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Cytological study of breast lesions in postmenopausal women: A 3-yearstudy

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Abstract:
Background:
Breast Cancer is one of the most common malignancies encountered in post-menopausal females in the developing countries worldwide. In post-menopausal women, breast mass is always suspected as malignancy. Various benign lesions of inflammatory etiology are also seen at this age.
Aims and Objectives*: - To evaluate cytomorphology of various breast lesions in postmenopausal women and its prevalence.*
Material and methods*: -A3-year retro-prospective study of postmenopausal breast lesion (October2015to2018). A total of 102FNAC procedures were performed in department of pathology GRMC, Gwalior (M.P.) India. The data was summarized and analyzed statistically.*
Result: *Total 102 FNAC cases; malignant 63 cases (61.7%) and benign 24 (23.5%). Most common lesion encountered in post-menopausal females with a palpable mass is carcinoma breast. Among benign diseases, most frequent lesion seen is fibrocystic-diseases (5.8%), breast-abscess (3.9%), benign-cystic-lesion (3.9%), fibroadenoma (3.9%), fat necrosis(2.0%), phyllodes tumor (2.0%), chronic granulomatous-mastitis (2.0%).A total of 09 (8.8%) cases has been diagnosed as C3 category i.e., as Benign proliferative disease with Atypia. 04 cases (04%) have been assigned C4 category as they have more atypical changes and pleomorphism but still do not meet the criteria to put into malignant category.*
The mean age of presentation of post-menopausal women with benign breast disease is 49.9 years in our study. It has come to notice in the present study that BBD in post-menopausal can be in a wide range of age group but are more commonly seen in post-menopausal women of age less than 50 years. Also, the malignant lesions can be seen in wide age range in the post-menopausal women but are more commonly seen in age group above 50 years.
Conclusion*: - We conclude that most frequent lesion was carcinoma breast. FNAC is a useful diagnostic tool in breast lesion particularly to differentiate malignant from benign pathology.*
Keywords: *Postmenopausal women breast lesion, breast cytology postmenopausal, breast FNAC, Post-menopausal breast mass.*

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I. Introduction:

Breast Cancer is one of the most common malignancies encountered in post-menopausal females in the developing countries worldwide, apart from uterine, lung and colorectal malignancies.In developed nations, it is the second cause of cancer-related deaths subsequent to lung cancer.[1]While in developing nation like ours it is one of the major causes of cancer related mortality. In India, the incidence rate is as high as 26 per 1,00,000 women population, whereas mortality rate is 13 per 1,00,000 women population.[2]Patients still presents to hospital at very advanced stage of the disease due to lack of awareness, low socioeconomic status, social circumstances, lack of screening facilities and hesitancy of being examined by male doctors. Triple assessment of breast in postmenopausal females includes clinical examination, imaging studies(Mammography/ Ultrasonography) and FNAC (Fine needle aspiration cytology) has been accepted for screening worldwide. Interpretation of the cytological findings should always be performed in conjunction with clinical and imaging findings.[3]

Menopause, also called as climacteric i.e., a crucial change. It is a permanent physiological change in females that affect almost every aspect of life. Menopause (natural menopause) – the term is defined as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity. **Natural menopause** is recognized to have occurred after 12 consecutive months of amenorrhea, for which there is no other obvious pathological or physiological cause. Menopause occurs with the **final menstrual period** (FMP) which is known with certainty only in retrospect a year or more after the event. An adequate biological marker for the event does not exist. [4]Menopausal transition – The term **menopausal transition** should be reserved for that period of time before the FMP when variability in the menstrual cycle is usually increased. This term can be used synonymously with "premenopausal", although this latter term can be confusing and preferably should be abandoned. [4]

Climacteric – The phase in the aging of women marking the transition from the reproductive phase to the non-reproductive state. This phase incorporates the perimenopause by extending for a longer variable period before and after the perimenopause. [4]**Climacteric syndrome** – The climacteric is sometimes, but not necessarily always, associated with symptomatology. When this occurs, it may be termed the "climacteric syndrome." [5]**Premenopause** – This term is often used ambiguously to refer to the one or two years immediately before the menopause or to refer to the whole of the reproductive period prior to the menopause. The group recommended that the term be used consistently in the latter sense to encompass the entire reproductive period up to the FMP. [4]**Post menopause** – It is defined as dating from the FMP, regardless of whether the menopause was induced or spontaneous. [4] Premature menopause – Ideally, premature menopause should be defined as menopause that occurs at an age less than two standard deviations below the mean established for the reference population. In practice, in the absence of reliable estimates of the distribution of age at natural menopause in populations in developing countries, the age of 40 years is frequently used as an arbitrary cut-off point, below which menopause is said to be premature. [4]**Induced menopause** –is defined as the cessation of menstruation which follows either surgical removal of both ovaries (with or without hysterectomy) or iatrogenic ablation of ovarian function (e.g., by chemotherapy or radiation). [4] Age of menopause varies geographically, and it shows a minor difference of age in regions within same country.

Table 1: Age of menopause in different region of India [7]

Region	Mean natural age of menopause
East	47.3 ± 3.91
West	46.2 ± 3.91
North	45.5 ± 4.86
South	46.1 ± 5.63
Central	47.8 ± 4.41

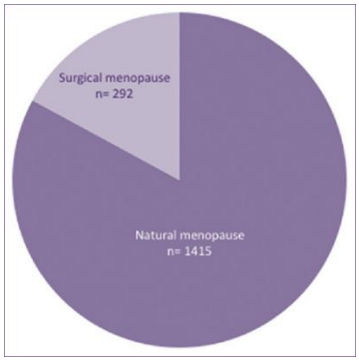

Fig 1: Natural versus Surgical menopause cases in India [7]

Breast lesion in postmenopausal women is always a suspicious finding because their breast tissue is no more biologically functional anddo notpossess hormonal receptor over it in an accountable density. Apart from this, there is a deficiency of activating hormones in this phase when compared to that of reproductive age group. But if somehow this genetically clocked inactive tissue is exposed to hormones, be it artificially or pathologically; these hormonally deprived cells do react to that intent hormonal exposure and they react much more when in familial or sporadically genetically prone female population. Apart from that a small population also shows some lesions which are not hormonally related but are due to histo-anatomical architecture related changes of tissue will cause various benign lesions.

Normal breast cytology shows scanty cellular smear comprising of few small clustersof cohesive ductal epithelial cells with small round to oval nuclei (6-10 micro) with smooth nuclear contours, vesicular chromatin and inconspicuous nucleolus. Few myoepithelial cells with nakedstripped or bipolar nuclei also present in background amidst adipocytes and stromal cells.

AIMS AND OBJECTIVES: Cytomorphological study of various breast lesion in postmenopausal women and their prevalence.

II. Material And Method

Study duration: Thisretro-prospective cohort studywas carried out on all the postmenopausal femaleswith a palpable breast lesion during a period of 3 years i.e., from October 2015 to October 2018 in Department of Pathology at G R Medical college.

Sample Size:FNAC was performed on a total of 102 cases (post-menopausal women with palpable breast lesions) following their detailed cyto-pathological examination and reporting was done.

Inclusion Criteria: The study includes all the post-menopausal aged females presenting to pathology department of our hospital for FNAC with a palpable breast lesion.

Exclusion Criteria: The exclusion criteria wereall the smears with inadequate material, improper sampling, field obscured by blood and menstruating females or those at premenopausal age.

Procedure Methodology: Patient was well informed about the procedure. After a relevant and detailed history, consent was taken for examination and FNAC was performed using a 22.5 gauze needle and 20 ml syringe attached to an FNAC handle.

Aspirate was smeared over a clean glass slide. In case of frank liquid aspirate, material is smeared over slide after centrifuge then stained with May Grunwald Giemsa and Papanicolaou stains. Where ever necessary, Leishman Geimsa stain was also done. After adequate drying, slides were mounted using DPX and thin glass cover slide. Smears were then examined under scanner (4x), low magnification (10x), and higher magnification (40x).Adequacy of the smear was assessed which includes presence of at least seven clusters of cells each comprising 20 or more epithelial cells along with the presence of myoepithelial cells. A final diagnosis was then made.

Statistical Analysis: The data was collected, retrieved, tabulated, summarized and compared statistically by frequency distribution and percentage Proportion. Chi-square (X2) test was applied to evaluate the significant (p-value) ratio of difference statistically. All the breast lesions were then classified according to The International Academy of Cytology Yokohama System of reporting breast cytology into five categories – insufficient, benign, atypical, suspicious, and malignant. [7]

III. Result

The average age of presentation of post-menopausal women with palpable breast lesion is 51.4 years. The 102 women in the present study experienced menopause at varying ages with an age range of 45 to 51 years. The average post-menopausal age in the present study is 48 years.

A total of 102 FNAC cases reported. In the present study the age range of post-menopausal females with a palpable breast lesion range from 45 to 74 years with a mean age of59.5 years. The earliest menopausal age in present study is 45 years.63 cases (61.7%) areof malignancyand 24 cases areof benign breast disease(23.5%).Among the malignant cases, most frequently and exclusively encountered entity was Invasive ductal carcinoma (IDC) with mean age of patient is 58.7 years. Other malignant lesion includes lobular, medullary, mucinous and poorly differentiated carcinoma. The mean age of presentation of post-menopausal women with benign breast disease is 49.9 years. Most of the malignant lesions were seen in women above 50 years of age which also includes women with category C3 and C4 while most of the benign lesions were seen in the post-menopausal women with age less than 50 years.

Among the benign breastdiseases (BBD), the most frequent entity is fibrocystic diseases (6 case, 5.8%) with a Mean age of 58.74 years followed by breast abscess (4 cases,3.9%) with a Mean age 55 years, Benign cystic lesion (4 cases ,3.9%) with a mean age of 54 years, Fibroadenoma (4 cases ,3.9%) with a mean age 53 years, fat necrosis (2 cases, 2.0%) with a mean age of 64 years, Phyllodes tumor (2 cases, 2.0%) with a Mean age of 65 years andChronic granulomatous mastitis (2 cases,2.0%) with a Mean age of 55 years.Most common benign breast disease encountered in our study in a post-menopausal woman is Fibrocystic disease.

A total of 09 (8.8%) cases has been diagnosed as C3 category i.e., as Benign proliferative disease with Atypia. 04 cases (04%) have been assigned C4 category as they have more atypical changes and pleomorphism but still do not meet the criteria to put into malignant category.

Table 2: Classification of breast lesions according to theIAC Yokohama System of reportingbreast cytology[7]

Category	Classification	Cases(n)	Cases (%)
C1	Insufficient	02	2.0
C2	Benign	24	23.5
C3	Atypia	09	8.8
C4	Suspicious of Malignancy	04	4.0

C5	Malignant	63	61.7
	Total Cases	**102**	**100**

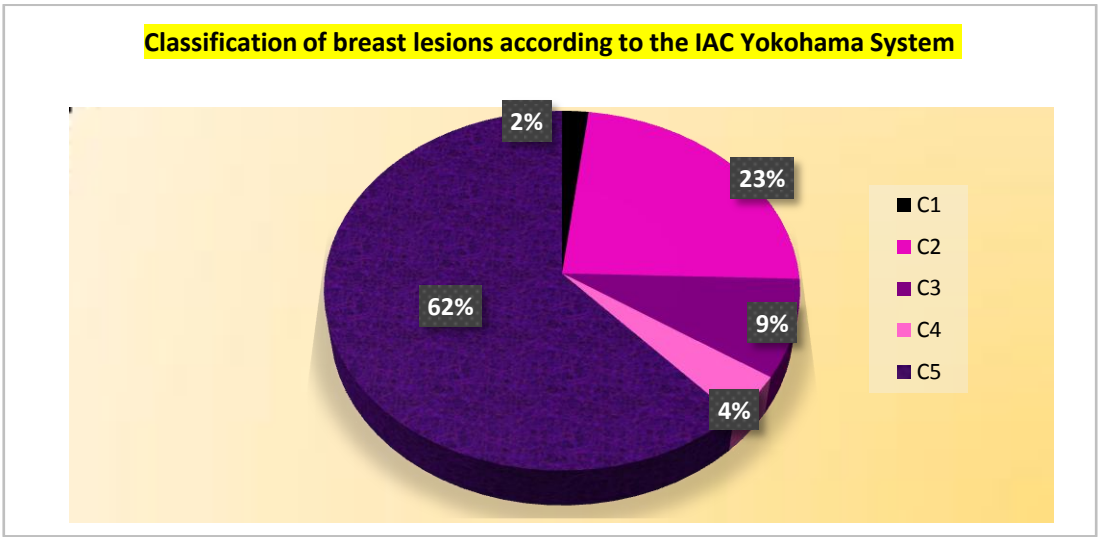

Table 3: Percentage of various Benign Breast Diseases (BBD) in Post-Menopausal Females

S.No.	Classification	Cases(n)	Cases(%)	Mean Age (yrs)
1	Fibrocystic disease	6	5.8 %	48.7
2	Breast abscess	4	3.9%	48.0
3	Benign cystic lesion	4	3.9%	47.0
4	Fibroadenoma	4	3.9%	46.8
5	Fat necrosis	2	2.0%	49.0
6	Phyllodes tumor	2	2.0%	52.0
7	Chronic granulomatous mastitis	2	2.0%	58.0
Total cases		**24**	**23.5**	**49.9**

Table 4: Mean age of various breast lesions in post-menopausal women.

S. No	Diagnosis	Mean Age (in years)
1	Invasive ductal carcinoma	58.7
2	Fibrocystic disease	48.7
3	Breast abscess	48.0
4	Benign cystic lesion	47.0
5	Fibroadenoma	46.8
6	Fat necrosis	49.0
7	Granulomatous mastitis	58.0
8	Atypia	52.5
9	Suspicious of Malignancy	55.2

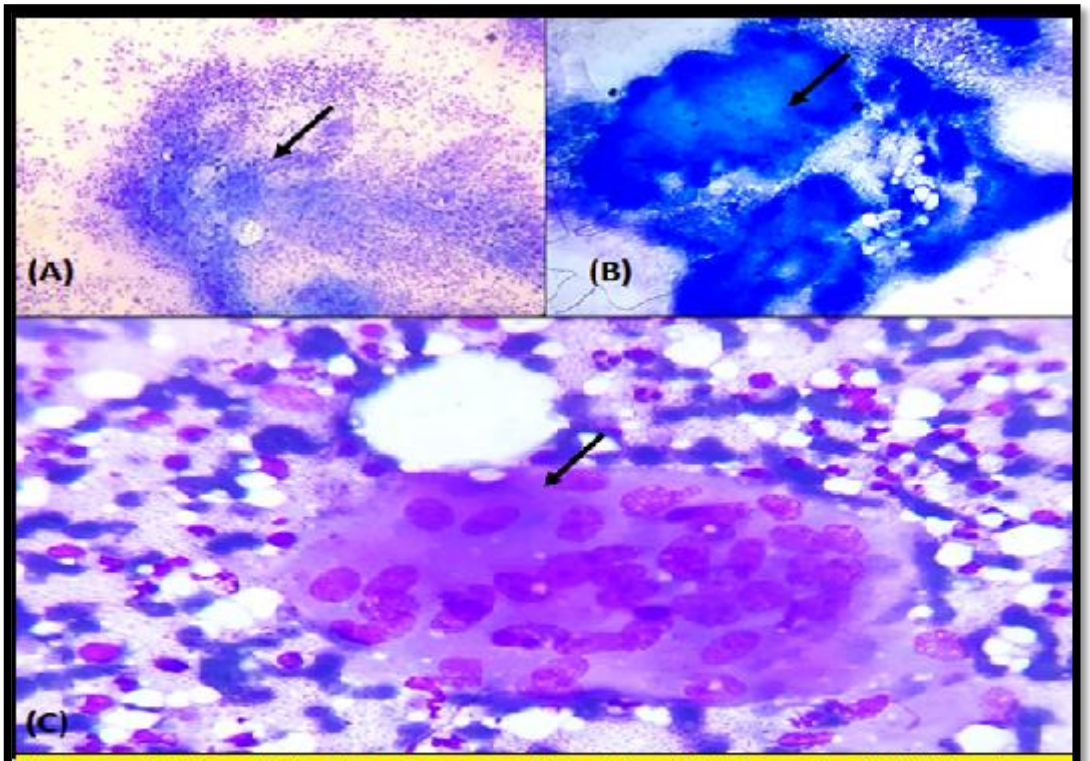

Figure 2 (LG 10x 40x): **Granulomatous Mastitis** – Well formed epithelioid cell granulomas(A) amidst numerous lymphocytes, caseous necrosis (B) and multinucleated giant cells (C).

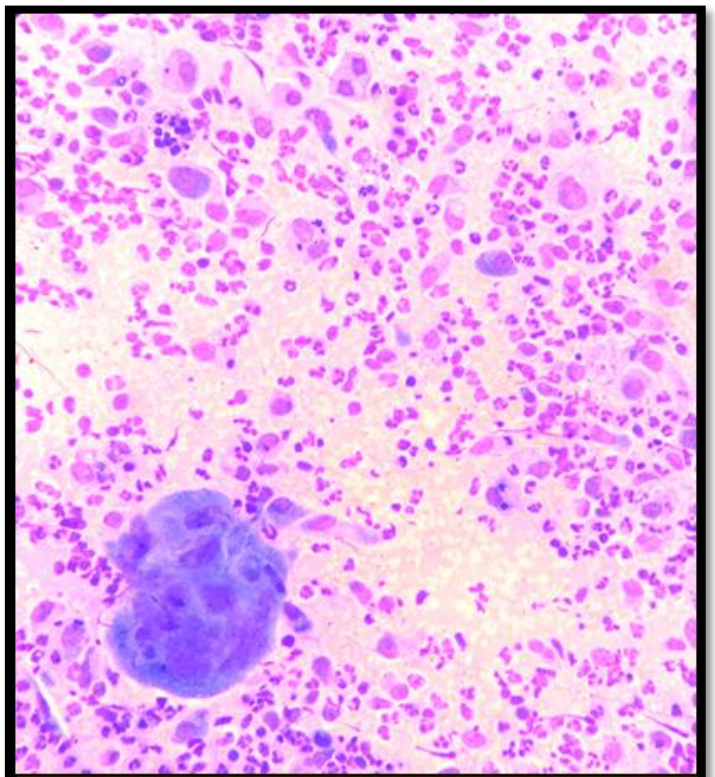

Figure 3: (MGG 40x) Breast abscess: Numerous inflammatory cells predominantly polymorphs and degenerated cells with giant cell reaction.

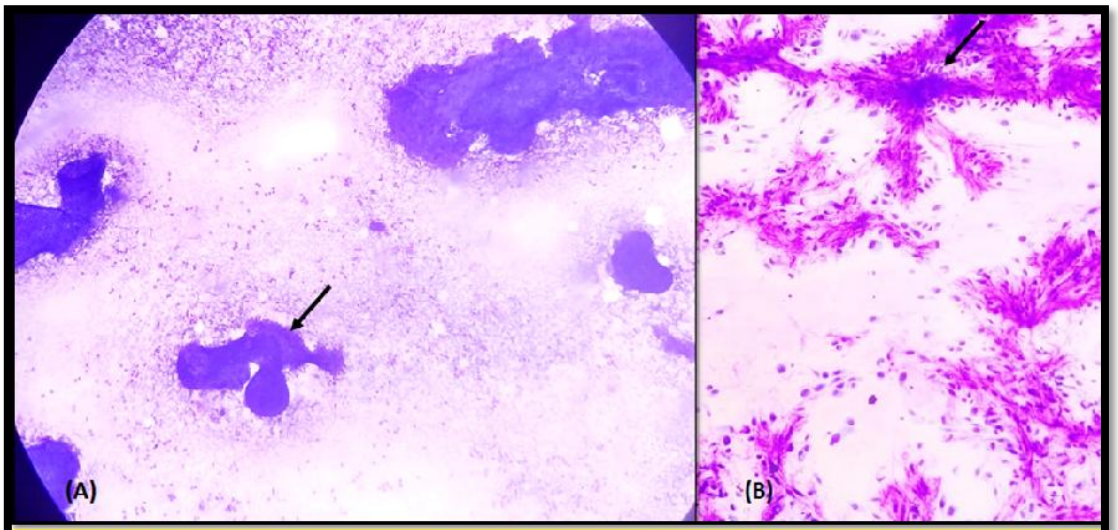

Figure 4: (LG & MGG 4x &10x) **(A) Fibroadenoma**: Numerous benign ductal epithelial cells in antler horn clusters and bare nuclei in background. (**B) Phyllodes tumor**: Large clusters of oval to spindle shape cells with spindle shaped blunt ended nuclei amidst deep magenta colored stroma.

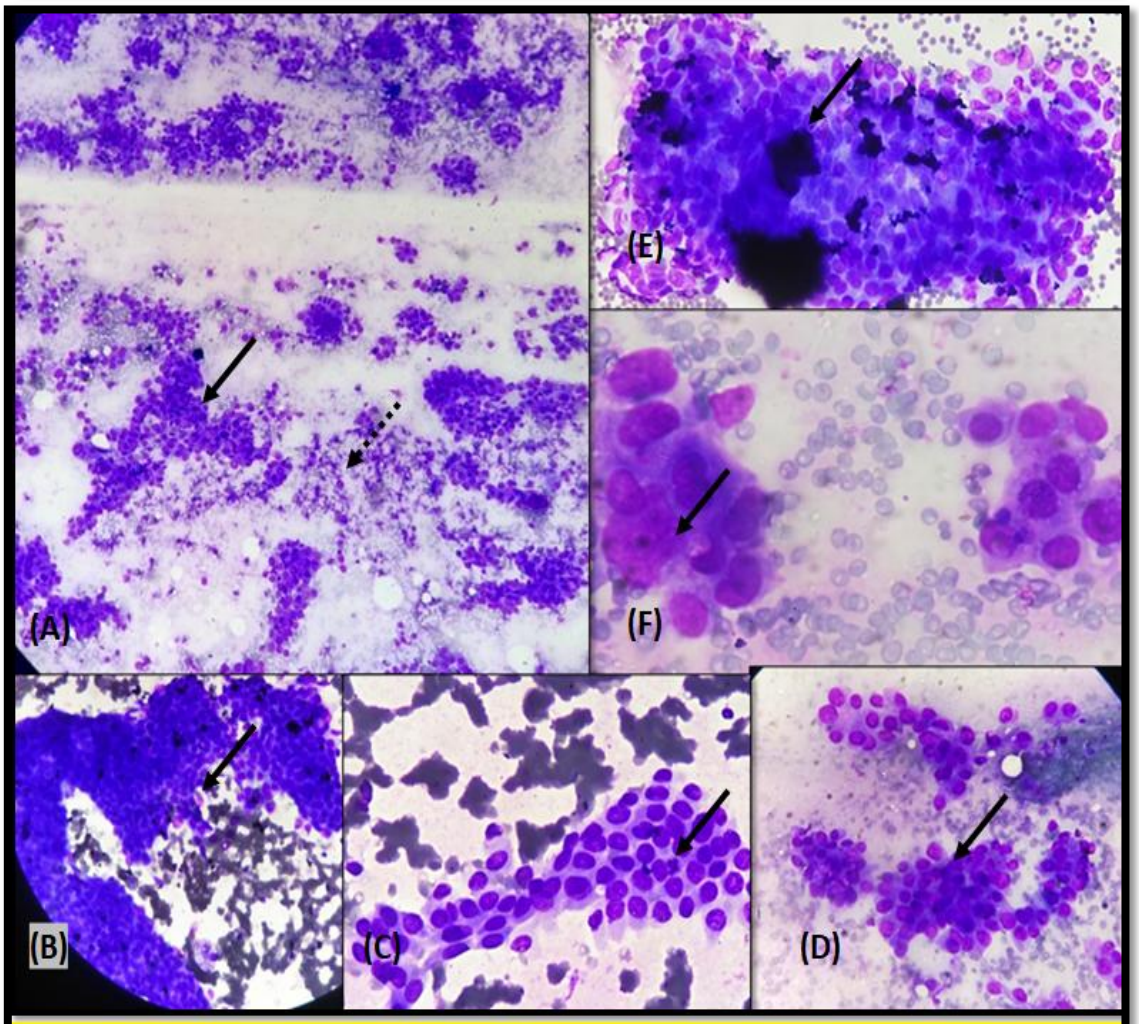

Figure 5: (LG & MGG: 4x, 10x & 40x) **Proliferative Breast disease with Atypia/AUS**: Smears are hypercellular (A) with benign ductal cells in tight cohesive (B) as well as loose cohesive clusters (C,D,E,F) amidst spindle shaped cells and bare nuclei (myoepithelial cells) (A,B,E). Few clusters show focal cytological and nuclear atypia, pleomorphism (E,F).

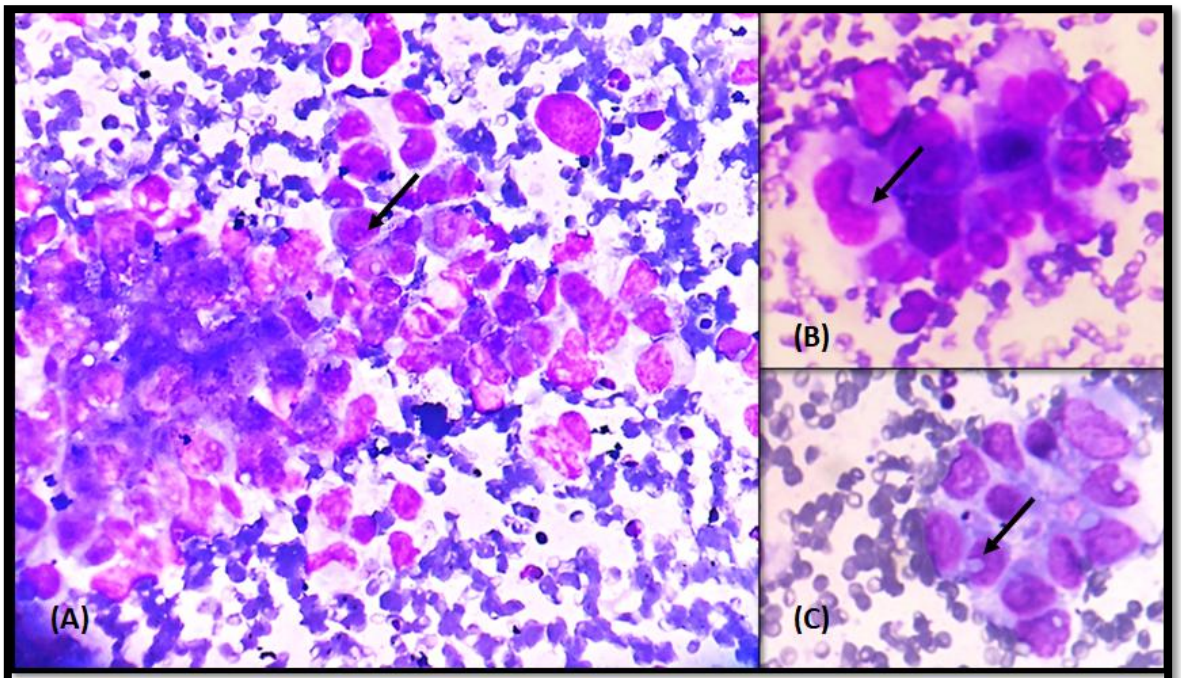

Figure 6: (MGG and LG) 40x **Invasive Ductal Carcinoma** : Loosely cohesive clusters & discrete malignant cells with cellular and nuclear pleomorphism, irregular clumped chromatin, nuclear crowding and prominent nucleoli. Absent myoepithelial cells.

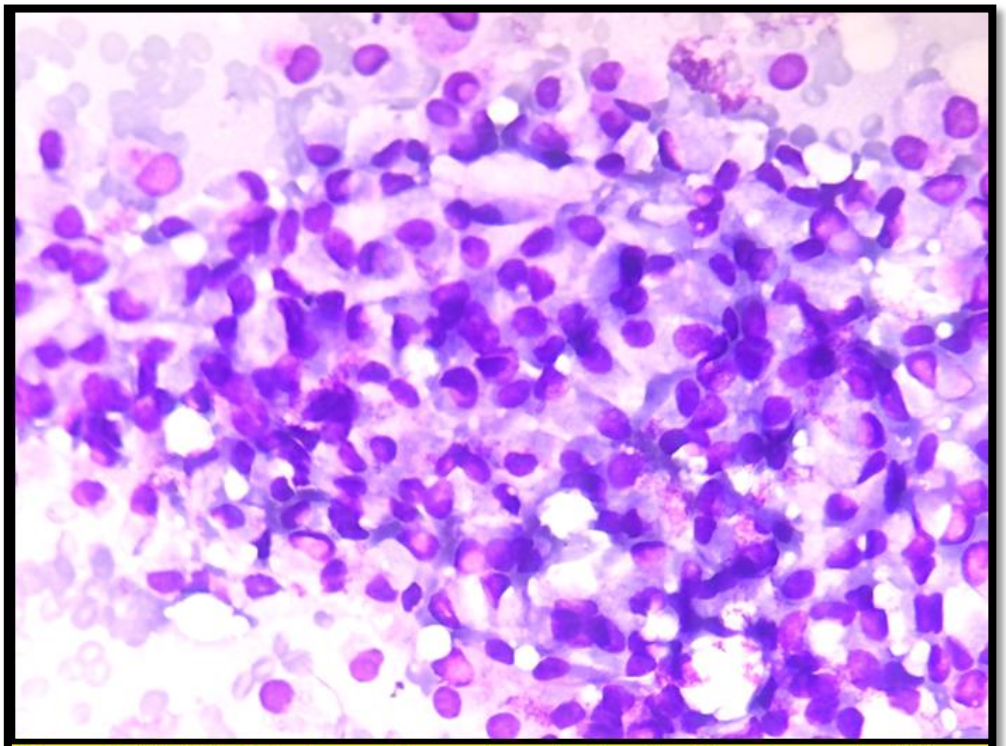

Figure 7: 40x LG: **Lobular carcinoma breast**: Abundant discrete round mildly pleomorphic ductal cells with moderate amount of cytoplasm and eccentric nucleus (plasmacytoid variant)

IV. Discussion:

Rates of breast cancer are highest in the age group of 60–64 years, but can affect women of all ages.[4]The risk factors for both pre-and post-menopausal breast cancer were found similar other than late menopause in postmenopausal patients. Most of the patients be it pre-and post-menopausal had dense breast tissue.[6]

Dense breast tissue means there is more glandular and less fatty tissue that is associated with epithelial proliferation and stromal fibrosis.The relation between these histological features and risk of breast cancer may be explained by the known actions of growth factors that play an important role in breast development and carcinogenesis. Breast cancers originate in epithelial cells, so greater areas of fibro glandular tissue may reflect a greater number of cells that are at risk of carcinogenesis and/or an increased rate of epithelial proliferation. [9,10] Menopause does not cause cancer, but the risk of developing cancer increases with ages. A woman who experiences menopause after age 55 has an increased risk of ovarian, breast, and uterine cancers. The risk is greater if a woman also began menstruating before age 12. A longer exposure to estrogen increases a woman's risk of breast cancers. Therefore, women who have been through natural menopause are more likely to develop cancer around as twice as high because of hormonal factor.

The average post-menopausal age in the present study is 48 years which is comparable with the average post-menopausal age of 45 years in the study by Surakasula A etal[6] and 46.2 years in the study by Ahuja et al [7]. The mean age of presentation of post-menopausal women with benign breast disease is 49.9 years in our study. It has come to notice in the present study that BBD in post-menopausal can be in a wide range of age group but are more commonly seen in post-menopausal women of age less than 50 years. Also, the malignant lesions can be seen in wide age range in the post-menopausal women but are more commonly seen in age group above 50 years.

In a study by Devitt JE. et.al it is stated that relative age specific incidences of benign disease has significantly dropped after menopause, where as in present study also we have found that the incidences of benign diseases are much lesser in post-menopausal women then premenopausal group.[11]

The most common short coming in FNAC breast is sampling error when the lesion is too small or large, located too deep, ill defined, degree of fibrosis is more, necrosis and cystic changes present. Others includes poor FNAC technique, ill experience handswill bring failure in FNAC and false negative diagnosis. Interobserver variability is accountable.Reasons for false positive are incorrect interpretation of atypical or proliferative lesions, rendering an incorrect diagnosis on inadequate and poorly preserved sample/ material.Also, the major limitation is breast FNAC cannot differentiate between atypical ductal hyperplasia &low-gradeDCIS as well as high grade Ductal carcinoma insitu &Invasive ductal carcinoma.

The major advantages in breast FNAC -simple, easy, economic and cost-efficient technique in short period of time, it is therapeutic many times and its useful for both palpable and as well as for image guided (nonpalpable) lesions.

However, in this modern era, core needle biopsy has gained much popularity over the FNAC for palpable breast lesions with added advantages of histological grading, hormonal receptor status contributing to predictive and prognostic criteria. However, there are many centers which cannot bear the financial burden of advanced techniques or the set ups available at remote areas. In such scenarios FNAC is the simplest and most cost effective available diagnostic tool. Also, a cell block can be prepared from the aspirated material for ancillary studies. With the triple assessment, the sensitivity and specificity of FNAC is comparable with the core needle biopsy. [14]. The use of international standardized reporting formats and protocols improves not only the interpretation and interobserver variabilityin cytopathology but also establish an easy communication link with clinicians and vice versa.

V. Conclusion:

We conclude that most frequent lesion was carcinoma breast. FNAC is a useful diagnostic tool in breast lesion particularly to differentiate malignant from benign pathology.With the triple assessment, the sensitivity and specificity of FNAC is comparable with the core needle biopsy.

References-

[1]. Ferlay J;Soerjomataram I;Dikshit R;Eser S;Mathers C;Rebelo M;Parkin DM;Forman D;Bray F; Cancer incidence and mortality worldwide: Sources, methods and major patterns in Globocan 2012 [Internet]. International journal of cancer. U.S. National Library of Medicine; [cited 2022Nov19]. Available from: https://pubmed.ncbi.nlm.nih.gov/25220842

[2]. Gupta S. Breast cancer: Indian experience, data, and evidence. South Asian J Cancer. 2016 Jul-Sep;5(3):85-6. doi: 10.4103/2278-330X.187552. PMID: 27606287; PMCID: PMC4991143.

[3]. Gray W, Kocjan G. Diagnostic cytopathology. Edinburgh: Churchill Livingstone; 2010.

[4]. Menopause. World Health Organization; [cited 2022Nov23]. Available from: https://www.who.int/news-room/fact-sheets/detail/menopause 2015 international menopausal, 27/ society (IMS) https://www.imsociety.org/menopause_terminology.php1/19

[5]. Surakasula A, Nagarjunapu GC, Raghavaiah KV. A comparative study of pre- and post-menopausal breast cancer: Risk factors, presentation, characteristics and management. J Res Pharm Pract. 2014 Jan;3(1):12-8. doi: 10.4103/2279-042X.132704. PMID: 24991630; PMCID: PMC4078652.
[6]. Ahuja M. Age of Menopause and determinants of Menopause age: A Pan India Survey by IMS. Journal of Mid-life Health. 2016;7(3):126.
[7]. Field AS, Schmitt F, Vielh P. IAC standardized reporting of breast fine-needle aspiration biopsy cytology. Acta Cytologica. 2016;61(1):3–6.
[8]. Boyd NF, Lockwood GA, Byng JW, Tritchler DL, Yaffe MJ. Mammographic densities and breast cancer risk. Cancer Epidemiol Biomarkers Prev. 1998 Dec;7(12):1133-44. PMID: 9865433.
[9]. Butt S, Borgquist S, Anagnostaki L, Landberg G, Manjer J. Parity and age at first childbirth in relation to the risk of different breast cancer subgroups. Int J Cancer. 2009 Oct 15;125(8):1926-34. doi: 10.1002/ijc.24494. PMID: 19569233.
[10]. Devitt JE. Benign disorders of the breast in older women. Surg Gynecol Obstet. 1986 Apr;162(4):340-2. PMID: 3961655.
[11]. VMC ,Breast Lumps and Lesions , https://www.myvmc.com/symptoms/breast-lumps-and-lesions/ 27/1/19
[12]. Aruna Surakasula,[1] Govardhana Chary Nagarjunapu,[2] and K. V. Raghavaiah , A comparative study of pre- and post-menopausal breast cancer: Risk factors, presentation, characteristics and management , J Res Pharm Pract. 2014 Jan-Mar; 3(1): 12–18. doi: 10.4103/2279-042X.132704
[13]. Wong S, Rickard M, Earls P, Arnold L, Bako B, Field AS. The international academy of cytology Yokohama system for reporting breast fine needle aspiration biopsy cytopathology: A single institutional retrospective study of the application of the system categories and the impact of rapid onsite evaluation. Acta Cytol. 2019; 63:280–91.
[14]. Andrew S. Field, Wendy A. Raymond, Fernando Schmitt, The International Academy of Cytology Yokohama System for Reporting Breast Fine- Needle Aspiration Biopsy Cytopathology: Recent research findings and the future, Cancer Cytopathology, 10.1002/cncy.22450, **129**, 11, (847-851), (2021).
[15]. Tse GM, Tan PH. Diagnosing breast lesions by fine needle aspiration cytology or core biopsy: which is better? *Breast Cancer Res Treat*. 2010; **123**: 1- 8.
[16]. Scopa CD, Koukouras D, Androulakis J, Bonikos D. Sources of diagnostic discrepancies in fine-needle aspiration of the breast. *Diagn Cytopathol*. 1991; **7**: 546- 548.

Dr.Rashmi Samele, et. al. "Cytological study of breast lesions in postmenopausal women: A 3-yearstudy." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(12), 2022, pp. 01-09.