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Community Medicine

BENIGN BREAST DISEASE: A COMMUNITY BASED COHORT STUDY

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ABSTRACT
Background: Benign breast diseases, in spite being more common and frequent than breast malignancy, is not accorded due importance in comparison to malignancy. Benign breast lesions in majority are symptomatic, though at times they are detected incidentally as part of screening programs for breast cancer. The management of benign breast disease includes detailed clinical history, complete breast examination, radiological, and if necessary histological diagnostic investigations to rule out malignancy; palliation of symptoms; treatment and counseling and monitoring of patients at increased risk of breast cancer. Investigations to rule out a malignancy and reassurance is very important apart from treatment. There is a paucity of studies from India, on Benign Breast diseases. The present study is an analysis of benign breast disease occurring in a closed community.
Methods: This is a prospective analysis of a retrospectively maintained data. Data of patients presenting with (BBD) were retrieved during the period from June 2013 to December 2015. Clinical Breast Examination (CBE) was performed in all, with subsequent breast imaging and cytology if required, followed by appropriate treatment. They were all followed up based on risk stratification for malignancy until January 2020.
Result: Of a total of 3033 cases presenting to us, 2972 patients were analyzed for benign breast disease. Of these 964 (32.44%) of the women with benign breast disease were symptomatic. Breast lump was the presenting complaint in 11.8 %. CBE was suggestive of benign breast findings in 33%. Breast imaging revealed benign findings in 20.7%. Both imaging and cytology (FNAC) revealed that Fibrocystic changes was the commonest lesion, followed by fibroadenoma. Clinical and radiological follow up of the benign lesions showed no progression of the lesion to malignancy. Though 5 cases developed malignancy, they were in another area of the breast, not related to benign lesions.
Conclusion: Benign breast disease is common. Most of them are symptomatic. Imaging and cytology provide conclusive diagnosis. The lesions are not precursors of malignancy.

INTRODUCTION

Any breast changes in a women is a cause of anxiety due to the possibility of it being a malignancy, Although breast cancer is detected in only 3% to 6 % of women with clinical symptoms, and in most cases the cause of the symptoms is benign, there is no evidence-based recommendations for the management of benign disease . This is primarily due to the focus of clinicians being on the diagnosis and treatment of breast cancer [1]. Benign breast diseases (BBD) include a wide and heterogeneous spectrum of non-malignant lesions [2], ranging from disorders of development, inflammatory lesions, proliferative diseases of the epithelium and stroma to different types of neoplasms. [3] Although there is literature evidence of community-based studies on BBD from west [4] which review common benign breast diseases stratified by future risk of breast cancer, the same from low- and middle-income countries (LMIC) is sparse [5]. The present study is a spectrum of benign breast disease occurring in an urban community from Mumbai.

MATERIAL AND METHODS:

This is a prospective analysis of a retrospectively maintained data. Data of patients presenting with (BBD) were retrieved during the period from June 2013 to December 2015. A prior institutional ethics committee approval was obtained (Ref no. BHMEC/06/2015 dated 23/6/2016).This study has been conducted in the setting of an 'awareness and clinical breast examination (CBE) based breast cancer screening program', conducted in a community covered under universal healthcare for about 100000 population in suburban Mumbai. All symptomatic as well as asymptomatic women who underwent CBE as part of the early detection program were included in the study. The clinical, imaging, pathology and treatment records were retrieved from Electronic Medical Records (EMRs) using Gail model [6] for risk stratification. A thorough medical history of all patients included in the study was taken, and they were subjected to complete breast examination. Women with positive CBE and/or presence of high-risk factor for development of breast cancer were referred to

specialty clinic, where a surgeon experienced in CBE examined all the referrals and decided regarding the need for triple testing based on clinical findings as well as risk factors. Breast ultrasound was the imaging modality of choice for symptomatic women less than 50 years of age. Mammography was performed for women above the age of 50 years or in asymptomatic women presenting with high risk factors for breast cancer. Reporting and Data system (BI-RADS) classification for reporting the imaging findings was used [7,8,9]. Triple assessment was completed with cytology of nipple discharge and FNAC of palpable breast lumps. The FNA breast report was categorized with the IAC breast group 5 stage system, Yokohama System [10] for reporting breast cytopathology into general categories C1 to C5 with an implicit probability/ risk of malignancy. Fibrocystic change in the benign category was divided into non-proliferative lesions and proliferative lesions without atypia using the Masood's scoring index [11]. Risk stratification on histopathology of the excised lumps was done using histology classification of BBD into non-proliferative lesion, proliferative lesion and atypical hyperplasia [12].

All women with BBD were followed for a mean 5 years to detect any development of malignancy.

Statistical Analysis

Data extracted from Hospital information system (HIS) was summarized into Microsoft Excel for Windows, Version 2010 and further analyzed using SPSS Version 24.0 (SPSS Inc., Chicago, IL, USA). Variables under consideration were presented as frequency in absolute numbers as well as percentages of the total.

RESULTS

The community comprises of 85870 total population with 38942 post pubertal women. Of these, 3033 (10.20 %) women presented to the breast clinic as part of the early cancer detection program in the study period. 61 women (2.01%), who were diagnosed with malignancy in this period were excluded from final analysis. Thus, a data of

2972women was analyzed. The demographic details of the patients analyzed is as shown in Table 1.

Table1. Demographic details of the women with the risk status
N=2972

Demographical details	No. of patients	Percentage (%)
Age distribution		
< 30	184	6%
30-39	614	21%
40-49	1079	36%
*50-59	694	23%
*60-70	345	12%
>70	56	2%
Menarche		
*<11	160	5.38%
>11	2812	94.61%
Parity		
*Nulliparous women	352	12%
Parous women	2620	88%
Age at 1st child		
<30	2150	82%
>30	470	18%
Lactational History		
Yes	2546	97%
*No	74	3%
Family h/o breast cancer		
*First degree relative with cancer of breast, uterus, ovary (ie mother, sister, daughter)	131	4.4%

* Refers to women in high risk group

As seen, the largest number of women presented were in 40-49 years age group (n=1079, 36.3%) followed by 50-59 years age group (n=694, 23.3%). 2008(67.6%) were clinically asymptomatic and had come to the breast clinic as part of the screening in the on-going breast awareness program. 964 women (32.4%) presented with breast related symptoms. Their presentation was varied as shown in Table 2.

Table 2: Clinical presentation of the women

Presentation	No of patients(n=2972)	Percentage (%)
Breast lump	352	11.84
Mastalgia	333	11.20
Nipple discharge	72	2.42
Multiple symptoms	207	6.94
Asymptomatic women	2008	67.6

Clinical breast examination (CBE) was performed in all 2972 women, and was found to be positive in 980 women (33%). Fibrocystic change was the commonest clinical diagnosis (13.4%), followed by fibroadenoma (5.4%) and inflammatory lesions. All women with a positive CBE and women in the high-risk category for developing cancer were subjected to breast imaging (n=1009).

Table 3. Results of Ultrasound Imaging

Diagnosis	Total No of women (n=1009)	Percentage(%)
Normal	395	39.14
Fibrocystic change	403	39.94
Fibroadenoma	139	13.77
Infections	36	3.56
Lipoma	02	0.19
Galactocele	15	1.48
Intraductal papilloma	02	0.19
Lymphadenopathy	04	0.39
Miscellaneous benign lesions	13	1.28

Table 3 summarizes the Ultrasound imaging findings. As seen, benign breast findings were seen in 614 women on ultrasound (20.7%) of which fibrocystic changes were commonest (65.63%) followed by fibroadenoma (22.63%). 428 women underwent mammography, of which 252 (58.87%) had benign beast findings corresponding to BI-RADS 2. Further, there were 162 women in BI-RADS 1 category and 3 in BI-RADS 3 category. There were 11 women in BI-RADS 4 category who on further assessment with FNAC and histopathology were found to have benign lesions. Following breast imaging, 139 women were

subjected to FNAC procedure, as a part of triple assessment. There were 19 cases in C1 category (Insufficient material), 116 cases in C2 category (Benign), 4 cases in C3 category (Atypical probably benign). The spectrum of benign lesions diagnosed on FNAC is shown in Table 4.

Table 4. Frequency of Specific Cytology Diagnosis of the 116 cases in C2 Category (Benign lesions) on FNAC

Broad Diagnostic Groups	Specific Cytology Diagnosis	No of cases (n=116)
Inflammatory lesions	Acute suppurative inflammation	06
	Granulomatous inflammation	03
Fibrocystic change	Cysts	12
	Non-proliferative	14
	Proliferative without atypia	36
	Duct ectasia	04
Neoplasms	Fibroadenoma	35
	Benign Phyllodes	03
	Lactating adenoma	01
	Lipoma	02

28 women underwent lumpectomy primarily to rule out malignancy, the histopathology details of whom are as given in Table 5.

Table 5 Categorization of BBD as defined by risk for subsequent development of carcinoma

Histology category	Relative risk*	Histopathology diagnosis	No of cases (n=28)	Cytology category
Non-proliferative or minimally proliferative lesions	1	Granulomatous mastitis	04	C2
		Duct ectasia	01	C2
		Simple Fibroadenoma	12	C2
Moderate or florid Proliferative lesions without atypia	1.5-2	Moderate or florid hyperplasia of usual type	03	C2
		Intraductal papilloma	02	C3
		Complex fibroadenoma	01	C3
		Phyllodes	04	C2
Atypical hyperplasia	5-10	Atypical ductal hyperplasia	01	C3

On correlating the FNAC-cytology and histopathological findings, there was 100% correlation with regard to specific cytology diagnosis, including the 4 cases, categorized as C3 on FNAC also revealing benign lesions on histopathology. All women with BBD were followed up for a mean 4 years 6 months period with imaging to assess progression to cancer. 5 cases with BIRADS 2 lesions developed malignancy , though in another segment of the breast, and one of them developed synchronous breast cancer. However, the initial BIRADS 2 lesions in all remained stable. 3 women in BI-RADS 3 category were re-categorized as BI-RADS 2 category as, on follow up their lesions remained stable. None of the 36 cases identified as proliferative FCC on FNAC or the 11 cases on histopathology with high risk showed progression to malignancy.

* (Fitzgibbons et al., 1998)

DISCUSSION:
Benign breast diseases represent a wide spectrum of conditions ranging from includes a heterogeneous group of conditions which range from normal, to aberrations in normal development and involution (ANDI), epithelial and stromal proliferations, inflammatory lesions and benign neoplasms [13]. It is often a cause of much anxiety due to is presumption of malignancy, leading to its relatively early presentation in its clinical course. Interestingly, its incidence is 10 times more common than breast cancer in the western world [2]. In the present study too, of a total of 3033 women presenting to the breast clinic, only 61 (2.01%) were detected to have malignancy, the rest being Benign Breast disease. Though it can occur beginning from 2nd decade, its peak incidence is in the 4th and 5th decade [2]. In our study, 36% of cases were in the 4th decade (40-49 years). Besides, there are studies in literature reporting varying period of peak incidence

between 21-40 years [14] and 11-30 years [15]. Majority of patients of BBD are asymptomatic, it being 67.6% in the present study. Most present to allay their anxiety of malignancy and as in our study due to ongoing breast screening program. This fact that most of them are asymptomatic, corroborates with the available literature evidence, as reported by Janaki et al [16] and Krishnaswamy [17] in their study. Amongst the symptomatic group breast lump (11.84%) and mastalgia (11.2.%) were the common presenting complaints in our study. Choudhary et al [18], Mallikarjuna et al [19] and Sagar et al [20] too have reported breast lump as the predominant presenting complaint in their studies. In a study by Karki et al [21] mastalgia was the main presenting complaint. As per our protocol, all patients presenting to the breast clinic, irrespective of the symptomatology were subjected to complete breast examination (CBE), and this yielded positive findings in 33%.

Establishing the benign nature of the breast lesions and further characterizing the lesion is essential to provide optimal and correct treatment. Further a multidisciplinary approach in form of Triple assessment i.e. a combination of clinical examination, imaging and FNAC/ biopsy, leads to accurate diagnosis of the breast lesions [22]. In the present study, women with positive CBE and those with high-risk factors for development of breast cancer were referred to specialty clinic where on clinical examination by a surgeon, a decision was made for the need of further need for triple testing. Breast ultrasound was performed on all symptomatic women less than 50 years age, whereas Mammography was performed for symptomatic women above the age of 50 and on those with high risk factors for breast cancer. The importance of breast ultrasound has been proved beyond doubt in the literature. Way back in 1995, Stavros et al [23] demonstrated characterization of solid breast lesions as benign or malignant lesions using high resolution gray-scale ultrasound imaging. Hooley et al [24] have described breast ultrasound as a preferred and important modality for breast imaging which complements both mammography and breast MRI. Joshi et al [25], have observed improvement in the diagnostic confidence and lesion characterization, following supplemental breast ultrasound. In our study mammography was done only in 29.2% women revealing BIRADS 2 category in 58.87 %. The reason for fewer mammography being done, was the fact that in our study 57.3% women were less than 50 years of age, a population which has mammographically dense breast parenchyma, decreasing its sensitivity.

Further, triple assessment was completed with cytology of nipple discharge and FNAC of palpable breast lumps.139 women underwent FNAC in our study, of whom 116 were diagnosed to be in benign category (C2). Treatment of benign lesions varies, hence a specific diagnosis based on cytomorphology is essential to institute an appropriate treatment. A varied diagnostic accuracy rates have been reported in literature. In a study by Maygarden et al [26], on sub-classification of benign breast disease by fine needle aspiration cytology, comparing cytological and histopathological findings in 265 palpable breast masses, found that overall, specific diagnosis was correct in only 80% of cases. Mendoza et al [27] stated that though various benign lesions could be easily diagnosed at FNAC; there were overlapping features with malignant lesions. In our study, histopathology correlation was available in only 28 cases, and all C2 cases were confirmed to be benign.

In our study, Fibrocystic change (FCC) was the commonest lesion, seen in 39.94% of patients. FCC includes combination of small or large cysts, apocrine metaplasia, focal fibrosis, adenosis and ductal hyperplasia. FCC with ductular cells on cytology were further subdivided into proliferative and non-proliferative using the Masood [11] scoring index for risk stratification and appropriate management. Fibroadenomas were the commonest benign neoplastic lesion with 35 cases in our study. The FNAC had 100% co-relation with histology in all the 13 cases which underwent excision. This was contrary to the study of Lopez-Ferrer et al [28] who reported sensitivity of the cytological diagnosis of fibroadenoma to be 86.9% with positive predictive value of 79.3%. The importance of FNAC is underlined by the fact that, we had 3 cases of Benign Phyllodes tumor diagnosed pre-operatively on FNAC. This helped us to plan surgical treatment as unlike fibroadenomas, phyllodes tumor requires excision with wide margin, as it is although being benign, is locally malignant. Besides it also overcame the need of doing diagnostic biopsy in 116 women. FNAC in the grey zone categories (C3&C4) further, provides risk assessment for malignancy. A lesion in C3 category should be considered for histopathological evaluation, because the morphological features of well- differentiated invasive and in situ carcinoma overlap with those

of benign entities on cytology [29]. In our study all the 4 cases of C3 category (atypical probably benign) were excised, and all were histologically proved benign lesions.

As per the recommendations of a consensus group sponsored by the College of American Pathologists, benign breast disease has been stratified into 3 categories based on the risk for subsequent development of carcinoma[12]. The lesions without significant increase in relative risk of cancer were non-proliferative or minimally proliferative, lesions associated with slightly increased relative risk (1.5 to 2 times) were with moderate to florid degrees of hyperplasia without atypia and the high-risk category (5 to 10 times) comprises all atypical hyperplasia. Worsham et al[30] and Krieger et al [31], too in their studies have reported similar risk of malignancy. In our study, none of the cases identified on FNAC or histology with or without proliferation and with or without atypia progressed to malignancy on follow-up where the patient was assessed both clinically and even on imaging. Follow up was done for all BIRADS 3 lesions and 3 of these cases which remained stable were re-categorized as BIRADS 2, similar to the results in the study of Sickle et al [32].5 women in our cohort in BIRADS 2 category developed malignancy. However, it is important to note that the benign lesions in these 5 women diagnosed initially on imaging, remained unchanged on follow up and cancers were detected in another segment of the breast, with one of them developing synchronous breast cancer. Interestingly, all these 5 women had family history of malignancy in 1st degree relative, family history being an independent risk factor as shown by Hartmann et al [33]. None of our lesions diagnosed as benign, developed malignancy irrespective of the cytological categorization of proliferative with atypia and proliferative lesions without atypia.

CONCLUSIONS:
Based on our present study we conclude that benign breast conditions are more common than breast cancer in the community. Breast lump is the commonest presentation followed by mastalgia. Among the benign breast lumps fibrocystic changes is the commonest. Triple assessment comprising of CBE, imaging and FNAC provides accurate. Follow-up of these patients based on risk stratification is important for early detection of progression to malignancy.

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