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Research

BENIGN BREAST DISEASE: A PROSPECTIVE CLINICAL STUDY FOR DETERMINATION OF RISK FACTORS AND FNAC IN POST-OPERATIVE PATIENTS

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Abstract

Background: Benign breast disease is one of the most common forms of tumors seen in women than malignant tumors, with clinical presentation of lumps associated with pain. The disease requires accurate clinicopathological and histopathological diagnosis for ruling out the type of tumors and to provide the ideal treatment. **Materials and Methods:** A clinical prospective study was conducted on patients diagnosed with benign breast disease in the Tirunelveli Medical College and Hospital. The duration of the study was 18 months (February 2015 – August 2016). The study evaluated 120 female patients over a duration of 18 months for different clinical assessments. The study also evaluated the histopathological correlation for fibroadenoma by using the FNAC scale. The given treatment for different benign breast diseases was also evaluated. **Result:** Out of 120 cases of BBD, fibroadenoma was the most common clinical condition with 79 cases (65.8%), followed by phyllodes in 17 cases (14.2%), fibrocystic disease in 13 cases (10.8%), tubular adenoma and breast abscess with 5 cases (4.2%) and epitheliosis was diagnosed in one patient. The study findings revealed that a significant number of the patients had unilateral breast lesion involvement in the age group of 20-30 years old. The use of oral contraceptives and family history was seen in 9 cases of fibroadenoma. The comparison of fibroadenoma with HPE was conducted with a 93.67% and specificity of 56.10%. A positive predictive value of 80.43% and a negative value of 82.14%. The correlation between HPE with FNAC was performed and seen with a consistent result among the patients. A notable case of phyllodes was diagnosed in a 13-year-old female without reaching menarche. **Conclusion:** Fibroadenoma is the most prevalent type of BBD in the Indian population, with no significant clinical symptoms except the painless lumps in the breast. The diagnosis of such conditions requires the use of clinicopathological and histological methods for appropriate treatment of the disease.

INTRODUCTION

Benign breast diseases (BBD) are one of the most common diseases seen in different aspects of age, ranging from early reproductive life to the postmenopausal stage, with increasing health concerns worldwide. Breast cancer is one of the most common forms of cancer seen in women, occurring in one in eight women during their lifespan. According to data from USA and Netherlands, 3% of women consult their general practitioner for symptoms related to breast diseases. Women may be associated with clinical symptoms of malignant cancer, however, only 3% to 5% of such women are diagnosed with breast cancer and evidence has suggested that the remaining population are diagnosed with benign tumors.[1,2] Benign breast disease is more common in women of childbearing age, peaking at the age between 30 to 50 age. Benign tumors of the breast are 4 to 5 times more common than malignant tumors, up to 30% of women can suffer from BBD which can require

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appropriate treatment over their ifetime. Over 80% of such population presented with clinical symptoms such as pain and breast lumps The etiology of BBD and its significant risk factors have been studied, however, there is limited data for such studies on the Indian population.[3] Hormonal factors; including reproductive and lifestyle factors are a few of the documented risk factors for cancer in women. The data for other risk factors including early menarche, irregular and short menstrual cycle, use of oral contraceptives, hormone replacement therapy, and other lifestyle factors can pose a risk to the incidence of BBD in females. However, this correlation of risk factors has not been evaluated for patients presented with BBD.[1,2] Benign breast disease covers a spectrum of non-invasive breast conditions, including epithelial proliferation with atypia (EPA) or epithelial proliferation without atypia (EP) hyperplasia, fibroadenomas (affecting younger women with a clinical condition of firm breast mass), papillomas (small discrete benign tumors), adenosis (lobules enlargement), calcifications, fluid-filled cysts, and fibrocystic changes (FCGs) which comprise of cysts and solid lesions. The management of such disease includes clinical, radiological, and if required histological diagnostic methods for ruling out malignancy.[5,6] Surgical removal of tumors has remained one of the most widely used methods due to its curative effect and prevention of the development of malignant tumors. However, the exact relationship between malignant and benign tumors is yet to be established. The study aims to analyze the spectrum of benign breast diseases concerning risk factors such as age, clinical presentation, symptoms, and their management. The study targets to represent the clinical treatment modalities, and correlation of the post-operative histopathological reports among the Indian population. According to the best of our knowledge, there are no such studies conducted to evaluate and present the current scenario of benign breast disease in Indian females.

MATERIALS AND METHODS

The prospective evaluated 120 cases of benign breast disease in patients admitted to the Tirunelveli medical college and hospital from February 2015 to August 2015 (18 months). The approval of the study was taken by the ethics committee. Patients with a clinical diagnosis of BBD were admitted for further evaluation after obtaining informed written consent. A detailed history and clinical examination were done with a self-designed questionnaire. Patients enrolled in the study was assessed with the aid of routine investigations, specific diagnostic test, and histopathological methods for confirming the clinical presentation of benign breast disease. Patients' detailed histories, medical reports, and clinical treatment were compiled to formulate a complete profile by collaborating with the different departments of the hospital.

Inclusion Criteria
Females above 12 years of age
Patients admitted with a provisional diagnosis of benign breast disease
Patients with a confirmed diagnosis of benign breast disease by clinicopathological examination

Exclusion Criteria
Females under the age of 12 years
Patients who were found to have malignant tumors during the clinical evaluation

Methodology
The study assessed the various risk factors, the spectrum of disease, histopathological correlation, and management based on patient interviews, lab reports, and discussion.
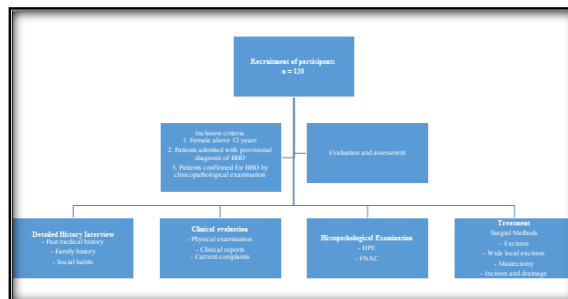

Figure 1: Methodology of the prospective study

Outcome Variables
The study determines each variable separately depending on the detailed history interview, clinical lab results, and histopathological correlation.

Analysis
The data from the study were presented as frequency and percentage, including bars and graphs.

RESULTS

During the study period, we assessed 120 cases of benign breast disease, based on the histopathological and clinical findings. From histopathological findings, fibroadenoma (FA) was the most prevalent that accounting for 79 cases out of which 9 were diagnosed with giant fibroadenoma (65.8%) followed by phyllodes in 17 (14.2%), fibrocystic disease (FCD) in 13 (10.8%), tubular adenoma (TA) in 10 (8.3%), and breast abscess (BA) and epitheliosis in 1 patient was recorded. Figure no 2 indicates the distribution of benign breast disease among the 120 patients.
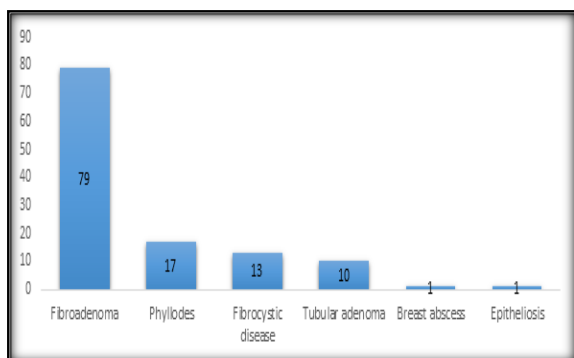
Figure 2: Distribution of BBD

Figure 3: Laterality of BBD in the study group

When we compared the age-wise distribution for different benign breast diseases, we found out that fibroadenoma was the most common presentation in the age group of 21-30 years (35 cases), followed by t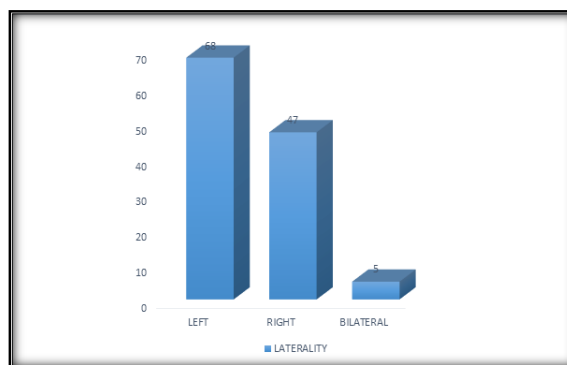he age group of 15-20 years (19 cases) and 31-40 years (11 cases). Phylloids were most common in the age group of 41-50 years (8 cases) followed by 31-40 years (7 cases) and 21-30 years of age (5 cases) [Table no. 1] denotes the clinical presentation of BBD with the age-wise distribution.

Table 1: Clinical presentation of BBD with age-wise distribution

Clinical Presentation	Age-wise distribution						
	<15 years	15-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years
FA	1	19	35	11	8	0	
FCD	1	4	0	6	2	0	
PHYLLODES	1	1	5	7	8	1	
BA		2	3	1		1	1
TA			1	1		0	
EPITHELIOSIS						0	

During the study, we evaluated the chief complaints stated by the patients, which revealed that 66 patients were found with lumps associated with pain and 54 cases were found to have just lump mass during the inspection. The data significantly revealed that lump and pain were predominantly seen in FCD and phyllodes patients study group whereas, a painless lump was only seen in patients with fibroadenoma and tubular adenoma. The study assessed the clinical symptoms with respect to different duration ranging from 1-6 months (60%), out of the 72 cases, 56 cases were diagnosed with fibroadenoma. The assessment of symptoms was conducted as; 8 cases for less than a month, and 9 cases for 7-12 months of duration [Table no. 2] portrays the overall assessment for different benign breast diseases.

Table 2: Assessment of clinical symptoms with respect to duration

Duration of months	FA	FCD	Phyllodes	TA	Breast abscess	Epitheliosis	Total	%
<1 month	8	3	4	4	5	0	24	20
1-6 month	56	7	8	0	0	1	72	60
7 - 12 month	9	2	4	1	0	0	16	13.3
> 12 month	6	1	1	0	0	0	8	6.7
Total	79	13	17	5	5	1	120	100.0

24 cases were evaluated to study the symptom for a period of less than a month where; 3 cases were detected as FCD, 4 were diagnosed with phyllodes, 4 patients were seen with tubular adenoma and 5 cases of breast abscess were observed. In the 9 observed cases of fibroadenoma, a significant family history correlation of breast lesions among the family members was found. 7 cases of such patients provided a history of breast lesions for their siblings whereas, 2 cases reported a history of lesions in the mother. 4 cases of fibroadenoma patients reported a history of operative breast lump surgery, and all of these individuals presented prior with a lump in their contralateral breast. The relapse of BBD was seen in 4 cases, where two reported the relapse of fibroadenomas and the other two were phyllodes. Inconsistencies of the menstrual cycle were seen in a few patients, where BBD was most found in postmenopausal women. A rare case was observed during the study which included the diagnosis of phyllodes in a 13-year-old female, without reaching the menarche. A majority of the patients diagnosed with BBD were seen after the birth of the second child. The use of oral contraceptives was observed in 9 cases of BBD. We observe a total of 8 confirmed cases of BBD who were in their menopause. The study also found that patients with BBD were incorporating a mixed diet 94.5% into their schedule and 5.5% were seen with a vegetarian diet. The prevalence of benign breast disease was

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more prevalent on the left side breast; comprising 68 cases (56.6%) when compared with right-sided 47 cases (39.2%). The study only observed 5 patients with bilateral involvement of the breast (4.2%). [Figure no. 3] denotes the laterality of distribution of the studies groups with BBD.

The most common size of the lesion was found to be between 2-5cms in 80 patients with different clinical conditions of BBD. A total of 35 patients were seen with lesions more than 5 cm. Fibroadenoma was found in a total of 79 cases out of which 62 cases were seen with breast lesion sizes between 2-5 cm

and 14 cases with lesion dimensions of more than 5 cm. Phyllodes were observed for a total of 17 patients out of which 13 phyllodes were more than the size of 5 cm and 4 were in the range of 2-5 cm. The study assessed the clinical correlation of patients with fibroadenoma by using the histopathological examination (HPE). The HPE revealed a positive correlation for 74 patients with fibroadenoma and 18 patients who had fibroadenoma without a significant correlation with HPE. Table no 3 shows the comparison of clinical diagnosis with HPE in fibroadenoma.

Table 3: Comparison of clinical diagnosis with HPE in fibroadenoma

Clinical Diagnosis	Fibroadenoma as H/P/E	Fibroadenoma as Not H/P/E	Total
Positive	74	18	92
Negative	5	23	28
Total	79	41	120
Septic Shock	16	30.8	0
Total	52	100	48

The fibroadenoma assessment with correlation as H/P/E was conducted with a sensitivity of 93.67% and specificity of 56.10%. A positive predictive value of 80.43% and a negative value of 82.14% were observed. The correlation of consistency with respect to FA with HPE and FNAC was evaluated during the study which revealed a positive consistent result for 72 patients and inconsistent result for 17 patients. Table no 4 denotes the overall comparison of FNAC in consistent with H/P/E.

Table 4: Comparison of FNAC in consistent with H/P/E

FNAC	Consistent with FA In H/P/E	Inconsistent with FA in H/P/E	Total
Positive	72	17	89
Negative	7	24	31
Total	79	41	120

Sensitivity: 91.14%, Specificity: 58.54%, Positive predictive value: 80.90% and Negative predictive value: 77.42%. A majority of the patients with BBD were treated with the excision method for FA (79 cases), FCD (13 cases), and phyllodes (11 cases). The other most used method was the wide local excision adapted for phyllodes (5 cases) and tubular adenoma (2 cases). Mastectomy was only performed on one patient diagnosed with phyllodes. Incision and drainage were most commonly used in the case of a breast abscess (5 cases). Table 5 denotes the overall use of different surgical methods adapted for the treatment of BBD.

Table 4: Surgical method adapted for treating BBD

Disease	Excision	WLE	Mastectomy	I & D	Total
FA	79	-	-	-	79
FCD	13	-	-	-	13
Phyllodes	11	5	1	-	17
Breast abscess	-	-	-	5	5
Tubular adenoma	3	2	-	-	5
Epitheliosis	1	-	-	-	1
Total	107	7	1	5	120

In the group of phyllodes, benign tumors were observed in 5 cases, followed by 6 low-grade cases, with two intermediate-grade cases, and 3 on borderline. Only one case of high-grade observation was detected. The study also found that 3 cases were detected with fibroadenoma with a focal duct epitheliosis. In addition, fibroadenoma with FCD was reported in a single case of a 39-year-old female. Another addition of rare case of benign phyllodes was recorded in a 13-year-old-female who did not reach her menarche.

DISCUSSION

The study evaluated a total of 120 patients with BBD for 18 months to assess the different clinicopathological aspects. Women presenting with breast complaints, especially with painless lumps or lumps associated with pain are often seen with

anxiety. It is imperative to distinguish such conditions from malignancy or benign tumors as they can lead to morbidity or mortality if not treated adequately. In the present study out of 120 cases, fibroadenoma was the most prevalent disease accounting for 65.8% of the patients. This observation was similar to the other studies conducted for BBD.[7,8] The study conducted by

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Sandhya et.al has shown that fibroadenoma was more prevalent accounting for 21 cases out of 60 (35%), followed by fibrocystic disease comprising 17 cases (28.33%).[7] Age can be one of the potent indicators for detecting the underlying etiology of breast lump or mass, as per the study findings by Annelie et.al, data of 61 617 women revealed that fibroadenoma was one of the most common forms of BBD among younger ages (45 per 100 000 persons at the age of 25 years) with an increasing prevalence during the age range of 30-40 years (81 per 100 000 person-years at the age of 40).[1] In the present study, most of the patients were in their active reproductive period (20-40 years) which has seen most of the breast-related complaints. However, the occurrence of BBD has also been seen in patients who have reached menopause (present study 8 cases). Hence, BBD occurrence can be seen across different age groups. The study conducted by Oluwole and Freeman has shown that BBD can be seen from the age of 10 years to 70 years of age. The incidence of BBD was more prevalent among 21-30 years (43%).[8] In the present study, we have also seen that most of the women between 21-30 years of age were more affected by BBD. The presenting study has shown that 45% of patients diagnosed with BBD with a presentation of painless lumps and 55% were seen with lump-associated pain, this study finding was similar to a study conducted by Forrest et.al which shows that 71% of patients with painless lump and was diagnosed with fibroadenoma and pain with lump was seen in FCD.[9] The study observed that 9 cases had a strong family history of BBD, which is not seen in a majority of the individuals. However, the study by Annelie et.al has revealed that premenopausal women with a family history are present with a higher risk of benign breast disease. The use of oral contraceptives was seen in 9 cases of BBD, several studies have suggested a risk associated with the use of oral contraceptives. The prevalence of fibroadenoma is much higher in patients with the use of oral contraceptives.[1] In the present study, irregularity of the menstrual cycle was only seen in a few cases, hence there are inconclusive results and the relation is yet to be established. The prevalence of BBD was much higher in women after their second childbirth, which results in a significantly higher risk of FCD. In lactating females, the most common complaints were breast abscesses. In addition, 8 cases were diagnosed with menopause, which can indicate that BBD is not limited to premenopausal women. The current study observed a higher prevalence of left-side breast involvement for BBD, there was no significant correlation for such unilateral association in females. Bilateral involvement was reported in 5 cases. We also find that the upper and outer quadrants of the breast were the most common quadrant for BBD. This data was correlated with the other studies, which shows a consistent result in the study conducted by Oluwole

et.al., Figure 4 shows the comparison of quadrants in both the studies.[8]
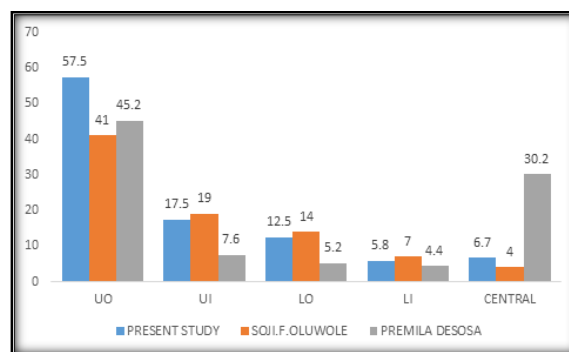

Figure 3: Comparison of BBD among quadrants in two studies.[8,10]

A majority of the studies have shown the involvement of specific quadrants for BBD, which can be due to the proportion of breast tissues in the respective quadrants. However, this correlation can also be seen in similarly in malignant tumors. The current study revealed that a majority of breast lesions were in the range of 2-5cm (66.7%) comprising their average overall size respectively from 2-10 cm. Literature has denoted that lesions can vary from 1 cm to 10 cm, depending on the clinical condition, whereas fibroadenoma is generally in the range of 2-5 cm.[8] The size of the lesion can be correlated with the type of BBD, clinical diagnosis has suggested that a larger size of the lesion is mostly associated with phyllodes. However, a size larger than 5 cm can be related to fibroadenoma of the breast. In the present study, all the patients were managed surgically with excision biopsy was the most common method used to treat fibroadenoma, fibrocystic disease, and tubular adenomas. In addition, the method varied depending on the size of the lesions. Wide local excision was adapted for phyllodes tumor and mastectomy for recurrent phyllodes. The breast abscess was treated by using the incision and drainage method. The positive predictive value of diagnostic methods can be enhanced to improve the accuracy of detecting undiagnosed cases, for preventing complications that can arise due to the tumor.

CONCLUSION

Fibroadenoma was one of the most common types of BBD followed by phyllodes. Based on the study, the Indian population is seen with a higher case of fibroadenoma and fibrocystic disease. A high prevalence of fibroadenoma is seen in the age of 20-30 years, which is the highest risk age for BBD. However, the data suggest that BBD can occur at any given age depending on the risk factors associated with an individual. Literature has suggested that the use of oral contraceptives can denote a higher risk of BBD but no such significant observations were found in the study. Benign breast

disease is one of the silent underlying conditions, which cannot be diagnosed until a physical examination or without the occurrence of symptoms. Patients with such benign tumors are always anxious about the condition of malignancy, hence we have seen an awareness of diagnosis among the patients. Due to socio-economic conditions, there is a delay in the follow-up of patients which is one of the limitations to receiving the appropriate management. The ideal management of such tumors is surgical removal, which enabled quick relief among patients without raising future complications.

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