Management of breast mass

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Dedication

To all my friends who help me in the research and my dear family specially my mother.

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List of abbreviations

Abbreviation	Full name
U/S	Ultrasound
FNAC	Fine needle aspiration cytology

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Abstract

Background: Breast masses have a variety of etiologies, benign and malignant. Fibroadenoma is the most common benign breast mass; invasive ductal carcinoma is the most common malignancy. [1] Most masses are benign, but breast cancer is the most common cancer and the second leading cause of cancer deaths in women.

Aim: to assess the patients with breast lump that consult the breast clinic in different age group.

Patient and method: This prospective descriptive study was carried out at the breast clinic in AlImamain AlKadhmain Medical City , during the period of 10 October 2018 to 1 April 2019 . A total 100 patients with palpable breast lump were included in the study. Age of the patients was between 18 to 59 years.

Result and discussion: In most of the patients with breast lump ultrasound and fine needle aspiration cytology were done . Among the study population 95% had benign lesions, Breast carcinoma accounted for 5% casess. Fibroadenoma was the most common benign lesion (59 %) followed by fibroadenosis (12%) . Here we attempted to find out the age incidence of breast lump and its correlation with clinical features, FNAC findings and histopathological report to improve the accuracy of diagnosis and management of breast disease.

Conclusion: From this study, we can say that most common breast mass are benign (95 %) Fibroadenoma followed by fibroadenosis and the malignant is (5%) . The probability of developing breast cancer increases with age, throughout life. Women who are at greater than normal risk of developing breast cancer, should be identified by proper health education and employing screening program by regular self examination of breast, physical examination by doctors and mammography. Any suspicious lesion must have a cytological diagnosis. Early detection of breast lump, differentiation between benign and malignant lesions and proper treatment has an immense value.

Introduction

Breast masses have a variety of etiologies, benign and malignant. Fibroadenoma is the most common benign breast mass; invasive ductal carcinoma is the most common malignancy. [1] Most masses are benign, but breast cancer is the most common cancer and the second leading cause of cancer deaths in women. [2] Although most breast cancers occur in women older than 50 years, 31 percent of women diagnosed with breast cancer between 1996 and 2000 were younger than 50 years. [3] An efficient & accurate evaluation can maximize cancer detection and minimize unnecessary testing and procedures.[2]

Initial Evaluation

HISTORY

A thorough patient history is necessary for the physician to identify risk factors for breast cancer. Some risk factors are well-established, and others indicate probable or possible increased risk (Tables 1 and 2). [4-14]

PHYSICAL EXAMINATION

A complete clinical breast examination (CBE) includes an assessment of both breasts and the chest, axillae, and regional lymphatics. In premenopausal women, the CBE is best done the week following menses, when breast tissue is least engorged. With the patient in an upright position, the physician visually inspects the breasts, noting asymmetry, nipple discharge, obvious masses, and skin changes, such as dimpling, inflammation, rashes, and unilateral nipple retraction or inversion. [15]

With the patient supine and one arm raised, the physician thoroughly palpates breast tissue on the raised-arm side in the superficial, intermediate, and deep tissue planes (i.e., the "triple touch"

TABLE 1
Relevant History in Women with Palpable Breast Masses

Breast lump characteristics	**Medical and surgical history**
Changes in size over time	Personal history of breast cancer
Change relative to menstrual cycle	Previous breast masses and biopsies
Duration of mass	Recent breast trauma or surgery
Pain or swelling	Recent radiation therapy or chemotherapy
Redness, fever, or discharge	Other exposure to radiation
Diet and medications	**Personal characteristics**
Current medications	Age at first childbearing
History of hormone therapy	Age at menarche
Family history	Age at menopause
History of breast disease	Current age
Relationship to patient	Current lactation status
Relative's age at onset	History of breastfeeding
	Number of children
	Social history
	Radiation and chemical exposure
	Smoking

Information from references 4 through 14.

technique); axilla; supraclavicular area; neck; and chest wall, assessing the size, texture, and location of any masses. [15] The physician should note the size of the masses to document changes over time. Next, the physician should inspect the areola-nipple complex for any discharge. CBE sensitivity can be improved by longer duration (i.e., five to 10 minutes) and increased precision (i.e., using a systematic pattern, varying palpation pressure, and using three finger pads and circular motions). [15,16]

Benign masses generally cause no skin change and are smooth, soft to firm, and mobile, with well-defined margins. Diffuse, symmetric thickening, which is common in the upper outer quadrants, may indicate fibrocystic changes. Malignant masses generally are hard, immobile, and fixed to surrounding skin and soft tissue, with poorly defined or irregular margins. [15] However, mobile or nonfixed masses can be cancerous. Infections such as mastitis and cellulitis tend to be erythematous, tender, and warm to the touch; they may be more circumscribed if an abscess has formed. Similar symptoms may occur in patients with inflammatory breast cancer. Therefore, caution should be used in assessing patients with suspected breast infections.[16]

TABLE 2
Risk Factors for Breast Cancer

Well-established risk factors	Probable risk factors
Age 50 or older	Alcohol consumption
Benign breast disease, especially cystic disease, proliferative types of hyperplasia, and atypical hyperplasia	Did not breastfeed
Exposure to ionizing radiation	Elevated endogenous estrogen levels
First childbirth after age 20	High BMI*
Higher socioeconomic status	Hormonal contraception therapy
History of breast cancer	Increased mammographic density of breast tissue
History of breast cancer in a first-degree relative	Menarche before age 12
Hormone therapy	Menopause after age 45
Nulliparity	Mutations in BRCA 1 and BRCA 2 genes
Obesity (i.e., BMI ≥ 30 kg per m²)*	**Possible risk factors**
	Chemical exposure
	Diet high in fat
	Diet low in beta carotene, folate, and vitamins A and C
	Diet low in fruits and vegetables

BMI = body mass index.

**—Breast cancer risk increases by 3 percent with every 1 kg per m² increase in BMI.*

Information from references 4 through 14.

Digital palpation of the breast is effective in detecting masses and can help determine whether a mass is benign or malignant. [15,17] CBE can detect up to 44 percent of cancers, up to 29 percent of which would not have been detected by mammography. [15] Despite its accuracy, CBE alone is not adequate for definitive diagnosis of breast cancer.Further evaluation, including follow-up examinations, imaging, and tissue sampling, is required in all patients with breast masses.[17]

Imaging

ULTRASONOGRAPHY

Ultrasonography can effectively distinguish solid masses from cysts, which account for approximately 25 percent of breast lesions. [18,19] When strict criteria for cyst diagnosis are met, ultrasonography has a sensitivity of 89 percent and a specificity of 78 percent in detecting abnormalities in symptomatic women. [18] Recurrent or complex cysts may signal malignancy; therefore, further evaluation of these lesions is required. [19]

Although ultrasonography is not considered a screening test, it is more sensitive than mammography in detecting lesions in women with dense breast tissue. 18,20 It is useful in discriminating between benign and malignant solid masses, [18,21] and it is superior to mammography in diagnosing clinically benign palpable masses (i.e., up to 97 percent accuracy versus 87 percent for mammography). [21]

DIAGNOSTIC MAMMOGRAPHY

Diagnostic mammography can help physicians determine whether a lesion is potentially malignant, and it also screens for occult disease in surrounding tissue. A radio-opaque ball bearing marks the location of the mass, and spot compression and magnificationviews can clarify the breast mass and determine its density. If old films are available, they are compared with the new images. Diagnostic mammography is up to 87 percent sensitive in detecting cancer. [22] Its specificity is 88 percent, and its positive predictive value may be as high as 22 percent. [22]

DIGITAL MAMMOGRAPHY

Digital mammography allows images to be enhanced and transmitted electronically.
The ability to alter contrast and brightness permits furtherevaluation of abnormal areasto identify features diagnosticof benign and malignant disease. [23-26] Although the overallcancer-detection rate is similar in screen-field and full-field mammography, screen-field imaging has better image quality and less artifact and requires fewer patient recalls. [24,25]

In addition to its usefulness in tele-mammography, digital mammography may be more accurate than traditional mammography; studies comparing the methods are underway. Potential new techniques include three-dimensional imaging, lower-dose radiation, dual energy subtraction, contrast-enhancement imaging, and computerassisted diagnosis. [23,24,26]

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) is being studied to determine its usefulness in diagnosing breast masses. Gadolinium contrast is used to enhance the vascularity of malignant lesions. Although MRI is highly sensitive (85 to 100 percent), it lacks specificity(47 to 67 percent). [27,28] MRI is inferior to mammography in detecting in situ cancers and cancers smaller than 3 mm, and it provides no cost benefit over excisional biopsy for verifying malignancy. [27,28]

Research suggests two potential roles for MRI in breast mass diagnosis: evaluating patients with silicone breast implants 29 and assessing patients in whom evaluation by ultrasonography and mammography is problematic. The latter group includes patients who have had breast-conserving surgery; patients with known carcinoma in whom multifocal, ipsilateral, or contralateral disease must be ruled out; patients with axillary metastasis and an unknown primary; patients with extensive postoperative scarring; and patients with extremely dense parenchyma. [28,30-32]

A recent study 33 compared the effectiveness of mammography and MRI in women with a family history of breast cancer or a genetic susceptibility to the disease. The sensitivity of MRI was higher than that of mammography in detecting breast cancer, and MRI was better able to discriminate between benign and malignant lesions. [30-32]

Although MRI improves detection of early breast cancers in carriers of BRCA mutations, it has lower specificity than mammography, which requires additional evaluations. It also has a limited sensitivity in detecting ductal carcinoma in situ.[31]

Tissue Studies

FINE-NEEDLE ASPIRATION

The first step in evaluating patients with palpable breast masses often is fine-needle aspiration (FNA), in which a 22- to 25gauge needle is used to aspirate cystic fluid or sample solid lesions for cytology. In some patients, the lesion completely resolves after FNA, and no further diagnostic work-up is required. However, when imaging is indicated after FNA, cyst wall disruption caused by the procedure may make imaging more difficult to evaluate. The problem may be avoided by scheduling imaging studies up to two weeks after FNA and notifying the radiologist of the recent procedure. [34]

FNA also is used with ultrasonography or stereotactic imaging to further assess poorly defined palpable masses. When sampling inpatients with solid lesions is adequate, FNA is highly sensitive for malignancy (98 to 99 percent) and has a positive predictive value of 99 percent and a negative predictive value of 86 to 99 percent. [35] Sample adequacies is of some concern; one study 36 rated 28 percent of samples as inadequate and another 22 percent as less than optimal. The physician's training and experience may be a key factor in obtaining adequate samples. [36]

CORE-NEEDLE BIOPSY

Core-needle biopsy (CNB) produces a larger tissue sample than FNA and may be used in conjunction with ultrasonography or stereotactic imaging for small or difficult-to-palpate lesions. Local anesthesia is required. A 14- to 18-gauge cutting needle is used to obtain two to six slender cores of tissue for histology. [37,38] The sensitivity of ultrasonography-guided CNB may be as high as 99 percent in diagnosing malignancy in palpable lesions and 93 percent in nonpalpable lesions. [1] Specimens can be used to differentiate between in situ and invasive carcinoma, and to identify hormone-receptor levels. [39] Results vary depending on radiographic guidance, the size of the needle, and the number of cores sampled. A minimum of four cores is suggested to achieve greater accuracy. [37,38] Insufficient specimens are rare. [1,38] Compared with FNA, CNB takes more time and requires specific training and patient anesthesia, but it has a higher positive predictive value for suspicious and atypical results and may provide an overall cost benefit. [38]

EXCISIONAL BIOPSY

Excisional biopsy is the gold standard for evaluating breast masses. It is performed in an operating room under local or general anesthesia and results in the removal of the entire lesion. Excisional biopsy is diagnostic and therapeutic: a completely removed mass with good margins of normal tissue may mean that further surgery is not required. An incisional biopsy (i.e., removal of a portion of the lesion) generally is used for tissue diagnosis in large tumors when CNB is non-diagnostic. Excisional biopsy is indicated in patients with clinically suspicious lesionsand lesions in which imaging or tissue studies are equivocal. 40-43 With the increased use of CNB, the need for diagnostic excisional biopsy has declined. [44]Triple Test The triple test is the combination of results from CBE, imaging, and tissue sampling. [41,45-47]
When the three assessments are performed adequately and produce concordant results, the triple testdiagnostic accuracy approaches100 percent. 41,45,46 Discordantresults or resultsthat cannot beevaluated may indicate the needfor excisional biopsy. [45]

The Triple Test Score (TTS) was developed to help physicians interpret discordant triple test results. [41,42]A three-point scale is used to score each component of the triple test (1 = benign, 2 = suspicious, 3 = malignant). A TTS of 3 or 4 is consistent with a benign lesion; a TTS of 6 or more indicates possible malignancy that may require surgical intervention. Excisional biopsy is recommended in patients with a TTS of 5 to obtain a definitive diagnosis.

DIAGNOSTIC EVALUATION PROCESS

After the patient history is obtained and the CBE is performed, the next diagnostic step is determined by the patient's age and the physician's experience with performing office-based FNA (Figure 1).Physicians trained in FNA may choose this procedure for two reasons: it is office-based and may be performed during the same clinical visit, and cystic lesions that resolve on aspiration spare the patient further work-up. [45]
If FNA reveals a solid lesion, evaluation with diagnostic mammography should be performed next [34,48]; ultrasonography may be considered in women younger than 40 years. 41 If all three elements (CBE, FNA, and imaging) indicate benign disease

(i.e., TTS of 3), the patient may be followed with another examination in four to six weeks. [42,48]

If all triple test elements are positive (i.e., suggestive of malignancy), surgical intervention is indicated. [45] Patients with discordant results and a TTS of 4 may be followed withrepeat examination, but excisional biopsy or referral to a breast specialist is indicated in patients witha TTS of 5 or higher. [42] CNB may be performed to enhance the triple test accuracy if it was not used previously. [38,47]If FNA is not feasible during the initial presentation, ultrasonography should be considered to rule out cystic disease and delineate lesion margins. [22,48] Cystic lesions may be aspirated. Solid lesions should be evaluated with mammography, which often can be done during the same visit, to further delineate lesion margins and to screen for occult disease in the ipsilateral and contralateral breast, particularly in women older than 40 years. [49] Solid lesions will then require FNA or CNB [48] to complete the triple test. Further management should be implemented as described in Figure 1.

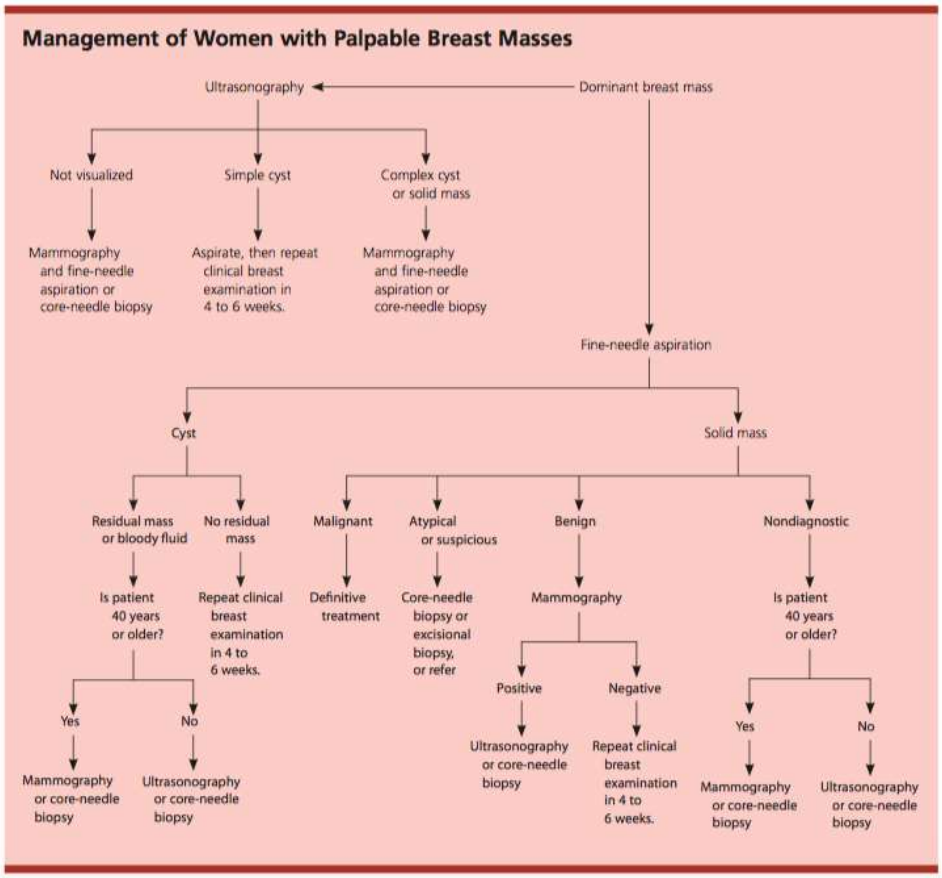

Figure 1. Diagnostic algorithm for patients with palpable breast mass.

Aim of the Study

Assessment of the patient with breast mass that consult Al-Imamain Alkadhmain Medical city.

Patients And Method

This is a prospective descriptive study carried out at the Departement of Surgery , Al-Imamain Alkadhmain Medical City in Baghdad at the breast clinic . all patient who presented with discrete breast mass to our hospital were included to the study for seven months in the period of 10 October 2018 to 1 April 2019 . triple assessment was done to the patients and this include full detailed history and clinical examination (history include patients name ,age ,occupation , residence ,marital status ,association of the breast mass such as pain nipple discharge...etc. family history of breast cancer ,history of OCP use ,breast feeding ,smoking ,clinical examination include examination of the diseased breast and compare with the other breast this include mass site ,size ,consistency ,shape and also examination of the axilla) .imaging that done to the patient was ultrasound and the histopathology was fine needle aspiration . modality of patients treatment was also included to the study .

Managementof Breast Mass | **Research sheet**

Patient name Age ( )

Marital status Residence:

Occupation

Chief complain and association

Past medical:

Past surgical:

Family history:

Gynecological history:

- Menarche:
- Regular irregular
- Using of OCP
- Using of HRT
- Social history :smoking alcoholic

Clinical examination:

- Site
- Size
- Shape
- Consistency

- Imaging:

- Histopathology:

- Treatment:

Results

Age

100 patients participate in the study, there age where ranging from 18 – 59 year, with mean of (35.46). As shown in table 3.

Table 3: Age of the patients in the study.

Age group	Number of patients
10 – 19	6(6%)
20 – 29	34(34%)
30 – 39	24(24%)
40 – 49	20(20%)
50 – 59	16(16%)

Marital Status

Twelve patients (12%) were single, while eighty-eight patients (88%) were married. As shown in table 4 and figure 2.

Table 4: patient number and percentage according to marital status in the study.

Marital status	Number of cases	Percentage
Married	88	88 %
Single	12	12 %

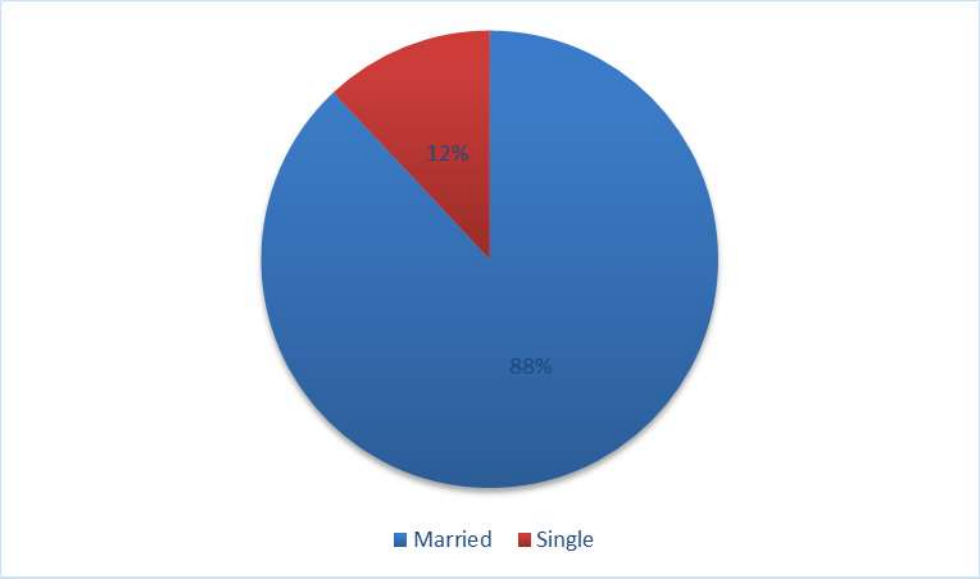

Figure 2: patient number and percentage according to marital status in the study

Breast feeding

Forty-six (46%) patients were have a negative history of breast feeding, while fifty-four (54%) of the patients were have a positive history of breast feeding. As shown in table 5 and figure 3.

Table 5: The number and percentage of the patients regarding the breast feeding.

Breast feeding	Number of cases	Percentage
No	46	46%
Yes	54	54%

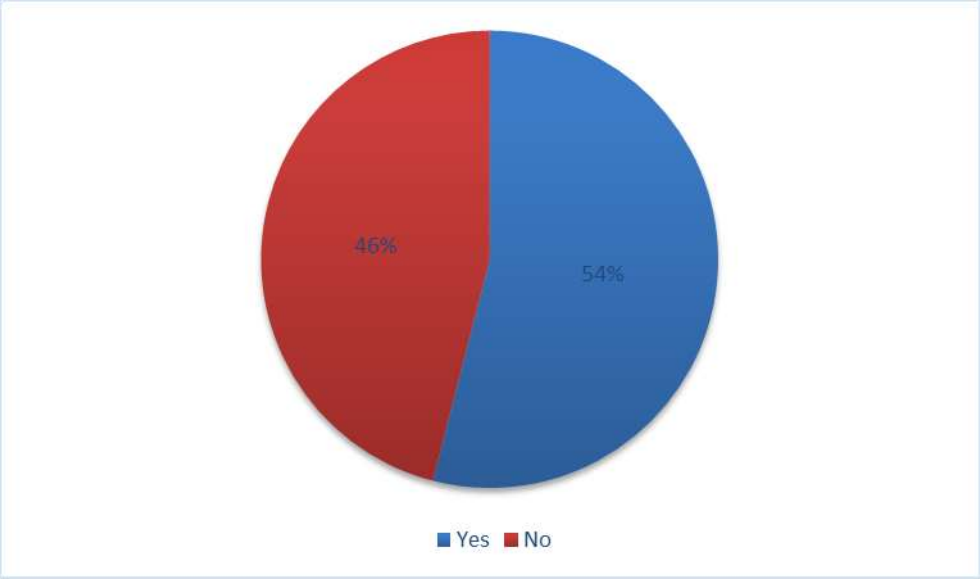

Figure 3: The number of the patients regarding the breast feeding.

Drug history (contraceptive pills)

Forty-nine (49%) patients were not taking oral contraceptive pills (OCP), while fifty-one (51%) of the patients were taking OCP. One the other hand none of the patients were taking hormone replacement therapy (HRT). As shown in table 6 and figure 4.

Table 6: The number and percentage of the patients regarding the contraceptive use .

Drug History (contraceptive use)	Number of cases	Percentage
Yes	51	51%
No	49	49%

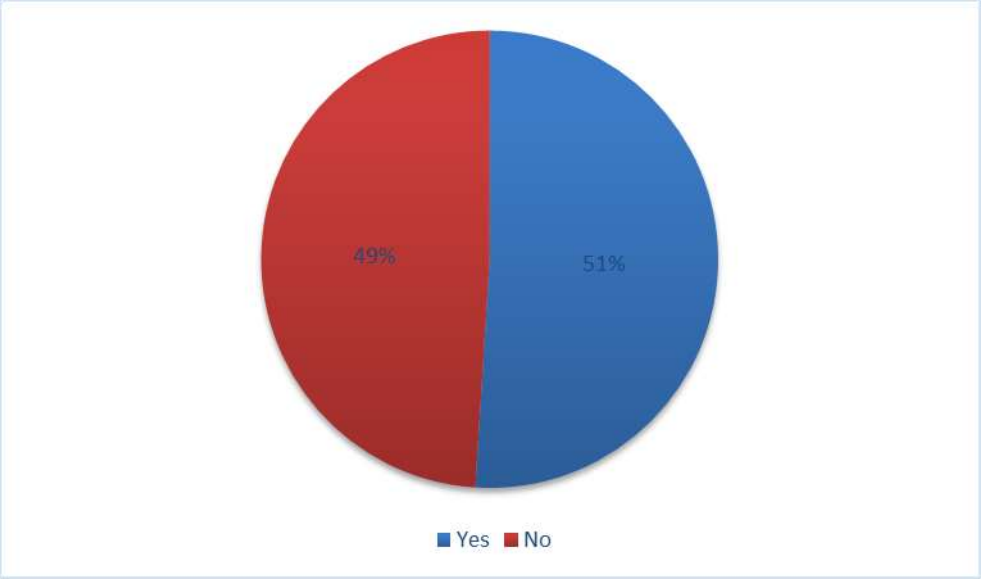

Figure 4: The number of the patients regarding the drug history.

Site

Regarding the site of the breast mass, 55% of the patients were having a left side breast mass and 42% of the patients were having a right-side breast mass, while only 3% of the patients were have a bilateral breast mass. As shown in table 7 and figure 5.

Table 7: The number and percentage of the patients regarding the site of the breast mass.

Site	Number of cases	Percentage
Bilateral	3	3%
Left	55	55%
Right	42	42%

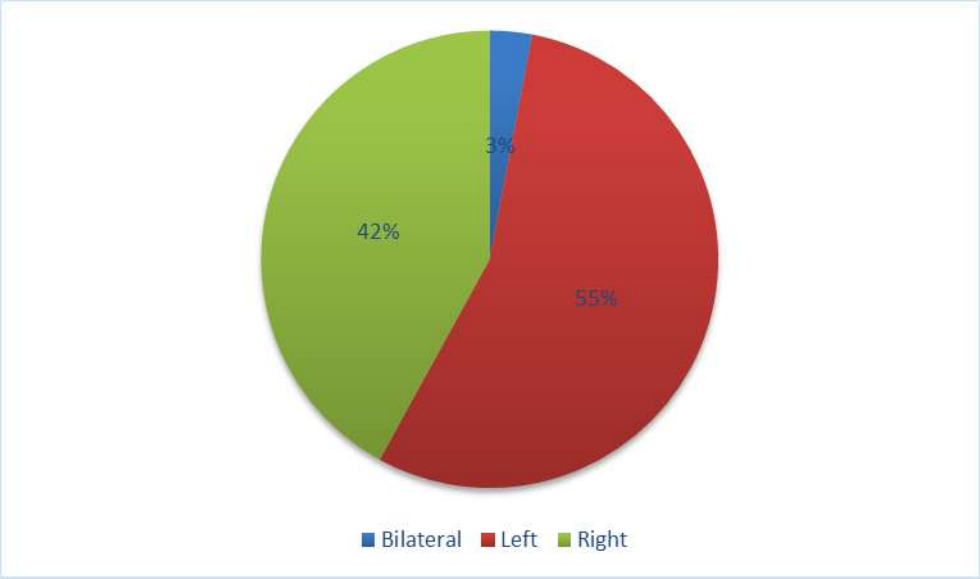

Figure 5: The percent of the patients regarding the site of the breast mass.

Diagnosis according to the ultrasound and fine needle aspiration

Regarding the diagnosis, 59% of the patients were having fibroadenomamass,12% of the patients were having fibroadenosis, 9% of the patients were having mastitis, 6% of the patients were having ductectasia, 4% of the patients were having abscess, 5% of the patients were having lipoma, while 3% and 2% of the patients were having mammary adenocarcinoma, invasive ductal carcinoma respectively. As shown in table 8.

Table 8: The number and percentage of the patients diagnosis according to ultrasound and fine needle aspiration.

Diagnosis	Number of cases	Percentage
Abscess	4	4%
Ductectasia	6	6%
Fibroadenoma	59	59%
Fibroadenosis	12	12%
Invasive ductal carcinoma	2	2%
Lipoma	5	5%
Mammary adenocarcinoma	3	3%
Mastitis	9	9%

Treatment and outcome:

Regarding the treatment, conservative method (64%) ,surgical (23%) , drainage and AB (4%) , analgesia and AB (9%). As shown in table 9.

Table 9: The number of the patients according to the modality of treatment.

Diagnosis	Number of cases	Treatment
Abscess	4(4%)	Drainage and Anti-biotics
Ductectasia	4(4%)	Conservative
	2(2%)	Surgical
Fibroadenoma	16(16%)	Surgical
	43(43%)	Conservative
Fibroadenosis	12(12%)	Conservative
Invasive ductal carcinoma	2(2%)	Surgical
Lipoma	5(5%)	Conservative
Mammary adenocarcinoma	3(3%)	Surgical
Mastitis	9(9%)	Analgesia and Anti-biotics

Table 10*:* Relation of age group to (marital status ,contraceptive use ,breast feeding and diagnosis.

Age group	Single	married	Contraceptive pills use	Breast feeding	Dx (benign)	Dx (malignant)
10 – 19	2(2%)	4(4%)	o	1(1%)	6(6%)	0
20 – 29	7(7%)	27(27%)	9 (9%)	11(11%)	33(33%)	1(%)
30 – 39	2(2%)	22(22%)	15(15%)	18(18%)	23(23%)	1(1%)
40 – 49	1(1%)	19(19%)	8(8 %)	14(14%)	19(19%)	1(1%)
50 – 59	0	16(16%)	11 (11%)	10(10%)	14(14%)	2(2%)

Discussion

100 patients participate in the study, there age where ranging from 18 – 59 year old the most common age presentation is in the second decade (20 – 29) followed by third decade (30 – 39) that agree with(Faridpur Med. Coll. J. 2013;8(2):56-58) (29)

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according to the marital status twelve patients (12%) were singles and eighty eight patients (88%) were married , married cancer patients have lower mortality than unmarried patients (30).

According to the breast feeding , Forty-six (46%) patients were have a negative history of breast feeding, while fifty-four (54%) of the patients were have a positive history of breast feeding ,the breast feeding lowering the risk of breast cancer (Barbara Wilson-Clay, BS, IBCLC).

Regarding the diagnosis most of the patients in this series (95%) show a benign feature clinically (most common benign lesion is fibroadenoma followed by fibroadenosis ,mastitis ,ductectasia,lipoma abcess) , while the patient that have a malignant features count about 5% (2% were invasive ductal carcinoma and 3% were mammary adenocarcinoma) , this agree with (between 41 and 55 the rate was 5%, and in those over 55 it was 21%.

The predominant finding in young women was a fibroadenoma. In the middle age range fibrocystic change was most common, and in postmenopausal women most of the lesions were malignant. (30).

according to the treatment of patient the conservative method is most common modality of treatment used in this study (64%).

Conclusion

From this study, we can say that most common breast mass are benign (95 %) Fibroadenoma followed by fibroadenosis and the malignant is (5%) . The probability of developing breast cancer increases with age, throughout life. Women who are at greater than normal risk of developing breast cancer, should be identified by proper health education and employing screening program by regular self examination of breast, physical examination by doctors and mammography. Any suspicious lesion must have a cytological diagnosis. Early detection of breast lump, differentiation between benign and malignant lesions and proper treatment has an immense value .

REFERENCES

1. Schoonjans JM, Brem RF. Fourteen-gauge ultrasonographically guided large-core needle biopsy of breast masses. J Ultrasound Med 2001;20:967-72.
2. American Cancer Society. Cancer facts and figures 2003.
3. Accessed online October 14, 2004, at: http://www. cancer.org/downloads/STT/CAFF2003PWSecured.pdf.
4. National Cancer Institute. SEER 1973-2001 public-use data. Accessed online October 14, 2004, at: http://seer. cancer.gov/publicdata/.
5. Madigan MP, Ziegler RG, Benichou J, Byrne C, Hoover RN. Proportion of breast cancer cases in the United States explained by well-established risk factors. J Natl Cancer Inst 1995;87:1681-5.
6. National Cancer Institute. Breast cancer (PDQ): prevention. Accessed online October 14, 2004, at: http:// www.cancer.gov/cancertopics/pdq/prevention/breast/ healthprofessional.
7. Newcomb PA, Titus-Ernstoff L, Egan KM, Trentham-Dietz A, Baron JA, Storer BE, et al. Postmenopausal estrogen and progestin use in relation to breast cancer risk. Cancer Epidemiol Biomarkers Prev2002;11:593-600.
8. Weiss LK, Burkman RT, Cushing-Haugen KL, Voigt LF, Simon MS, Daling JR, et al. Hormone replacement therapy regimens and breast cancer risk (1). ObstetGynecol2002;100:1148-58.
9. Key TJ, Appleby PN, Reeves GK, Roddam A, Dorgan JF, Longcope C, et al. Body mass index, serum sex hormones, and breast cancer risk in postmenopausal women. J Natl Cancer Inst 2003;95:1218-26.
10. Boyd NF, Jensen HM, Cooke G, Han HL, Lockwood GA, Miller AB. Mammographic densities and the prevalence and incidence of histological types of benign breast disease. Reference Pathologists of the Canadian National Breast Screening Study. Eur J Cancer Prev2000;9:15-24.
11. Byrne C, Connolly JL, Colditz GA, Schnitt SJ. Biopsy confirmed benign breast disease, postmenopausal use of exogenous female hormones, and breast carcinoma risk. Cancer 2000;89:2046-52.
12. Kumle M, Weiderpass E, Braaten T, Persson I, Adami HO, Lund E. Use of oral contraceptives and breast cancer risk: the Norwegian-Swedish Women's Lifestyle and Health Cohort Study. Cancer Epidemiol Biomarkers Prev2002;11:1375-81.

13. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. Collaborative Group on Hormonal Factors in Breast Cancer. Lancet 1996;347:1713-27.
14. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA 2002;288:321-33
15. Budai B, Szamel I, Sulyok Z, Nemet M, Bak M, Otto S, et al. Characteristics of cystic breast disease with special regard to breast cancer development. Anticancer Res 2001;21:749-52.
16. Barton MB, Harris R, Fletcher SW. The rational clinical examination. Does this patient have breast cancer? The screening clinical breast examination: should it be done? How? JAMA 1999;282:1270-80.
17. Campbell HS, Fletcher SW, Pilgrim CA, Morgan TM, Lin S. Improving physicians' and nurses' clinical breast examination: a randomized controlled trial. Am J Prev Med 1991;7:1-8.
18. Baines CJ, Miller AB. Mammography versus clinical examination of the breasts. J Natl Cancer Inst Monogr 1997;(22):125-9.
19. Moss HA, Britton PD, Flower CD, Freeman AH, Lomas DJ, Warren RM. How reliable is modern breast imaging in differentiating benign from malignant breast lesions in the symptomatic population? ClinRadiol1999;54:676-82.
20. Berg WA, Campassi CI, Ioffe OB. Cystic lesions of the breast: sonographic-pathologic correlation. Radiology 2003;227:183-91.
21. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology 2002;225:165-75.
22. Lister D, Evans AJ, Burrell HC, Blamey RW, Wilson AR, Pinder SE, et al. The accuracy of breast ultrasound in the evaluation of clinically benign discrete, symptomatic breast lumps. ClinRadiol1998;53:490-2.
23. Barlow WE, Lehman CD, Zheng Y, Ballard-Barbash R, Yankaskas BC, Cutter GR, et al. Performance of diagnostic mammography for women with signs or symptoms of breast cancer. J Natl Cancer Inst 2002;94:1151-9.
24. Leichter I, Buchbinder S, Bamberger P, Novak B, Fields S, Lederman R. Quantitative characterization of mass lesions on digitized mammograms for computerassisted diagnosis. Invest Radiol2000;35:366-72.

25. Obenauer S, Luftner-Nagel S, von Heyden D, Munzel U, Baum F, Grabbe E. Screen film vs full-field digital mammography: image quality, detectability and characterization of lesions [published correction appears in EurRadiol 2002;12:2388]. EurRadiol2002;12:1697-702.
26. Lewin JM, Hendrick RE, D'Orsi CJ, Isaacs PK, Moss LJ, Karellas A, et al. Comparison of full-field digital mammography with screen-film mammography for cancer detection: results of 4,945 paired examinations. Radiology 2001;218:873-80.
27. Fischer U, Baum F, Obenauer S, Luftner-Nagel S, von Heyden D, Vosshenrich R, et al. Comparative study in patients with microcalcifications: full-field digital mammography vs screen-film mammography. EurRadiol2002;12:2679-83.
28. Hrung JM, Sonnad SS, Schwartz JS, Langlotz CP. Accuracy of MR imaging in the work-up of suspicious breast lesions: a diagnostic meta-analysis. AcadRadiol1999;6:387-97.
29. ABMZ Sadik1 , MM Hasan2 , HEZA Haque3 , FU Ahmed4 , MZ Kabir
30. Can J Surg. 1992 Feb;35(1):41-5.