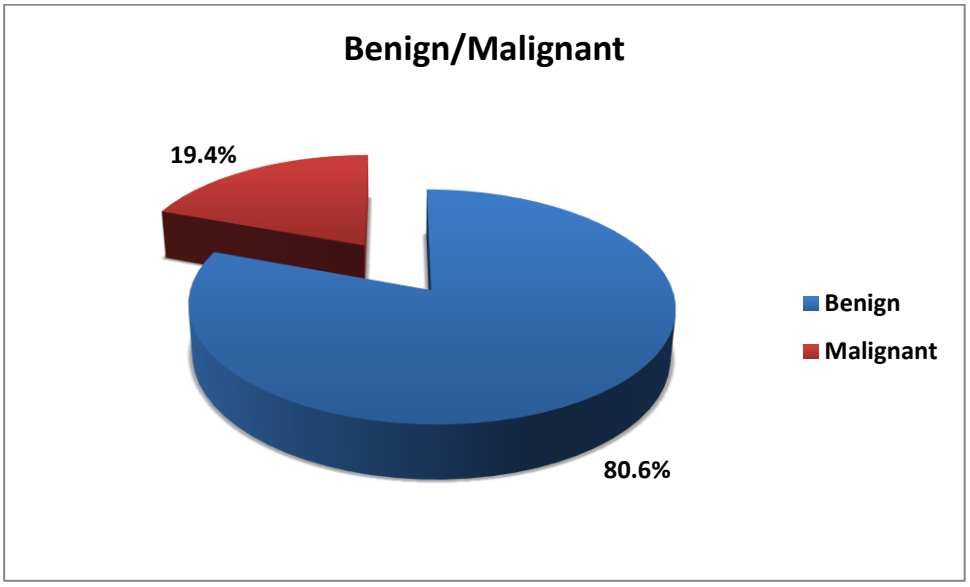

Chart 8: Distribution of cases according to Benign/Malignant

Out of 124 cases, 100 cases (80.6%) were benign and 24 cases (19.4%) were malignant. Table 9 & chart 8

9. Distribution of cases and ME cells according to Cytological Diagnosis

Table 10: Distribution of cases and ME cells according to Cytological Diagnosis						
				ME cells		
Diagnosis cytology		**N**	**%**	**Mean**	**SD**	**P value**
Benign Non Neoplastic	Acute mastitis	2	1.6	215.0	21.2	
	Acute Suppurative Inflammation	5	4	201.4	53.5	
	Benign cystic lesion of breast	2	1.6	0.0	0.0	
	Epidermal cyst	1	0.8	0.0	0.0	
	Galactocele	2	1.6	0.0	0.0	
	Granulomatous mastitis	3	2.4	325.0	25.0	
	Gynecomastia	6	4.8	121.7	160.1	
	Epithelial Hyperplasia	25	20.5	291.1	142.7	
	Simple cyst with suppurative inflammation	1	0.8	0.0	0.0	
	Total	**47**	**37.9**	**156.8**	**141.9**	
Benign Neoplastic	Benign phyllodes tumor	1	0.8	9.0	0.0	<0.001*
	Fibroadenoma	50	40.3	369.6	76.1	
	Papillary Neoplasm	2	1.6	25.0	7.1	
	Total	**53**	**42.7**	**352.1**	**45.2**	
Malignant	Ca with prominent mucinous features/ Ductal ca with mucinous change	1	0.8	0.0	0.0	
	Ductal carcinoma	5	4	4.0	5.7	
	High grade invasive carcinoma	1	0.8	0.0	0.0	
	Infiltrating Ductal Carcinoma	3	2.4	0.0	0.0	
	Invasive carcinoma NST	12	9.6	4.3	7.1	
	Papillary carcinoma	2	1.6	2.0	2.8	
	Total	**24**	**19.4**	**3.1**	**5.7**	
	Total cases	124	100			

Note: * significant at 5% level of significance ($p<0.05$)

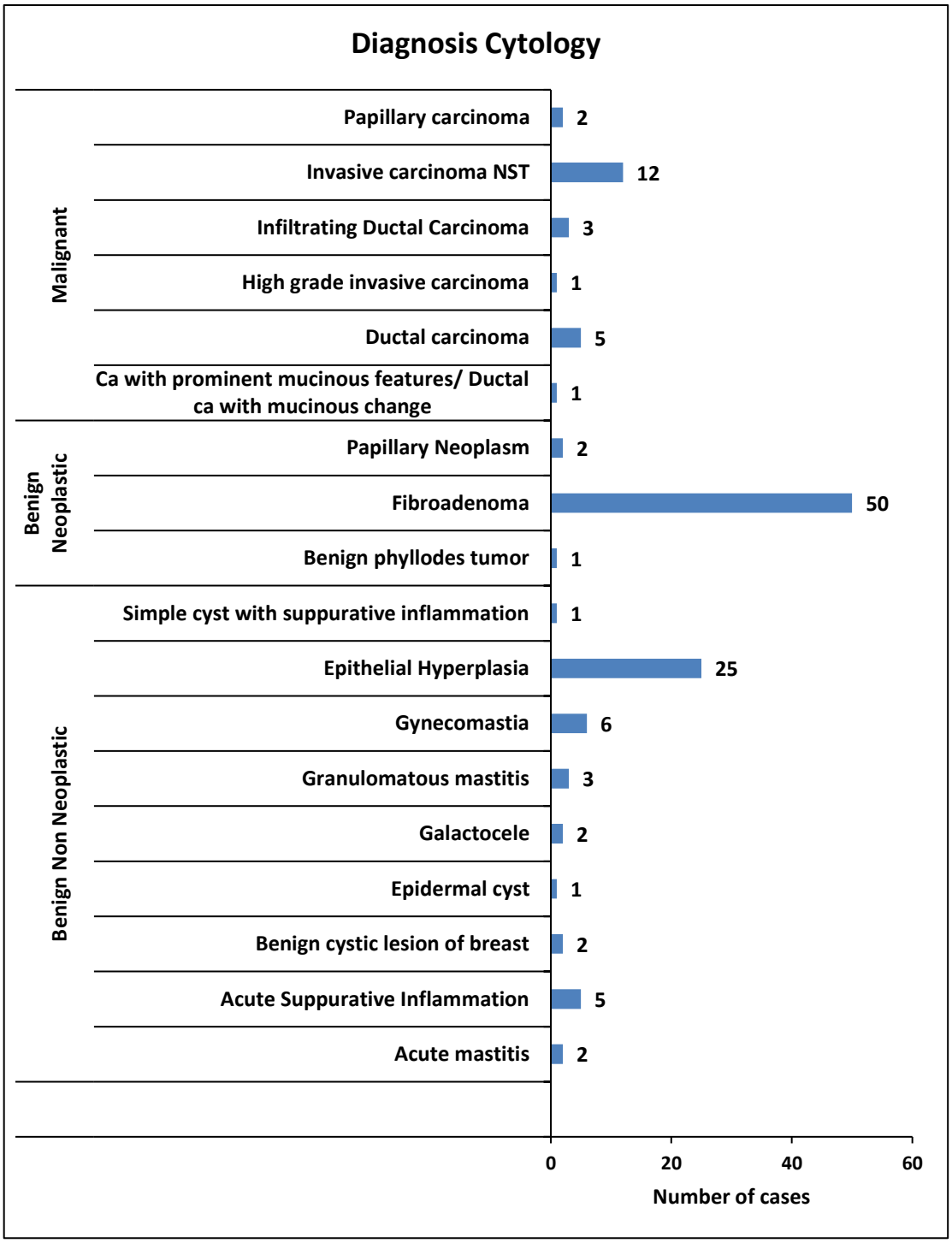

Chart 9: Distribution of cases according to Cytology Diagnosis

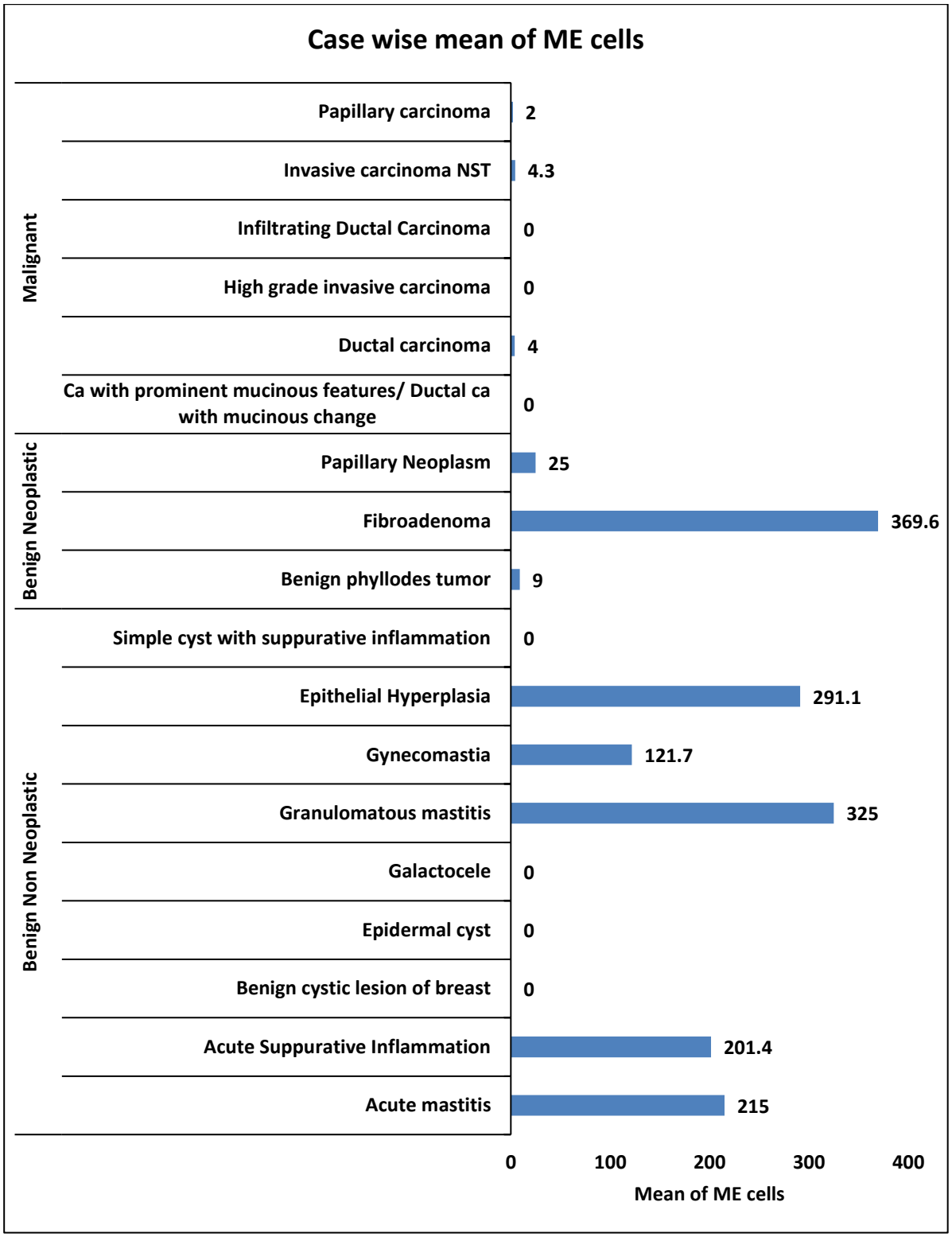

Chart 10: Case wise distribution of No. of ME Cells/1000 ductal cells

Out of 124 cases, maximum cases (100) were benign, among these benign cases, 47 cases benign non-neoplastic and 53 were of benign neoplastic lesions. There were 25 cases of epithelial hyperplasia(20.5%), 50 cases (40.3%) of fibroadenoma and out of 24 malignant cases, 12 cases (9.6%) were of Invasive carcinoma NST. The details of which are mentioned in the Table 10 & Chart 9.

Myoepithelial cells were counted as cells with same or smaller size than that of epithelial cells with bipolar shape, dense, homogeneous chromatin, and smooth nuclear outline without any nucleoli, with definable cytoplasm, distributed within the epithelial clusters or scattered singly in the background.

Among benign non-neoplastic lesions, granulomatous mastitis had the maximum number of ME cells i.e. 325 $\pm$ 25, followed by epithelial hyperplasia (291.1 ± 142.7), followed by acute mastitis (215 $\pm$ 21.2). Among benign cases, fibroadenoma had highest no. of Me cells (369.6 ± 76.1). The papillary carcinoma had very less number of myoepithelial cells with a mean of 2.0 $\pm$ 2.8. Invasive ductal carcinoma and high grade invasive carcinoma had 0 ME cells.

Details of which are mentioned in Table 10 and Chart 10.

10. Presence/ Absence of No. of ME cells in Benign/Malignant cases

Table 11: Presence/ Absence of No. of ME cells in Benign/Malignant cases					
No. of ME	**Benign**		**Malignant**		**p value**
	N	**%**	**N**	**%**	
Present	86	86%	7	29%	<0.001*
Absent	14	14%	17	71%	
Total	100	100%	24	100%	

Note: * significant at 5% level of significance (p<0.05)

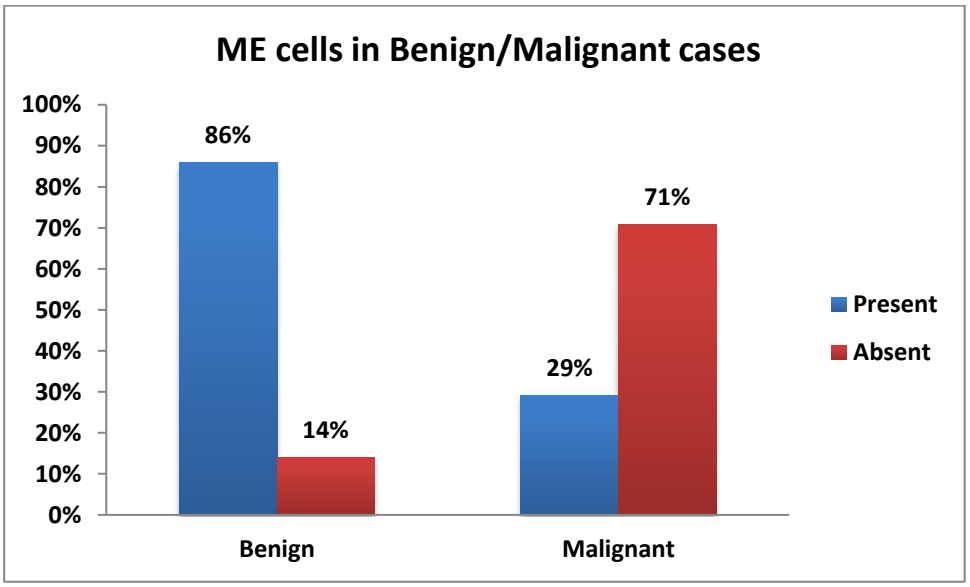

Chart 11: Presence/ Absence of No. of ME cells in Benign/Malignant cases

Among 100 benign cases, ME cells were present in 86 cases (86%) and absent only in 14 cases (14%). Among 24 malignant cases ME cells were absent in 17 cases (71%) and present only in 7 cases (29%). The presence/absence of ME cells was significant in benign and malignant lesion. (Table 11, Chart 11).

11. Mean of ME Cells in Benign/Malignant

Table 12 : Mean of ME Cells in Benign/Malignant					
Mean of ME Cells	Benign		Malignant		p value
	Mean	SD	Mean	SD	
	287.3	163.6	3.1	5.7	<0.001*

Note: * significant at 5% level of significance (p<0.05)

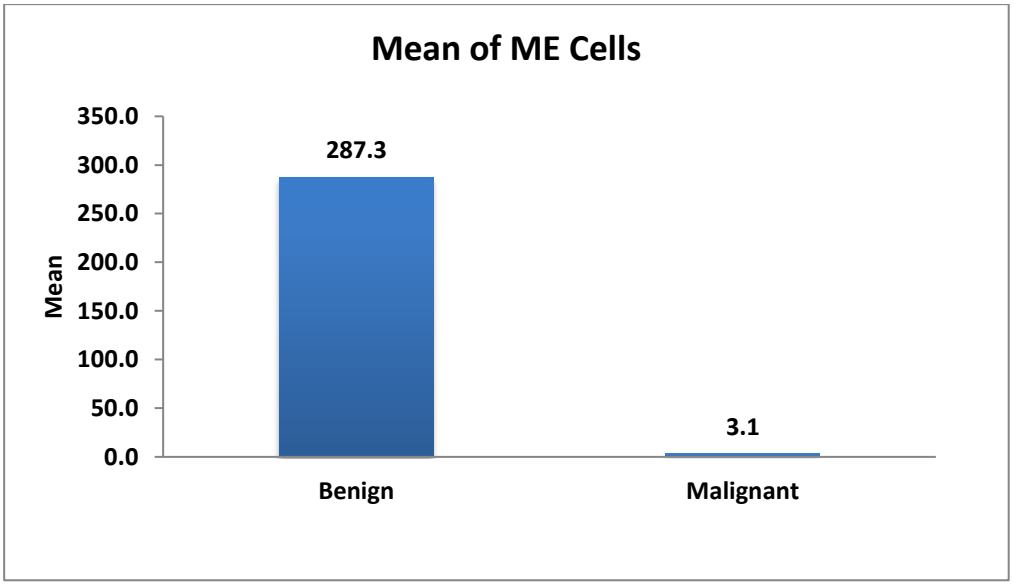

Chart 12: Mean of ME Cells in Benign/Malignant

Table 13: Mean of ME Cells in Benign non-neoplastic, Benign neoplastic & Malignant lesions			
Diagnosis	No. ME		p value
	Mean	SD	
Benign Non-Neoplastic	156.8	141.9	<0.001*
Benign Neoplastic	352.1	45.2	
Malignant	3.1	5.7	

Note: * significant at 5% level of significance (p<0.05)

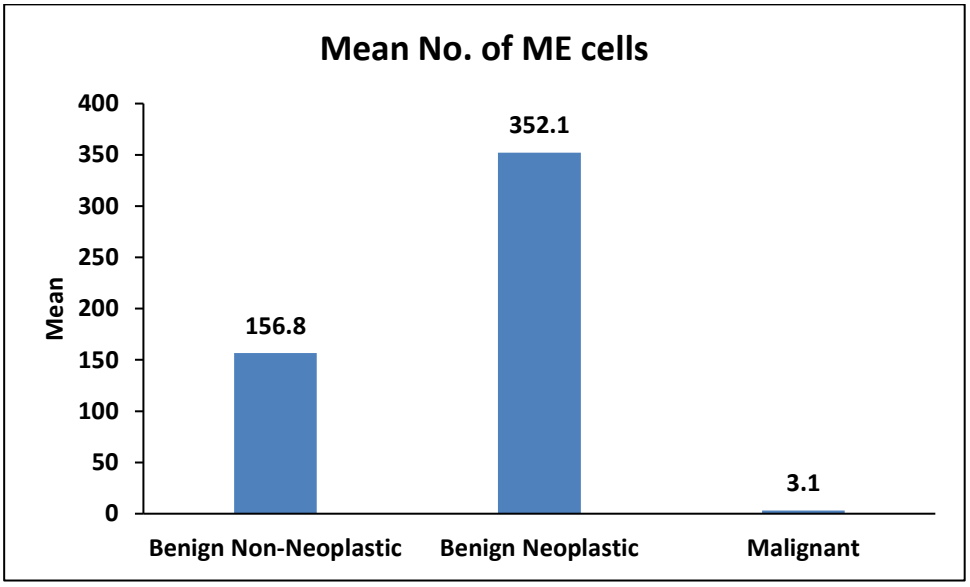

Chart 13: Mean of ME Cells in Benign non-neoplastic, Benign neoplastic & Malignant lesions

The difference of mean of ME cells in inflammatory lesions and others, benign and malignant lesions were significant (<0.001). Table 12 & Chart 12. Also the mean ME cells in benign non-neoplastic lesion was 156.8 ± 141.9, benign neoplastic lesions was 352.3 ± 45.2 whereas mean ME cells in malignant lesions was 3.1 ± 5.7. Details of which are mentioned in Table 13 and chart 13.

12. Test Characteristics

Table 14: Test Characteristics	
	No. of ME Cells
Sensitivity	86.0%
Specificity	70.8%
PPV	92.5%
NPV	54.8%
Accuracy	83.1%

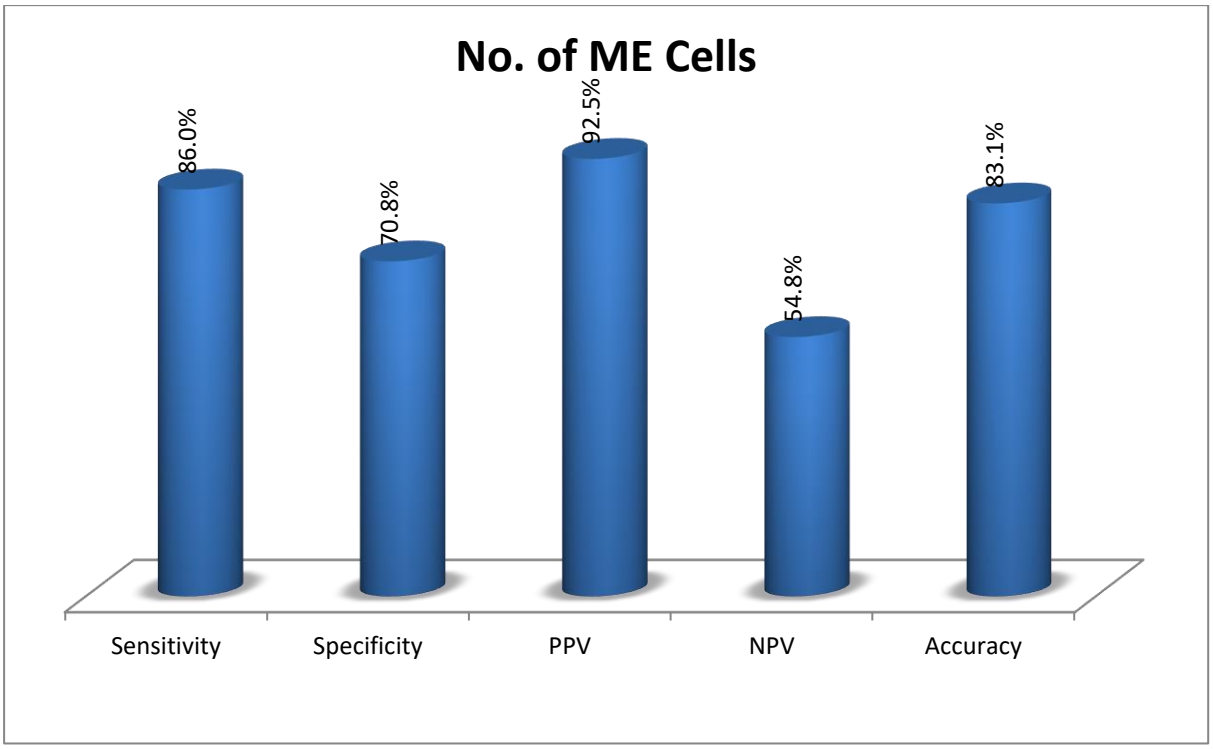

Chart 14: Test Characteristics

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ME cells, benign pairs and bipolar nuclei are 86%,70.8%, 92.5%, 54.8% and 83.1% respectively. Details are mentioned in Table 14 and Chart 14.

13. TP,TN,FP,FN OF ME CELLS

Table- 15 : TP,TN,FP,FN OF ME CELLS	
	No. of ME Cells
TP (true positive)	86
FN (false negative)	14
FP (false positive)	7
TN (true negative)	17

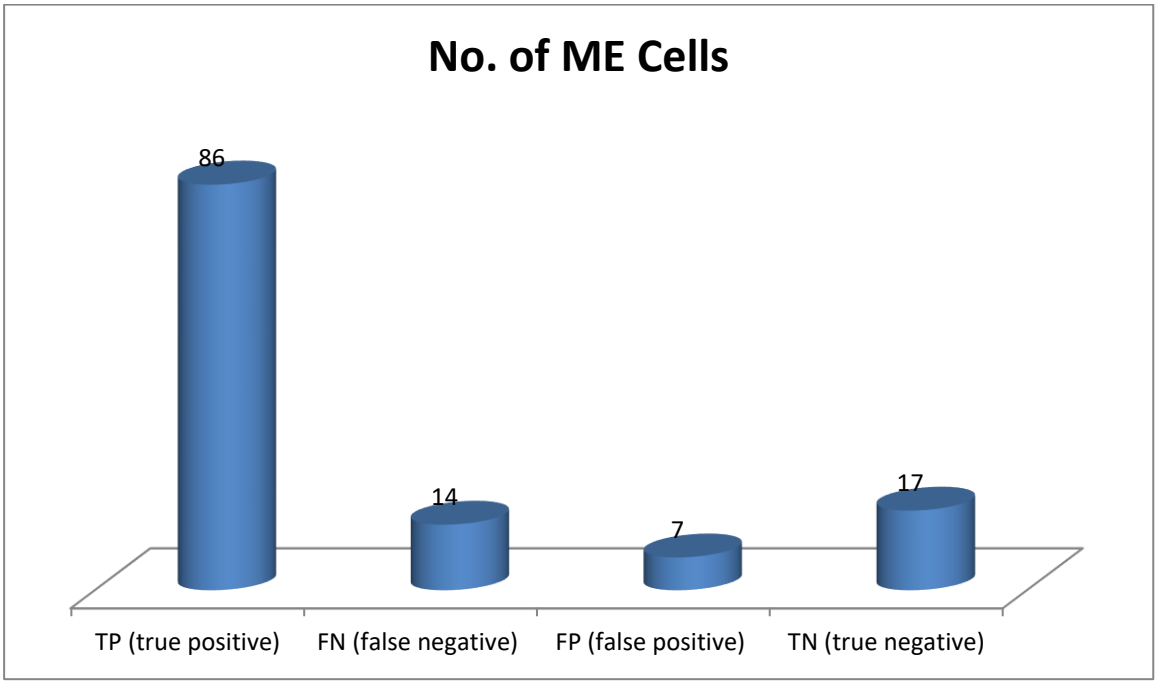

Chart 15: TP, FN, FP, TN

True positivity of ME cells is 86, whereas false positivity is 7. Details of which are mentioned in Table 15 and Chart 15.

14. Cytohistological correlation showing Concordance and Discordance

Table 16: Cytohistological correlation showing Concordance and Discordance		
Concordance	**N**	**%**
Concordant	25	83.3
Discordant	5	16.7
Total	30	100.0

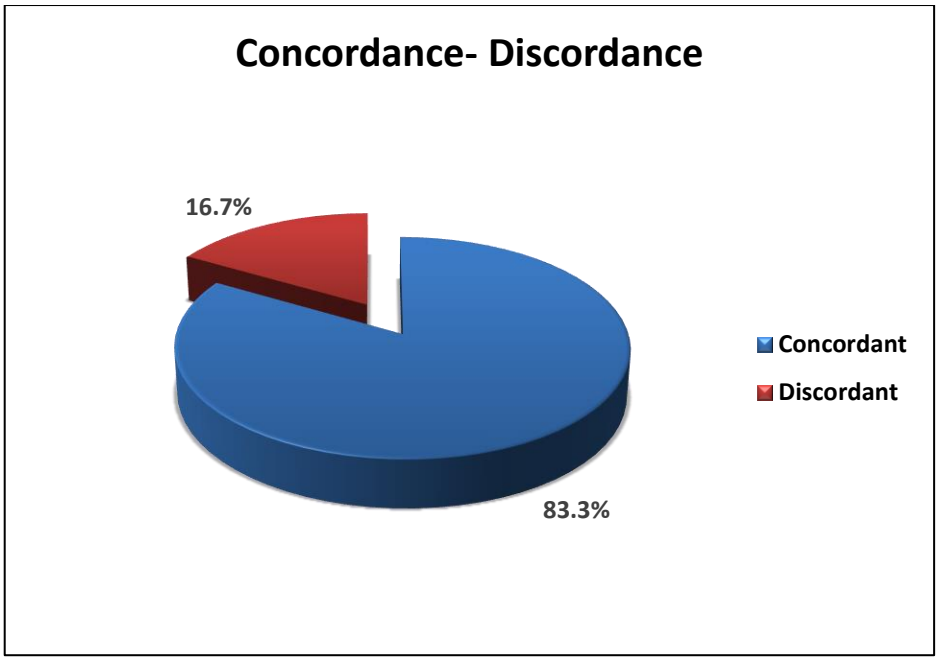

Chart 16: Cytohistological correlation showing Concordance and Discordance

Out of 124 total cases, histopathology correlation was available for 30 cases, out of which 25 cases (83.3%) were concordant and 5 cases (16.7%) were discordant. Details are mentioned in Table 16 and Chart 16.

15. Cytohistological correlation in Benign & Malignant cases

Table 17: Cytohistological correlation in Benign & Malignant cases			
	Benign (n=100)	Malignant(n=24)	Total(n=124)
Histopathology Available	19 (19%)	11(45%)	30
Concordant	15	10	25
Discordant	4	1	5

Out of 100 benign cases, histopathology correlation was available for 19 cases (19%) out of which 15 were concordant. Out of 24 malignant cases, histopathology was available for 11 cases (45%), out of which 10 were concordant. (Table 17)

16. Cytohistological correlation: Case Wise

Table 18 : Cytohistological correlation: Case Wise					
		Cases	Histopathology Correlation		
Diagnosis cytology		**Total**	**Available**	**Concordant**	**Discordant**
Benign Non-Neoplastic	Acute mastitis	2	0	0	0
	Acute Suppurative Inflammation	5	0	0	0
	Benign cystic lesion of breast	2	0	0	0
	Epidermal cyst	1	0	0	0
	Galactocele	2	0	0	0
	Granulomatous mastitis	3	1	1	0
	Epithelial Hyperplasia	25	3	1	2
	Gynecomastia	6	1	1	0
	Simple cyst with suppurative inflammation	1	0	0	0
Benign	Papillary Neoplasm favoring benign lesion	2	0	0	0
	Benign phyllodes tumor	1	0	0	0
	Fibroadenoma	50	14	12	2
Malignant	Papillary carcinoma	2	2	1	1
	Ca with prominent mucinous features/ Ductal ca with mucinous change	1	0	0	0
	Ductal carcinoma	5	2	2	0
	High grade invasive carcinoma	1	1	1	0
	Infiltrating Ductal Carcinoma	3	1	1	0
	Invasive carcinoma NST	12	5	5	0
Total		124	30	25	5

Out of 50 cases of fibroadenoma, 14 cases had histopathology correlation and out of which 12 were concordant with and 2 was discordant. Also out of 12 cases of invasive carcinoma NST, 5 cases had histopathology correlation and all 5 were concordant. Details of which are mentioned in Table 18.

Illustrations

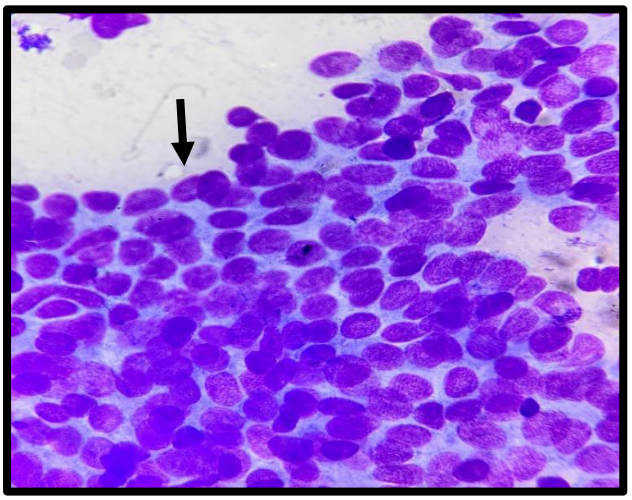

Fig 1: Ductal epithelial cells in sheets 1000x Geimsa

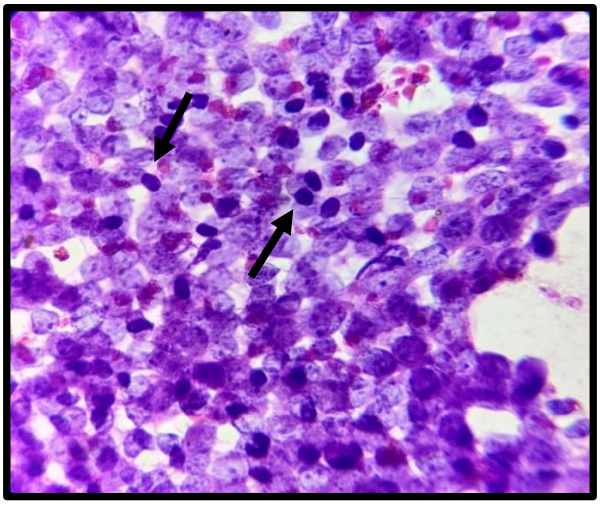

Fig 2: ME cells Fibroadenoma 1000x PAP

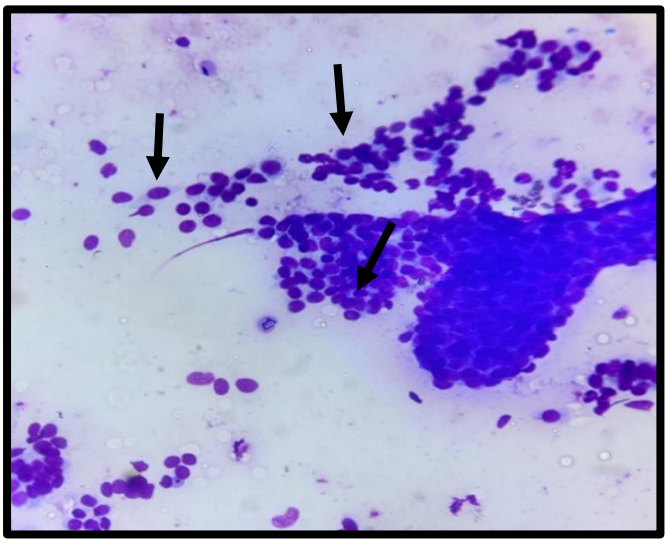

Fig 3: Fibroadenoma showing ductal cells and ME cells 400x Geimsa

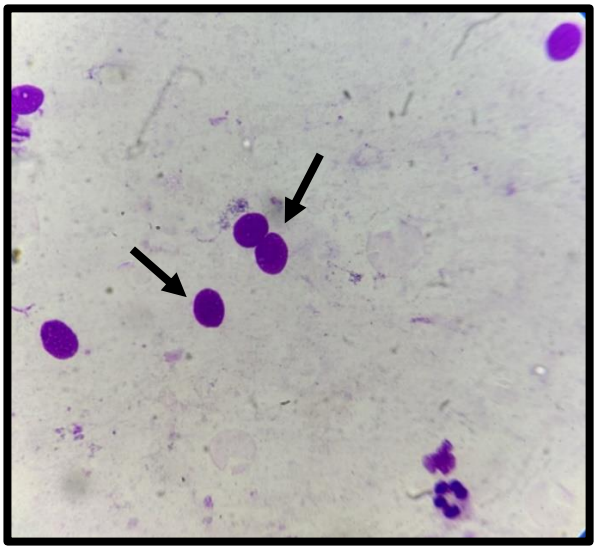

Fig 4: Benign pairs and Bipolar nuclei 1000x Geimsa

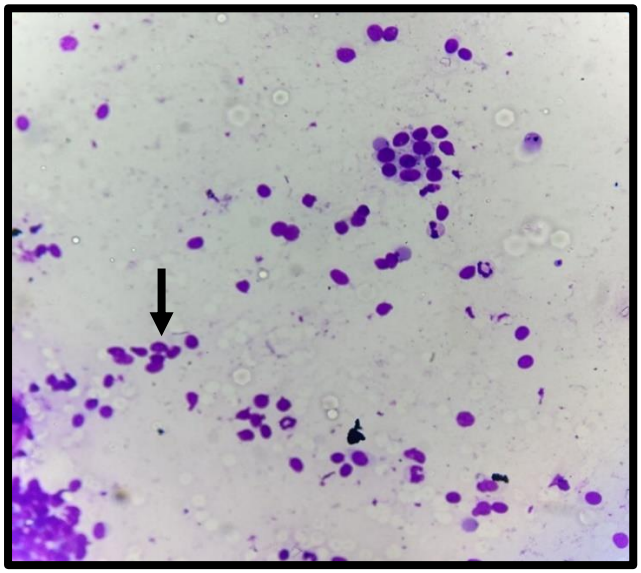

Fig 5: Gynaecomastia showing ME cells **400x Geimsa**

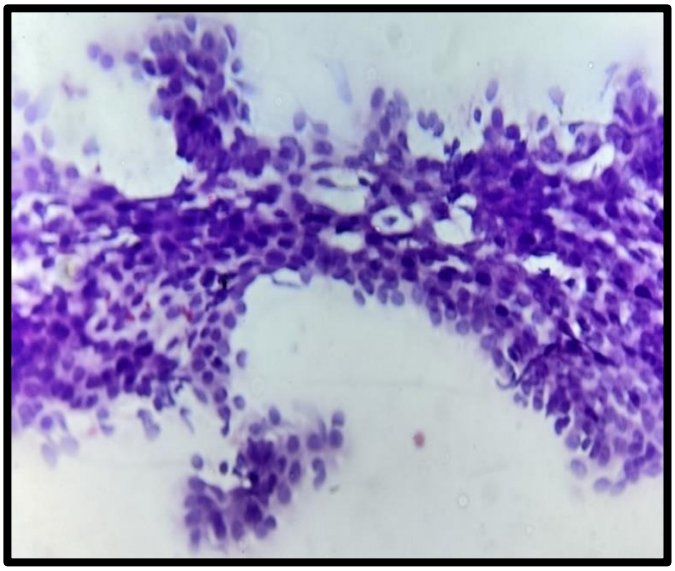

Fig 6: Aypical Ductal hyperplasia **400x PAP**

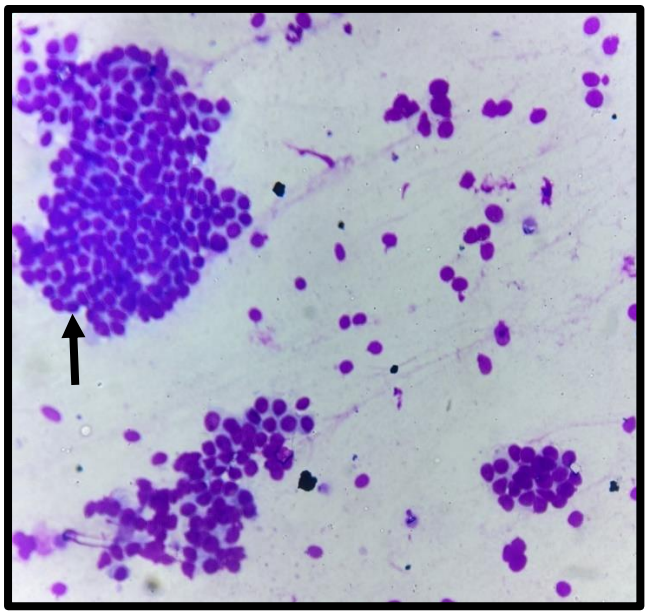

Fig 7: Benign ductal proliferation without atypia showing ME cells **400x Geimsa**

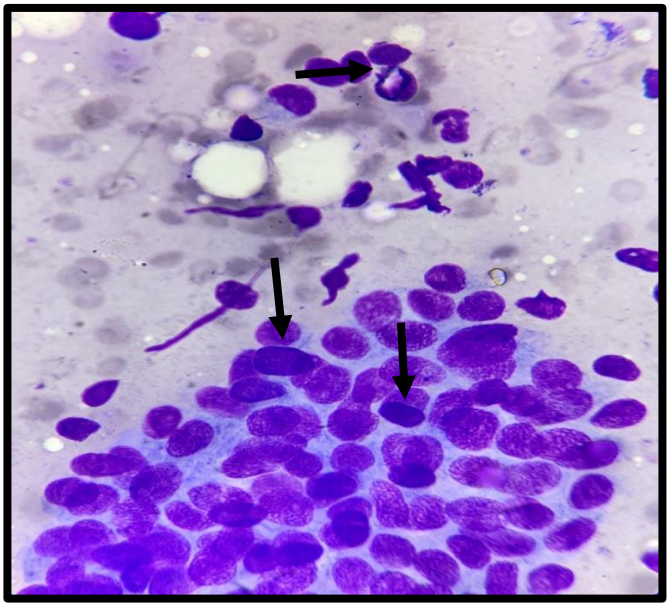

Fig 8: Benign ductal proliferation without atypia showing ME cells **1000x Geimsa**

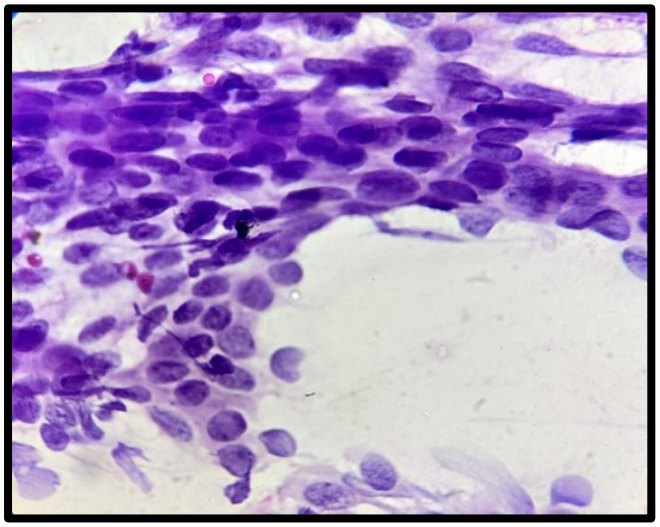

Fig 9: Benign Pyllodes tumor **1000x PAP**

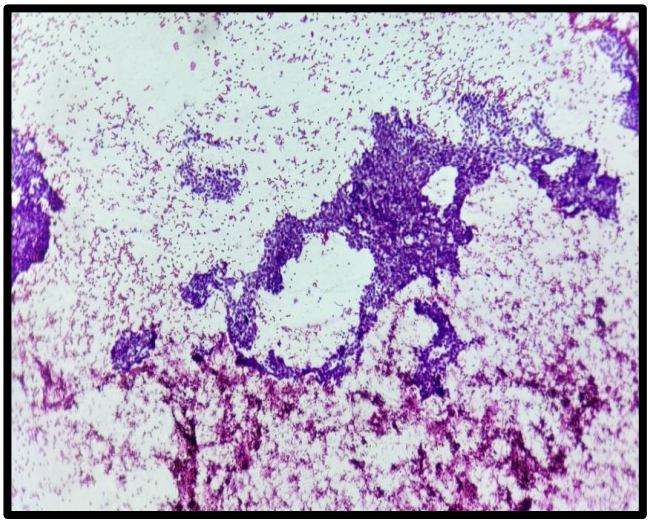

Fig 10: Papillary Neoplasm favouring benign lesion **100x PAP**

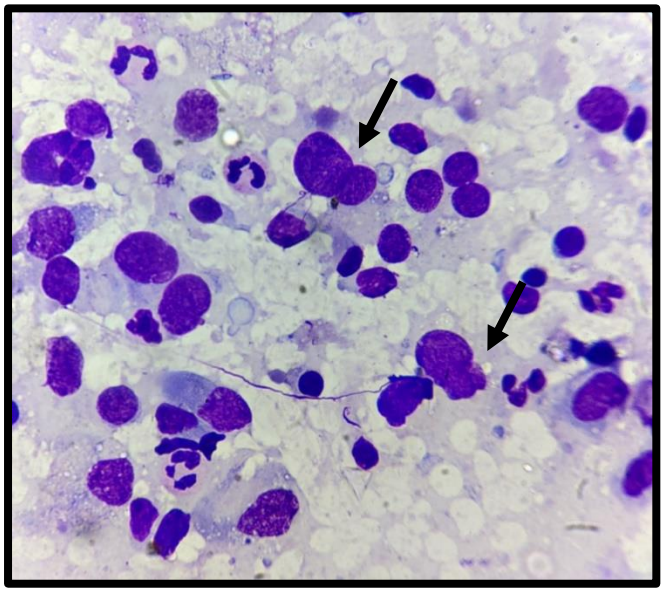

Fig 11: Infiltrating Ductal Carcinoma. Note the nuclear atypia, pleomorphism, Irregular nuclear membrane and absence of ME cells **1000X Geimsa**

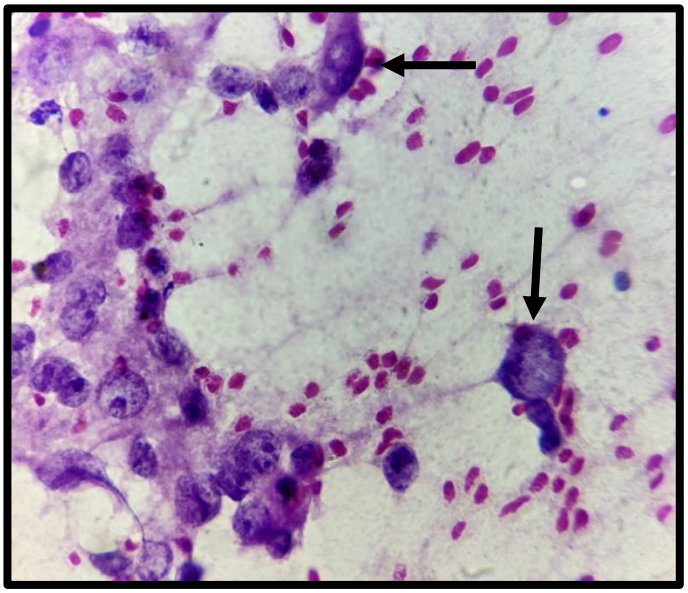

Fig 12: Infiltrating Ductal Carcinoma showing pleomorphism & absence of ME cells **1000x PAP**

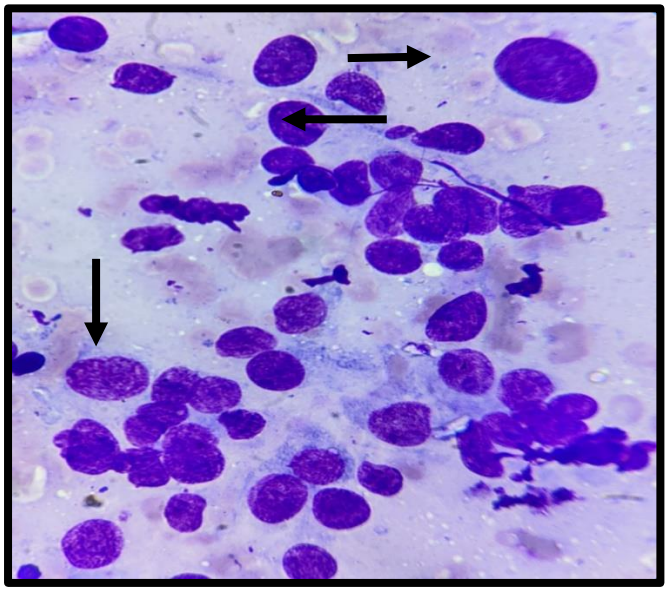

Fig: 13 A

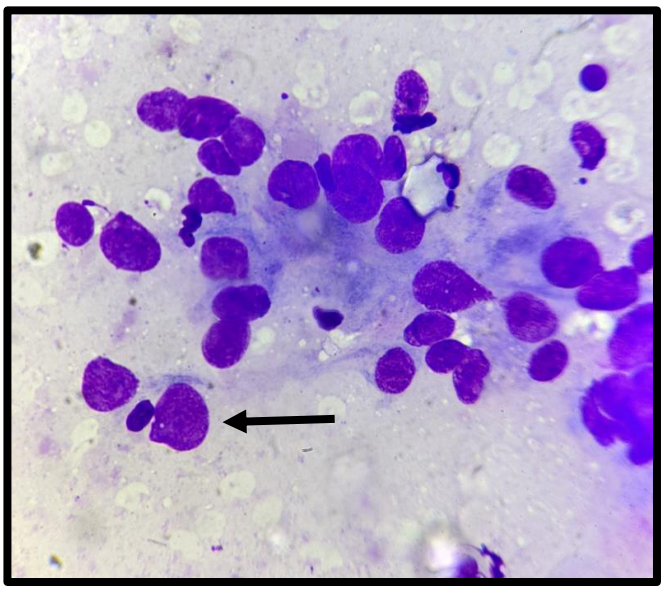

Figure 13 B

Fig 13 A & 13 B: High Grade Invasive Carcinoma. Note the severe nuclear atypia, pleomorphism, Irregular nuclear membrane & absence of ME cells **1000X Geimsa**

Discussion

FNA is used to assess palpable breast masses and cysts as well as non-palpable mammographic deviations.[50] FNA does not necessitate anesthesia or hospitalization, and it takes a few minutes to perform. So it is the most rapid and most versatile for diagnosis of a malignant tumor and it also permit the patient to participate in the choice of therapies that lead to preservation of the breast [i.e., local or segmental resection (lumpectomy)], followed by radiotherapy and chemotherapy. So FNA saves anxiety, time, and money. FNA is principally valuable when the level of clinical suspicion is low, which can either be because of the type of aberration involved or the young age of the patient. Under these circumstances, the probabilities that the lesion will be benign are very high, and thus the health care provider may be hesitant to vouch for a traumatic and costly tissue biopsy

Myoepithelial cells are identifiable as small, spindly, occasionally curved, dark homogeneous bipolar nuclei with very scanty cytoplasm that may either appear singly or adhere to epithelial fragments. In very well processed, air-dried aspiration smears, slender wisps of extended cytoplasm at both ends of the oval nucleus may be observed occasionally. The presence and acknowledgment of myoepithelial cells are of major diagnostic significance[53]

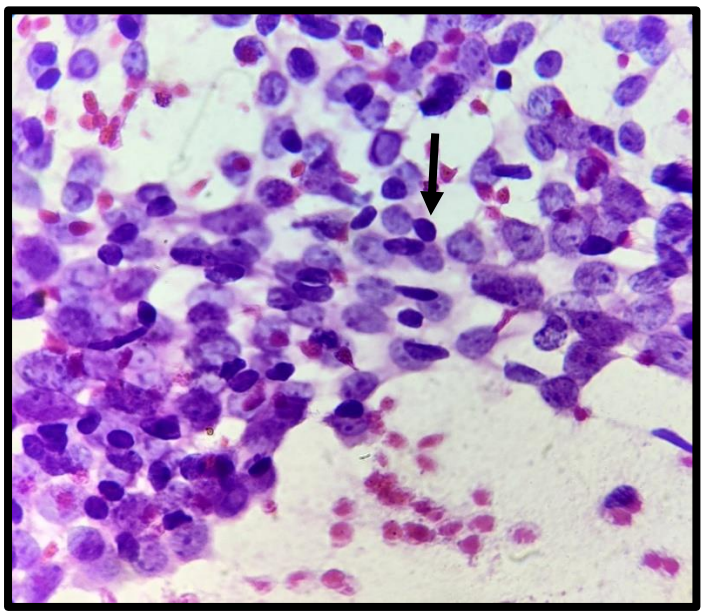

Figure 14A

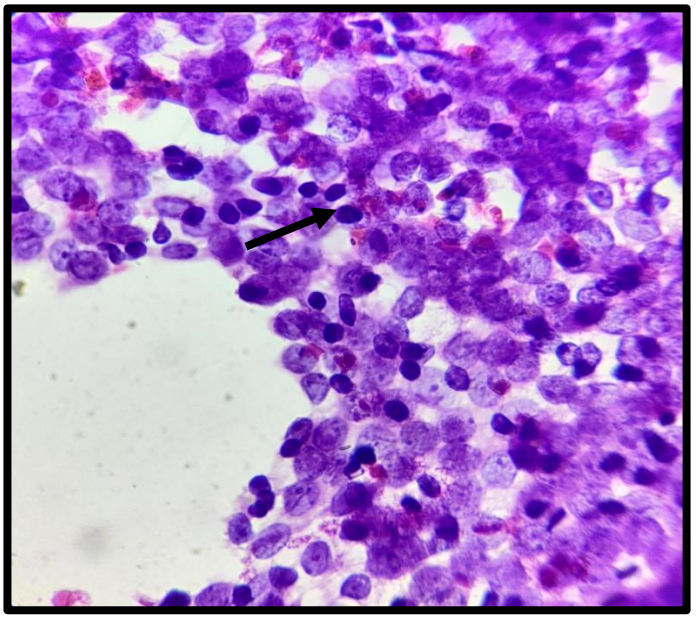

Figure 14B

Fig: 14A & 14B ME cells 1000x PAP

The presence of myoepithelial cells has been documented as a prominent feature of benign breast disease which distinguishes it from malignant lesions. However, its existence has rarely been studied.[2]

Among benign cases, fibroadenoma had the maximum number of ME cells i.e. 369.6 ± 76.1. Among benign non-neoplastic lesion, granulomatous mastitis had maximum no. of ME cells (325 ± 25). The papillary carcinoma had very less number of myoepithelial cells with a mean of 2.0 ± 2.8. Invasive ductal carcinoma and High grade invasive carcinoma had 0 myoepithelial cells. (Table 10)

Thus the difference in the number of myoepithelial cells was not much between some benign lesions but the myoepithelial cells were markedly decreased or seldom found in malignant lesions. Also there was significant difference of mean of ME cells between benign non-neoplastic and benign neoplastic lesions. P value between the benign and malignant cases & benign neoplastic and Benign non-neoplastic cases for the average number of myoepithelial cells was found to be significant ($p<0.001$). The present study also showed insignificant differences for the number of myoepithelial cells between various benign conditions except for: Epithelial hyperplasia (291.1 ± 142.7) and papillary neoplasm favoring benign lesion (ME cells=25.0±7.1), fibroadenoma (ME cells=391 ± 86.2) and gynecomastia (ME cells=121.7±160.1), benign phyllodes tumor (ME cells9±0) and

acute mastitis (ME cells=215.0±21.2.

In a study done by Pattari SK et al[2] in 2008, he found the mean number of ME cells per 1000 ductal cells on cytology smears in malignant lesions was 5.1 ± 5.5, in carcinoma in-situ was 30.8 ± 25, Proliferative breast disease was 28.3 ± 20.2, and in benign breast lesions was 38.4 ± 38.8. His study favors our study.

Agarwal P et al[41] in 2017 studied 50 cases in her study and found out that ME cells were maximum in cases of benign breast disease with non-specific descriptive (359.1) followed by fibroadenoma (161.1) and granulomatous mastitis (92). No. of ME cells were very less in ductal carcinoma with a mean of 5.8, and there was statistically significant difference between the mean of myoepithelial cells/1000 ductal cells in benign and malignant lesions. Our findings also matches the findings of her study.

The sensitivity, specificity and accuracy of ME cells to detect benign lesion is 86%, 70.8% and 83.1% respectively. (Table 14)

In our study of 124 cases, ME cells were maximally present in benign cases (86 cases, 86%) only 7 malignant cases (29%). The presence/absence of ME cells was significant in benign and malignant lesion. (Table 11).

Andra R et al[62] in 2000, also found the presence of ME cells more in Benign cases (94%) than in malignant cases(17%)

Bofin et al[61] in 2004, found myoepithelial cells in 87% of benign cases and 26% of malignant cases. He only labelled the presence or absence of ME cells in breast lesions and found that myoepithelial cells were absent or markedly reduced in invasive carcinomas. Their results are similar to the results of our study.

Choi YD et al[59] in 2006, also found similar results in his studies. Hence their findings are in favor of our study.

Also it was found that the cases under our study were between 04-84 years of age. Maximum number of cases were in age group of 21-30 years (37.1%). (Table 2).

Hussain et al[54] in 2005, studied 50 patients and found the age distribution was between 15-65 years and the maximum patients were seen in age group of 31-40 yrs**.**

Homesh et al[55] in 2005, also revealed similar findings having maximum number of cases between the age group of 22-44 years.

Khemka et al[56] in 2009, found in his study that The maximum number of women was in the age group of 40-44

years, followed by 30-34 years.

The age of all benign cases ranged from 12 to 80 years with majority of cases in between 21-30 years (46%), Table 3.

Khemka et al[56] in 2009, observed that benign lesions of breast were more commonly seen in younger age groups with maximum patients in 30-34 years of age. Our findings are in concordance with his study.

The age of all malignant cases ranged from 04 to 84 years with majority of cases in between >50 years (50%) (Table 4).

Khemka et al[56] reported the maximum number of patients with malignant cases in between 40-44 yrs.

Ganiat et al[57] reported maximum number of patients with malignant lesions in 4th to 7th decade which is in concordance with our study.

In our present study Out of 124 cases, females patients were 91.1% of cases and male patients with breast lump were only 8.9% of cases.

GPS Yeoh et al[58] in 1998 studied a total of 1533 FNAC cases from 1447 patients were submitted during the study period. Six of the patients were male. Our study is similar to his study.

In our study right breast was involved more than the left breast having 62 cases (50%) and 59 cases (47.6%) respectively. Bilateral involvement of breast was noted in 3 cases (2.4%). Table 6.

Tavassoli et al[34] in 1991, studied 31 cases, out of which 16 cases were present in right breast and 14 cases were present in left breast which favors our study.

Hussain et al[54] in 2005, showed left breast involvement in 27 patients (54%) and right breast involvement in 23 cases (46%) and concluded that left breast was involved more commonly than right.

Khemka et al[56] in 2009, observed in their patient that left breast was more commonly involved than the right breast. They found that right breast was involved in 22 patients while left breast was involved in 28 cases.

Pooja Agarwal et al[41] in 2017 studied 50 cases, out of which cases, 32 were left-sided (68%).

Among all four quadrants, superolateral quadrant was most common quadrant involved for breast lesion in present study (51 cases, 41.1%). (Table 7).

Hussain et al[54] in 2005 in their study, had 29 patients (58%) with lump in upper- outer and thus concluded that

upper-outer quadrant was most commonly involved quadrant in breast lesions.

Khemka et al[56] in 2009, also observed upper-outer quadrant as the commonest quadrant to be involved in breast lesions. The presently study is in concordance with above studies.

Out of 124 cases, maximum cases had single lump in the breast (118 cases, 95.2%) and few cases (6 cases, 4.8%) had multiple (2) lumps in the affected breast.

Choi YD et al[59] in 2006, studied 55 cases out of which 18 cases were multiple breast lumps. Hence majority of cases had single breast lump which is similar to our study.

In this study of 124 cases, 100 cases (80.6%) were benign and 24 cases (19.4%) were malignant. Among these benign cases, 47 cases were of benign non-neoplastic lesions and 53 were of benign neoplastic lesions. (Table 10).

GPS Yeoh et al[58] in 1998 studied 1533 breast masses on FNAC and found that 70.4 percent cases were benign, followed by malignant cases (4.4 %), followed by atypical cases (3.3 %) followed by suspicious cases (1.2 %), his results were similar to our study.

Ganiat et al[57] in 2009, studied 757 cases on FNAC and found out that maximum number of cases were benign (50.2 %) followed by malignant cases (31.4 %) followed by suspicious malignant case (9.5 %) and inflammatory cases (7.4 %).

In present study, out of 124 cases, maximum cases (100) were benign, among which 50 cases (40.3%) were of fibroadenoma followed by epithelial hyperplasia (25 cases, 20.5%) followed by Gynecomastia (6 cases, 4.8%). 24 cases were malignant in the present study., among which Invasive Carcinoma was most common (12 cases, 9.6%) (Table 15).

Jayaram et al[42] in 1996 studied 543 cases on FNAC with fibrocystic disease (39.8%) as the most common lesions followed by fibroadenoma (32.8 %).

Alexandre et al[60] in 2008, documented fibroadenoma as most common benign lesion (19 cases out of 42 benign cases, 45.2%) in their study.

Pattari SK et al[2] in 2008, studied 71 cases and documented infiltrating ductal carcinoma as the most common lesion (24/71) in their study amongst the histologically confirmed breast aspirates. Our observation was close to

the studies performed by Alexandre et al.[60]

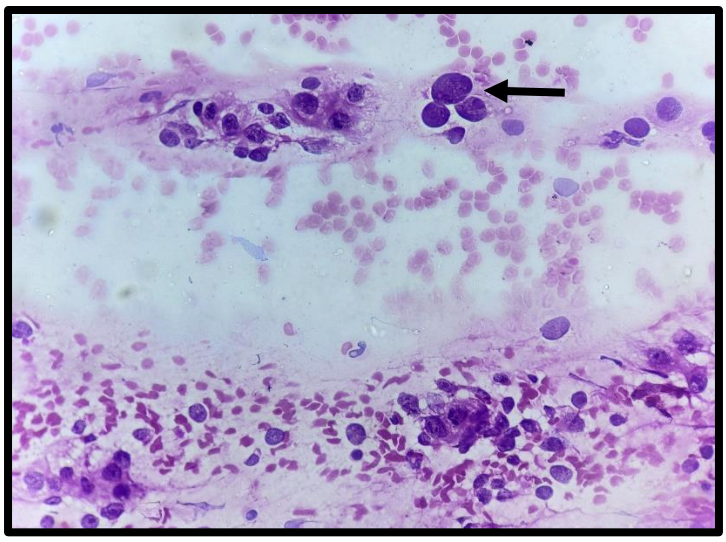

Figure 15A

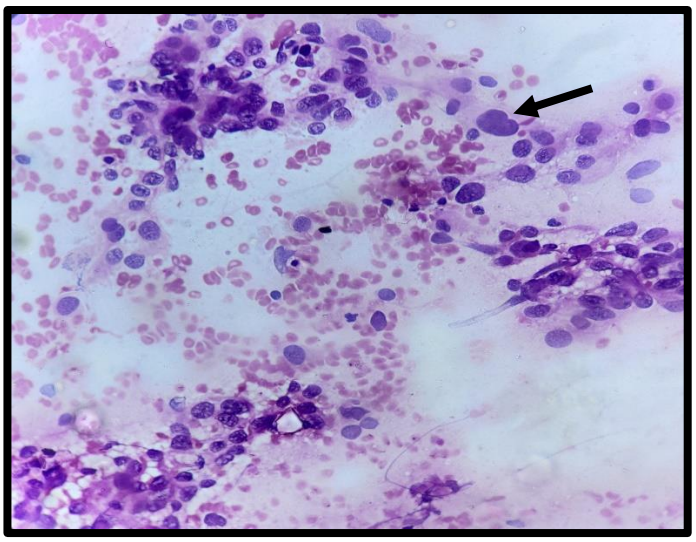

Figure 15B

Fig: 15A & 15B Invasive Carcinoma NST showing plemorphism & absence of ME cells 400x H&E

Out of 100 benign cases, histopathology correlation was available for 19 cases (19%) out of which 15 were concordant. Out of 24 malignant cases, histopathology was available for 11 cases (45%), out of which 10 were concordant. (Table 25). Out of 50 lesions reported as fibroadenoma, histology was available for 14 cases. Out of these 12 were confirmed histologically (Table 26) 1 case was diagnosed as lactating adenoma and 1 case was diagnosed as fibrocystic change on histology. Also 2 cases of Epithelial hyperplasia were diagnosed as fibroadenoma and fibrocystic disease. Out of 2 cases of papillary carcinoma 1 was diagnosed as Invasive carcinoma NST on HPR.

Jayaram et al[42] in 1996, performed FNAC on breast lumps and reported that out of 93 cytologically benign cases, 3 cases (3.22 %) were malignant and out of 61 malignant cases, 1 case (1.66 %) was benign on histology. The present study is in concordance with his study.

GPS Yeoh et al[58] in 1998, reported that out of 103 benign and atypical cases on cytology, 97 cases (94.17 %) were benign and 6 cases (5.8 %)were malignant on histology whereas out of 25 suspicious or malignant cases on FNAC, 2 cases (8%) were benign and 23 (92%) were malignant on histology.

Kollur SM[43] in 2006, did a retrospective analysis of 110 cases of FNA smears, diagnosed as fibroadenoma of which surgical pathology follow-up was done in 33. The cytohistological correlation was obtained in 26 of 33 (79%) cases.

Conclusion

In the present study, it was found that on quantification, the mean of ME cells in benign breast lesions was much more than that found in malignant breast lesions where they were either very much reduced or absent, making the occurrence of ME cells and its frequency a characteristic feature of benignancy. Quantification of ME cells was helpful to not only differentiate between benign and malignant lesions but also to differentiate between benign non-neoplastic and benign neoplastic lesions where the difference of their mean of ME cells was statistically significant.

We hereby conclude that quantification of myoepithelial cells is a key to distinguish benign from malignant lesions in fine-needle aspiration cytology of the breast.

Summary

FNAC has become popular as a valuable tool in preoperative assessment of breast masses, and because of its high accuracy, sensitivity, and specificity. It has grown popular as it provides a fast and easy approach. Being inexpensive, it makes it affordable and can be performed with little complications.

ME cells, benign pairs and bipolar nuclei assessment by FNAC of patients with breast lumps not only reduce the cost of management but also save the patient from unnecessary operative procedures and overtreatment.

In our study, a total of 124 cases have been studied, the majority being females. The age of the patients ranged between 4-84 years having the right breast more commonly involved. Superolateral quadrant was the most commonly involved.

Among 124 cases, 47 cases were benign non-neoplastic, 53 cases were benign neoplastic and 24 cases were malignant. On quantification, it was found that the number of ME cells was very much higher in benign lesions when compared to malignant ones and the difference was statistically significant. Also, quantification was helpful to distinguish between non-neoplastic benign lesions and neoplastic benign lesions. Besides having a very less no. of ME cells in carcinoma cases, ME cells were also found to be absent in many such cases.

Hence, this study not only helps to reduce mortality and morbidity of the patient by preventing over treatment, but also promotes timely management. This justifies the time and energy spent in understanding the importance of these entities in breast lesions whose significance was not much explored till yet.

Bibliography

1. Dey P. Diagnostic cytology. 2nd ed. New Delhi: Jaypee Brothers; 2018. p. 347-376.
2. Pattari SK, Dey P, Gupta SK, Joshi K. Myoepithelial Cells: Any role in aspiration cytology smears of breast tumors?. Cytojournal. 2008;5:9.
3. Orell S, Sterrett G, Orell S. Orell & Sterrett's fine needle aspiration cytology. 5th ed. Edinburgh: Churchill Livingstone/Elsevier; 2012. p. 156-209
4. Dudgeon LS, Patrick CV. A new method for the rapid microscopical diagnosis of tumors: with an account of 200 cases so examined. British Journal of Surgery. 1927 Oct;15(58):250-61
5. Martin HE. Ellis. EB Aspiration biopsy. Surg. Gynaecol. Obstet. 1934;59:578-89.
6. Cowin P, Wysolmerski J. Molecular mechanisms guiding embryonic mammary gland development. Cold Spring Harbor perspectives in biology. 2010 Jun 1;2(6):a003251.
7. Van Keymeulen A, Rocha AS, Ousset M, Beck B, Bouvencourt G, Rock J, Sharma N, Dekoninck S, Blanpain C. Distinct stem cells contribute to mammary gland development and maintenance. Nature. 2011 Nov;479(7372):189-93.
8. Olin PP, Anbazhagan R. Bartko Ya J, et al Breast development gives insights into breast disease. Histopathology 1998;33:275-2&3.
9. Hoda SA, Brogi E, Koerner F, Rosen PP. Rosen's breast pathology. Lippincott Williams & Wilkins; 2014. P. 1-217
10. Masood S, Lu L, Assaf-Munasifi M, McCaulley K. Application of immunostaining for muscle specific actin in detection of myoepithelial cells in breast fine-needle aspirates. Diagnostic cytopathology. 1995 Jul;13(1):71-4.
11. Orell S, Sterrett G, Orell S. Orell & Sterrett's fine needle aspiration cytology. 5th ed. Edinburgh: Churchill Livingstone/Elsevier; 2012. p. 1-7
12. Bibbo M, Wilbur D. Comprehensive Cytopathology. 3rd ed. London: Elsevier Health Sciences; 2014. p. 713-762.
13. Lee KC, Chan JK, Ho LC. Histologic changes in the breast after fine-needle aspiration. The American journal of surgical pathology. 1994 Oct;18(10):1039-47.
14. Fornage BD, Sneige N, Singletary SE. Masses in breasts with implants: diagnosis with US-guided fine-needle aspiration biopsy. Radiology. 1994 May;191(2):339-42.
15. Lieske B, Ravichandran D, Wright D. Role of fine-needle aspiration cytology and core biopsy in the preoperative diagnosis of screen-detected breast carcinoma. British journal of cancer. 2006 Jul;95(1):62-6.

16. Silverman JF. Diagnostic accuracy, cost-effectiveness, and triage role of fine-needle aspiration biopsy in the diagnosis of palpable breast lesions. The Breast Journal. 1995 Jan;1(1):3-8.
17. Collaço LM, de Lima RS, Werner B, Torres LF. Value of fine needle aspiration in the diagnosis of breast lesions. Acta cytologica. 1999;43(4):587-92.
18. Wang HH, Ducatman BS, Eick D. Comparative features of ductal carcinoma in situ and infiltrating ductal carcinoma of the breast on fine-needle aspiration biopsy. American journal of clinical pathology. 1989 Dec 1;92(6):736-40.
19. Al-Kaisi N. The spectrum of the" gray zone" in breast cytology. A review of 186 cases of atypical and suspicious cytology. Acta cytologica. 1994;38(6):898.
20. Layfield LJ, Mooney EE, Glasgow B, Hirschowitz S, Coogan A. What constitutes an adequate smear in fine-needle aspiration cytology of the breast?. Cancer Cytopathology: Interdisciplinary International Journal of the American Cancer Society. 1997 Feb 25;81(1):16-21.
21. Uniform approach to breast fine-needle aspiration biopsy. National Cancer Institute Fine-Needle Aspiration of Breast Workshop Subcommittees. Diagn Cytopathol. 1997;16(4):295-311.
22. Zajdela A, Zillhardt P, Voillemot N. Cytological diagnosis by fine needle sampling without aspiration. Cancer. 1987 Mar 15;59(6):1201-5.
23. Eckert R, Howell LP. Number, size, and composition of cell clusters as related to breast FNA adequacy. Diagnostic cytopathology. 1999 Aug;21(2):105-11.
24. Tot T. The theory of the sick breast lobe and the possible consequences. International Journal of Surgical Pathology. 2007 Oct;15(4):369-75.
25. Rosai J. Rosai and Ackerman's surgical pathology. 11th ed. Edinburgh: Mosby; 2018. p. 1434-1512.
26. Gray W, Kocjan G. Diagnostic cytopathology. 3rd ed. Edinburgh: W.B. Saunders; 2010. p. 179-230.
27. Field A, Raymond W, Schmitt F. The International Academy of Cytology Yokohama System for reporting breast fine needle aspiration biopsy cytopathology. 1st ed. Switzerland: Springer; 2020. p. 1-130.
28. Isa NA, Subramaniam E, Mashor MY, Othman NH. Fine needle aspiration cytology evaluation for classifying breast cancer using artificial neural network. In American Journal of applied sciences 2007.Altaf FJ. Pattern of breast diseases: King Khalid National Guard Hospital experience. Annals of Saudi medicine. 2001 May;21(3-4):239-41.
29. Ohtani H, Sasano N. Myofibroblasts and myoepithelial cells in human breast carcinoma. Virchows Archiv A. 1980 Feb 1;385(3):247-61.
30. Gusterson BA, Warburton MJ, Mitchell D, Ellison M, Neville AM, Rudland PS. Distribution of myoepithelial cells and basement membrane proteins in the normal breast and in benign and malignant breast diseases. Cancer research. 1982 Nov 1;42(11):4763-70.

31. Nagle RB, Böcker W, Davis JR, Heid HW, Kaufmann M, Lucas DO, Jarasch ED. Characterization of breast carcinomas by two monoclonal antibodies distinguishing myoepithelial from luminal epithelial cells. Journal of Histochemistry & Cytochemistry. 1986 Jul;34(7):869-81.
32. Tsuchiya S, Maruyama Y, Koike Y, Yamada K, Kobayashi Y, Kagaya A. Cytologic characteristics and origin of naked nuclei in breast aspirate smears. Acta cytologica. 1987 May 1;31(3):285-90.
33. Gottlieb C, Raju U, Greenwald KA. Myoepithelial cells in the differential diagnosis of complex benign and malignant breast lesions: an immunohistochemical study. Modern pathology: an official journal of the United States and Canadian Academy of Pathology, Inc. 1990 Mar 1;3(2):135-40.
34. Tavassoli FA. Myoepithelial lesions of the breast: myoepitheliosis, adenomyoepithelioma, and myoepithelial carcinoma. The American journal of surgical pathology. 1991 Jun 1;15(6):554-68.
35. McCluggage WG, McManus DI, Caughley LM. Fine needle aspiration (FNA) cytology of adenoid cystic carcinoma and adenomyoepithelioma of breast: two lesions rich in myoepithelial cells. Cytopathology. 1997 Jan;8(1):31-9.
36. Moriki T, Takahashi T, Ueda S, Wada M, Ichien M, Hashimoto M. Cytopathology of the breast--benign and malignant neoplastic conditions. Rinsho byori. The Japanese Journal of Clinical Pathology. 1999 Jul 1;47(7):585-92.
37. Barbareschi M, Pecciarini L, Cangi MG, Macrì E, Rizzo A, Viale G, Doglioni C. p63, a p53 homologue, is a selective nuclear marker of myoepithelial cells of the human breast. The American journal of surgical pathology. 2001 Aug 1;25(8):1054-60.
38. Reis-Filho JS, Albergaria A, Milanezi F, Amendoeira I, Schmitt FC. Naked nuclei revisited: p63 immunoexpression. Diagnostic cytopathology. 2002 Sep;27(3):135-8.
39. Böcker W, Moll R, Poremba C, Holland R, Van Diest PJ, Dervan P, Bürger H, Wai D, Diallo RI, Brandt B, Herbst H. Common adult stem cells in the human breast give rise to glandular and myoepithelial cell lineages: a new cell biological concept. Laboratory investigation. 2002 Jun;82(6):737-46.
40. Bofin AM, Lydersen S, Hagmar BM. Cytological criteria for the diagnosis of intraductal hyperplasia, ductal carcinoma in situ, and invasive carcinoma of the breast. Diagnostic Cytopathology. 2004 Oct;31(4):207-15.
41. Agarwal P, Prakash P, Bhadhkaria T, Prakash S, Bhagat R. A Study of Myoepithelial Cells in Fine Needle Aspirates from Breast Lump Using Antibody to p63. Annals of Pathology and Laboratory Medicine. 2017 Feb 19;4(1):p. 63-68.
42. Jayaram G, Alhady SF, Yip CH. Cytological analysis of breast lesions: A review of 780 cases. Malaysian Journal of Pathology. 1996 Dec 1;18:81-8.
43. Kollur SM, El Hag IA. FNA of breast fibroadenoma: observer variability and review of cytomorphology with cytohistological correlation. Cytopathology. 2006 Oct;17(5):239-44.

44. O Obaseki DE, Olu-Eddo AN, Ogunbiyi JO. Diagnostic accuracy of fine needle aspiration cytology of palpable breast masses in Benin City, Nigeria. West African Journal of Medicine. 2010 Jul 1;29(4).
45. Sneige N. Fine-needle aspiration of the breast: a review of 1,995 cases with emphasis on diagnostic pitfalls. Diagnostic cytopathology. 1993 Jan;9(1):106-12.
46. Greenberg M. Diagnostic pitfalls in the cytological interpretation of breast cancer. Pathology. 1996 Jan 1;28(2):113-21.
47. Arshid FR. False-positive reports in fine needle biopsy of breast lesions. Pathology. 2001 Jan 1;33(4):428-36.
48. Farshid G, Moinfar F, Meredith D, Peiterse S, Tavassoli F. Spindle cell ductal carcinoma in situ. Virchows Archiv. 2001 Jul 1;439(1):70-7.
49. Foxcroft LM, Evans EB, Porter AJ. Difficulties in the pre-operative diagnosis of phyllodes tumours of the breast: a study of 84 cases. The Breast. 2007 Feb 1;16(1):27-37.
50. Cibas E, Ducatman B. Cytology. 4th ed. China: Elsevier Saunders; 2014. p. 233-266.
51. Rogers LA, Lee KR. Breast carcinoma simulating fibroadenoma or fibrocystic change by fine-needle aspiration: a study of 16 cases. American journal of clinical pathology. 1992 Aug 1;98(2):155-60.
52. Shabb NS. Phyllodes tumor. Fine needle aspiration cytology of eight cases. Acta cytologica. 1997;41(2):321-6.
53. Koss L. Koss' diagnostic cytology and its histopathologic bases. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 1081-1147.
54. Hussain MT. Comparison of fine needle aspiration cytology with excision biopsy of breast lump. Journal of the College of Physicians and Surgeons--Pakistan: JCPSP. 2005 Apr;15(4):211-4.
55. Homesh NA, Issa MA, El-Sofiani HA. The diagnostic accuracy of fine needle aspiration cytology versus core needle biopsy for palpable breast lump (s). Saudi medical journal. 2005 Jan;26(1):42-6.
56. Khemka A, Chakrabarti N, Shah S, Patel V. Palpable breast lumps: fine-needle aspiration cytology versus histopathology: a correlation of diagnostic accuracy. Internet J Surg. 2009;18(1).
57. Omoniyi G. Cytopathological Review of Breast Lesions In Ile-Ife Nigeria. The Internet Journal of Third World Medicine. 2009;8(1):10-25.
58. Yeoh GP, Chan KW. Fine needle aspiration of breast masses: an analysis of 1533 cases in private practice. Hong Kong Medical Journal. 1998 Sep;4:283-8.
59. Choi YD, Gong GY, Kim MJ, Lee JS, Nam JH, Juhng SW, Choi C. Clinical and cytologic features of papillary neoplasms of the breast. Acta cytologica. 2006;50(1):35.
60. Barra AD, Gobbi H, de L. Rezende CA, Gouvêa AP, de Lucena CÊ, Reis JH, Costa e Silva SZ. A comparision of aspiration cytology and core needle biopsy according to tumor size of suspicious breast lesions. Diagnostic cytopathology. 2008 Jan;36(1):26-31.

61. Bofin AM, Lydersen S, Hagmar BM. Cytological criteria for the diagnosis of intraductal hyperplasia, ductal carcinoma in situ, and invasive carcinoma of the breast. Diagnostic Cytopathology. 2004 Oct;31(4):207-15.
62. Frost AR, Tabbara SO, Poprocky LA, Weiss H, Sidawy MK. Cytologic features of proliferative breast disease: a study designed to minimize sampling error. Cancer Cytopathology. 2000 Feb 25;90(1):33-40.

ANNEXURE-I

B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC NO: 285/2018
17-11-2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : A quantitative study of myoepithelial cells in fine needle aspirate from breast lumps.

Name of P.G. Student : Dr Toshi Agarwal.
Department of Pathology.

Name of Guide/Co-investigator: Dr.Surekha.B.Hippargi, Professor of Pathology.

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College, VIJAYAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

ANNEXURE-II

B.L.D.E (Deemed to be University),
SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER,
VIJAYAPURA-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

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

Further Doctor has informed me that my participation in this study help in evaluation of the results of the study which is useful reference to treatment of other similar cases in near future, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not assessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on information given by me, I can ask any clarification during treatment / study related to diagnosis, procedure of treatment, result of treatment or prognosis. At the same time I have

been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

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

Signature of patient:

Signature of doctor:

Witness: 1.

2.

Date:

Place

ANNEXURE-III

PROFORMA

CASE-

- **Demographic Details:**

Name: Age : Sex:

OPD / IPD No. : Laboratory number: FNAC No.-

- **Chief complaints:**
- **History of present illness:**
- **Past History**
- **Local examination**
  - **Size**
  - **Quadrant**
  - **Single/multiple**
  - **Unilateral/Bilateral**
  - **Consistency**
- **Proivisional Diagnosis**
- **Cyotological diagnosis:**
- **Number of ME cells on cytology FNAC:**
- **Histopathological follow up- Yes/No:**
  - **Concordant/ Discordant with cytological diagnosis:**

KEY TO MASTER CHART

S.NO.	Serial Number
U/L	Unilateral
B/L	Bilateral
NO. ME.	Number of Myoepithelial cells/1000 ductal cells
P	Present
AB	Absent
C/D	Concordant/ Discordant
HPR	Histopathological Report

MASTER CHART

S.No	Name	Age	Sex	IP/OP	UL/BL/	Quadrant	Single/ Multiple	Consistency	Size (cm)	No. ME	Diagnosis cytology	C/D	HPR Diagnosis
1	B M Hiremath	63	M	429225	Right	Central	Single	soft to firm	2.5x3.5	4	Papillary carcinoma	Concordant	Encapsulated low grade papillary ca
2	Chandragouda Shankargouda Sasanur	50	M	42671	Right	Central	Single	Firm	6x6	110	Acute Suppurative Inflammation		
3	Shahira Banu Yalagar	27	F	437545	Right	Superolateral	Single	Firm	3x2	400	Fibroadenoma		
4	Savita Pujari	35	F	449838	Left	Superolateral	Single	soft	2x2	430	Fibroadenoma		
5	Jyoti Jain	28	F	445359	Left	Superolateral	Single	Firm	2x2	237	Acute Suppurative Inflammation		
6	Hema Kondaguli	25	F	2762	Left	Superolateral	Single	Firm	2.5x2	308	Fibroadenoma		
7	Jayashree vishwanath Anagond	23	F	737	Left	Superolateral	Single	Firm	2x2	489	Fibroadenoma		
8	Chaya Mali	30	F	11829	Right	Superolateral	Single	Firm	3x3	379	Fibroadenoma	Concordant	Fibroadenoma
9	Arati Kadakol	27	F	15451	Right	Superolateral	Single	Soft to firm	4x3	135	Epithelial hyperplasia		
10	Laxmi S Madar	24	F	37185	Left	Superolateral	Single	Soft to firm	2x2	479	Fibroadenoma		
11	Shivleela P Kolamali	24	F	43726	Right	superomedial	Single	Firm	3x2	0	Galactocele		
12	Suvarna Sarawad	40	F	44507	Right	superomedial	Multiple-2	Firm	2x2	203	Epithelial hyperplasia		
13	Laxmi B H	18	F	47909	Left	Superolateral	Single	Firm	3x2	507	Fibroadenoma		
14	Savita M Magadi	16	F	47908	Left	superomedial	Single	Firm	4x4	280	Fibroadenoma		
15	Vidyashree	21	F	49267	Left	Inferolateral	Single	Firm	3x2	442	Fibroadenoma	Concordant	Fibroadenoma
16	Vijaylaxmi Rajkumar Hattarsang	35	F	3741	Left	Superolateral	Single	Soft	3x3	0	Galactocele		
17	Soumya	47	F	465786	Left	Central	Single	Soft	1x1	368	Fibroadenoma		
18	Renuka	19	F	5549	Left	superomedial	Single	Firm	3x2	298	Fibroadenoma	Concordant	Fibroadenoma
19	Shivaningawwa Kannal	60	F	67988	Right	Superolateral	Single	Firm	2x2	8	Ductal carcinoma		
20	Supriya Hattalli	22	F	79090	Right	Central	Single	Firm to hard	5x3	365	Fibroadenoma		
21	Laxmibai Basappa Biradar	40	F	84396	Right	Superolateral	Single	Firm	3.5x2	479	Fibroadenoma		
22	Basappa Dodamani	75	M	84778	Right	superolateral	single	Firm	3x2	12	Ductal carcinoma		
23	Sangamma B Goragundagi	55	F	8039	Left	Inferomedial	Single	Firm	4x5	0	Papillary carcinoma	Discordant	Invasive Carcinoma NST
24	Geeta Yalameli	40	F	85147	Left	superolateral	Single	Firm	1.5x1	0	Simple cyst with suppurative inflammation		
25	Anjana Gornal	50	F	90599	Left	Inferolateral	Single	soft to firm	3x2	0	Benign cystic lesion of breast		
26	Channamma	55	F	7685	Left	inferomedial	single	firm	3x5	300	Granulomatous mastitis		
27	Basamma Waddar	30	F	92099	Left	Inferolateral	single	Firm	4x3	148	Epithelial hyperplasia		
28	Ishwaramma Math	28	F	98287	Left	superolateral	single	firm	3x2	285	Fibroadenoma	Concordant	Fibroadenoma
29	Parshuram chavan	75	M	99966	Right	Central	single	soft	2x1	130	Gynecomastia		
30	Asha kiran rathod	23	F	106843	Right	superolateral	single	soft to firm	3x2	0	Epithelial hyperplasia	Concordant	Fibrocystic ds
31	Mahadevi sharanappa	55	F	9222	Right	superomedial	single	Hard	6x4	0	Ductal carcinoma	Concordant	Invasive ductal Ca NST
32	Ganga Patil	52	F	107162	Right	central	single	firm	1x1	200	Acute mastitis		
33	Vanita Matali	35	F	110959	Right	Superomedial	single	firm	1x1	0	Epidermal cyst		
34	Raghuveer Desai	13	M	112312	Left	Central	Single	firm	2x2	400	Gynecomastia		
35	Manjula sunagad	24	F	118219	Left	Superomedial	single	firm	2x1	460	Fibroadenoma		
36	Shanta Rathod	50	F	123487	Left	Central	single	firm	2x2	200	Acute Suppurative Inflammation		
37	Shivamma Jalawadi	65	F	127685	Right	Inferolateral	single	firm	2.5x2	465	Epithelial hyperplasia		
38	Mangala somu	30	F	12654	Left	Superolateral	single	firm	2x2	300	Epithelial hyperplasia		
39	Shridevi basavraj	35	F	13053	Right	Central	single	firm	5x4	250	Fibroadenoma	Discordant	Fibrocystic change
40	seetawwa maruti	30	F	13133	Right	superolateral	single	firm	8x8	461	Fibroadenoma	Concordant	Fibroadenoma
41	Narasawwa Talawar	45	F	149347	Left	Superior	single	Firm to hard	10x9	0	Ca with prominent mucinous features/ Ductal ca with mucinous change		

42	Mahadevi	29	F	150457	Right	Superior	single	hard	4x3	0	Epithelial hyperplasia		
43	Lalitabai patil	37	F	150716	Left	Superior	single	firm	2x2	457	Fibroadenoma	Concordant	Benign breast ds C/W FA
44	Gayatri sutar	32	F	151251	Left	superolateral	single	firm	3x2	556	Fibroadenoma		
45	Bismilla	50	F	14454	Left	All quadrants	single	hard	20x10	0	Ductal carcinoma		
46	Rakesh marate	16	M	163065	B/L	Central	Single	soft	2x2	0	Gynecomastia		
47	Lalabi nadaf	30	F	169038	left	superolateral	single	firm	3x2	230	Acute mastitis		
48	Malakavva	57	F	15664	Right	All quadrants	single	hard	10x10	0	Invasive carcinoma of NST	Concordant	Invasive Carcinoma NST
49	Yallamma Sasnur	29	F	176361	Right	superolateral	single	firm	3x2	400	Epithelial hyperplasia		
50	Nainsaba B Gheewale	28	F	176542	Right	Inferolateral	single	firm	2x2	300	Fibroadenoma		
51	Neelamma S Patangi	20	F	177410	Right	Inferolateral	single	firm	3x3	415	Fibroadenoma	Concordant	Fibroadenoma
52	Shivalila biradar	18	F	177868	Right	Inferolateral	multiple (2)	firm	2x2, 0.5x0.5	341	Fibroadenoma		
53	chandabee nadaf	40	F	182910	Left	Inferolateral	single	firm	1x1	0	Benign cystic lesion of breast		
54	Padmavati	43	F	440505	Left	Inferolateral	single	firm	1x1	370	Fibroadenoma		
55	Bhagyashree Laxman Kalli	21	F	18375	Left	superolateral	Single	firm	3x2	299	Fibroadenoma	Concordant	Fibroadenoma
56	Chandarkala Mallanna Hugar	25	F	17962	Left	Inferolateral	single	firm	2x1	200	Epithelial hyperplasia		
57	Ishwari	35	F	459902	Right	superolateral	Single	Firm	3x3	369	Fibroadenoma		
58	Malanbee	50	F	19654	Right	All quadrants	Single	Hard	10x10	0	Ductal carcinoma	Concordant	Invasive Ductal Ca
59	Prabhavati Bidan	26	F	215902	Right	Superomedial	Single	firm	2x2	340	Epithelial hyperplasia		
60	Anusuya Madar	30	F	218479	Left	Superomedial	Single	firm	2x2	452	Fibroadenoma		
61	Shakuntala	35	F	20192	Right	superolateral	single	firm	2x2	321	Epithelial hyperplasia	Concordant	Fibroadenoma
62	Shantabai Chavan	37	F	222952	Right	Inferolateral	Multiple	Firm	L-3x4, S-2x2	245	Epithelial hyperplasia		
63	Kamalabai Biradar	24	F	227247	Left	Superomedial	single	Firm	2x2	300	Epithelial hyperplasia		
64	Sudha Natikar	28	F	231354	Left	superolateral	Single	firm	5x4	350	Granulomatous mastitis		
65	Sharada Betageri	33	F	237335	Left	superolateral	single	Firm	3x4	424	Fibroadenoma		
66	Lakshambai Madar	45	F	238876	Left	superolmedial	Single	Hard	4x3	07 cells	Invasive carcinoma		
67	Bhagyashree Halleppanavar	12	F	241392	Right	All quadrants	single	Firm	10x6	417	Fibroadenoma		
68	Kavita S Rathod	23	F	242535	Right	Superomedial	Single	firm	2x2	501	Fibroadenoma		
69	Preeti Bange	18	F	244776	Right	superolateral	single	firm	4x3	433	Fibroadenoma		
70	Tasmaniya Nadaf	22	F	246086	B/L	Right- SM, Left-IL	Single in each	firm	Rt-2x1, Lt- 2x2	267	Epithelial hyperplasia		
71	Roopa Ibrahimpur	21	F	251590	Right	Central	single	Soft to firm	3x3	220	Acute Suppurative Inflammation		
72	Mahananda Vani	38	F	256113	Right	superolateral	single	firm	3x2	389	Fibroadenoma		
73	Renuka	35	F	256724	Right	superolateral	single	firm	2x2	230	Epithelial hyperplasia		
74	Shreyaseddy	13	M	259037	Right	Central	single	firm	1.5x1	0	Gynaecomastia		
75	Anasubai Hiremath	55	F	259690	Left	Superomedial	single	Hard	3x2	10	Invasive carcinoma of NST	Concordant	Invasive Ca NST & invasive papillary Ca
76	Ganesh	20	M	260942	Left	Central	single	firm	1x1	200	Gynaecomastia	Concordant	Gynaecomastia
77	Pooja talawar	17	F	262268	Right	Superolateral	single	firm	1x1	321	Fibroadenoma		
78	Pallavi Bijargi	20	F	262387	Right	superolateral	single	Hard	4x3	325	Granulomatous mastitis	Concordant	Granulomatous mastitis
79	Sunanda Irappa badiger	40	F	24518	Left	Inferolateral	single	firm	2x3	482	Epithelial hyperplasia	Discordant	Fibroadenoma
80	Bhogavati chandrakanth	19	F	25020	Right	Inferolateral	single	firm	2x2	379	Epithelial hyperplasia		
81	Mahadevi Kabade	35	F	270120	Right	Central	single	Hard	3x3	0	Invasive carcinoma		
82	Neelabai Patil	84	F	270975	Right	Superomedial	single	Hard	2x2	0	Invasive carcinoma of NST		
83	Suvaran mathapti	26	F	272512	Left	superolateral	single	firm	2x2	511	Fibroadenoma		
84	Savita golasangi	27	F	272567	Left	Inferomedial	single	hard	3x2	240	Suppurative inflammation		
85	Savita Rajendra gulagi	25	F	25553	Left	Superomedial	single	Firm	1x1	263	Fibroadenoma	Concordant	Fibroadenoma
86	Shabana Nagur	45	F	282859	Left	All quadrants	Single	Firm	12x8	9	Benign phyllodes tumor		

87	Soundrya Patil	16	F	283784	Left	Inferomedial	single	firm	4x3	463	Fibroadenoma	Concordant	Fibroadenoma
88	Vanishree Karade	23	F	285548	Right	superolateral	Single	firm	3x2	368	Epithelial hyperplasia		
89	Basamma Biradar	28	F	289396	Left	Superomedial	Two	firm	L-2x2, S-1x1	280	fibroadenoma with lactational change		
90	Mandakini Gayakwad	38	F	302933	Left	Inferomedial	Single	Hard	2x1	8	Invasive Carcinoma		
91	Laxmi Thabad	19	F	304387	Right	Inferolateral	Single	Firm	2x2	309	Fibroadenoma		
92	Vaishanavi Patil	21	F	303561	Left	superolateral	Single	firm	1x1	411	Fibroadenoma		
93	Bhagyashree Indi	28	F	309297	Right	Inferolateral	single	firm	1x1	502	Epithelial hyperplasia		
94	Laxmibai	80	F	313553	Right	1st- Inferolat, 2nd-Supmed	Multip le (2)	Hard	1st- 5x4, 2nd-4x3	30	Papillary Neoplasm		
95	Laxmibai Pudlik Koudi	4	F	29657	Left	1st-supmed, 2nd-infmed	Multip le(2)	firm	1st-4x3, 2nd- 8x3	0	High grade invasive carcinoma	Concordant	Infiltrating Ductal Ca
96	Boramma	17	F	31457	Left	Superomedial	single	firm	3x2	545	Fibroadenoma		
97	Shobha Nidoni	26	F	344753	Left	superolateral	single	firm	1x1	252	Fibroadenoma		
98	Kamalabai Arjunagi	45	F	347671	Left	Inferolateral	Single	Firm	2x1	165	Epithelial hyperplasia		
99	Surekha Shivbasappa hosamani	21	F	34370	Right	Inferolateral	single	firm	2x2	410	Fibroadenoma	Concordant	Multiple cellular Fibroadenoma
100	Anita Pradani	46	F	372140	Left	Superomedial	single	firm	3x2	339	Fibroadenoma	Concordant	Fibroadenoma with Fibrocystic change
101	Manjawwa Badiger	35	F	372324	Right	superolateral	single	firm	4x3	275	Epithelial hyperplasia		
102	Sangeeta Rathod	28	F	373376	Right	superolateral	single	firm	3x2	221	Epithelial hyperplasia		
103	Arati Gouli	23	F	379425	Left	superolateral	single	firm	1x1	326	Epithelial hyperplasia		
104	Rekha Natikar	30	F	394612	Left	superolateral	Single	soft	3x3	493	Epithelial hyperplasia		
105	Sudharani Rajakumar	30	F	396223	Left	superolateral	single	firm	4x3	391	Fibroadenoma		
106	Dundappa Naik	42	M	396365	B/L	Central	single in each	soft	2x2	0	Gynaecomastia		
107	Jannathbee Jamadar	38	F	397808	Right	superolateral	Single	firm	4x4	401	Fibroadenoma		
108	Seema Chopra	31	F	400443	Right	Inferolateral	single	firm	4x3	305	Fibroadenoma		
109	Niramaladevi	42	F	403152	Right	Inferolateral	single	firm	4x4	20	Papillary neoplasm		
110	Boramma Siddaram Wangi	28	F	405133	Right	Inferolateral	single	firm	3x3	512	Epithelial hyperplasia		
111	Sudhabai	34	F	413259	Left	superolateral	Single	Firm	2x2	560	Fibroadenoma		
112	Pramila Betageri	21	F	422428	Left	superolateral	single	Firm	2x2	243	Fibroadenoma	Discordant	Lactating adenoma
113	Yankawwa Jabannavar	35	F	427152	Right	superolateral	Single	Firm	2x2	289	Fibroadenoma		
114	Reshma Lamani	25	F	431106	Left	Superomedial	Single	Firm	3x2	357	Fibroadenoma		
115	Shankaremma B Sajjan	60	F	432136	Left	All quadrants	Single	Firm	8x8	0	Infiltrating Ductal Carcinoma		
116	Renuka Y Chalawadi	40	F	433372	Left	superolateral	single	Firm	4x4	0	Infiltrating Ductal Carcinoma	Concordant	Invasive Carcinoma NST
117	Sumitra Dalawai	29	F	433733	Right	superolateral	single	Firm	2x2	309	Fibroadenoma		
118	Savitri Ramu Gadiwaddar	55	M	41126	Right	superolateral	single	Hard	5x5	0	Invasive carcinoma NST	Concordant	Invasive carcinoma NST
119	Padmavati shreeshail meti	50	F	2181	Right	superolateral	single	Hard	3x3	11	Invasive carcinoma	Concordant	Invasive carcinoma NST
120	Nagamma S Patil	50	F	45158	Right	central	single	hard	3x3	0	invasive carcinoma NST		
121	Sangeeta Jagadev Deshmukh	54	F	4271	Right	superolateral	Single	Hard	6x5	0	Invasive carcinoma		
122	Mahadevi Anil Navi	42	F	5287	Right	superolateral	Single	Hard	3x3	22	Invasive Carcinoma	Concordant	Invasive carcinoma NST
123	Soroaja	64	F	100955	Right	superolateral	single	Hard	4x3	0	Invasive Carcinoma		
124	Mamataz Hanif hadimani	38	F	12517	Right	all quadrants	Single	Hard	7x5	0	Infiltrating Ductal Carcinoma		