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CLINICOPATHOLOGICAL ASSESSMENT OF BENIGN BREAST LESIONS IN A SAMPLE OF IRAQI PATIENTS

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ABSTRACT

Introduction; Benign lesions are the most common cause of breast problems in females, they are 10 times more common than breast cancer in the western world and make up 90% of breast illnesses worldwide. **Method;** A retrospective study included an analysis of 200 cases of benign breast lesions, The clinic-pathological data that were collected from patient's pathology reports included age, laterality, quadrant, clinical presentation, site, and any associated incidental microscopic findings (UDH, ADH, DCIS, LCIS, and CA). **Results;** the mean age for diagnosing benign breast lesions is 32, fibroadenoma is the commonest lesion (38.5%) followed by fibrocystic changes (19.5%) and duct ectasia (12%), benign lesions are most commonly bilateral (46.5%) followed by right side (43%), (31%) of them are located in the upper outer quadrant and (72%) of them presented as a breast mass. **Conclusion;** Fibroadenoma followed by fibrocystic changes constitute the majority of benign breast lesions, they are most commonly bilateral, located in the upper outer quadrant and presented as a lump. There is a significant association between the histopathological diagnosis of a benign lesion with side, site and age of presentation.

INTRODUCTION

Benign lesions are the most common cause of breast problems in females; they are 10 times more common than breast cancer in the western world.[1] And make up 90% of breast illnesses worldwide.[2]

Based on the likelihood of developing breast cancer, benign epithelial lesions are categorized as proliferative and non-proliferative. Non-proliferative changes are not linked to a higher risk of breast cancer. A slight increase in the chance of developing cancer in either breast later on is linked to proliferative breast disease, which is characterized by the proliferation of epithelial cells without atypia.[3]

Benign breast illnesses include developmental abnormalities, inflammatory lesions, epithelial and stromal proliferation, and neoplasms, including fibroadenomas, hyperplasia, intraductal papilloma, sclerosing adenosis, radial scars, fat necrosis, cysts, mastitis, duct ectasia, and granular cell tumors.[4]

Pain and swelling are the most prevalent symptoms of these lesions.[5] Clinical examination, mammography, ultrasound, and FNAC are simple methods for diagnosing benign lesions, which can be confirmed through an excision biopsy or a core needle biopsy.[6]

Millions of women worldwide are diagnosed with fibrocystic breast disease, the most prevalent benign form of breast illness. Up to 50% of women will experience symptoms at some point in their lives.[7,8]

Fibroepithelial lesions are a distinct class of breast illnesses that share similar histologic characteristics but differ clinically. Examples of these lesions are fibroadenomas and phyllodes tumors. The most frequent benign breast mass is a fibroadenoma, while phyllodes tumors are less common and can be benign neoplasms or malignant tumors with the ability to spread to distant locations.[9]

Breast fibroadenoma is a frequent biphasic tumor that peaks in occurrence in the second and third decades of life and affects women of all ages.[10]

Breast sclerosing lesions known as radial scars are benign and are distinguished by a central fibroelastotic core with benign glands radiating from the center. Radial scars are benign but have an association with occult cancer, according to numerous studies.[11]

Benign intraductal papilloma, the most common breast papillary lesion, has increased in incidence over the past 20 years, currently ranging from 1 to 9%.[12,13]

Microglandular adenosis is a benign, poorly confined proliferation of glandular structures infiltrating breast stroma and adipose tissue, defying the "2-cell-type rule" for benign breast lesions.[14]

The spectrum of benign spindle-cell breast lesions is broad and diverse, encompassing both myofibroblastic and fibroblastic lesions.[15]

A benign mesenchymal breast lesion called pseudoangiomatous stromal hyperplasia is typified by myofibroblast growth that mimics a vascular lesion.[16]

This study aims to assess benign breast lesions according to age, laterality, quadrant, clinical presentation, site, size, ultrasound findings, and any associated incidental microscopic findings (UDH, ADH, DCIS, LCIS and CA) among a sample of Iraqi women.

MATERIALS AND METHODS

A retrospective study included an analysis of 200 randomly selected cases of benign breast lesions collected from the Teaching Laboratories of Al-Emamain Al-Kadhmain Medical City (AS), Baghdad Medical City, from January 2022 to October 2023. The cases included 125 excisional biopsies, 47 core biopsies, and 28 trucut biopsies.

Hematoxylin and eosin-stained slides were collected, and the diagnosis was revised by two pathologists.

The clinic-pathological data that were collected from patient's pathology reports included age, laterality, quadrant, clinical presentation, site, and any associated incidental microscopic findings (UDH, ADH, DCIS, LCIS, and CA).

Exclusion Criteria

- Cases diagnosed with malignant neoplasms.
- Reports with incomplete clinical or pathological data.

All statistical analyses were performed utilizing SPSS version 26 and included mean, standard deviation, frequency, and percentage using Chi square, with a p-value <0.05 regarded as statistically significant.

RESULTS

The study sample

A total number of 200 patients were included in the study sample.

Age distribution of the studied sample

The age distribution of the studied sample ranged from 14 -57 years with a mean of 32.6 ± 10.7 SD. Regarding age group distribution, 83 (41.5%) patients were in the age group 14-30 years, 97 (48.5%) between 31-45 years, and 20 (10.0%) >45 years; as shown in figure (1).

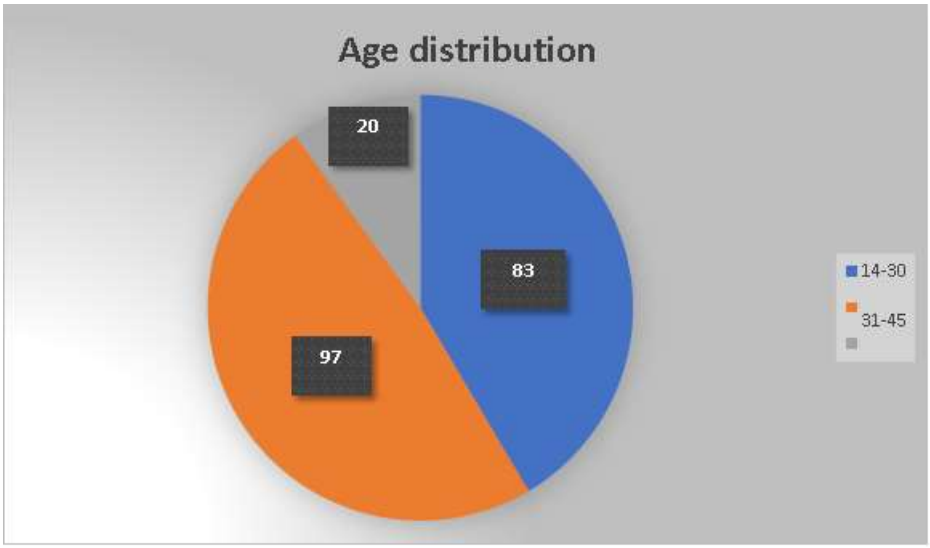

Figure (1): Age distribution of the studied sample.

Clinical characteristics

Regarding affected side; most cases were on the right side (84.4%). Concerning the affected site, the upper outer quadrant was the most common (31.0%), followed by lower inner quadrant (22.5%). As for clinical presentation, most patients presented with breast mass (72.5%); as shown in table (1).

Table (1): Clinical characteristics of the studied sample.

Variable	Frequency (N=200)	Percentage (%)
Affected side		
Right	86	84.4
Left	21	19.6
Affected site		
Upper inner	26	13.0
Lower inner	45	22.5
Upper outer	62	31.0
Lower outer	23	11.5
Areolar	38	19.0
Nipple	6	3.0
Clinical presentation		
Mass	145	72.5
Abscess	14	7.0
Calcification	12	6.0
Nipple discharge	13	6.5
Cysts of U/S	6	3.0
Densities on mammography	2	1.0
Galactorrhea	2	1.0
Nipple retraction	2	1.0
Skin bruising	2	1.0
Breast enlargement	2	1.0

Histopathological diagnosis

Regarding histopathological diagnosis; fibroadenoma (figure 2) was the most common diagnosis 38.5%, followed by fibrocystic changes 19.5% (figure 3), duct ectasia 12.0% (figure 4) and intraductal papilloma 6% (figure 5); as shown in table (2).

Table (2): Distribution of cases according to histopathological diagnosis.

Variable	Frequency (N=200)	Percentage (%)
Fibroadenoma	77	38.5
Fibrocyastic changes	39	19.5
Duct ectasia	24	12.0
Intraductal papilloma	12	6.0
Abscess	10	5.0
Fat necrosis	8	4.0
Chronic granulomatous mastitis	6	3.0
Cystic neutrophilicgranulomatous	6	3.0
Adenosis with inflammation	4	2.0
Sclerosing adenosis	4	2.0
Apocrine metaplasia	4	2.0
Keratinous cyst	4	2.0
UDH	2	1.0
Total	200	100.0

Relationship between clinical parameters

Association between histopathological diagnosis and age

A statistically significant association was detected between histopathological diagnosis and age (P value < 0.001); as shown in table (3).

Table (3): Association between histopathological diagnosis and age.

Histopathological diagnosis	Age			Total
	14-30 years	31-45 years	>45 years	
Fibroadenoma	59	18	0	77
	76.6%	23.4%	0.0%	100.0%
Fibrocyastic changes	0	37	2	39
	0.0%	94.9%	5.1%	100.0%
Ductectasia	6	12	6	24
	25.0%	50.0%	25.0%	100.0%
Intraductal papilloma	6	0	6	12
	50.0%	0.0%	50.0%	100.0%
Abcess	0	10	0	10
	0.0%	100.0%	0.0%	100.0%
Fat necrosis	4	4	0	8
	50.0%	50.0%	0.0%	100.0%
Chronic granulomatousmastitis	4	2	0	6
	66.7%	33.3%	0.0%	100.0%
Cystic neutrophilicgranulomatous	2	4	0	6
	33.3%	66.7%	0.0%	100.0%
Adenosis withinflammation	0	2	2	4
	0.0%	50.0%	50.0%	100.0%
Sclerosing adenosis	0	2	2	4
	0.0%	50.0%	50.0%	100.0%
Apocrine metaplasia	0	4	0	4
	0.0%	100.0%	0.0%	100.0%
Keratinous cyst	2	2	0	4
	50.0%	50.0%	0.0%	100.0%
UDH	0	0	2	2
	0.0%	0.0%	100.0%	100.0%
Total	83	97	20	200
	41.5%	48.5%	10.0%	100.0%

Association between histopathological diagnosis and laterality

No statistically significant association was detected between histopathological diagnosis and laterality (P value = 0.092); as shown in table (4).

Table (4): Association between histopathological diagnosis and laterality.

Histopathological diagnosis	Laterality		Total
	Bilateral	Unilateral	
Fibroadenoma	37	40	77
	48.1%	51.9%	100.0%
Fibrocyastic changes	20	19	39
	51.3%	48.7%	100.0%
Ductectasia	8	16	24
	33.3%	66.7%	100.0%
Intraductal papilloma	6	6	12
	50.0%	50.0%	100.0%
Abcess	8	2	10
	80.0%	20.0%	100.0%
Fat necrosis	2	6	8
	25.0%	75.0%	100.0%
Chronic granulomatous mastitis	2	4	6
	33.3%	66.7%	100.0%
Cystic neutrophilic granulomatous	2	4	6
	33.3%	66.7%	100.0%
Adenosis with inflammation	0	4	4

	0.0%	100.0%	100.0%
Sclerosing adenosis	2	2	4
	50.0%	50.0%	100.0%
Apocrine metaplasia	2	2	4
	50.0%	50.0%	100.0%
Keratinous cyst	4	0	4
	100.0%	0.0%	100.0%
UDH	0	2	2
	0.0%	100.0%	100.0%
Total	93	107	200
	46.5%	53.5%	100.0%

Association between histopathological diagnosis and affected site

A statistically significant association was detected between histopathological diagnosis and affected breast site (P value < 0.001); as shown in table (5).

Table (5): Association between histopathological diagnosis and affected breast site.

Histopathologicaldiagnosis	Affected breast site						Total
	Upperinner	Lowerinner	Upperouter	Lowerouter	Areolar	Nipple	
Fibroadenoma	12	14	20	15	16	0	77
	15.6%	18.2%	26.0%	19.5%	20.8%	0.0%	100.0%
Fibrocyasticchanges	0	17	14	4	4	0	39
	0.0%	43.6%	35.9%	10.3%	10.3%	0.0%	100.0%
Ductectasia	6	4	4	0	6	4	24
	25.0%	16.7%	16.7%	0.0%	25.0%	16.7%	100.0%
Intraductalpapilloma	2	4	2	2	0	2	12
	16.7%	33.3%	16.7%	16.7%	0.0%	16.7%	100.0%
Abcess	2	4	4	0	0	0	10
	20.0%	40.0%	40.0%	0.0%	0.0%	0.0%	100.0%
Fat necrosis	0	0	4	0	4	0	8
	0.0%	0.0%	50.0%	0.0%	50.0%	0.0%	100.0%
Chronic granulomatousmastitis	0	0	6	0	0	0	6
	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
Cystic neutrophilicgranulomatous	2	0	0	2	2	0	6
	33.3%	0.0%	0.0%	33.3%	33.3%	0.0%	100.0%
Adenosis withinflammation	2	0	2	0	0	0	4
	50.0%	0.0%	50.0%	0.0%	0.0%	0.0%	100.0%
Sclerosingadenosis	0	0	2	0	2	0	4
	0.0%	0.0%	50.0%	0.0%	50.0%	0.0%	100.0%
Apocrinemetaplasia	0	0	2	0	2	0	4
	0.0%	0.0%	50.0%	0.0%	50.0%	0.0%	100.0%
Keratinous cyst	0	2	2	0	0	0	4
	0.0%	50.0%	50.0%	0.0%	0.0%	0.0%	100.0%
UDH	0	0	0	0	2	0	2
	0.0%	0.0%	0.0%	0.0%	100.0%	0.0%	100.0%
Total	26	45	62	23	38	6	200
	13.0%	22.5%	31.0%	11.5%	19.0%	3.0%	100.0%

Association between histopathological diagnosis and associated diagnosis

No statistically significant association was detected between primary histopathological diagnosis and any associated diagnosis (P = 0.083); as shown in table (6).

Table (6): Association between histopathological diagnosis and associated diagnosis.

Histopathologicaldiagnosis	Associated diagnosis				Total
	None	Adenosis	UDH	Atypical intraductal hyperplasia	
Fibroadenoma	60	2	9	6	77
	77.9%	2.6%	11.7%	7.8%	100.0%
Fibrocyasticchanges	37	2	0	0	39
	94.9%	5.1%	0.0%	0.0%	100.0%
Ductectasia	24	0	0	0	24
	100.0%	0.0%	0.0%	0.0%	100.0%
Intraductalpapilloma	10	2	0	0	12
	83.3%	16.7%	0.0%	0.0%	100.0%
Abcess	8	0	2	0	10
	80.0%	0.0%	20.0%	0.0%	100.0%
Fat necrosis	8	0	0	0	8
	100.0%	0.0%	0.0%	0.0%	100.0%
Chronic granulomatousmastitis	4	2	0	0	6
	66.7%	33.3%	0.0%	0.0%	100.0%
Cystic neutrophilicgranulomatous	6	0	0	0	6
	100.0%	0.0%	0.0%	0.0%	100.0%
Adenosis withinflammation	4	0	0	0	4
	100.0%	0.0%	0.0%	0.0%	100.0%
Sclerosing adenosis	4	0	0	0	4
	100.0%	0.0%	0.0%	0.0%	100.0%
Apocrine metaplasia	4	0	0	0	4
	100.0%	0.0%	0.0%	0.0%	100.0%
Keratinous cyst	4	0	0	0	4
	100.0%	0.0%	0.0%	0.0%	100.0%
UDH	2	0	0	0	2
	100.0%	0.0%	0.0%	0.0%	100.0%
Total	175	8	11	6	200
	87.5%	4.0%	5.5%	3.0%	100.0%

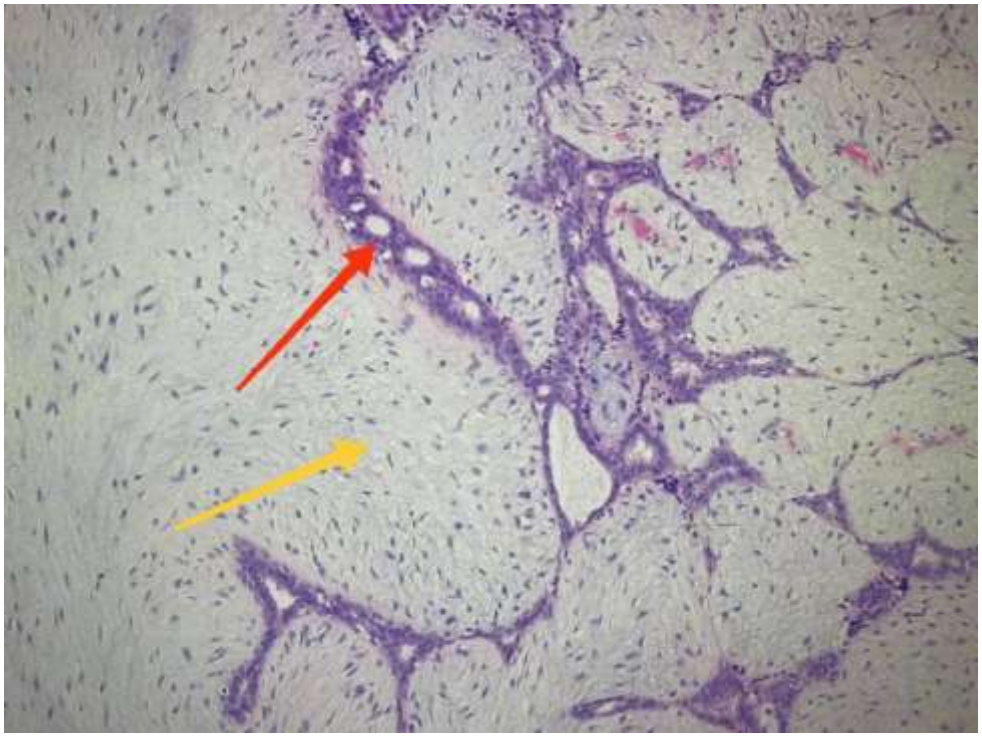

Figure (2): fibroadenoma. The image shows the proliferation of benign mammary glands lined by epithelial and myoepithelial layers (red arrow) surrounded by the myxoid stroma (yellow arrow). (H&E, 20x).

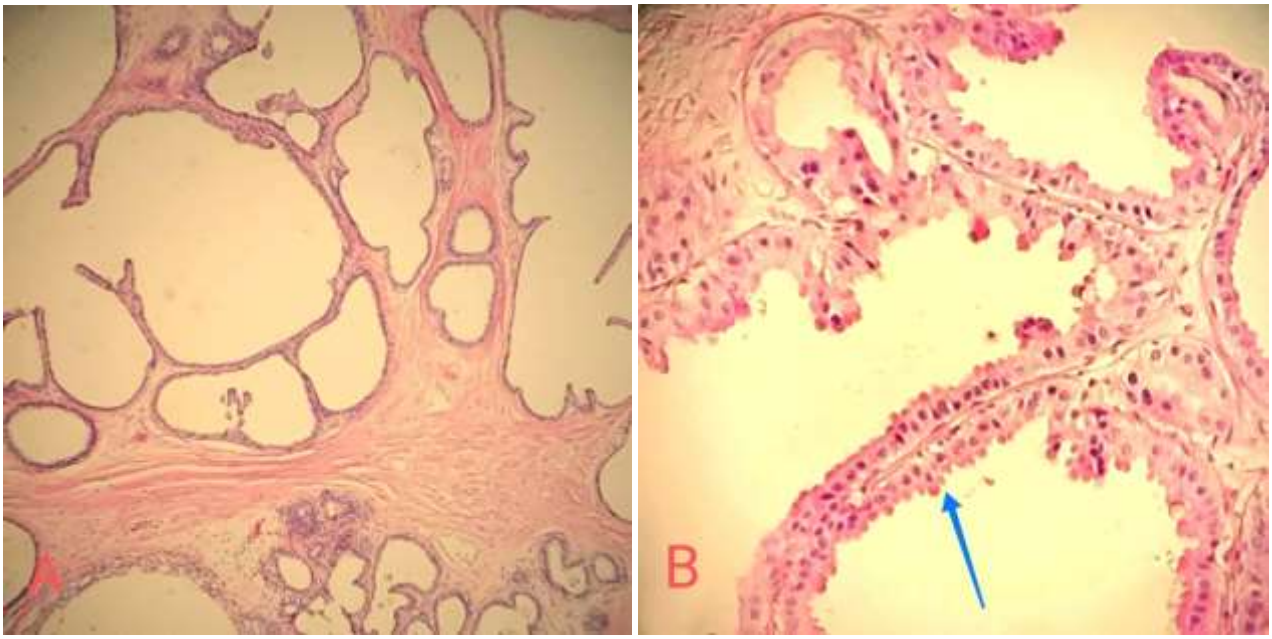

Figure (3): fibrocystic change. The images show increased acini per lobule, cystically dilated benign ducts surrounded by fibrosis (A); the ducts show apocrine metaplasia (blue arrow). (B). (H&E, 10X, 20X).

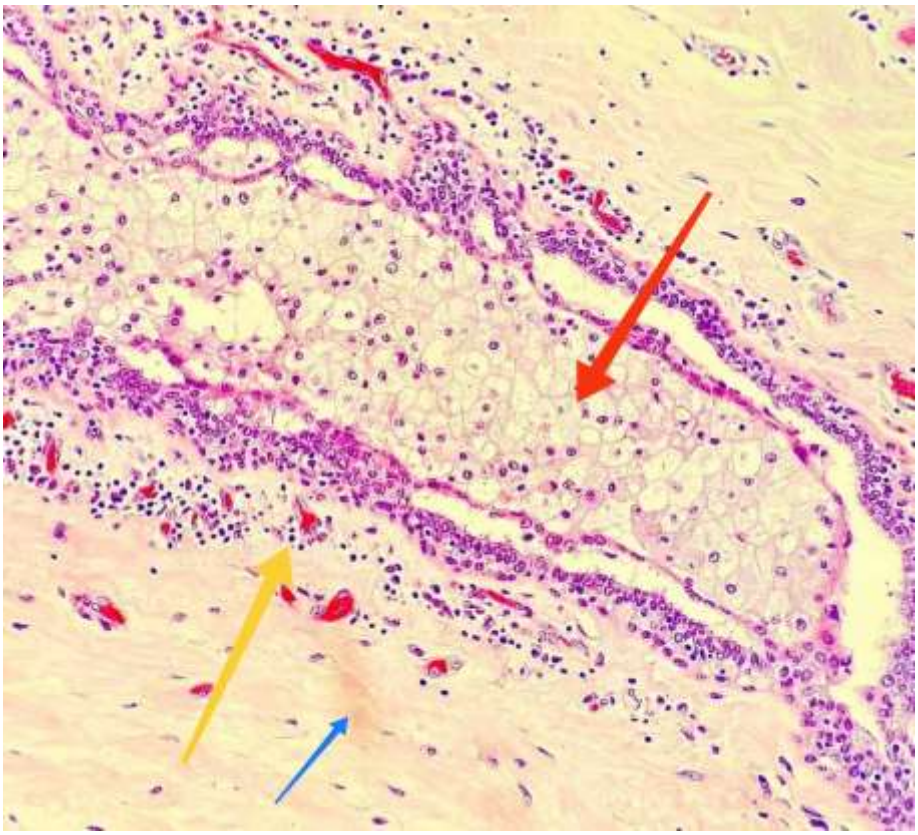

Figure (4): ductectasia. The image shows dilated duct filled with macrophage (red arrow) and surrounded by fibrosis (blue arrow) and inflammation (yellow arrow). (H&E, 20X).

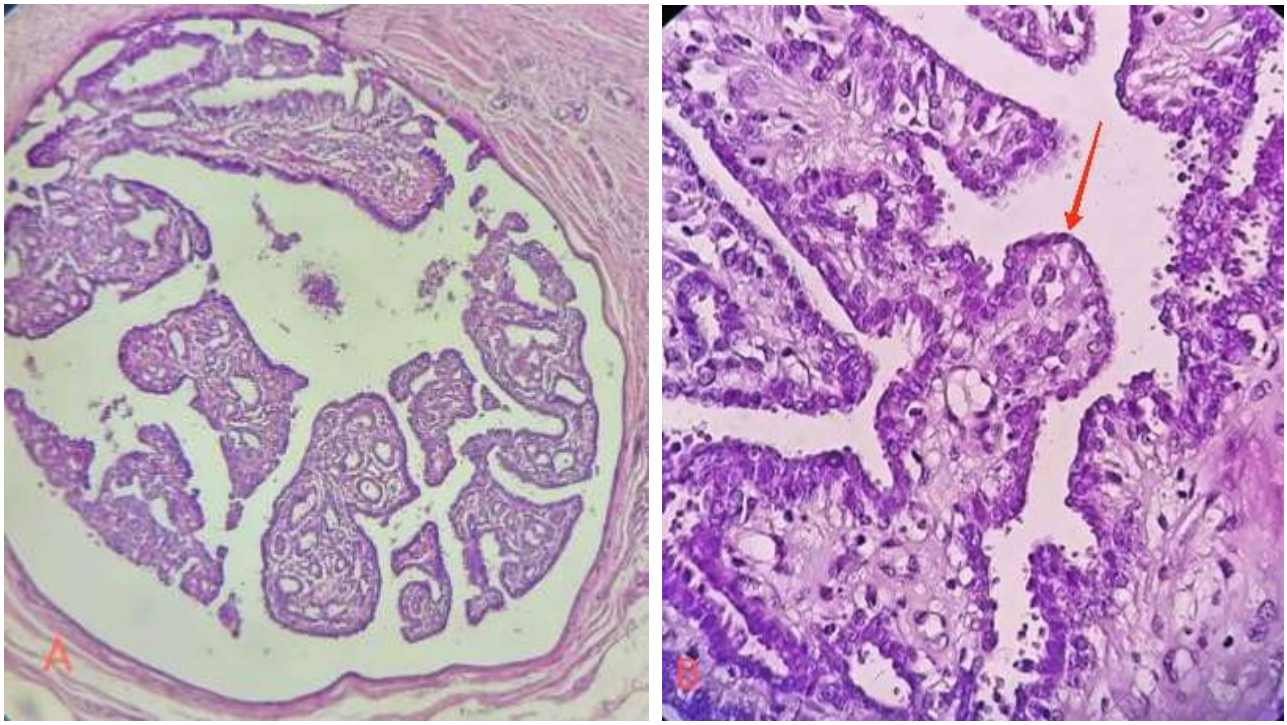

Figure (5): intraductal papilloma. The images show papillary proliferation within a dilated duct (A), the papillae have a fibrovascular core and lined by benign cuboidal cells (red arrow). (B). (H&E, 10X, 20X).

DISCUSSION

Overview; Given the widespread public awareness, women presenting with breast complaints—particularly lumps—are a regular finding and a major source of anxiety. Therefore, a surgeon's ability to differentiate benign from malignant illnesses and their frequency becomes crucial. Every year, 200,000 new cases of breast diseases are reported, with the majority of the palpable lesions being benign.[17] A significant portion of research on benign breast diseases is concerned with how it may be related to the eventual development of cancer. Breast lesions with little to no increased risk of breast cancer should be identified from those with a little or moderate increase in risk and the classification of benign breast disease should take this stratification into account.[18]

Regarding histopathological diagnosis; fibroadenoma was the most common diagnosis (38.5%) in this research, followed by fibrocystic changes (19.5%), duct ectasia (12.0%) and intraductal papilloma (6.0%) and other less frequent lesions.

These results are consistent with other studies like **ameet et al**. (**2022),** which found Fibroadenoma (58.6%) was the commonest followed by Fibrocystic disease in (11.4%) of cases. (2) And **Kanpurwala et al. (2017)**, which mentioned that the commonest benign breast lesion was fibroadenoma (77.62%), followed by fibrocystic disease (4.3%).(1) While in another study conducted by **Nazma et al (2022)** most frequently encountered lesion was fibroadenoma (45.8%), breast abscess (22.6%) and fibrocystic change (11.6%).[19]

Regarding age; the mean age in our study was 32, (48.5%) were between 31-45 years, (41.5%) patients were in the age group 14-30 years, and (10%) >45 years. And there was significant association between benign breast lesions and age.

According to **Mugdha et al. 2018**, The mean age of patients with benign breast lesions was 30 years.[20] The majority of patients were between 31-40 years of age in a study by **Kotte Nagarjuna Reddy and G. Harshitha. (2022).**[21] both of these studies agree with ours, however (11-30) years was the commonest age group according to **Krishnareddy et al.**[22] And was (21-30) according to **Sravanthi Kanumuri et al 2022**.[23]

In this study, fibroadenoma had significantly higher rate in patients within the age group (14-30) while fibrocystic change was significantly higher in prevalence among patients (31-45) old.

This finding is comparable to other studies in the literature, like **Nazma et al. (2022) and Kumar N and Prasad J (2019)** where fibroadenoma was more frequent in the years 15-2.[19,24] **Shweta Pai (2011)** and **Nazma et al. (2022)**, both studies found significantly higher prevalence of fibrocystic disease in third and fourth decades.[25]

These findings are reasonable as fibrocystic changes are due to hormonal changes that occur during ovulation and just before menstruation; the breast cells that cause fibrocystic illness create cysts by retaining fluid.[26] While fibroadenoma is more common in younger age group because breast fibroadenoma arises from lobules

that are more active and prone to growth during this period.[27]

Regarding affected side; in the current study, most cases were on the right side (84.4%).

this aligns with other studies like **Abbadi Venkat Reddy, 2019** and **Jetendra Yede et al, 2015**, who studied benign breast lesions and showed that right side was more common.[28,29] the left side was most prevalent according to **Oluwole and Ajao, 1997.**[30]

Regarding the affected quadrant; the upper outer quadrant was the most commonly affected side (31.0%), followed by lower inner quadrant (22.5%). Furthermore we found that the site of involvement was significantly associated with benign diagnoses.

this finding aligns with other studies in the literature like **Krishnareddy et al**. **2020**[22] and **shobha et al 2016**.,[6] both reported the upper outer quadrant as the commonest site of involvement in benign breast lesions.

As for clinical presentation, most patients presented with breast mass (72.5%). Followed by abscess. (7), nipple discharge (6.5%) and calcification (6%) among other less prevalent symptoms according in our sample.

According to **Mallikarjuna et al**., the most common symptom (80%) was the existence of a painless lump. According to **Sagar et al**., 78.13% of cases had a painless lump.[31,32] The clinical presentation was mainly also a painless lump according to **Krishnareddy et al**.,[22] **Jetendra et al**,[29] and **Abbadi Venkat Mohan Reddy.**[33]

Out of 200 cases, in the present study, adenosis was found in 8 cases (2 in chronic granulomatous mastistis, 2 of papillomas, 2 in fibrocystic disease cases and 2 in fibroadenomas), UDH was present in 11 of cases (2 within abscess cases and 9 within fibroadenoma cases), ADH was detected in 6 cases (3%), all of them were within fibroadenomas. However there was no significant association between the associated/ incidental finding and the histopathological diagnosis.

Atypical hyperplasia was found in just 4% of the biopsy samples in a study conducted by (**Dupont and Page 2010)**.[34] 4.6% of cases had ADH according to (**Mima Maychet B. and Sangma 2013)**.[35] Our study's results were close to the above investigations. Our sample, however, was fewer in quantity than theirs.

CONCLUSION

Benign breast lesions constitute a heterogeneous group of diseases, fibroadenoma followed by fibrocystic changes constitute the majority of them, they are most commonly bilateral, located in the upper outer quadrant and presented as a lump. There is a significant association between the histopathological diagnosis of a benign lesion with side, site and age of presentation.

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