



**ORIGINAL RESEARCH PAPER**

**Pathology**

**STUDY OF HISTOMORPHOLOGICAL SPECTRUM OF BREAST LESIONS IN TERTIARY CARE HOSPITAL**

**KEY WORDS:** Triple Marker, Benign Breast Lesion, Inflammatory Breast Lesion, Malignant Breast Lesion, Histomorphological Spectrum

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**ABSTRACT**

**Introduction:** Breast is a site of a broad array of pathological alterations ranging from inflammatory lesions to life threatening invasive cancers. The present study carried out to study the spectrum of breast lesions in tertiary care hospital. **Methodology:** The present study was a retro-prospective observational cross-sectional study that encompassed all breast specimens received in the Department of Pathology from March 2022 to March 2024. **Results:** Total 230 breast specimens were included. As 17 cases were inconclusive and 3 cases had skin lesions of breast, so they were excluded and total 210 cases included. Mean age was 49.16 years. Females outnumbered males with 97% of the cases. Maximum number of cases of breast lesion were found in the age group of >60yrs. Nearly half (49.5%) of the cases had predilection for left breast. The upper outer quadrant (66%) was the most common site of involvement. Lumpectomy was the most common specimen received (59%). The commonest contributor was neoplastic lesions accounting for 82.87% of the cases. The maximum number of malignant cases were found in the age group of 51-60 years. Right breast predilection was seen in 47% of cases. The upper outer quadrant (68%) was the most common site of involvement. Invasive breast carcinoma NST was the most common malignancy accounting for 83.5% of the cases. Maximum number of cases (69.34%) had 2- 5cm of size. Maximum cases (40%) had 1-3 lymph node involvement. Grade II tumors were predominant accounting for 88% of cases. Triple negative was the most common molecular subtype comprising 36% of cases. **Conclusion:** From this study we conclude that, Benign lesions were more common than malignant and inflammatory lesions. Acute mastitis was the most frequent inflammatory lesion, fibroadenomatoid mastopathy was the commonest benign non-neoplastic lesion, and fibroadenoma was the predominant benign tumor. Triple-negative breast carcinoma was the most common molecular subtype, followed by luminal A and luminal B tumors. Overall, the study highlights the importance of histopathological evaluation and molecular subtyping in the diagnosis and management of breast lesions. Early detection and appropriate treatment are essential for improving prognosis and reducing breast cancer-related morbidity and mortality.

**INTRODUCTION**

Breast is a site of a broad array of pathological alterations ranging from inflammatory lesions to life threatening invasive cancers.[1,2,3,4]

Reports by Global Cancer Incidence, Mortality and Prevalence (GLOBOCAN) show that breast cancer is the most common cancer among women with an estimated 1.67 million new cases diagnosed in 2012.[1,2,3,4] According to GLOBOCAN 2020, Female breast cancer has now surpassed lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3 million new cases, representing 11.7% of all cancer cases.[2] Around 200,000 cases of breast lesions are diagnosed annually.[4]

The most common cancer among Indian women is breast cancer accounting for 25.8/100,000 women and mortality 12.7 per 100,000 women.[4] In India, breast cancer is second most common cancer after cervical cancer.[3] The breast is composed of two major structures (ducts & lobules), two types of epithelial cells (ductal & luminal) and two type of stroma (interlobular & intralobular). Each of this is source of both benign & malignant lesions.[2,5,6,7]

The most important risk factors are gender (99% of those affected are female), age, lifetime exposure to estrogen, genetic inheritance, and, to a lesser extent, environmental and lifestyle factors. There is a concern that environmental contaminants, such as organochlorine pesticides and certain plastics, have estrogenic effects on humans that may increase the risk of breast cancer.[2,3,4] Common inflammatory lesions of breast include acute mastitis, granulomatous mastitis, duct ectasia, fat necrosis and lymphocytic mastopathy.[5,6,7]

Common benign lesions of breast include benign proliferative and nonproliferative breast lesions, sclerosing lobular hyperplasia, pseudo-angiomatous stromal hyperplasia, radial scar and complex sclerosing lesions.[5,6,7] Common benign tumors of the breast include fibroadenoma, phyllodes tumor, lactating adenoma and tubular adenoma.[8,5,6,7] Common malignant tumors of breast include invasive breast carcinoma no special type (IBC NST), invasive lobular carcinoma, papillary carcinoma, tubular carcinoma, mucinous carcinoma and medullary carcinoma.[5,6,7]

More than 95% of breast malignancies are adenocarcinoma that arises from the ductal or lobular system early as a carcinoma in situ, but at a time of clinical detection, the majority (>70%) will breach the basement membrane and invade the stroma.[2,5,6,7] Multiple factors viz. age at presentation, size of tumor, morphological grading, lymph node involvement and prognostic markers play role in prognosis of breast malignancies. Among them, axillary lymph node metastasis and prognostic markers play a critical role in prognosis.[9,10,11] The present study carried out to study the spectrum of breast lesions in tertiary care hospital.

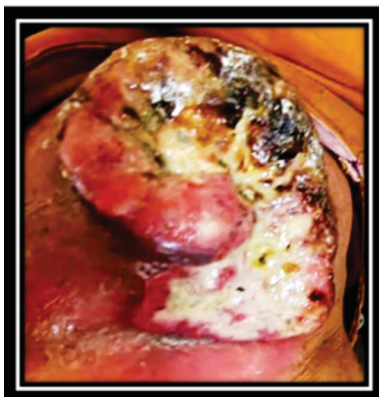
**Methodology**

The present study was a retro-prospective observational cross-sectional study that encompassed all breast specimens received in the Department of Pathology from March 2022 to March 2024. Initially, 230 specimens were included; however, 17 cases were inconclusive, and 3 had cutaneous lesions over breast. So, 20 cases were excluded and total 210 cases were included in the study. The study included all breast specimens received in the Department of Pathology during the period

mentioned in the study design. All known malignancy patients undergoing chemoradiation and patients of skin lesions on the breast were excluded from the study.

Relevant clinical data were obtained from medical records and requisition forms for retrospective and prospective cases respectively. The study encompassed all specimen types, including tru-cut biopsies, lumpectomies, and modified radical mastectomies with axillary clearance. A detailed gross examination of all specimens was performed, focusing on tumor size, location, consistency, margins, and cut surfaces in lumpectomy and mastectomy specimens. Biopsy specimens were processed on the same day, while lumpectomy and mastectomy specimens were fixed overnight in 10% neutral buffered formalin. For modified radical mastectomy specimens, grossing and trimming followed the guidelines outlined in the Surgical Manual of Grossing by Tata Memorial Hospital, with minor adaptations to fit institutional protocols.

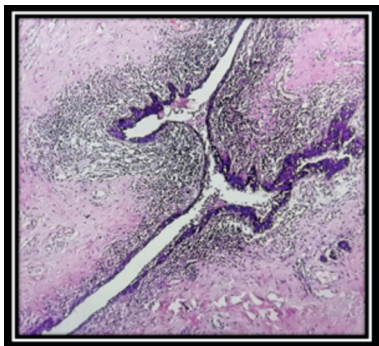
Data were analyzed, tumors were categorized as per -WHO classification of tumor 5th edition and compared with other studies.



**Fig 1 : Clinical Photograph -breast Carcinoma Showing an Ulcero Infiltrative Tumor.**

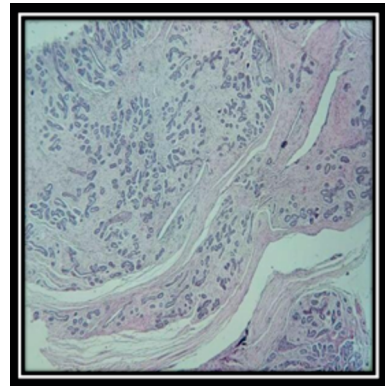


**Fig 2: Modified Radical Mastectomy Specimen, Cut Surface Shows a Grey White Infiltrative Tumor (Arrow Mark)**



**Fig 3 : Microphotograph of Duct Ectasia Showing**

**Dilatation of Duct With Peri-ductal Inflammation (10x H&E) Inset (40x)**



**Fig 4: Microphotograph of Sclerosing Lobular Hyperplasia Showing Proliferation of Intra-lobular Stroma Containing Epithelial Elements Resembling a Microfibroadenoma**

**RESULTS**

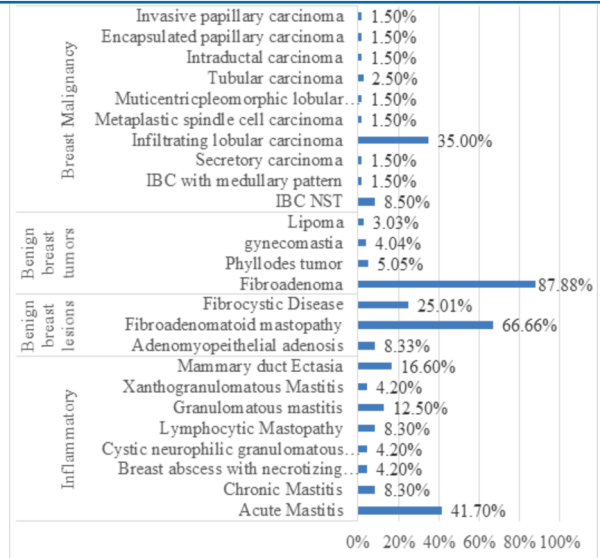
Total 230 breast specimens were included. As 17 cases were inconclusive and 3 cases had skin lesions of breast, so they were excluded and total 210 cases included. Mean age was 49.16 years.

**Table 1: Distribution of Cases According to Demographic Parameter**

Demographic Parameter	Frequency	Percentage	
Gender	Male	7	3
	Female	203	97
Age	10-20	23	13
	21-30	45	20
	31-40	42	19
	41-50	34	16
	51-60	18	10
	>60	48	22
Laterality of breast lesion	Bilateral	7	4
	Left	104	49.5
	Right	99	46.5
Involvement of quadrant	Lower Inner	30	13
	Lower Outer	17	9.5
	Retro-areolar	5	2
	Upper Inner	17	9.5
	Upper outer	141	66
Type of specimen	Biopsy	61	27
	Mastectomy	25	14
	Lumpectomy	124	59
Type of lesion	Benign tumors	99	47.15
	Malignant tumors	75	35.72
	Inflammatory lesions	24	11.42
	Benign lesions	12	5.71

Females outnumbered males with 97% of the cases. Maximum number of cases of breast lesion were found in the age group of >60yrs followed by 21-30 years of age group. Nearly half (49.5%) of the cases had predilection for left breast. The upper outer quadrant (66%) was the most common site of involvement, followed by the lower inner quadrant (13%). Lumpectomy was the most common specimen received (59%), followed by biopsy (27%) and mastectomy (14%). In 210 cases of breast lesions the commonest contributor was neoplastic lesions accounting for 82.87% of the cases. Amongst it, benign tumors were commonest, accounting for 47.15% of the total cases. Non-neoplastic lesions comprised of 17.13% of cases. (Table 1)

Fig 5 shows the, distribution of cases according to histomorphological spectrum of breast lesion.



**Fig 5: Distribution of Cases According to Histomorphological Spectrum of Breast Lesion**

The maximum number of cases were found in the age group of 51-60 years, followed by 61-70 years of age group. Right breast predilection was seen in 47% of cases and left breast involvement was found in 53% of the cases. The upper outer quadrant (68%) was the most common site of involvement, followed by the upper inner quadrant (12%). Invasive breast carcinoma NST was the most common malignancy accounting for 83.5% of the cases followed by infiltrating lobular carcinoma (3.5%) and tubular carcinoma (2.5%). Maximum number of cases (69.34%) had 2-5cm of size followed by >5cm (22.66%). Maximum cases (40%) had 1-3 lymph node involvement, followed by 4-9 lymph node involvement in 32% of cases. Grade II tumors were predominant accounting for 88% of cases followed by grade I in 12% of cases. Triple negative was the most common molecular subtype comprising 36% of cases, followed by Luminal A (28%), Luminal B (24%), other subtypes (8%) and Her2/neu enriched (4%). (Table 2)

**Table 2: Distribution of Malignant Cases According to Clinico-demographic Parameter**

Clinico-demographic parameter (n=75)		Frequency	Percentage
Age	30-40	15	20
	41-50	11	15
	51-60	18	24
	61-70	17	23
	>70	14	18
Laterality	Right	35	47
	Left	40	53
Quadrant Involvement	Upper outer	51	68
	Lower outer	7	9
	Upper inner	9	12
	Lower inner	5	7
	Retro-areolar	3	4
Size	<2 Cm	6	8
	2-5 Cm	52	69.34
	>5 Cm	17	22.66
Lymph node involvement	No LNs	6	24
	1- LNs	10	40
	4-9 LNs	8	32
	>10 LNs	1	4
Grade	Grade I	3	12
	Grade II	22	88
	Grade III	0	0
Molecular Subtype	Luminal A	7	28
	Luminal B	6	24

Her2/NEU Enriched	1	4
TNBC	9	36
Other	2	8

**DISCUSSION**

Present study found frequency of breast lesions as 3.77% which was comparatively low with other studies. Guo Y et al [12] and Chukwuemeka Charles Nwafor et al [1] found frequency of breast lesions as 7.77% and 15.99% respectively. This may be because of tertiary care center catering the services to adjoining rural area of Karnataka state and Marathwada region. Majority of the patients belong to lower social economic strata. The patients above this stratum also form a major chunk and seek medical consultation from private and corporate hospitals. Present study found mean age as 49.16 years which was well in concordance with Li Peng et al [13] and Doval et al [14]. Present study found female to male ratio of breast lesions as 29:1 which was well in concordance with Greta Pandey et al [1] and Fekade Yerakly et al [2]. In present study breast lesions had predilection for left breast (49.5%) than right breast. The finding was well in concordance with study conducted by Dr. C Bhavani et al [15] & Fekade Yerakly et al [2]. Present study also observed the upper outer quadrant as the predominant quadrant affected by breast lesions. The finding was well in concordance with Khoda et al [16] in his study of 50 cases found upper outer quadrant as the most common quadrant involved in breast lesions in 52% of cases followed by upper inner quadrant in 24% of cases. Present study found benign breast lesions (non-neoplastic lesions and benign tumors combined) as the dominant lesions in 52.8% of cases followed by malignant breast lesions in 35.8% of cases and inflammatory breast lesions in 11.4% of cases. The finding was well in concordance with Dr. C Bhavani et al [15], Anushree C.N et al [4] & Dr. J. Bhagya Lakshmi et al [3]. In present study most common inflammatory lesion was acute mastitis which was in concordance with Anushree C.N et al [4] and Dr. C Bhavani et al [15].

Anushree C.N et al [4] found fibrocystic disease (75%) as the predominant benign breast lesion followed by sclerosing adenosis (25%). Fekade Yerakly et al [2] identified fibrocystic disease (72.73%) as the dominant benign breast lesion followed by atypical ductal hyperplasia (27.27%). Present study noted Sclerosing lobular hyperplasia (fibro-adenomatoid mastopathy) (66.66%) as the dominant lesion, followed by fibrocystic disease (25.01%) and adenomyoepithelial adenosis (8.33%). Proliferative breast lesions are of particular concern, warranting further investigations into their potential malignancy risk. Present study observed fibroadenoma as the predominant benign tumor comprising of 87.88%, followed by benign phyllodes tumor (5.05%), gynecomastia (4.04%) and lipoma (3.03%). In the present study, fibroadenoma was the most common benign breast tumor which was well in concordance with other studies. Deepthi Raj Madampithara et al [17] found fibroadenoma (95.1%) as the most common benign breast lesion, followed by benign phyllodes tumor (3.99%).

Present study found the mean age of breast malignancy as 54.18 years, which was in concordance with Rao et al [18] & Sengal A.T. et al [19]. In present study, left breast had predilection for malignant breast lesions which was well in concordance with Sassi A et al [20]. Present study observed the upper outer quadrant as the dominant quadrant involved in malignant breast tumors comprising of 68% cases followed by upper inner quadrant in 12% of cases. Seth R et al [21], & Shaoqing Niu et al [22] found upper outer quadrant as the most common quadrant involved in malignant breast tumors. Amongst invasive breast carcinoma, invasive breast carcinoma no special type (IBC NST) stands as the most prevalent subtype. The observation of present study was in concordance with study conducted by Bhagat VM et al [23] & Hawary AK et al [24], with IBC NST being the predominant tumor accounting for 83.5% of cases. In present study

comparatively wide spectrum of special variants was observed with tubular carcinoma in 2.5% of cases, IBC NST with medullary pattern, encapsulated (intracystic) carcinoma breast, secretory carcinoma, metaplastic carcinoma, papillary carcinoma and intraductal carcinoma in a single case each accounting for 1.5% of cases. The observed variations are challenging to elucidate but may be attributed to variations in sample sizes and demographic factors. Nonetheless, the possibility of chance findings cannot be disregarded. However new approaches or strategies for the treatment modalities need comprehensive understanding of the molecular characteristics underlying specific types of breast cancer. Entire strategic management of breast malignancies are dependent on molecular subtypes, nodal status and grade of the tumor. Majority of the studies had largest dimension of 2-5cm as the predominant finding. This can be attributed to the lack of awareness, shyness on part of patients. They seek the consultation late which makes the tumor grow and attain a large size to be noticed by the patient to proactively tell family members about breast lump. Additionally, in the majority of the institutions and hospitals robust mammography or other screening programs are not a part of routine to detect tiny to small tumors. Fekade Yerakly et al [2] in his study of 114 cases found that 50.9% of cases had >5cm as the largest dimension followed by 42.1% of malignant breast tumors had largest dimension of 2-5cm. It is well known that in breast cancer the number of positive lymph nodes has an inverse linear relationship with prognosis and survival. [25] Fekade Yerakly et al [2] found that 49,5% of cases had no lymph node metastasis, 1-3 lymph nodes were involved in 27.8% of cases, 15.8% of cases had 4-9 lymph nodes involvement and >10 lymph nodes involvement was seen in 6.9% of cases. The studies of Dogra et al [26], Dovel et al [14] and Bhattacharjee et al [27] observed grade II tumours were the main contributors consisting of 70.1%, 72.5% and 71.1% of cases respectively. Present study had similar observations with grade II tumours in 75% of cases. But alone grading does not impact the prognosis and outcome of breast cancer. The literature mentions Luminal A is the most common subtype, in India followed by TNBC. Luminal A is said to be of low grade, good prognosis and sensitive to hormonal therapy. Luminal B tends to have higher grade, worst prognosis and resistant to hormone therapy. HER2/neu enriched are usually of higher grade with aggressive course. But with the advent of anti HER2/neu targeted therapy they respond to Herceptin[28]. Early age of cancer onset, lifestyle factors such as diet and obesity, reproductive factors such as multiparity, socioeconomic factors, and potential genetic susceptibility of Indians to TNBC are the factors that might have accounted for the higher prevalence of TNBC reported by studies conducted among Indian patients[29].

**CONCLUSION**

From this study we conclude that, Benign lesions were more common than malignant and inflammatory lesions. Acute mastitis was the most frequent inflammatory lesion, fibroadenomatoid mastopathy was the commonest benign non-neoplastic lesion, and fibroadenoma was the predominant benign tumor. Among malignant tumors, invasive breast carcinoma of no special type (IBC-NST) was the most common histological subtype.

Most malignant tumors measured 2–5 cm and were predominantly of nuclear grade II. Lymph node involvement was observed in many malignant cases. Triple-negative breast carcinoma was the most common molecular subtype, followed by luminal A and luminal B tumors.

Overall, the study highlights the importance of histopathological evaluation and molecular subtyping in the diagnosis and management of breast lesions. Early detection and appropriate treatment are essential for improving prognosis and reducing breast cancer-related morbidity and mortality.

**REFERENCES**

1. Nwafor, Chukwuemeka Charles & Udo, Isaac Assam. (2018). Histological Characteristics of Breast Lesions in Uyo, Nigeria. Nigerian Journal of Surgery. 24. 76. 10.4103/njs.NJS\_29\_17.
2. Clinics in Oncology Histopathologic Patterns of Breast Lesions in Hawassa [Internet]. 2022 [cited 2024 Jul 29]. Available from: <https://www.clinicsinoncology.com/open-access/histopathologic-patterns-of-breast-lesions-in-hawassanbspuniversity-comprehensive-8495.pdf>
3. Lakshmi JB Spectrum Of Breast - Google Search [Internet]. Google.com. 2024 [cited 2024 Aug 30].
4. C.n A, M.r P, Y.a M. Histopathological spectrum of neoplastic and non neoplastic lesions of breast in a tertiary care centre in Bangalore. Indian Journal of Pathology and Oncology [Internet]. [cited 2024 Jul 29];6(2):203–6. Available from: <https://www.ijpo.co.in/article-details/8953>
5. 134. Goldblum JR, Lamps LW, McKenney JK, Myers JL, Rosai and Ackerman's Surgical Pathology E-Book. 11th ed. Elsevier; 2017.
6. Longacre TA. Mills and sternberg's diagnostic surgical pathology. 7th ed. Baltimore, MD: Wolters Kluwer Health; 2022.
7. Hoda SA, Rosen PP, Brogi E, Koerner FC. Rosen's breast pathology. 5th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2020.
8. A prospective study of histopathological spectrum of benign breast lesions in a tertiary hospital Karattupalayam Sampath Mouleeswaran 1%2C B.S. Sangeetha 2 - Google Search [Internet]. www.google.com. [cited 2024 Jul 29].
9. American Joint Committee on Cancer: AJCC cancer staging manual, edition 7, New York: Springer; c2009
10. 127. Liu Y, He M, Zuo WJ, Hao S, Wang ZH, Shao ZM. Tumor Size Still Impacts Prognosis in Breast Cancer With Extensive Nodal Involvement. Frontiers in Oncology. 2021 Apr 9;11.
11. Hernandez-Aya LF, Chavez-MacGregor M, Lei X, Funda Meric-Bernstam, Buchholz TA, Hsu L, et al. Nodal Status and Clinical Outcomes in a Large Cohort of Patients With Triple-Negative Breast Cancer. Journal of clinical oncology. 2011 Jul 1;29(19):2628–34.