

# Comparison of mammography findings in women referred to breast pain and those referring for breast screening to hospital associated with cancer

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## SUMMARY

**Background:** Breast cancer is one of the most common cancers and the second leading cause of death after cardiovascular disease and breast pain is a common breast complains that affects a large number of women in reproductive age. In addition to the fear of cancer, it causes frequent medical referrals and disruptions occupational, social, and family activities. The aim of this study was to compare mammography findings in two groups of patients with breast pain and natural examination, and those referring to Imam Reza Hospital, Birjand during 2016-2017.

**Methods:** In this cross-sectional descriptive study, 400 women over 40 years of age complaining of breast pain were examined over a period of one year by a general practitioner. A total of 386 patients were evaluated for routine breast cancer screening (control group) who were matched to the case group for age, marital status, age of menarche, age of first pregnancy and number of children. They were selected through convenience sampling and entered the study. All mammograms were performed by a radiology technician. Data were analyzed by SPSS 15 software using Chi-square and Fisher exact tests.

**Results:** Our results demonstrated benign lesions in 39.4% of women in breast pain group and 42.2% of women in screening group. Findings also showed suspected lesions in 1% of women in breast pain group and 1.3% of women in screening group ( $p=0.45$ ). Mammography findings revealed benign lesions in 51.2% of women in breast pain group and 32.6% of women in screening group based on the in IUD prevention method. The frequency distribution of mammography findings in women in the two groups was not significantly different regarding contraceptive methods (ampoules, tubectomy, condoms and normal). In addition, the frequency distribution of mammography findings in women in both groups was not significantly different in terms of menarche age and menopause ( $p>0.05$ ).

**Conclusion:** According to the results of the present study, breast pain can rarely be a symptom of breast cancer, associated with various factors.

**Key words:** breast pain, screening, mammography findings, natural examination

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## INTRODUCTION

Breast cancer is one of the most common cancers and the second leading cause of death after cardiovascular disease [1]. It accounts for about 33% of all types of cancer in women, with prevalence ranging from 8% to 10% in the general population worldwide. Its incidence in Iran is reported to be 31 per 100,000 women, as indicated to be high in age group between 42 and 49 years [2,3]. Prevention of this disease seems almost impossible due to unknown factors. Therefore, early detection and diagnosis is one of the essential factors in the treatment of this disease so that early diagnosis can lead to 85% chance of survival [4]. Timely diagnosis strategies include awareness of early signs and symptoms, breast self-exam, clinical screening by a physician, and mammography [5]. Mammography is the most effective method for diagnosis of breast cancer with an accuracy of about 97-83% depending on the patient's age and is the only method capable of detecting microcalcifications that has reduced mortality rates by up to 25% [6]. Mammography is far more accurate than clinical examinations in the early detection of Occult primary tumor (before reaching 5 mm), therefore, current guidelines recommend screening women over 40 years of age [7]. However, many women still refrain from doing mammography courses and are less likely to refer to mammography [8] and those referred to health care centers for mammography are due to breast pain [9]. In a study by Yousefi et al. it has been reported that 54.3% of the study population referred for breast pain and only 15.3% for breast cancer screening [10]. Kaviani

reported the causes of breast pain (32%) in a study of 1442 patients referred to the breast clinic [11]. Mastalgia or breast pain is one of the most common and important clinical symptoms of breast cancer [12], accounting for 50% to 70% of cases referred to breast clinics [13]. Most women experience breast pain during their reproductive years [14]. This unpleasant experience results in frequent visits to health care centers for fear of breast cancer, and sometimes these pains lead to unnecessary treatments [9]. The severity of the pain varies from a breast heaviness to severe pain [14], therefore, they may even avoid exercise, sexual activity, or having a close relationship with others because of breast pain, which may contribute to lower quality of life [9]. Various factors such as psychological factors, nutrition, elevated levels of unsaturated fatty acids, increased receptors sensitivity, water retention, inflammatory cytokines, hormonal factors (e.g. high estrogen levels, low progesterone levels, increased estrogen/progesterone imbalance, increased prolactin levels) are some of the causes that can stimulate breast tissue and cause breast pain [15,16]. Studies have also shown associations between breast pain and psychological symptoms such as depression, anxiety, and physical reaction [17,18]. Breast pain appears to be exacerbated by irregular menstrual cycles, and is more likely to occur when exogenous ovarian hormones are administered during or after menopause [19]. In addition, fibrocystic changes may also cause breast pain [14]. Patients with breast pain are often more concerned about being diagnosed with a malignant condition such as breast cancer. Evaluation of a patient with breast pain first needs to rule out malignancy. Many patients with breast pain undergo ultrasound and mammography [20]. Tumyan et al. reported that 95% of mammography and sonographic findings were normal in 86 patients with localized breast pain, where the negative predictive value of sonography and mammography in patients with localized breast pain was determined as 100%. Therefore negative sonography and mammography are reassuring and follow-up is recommended only if clinical examination is normal [21]. However, there is a 5 to 10% false-negative probability, so mammography cannot be substituted for patient examinations [22].

After rejecting major illnesses with evaluations, most patients recover with confidence [20]. In many patients, reassurance from a physician after a careful assessment of the absence of breast cancer is sufficient for treatment and other therapies may be required only for a small percentage of patients [23]. Given the high prevalence of breast pain in women and the consequences of this pain on quality of life and their unnecessary referral for mammography by physicians and the high false positive rate of these women, a study is needed to investigate mammographic findings in women with breast pain.

The aim of this study was to compare mammography findings in two groups of patients with breast pain and natural examination, and those referring to Imam Reza Hospital, Birjand for one year.

## MATERIALS AND METHODS

In this cross-sectional descriptive study, 400 women over 40 years of age complaining of breast pain were examined over a period of one year by a general practitioner who referred to Imam Reza Hospital in Birjand (>5 days). Their severity was assessed using the Visual Analog Scale (VAS). Furthermore, 401 people were selected by convenience sampling from among those who had pain intensity of 5 and above. Then, 386 women were selected for routine screening of breast cancer in this period and were considered as control group. The control group was matched for age, marital status, age of menarche, age at first pregnancy and number of children.

Inclusion criteria included over 40 years old, no symptoms of breast cancer in clinical examination by GP, willingness to participate in study and pain intensity 5 and above based on VAS.

Exclusion criteria included abnormal nipple discharge, Saggy breasts in comparison with age, breast asymmetry, nipple asymmetry, palpate breasts, mass in the lymph nodes of the neck and armpits, and having other indications of diagnostic mammography for breast cancer. Sample size was calculated to be 382 according to the following formula: (natural finding: 55% and benignant lesions

and mass: 45% in mammographic results) based on the study by Nizadeh et al. [23].

Study goals were explained to patients and individuals were encouraged to participate in the study and they were assured that their personal information would remain confidential. Then, mammography were performed by a radiology technician. Data were collected using a two-part questionnaire. The first part consisted of socio-demographic characteristics, midwifery (age, occupation, height and weight (BMI), marital status, infertility history, menarche age, age of menopause, age of first pregnancy, method of contraception and number of children) and second part of the questionnaire was related to mammography. Mammography was performed at Imam Reza Hospital Birjand and interpretation was performed by a skilled radiologist based on the standard mammography report (BIRADS reporting system). The system is graded and interpreted as follows:

A) The evaluation is incomplete:

Grade zero: Complementary evaluations may be required, which may include comparing mammography with previous mammography, with or without ultrasound.

B) The evaluation is complete:

Class 1) Negative: Breasts were symmetrical without mass or suspicious findings.

Class 2) Benign lesions: Like grade 1, the assessment is normal and there is no evidence of malignant changes. The radiologist may have described evidence of benign fibroadenoma, lipoma, cysts, galactocellus, hamartoma.

Class 3) Possible Benign Lesions: The risk of malignancy is 2% or less, and given the very high probability of benign, regular follow-up is recommended.

Class 4) Suspected lesions: The risk of malignancy is 2 to 95%. This class is divided into three subgroups 4A (malignancy >2% and <10%), 4B (between 10% to 50%), 4C (between 50% and 95%), biopsy is recommended because of the probability of malignancy.

Class 5) malignant lesions proven by non-surgical biopsy.

Data were analyzed by SPSS 15 software using Chi-square and Fisher exact tests. A p-value <0.05 was statistically considered as significant.

## RESULTS

In the present study, 401 (51%) of women were examined for breast pain and 386 (49%) for routine breast cancer screening. The findings showed mammography class 2 (benign lesions) in 39.4% of women in breast pain group and 42.2% of women in screening group. Findings also showed class 4 (suspected lesions) in 1% of women in breast pain group and 1.3% of women in screening group but these differences were not statistically significant (p=0.45).

In the menarche age of 14 years, the relative frequency of class 1 was significantly higher in women with breast pain (34.5%) as compared to women in screening group (22%), (p=0.03), but no significant difference was found between menarche and menopause age (p>0.05; Table 1 and Table 2).

**Tab. 1.** Comparison of the relative frequency of mammography findings in women in the two study groups by age of menarche

Age of menarche	Category Group	1 Number (%)	2 Number (%)	3 Number (%)	4* Number (%)
13 years and under	Breast Pain (n=127)	28 (22)	52 (40/9)	45 (35/4)	(1/6) 2
	Screening (n=117)	27 (23/1)	46 (39/3)	38 (32/5)	(1/7) 2
	$\chi^2$ test p-value	0/85	0/80	0/63	1/00
14 Years	Breast Pain (n=119)	41 (34/4)	47 (39/5)	27 (22/7)	(0/8) 1
	Screening (n=118)	26 (22)	59 (50)	27 (22/9)	(0/8) 1
	$\chi^2$ test p-value	0/03	0/10	0/97	1/00
15 years	Breast Pain (n=71)	22 (31)	26 (36/6)	19 (26/8)	(0) 0
	Screening (n=76)	21 (27/6)	28 (36/8)	24 (31/6)	(2/6) 2
	$\chi^2$ test p-value	0/66	0/98	0/52	0/50
16 years and more	Breast Pain (n=84)	24 (28/6)	33 (39/3)	25 (29/8)	(1/2) 1
	Screening (n=75)	24 (24)	40 (40)	32 (32)	(0) 0
		18	30	24	(0) 0

$\chi^2$ test p-value		0/51	0/93	0/76	1/00
Fisher Exact Test*					

**Tab. 2.** Comparison of the relative frequency of mammography findings in women in the two study groups based on the age of menopause

Age of menopause	Category	1 Number (%)	2 Number (%)	3 Number (%)	4* Number (%)
No menopause	Breast pain (n=264)	(26/5) 70	(41/7) 110	(30/3) 80	(0/8) 2
	Screening (n=242)	(23/6) 57	(40/5) 98	(31) 75	(1/2) 3
p-value $\chi^2$ test		0/44	0/79	0/87	0/67
Less than 45 years	Breast pain (n=27)	(40/7) 11	(25/9) 7	(29/6) 8	-
	Screening (n=34)	(20/6) 7	(50) 17	(29/4) 10	-
p-value $\chi^2$ test		0/09	0/06	0/99	-
45-50 years	Breast pain (n=62)	(29) 18	(37/1) 23	(25/8) 16	(1/6) 1
	Screening (n=74)	(24/3) 18	(43/2) 32	(29/7) 22	(0) 0
p-value $\chi^2$ test		0/54	0/47	0/61	0/46
More than 50 years	Breast pain (n=48)	(33/3) 16	(37/5) 18	(25) 12	(2/1) 1
	Screening (n=36)	(27/8) 10	(44/4) 16	(16/7) 6	(5/6) 2
p-value $\chi^2$ test		0/59	0/52	0/36	0/57
Fisher Exact Test*					

In people with IUD contraception, the relative frequency of class 3 in screening group (39.1%) was significantly higher than women in breast pain group (17.1%) (p=0.02), but the relative frequency of other mammography findings were not significantly different in women of both groups by method of contraception (p>0.05; Table 3).

**Tab. 3.** Comparison of the relative frequency of mammography findings in women in the two study groups based on the contraceptive method

Contraceptive Method	Category	1 Number (%)	2 Number (%)	3 Number (%)	4* Number (%)
No contraceptive	Breast pain (n=146)	(28/8) 42	(34/2) 50	(32/9) 48	(2/1) 3
	Screening	(25) 34	(44/1) 60	(28/7) 39	(0/7) 1

	(n=136)				
p-value $\chi^2$ test		0/48	0/09	0/45	0/62
Tablets and ampoules	Breast pain (n=108)	(31/5) 34	(40/7) 44	(25/9) 28	(0) 0
	Screening (n=124)	(21/8) 27	(46) 57	(26/6) 33	(2/4) 3
p-value $\chi^2$ test		0/09	0/42	0/91	0/25
Tubectomy	Breast pain (n=22)	(9/1) 2	(40/9) 9	(45/5) 10	(0) 0
	Screening (n=9)	(22/2) 2	(22/2) 2	(44/4) 4	(11/1) 1
p-value $\chi^2$ test		0/32	0/32	0/96	0/29
condom	Breast pain (n=62)	(32/3) 20	(38/7) 24	(29) 18	-
	Screening (n=52)	(25) 13	(46/2) 24	(23/1) 12	-
p-value $\chi^2$ test		0/40	0/42	0/47	-
Normal	Breast pain (n=22)	(18/2) 4	(45/5) 10	(22/7) 5	(4/5) 1
	Screening (n=19)	(26/3) 5	(26/3) 5	(36/8) 7	(0) 0
p-value $\chi^2$ test		0/53	0/21	0/32	1/00
IUD	Breast pain (n=41)	(31/7) 13	(51/2) 21	(17/1) 7	-
	Screening (n=46)	(23/9) 11	(32/6) 15	(39/1) 18	-
p-value $\chi^2$ test		0/42	0/08	0/02	-
Fisher Exact Test*					

## DISCUSSION

The results of this study showed that 401 (51%) of the women were examined for breast pain and 386 (49%) for routine breast cancer screening. The findings revealed mammography class 2 (benign lesions) in 39.4% of women in breast pain group and 42.2% of women in screening group, followed by class 4 (suspected lesions) in 1% of women in breast pain group and 1.3% of women in screening group, however, these differences were not found to be statistically significant (p=0.45).

Tumyan et al. (2005) reported that 95% of mammograms and ultrasound findings were normal or benign in 86 patients with localized breast pain [21]. Sina et al. evaluated the results of 1004 mammograms performed at Imam Khomeini Medical Center, of which 15.4% had mass, 56% of which were benign, 7% malignant and the rest were non-tumoral. [24]. In Pakistan, a study examined 207 women referred to the

Mammography and Ultrasound Center of Aga Khan Hospital in Karachi due to localized and diffuse breast pain, in which 62% of women reported with benign findings [25].

Another study conducted by Naz et al. on women aged 15-65 in 2010 to evaluate usefulness of breast imaging in patients with breast pain. Of the 175 participated women in the study, 24.5% had benign masses [26], which was similar to benign lesions in the present study. The lesions were found to be benign lesions as was seen in the present study.

According to the results of this study, it can be stated that mastalgia or breast pain is one of the common clinical symptoms. Breast pain is the most common complaint associated with breast in primary care clinics and fear of breast cancer is a major cause of referral [23]. Sometimes the severity of pain can disrupt daily activities. Pain leads to frequent referrals to health care centers for counseling [9]. Yousefi et al. showed that 54.3% of the study population referred for breast pain and only 15.3% for breast cancer screening [10]. Kaviani indicated that, the reasons for referring patients were breast pain (32%) and mammary mass (24%), respectively [11].

In the present study, among 401 patients with breast pain and 386 with routine screening for breast cancer, mammographic findings showed benign lesions, but these differences were not statistically significant. Therefore, breast pain can rarely be a symptom of breast cancer and can be caused by a variety of factors. Although breast cancer worries and fears are more common in people with recurrent breast pain, but breast pain is rarely a symptom of breast cancer [27]. The results indicate that breast pain is usually originated from a member of the body and is rarely a symptom of breast cancer, and only 5.4% of patients with breast cancer presented pain [20].

The causes of breast pain are unclear, but causes such as increased estrogen levels, decreased progesterone, and an estrogen-progesterone ratio imbalance can be indicated [28]. Mammary tissue receptors are more susceptible to hormonal stimulation due to increased fatty acid ratio, according to theories in breast pain.

Therefore, changes in the ratio of fatty acids in the bloodstream through diet, dietary supplements and medications can affect breast pain. Breast pain interference with sexual, physical and social activities, work and school has also been reported [29].

Mirghoforvand et al. [30] demonstrated that there was a positive and significant relationship between duration and severity of mastalgia with anxiety. Other study reported a relationship between breast pain and psychological symptoms such as depression, anxiety, and physical reaction [31]. It has been indicated that postulated mechanisms are changed ratios of fatty acid esters, increased basal prolactin, elevated prolactin response to stimulation, and high dietary fat [32]. In addition, breast pain appears to be exacerbated by irregular menstrual cycles, and is more likely to occur when exogenous ovarian hormones are administered during or after menopause [19], which may also cause fibrocystic changes in the breast [14]. The results of this study also showed that the frequency distribution of mammographic findings was significantly different between the two groups of breast pain and screening by IUD prevention method ( $p=0.05$ ). Mammography findings revealed class 2 in 51.2% of women in breast pain group and 32.6% of women in screening group based on the in IUD prevention method.

But the frequency distribution of mammography findings in women in the two groups was not significantly different regarding contraceptive methods (ampoules, tubectomy, condoms and normal). In addition, the frequency distribution of mammography findings in women in both groups was not significantly different in terms of menarche age and menopause ( $p>0.05$ ).

Kaviani et al. showed that contraceptive pills were significantly more common in people with breast pain [11], which is inconsistent with the results of the present study.

## CONCLUSION

Based on the results presented herein, it can be concluded that breast pain is rarely a symptom of breast cancer and can be due to

various factors. Given the role of mammography in the early detection of breast cancer, regular visit for mammography is recommended for women over 40 years of age without regard to pain and ensure that pain alone is not a significant symptom of breast cancer.

## CONFLICT OF INTEREST

None.

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