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Clinicopathological study of benign breast disease and special reference to treatment regime : A prospective study

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ABSTRACT
Benign Breast Disease includes heterogeneous group of lesions that constitutes developmental abnormalities, inflammatory lesion, epithelial and stromal proliferations and neoplasm . However incidences of Benign Breast Disease rise in second decade of life and peak in fourth and fifth decade of life while in malignant condition incidence continues to increase after the menopause. Fibroadenoma, fibrocystic disease and breast abscess have common incidence of benign breast disease whereas the commonest age group of patients 21 to 30 years while fibroadenoma more common in 10 to 20 year age group of patient in BBD although painless lump were most common symptom of the disease. However excision, incision & drainage were commonly performed surgical procedure for this study. while the sensitivity of clinical examination of Benign Breast Disease were 89.18%, 100% and 86.66% for fibroadenoma, fibro cystic disease and breast abscess respectively
Key Words: Fibroadenoma, Benign Proliferative lesion, FIbrocystic Disease, BBD, ANDI,

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INTRODUCTION

The breast is highly modified sudoriferous gland that develops as ingrowths from ectoderm from the alveoli and ducts. Supporting vascularized connective tissue takes derivation solely from mesenchyme.
The breast is subjected to constant physical and physiological alterations that relate to menses, pregnancy, gestation and menopause for every woman from puberty to death.[1]
The term "Benign breast diseases" encompasses a heterogenous group of lesions that constitute developmental abnormalities, inflammatory lesions, epithelial and stromal proliferation and neoplasms. It's present with wide range of symptoms or may be detected as incidental microscopic finding. While incidence of Benign breast disease rise in 2nd decade of life and have a peak in fourth and fifth decade of life while in malignant condition incidence continue increase after the menopause.[2]
According to classification of benign breast diseases which are based on aberration of normal development and involution (ANDI) lead to confusion and lack of clarity between normal physiological and pathological changes. However more satisfying classification would be coined by Love S et al[3] proposed as Nashville classification which divided into two category: pathological BBDs and clinical BBDs.
Pathological BBDs further divided into
1. Non proliferative lesions with atypia or without atypia.
2. Proliferative lesions with atypical lesion or without atypical lesion.
While clinical BBD is classified according to their clinical symptoms like swelling, tenderness, nodularity, breast pain, palpable lump, nipple discharge and infection or inflammation.
Benign breast disease need attention because their high prevalence in premenopausal age and impact on women life due to cancerous potential of some histological type.[4-6] Hence awareness and terminologies of benign breast disease and malignancy must be clear in general population and physician. So, histopathology play an important role for diagnosis and management.
However the aims of this study was to know the incidence rate, various presentation and their treatment or various surgical intervention performed in BBD.

MATERIAL AND METHODS

It was descriptive and prospective study which were conducted in outpatient or indoor patients who were admitted in J.A. Group of Hospitals and Gajraraja Medical College, Gwalior over three years periods

(2016-2019) which includes 118 patients of female BBD and consent taken prior to enrollment of the study and also ethical clearance was taken by the institutional ethical committee as per their guidelines.

Inclusion criteria: Female patients with age group of 10 years to 65 years of women and negative history of breast carcinoma in their family .

Exclusion criteria:

1. Male benign breast diseases
2. Positive history of carcinoma of breast in their Family
3. Women with obvious malignant diseases and who have been treated for malignancy.

118 cases of breast lesion were studied in detailed with relation to clinical and pathological data.

A detailed clinical data (like age of patient, age of menarche, age of menopause, duration of lump, size of lump, consistency etc.) and physical examination were noted as per proforma. After that we made a clinical diagnosis with the help of physical examination and by using one or more of this special investigations – like FNAC/core needle biopsy, USG/mammography were carried out for confirmation of the diagnosis all routine investigation had been done for all patients for excision biopsy/lumpectomy/ mastectomy.

While the FNAC, cytology smear and histopathology were diagnosed according to standardized criteria. They were categorized into nonproliferative/proliferative with atypia without atypia /carcinoma in situ.

The clinical diagnosis was compared with cytological diagnosis or histological finding and sensitivity, specificity, positive predictive value, negative predictive value and accuracy were evaluated in it.

Data analysis were done by SPSS software

RESULT

A total 118 cases from Surgery out patients department for breast disease were studied in the Department of General Surgery. The patients were broadly divided into different category Benign breast symptoms like breast lump, pain, nipple discharge and axillary lump.

The commonest presentation was breast lump found in 80 cases (68.0%) all lump were painless with distinct border while among the 38 cases in which 10case (5.885) were present as symptoms of breast pain (Mastalgia) associated with menses while 9 (5.88) case has indistinct lump with pain,

However, 16 cases (13.45%) lump were found with symptoms of breast lump ,pain & nipple discharge they were having elicited tenderness & fluctuation which is associated with fever.

whereas various different single presentation were revealed as nipple discharge and pain, Bilateral axillary lump and periareolar infected cyst.

Table 1 : Incidence of benign breast disease according to clinical breast examination in different age group

Types of lesion	Age groups (No. of patients)					Total	%age
	10-20	21-30	31-40	41-50	Above 51		
Fibroadenoma	32	25	11	5	3	76	64.4
Fibroadenosis Fibrocystic breast disease	1	6	5	6	1	19	16.10
Breast abscess	2	10	3	0	1	16	13.55
Phylloid tumor	0	1	0	3	0	4	3.38
Montagmery cyst (infected)	0	1	0	0	0	1	0.84
Bilatral axillary accessory breast	1	_	_	_	_	1	0.84
Nipple discharge	_	_	_	1	-	1	0.84
Total	36	43	19	15	5	118	100

Table 2:The different type of clinical presentation and their incidence

Presentation/Symptoms	No. of case	Percentage
Painless lump	80	68.07
Breast pain	10	5.88
Indistinct lump + pain	9	5.88
Pain + Swelling + nipple discharge	16	13.45
Nipple discharge + pain	1	0.84
Bilateral axillary lump	1	0.84
Periareolar infected swelling	1	0.87
Total	118	100

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The age distribution of cases with BBD ranged from 10 years to 65 years while average was 28.5 year and 21-30 age group of cases were having maximum 43 cases (36.44%) of BBD in this study while common

incidence of fibroadenomaa 21-30 age group of cases were as commonest 43 cases (36.44) of benign breast disease found in this study. While common incidence of fibroadenoma were 32 cases found in 10-20 years of age group of patients however painless lump or fibroadenoma 76 cases [64.4%] as common lesions in this study benign breast lesion were affected 71 cases (60,66%) in married women while 47 case(47%) affected in unmarried women and 86 case (72.38) affected in premenopausal women.
Out of 118 case, 76cases [76.64%] fibroadenoma, 19 cases (16.10%),fibrocystic changes or fibroadenosis &16 cases (13.65) breast abscess were the commonest benign breast disease revealed in the study.
Among the 76(63.3%) of fibroadenoma all were painless and average size of tumor was 2.25 cm. In which it includes 1 case of giant fibroadenoma (5 cm), 7 patients of bilateral fibroadenoma and 5 cases of multiple fibroadenoma .These mainly affected in upper and outer quadrant of the breast in the study while 1 case was of recurrent fibroadenoma and its FNAC was positive for phylloid tumor with mild atypia.
Benign breast lesion were affecting left side in 57case (48.31%), 48 case (44.6) right side and bilateral in13 case (11.02%). In this study only 6 cases were having family history of BBD in grade one family member. Mean age of menarche was 14.14 years.

Table 3 : Incidence of benign breast disease according to their side involvement

Breast disease	Right side	Left side	Bilateral side	Total	%
Fibroadenoma	29	40	7	76	63.03
Fibrocystic breast disease/ Fibroadenosis	9	6	4	19	7.56
Breast abscess	8	8	0	16	13.45
Phylloid tumor	1	3	0	4	4.20
Montgomery cyst	1	0	0	1	0.84
Bilateral axillary accessory breast	0	0	0	1	0.84
Nipple discharge	0	0	0	1	0.84

Out of 118 cases in this series of BBD found 19 cases of fibrocystic disease or fibroadenosis so it was a second common incidence and 16 cases of breast abscess were third common incidence found in the study. Among the 16 patients of breast abscess, 10 patients found to be at the age group of 21-30 years. All were lactating mother except one patient who had postpuperal period and her delivered still born baby 1 month before presentation, clinically she was diagnosed as breast abscess but her FNAC and USG breast show breast abscess associated with phylloid tumor. So we planned for incision and drainage and wide excision of tumor later it was planned for definitive (simple mastectomy) surgery.
However, 4 cases of phylloid tumor found in which 1 case had recurrent phylloid tumor although one case each of lactational adenoma and Montgomery cyst, nipple discharge and bilateral accessory axillary breast lump were also found in the study.
Two breast lump which were clinically diagnosed fibrocystic disease but their FNAC and histopathological examination differed from its excision biopsy which revealed infiltrating ductal carcinoma and ductal cell carcinoma while one lump was clinically diagnosed as fibroadenoma and its histopathology report revealed ductal cell carcinoma.
one breast lump was also differed from FNAC while their histopathological examination revealed tubercular granuloma but in past she was not having history of tuberculosis .

Clinical and histocytological correlations:

The diagnosis of lump were confirmed either by Cytology or histopathological examination or in both way for 118 cases through FNAC & Biopsy except 11 cases of fibroadenosis without nodularity which were associated with cyclical mastalgia .Hence FNAC was not done & their USG breast was normal.
In this study, we have compared clinical diagnosis with FNA cytology for this F.N,A.C has gold standard test whereas when we compared with histopathological diagnosis biopsy was gold standard test for the statistically evaluation (Table-4).

Table no. 4: Shows statistical analysis of clinical diagnosis

Disease	Measures				
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Fibroadenoma	**89.18**	**100**	**100**	**20**	**89.47**
Fibrocystic Disease	**100**	**100**	**90.9**	**100**	**90.90**
Breast bscess	**86.66**	**100**	**100**	**100**	**87.6**
Phylloides tumor	**100**	**100**	**100**	**100**	**100**

Through the clinical examination 66 cases was correctly diagnosed as fibroadenoma & their clinical sensitivity & specificity were 89.18%,100%respectively while PPV& NPV were 100% & 20% respectively in BBD cases whereas accuracy was 89.47.while 10 cases were correctly diagnosed as fibrocystic disease by clinical examination & their sensitivity ,specificity, PPV& NPV had 100%.100%,90.9% & 100% respectively in BBD cases accuracy was 90.90%.

Although clinical sensitivity of breast abscess 86.66%,specificity 100%, &PPV ,NPV were 100%each,while accuracy was 87.6% in BBD cases.

Whereas in phylloides tumor their clinical sensitivity & specificity 100% each this observation may be due to less number of cases in this group

Table 5: Statistical analysis of Histopathology Diagnosis in BBD cases
(Biopsy is Gold Standard Test)

Disease	Measures				
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Fibroadenoma	**95.94**	**50**	**98.6**	**25**	**94.73**
Fibrocystic Disease	**77.77**	**100**	**100**	**100**	**77.77**
Breast bscess	**86.66**	**100**	**100**	**100**	**100**
Phylloides tumor	**100**	**100**	**100**	**100**	**100**

We also compared FNAC with Histopathological report and found out sensitivity and specificity which was 95.94% and 50% respectively in fibroadenoma, while sensitivity and specificity was 77.7%, 100% respectively in fibrocystic disease whereas overall clinical sensitivity was 94.94% and specificity was 83.3% and accuracy was 94.28% in BBD cases

The majority of patient underwent for surgical treatment of which excision was most common surgical procedure performed.

76 cases, out of 118 patients undergoes excision followed by incision and drainage (16 cases), 11 patients were treated conservatively with reassurance, analgesics and antibiotics while 9 cases were undergoes lumpectomy, 4 cases for simple mastectomy and 2 cases were performed wide excision. One case underwent for microdectomy as a surgical procedure [Table 6].

Table 6 : Distribution of patients according to surgical procedure performed (n=118)

Types of surgical procedure performed	No. of patients	Percentage
Excision	76	63.55
Incision and drainage	16	13.55
Lumpectomy	9	7.62
Systematic/conservative	11	9.32
Simple mastectomy	4	3.38
Miscellaneous	2	1.69

DISCUSSION

Globally benign lesion of breast are the most common lesions which account for 90% of the clinical presentation on related to breast. Histopathologically it is heterogenous group of lesion while clinically present with combination of these complaints like breast pain, breast lump, breast lump with pain and nipple discharge. Therefore we proposed that any discrete breast lump should be screened by the triple assessment to make an early diagnosis. By this prospective, we have attempted to diagnosis of benign breast disease within 72 hrs of the first consultation.

In several studies and the present study revealed that fibroadenoma was common benign proliferative lesion found in premenopausal women [5, 6].

It may occur an oestrogen has influence on proliferation of breast lesion. So, normal proliferation of cells occur due to action of endogenous steroid, hormones that leads to breast enlargement seen at puberty and reproductive period [7]. However, oestrogen helps in elongation and proliferation of ductal tissue whereas progesterone help in lobuloalveolar development in every month during each menstrual cycle and 15% increase of breast size in premenopausal age while number of lobule decrease at menopause [8].Oestrogen has a intracellular receptor that mediate a cascade of genetic process that consequently result of protein synthesis oestrogen is physiologically affecting cell proliferation and differentiation during cell cycle.

Possibly in benign breast disease this steroid hormone antagonized cell differentiation and apoptosis[9-10]. So, due to impairment of this process lead to development of fibrocystic changes in breast that eventually present as breast lump [10, 11].

So fibroadenoma is more common benign proliferative lesion of the breast which was 63.3% that has consistent with finding of other authors like Yogalakshmi *et al* 45%, Kapoor *et al* 53.3%, Kumar et al 46.66% and Samal S et al 55% [5, 12, 13, 16].

However, the proliferation of cells that lead to formation of lump which are painless process until and unless if it has involved any intercurrent pathology such as milk stasis, infection of the lactiferous ducts, trauma and pressure effect occurred in blood vessels and nerves.

In this study, we have account the common incidence of benign breast disease revealed as fibroadenoma (63.3%) followed by fibrocystic change (7.56%) and breast abscess (13.4%) which are similar to same sequence of several other authors' studies [14-16].

We also found that common presentation of benign breast disease were painless lump which are similar to other authors' studies [4, 12, 13].

we also found that upper and outer quadrant (45%) commonly involved in fibroadenoma which was accordance to other literature [12, 13, 17] while BBD has affected more commonly on left side in this study as compared to other studies. whereas other Author results was affecting right side, but Shashikala *et al* [18] their result accordance with present study.

In our study clinical sensitivity and specificity of fibroadenoma were 89.18%, 100% respectively while PPV and NPV were 100% and 20% respectively. These result has accordance with the study by Bhavuk *et al* they found 87.5% sensitivity and 92.8 % specificity for clinical diagnosis while they had found PPV 93.3% and NPV 86.6% respectively [19] also in accordance with other author results 92 % and 95.4% of fibroadenoma [20, 21].

However sensitivity of fibrocystic disease was 100% whereas specificity found was 100% while PPV and NPV was90.9%, 100% respectively which was accordance with other author's study in which they found sensitivity was 100% .[18]

In our study we also found out clinical sensitivity and specificity for breast abscess which was 86.6% and 100% respectively while other author's result were 100% for each case. Although specificity and sensitivity of phylloides tumour was 100% each case which was accordance with the other study [19,11].

In the study we compare sensitivity and specificity as compared to hisotpathology which was 90.5% and 50% for fibroadenoma while 77.7% and 100% for fibrocystic disease but in accordance to Bhavuk Kapoor *et al* result shows 100% while Jabbo NS shows that sensitivity of FNAC was 85% and specificity was 95% [19, 27] So it concludes that FNAC is an excellent method for diagnosis of breast lesion according to Abdel-Hadi *et al* 2010 [28] but a study conducted in Verona(1999-2004) screening programme for breast cancer they advised open biopsy in benign breast lesion because some time benign proliferative lesion(pre-malignant condition) have been undiagnosed [22] hence open biopsy will reduce the mortality and this lesion need to be counted separately for future evaluations. Overall clinical sensitivity and specificity in this study was 94.94% and 83.3% respectively whereas other author's had a sensitivity and specificity reading of 90% and 98% respectively [19, 21]. The overall accuracy was 94.28% in our study which were accordance with other various studies the readings seen were 88%, 86.7%, 91.3% and 85% respectively [23-25].

CONCLUSION

Globally, benign breast disease is a common problem in premenopasual women. This may be due to endogenous steroid hormone which increase antagonized cell differentiation and apoptosis. So, due to failure of this process lead to BBD or it may be responsible for conversion of breast cancer in this age group. Hence, we have proposed in future molecular diagnostic tools which detect pathogenic events at genomic level in early phase and will reduce morbidity or prevention by chemoprophylaxis in sporadic cancer.

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Abbreviations: (BBD: Benign Breast Disease) , (ANDI: Aberration of Normal Development and Involution) (PPV: Positive Predictive Value); (NPV: Negative Predictive Value) ; (FNAC: Fine Needle Aspration cytology)

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