COMPARATIVE STUDY BETWEEN LIQUID BASED CYTOLOGY AND CONVENTIONAL SMEAR IN FNA SAMPLES OF BREAST LESIONS

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M.D.Degree

in PATHOLOGY – BRANCH III

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THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY CHENNAI, TAMILNADU

DECLARATION

I solemnly declare that the dissertation entitled COMPARATIVE STUDY BETWEEN LIQUID BASED CYTOLOGY AND CONVENTIONAL SMEAR IN FNA SAMPLES OF BREAST LESIONS was done by me in the Department of Pathology at Coimbatore Medical College, Coimbatore during the period of July 2015 to July 2016 under the guidance and supervision of **DR. C. LALITHA, MD.,** Professor and Head, Department of pathology, Coimbatore Medical College, Coimbatore.

This dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai towards the partial fulfillment of the requirement for the award of M.D., Degree in Pathology.

Place:

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CERTIFICATE

This is to certify that the dissertation entitled **COMPARATIVE STUDY BETWEEN LIQUID BASED CYTOLOGY AND CONVENTIONAL SMEAR IN FNA SAMPLES OF BREAST LESIONS** is a record of bonafide work done by **Dr.R.Kousalya**, post graduate student in the Department of Pathology, Coimbatore Medical College and Hospital, Coimbatore under the supervision and guidance of **Dr.C.Lalitha, M.D.,** Professor and Head, Department of Pathology, Coimbatore medical college and Hospital, Coimbatore in partial fulfillment of the regulations of the Tamilnadu Dr.M.G.R. Medical University, Chennai towards the award of M.D. Degree (Branch III) in Pathology.

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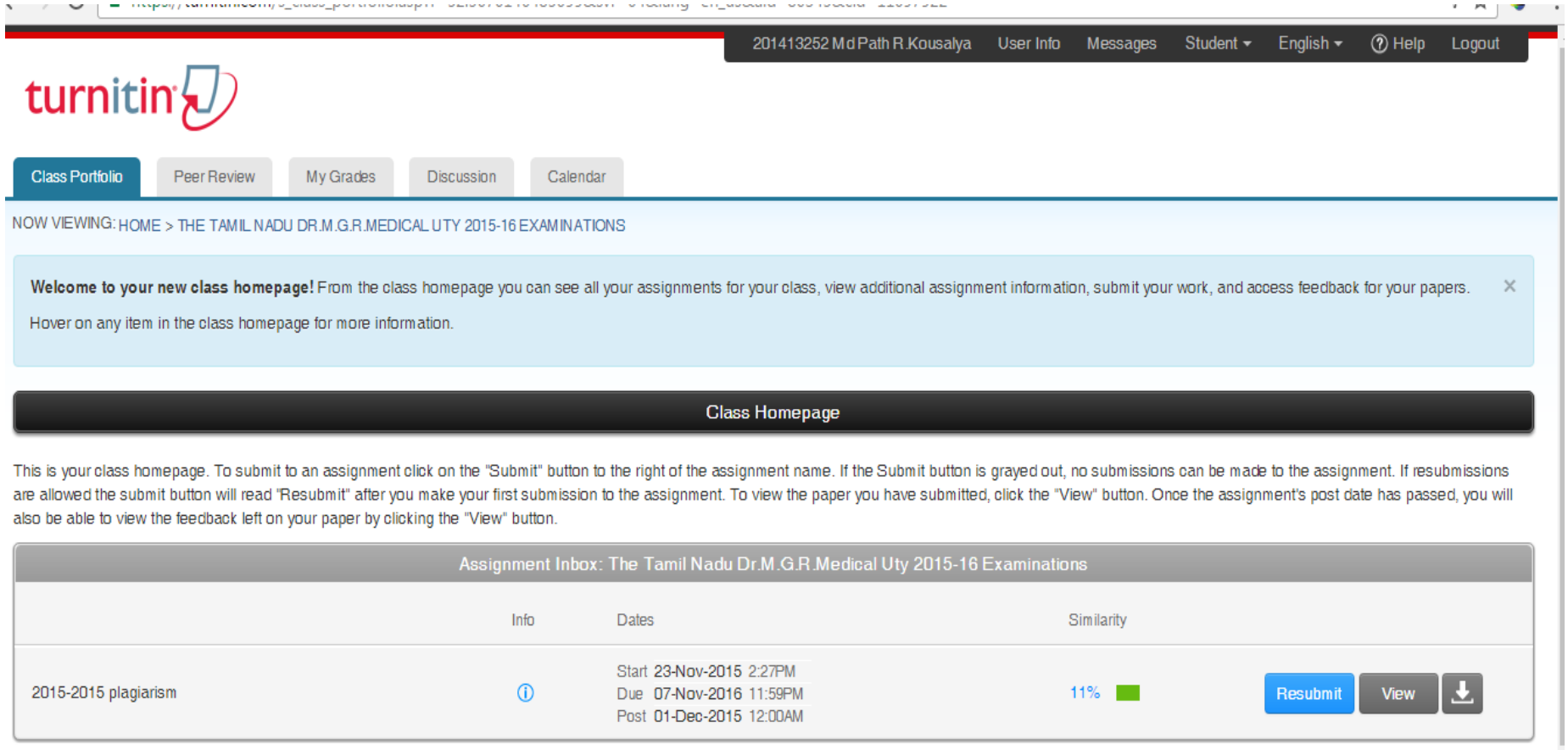
INTRODUCTION

Breast lesions can be of various types from inflammatory to malignant. Some lesions are common in younger age group while others are more common in elderly age group.

Benign lesions of the breast are the most common lesions which account for 90% of the clinical presentations related to breast[1]. Patients present with palpable breast lump and pain[2]. Breast Benign lesions existing already may result in carcinoma and deformity[3]. Breast tissue is under hormonal influence which causes changes in breast, present throughout life[4]. Fibroadenoma of the breast is the common cause of benign breast lump[5]. Breast cancer is the frequent cancer in women worldwide. Incidence rate differs worldwide from 27/100000 (females in Eastern Africa) to 90/100000 females in Europe.

Breast cancer is common among women in India according to National cancer registry programme 2011 report. A woman has one in eight chance of developing breast cancer during her lifetime. By the year 2000 global burden of breast cancer will be more than two million every year.

In India the incidence of carcinoma of breast is increasing and the crude(life) rate for breast cancer in India is 111 per 10,000. Overall, breast cancer are more common in women.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INTRODUCTION

Breast lesions can be of various types from inflammatory to malignant. Some lesions are common in younger age group while others are more common in elderly age group.

Benign lesions of the breast are the most common lesions which account for 90% of the clinical presentation related to breast[1]. Patients present with palpable breast lump and pain[2]. Breast lumps besides creating anxiety may result in carcinoma and deformity[3]. Breast tissue is under hormonal influence which causes changes in breast, present throughout life[4]. Fibroadenoma of the breast is the common cause of benign breast lump[5]. Breast cancer is the frequent cancer in women worldwide. Incidence rate differs worldwide from 27/100000 females in Eastern Africa to 96/100000 females in Europe.

Breast cancer is common among women in India according to National cancer registry programme 2011 report. A woman has, one in eight chance of developing breast cancer during her lifetime. By the year 2030 global burden of breast cancer will be more than two million every year.

In India the incidence of carcinoma of breast is increasing and the mortality rate for breast cancer in India is 11.1 per 10,000. Overall, breast nodules are more common in women.

Fine-needle aspiration cytology is a safe and cost-effective, first line diagnostic tool in diagnosing breast lumps. FNAC helps in reducing the number of unnecessary surgeries in benign breast lesions.

For many years, conventional smears have been regarded as the gold standard technique for diagnosing breast lesions in cytology. From the aspirated material, smears of variable number are prepared. It consumes time and has been tedious for the cytologists to screen the slides. Technical aspects add to the problem, which include improper smear preparation and fixation leading to poor preservation of cellular details. Thick smears, cellular overlapping and obscuring inflammatory infiltrate all interfere in reporting the smears.

To overcome the above disadvantages posed by conventional method, the Liquid-based technique has been used with increasing frequency worldwide in most of the centers for gynecological as well as non-gynecological samples. Two systems named Thin-prep and Sure-path approved by US Food and Drug Administration (FDA) are commonly used. Both represent first generation liquid based cytology systems, and they consist of automated equipments, filters, plastic containers, and vacuum devices. When compared with conventional smear, the cost of preparing slides using the above two systems was increased to a greater extent, making the improved method potentially inaccessible.

Liquid-PrepTM, the second generation technique is a simpler one. It requires low cost, because most of the automated machines and devices are not used in this liquid based cytology system. It also enhances clear visualization due to monolayer spread of cells.

The objective of the investigator in this study, is to use a commonly available instrument (centrifuge), and to prepare slides from fine needle aspirates. The results are interpreted using standard morphologic criteria proposed for liquid based smears.

Finally, the left over liquid based sample can be used for ancillary tests such as immunocytochemistry and molecular studies. Cell block could be prepared as well from them. However, in this study they are not included.

AIM AND OBJECTIVES

AIM:

To compare liquid based cytology technique with conventional smear method and to correlate with histopathological diagnosis.

OBJECTIVES:

- To compare the cyto-morphological features of manual liquid based preparation with conventional cytology in breast lesions using FNA technique.
- To compare the diagnostic value of Liquid based method with Conventional one.
- To correlate with final histopathological diagnosis whenever available.

REVIEW OF LITERATURE

Over the past three decades, in the work-up of breast lesions, fine needle aspiration has been commonly used as first line diagnostic tool. It is widely accepted as simple, safe and cost effective and helps in selecting the patients for surgical excision instead of managing them clinically[6].

A low false-negative rate **(FNR)** and high true positive rate **(TPR)** indicates the success of breast fine needle aspiration. A low FNR depends upon the high quality of samples that are procured by technically-skilled persons to prepare slides that are representative of the lesion with sufficiently good quantity and quality for the interpretation of results. A high TPR depends upon the accurate interpretations using established criteria for sample adequacy and cellular morphology[7,8]

The smear can be prepared by Conventional method or can be processed by either of the following methods - liquid preparations or cytospin[8,10,45].

For years, **conventional smears (CS)** have been the gold standard technique in diagnosing breast lesions. The main drawback with conventional smear is bloody background, which hinders the evaluation of breast ductal cells; it also requires some skill. Finally slide transportation can be an issue[6,9].

In 1996, to overcome the problems faced by conventional method, a newer technique called **liquid based cytology** has been applied in the cytological sample collection and preparation. This method originally developed for cervical cytology smears[10], has gradually been applied to non gynaecological specimens[7,11,12] and especially to aspiration cytology samples with better outcome.

In LBPs, instead of smearing, the sample is collected are rinsed in preservative medium and processed in automated or semi-automated machines or they are processed manually [12].

A newer LBC method, **liquid-PREP (LP)** was introduced in the recent years because of low cost when compared with the older liquid based method[13,14].

A decreased non-diagnostic rate and an increased rate of accurate diagnosis were observed with conventional smears in some studies. More comparable or better results with liquid-based methods were obtained in later studies.

ADVANTAGES OF LBP [6,10]

- Liquid based preparations are considered best alternative method to conventional smear because of its easy processing technique, faster screening time and other interpretation advantages. They include:
- Procedure of collecting the sample is uniform and 100%; collection can be done by cytologists or by the clinicians;
- Hazards of handling needle while preparing conventional smears are minimized;
- Transportation even from remote places to the diagnostic centre is easy;
- The technique can be done in automated (ThinPrep) or semi-automated (SurePath) equipments or can be processed manually (Liquid-prep);
- Air drying artifact is avoided and the morphology is preserved well due to immediate fixation in the liquid based solution;
- Processing technique is standardized and is uniform which gives an enriched cell sample with uniform distribution of cells
- Enables the cytologists to examine less number of slides for each case.
- Easier for the cytologists to interpret liquid based slides because the smear is spread has bloodless background and the cells are spread in monolayer.
- The time required for interpretation is less;

- Leftover sample can be stored at room temperature for few months (average-six months). This provides the chance of making additional slides or cell block and immunohistochemistry/ molecular studies[15,16,17,18,19] to be performed at a later date.
- Many studies reported that the diagnostic accuracy of liquid based technique has improved or remained equal to that of conventional method; almost all acknowledge that liquid based preparations produced cytological changes in the morphology of cells.
- With all the advantages discussed above, the cyto-pathologist should be aware and be familiar with the minor cyto-morphologic alterations produced by LBPs, although the architectural features are maintained[6,20].

ALTERATIONS RECOGNISED IN LBP

The alterations noted in liquid based preparations are in the cellularity, distribution of cells, cellular architecture, morphology and the background elements[7]. Michael et al (2000)[21] stated that these alterations are attributed by processing techniques involved in preparing the liquid based slides.

Cellularity

A high cell yield with minimum loss of cells can be obtained when the aspiration sample is processed wholly in liquid based technique. This can be achieved when the sample is collected through a special pass[21].

Background Elements

Liquid based preparations provide a clean background which is achieved by adding lytic agents to the sample that reduces the background blood cells. This has been quoted in almost all reference studies.

Architecture

LBP usually retains the architectural patterns like syncytial cell clusters. However, apparent discohesion with more single cells are noted with breakage of large sheets. The cell dispersion is due to the processing technique involved in liquid based preparations.

Distribution of cells

The cell distribution is almost uniform, as thin monolayer with minimal overlapping[21,22].

Cellular morphology

Morphology of cells are well preserved and are seen enhanced in liquid based preparations[21,22]. The cell shape and the nuclear details are usually retained but the nucleus appears slightly shrunken in liquid based preparations. Nuclear features like pleomorphism, irregular nuclear membrane, chromatin appearance are better visualized[21,22,23]. Cytoplasm looks denser and is readily seen in lymphocyte[21]. The artefacts introduced by liquid based preparation emphasizes the need to develop better experience in reporting the liquid based

smears to avoid diagnostic errors. These artifacts have also been observed in few of the studies done on fine needle aspiration specimens as well as with other non-gynecologic samples[10,11,12].

ANATOMY OF NORMAL BREAST [24]

The female breast is modified sweat glands. Nonlactating adult breast contains glandular portion. It is made up of clusters of small secretory lobules. These lobules connected to main excretory duct. The stroma is made up of loose connective tissue and fat. After menopause these glandular portion undergoes atrophy.

Each acinus or lobule in the resting state is composed of small cuboidal cells. The small ducts, lined by small cuboidal cells, with an outer layer of myoepithelial cells. The large lactiferous ducts are lined by one to two layers of cuboidal cells. The lining of the smaller ducts may undergo apocrine metaplasia. Nipple is made up of thick epidermis. The male breast contains sparse duct, scarce fat and connective tissue. The lobular apparatus is absent in male breast.

Normal cytology [6,20,24]

Normal breast is difficult to aspirate. In conventional cytologic preparations, normal breast usually shows scant cellularity cohesive ductal

fragments with uniform round nuclei with dense chromatin and small inconspiscous nucleoli.

The breast ductal epithelial cells in the liquid based preparations appear as small clusters with three dimensional arrangement. The cells are round with scant basophillic cytoplasm. Nucleus look small, regular and round with clumped chromatin. There is elimination of obscuring elements such as blood, excessive inflammation and cellular debris.

DIAGNOSTIC TERMINOLOGY [46]

Accurate diagnosis of breast lesions depend upon triple assessment approach. It has clinical, imaging and pathologic examination. Fine needle aspiration cytology is widely adopted for pathologic assessment because of the accuracy and ease of use. In literature, few of the classification schemes are recommended in the reporting of breast aspiration cytology. Each one of them was based on their individual or institutional experience and also on clinical organisation. Perceptions of these diagnostic terminology and reporting according to the classification scheme, lead to disordence between the clinician and cytopathologist which altered the patient management.

The most commonly used reporting system is “Five tier method of reporting system” (C1-C5). Categories ranges from insufficient materials (C1), benign (C2), atypical(C3), suspicious of malignancy (C4), frankly malignant

(C5). This categorisation was initiated by the NATIONAL COORDINATING COMMITTEE FOR BREAST SCREENING and UK NATIONAL BREAST SCREENING PROGRAM. Diagnostic Terminology Reporting terminology. The M.D. Anderson Cancer Center proposal. The category also includes the following points

Adequacy/diagnostic category

Specimen adequacy

Satisfactory for evaluation.

Insufficient for evaluation - scant cellularity (<4–6 cell groups).

Unsatisfactory for evaluation - distortion artifact, obscuring blood

(1) Benign lesions

Specification of lesion (e.g., fibroadenoma, adenosis, FCD)

(2) Proliferative breast lesion

A. Presence of cytological atypia (e.g., crowded, pleomorphic nucleus, loss of cohesion, hyperchromasia)

B. Architectural pattern.

a. Ductal hyperplasia

b. Atypical hyperplasia/low-grade carcinoma in situ

(3)Suspicious for carcinoma

- Insufficient cellularity.

- Benign ductal elements with low grade carcinoma in same slide.

(4) Malignant

- specification of type (e.g., ductal, lobular, mucinous)

- Other types (sarcoma, metastasis, lymphoma etc.)

Diagnostic terminology given by E.C. Working Group

C1. Unsatisfactory :

Hypocellularity sample, aspiration error.

C2. Benign Adequate:

Sample with absence of malignancy features

C3. Atypia probably benign :

Adequate sample with characteristics of benign aspirate with one or more of the following features:

a) Nuclear pleomorphism

b) Loss of Cellular cohesiveness

c) Nuclear and cytoplasmic changes.

d) High cellularity

C4. Suspicious of malignancy:

Adequate sample with atypical features. Accurate diagnosis of malignancy cannot be made due the following:

a) Scant, poorly preserved and prepared smear
b) Detection of few malignant features without presence of malignant cells
c) Few cells showing malignant features.

C5. Malignant:

Adequate sample containig characteristics of carcinoma or other malignancy

Non- gynecologic cytology developed as a poor stepchild in the world of pathology. Papanicolaou "Class" system was widely used and often applied to non-gynecologic cytlogypathology. The 1996 concensus conference on breast cytology by Bethesda,M.D., proffered a categorized reporting format consisting of five categories with negative, benign, atypical, suspicious, malignant.

Recently, The American society of cytopathology published the guidelines for non–gynecologic cytology speciemens. In addition to the obvious need in the report for demographics [name or unique identification or both, age or birth date, and the name of the ordering physician].

1) The ASC guidelines recommended that the final report include useful data that are legible, accurate and released to the authorized person.

2) The ASC guidelines also indicates there are no universal criteria for adequacy, but that the laboratory must indicate the reason if the sample cannot be tested(for example, lack of proper fixation, broken slide)
3) The ASC guidelines say, the report should be as specific as possible using histopathologic terms and, if a specific diagnosis cannot be rendered, a differential diagnosis should be given, when appropriate.
4) History and clinical information should be incorporated into the report.

The pathologists who are opposed to general categorization feel passionately that non-gynecologic cytology report should be as close to surgical pathology report. Regardless of whether report is Bethesda like or histopathogic like, there are key requirements for a good non-gynecologic pathology report.

A report should convey information in such a way that the health care professionals who read the report will have clear understanding of the presence, absence or uncertainity of the disease.

Speciemen adequacy for breast fine needle aspiration cytology

Solid lesions

There is no specific requirement.

Sample adequacy depends upon aspiration.

Benign breast lesions

The amount of epithelial cells present has to be reported.

Individual laboratory may consider specific cell count, as their own criteria.

Cystic lesions

There is no minimal criteria for cell count.

If the fluid is thin, watery, and not bloody, the fluid is examined or discarded at the aspirators decision, provided the FNA completely evacuates the cyst and there is no residual palpable mass left.

Any residual mass or nodule requires FNA from the residual mass

Cysts with brown reddish fluid (not related to trauma of the FNA) require careful evaluation or further workup.

BENIGN CONDITIONS :

Fibrocystic Changes

Fibroadenoma

Fat Necrosis

Pregnancy and Lactational Changes

Mastitis

Radiation Change

Gynecomastia

PAPILLARY NEOPLASMS

PHYLLODES TUMOR

Breast carcinomas

Ductal Carcinoma (invasive)

Lobular Carcinoma (invasive)

Mucinous Carcinoma

Medullary Carcinoma

Metaplastic Carcinomas

Tubular Carcinoma

UNCOMMON BREAST TUMORS

Sarcoma

Apocrine Carcinoma

NHL

Adenoid Cystic Carcinoma

METASTATIC TUMORS

Benign breast lesions:

Fibrocystic changes:

One of the common breast lesion is fibrocystic change. It is composed of small cysts, large cysts, focal fibrosis, apocrine metaplasia, adenosis, intraductal hyperplasia. Moderate amount of ductal hyperplasia is seen. Two types of fibrocystic changes are seen proliferative and non proliferative. This is based on presence of ductal hyperplasia[24,47]

Cytological features:

Clusters of cells without nuclear overlap with fine granular chromatin and inconspiscous nucleoli.

Fibroadenoma:

Fibroadenoma, the most common benign tumor of the female breast. Can occur in any age group. They are solitary, well circumscribed lesion, which is freely mobile and rubbery due to stromal and glandular proliferation. They can occur as multiple lesions.

Cytological features of fibroadenoma:

• Hypercellular lesions, with large sheets of three-dimensional clusters. Two cell population epithelial and myoepithelial. Bipolar cells with oval nuclei. Stromal fragments are fibrillar. Nuclear atypia is present. Epithelial cohesion is lost. Nuclear spacing is regular. Chromatin is finely granular. Nucleolus is small and round [24].

Generally both conventional smears and liquid based preparations show similar cytological features with minor differences, which includes

1. Benign appearing ductal cells in LBPs are arranged in flat sheets, clusters or aggregates. They are small uniform in size with rare small nucleoli. Myoepithelial cells are present admixed with the benign epithelial cells.
2. Compared to conventional smears, liquid based preparations have decreased or absent stromal components.

Many authors observed loss of stromal components as limitations of thinprep. Dey et al (2000) & Ali et al (2004) observed similar features as in conventional smears like cells arranged in staghorn clusters, isolated myoepithelial cells and stromal fragments.

Mygdakos et al (2009) stated that stromal elements were reduced or absent, but the diagnosis of fibroadenoma is made based on the features like ductal cell aggregates and bipolar cells.

Michael et al (2000), Leung et al (1997) & Perez-Reyes et al (1994) observed that cells are arranged in small aggregates, with decrease in myoepithelial cells and paucity or loss of stromal fragments.

Pregnancy, Lactational Changes:

Pregnancy and lactation causes hyperplasia of terminal lobular unit.

Cytological features of pregnancy and lactational changes:

Smears are moderately cellular. Smear contains many isolated epithelial cells. Nucleus is enlarged with no change in size and shape. Prominent nucleolus is seen. Cytoplasm is abundant and finely vacuolated. Proteinaceous foamy material is seen in the background. Numerous naked nuclei are seen. The lactational adenoma may be confused with ductal carcinoma but, carcinoma do not have foamy background [6,24,26,35].

Fat Necrosis:

Fat necrosis can mimic carcinoma. Most common in patients with previous history of biopsy and trauma to the breast.

Cytological features of fat necrosis:

- Hypocellular smears.
- Contains many histiocytes.
- Round to kidney-bean shaped nucleus.
- Low N/C ratio.
- Multinucleated, atypical cells are seen.
- Neutrophils, plasma cells and lymphocytes seen in the background[28,29].

Radiation Changes:

Cytological features of radiation changes:

Hypocellular smears with low N/C ratio. Hyperchromatic nucleus with prominent nucleoli. Cytoplasmic vacuolization is seen [30].

Mastitis:

Acute mastitis:

Bacterial infection is the most common cause.

Cytological features of acute mastitis:

Numerous neutrophils with ductal cells showing reactive changes.

Chronic mastitis:

It is due to complication of acute mastitis. Etiology is unknown[31].

Cytological features of chronic mastitis:

- Cellular smears.
- Inspissated ducts produce amorphous granular debris.
- Lymphocytes, plasma cells are common inflammatory infiltrate.

Both acute and chronic mastitis on LBC preparations are classified based on the inflammatory cells.

Kalpalata Tripathy et al (2015) described that the chronic mastitis is diagnosed on LBC preparations due to clarity of the nuclear features and also the presence of inflammatory cells.

Granulomatous mastitis:

The term granulomatous lobular mastitis is a clinical syndrome of unknown etiology. Most common in pregnancy age group [31].

Cytological features of granulomatous mastitis:

- Clusters of epithelioid histiocytes.
- Cytoplasm is vacuolated.
- Folded or round nucleus.
- Dispersed chromatin.
- Nucleoli is large.
- Lymphocytes, eosinophils, plasma cells and giant cells are seen in the stroma.

Subareolar Abscess:

It is also known as "recurring subareolar abscess". It arises in areola due to squamous metaplasia of lactiferous ducts. It is also due to keratin plugging, rupture and dilatation of ducts. If lesions are not completely exicised, it will recur.

Cytological features of subareolar abscess:

Anucleate squames are many with histiocytes, neutrophils and multinucleated giant cells [32]. Granulation tissue fragments are noted.

Gynecomastia:

Gynecomastia is a common lesion of male breast. It is diffuse or nodular enlargement of breast and is frequently bilateral.

Cytological features of gynecomastia:

Most commonly resembles Fibroadenoma. Cellularity is variable. Ductal cells arranged in groups with small, oval nucleus and scant cytoplasm [33]. Isolated bipolar cells are seen.

Papillary Neoplasms:

They are solitary tumors. They arise in subareolar lactiferous ducts. The common presentation is bloody nipple discharge. So nipple discharge cytology should be done. Papillary carcinoma represents 1% to 2% of breast carcinomas. It may be cystic or solid, invasive or noninvasive. The prognosis is favourable. The distinction between malignant and benign are difficult to diagnose in fine needle aspiration. Papillary carcinomas show, singly scaterred columnar cells. Sclerosing papillary lesions may mimic as malignant lesion in fine needle aspiration [32]. Therefore excision biopsy should be done to confirm whether the lesion is benign or malignant.

Cytological features of benign papillary neoplasm:

Smears are moderate to high cellular. Cells are arranged in three-dimensional papillary groups with fibrovascular core. Cuboidal to columnar cells. Nucleus is round to oval. Chromatin is finely granular[32].

Cytological features of malignant papillary neoplasm :

Smears are moderate to markedly cellular. Cells are arrangend in papillary pattern, cribriform, tubular pattern. Absence of myoepithelial cells. Tall columnar cells are commonly seen with elongated uniform nuclei [24]. Many naked nuclei and blood and hemosiderin-laden macrophages seen.

Phyllodes Tumor:

It is a biphasic tumour. It has epithelial and stromal component with increased stromal cellularity. The incidence is less than 1% of breast tumors. Many grow as massive masses most commonly infiltrating the skin. They can be classified as benign, borderline and malignant.

Cytological features of phyllodes tumor:

Cytological features are similar to fibroadenoma but phyllodes tumor is more cellular with more cellular stromal component[24,35]. Epithelial atypia also noted and it will mimics like carcinoma [34].

Breast Carcinomas:

Invasive Ductal Carcinoma:

Invasive ductal carcinoma, common malignant tumor of breast and it accounts for 40% to 75% of all breast cancers. IDC is mostly solid. Palpation and mammography helps in detection of these lesions. During fine needle aspiration IDCs are found to be gritty in consistency. FNA is of limited use on grading breast carcinomas.

Cytological features of of invasive ductal carcinoma:

They are hypercellular. Cells are isolated and they are poorly cohesive. Nucleus is often protruding from the cytoplasm. Enlarged hyperchromatic nuclei is seen, with size and shape variation [36,37] and fine to coarsely granular chromatin. Nucleoli is prominent [6,24].

Both type of cytological preparations (conventional smear and liquid based smear) have more or less same features for detection of breast carcinomas. LBC picture of ductal carcinoma shows clusters of malignant ductal epithelial cells having pleomorphic hyperchromatic nucleus with scant to moderate amount of cytoplasm. Background is free from haemorrhage or necrosis.

Dey et al (2000) stated that it was easier to diagnose invasive ductal carcinoma in liquid based preparation, due to clear background and detailed

nuclear features of the neoplastic cells. However clean background means an uninformative background because, traditional diagnostic clues associated with malignancy like blood and necrotic material are lost in liquid based preparations.

Ryu et al (2013) found that there are remarkable differences of nuclear features in breast carcinomas processed by liquid based cytology in comparison to conventional smear, including more prominent nucleoli, hyperchromasia and less coarse chromatin.

Michael et al (2000), Dey et al (2000) stated that large clusters of cells are reduced to smaller aggregates. Ryu et al (2013) described that three dimensional clusters are more common in liquid based preparations in contrast with Michael et al (2000) which revealed the more common flattened cell aggregates present in TP slides.

Mygdakos et al (2009), Kalpalata Tripathy et al (2015), Gerhard et al (2014) described that ductal carcinoma can easily be diagnosed by liquid based preparation than that of conventional smear because of clean background and better nuclear features.

Invasive Lobular Carcinoma:

It constitutes about 5% to 15% of invasive breast carcinomas.

Cytlogical features of invasive lobular carcinoma:

Smears are hypocellular due to stromal fibrosis. Cells arranged in singles, small groups and linear arrays. The cells are small to medium sized with cytoplasmic vacuole [37] . The nucleus is hyperchromatic with small nucleolus.

Medullary Carcinoma:

Incidence of medullary carcinoma is 1% to 7% of breast tumors.

Cytological features of medullary carcinoma:

Smears are hypercellular with isolated cells and loose clusters. Macronucleolus is more prominent and irregular [37]. Numerous mitoses are seen. Cytoplasm is granular. Many lymphocytes are seen.

Mucinous Carcinoma (colloid):

Incidence of mucinous carcinoma is 2% of invasive breast. Distinction between mucinous carcinoma and IDC with mucinous change is not possible with help of FNA.

Cytological features of mucinous carcinoma:

Cohesive tight clusters of cells with three-dimensional balls like arrangement [24,37]. Capillary structures are branched. Nucleus is uniform with small cytoplasmic vacuolisation.

Mucinous carcinoma cannot be diagnosed with the help of LBC because the important feature of mucinous carcinoma, the mucoid background is lost during liquid based preparation.

Michael et al (2000) described that mucinous carcinoma and low grade carcinomas(invasive and in situ ductal carcinomas, tubular and lobular carcinomas) of the breast are reported to be difficult to diagnose using LBC preparation.

Veneti et al (2003) described that the mucinous carcinoma diagnosed by cytology depends upon the presence of mucus in the background which is lost during LBC preparations. In one study this diagnosis was missed because this material was not present on the slides.

Tubular Carcinoma:

Incidence of this carcinoma is less than 2%. Prognosis is favourable. The sensitivity for diagnosing tubular carcinoma is lower for FNA than for core biopsy.

Cytological features of tubular carcinoma:

Hypocellular smears due to dense fibrosis. Cohesive angular clusters of cells. Peripherally perpendicular cells arranged around tubular clusters [41].

Metaplastic Carcinomas:

Incidence is less than 1% of breast carcinomas.

Cytological features of metaplastic carcinomas:

Cells show moderate to marked cytologic atypia. Clusters and isolated tumor cells are seen. Pleomorphic, spindle-shaped cells. Intermingled with malignant squamous or glandular cells[41]. Amorphous debris and inflammatory cells are present in the background.

Metastatic Tumors:

Non-mammary tumors can metastasize to the breast parenchyma. The common tumors that metastasize to breast are lung cancer, renal cell carcinoma, melanoma, adenocarcinoma of the stomach and intestinal carcinoid tumors.

Cytological features of metastatic tumors:

Consider the metastatic tumor whenever the cytologic findings are not typical for breast carcinoma.

MATERIALS AND METHOD

STUDY PLACE:

Coimbatore Medical College Hospital, Coimbatore

STUDY DESIGN:

This study includes a total of 100 breast fine needle aspirates obtained prospectively from patients who come to our pathology department with breast lump during the study period July 2015 to July 2016.

Inclusion criteria

Both female and male patients

Age: 18 to 80 years

Patients with clinically palpable breast enlargement

Exclusion criteria

Age: less than 18 years

Uncooperative patients

DATA COLLECTION:

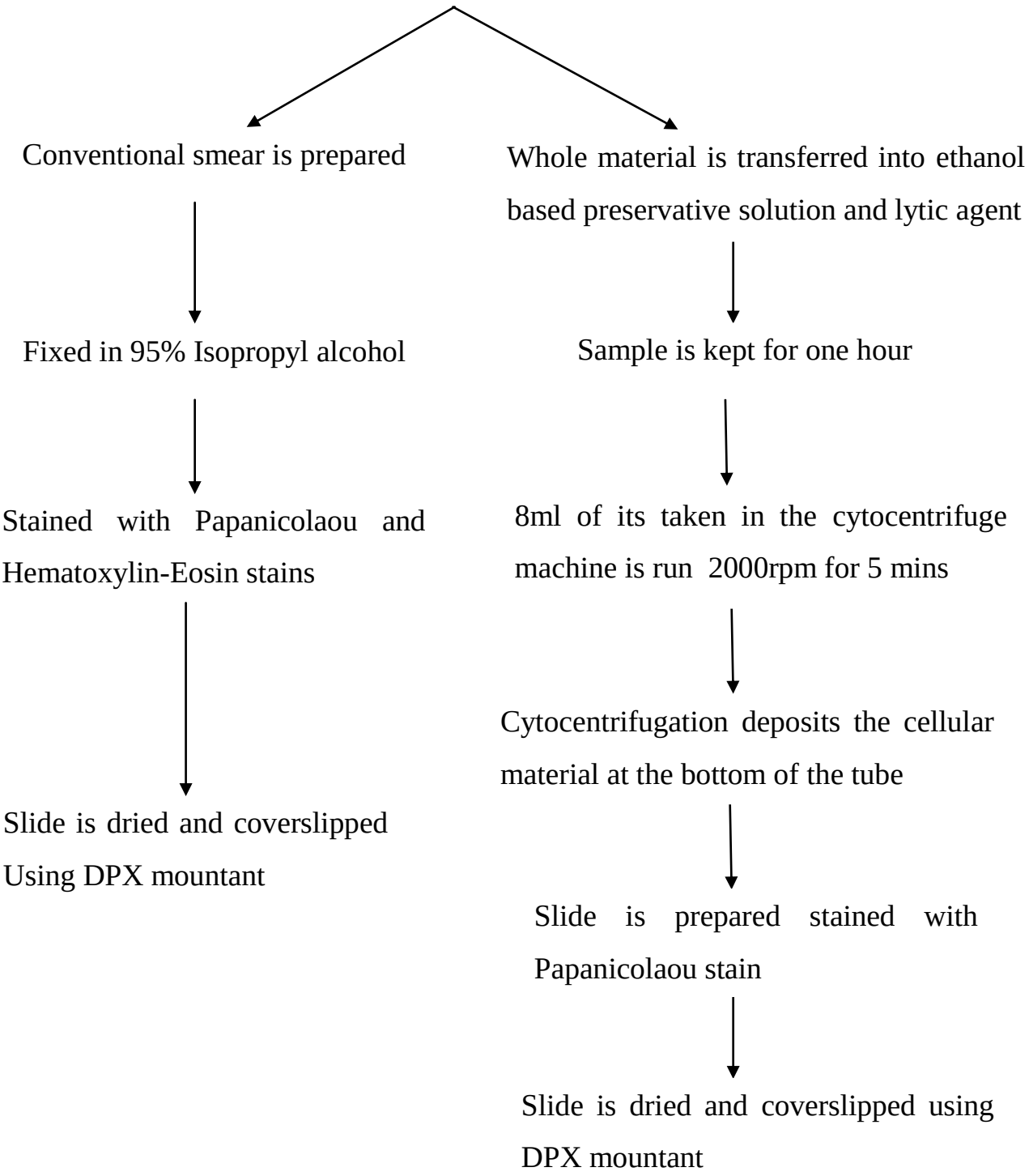
Both male and female patients with palpable breast lesions are included in the study. Patient's age, clinical history and ultrasound findings (if available) were recorded. Consent from the patient was obtained.

METHODOLOGY AND TECHNIQUE USED:

Conventional and liquid based smears were prepared using cytological material obtained by separate needle passes. The aspirates were performed using 26 gauge needle connected to 10ml syringe. Non-aspiration technique was followed to minimize bloody samples.

Liquid based cytology smears were prepared using centrifuge machine.

Fine needle aspiration cytological material



Note:

1. Conventional smears were stained in Hematoxylin and Eosin and the original cytological diagnoses were made using conventional slides.
2. To eliminate and minimize the variation in sampling, the principle investigator of the study was involved in performing fine needle aspiration procedure.

Stained conventional and liquid based smears were interpreted using the diagnostic categories recommended by E.C. Working Group on Breast Screening.

C1. Unsatisfactory

C2. Benign Adequate

C3. Atypia probably benign

C4. Suspicious of malignancy

C5. Malignant

The sensitivity, the specificity, the diagnostic accuracy, the positive predictive value and the negative predictive values were analysed for liquid based smears and they were compared with the conventional one. In addition, both liquid based and conventional methods were correlated with histopathological diagnosis whenener available.

Available corresponding mastectomy specimens were received and fixed in 10% formalin. Paraffin embedded sections obtained from routine processing were cut at a thickness of 3microns using Leica microtome. The slides were then stained with Hematoxylin and Eosin.

PROCEDURE FOR HEMATOXYLIN AND EOSIN STAINING FOR CYTOLOGICAL SMEARS

1. Fix in (95%)isopropyl alcohol -20 minutes
2. Hematoxylin-15 minutes
3. Blueing in tap water-10minutes
4. Eosin-7dips
5. Rinse in tap water
6. Dry, xylene, Mount with DPX

PROCEDURE FOR PAPANICOLAOU STAINING

1. Fix smears in 95% isopropyl alcohol-20 minutes
2. Isopropyl alcohol (80%)-1minute
3. Isopropyl alcohol (75%)-1 minute
4. Isopropyl alcohol (50%)-1 minute
5. Wash in tap water-10 minutes
6. Harris hematoxyline- minutes
7. Wash in tap water-gently& briefly

8. Differentiate in 1% acid alcohol(1-2 dips)

9. Blueing in tap water-1 minutes

10. 70% isopropyl alcohol-5 minutes

11. 90% isopropyl alcohol-5 minutes

12. OG-6 – 2 minutes

13.95% isopropyl alcohol-1 minute

14.95% isopropyl alcohol-1 minute

15.95% isopropyl alcohol-1 minute

16. Eosin Azure50 – 4 minutes

17. 95% isopropyl alcohol-1 minute

18.95% isopropyl alcohol-1 minute

19.95% isopropyl alcohol-1 minute

20. Xylene : Alcohol (1:)-5 minutes

21. Xylene I, II-each 10 minutes

22. Mount with DPX

In order to standardize the present study the following scoring system followed[39]

Parameters for cytomorphological correlation

Cytologic features	Score 0	Score 1	Score 2	Score 3
Cellularity	Nil	Scanty	Adequate	Abundant
Background blood, cell debris	Nil	Occasional	Good amount	Abundant
Informative background	Absent	Present		
Monolayer	Absent	Occasional monolayer cells	Many monolayer cells	
Cell architecture	Not recognised	Partially recognised	Well recognised	
Nuclear detail	Poor	Fair	Good	Very good
Cytoplasmic detail	Poor	Fair	Good	Very good

RESULTS

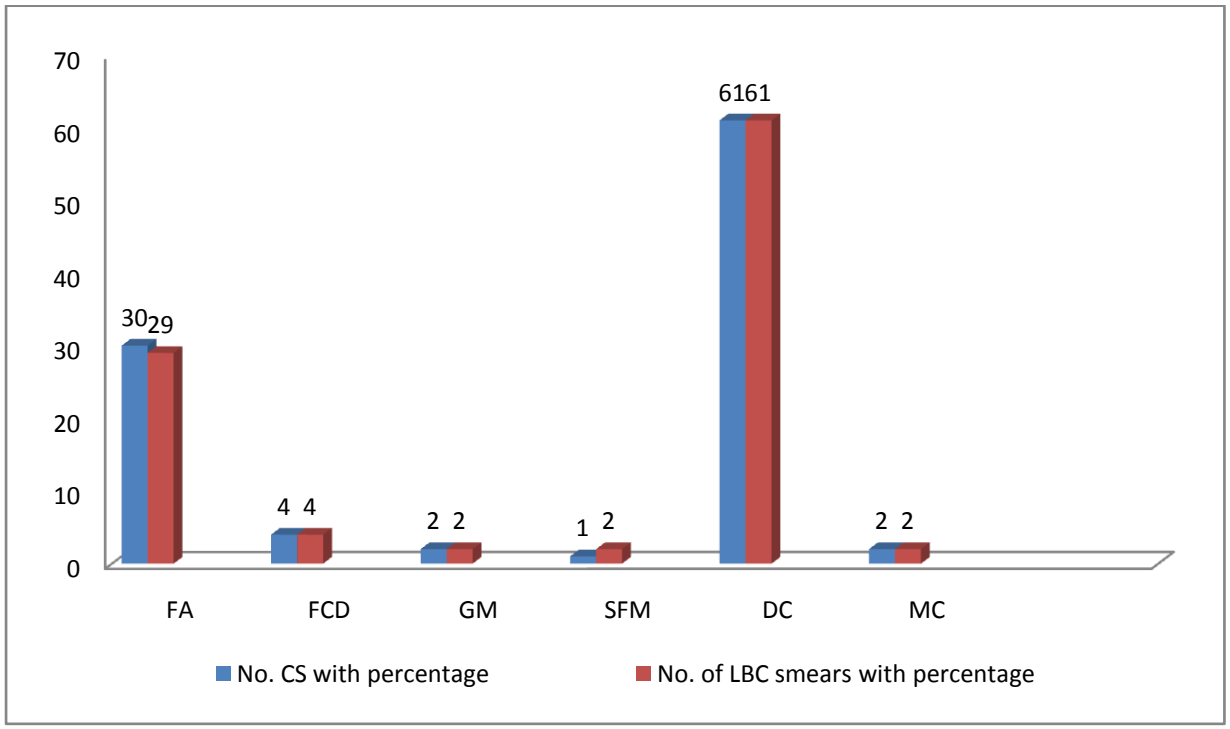
Total of 100 fine needle aspiration samples (98 from women and 2 from men) were included in the study. Both conventional and liquid based smears were prepared for all 100 fine needle aspiration specimens.

Table – 1: Total number of cases done in Conventional method and Liquid based cytology method.

S.No	Cytological diagnosis	No. of CS with percentage	No.of LBC smears with percentage
1.	FA	**30(30%)**	**29(29%)**
2.	FCD	**4(4%)**	**4(4%)**
3.	GM	**2(2%)**	**2(2%)**
4.	SM	**1(1%)**	**2(2%)**
5.	DC	**61(61%)**	**61(61%)**
6.	MC	**2(2%)**	**2(2%)**
	TOTAL NO. OF CASES	**100**	**100**

The above table shows total number of cases in each one of the study category. Benign category includes fibroadenoma, fibrocystic disease of breast and gynecomastia constituting about 35% of cases in each method. Suspicious of malignant category constitutes 2% cases in LBC preparation and 1% case in conventional method. Malignant category had equal incidence in liquid based and conventional methods, constituting 61 cases of ductal carcinoma and 2 cases of mucinous carcinoma.

CHART -1: Total number of cases done in Conventional method and Liquid based cytology method.



[FA – Fibroadenoma, FCD - Fibrocystic disease of breast, GM – Gynecomastia, SM – Suspicious of malignancy, DC – Ductal carcinoma, MC – Mucinous carcinoma

CHART – 2: Age distribution in benign lesions

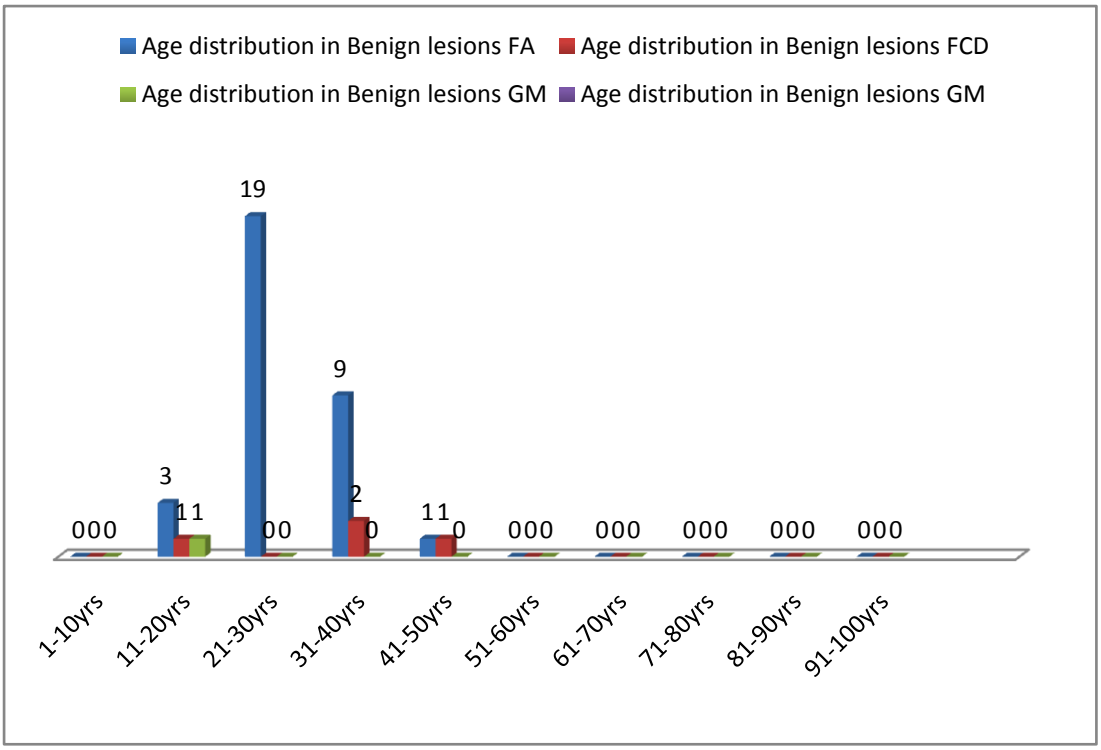
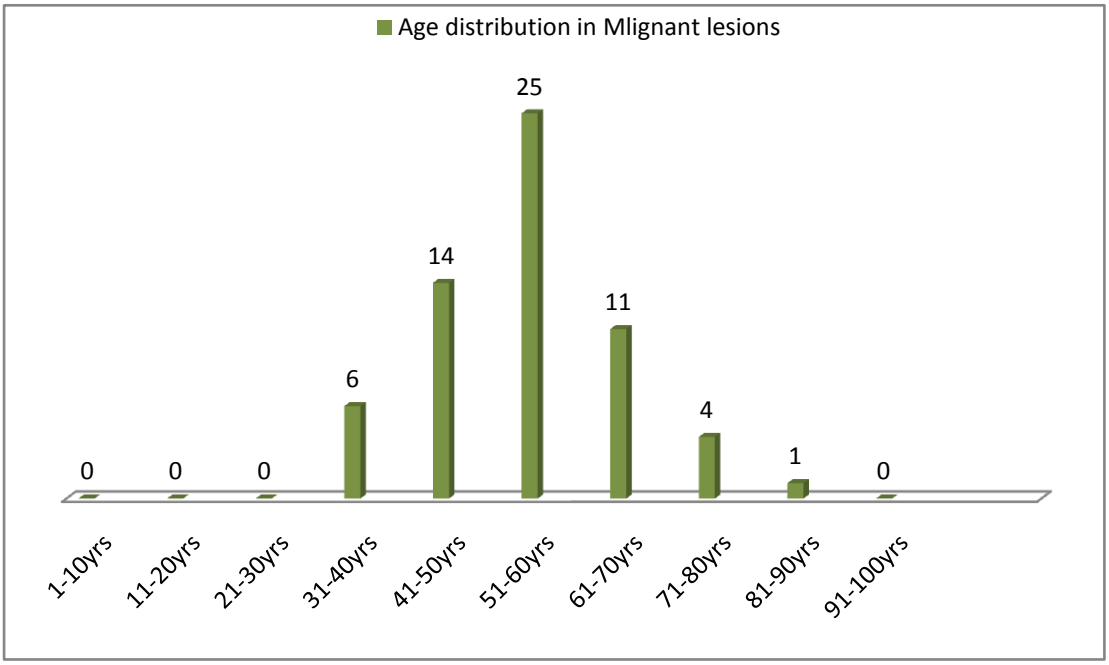


CHART -3: Age distribution in malignant lesions



CYTOMORPHOLOGICAL CORRELATION

Table-2: Comparison of cellularity between Liquid based and Conventional method

	CELLULARITY	
	LBC	**CS**
0-ZERO	0	0
1-SCANTY	1	3
2-ADEQUATE	33	93
3-ABUNDANT	66	4

CHART-4: Comparison of cellularity between Liquid based and Conventional method

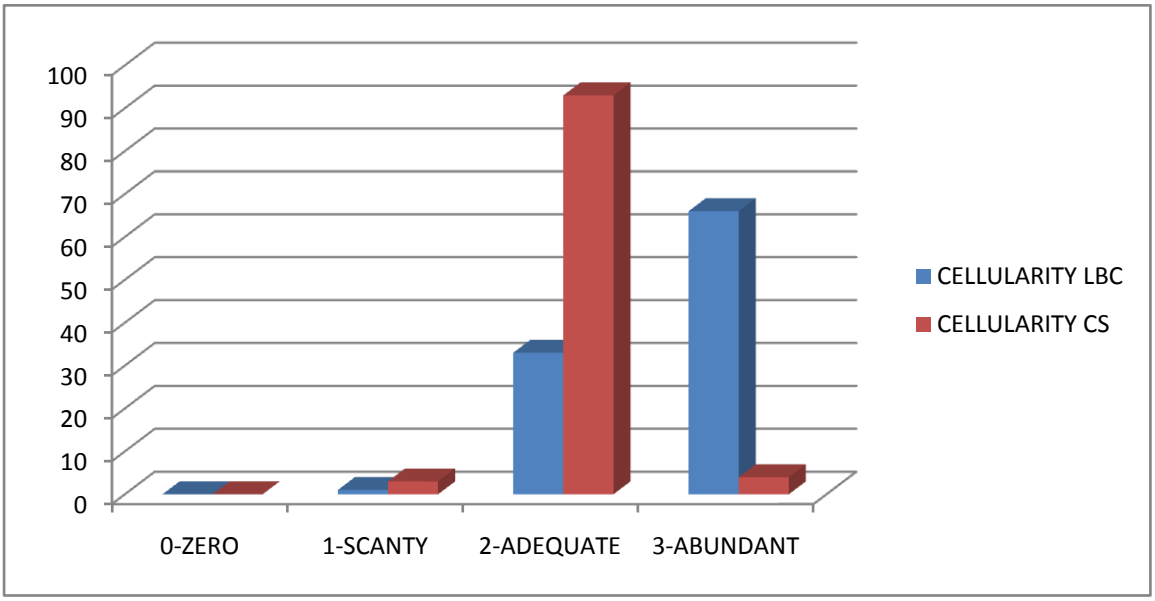


Table -3: Comparison of background material (blood, cell debris) between Liquid based and Conventional method

	LBC	CS
0-ZERO	100	0
1-OCCASIONAL	0	16
2-GOOD AMOUNT	0	40
3-ABUNDANT	0	44

CHART-5: Comparison of background material (blood, cell debris) between Liquid based and Conventional method

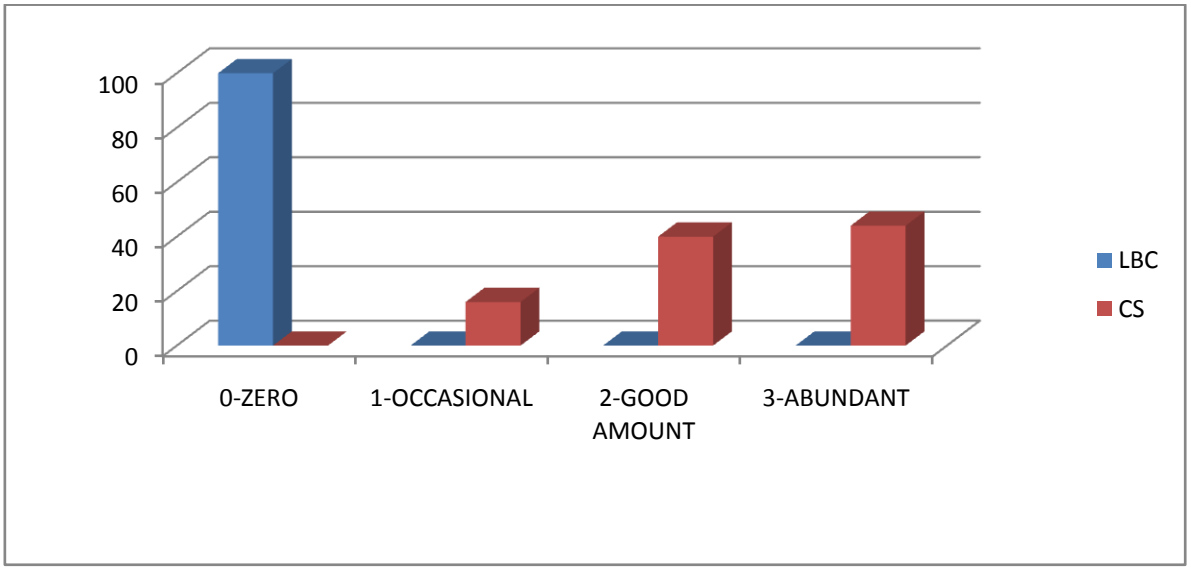


Table -4: Comparison of Informative background between Liquid based and Conventional method

INFORMATIVE BACKGROUND		
	LBC	**CS**
0-ABSENT	70	44
1-PRESENT	30	66

CHART –6: Comparison of Informative background between Liquid based and Conventional method

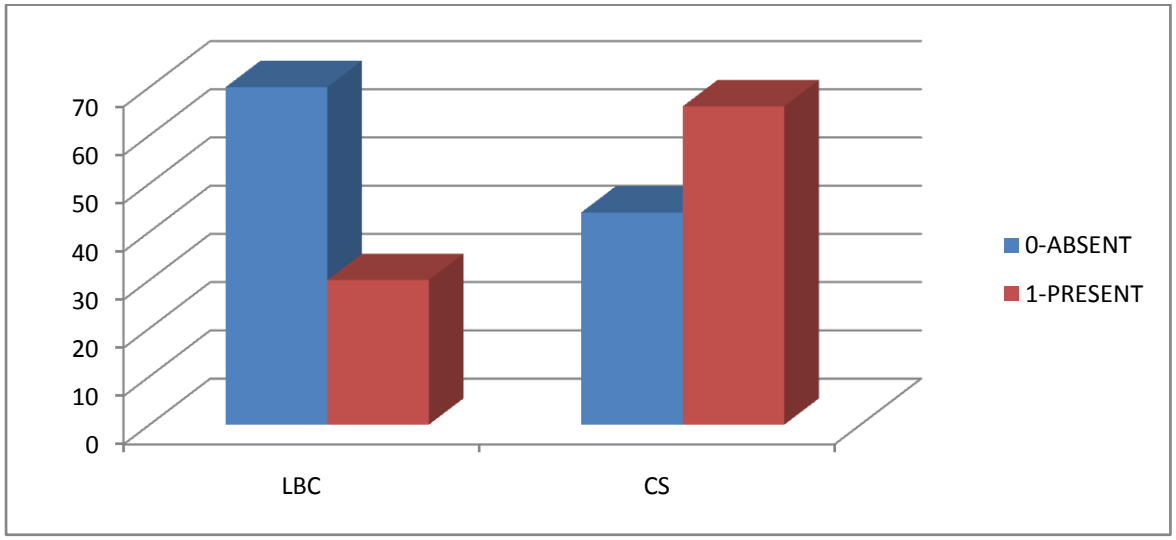


Table -5: Comparison of monolayer arrangement between Liquid based and Conventional method.

	MONOLAYER ARRANGEMENT	
	LBC	**CS**
0- ABSENT	0	75
1-OCCASIONAL	14	14
2-GOOD AMOUNT	86	16

CHART – 7: Comparison of monolayer arrangement between Liquid based and Conventional method.

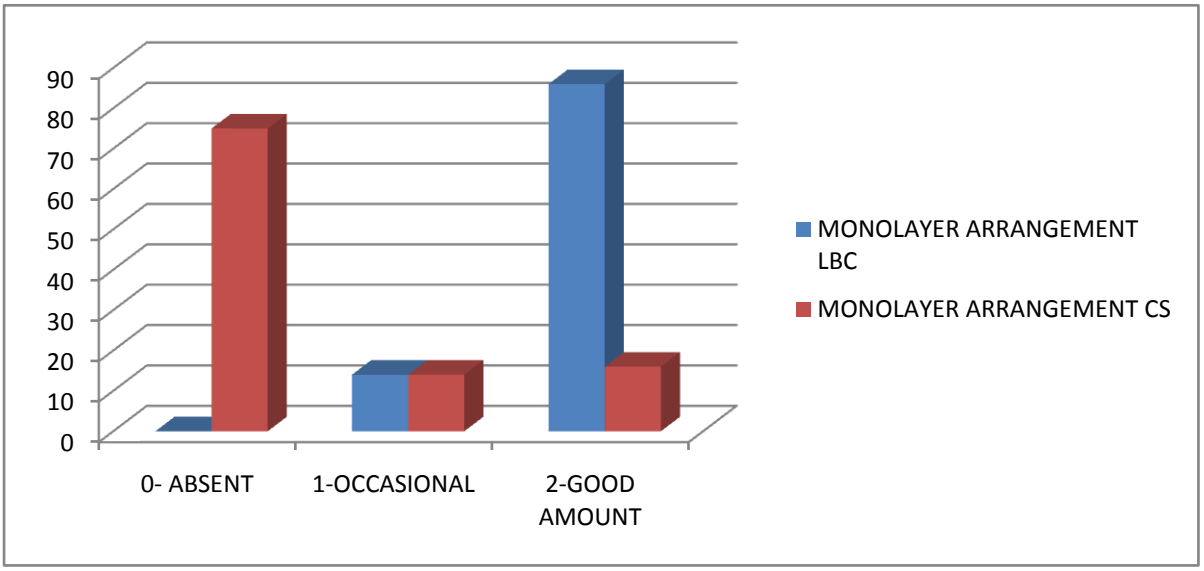


Table -6: Comparison of Cell architecture recognized by Liquid based and Conventional method.

	CELL ARCHITECTURE	
	LBC	**LBC**
0-NOT RECOGNISED	0	0
1-PARTIALLY RECOGNISED	14	26
2-WELL RECOGNISED	86	74

CHART – 8: Comparison of Cell architecture recognized by Liquid based and Conventional method.

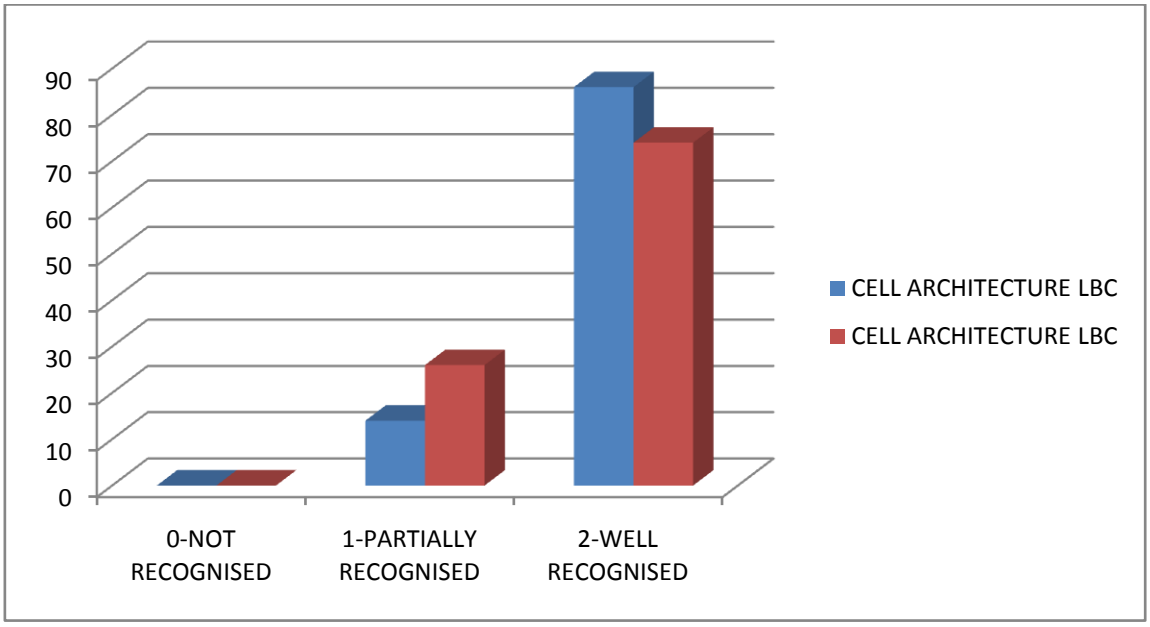


Table -7: Comparison of Nuclear detail between Liquid based and Conventional method

	Nuclear Detail	
	LBC	**CS**
0-Poor	0	0
1-Fair	14	18
2-Good	86	82
3-Very good	0	0

CHART – 9: Comparison of Nuclear detail between Liquid based and Conventional method

Table -8: Comparison of cytoplasmic details between Liquid based and Conventional method.

	Cytoplasmic Details	
	LBC	**CS**
0-Poor	0	0
1-Fair	0	0
2-Good	100	100
3-Very good	0	0

CHART – 10

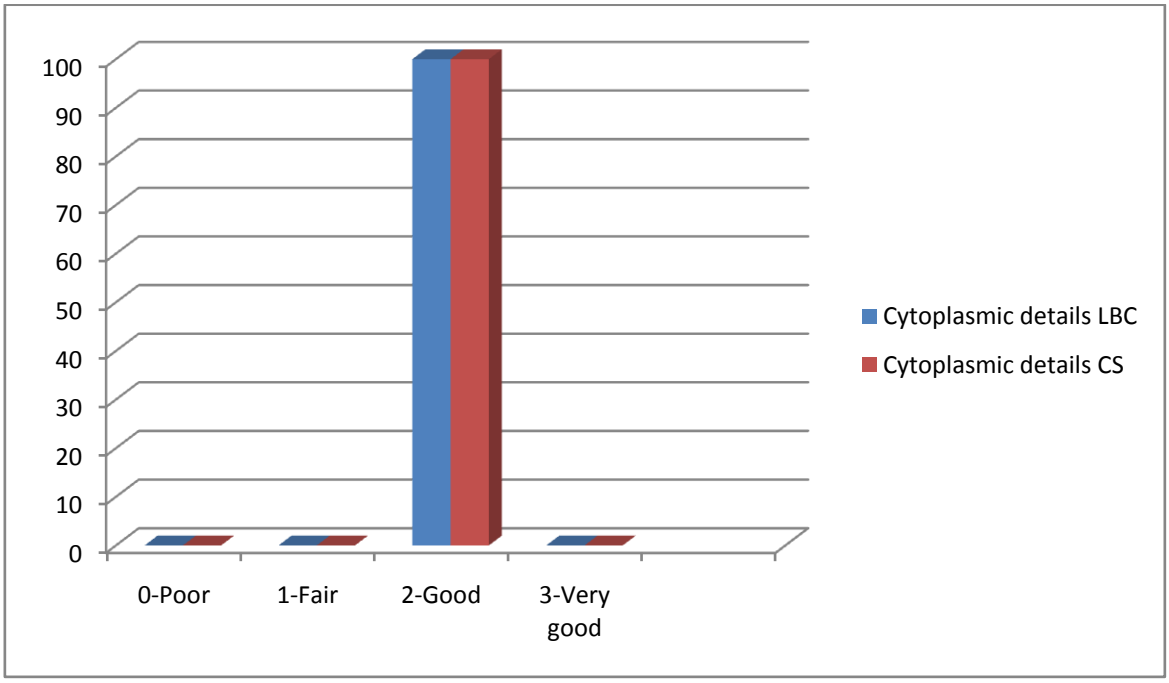


Table – 9:

Comparison of liquid based method and Conventional method in Bengin lesions			
	CS		
LBC	**Positive**	**Negative**	**Total**
Positive	32	3	35
Negative	0	63	63
TOTAL	32	66	98

Sensitivity - 100.00%

Specificity - 95.45%

Positve Predictive value - 91.42%

Negative Predictive value - 100.00%

Diagnostic Accuracy - 96.93%

CHART - 11

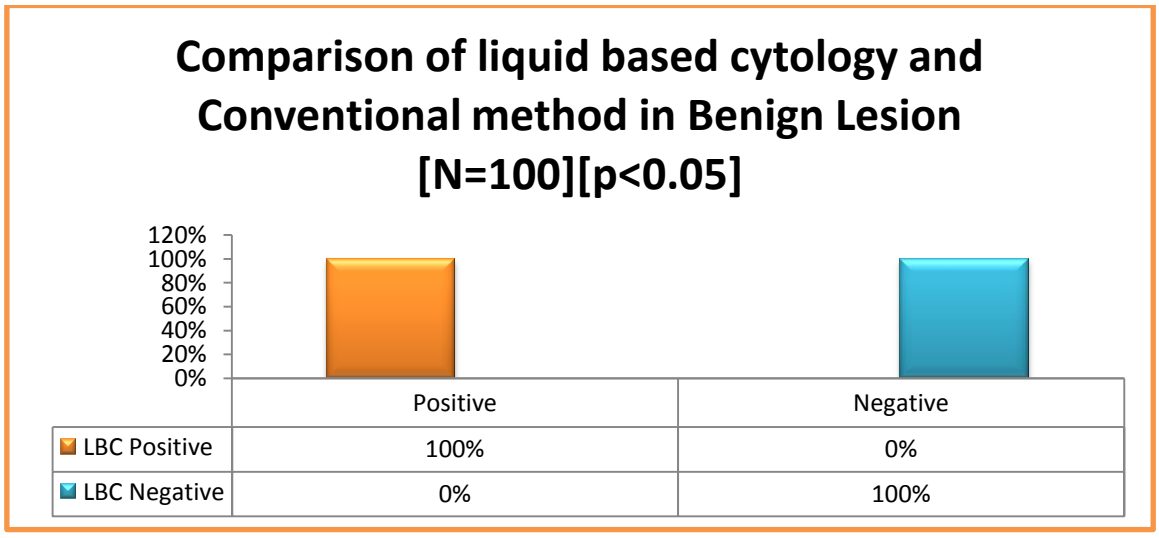


Table -10 COMPARISON OF LIQUID BASED METHOD AND CONVENTIONAL METHOD IN MALIGNANT LESIONS

	CS		
LBC	**Positive**	**Negative**	**Total**
Positive	63	0	63
Negative	0	37	37
TOTAL	63	37	100

Sensitivity - 100.00%

Specificity - 100.00%

Positve Predictive value - 100.00%

Negative Predictive value - 100.00%

Diagnostic Accuracy - 100.00%

CHART - 12

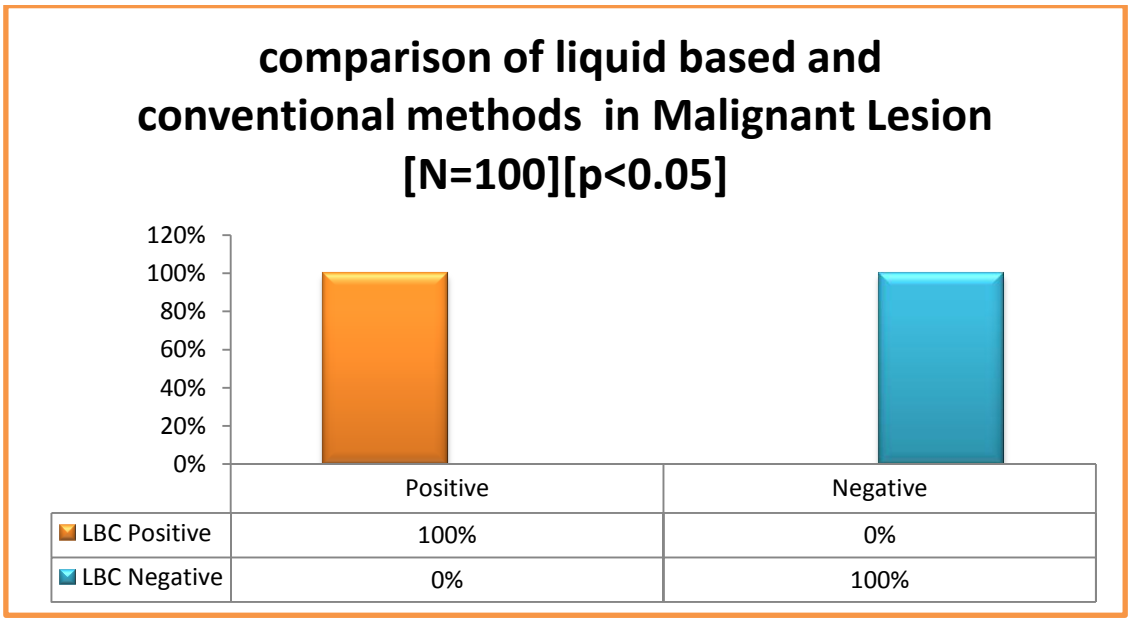


Table -11: Comparison of Liquid based method and Conventional method in Fibroadenoma (FA) cases.

Comparison of Liquid based method Conventional method in FA				
	CS			
LBC	**Positive**	**(%)**	**Negative**	**(%)**
Positive	27	100%	2	3%
Negative	0	0%	69	97%
TOTAL	27		71	

Sensitivity of LBC - 100.00%

Specificity of LBC - 97.18%

Positve Predictive value of LBC - 93.55%

Negative Predictive value of LBC - 100.00%

Diagnostic Accuracy of LBC - 98.00%

Table -12: Comparison of Liquid based method and Conventional method in Fibrocystic disease of breast (FCD) cases.

Comparison of Liquid based method and Conventional method in FCD				
	CS			
LBC	**Positive**	**(%)**	**Negative**	**(%)**
Positive	3	100%	1	1%
Negative	0	0%	96	99%
TOTAL	3		97	

Sensitivity of LBC - 100.00%

Specificity of LBC - 98.96%

Positve Predictive value of LBC - 75.00%

Negative Predictive value of LBC - 100.00%

Diagnostic Accuracy of LBC - 99.00%

Table -13: Comparison of Liquid based method and Conventional method in Gynecomastia (GM) cases.

Comparison of Liquid based method and Conventional method in GM				
	CS			
LBC	**Positive**	**(%)**	**Negative**	**(%)**
Positive	2	100%	0	0%
Negative	0	0%	98	100%
TOTAL	2		98	

Sensitivity of LBC - 100.00%

Specificity of LBC - 100.00%

Positve Predictive value of LBC - 100.00%

Negative Predictive value of LBC - 100.00%

Diagnostic Accuracy of LBC - 100.00%

Table 11, 12 & 13 – show that Liquid based method was 100% sensitive in detecting the benign cases (Fibroadenoma, Fibrocystic disease of breast, Gynecomastia). The diagnostic accuracy of Liquid based smears was 98%-100% comparable to the Conventional smears.

Table -14: Comparison of Liquid based and Conventional method in Suspicious of Malignancy (SM) cases.

Comparison of Liquid based method and Conventional method in SM				
	CS			
LBC	**Positive**	**(%)**	**Negative**	**(%)**
Positive	1	100%	1	1%
Negative	0	0%	98	99%
TOTAL	1		99	

Sensitivity of LBC - 100.00%

Specificity of LBC - 98.99%

Positve Predictive value of LBC - 50.00%

Negative Predictive value of LBC - 100.00%

Diagnostic Accuracy of LBC - 99.00%

Table -15: Comparison of Liquid based method and Conventional method in Ductal carcinoma (DC) cases.

Comparison of Liquid based method and Conventional method in DC				
	CS			
LBC	**Positive**	**(%)**	**Negative**	**(%)**
Positive	61	100%	0	0%
Negative	0	0%	39	100%
TOTAL	61		39	

Sensitivity of LBC - 100.00%

Specificity of LBC - 100.00%

Positive Predictive value of LBC - 100.00%

Negative Predictive value of LBC - 100.00%

Diagnostic Accuracy of LBC - 100.00%

Table -16: Comparison of Liquid based method and Conventional method in Mucinous carcinoma (MC) cases.

Comparison of liquid based method and Conventional method in MC				
	CS			
LBC	**Positive**	**(%)**	**Negative**	**(%)**
Positive	2	100%	0	0%
Negative	0	0%	98	100%
TOTAL	2		98	

Sensitivity of LBC - 100.00%

Specificity of LBC - 100.00%

Positve Predictive value of LBC - 100.00%

Negative Predictive value of LBC - 100.00%

Diagnostic Accuracy of LBC - 100.00%

Tables 14 & 15, show that the LBP was equally sensitive to conventional one in diagnosing malignant category.

Table -17: Correlation of Liquid based method with histological diagnoses

LBC method / Hist. Diagnosis	FA	FCD	GM	SM	DC	MC	TOTAL
FA	10	0	0	1	0	0	11
FCD	0	1	0	0	0	0	1
GM	0	0	1	0	0	0	1
DC	0	0	0	1	20	0	21
MC	0	0	0	0	0	1	1
TOTAL	**10**	**1**	**1**	**2**	**20**	**1**	**35**

[FA – Fibroadenoma, FCD - Fibrocystic disease of breast, GM – Gynecomastia, SM – Suspicious of malignancy, DC – Ductal carcinoma, MC – Mucinous carcinoma, LBC- Liquid based cytology]

Among 100 fine needle aspiration cases, it was possible to compare cytology results with mastectomy speciemens in 36 cases only. Correlating LBP with available histological diagnoses, the following results were inferred. Out of 10 cases of fibroadenoma, all the 10 correctly diagnosed. 1 case of FCD correctly interpreted. 1 case of GM correctly diagnosed. 1 case of SM in LBC diagnosed as fibroadenoma in histopathology and another case of SM in LBC preparation diagnosed as ductal carcinoma in histopathology.

Table -18: Correlation of Conventional method with histological diagnoses.

CS / Hist. Diagnoses	FA	FCD	GM	SM	DC	MC	TOTAL
FA	8	0	0	0	0	0	8
FCD	0	1	0	0	0	0	1
GM	0	0	1	0	0	0	1
DC	0	0	0	1	21	0	22
MC	0	0	0	0	0	1	1
TOTAL	**8**	**1**	**1**	**1**	**21**	**1**	**33**

[FA – Fibroadenoma, FCD - Fibrocystic disease of breast, GM – Gynecomastia, SM – Suspicious of malignancy, DC – Ductal carcinoma, MC – Mucinous carcinoma, CS- conventional smear]

Totally 33 cases of Conventional preparation were correlated with histopathology findings. Malignant category of conventional smears correlated very well with histopathological diagnosis. Out of 10 cases of fibroadenoma 8 cases correlated with histopathology. 2 cases of fibroadenoma were not diagnosed in CS method due to very low cellularity. Gynecomastia and fibrocystic change cases of conventional smear preparation correlated very well with histopathology findings.

Table – 19: Diagnostic accuracy of Liquid based method

	Histological diagnoses				
	FA	**FCD**	**GM**	**DC**	**MC**
Sensitivity	100%	100%	100%	100%	100%
Specificity	96%	100%	100%	100%	100%
PPV	90.90%	100%	100%	100%	100%
NPV	100%	100%	100%	100%	100%
D.A	97.14%	100%	100%	100%	100%

[FA – Fibroadenoma, FCD - Fibrocystic disease of breast, GM – Gynecomastia, DC – Ductal carcinoma, MC – Mucinous carcinoma, PPV – positive predictive value, NPV- negative predictive value, D.A – diagnostic accuracy]

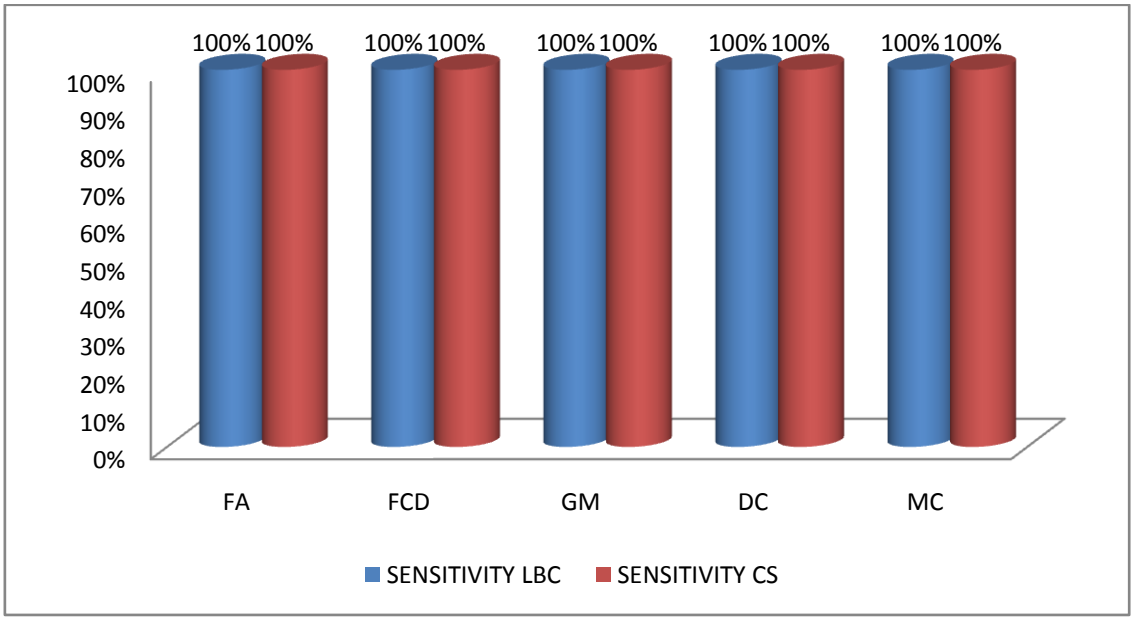
Table 20: Diagnostic accuracy of Conventional method

Histological Diagnoses					
	FA	**FCD**	**GM**	**DC**	**MC**
Sensitivity	100%	100%	100%	100%	100%
Specificity	92.59%	97.05%	100%	100%	100%
PPV	80%	50%	100%	100%	100%
NPV	100%	100%	100%	100%	100%
D.A	94.28%	97.14%	100%	100%	100%

[FA – Fibroadenoma, FCD - Fibrocystic disease of breast, GM – Gynecomastia, DC – Ductal carcinoma, MC – Mucinous carcinoma, PPV – positive predictive value, NPV- negative predictive value, D.A – diagnostic accuracy]

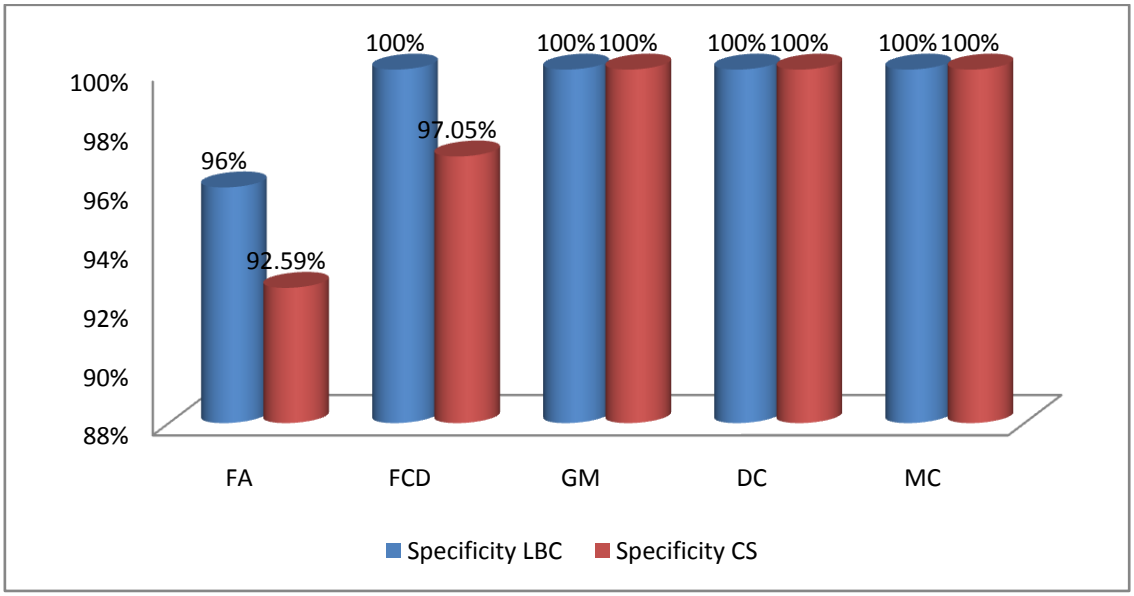
It was clearly evident from the above tables 19 & 20, that, Liquid based method was equally sensitive to conventional one (100%) in detecting the cases of FCD, FA, GM, DC. The specificity and diagnostic accuracy of Liquid based method were also equally comparable in all groups, except in suspicious for malignancy cases.

CHART – 13: Sensitivity of LBC and CS



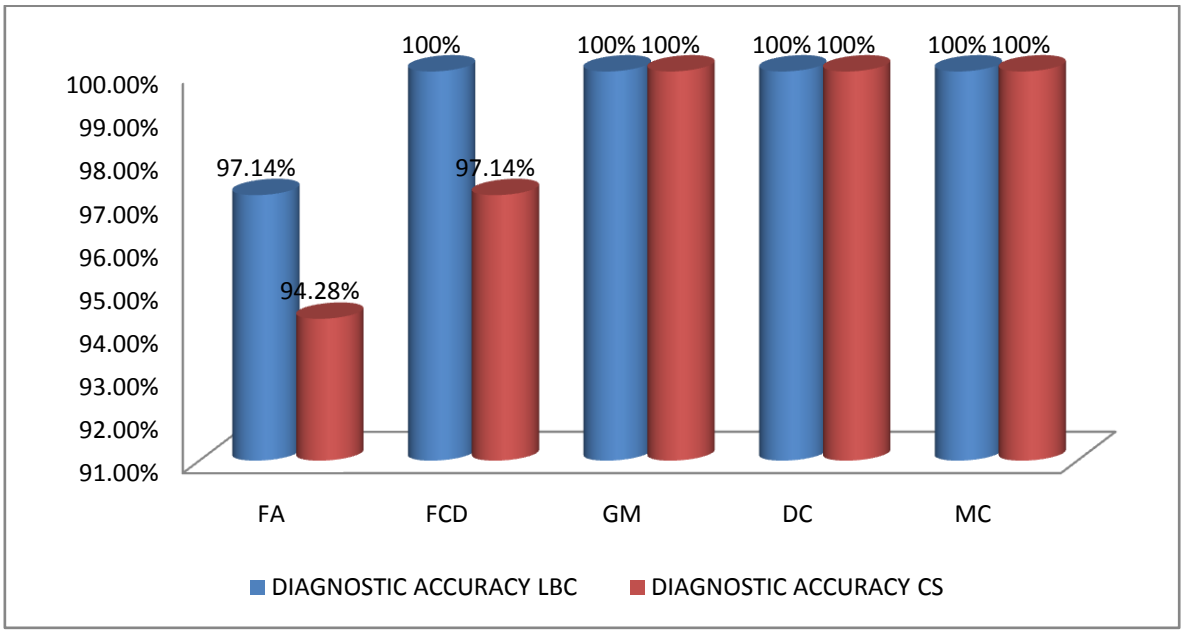
[FA – Fibroadenoma, FCD - Fibrocystic disease of breast, GM – Gynecomastia, DC – Ductal carcinoma, MC – Mucinous carcinoma, LBC- liquid based cytology, CS- Conventional smear]

CHART – 14: SPECIFICITY OF LBC & CS



[FA – Fibroadenoma, FCD - Fibrocystic disease of breast, GM – Gynecomastia, DC – Ductal carcinoma, MC – Mucinous carcinoma, LBC- liquid based cytology, CS- Conventional smear]

CHART -15: DIAGNOSTIC ACCURACY OF LBC & CS



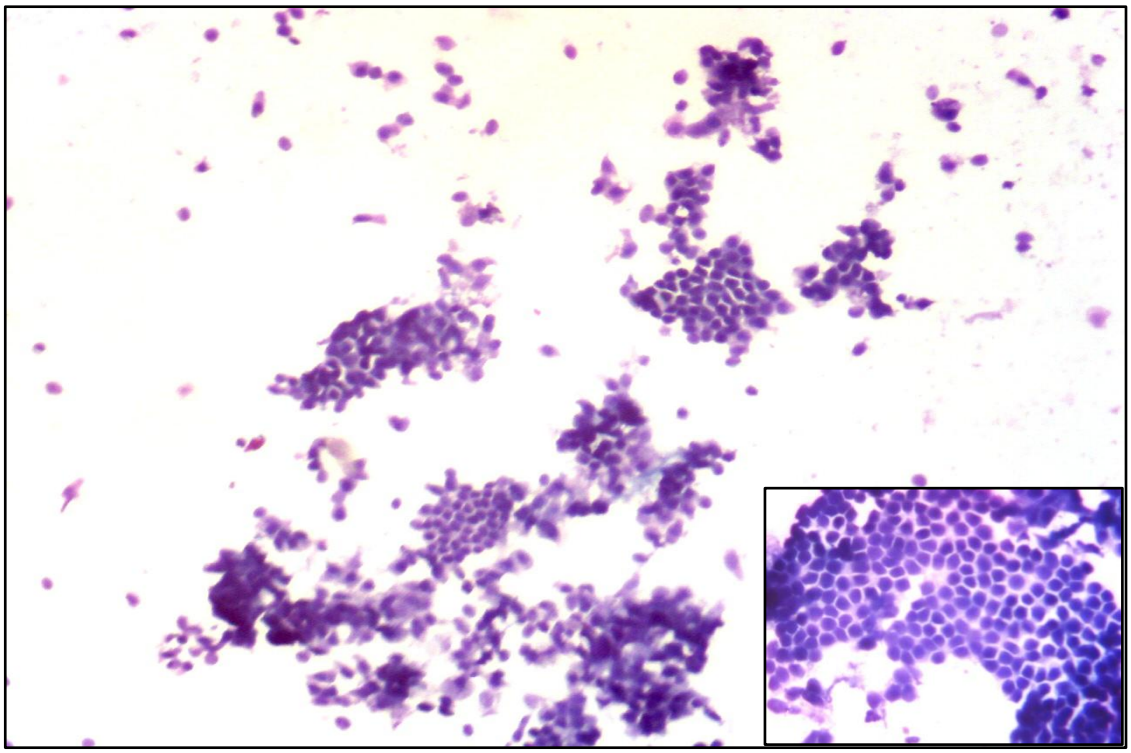


Fig.1: Fibroadenoma – predominantly arranged in monolayered sheets and scaterred bipolar cells in the clean background (10X). Inset (40X) shows monolayer arrangement. (Liquid based smear – Pap stain)

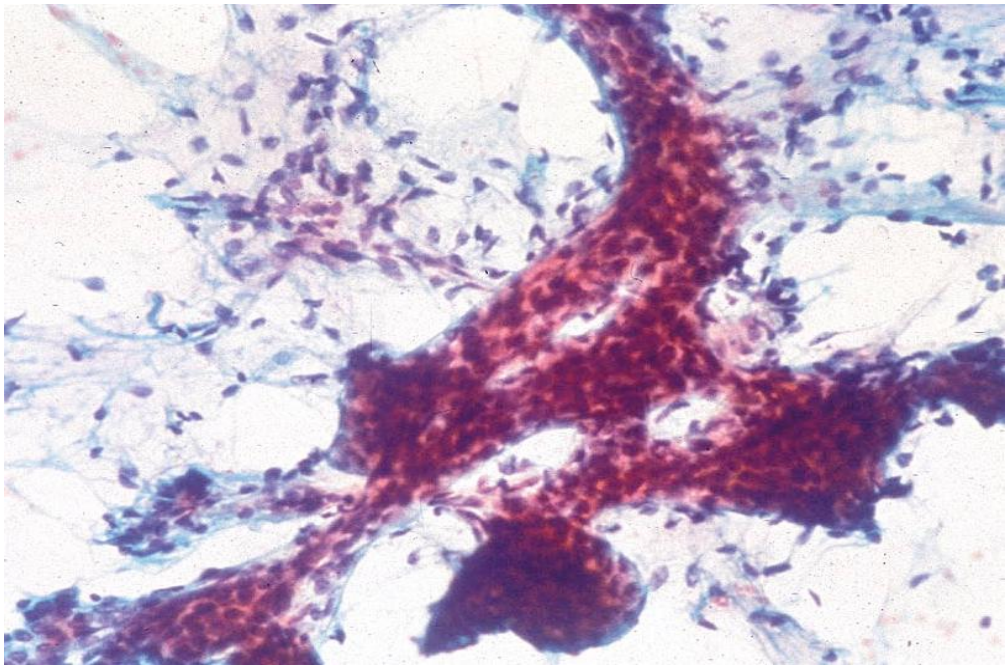


Fig .2: Fibroadenoma – sheets of ductal epithelial cells entangled within the blood, fibromyxoid stroma, naed bipolar cells (Conventional smear – pap stain)10 X

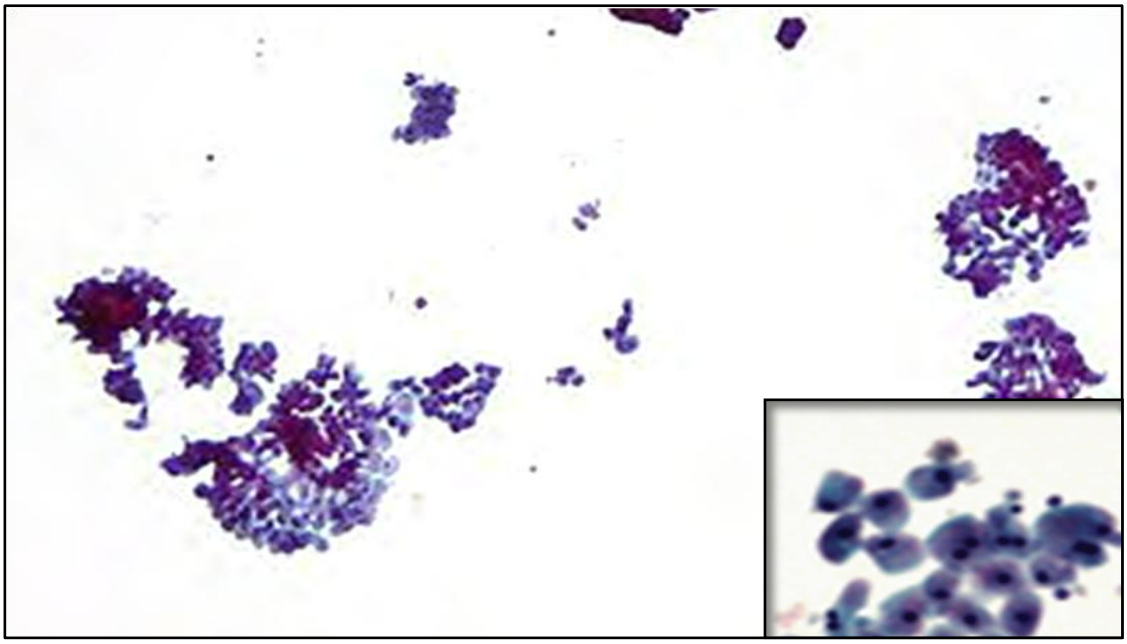


Fig.3: Fibrocystic disease of breast – monolayered arrangement of ducta epithelial cells and apocrine metaplastic cells (10X). Inset (40X) shows apocrine metaplastic cells (Liquid based smear – Pap stain).

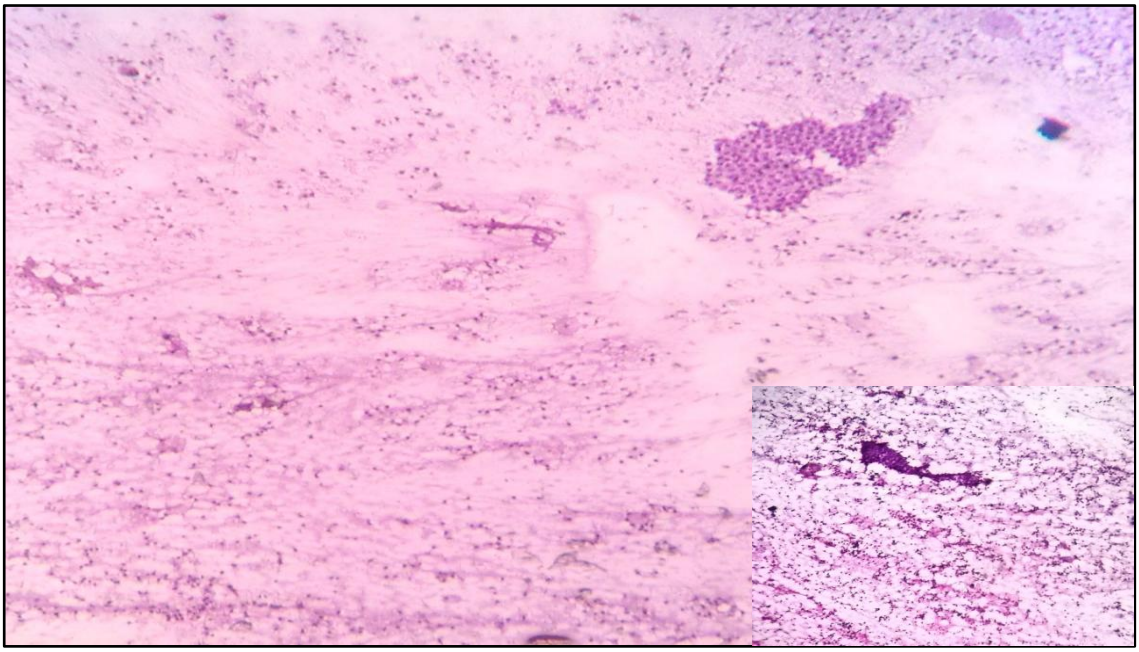


Fig .4: Fibrocystic disease of breast – scattered ductal epithelial cells and apocrine metaplastic cells in the fluid background. (Conventional smear – pap stain) 10 X

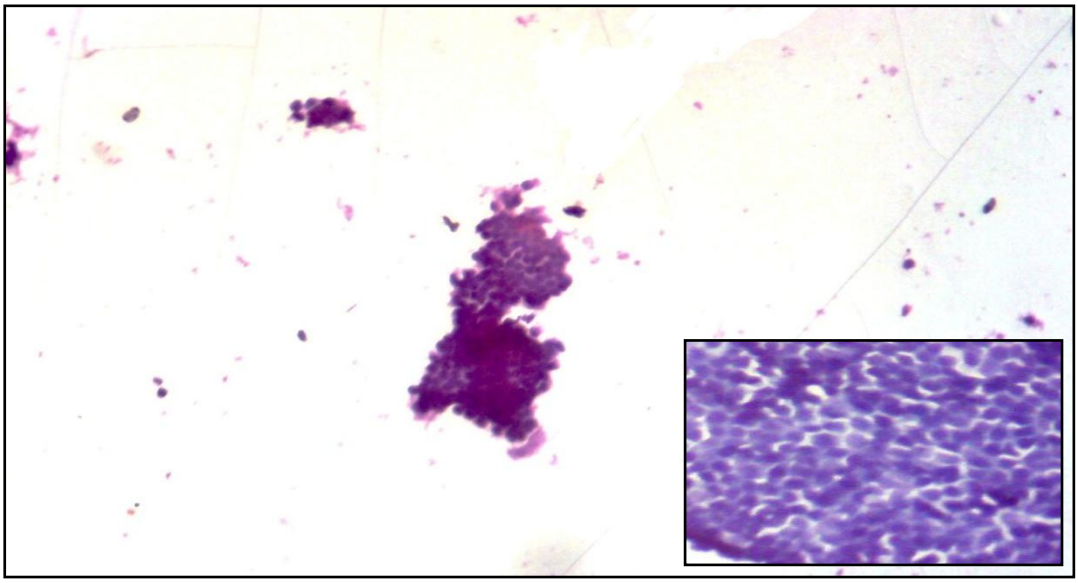


Fig .5: Gynecomastia – sheets of benign ductal epithelial cells in the clean backround (10X) (Liquid based smear – Pap stain)

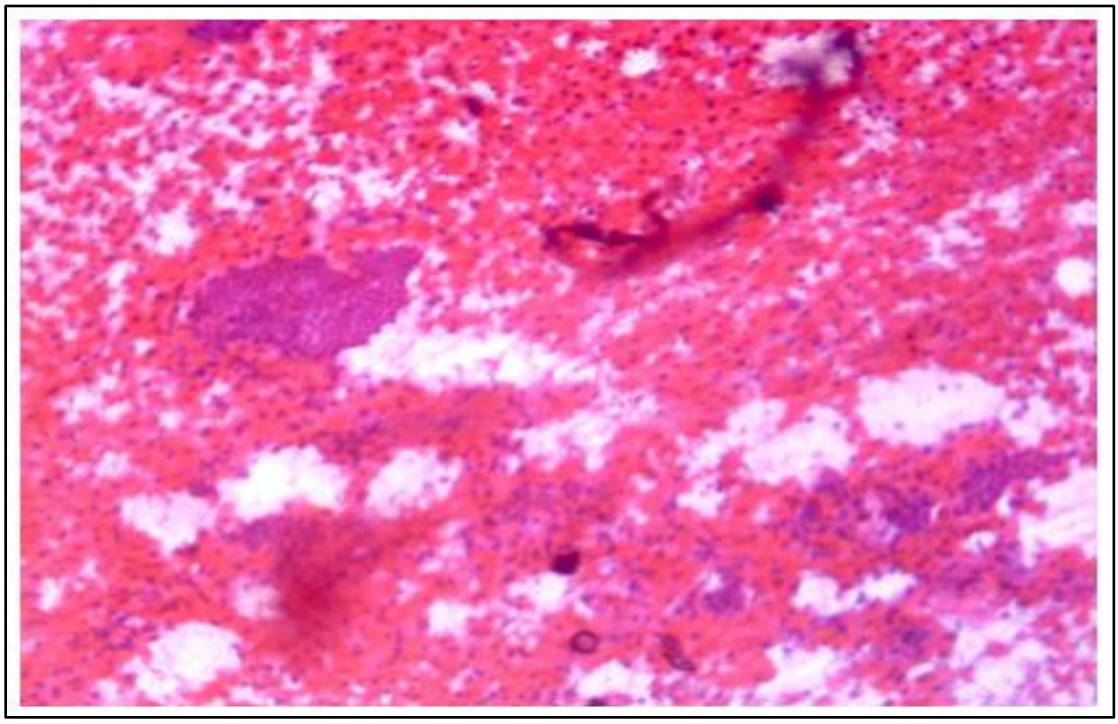


Fig. 6: Gynecomastia – small clusters of ductal epithelial cells in the bloody backgound. (Conventional smear – pap stain)10 X

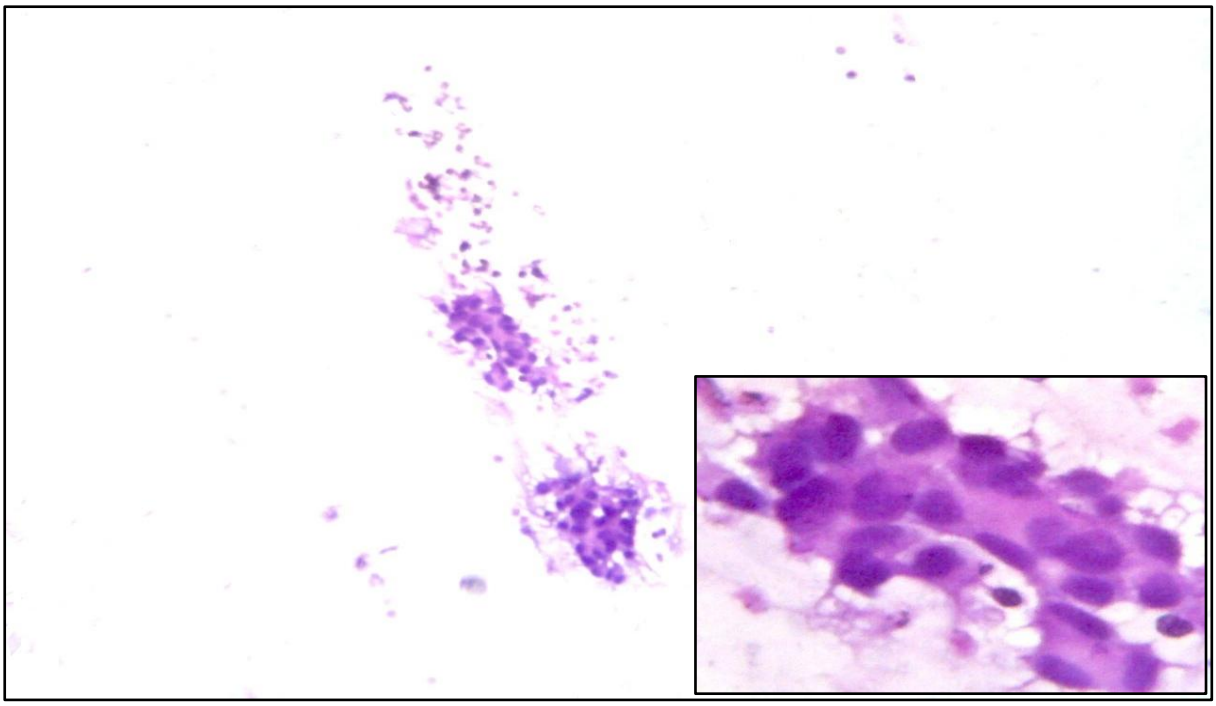


Fig .7: Suspicious for malignancy – small three dimensional clusters of cells with scant cytoplasm and mild to moderate pleomorphism (10X). Inset (40X) Liquid based smear – Pap stain

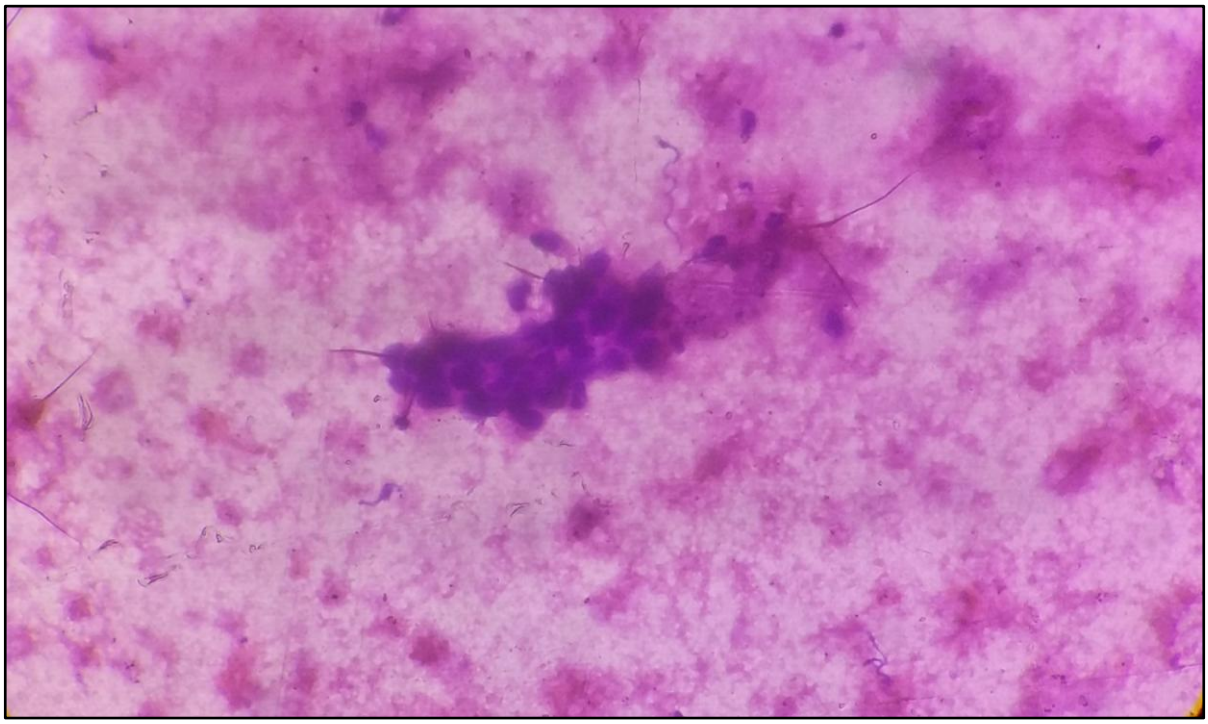


Fig .7A:Conventional smear – small clusters ductal epithelial cells with nucleus showing mild pleomorphism (10X).

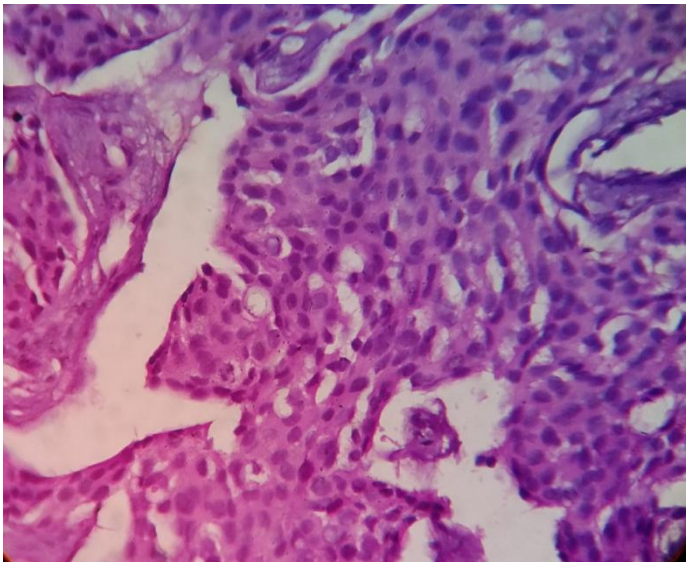
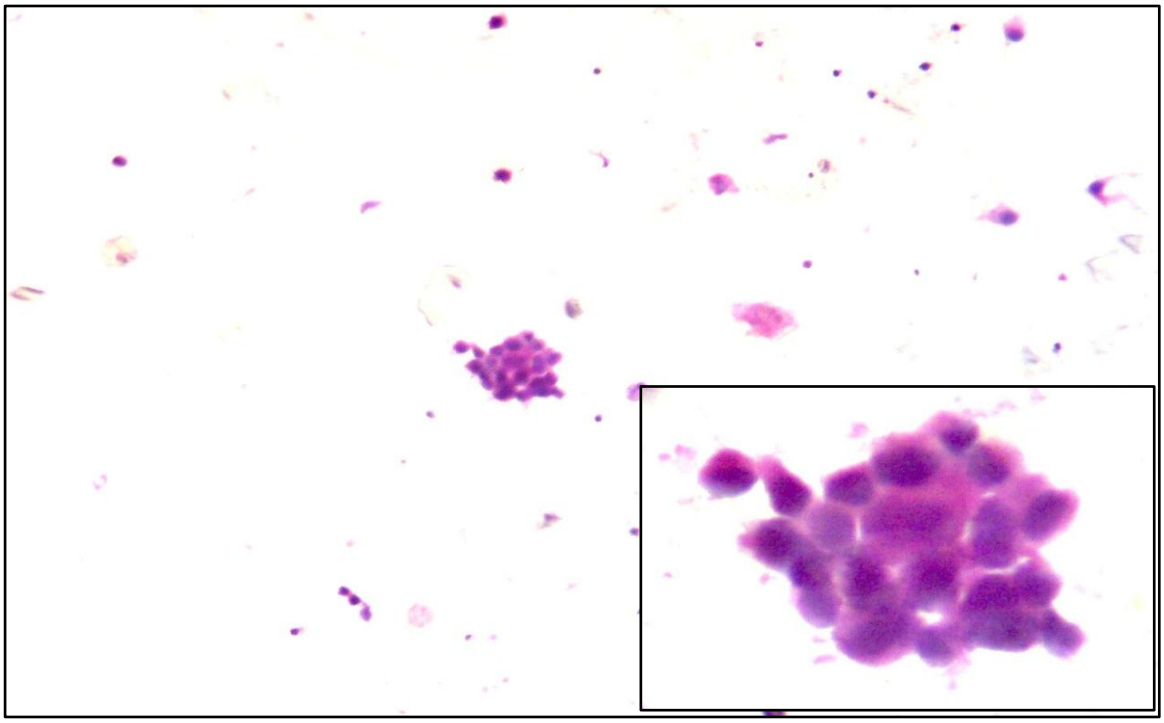


Fig.7B: H & E – microscopic view of ductal carcinoma (HPE No. 846/16)



8: Suspicious for malignancy – small three dimensional clusters of cells with scant cytoplasm and mild to moderate pleomorphism (10X). Inset (40X) (Liquid based smear – Pap stain)

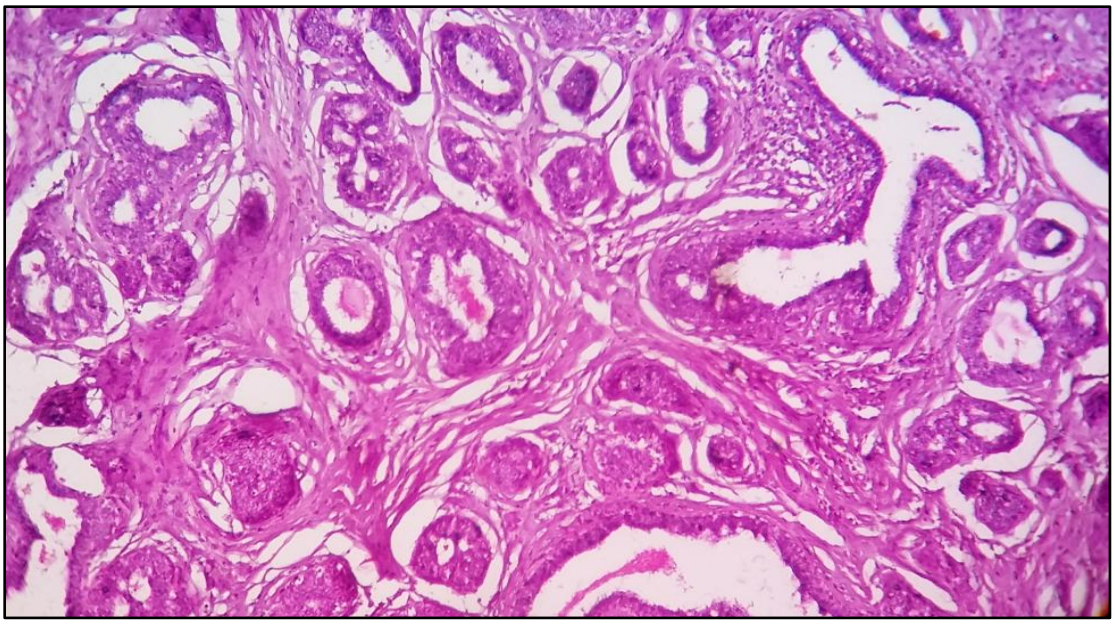


Fig.8A: Microscopic view of fibroadenoma with epithelial hyperplasia (40X). (HPE No.1335/16)

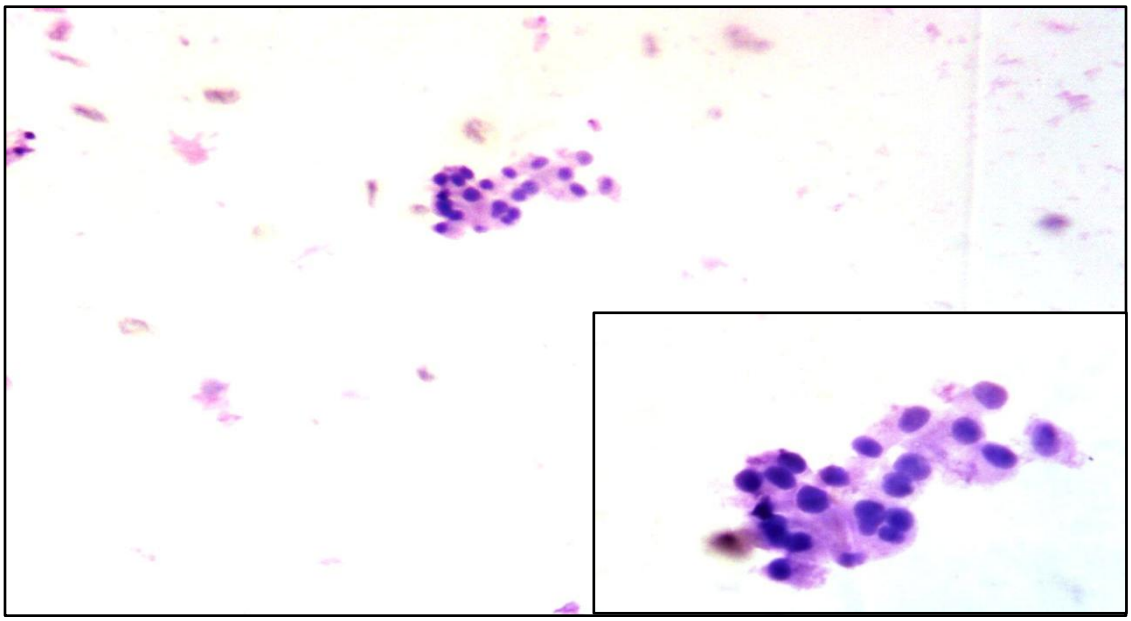


Fig. 9: Ductal carcinoma – small clusters and singly scaterred malignant ductal epithelial cells with nuclear pleomorphism in clean background (10X). Inset (40X) Malignant ductal epithelial cells (Liquid based smear – Pap stain)

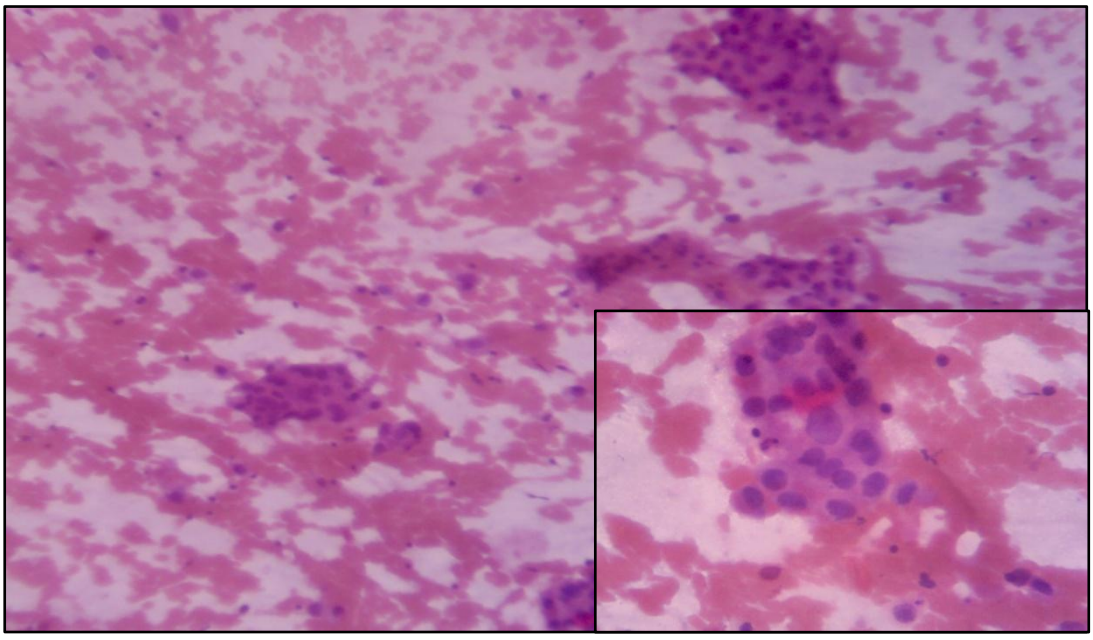


Fig .10: Ductal carcinoma- Conventional smear – (pap stain)10 X . Inset (40X)

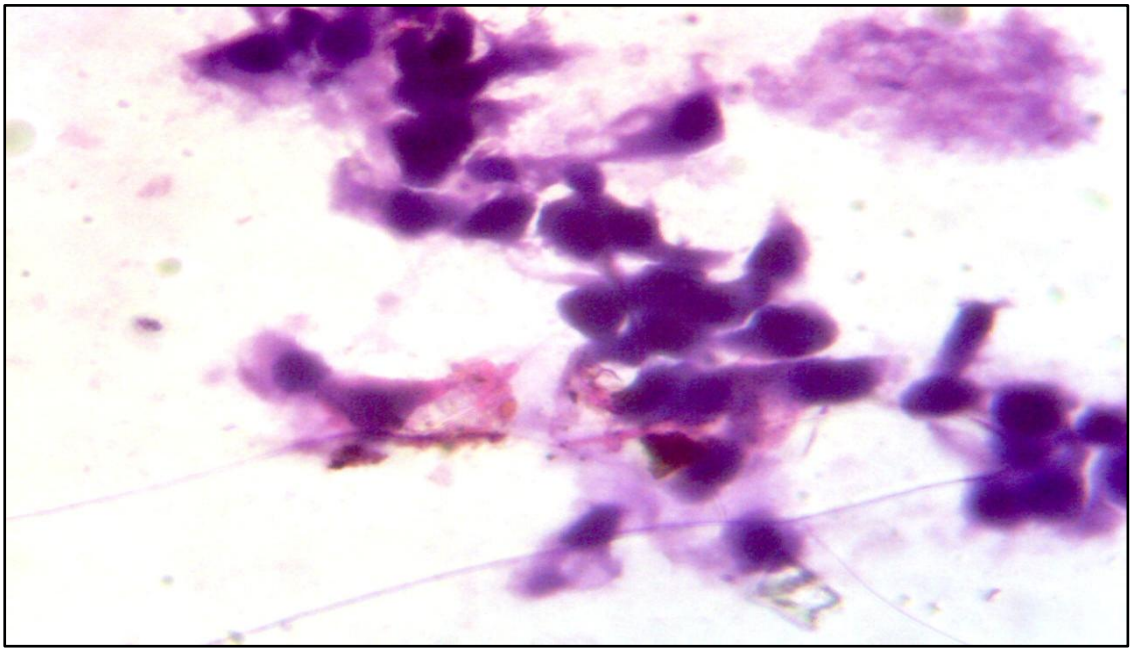


Fig.11: Mucinous carcinoma – small clusters of malignant ductal cell. Mucin reduced in the background and it present focally (40X). (Liquid based smear – Pap stain).

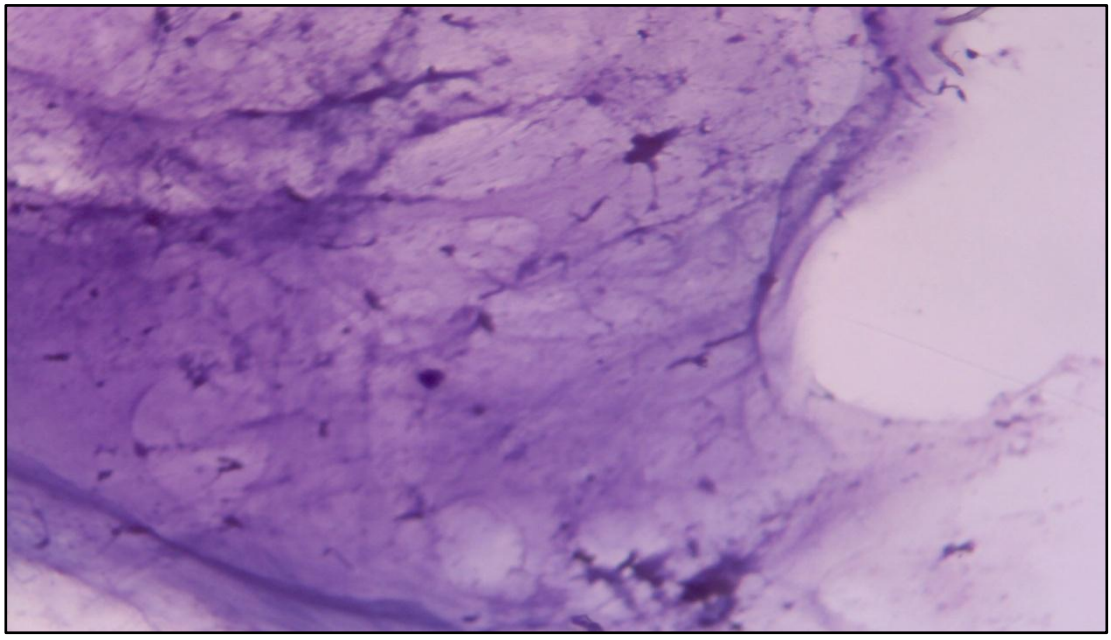


Fig.11: Mucinous carcinoma –Mucin reduced in the background and it present focally (40X). (Liquid based smear – Pap stain).

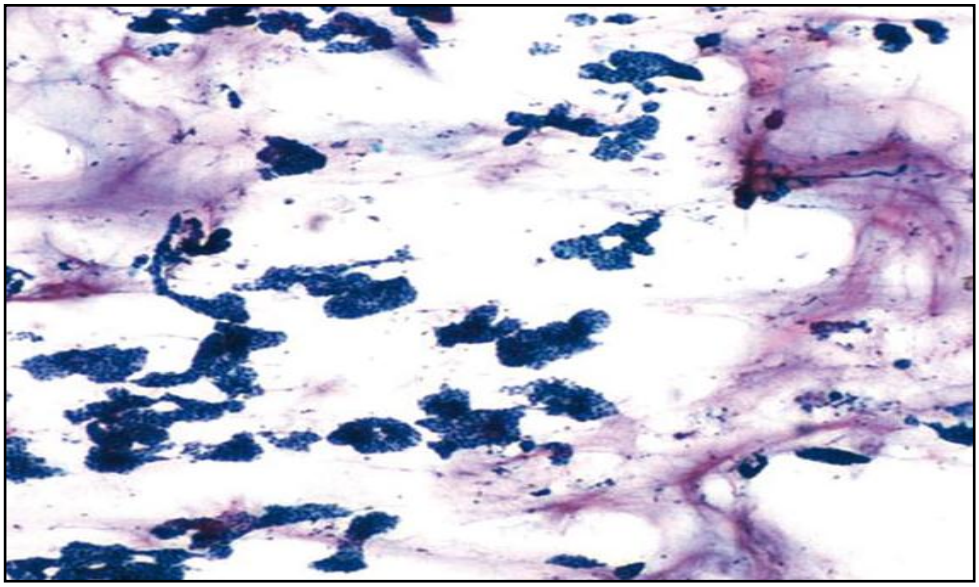


Fig.12: Mucinous carcinoma – malignant ductal cells in the dense mucinous background (Conventional smear – pap stain)10 X

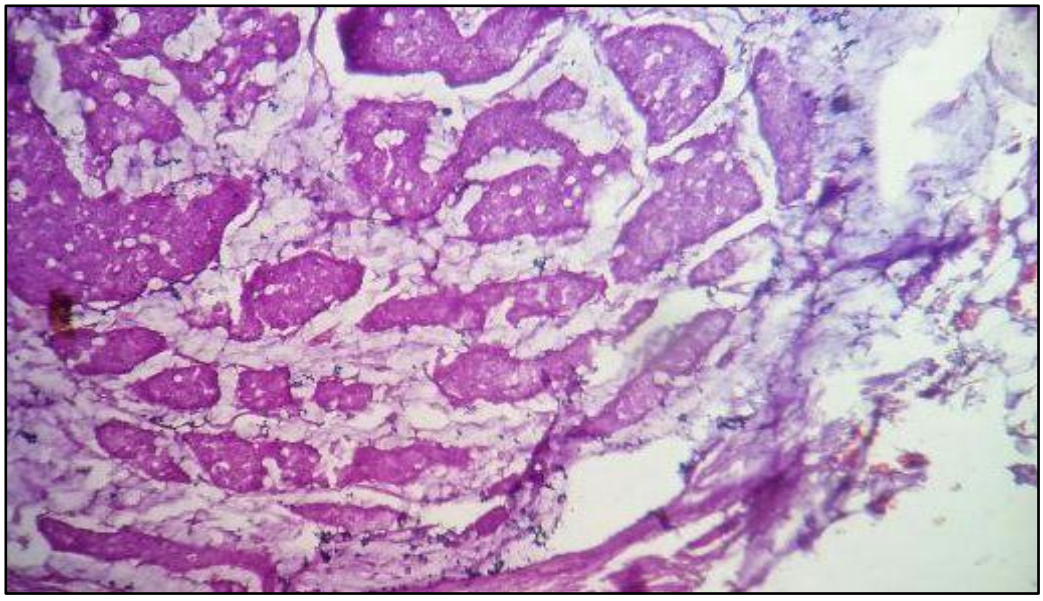


Fig.13: Microscopic view of mucinous carcinoma in dense mucinous background. (HPE No. 2321/16)

DISCUSSION

Over the past two decades, liquid based method has emerged as a newer technique in the field of cytology. Even though this technique has been in routine use at many diagnostic centers, it has not completely replaced the conventional method. The opinion regarding the best method is still controversial among the cytopathologists. The advantages offered by liquid based preparations include less number of slides to be screened, uniform cellular layer, clean bloodless background, better preservation of cell morphology.

Few authors [7,12,21] stated that LB smears made from rinsing the residual material left in the syringe or needle hub after initial preparation of conventional smear, showed loss of significant number of cells, background elements and alterations in cellular architecture and morphology. They suggested a special pass (ie., direct to vial technique) from the collection of liquid based sample, and many a times they observed that the liquid based smears had adequate number of cells, preserved background elements and well preserved cellular architecture and morphology. In view of the above suggestions, in this study, liquid based sample was collected from a separate needle pass. The lytic agents added to collecting media allowed the sample to be of better quality with less obscuring background elements than that of the conventional smears which are

thick with obscuring blood and inflammatory cells. The nature of the liquid based processing technique allows a thin layer of representative sample to be deposited on liquid based slide in a well defined area and enables cytologist to screen the slides at a faster rate.

The results obtained in our study, implies that during the initial introduction period, liquid based preparation has to be combined with conventional one for the purpose of gaining experience in interpretation and also to avoid errors in the final diagnosis. This would lower the individual diagnostic differences.

CELLULARITY:

In a broader terminology, sample is said to be adequate if it is cellular and of good quality with well preserved cellular morphology. Also it should be, representative of the lesion.

Dey P et al (2000), reported the cellularity in LBC was equal to conventional preparation.

Gerhard et al, Ryu et al (2013) described that cellularity in LBC and conventional preparations was same for both.

Michael et al (2000) and Leung et al (1997) reported that the cellularity in LBC preparations is slightly inferior or superior to the conventional smears.

Ryu et al (2013) and Jose et al (2015) both described that the cellularity between the LBC preparation and the conventional smear preparation are same. Almost all the above studies mentioned that the cellularity in both the LBC and conventional smear preparation are equal [15,21,38,39].

In the present study almost all the cases in LBC showed moderate to high cellularity except very few cases which showed low cellularity. For those cases which showed low cellularity second slides were made with the remaining material and the diagnosis given. This is one of the advantages in LBC preparation.

Conventional smears showed moderate cellularity in most of the cases. Very few of the cases showed low cellularity. In low cellularity cases when opinion was not easily made another prick was done to give the opinion.

In two cases where the conventional smear showed scant cellularity LBC slides show adequate cellularity (possibly due to centrifugation).

In our study, the cellularity in both LBC and CS preparations was almost equal.(Table – 2, Chart – 4)

This is in concordance with the above studies.

Background material (blood, necrosis, debris):

Gerhard et al (2013), Dey P et al (2000) describe that the background material like blood and necrosis are lost in LBC preparation, which gives clean background and helps in easier screening.

In our study, most of cases of LBC preparation showed clean background with absence of blood, cell debris and necrosis in the background. This is one of the advantages of the LBC preparation which helps in easy screening. In CS preparation most of the cases show bloody material in the background which obscures the cells. This is one of the disadvantages of the CS method (Table 3, chart 5). This is in concordance with the above studies.

Informative background:

Veneti et al (2003), Dey P et al (2000) and many authors described that the informative background was lost in LBC preparation which is one of the disadvantages in diagnosing the benign cases like fibroadenoma and malignant cases like mucinous carcinoma.

Informative background is one of the most important clue in diagnosing the lesions in cytology preparation. In our study informative background was found to be reduced but not lost in cases of LBC. This is one of the disadvantages in LBC method as described by many authors [21,38,39,40,48]. But in

CS method informative background is preserved which helps in diagnoses.(Table – 4, Chart – 6)

Cell architecture:

In the present study cell architecture was well recognized with LBC (86/100). Conventional smear showed well recognizable architecture in 74/100 cases. This is probably due to there being less overlapping of cells in LBC, which resulted in better assessment of cell morphology and architecture in LBC method (table-6). Many authors described the same features [21,43]. (table – 6,8 and chart – 6,8)

Nuclear detail and cytoplasmic detail:

Nuclear and cytoplasmic details are of equally good quality in almost all cases in both LBC and CS method (table 7,8 and chart 9,10).

BENIGN LESIONS:

The benign category included in the present study are fibroadenoma and fibrocystic disease of breast and gynecomastia. They constitute about 30 %, 4% and 2% respectively of all the breast lesions diagnosed in conventional and LBC methods.

FIBROADENOMA:

Current study showed that the diagnostic accuracy for LBC and CS preparation are 97% and 94 % respectively. These values imply that our study results are almost equal to that observed in many studies. The sensitivity and specificity in our study is 100% and 96%.

LBC preparation in fibroadenoma showed benign looking ductal epithelial cells, arranged in sheets, small clusters and three dimensional clusters. Some of the cases showed staghorn clusters. Isolated myoepithelial cells are seen. Most of the cases showed loss or paucity of the stromal elements like fibromyxoid stroma. Benign looking ductal epithelial cells without increase in nuclear cytoplasmic ratio arranged in small clusters and isolated myoepithelial cells helps us to diagnose fibroadenoma, eventhough there is loss or paucity of fibromyxoid stroma in the background. Continuous practice helps one to diagnose fibroadenoma.

Mygdakos et al (2009), Michael et al (2000), Leung et al (1997) and many other authors also observed decrease in myoepithelial cells and paucity or loss of stromal elements in fibroadenoma cases.

Ryu et al (2013) has interpreted some of the breast lesions, which showed false increase in ductal epithelial cells due to decrease in the fibromyxoid

stroma and myoepithelial cells, thus misdiagnosing these cases as suspicious for malignancy.

Leung et al (1992), Perez et al (1994), Kollur et al (2006) and many authors encountered same problem.

We also encountered a similar problem, but upon review of the doubtful cases, we could identify the predominance of cell clusters arranged in small clusters and three dimensional clusters without crowding or overlapping. Eventhough there is loss or paucity of background material, presence of uniform cell morphology, without increase in nuclear cytoplasmic ratio and the arrangement helps us to diagnose fibroadenoma in LBC.

In conventional preparation the diagnosis of fibroadenoma is easily done because of the staghorn arrangement of the cells with myoepithelial cells and background fibromyxoid stroma. But some cases are difficult due to the bloody background, the nuclear features are not seen clearly and the whole slide has to be searched. Two to three slides might have been made and all have to be screened, which consumed more time when compared to LBC were most of the cases are reported with a single slide. Two cases in conventional preparation had insufficient material to interpret.

The diagnosis of fibrocystic disease of breast by CS and LBP preparation shows similar features in both method. Ductal epithelial cells and scattered

apocrine metaplastic cells. But the cellularity in the conventional preparation is low. So another prick is usually done to diagnose the case. But LBC preparation shows moderate cellularity in such cases due to centrifugation which helps in diagnosing the case, one of the advantages of LBC.

Gynecomastia cases in both the method showed ductal epithelial cells. In CS preparation cellularity is low to moderate, so two to three slides are needed to report whereas in LBC, the cells are subjected to centrifugation and the diagnosis is made with a single slide itself.

SUSPICIOUS OF MALIGNANCY:

Two cases of the category, suspicious of malignancy were encountered in our study. One case in LBC method showed small clusters, three dimensional clusters and singly scaterred epithelial cells with moderate amount of cytoplasm and nucleus showing mild pleomorphism. Features in CS preparation showed sheets of epithelial cells and with nucleus showing mild pleomorphism. On histopathological correlation one of the two turned out to be fibroadenoma, other case was diagnosed as ductal carcinoma.

Bedard et al described that in their study 75% and 71% of the category suspicious for malignancy in CS and LBC preparation turned out to be malignant in histopathology study.

MALIGNANT CASES:

Most of the breast carcinomas are easily diagnosed with the help of FNA. Veneti et al(2003), Biscotti et al (1999), Ryu et al(2013) described that both the types of cytological preparations CS and LBC preparations have comparable features for detection of ductal carcinoms.

Dey et al (2000) stated that it was easier to diagnose the ductal carcinoma in LBC preparation because of the clean background. They also described that the clean background means uninformative background because main features of carcinomas like blood and necrosis are lost in LBC preparations.

The results of the present study is in concordance with the observation made by most of the above authors.

The sensitivity, specificity and the diagnostic accuracy for ductal carcinoma in CS and LBC preparations showed 100%.

LBC preparation showed malignant ductal epithelial cells arranged in three dimensional clusters, small clusters and also singly scattered in a clean background. Cells have scant to moderate amount of cytoplasm with nucleus showing marked pleomorphism. Most of the cases show fine chromatin.

CS preparation showed sheets of ductal epithelial cells in the background of blood. Nucleus features are almost the same for both preparations as described by Dey et al, Ryu et al and many authors [12,38,39,40].

But cytology preparation may not help to categorise the ductal carcinomas which is a major disadvantage of all FNA samples of both LBC and CS preparations.

Two cases of mucinous carcinomas were encountered in our study.

Komastsu et al detected mucinous carcinoma in a single case by the presence of mucous.

Michael et al(2000), Veneti et al(2003) and many other authors described that the mucinous carcinomas diagnosed by cytology depends largely on the presence of mucous in the background, which can be reduced or lost in LBC preparation. But this feature is preserved in CS preparation.

In our study both the cases in LBC preparation revealed 3D clusters of malignant ductal epithelial cells with the background showing focal areas of mucous and entrapped capillaries. This helped to make diagnosis as mucinous carcinomas. One of the cases was confirmed with histopathological diagnosis.

In CS preparations background mucus is preserved with sheets of malignant ductal epithelial cells which makes it easier to interpret.

Our study is in concordance with the study by the above authors.

Advantages of liquid based cytology:

1. Less time consuming.
2. Less number of slides - mostly single slide is enough for reporting.
3. Absence of artifact in preservation.
4. Absence of obscuring background elements (RBCs, necrosis)
5. Presence of cells in monolayers.
6. The remaining sample can be used for adjuvant study like immunocytochemistry, cell block preparation, immunohistochemistry.
7. Cell morphology and nuclear details are similar in both the preparations.
8. Abundant cellularity in LBC with no overlapping of the cells along with absence of obscuring background material is very helpful in diagnoses with some exception.
9. Cytoplasmic and nuclear details are similar to conventional smear.

Disadvantages Liquid based cytology:

1. Loss or paucity of informative background (fibromyxoid stroma, mucus).
2. Loss of architectural pattern.

Advantages of conventional preparation:

1. Preserved architectural arrangement.
2. Presence of informative background.

Disadvantages of conventional smears:

1. Presence of obscuring background material.
2. Screening time for the number of slides is long and exhaustive, especially when the smears are paucicellular.
3. Two or more slides needed on an average.
4. If cellularity is low second prick has to be made.
5. Less monolayering with more overlapping of cells.

SUMMARY

Liquid based cytology has evolved as a newer method in the field of fine needle aspiration cytology. The introduction of liquid based technique tries to overcome the limitations faced by conventional method. Liquid based smears are easier to screen and less time consuming due to spread of cells in monolayer with a clean background. The cellular morphology is always well preserved. Only a small amount of is used for LBC preparation and the remaining solution is stored in appropriate preservative solution for few months at an appropriate temperature for future studies.

In the present study, the diagnostic rate observed using liquid based method is equally comparable with that of conventional one. It is also found to be a reliable diagnostic method to differentiate between benign and malignant lesions.

The relatively low cost and easier method of preparing the slides are added advantages of this method. In addition, Immunohistochemistry can be performed on liquid based samples in equivocal cases or to confirm the nature of neoplasm.

The results obtained in our study, implies that during the initial introduction period, liquid based preparation has to be combined with

conventional one for the purpose of gaining experience in interpretation and also to avoid errors in the final diagnosis. This would lower the individual diagnostic differences.

To conclude, both the techniques have both advantages and disadvantages. Liquid based method may become a promising and reliable one for preoperative diagnosis of palpable breast lesions. But alterations in smear background and minor changes in the cellular architecture and morphology should be borne in mind while interpreting liquid based smears to avoid false diagnosis in general cytological practice.

Further studies with larger sample sizes are necessary to demonstrate the real diagnostic significance of this method among other liquid based techniques.

CONCLUSION

Fine needle aspiration method is a safer and cost effective method for the diagnosis of breast lesions. However, proper preparation of cytological smears determine the quality of diagnosis. Liquid based cytology of breast aspirates provides a better cellular preservation, less cellular overlapping and elimination of obscuring background when compared to that of Conventional smears. But the loss or paucity of informative background is a disadvantage in Liquid based cytology. Studies have shown similar accuracy between Liquid based cytology and Conventional smear for the diagnosis of breast lesions. Thus, Liquid based cytology can be used as important ancillary technique along with the Conventional smear for diagnostic accuracy.

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PROFORMA

Name : IP/OP No:

Age : FNAC No:

Sex:

Presenting Complaints :

Breast Lump :

Duration :

Pain :

Nipple Discharge :

Past History:

Family History :

History of previous surgery / FNAC for breast lumps :

Examination of breast :

Right side / left side breast :

Single / multiple swelling :

Size :

Consistency :

Mobile / fixed to underlying structures :

Nipple Discharge :

Examination of axillary nodes :

Ultrasound breast (if available) :

Previous FNAC report (if available) :

Previous surgery- HPE report (if available) :

Conventional smear diagnosis :

Liquid based cytology diagnosis :

ஒப்புதல் படிவம்

எனது மார்பக கட்டியில் இருந்து ஊசியின் மூலம் திசு / நீர் எடுத்து பரிசோதனை செய்வதற்கு முழு மனதுடன் சம்மதிக்கிறேன்.

இப்படிக்கு,

S.NO	FNAC.NO	HPE.NO	AGE	SEX	CS	LBC	HPE	SCORING SYSTEM													
								CELLULARITY		BACKGROUND BLOOD DEBRIS		INFORMATIVE BACKGROUND		MONOLAYER		CELL ARCHITECTURE		NUCLEAR DETAILS		CYTOPLASMIC DETAILS	
								0=ZERO		0=ZERO		0=ABSENT		0=ABSENT		0=NON-REC0GNIZED		0=POOR		0=POOR	
								1=SCANTY		1=OCCASIONAL		1=PRESENT		1=OCCASIONAL		1=MODERATELY RECOGONISED		1=FAIR		1=FAIR	
								2=ADEQUATE		2=GOOD AMOUNT				2=GOOD AMOUNT		2=WELL RECOGONISED		2=GOOD		2=GOOD	
								3=ABUNDANT		3=ABUNDANT								3=EXCELLENT		3=EXCELLENT	
								CS	LBP	CS	LBP	CS	LBP	CS	LBP	CS	LBP	CS	LBP	CS	LBP
1	1014/15	3983/15	67	FEMALE	DC	DC	DC	2	2	2	0	1	0	1	2	2	2	2	2	2	2
2	1133/15		60	FEMALE	DC	DC		2	2	3	0	1	0	1	2	2	2	2	2	2	2
3	1144/15	2216/15	57	FEMALE	DC	DC	DC	2	2	2	0	1	0	2	2	2	2	2	2	2	2
4	1146/15		29	FEMALE	FA	FA		2	2	3	0	1	1	2	2	2	2	2	2	2	2
5	1148/16		34	FEMALE	FA	FA		2	3	2	0	1	0	2	2	2	2	2	2	2	2
6	1152/16		60	FEMALE	DC	DC		2	3	2	0	1	0	1	2	2	2	2	2	2	2
7	1154/15		24	FEMALE	FA	DC		2	3	2	0	1	0	2	2	2	2	2	2	2	2
8	1160/15	2312/15	63	FEMALE	DC	DC		2	3	2	0	1	1	2	2	2	2	2	2	2	2
9	1164/15		52	FEMALE	DC	DC		2	3	2	0	1	0	2	2	2	2	2	2	2	2
10	1165/15		55	FEMALE	DC	DC		2	3	2	0	1	0	2	2	2	2	2	2	2	2
11	1167/15		37	FEMALE	FCD	FCD		1	1	3	0	1	0	2	2	2	2	2	2	2	2
12	1173/15	3067/15	72	FEMALE	DC	DC	DC	2	3	3	0	1	0	2	2	2	2	2	2	2	2
13	1188/15		51	FEMALE	DC	DC		2	2	2	0	1	0	2	2	2	2	2	2	2	2
14	1194/15		55	FEMALE	DC	DC		2	2	3	0	1	0	2	2	2	2	2	2	2	2
15	1201/15		24	FEMALE	FA	FA		2	2	3	0	1	0	1	2	2	2	2	2	2	2
16	1208/15		82	FEMALE	DC	DC		2	3	3	0	1	0	2	2	2	2	2	2	2	2
17	1209/15		70	FEMALE	DC	DC		2	3	3	0	1	0	1	2	2	2	2	2	2	2
18	1210/15		19	FEMALE	-	FCD		1	1	3	0	1	0	1	2	2	2	2	2	2	2
19	1222/15		29	FEMALE	FA	FA		2	3	3	0	1	1	2	2	2	2	2	2	2	2
20	1231/15		45	FEMALE	DC	DC		2	2	3	0	1	0	1	2	2	2	2	2	2	2
21	1239/15	2353/15	45	FEMALE	FA	FA	FA	2	3	2	0	1	1	2	2	2	2	2	2	2	2
22	1242/15		55	FEMALE	DC	DC		2	3	2	0	1	0	1	2	2	2	2	2	2	2

23	1298/15		55	FEMALE	DC	DC		2	2	2	0	1	0	1	2	2	2	2	2	2	2
24	1320/15		14	MALE	GM	GM		2	3	3	0	1	0	1	2	2	2	2	2	2	2
25	1372/15	2316/15	29	FEMALE	FA	FA	FA	2	2	2	0	1	1	2	2	2	2	2	2	2	2
26	1340/15	2380/15	75	FEMALE	DC	DC	DC	2	3	2	0	1	0	1	2	2	2	2	2	2	2
27	1426/15	2429/15	27	FEMALE	FA	FA	FA	2	3	3	0	1	1	2	2	2	2	2	2	2	2
28	1439/15		43	FEMALE	DC	DC		2	2	3	0	1	0	1	2	2	2	2	2	2	2
29	1446/15		37	FEMALE	FA	FA		2	3	3	0	1	1	2	2	2	2	2	2	2	2
30	1453/15		32	FEMALE	No cells	FA		2	2	3	0	1	0	2	2	2	2	2	2	2	2
31	1459/15		30	FEMALE	FA	FA		2	3	2	0	1	0	2	2	2	2	2	2	2	2
32	1496/15	2581/15	43	FEMALE	FA	FA	FA	2	2	2	0	1	0	2	2	2	2	2	2	2	2
33	1499/15		55	FEMALE	DC	DC		2	3	3	0	1	0	1	2	2	2	2	2	2	2
34	1504/15		21	FEMALE	FA	FA		2	2	3	0	1	0	2	2	2	2	2	2	2	2
35	1574/15	2612/15	24	FEMALE	FA	FA	FA	2	3	2	0	1	0	2	2	2	2	2	2	2	2
36	1601/15		46	FEMALE	DC	DC		2	3	3	0	1	0	1	2	2	2	2	2	2	2
37	1602/15		28	FEMALE	FA	FA		2	3	2	0	1	0	2	2	2	2	2	2	2	2
38	1663/15		25	FEMALE	No cells	FA		2	3	3	0	1	0	2	2	2	2	2	2	2	2
39	1701/15	2778/15	55	FEMALE	DC	DC	DC	2	2	3	0	1	0	1	2	2	2	2	2	2	2
40	1718/15	2728/15	30	FEMALE	FA	FA	FA	2	3	2	0	1	1	2	2	2	2	2	2	2	2
41	1736/15		38	FEMALE	DC	DC		2	2	3	0	1	0	1	2	2	2	2	2	2	2
42	1753/15		48	FEMALE	DC	DC		2	3	3	0	1	0	1	2	2	2	2	2	2	2
43	1775/15		40	FEMALE	FA	FA		2	3	3	0	1	1	1	2	2	2	2	2	2	2
44	1786/15		24	FEMALE	FA	FA		2	2	2	0	1	1	2	2	2	2	2	2	2	2
45	1855/15	3058/15	56	FEMALE	DC	DC	DC	2	3	2	0	1	0	1	2	2	2	2	2	2	2
46	2022/15	4045/15	70	FEMALE	DC	DC	DC	2	3	2	0	1	0	1	2	2	2	2	2	2	2
47	26/16		23	FEMALE	FA	FA		2	3	3	0	1	1	2	2	2	2	2	2	2	2

48	39/16	1384/16	65	FEMALE	DC	DC	DC	2	3	2	0	1	0	1	2	2	2	2	2	2	2
49	55/16	227/16	48	FEMALE	DC	DC	DC	2	3	2	0	1	0	1	2	2	2	2	2	2	2
50	72/16	374/16	35	FEMALE	DC	DC	DC	1	1	2	0	1	0	1	2	2	2	2	2	2	2
51	80/16	322/16	42	FEMALE	DC	DC	DC	2	3	3	0	1	0	1	2	2	2	2	2	2	2
52	92/16		46	FEMALE	DC	DC		2	3	2	0	1	0	1	2	2	2	2	2	2	2
53	119/16		19	FEMALE	FA	FA		2	3	2	0	1	1	2	2	2	2	2	2	2	2
54	156/16		27	FEMALE	FA	FA		2	3	3	0	1	1	2	2	2	2	2	2	2	2
55	164/16	895/16	40	FEMALE	DC	DC	DC	2	2	3	0	1	0	1	2	2	2	2	2	2	2
56	166/16	846/16	40	FEMALE	SFM	SFM	DC	2	3	3	0	1	0	1	2	2	2	2	2	2	2
57	173/16		59	FEMALE	DC	DC		2	2	3	0	1	0	1	2	2	2	2	2	2	2
58	178/16		34	FEMALE	FA	FA		2	3	2	0	1	1	2	2	2	2	2	2	2	2
59	221/16		28	FEMALE	FA	FA		2	2	3	0	1	0	2	2	2	2	2	2	2	2
60	2O7/16	959/16	39	FEMALE	FCD	FCD	FCD	2	2	3	0	1	1	1	2	2	2	2	2	2	2
61	253/16		33	FEMALE	FA	FA		2	2	3	0	1	1	2	2	2	2	2	2	2	2
62	303/16		19	FEMALE	FA	FA		2	3	2	0	1	1	2	2	2	2	2	2	2	2
63	306/16		51	FEMALE	DC	DC		2	3	2	0	1	0	1	2	2	2	2	2	2	2
64	317/16		68	FEMALE	DC	DC		2	3	2	0	1	0	1	2	2	2	2	2	2	2
65	321/16		67	FEMALE	DC	DC		2	2	3	0	1	0	1	2	2	2	2	2	2	2
66	329/16	775/16	25	FEMALE	FA	FA	FA	2	3	3	0	1	1	2	2	2	2	2	2	2	2
67	332/16		55	FEMALE	DC	DC		2	3	3	0	1	0	1	2	2	2	2	2	2	2
68	341/16		67	FEMALE	DC	DC		2	2	3	0	1	0	1	2	2	2	2	2	2	2
69	348/16	1046/16	40	FEMALE	DC	DC	DC	2	3	3	0	1	0	1	2	2	2	2	2	2	2
70	370/16		21	FEMALE	FA	FA		2	3	2	0	1	1	2	2	2	2	2	2	2	2
71	383/16		73	FEMALE	DC	DC		2	3	3	0	1	0	1	2	2	2	2	2	2	2
72	386/16		65	FEMALE	DC	DC		2	2	3	0	1	0	1	2	2	2	2	2	2	2
73	409/16		45	MALE	GM	GM		2	3	2	0	1	0	1	2	2	2	2	2	2	2

74	428/16	1032/16	48	FEMALE	DC	DC	DC	2	2	3	0	1	0	1	2	2	2	2	2	2	2
75	435/16		19	FEMALE	FA	FA		2	3	2	0	1	1	1	2	2	2	2	2	2	2
76	440/16		56	FEMALE	DC	DC		2	3	3	0	1	0	2	2	2	2	2	2	2	2
77	445/16		42	FEMALE	DC	DC		2	2	3	0	1	0	2	2	2	2	2	2	2	2
78	453/16		31	FEMALE	FA	FA		2	3	2	0	1	1	1	2	2	2	2	2	2	2
79	481/16	1142/16	60	FEMALE	DC	DC	DC	2	3	3	0	1	0	2	2	2	2	2	2	2	2
80	495/16		47	FEMALE	DC	DC		2	3	3	0	1	0	2	2	2	2	2	2	2	2
81	519/16		33	FEMALE	FA	FA		2	3	2	0	1	0	1	2	2	2	2	2	2	2
82	520/16		42	FEMALE	DC	DC		2	3	3	0	1	1	2	2	2	2	2	2	2	2
83	521/16		55	FEMALE	DC	DC		2	3	3	0	1	0	1	2	2	2	2	2	2	2
84	547/16	821/16	38	FEMALE	DC	DC	DC	2	2	2	0	1	1	2	2	2	2	2	2	2	2
85	559/16	1226/16	42	FEMALE	DC	DC	DC	2	3	3	0	1	0	1	2	2	2	2	2	2	2
86	560/16	2321/16	50	FEMALE	MC	MC	MC	2	3	2	0	1	1	2	2	2	2	2	2	2	2
87	604/16		40	FEMALE	DC	DC		2	3	3	0	1	1	2	2	2	2	2	2	2	2
88	608/16		70	FEMALE	DC	DC		2	3	3	0	1	0	2	2	2	2	2	2	2	2
89	612/16		75	FEMALE	DC	DC		2	3	3	0	1	0	2	2	2	2	2	2	2	2
90	463/16	973/16	43	FEMALE	FCD	FCD	FCD	2	3	2	0	1	0	1	2	2	2	2	2	2	2
91	628/16		58	FEMALE	DC	DC		2	2	3	0	1	0	2	2	2	2	2	2	2	2
92	677/16		56	FEMALE	DC	DC		2	3	2	0	1	0	1	2	2	2	2	2	2	2
93	688/16		60	FEMALE	MC	MC		2	3	3	0	1	1	2	2	2	2	2	2	2	2
94	718/16	1484/16	45	FEMALE	DC	DC	DC	2	3	2	0	1	1	1	2	2	2	2	2	2	2
95	719/16		57	FEMALE	DC	DC		2	2	3	0	1	0	2	2	2	2	2	2	2	2
96	720/16	1335/16	34	FEMALE	FA	SFM	FA	2	3	2	0	1	0	1	2	2	2	2	2	2	2
97	739/16	1384/16	54	FEMALE	DC	DC	DC	2	3	3	0	1	0	2	2	2	2	2	2	2	2
98	765/16	1584/16	50	FEMALE	DC	DC	DC	2	3	2	0	1	0	2	2	2	2	2	2	2	2
99	768/16		55	FEMALE	DC	DC		2	3	3	0	1	0	2	2	2	2	2	2	2	2
100	790/16		54	FEMALE	DC	DC		2	3	3	0	1	0	1	2	2	2	2	2	2	2

KEY TO MASTER CHART

1. FA- Fibroadenom
2. FCD- Fibrocystic disease of breast
3. GM – Gynecomastia
4. SM – Suspicious of malignancy
5. DC – Ductal carcinoma
6. MC – Mucinous carcinoma
7. LBC – Liquid based cytology
8. CS – Conventional smear
9. FNAC – Fine needle aspiration cytology
10. HPE – Histopathological examination

GLOSSARY

1. FNAC – fine needle aspiration cytology
2. CS – Conventional smear
3. LBC – Liquid based cytology
4. LBP – Liquid based preparation
5. TP – Thinprep
6. SP- Surepath
7. Lp – liquiprep
8. FA – Fibroadenoma
9. FCD – Fibrocystic disease of breast
10. GM – Gynecomastia
11. SM – Suspicious of malignancy
12. DC – Ductal carcinoma
13. MC – mucinous carcinoma
14. H&E – Hemotoxylin & Eosin
15. Pap stain – Papanicolaou stain