

Prevalence of benign proliferative breast lumps among females with benign breast diseases in Sohag governorate

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Background: *Benign breast disease is an important risk factor for a later breast cancer, which can develop in either breast. It includes a spectrum of histologic entities, usually subdivided into non-proliferative lesions, proliferative lesions without atypia, and atypical hyperplasia, with an increased risk of breast cancer associated with proliferative or atypical lesions.*

Aim: *To estimate the prevalence of benign proliferative breast lumps that carry a risk of developing breast cancer in Sohag governorate.*

Patients and methods: *This prospective study included 416 female patients presented to Breast Clinic with clinically palpable benign breast lump(s) at Sohag University Hospital; only 390 of them were enrolled in the study. All patients were subjected to thorough clinical examination, sono-mammography and fine needle aspiration cytology. Those who were pregnant or proved to be malignant were excluded. Data including use of contraceptives, Parity, menarche, menopausal status, family history of breast cancer were collected prospectively using a pre-test questionnaire in a face to face interview. All biopsies taken from the excised lumps were examined by three pathologists with experience in breast diseases.*

Results: *Of 416 females with clinically benign breast lump(s), only 390 were recruited in the study. The prevalence of BPBD was 78/390 (20%) while non BPBD was 312/390 (80%). BPBD with atypia was 24/390 (6.1%), while BPBD without atypia was 54/390 (13.8%). The commonest breast lesions were fibroadenoma, fibrocystic disease and duct ectasia (54.1%), (25.6%) and (5.6%) respectively.*

Conclusion: *Benign proliferative breast lumps are common among premenopausal women in Sohag governorate and a significant proportion of BPBD had atypical proliferation.*

Key words: *Breast, benign proliferative disease, atypia, risk factor, aetiology.*

Introduction:

Benign breast disease (BBD) account for about 90% of whole breast diseases. Because of the increased awareness of breast cancer, benign breast lumps have assumed increasing attention nowadays.¹⁻³ Benign breast lesions carry a risk factor for development of either unilateral or contralateral breast cancer.⁴ Histologic entities of benign breast lesions are usually subdivided into non-proliferative breast lesions, proliferative breast lesions without atypical hyperplasia, and proliferative breast lesions with atypical hyperplasia.⁵⁻⁷ It has been postulated that inflammatory breast disease and non proliferative breast disease do

not increase the risk of cancer. Proliferative breast disease without atypia and with atypia confers mild and moderate risk respectively, whereas carcinoma in situ is associated with substantial risk,⁸ so it is important to pick up the benign lesions having risk of breast cancer development and know its incidence. The aim of our study is to determine the prevalence of benign proliferative breast diseases at risk of developing breast cancer.

Patients and methods:

This prospective study was conducted at general surgery department, Sohag University Hospital From February 2009 to June 2013;

it included 416 female patients presented to Breast Clinic with clinically palpable benign breast lump(s).

All patients were subjected to thorough clinical examination, sono-mammography and fine needle aspiration cytology. Those who were pregnant or with clinical and/or radiological signs of malignancy were excluded. Fine needle aspiration cytology (FNAC) was done as an out patients procedure using Fine-gauge number 23 single-use disposable needles in combination with regular 10 cc single-use airtight disposable plastic syringe. Two to three dry clean slides were used for preparing the smears. All slides were labelled with a glass pencil and air-dried then were fixed with 95% alcohol and stained with eosin and haematoxylin stain. Those who had cytological report negative for malignancy were included in the study. Data including use of contraceptives, Parity, menarche, menopausal status, family history of breast cancer were collected prospectively using a pre-test questionnaire in a face to face interview. A written informed consent was obtained from all patients. The study design was approved by the local research ethics committee. All biopsies taken from the excised lumps were examined by three pathologists with experience in breast diseases each one was initially blinded from findings of the others. In case of discrepancy in reporting, the final decision was by consensus. Gathered data were processed using SPSS version 15 (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as mean \pm SD while qualitative data were expressed as numbers and percentages (%). Student t test was used to test significance of difference for quantitative variables while Chi square was used to test significance of difference for qualitative variables. A probability values (p-value) ≤ 0.05 was considered statistically significant.

Results:

This prospective study was carried out in the period from February 2009 to June 2013 at department of general surgery, Sohag University hospital, Egypt. It included 416

patients attended breast clinic with clinical features of benign breast lumps, only 390 of them were enrolled in the study. All patients were females; their ages ranged from (12-67 years) with average 27.6 years. The average diameters of the masses were 2.9cm (range: 1.0-7.0 cm). The patients, characteristics are shown in **Table (1)**. Benign proliferative breast lesions (BPBL) were found in (20%) 78/390, while (80%) 312/390 were non proliferative. Among the BPBL there were 50 patients who did not use hormonal contraception while 28 had been using contraception. The prevalence of BPBL was 7.1 and 12.8% among hormonal contraceptive users and non-hormonal contraceptive users respectively. 35.8% (24/78) patients with BPBL had atypia while (69.2%) 54/78 patients with BPBL were without atypia. The prevalence of BPBL with atypia was 6.1% (24/390) and prevalence of BPBL without atypia was 13.8% (54/390).

As regard the histological diagnosis of the breast lesions, (54.1%) 211/390 patients had fibroadenoma; this was followed by Fibrocystic disease in (25.6%) 100/390 patients. Duct ectasia, the third commonest diagnosis was found in (5.6%) 22/390 patients. Chronic abscess, lactating adenoma and fat necrosis were found in (4.6%) 18, (3.5%) 14, and (2%) 8 patients respectively and 17 patients (4.3%) had other diagnoses as shown in **Table (2)**. The proliferative nature of all lesions was limited to the fibrocystic disease and fibroadenoma, 35/78 (44.8%) and 24/78 (30.7%) respectively.

Discussion:

Benign breast disease is a well-established risk factor for a later breast cancer, which can develop in either breast.⁴ It encompasses a spectrum of histologic entities, usually subdivided into non proliferative lesions, proliferative lesions without atypical, and atypical hyperplasia, with an increased risk of breast cancer associated with proliferative or atypical lesions.⁹⁻¹¹ Studies of benign breast disease can clarify whether there is a continuum of breast alterations that culminates in breast cancer. However, it remains unclear which of the benign entities are actual

Table 1: Participants' characteristics with BPBD and non BPBD.

Variable	Parameters	All women (N=390)	Non BPBD (N=312)	BPBD (N=78)	Atypical Hyperplasia (N=24)	P-value
Percentage of total		100 %	80 %	20%	6.1 %	
Age	10-20	76	48 (15.4)	28(35.9)	1 (4.1)	0.001
	21-30	140	128(41.0)	12(15.4)	6 (25)	
	31-40	111	98 (31.4)	14(17.9)	8 (33.3)	
	40+	63	38(12.1)	24(30.8)	9 (37.5)	
Menarche	≤13 years	372	309 (99)	78(100)	24(100)	0.00
	>13 years	18	3 (1)	0.0	0.0	
Menopause	yes	42	24(7.7)	16(20.5)	4 (16.6)	0.00
	No	348	288(92.3)	62(79.5)	20(83.4)	
Parity	Null	144	96(30.7)	48(61.5)	13(54.2)	0.0002
	Low(1-2)	126	107(34.4)	19(24.4)	7(29.2)	
	High(≥3)	120	109(34.9)	11(14.1)	4(16.6)	
Family history of breast cancer	Yes	64	10(3.2)	54(69.2)	16(66.6)	0.00
	No	326	302(96.8)	24(30.8)	8(33.3)	
Contraceptive use	Yes	130	102(32.7)	28(35.9)	7(29.2)	0.0007
	No	260	210(67.3)	50(64.1)	17(70.8)	

(P-value ≤0.05) =significant

Table 2: Frequency of histological types of breast lesions.

Histological diagnosis	Frequency	Percentage
fibroadenoma	211	54.1%
Fibrocystic disease	100	25.6%
Duct ectasia	22	5.6%
Chronic abscess	18	4.6%
Lactating adenoma	14	3.5%
Fat necrosis	8	2.0%
Others	17	4.3%
Total	390	100%

precursors and which reflect a background of increased risk involving all breast tissue in a woman.¹² Retrospective and prospective studies have shown a relative risk of breast cancer of 1.5 to 1.6 for women with benign breast disease as compared with women in the general population. The histologic appearance of the benign lesion is strongly associated with the risk of breast cancer; with non-proliferative changes the relative risk was 1.27 as compared with a relative risk of 1.88 for proliferative changes but no atypia and of 4.2 for atypical hyperplasia.^{9,13-18} Among

women with BBD, a family history of breast cancer (BC) further increases BC risk and women with a family history of BC are more likely to be diagnosed with BBD, especially at younger ages.¹² Important questions remain, however, about the degree of risk associated with the common non-proliferative benign entities and the extent to which family history influences the risk of breast cancer in women with proliferative or atypical lesions. Dupont and Page found that women with non-proliferative disease did not have an increased risk of a later breast cancer.⁹ By contrast, a

companion study to the National Surgical Adjuvant Breast and Bowel Project (NSABP) found a relative risk of 1.6 for women who received a diagnosis of a “lower category” of benign breast.¹³ In our governorate where a large proportion of women with breast cancer are pre-menopausal, it was important to examine and characterize the nature of benign breast lesions encountered in routine clinical practice in our locality. We set out to establish the prevalence of benign proliferate breast lesions with atypia and without atypia. We found that benign breast lesions are a common presentation; 93.7% as the case elsewhere. In our study 20% (78/390) of all benign breast lumps were proliferative in nature. Atypia which is considered to carry two to four folds risk for developing breast cancer (19, 20) was present in 6% (24/390) of the benign proliferative lumps. Also we found that 83% (20/24) of the women with atypia were premenopausal. This came in accordance with a study by Schnitt et al, 1993, which found the prevalence of BPBD in Japan was as high as 18% among women younger than 40 years.²¹ A similar finding was documented in North America.²² In our series Fibroadenoma was the most frequently diagnosed lesion 54.1%, followed by fibrocystic change 25.6%. Duct ectasia was the third most commonly diagnosed lesion. Almost all of the benign proliferative lesions were found in the fibrocystic change and fibroadenoma categories. This result came in accordance with result of Chengqu an et al, Shrestha et al and Okota et al.²³⁻²⁵ As regard family history we found that there is a significant association between the positive history of breast cancer and BPBD. In literature the association between family history of breast cancer and risk of BPED is mixed, with some studies finding a positive association²⁶⁻²⁷ and others²⁸⁻³³ observing no association. In relation to parity; we found that there is an inverse association between the parity and the risk of BPBD and there are only three studies^{27,29,32} that support this result, while the remaining studies observed no association.^{28-30,33-36}

Several studies have also examined the

etiological role of exogenous hormone use.^{29,33,37-41,42} Four studies, two cohort^{33,42} and two case-control,^{29,37} have presented results for the association between oral contraceptive (OC) use and risk of BPBD, with two showing that risk of BPBD was reduced in association with OC use^{29,42} and the others^{37,33} showing no association. Several other studies (all case-control) have reported on the association between OC use and risk of BBD by degree of histological atypia.³⁶⁻⁴⁰ Findings for these studies have varied from those showing reduced risk of all grades of atypia³⁶ to those showing no reduction in risk with any grade of atypia.³⁷ In this study, no association is found between any measure of oral contraceptive use and risk of BPBD. The association between age at menarche and BPED of the breast has been investigated in nine case-control studies^{26-29,31,32,34,35} and one cohort study,³³ none of which has shown alterations in risk and this came in agreement with our result.

Conclusion:

Benign proliferative breast lumps are common among premenopausal women in Sohag governorate and a significant proportion of it had atypical proliferation. Fibroadenoma and fibrocystic disease were the commonest benign breast disease in our locality. An accurate breast cancer risk estimate study for BPBD is recommended.

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