

## RESEARCH ARTICLE

# Pathological Profile of Patients with Breast Diseases in Shiraz

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### Abstract

**Background:** Around 200,000 breast disorders are annually diagnosed all over the world. Fibrocystic changes are the most common breast disorder and fibroadenoma is the most prevalent benign breast tumor. The present study aimed to determine the spectrum, type and prevalence of breast masses in women referred to Shiraz University of Medical Sciences between 2004 and 2012. **Materials and Methods:** A cross-sectional study was conducted on the diagnostic reports data. **Results:** A total of 640 samples were studied. Most 57.3% of masses were detected in the left breast, 65%, 28.2% and 6.1% of cases presenting with benign, malignant, and inflammatory lesions, respectively. Among all the samples the most prevalent diagnosis (37.7%) was fibroadenoma and fibrocystic lesions (17%). 174 samples (96% of the malignant cases) were invasive. 6.5% of the benign, and 37% of the malignant cases occurred in post menopause women and the differences were statistically significant. Among those with malignant tumors lymph nodes were involved in 25.6% of menopausal women and 44.2% of non-menopausal ones, and the difference was statistically significant. **Conclusions:** Regular clinical breast examination beside mammographic follow-ups, especially during menopause, should be carried out as a priority and a national organized program should be designed for screening breast disorders.

**Keywords:** Breast diseases - benign - malignant - fibroadenoma - Iranian women

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### Introduction

Breasts undergo various changes during puberty, pregnancy, and menopause due to hormonal changes which might result from different reasons in different countries and ethnicities. In general, 1 out of every 6 women around the world undergoes biopsy due to breast problems; such a way that around 200,000 breast disorders, including inflammatory changes and malignant as well as benign lesions, are annually diagnosed all over the world. Breast cancer is the most common cause of mortality among women accounting for 23% all cancers (Perez et al., 2009). The risk factors of malignant and benign breast disorders include low parity, low age at the first pregnancy, and high age at menopause (Hislop and Elwood, 1981). Overall, malignant lesions are less prevalent compared to benign ones. Besides, fibrocystic changes are the most common breast disorder and fibroadenoma is the most prevalent benign breast tumor (Templeman and Hertweck MD, 2000; Hartmann et al., 2005; Degnim et al., 2007). Fibroadenoma are normally asymptomatic lesions sizing about 1-10 cm which have a smooth rubbery texture and can move under the skin. These lesions slightly increase the risk of breast cancer (Dupont et al., 1993; Templeman and Hertweck MD, 2000; Hartmann et al., 2005; Degnim et al., 2007; Worsham et al., 2009).

The rate of breast malignancies is higher in North

America and Western Europe compared to Asia and Africa, which might be due to difference in the individuals' lifestyles (Jemal et al., 2011). In Iran, although the prevalence of breast disorders is lower in comparison to western countries (Rezaianzadeh et al., 2011), breast cancer is still the most prevalent malignancy among women (Harirchi et al., 2004). During 2001-2006 average incidence of breast malignancies increased from 13.02 to 17.88 in Iran (Abbastabar et al., 2013). After 2004, a significant increase was observed, particularly after menopause, in Fars province, Iran (Mehrabani et al., 2012).

Imaging methods can be employed in order to examine, diagnose, follow up, and screen breast masses. Nevertheless, the final decision regarding the disease stage and treatment is made based on the pathology report (Brunicardi et al., 2009). The present study aims to determine the spectrum of breast lesions, so that after identification of the type and prevalence of masses, necessary measures can be taken towards diagnosis and treatment of the cases.

### Materials and Methods

This cross-sectional study was conducted on the diagnostic reports data of the women referring to the breast disease clinic affiliated to Shiraz University of

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Medical Sciences between 2004 and 2012. The study population included the patients who had undergone FNA, lumpectomy, mastectomy, and lymph node removal and their reports were available. The inclusion criterion of the study was having sufficient information in medical records. After all, the collected data were analyzed using the SPSS statistical software (v. 16). Quantitative variables were analyzed using mean and Standard Deviation (SD), while the qualitative ones were analyzed through relative frequency. In addition, Chi-square test was used to investigate the relationship between menopause status and disease diagnosis (malignant or benign) and lymph node involvement.  $p < 0.05$  was considered as statistically significant.

## Results

This study was conducted on 640 samples which had been referred to the laboratory between 2004 and 2012 and had the inclusion criteria of the study. The study women's age ranged from 20 to 68 years old, with the mean age of  $39.9 \pm 11.5$  years. Most of the masses were detected in the left breast (57.3%). Additionally, 420 (65.6%), 181 (28.2%), and 39 (6.1%) cases presented with benign, malignant, and inflammatory lesions, respectively. Besides, 241 cases had fibroadenoma which was the most prevalent diagnosis among all the samples (37.7%) as well as among the benign ones (57%). This lesion had mostly occurred in 20-30 years of age and the mean age at its occurrence was  $27.9 \pm 7.5$  years. Moreover, 109 cases presented with fibrocystic lesions (17% of the whole sample and 25% of the benign cases). In this regard, the mean age of the patients was  $36.7 \pm 10.8$  years. Finally, inflammatory lesions were detected in 39 cases, accounting for 6.1% of all the samples and 8% of the benign ones. The mean age of the patients with inflammatory lesions was  $37.4 \pm 10.1$  years. The inflammatory lesions were mostly in the form of mastitis. Besides, two cases of mastitis (0.3%) were granulomatous and had occurred in non-menopausal women.

Among the study population, 181 samples (28.2%) were identified as malignant (Tables 1 and 2). Out of these samples, 174 ones (27% of the total population and 96% of the malignant cases) were invasive and had occurred within 40-50 years of age, with the mean age at occurrence being  $48.8 \pm 8.7$  years. The rest of malignant samples were in situ, with the mean age at occurrence being  $47.1 \pm 6.4$  years.

According to the results, menopausal women comprised 15.2% of the total population (97 patients), 6.5% of the benign cases (30 patients), and 37% of the malignant cases (67 patients), and the differences were statistically significant (Table 3). On the other hand, 79% of the premenopausal women were diagnosed with benign and inflammatory cysts, while fibroadenoma was the most prevalent diagnosis in this group (42.7%). Moreover, the number of cases with carcinoma in situ was lower among the menopausal women compared to the non-menopausal ones (1 case (1.5%) vs. 6 cases (5.2%)). Among the menopausal women, malignancy was the most common diagnosis. Furthermore, ductal carcinoma was

the most prevalent malignancy in both menopausal and non-menopausal women (97% and 86.2%, respectively). Among the malignant tumors, lymph nodes were involved in 37.2% of the samples. This measure was 25.6% in menopausal women and 44.2% in non-menopausal ones, and the difference was statistically significant (Table 3). Furthermore, the malignant masses were 0.5-7.3 cm, with

**Table 1. Distribution and Pattern of Breast Diseases**

Variables	Frequency (% of total)	% of Diagnosis Category	Mean of age $\pm$ SD
<b>Menopausal status</b>			
Menopause	97 (15.2)		56.3 $\pm$ 5.2
Pre-Menopause	543 (84.4)		37.0 $\pm$ 9.8
<b>Diagnosis</b>			
<b>Inflammatory lesions</b>			
a) Mastitis	23 (5.0)	58	38.5 $\pm$ 9.9
b) Abscess	3 (0.4)	7	44.6 $\pm$ 14.5
c) Ectasia	1 (0.1)	2	
d) Other	12 (1.8)	30.7	46.3 $\pm$ 13.5
Total	39 (6.1)	100	37.4 $\pm$ 10.1
<b>Benign</b>			
a) Fibro adenoma	241 (37.7)	57	27.9 $\pm$ 7.5
b) Fibrocystic	109 (17.0)	25	36.7 $\pm$ 10.8
c) Cyst	12 (1.9)	2.8	40.6 $\pm$ 8.3
d) Other	58 (9.1)	13.8	39.7 $\pm$ 10.9
Total	420 (65.6)	100	36.4 $\pm$ 10.6
<b>Malignant (carcinomas)</b>			
a) Invasive ductal	163 (89.5)	90	49.0 $\pm$ 8.9
b) Invasive lobular	11 (1.7)	6	47.3 $\pm$ 7
b) In situ	7 (1.0)	3.8	47.1 $\pm$ 6.4
Total	181 (28.2)	100	48.9 $\pm$ 8.7
Lymph node Involvement	67 (10.5)	37.2	47.6 $\pm$ 8.4
Total Breast diseases	640 (100)	-----	39.9 $\pm$ 11.5

**Table 2. Age Distribution of Breast Diseases**

Variables	Age in years						Total
	10-20	20-30	30-40	40-50	50-60	60-70	
<b>Inflammatory lesions</b>							
a) Mastitis	1	5	6	9	2	0	23
b) Abscess	0	1	0	1	1	0	3
c) Ectasia	0	0	0	1	0	0	1
d) Other	1	3	6	2	0	0	12
Total	2	9	12	13	3	0	39
<b>Benign</b>							
a) Fibro adenoma	12	103	61	49	13	3	241
b) Fibrocystic	4	20	31	42	11	1	109
c) Cyst	0	2	3	6	1	0	12
d) Other	2	12	15	22	6	1	58
Total	18	137	110	119	33	5	420
<b>Malignant</b>							
a) Invasive ductal	0	2	29	60	55	17	163
b) Invasive lobular	0	0	3	5	2	1	11
b) In situ	0	0	1	5	1	0	7
Total	0	2	23	70	58	18	181
Total breast diseases	20	148	155	202	92	23	640
Lymph node involvement	0	0	14	29	18	5	67

**Table 3. Frequency of Benign and Malignant Diagnoses and Lymph Node Involvement with Respect to Menopause**

	Pre-Menopause Frequency (%)	Menopause Frequency (%)	p-value
Benign&Inflammatory lesions	(79) 429	(30.9)30	<0.0001
Malignan lesions	(21) 114	(69.1)67	
Total	(100)543	(100)97	
Lymph node not involved	(74.6)50	(55.8)63	0.01
Lymph node involved	50(44.2)	17(25.6)	
Total	113(100)	67(100)	

the mean size of  $2.4 \pm 1.1$  cm.

## Discussion

Breast disorders comprise nearly 40% of the reasons for women's reference to diagnostic centers and breast masses are the most common complaints among women (Barton et al., 1999). The present study was conducted on 640 samples collected from the women referring to the breast clinic of Shiraz University of Medical Sciences in order to extract and investigate epidemiological data on the prevalence of breast masses. In general, the frequency of benign masses is higher compared to malignant ones (Caleffi et al., 2004; Pollitt and Gateley, 2004; Sirous and EBRAHIMI, 2008; Olu-Eddo and Ugiagbe, 2011). According to the present study 420 (65%), 181 (28.2%), and 39 (6.1%) cases presented with benign, malignant, and inflammatory lesions, respectively, which is consistent with the results of the previous studies (GHASEMZADEH et al., 2008; Kochhar et al., 2013). In addition, most of the masses (57.3%) were detected in the left breast, which is also in agreement with the results of other studies conducted on the issue (Egwuonwu et al., 2009). Moreover, similar to other Asian studies (Khurshid et al., 2013) the most prevalent lesion were fibroadenoma prior to menopause and ductal carcinoma after menopause. This indicates the importance of breast masses, particularly during menopause. The results of the present study showed that fibroadenoma comprised 52% of the benign cases and 37.7% of the whole samples. This lesion had mostly occurred within 20-30 years of age, with the mean age at occurrence being  $27.9 \pm 7.5$  years. This findings was in line with that of other studies (Tiwari and Tiwari; DAHRI et al., 2010). Furthermore, fibroadenoma was most prevalent before menopause, which is corresponding with the results of other studies indicating fibroadenoma as the most common breast mass in young women. (Bock et al., 2005; Khanzada et al., 2009; Taj et al., 2009; Al-Rikabi and Husain, 2012) In general, fibroadenoma and fibrocystic changes are the most prevalent benign breast disorders (Sirous and EBRAHIMI, 2008). In the present study, fibrocystic changes were shown to be the second most frequent breast disorder; such a way that it comprised 25% of the benign cases, with the mean age at occurrence being  $36.7 \pm 10.8$  years. This is also in line with other studies conducted on the issue. Similar to the current study, the one by Chaudhary et al. reported most of the fibrocystic cases in the fifth decade of life (Chaudhary et al., 2003). Other studies, on the other hand, have reported the highest frequency of these cases in the third decade of life (Kamal et al., 2000; Tiwari and Tiwari, 2000; DAHRI et al., 2010). This difference might be due to cultural variables such as knowledge level, fertility variables, breastfeeding methods, consumption of oral contraceptive pills, etc. in different societies. According to the current study results, ductal carcinoma was the most prevalent malignancy during menopause, which is in agreement with the results of the previous studies (Ballard-Barbash, 1994; Franceschi et al., 1996; La Vecchia et al., 1997; Hussain et al., 2005; Aslam et al., 2013). Moreover, the total number of malignant masses was higher among the

menopausal women compared to those in the reproductive ages, which is similar to the results obtained by Mehrabani et al. (Mehrabani et al., 2012). This might result from the protective effects of hormonal cycles against malignancies during the reproductive ages (Bock et al., 2005; Hartmann et al., 2005). In general, fibrocystic changes are highly prevalent. The present study revealed a strong relationship between fibrocystic changes and women's menopausal status; such a way that these changes were more prevalent among the pre-menopausal women compared to the menopausal ones (Tiwari and Tiwari; Guray and Sahin, 2006). It should be noted that fibrocystic changes are lesions without hyperplasia which do not normally increase the risk of malignancies (Schnitt, 2003). In this study, 39% of the diagnoses were benign inflammation and mastitis was the most prevalent type of inflammation, which is consistent with the findings of other studies (Bukhari et al., 2011). Granulomatous mastitis can result from infectious factors such as mycobacterium tuberculosis, non-infectious factors such as sarcoidoses, or external factors such as paraffin and silicon. This lesion mostly occurs prior to menopause and its prevalence has been reported to be 3-4% in undeveloped countries and below 0.1% in developed ones. In the present study, two mastitis cases (0.3%) were granulomatous and both were detected in non-menopausal women. These findings were in accordance with other previous studies (Tiwari and Tiwari; Aslam et al., 2013).

The findings of the present study in consistent with other studies (Fouladi et al., 2012; Kadivar et al., 2012; Khokher et al., 2012; Afsharfard et al., 2013; Kotepui and Chupeerach, 2013) demonstrated that ductal carcinoma was the most prevalent malignancy in both menopausal and non-menopausal women (97% and 86.2%, respectively) and the rate of malignant masses was higher in menopausal women. This can be justified by the fact that the menopausal women's mean age is normally high and above 50-year-old ages are directly associated with the incidence of breast malignancies in women (Otu, 1990; Jemal et al., 2011). This can also result from increased consumption of estrogenic hormones after menopause (Heiss et al., 2008). However, controversies still exist in this regard (Wrensch et al., 2003). Overall, regular examinations with appropriate intervals are recommended to be performed particularly for the women above 50 years old and the menopausal women with suspicious findings. One of the limitations of the present study was the insufficient information in the patients' electronic medical records which led to exclusion of the incomplete cases from the research. Another limitation of the study was its cross-sectional design. This study did not include all the population of Shiraz. In addition, since Shiraz University of Medical Sciences is a major referral center in south of Iran, the population under study might not be representative of all the population living in Shiraz.

In conclusion, according to the study results, most of the masses were benign before menopause, but malignant after that. Considering the fact that most women refer to clinics due to breast complaints, clinical breast examination should be considered as a priority, regular examinations should be carried out, and mammographic

follow-ups should be conducted during menopause. Moreover, a national organized program should be designed for screening breast disorders.

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