

Impact of social and clinical factors on diagnostic delay of breast cancer

A Cross-sectional Study

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Abstract

One of the reasons for high mortality of breast cancer is long delay in seeking medical care. This study was designed to measure the association of a wide range of socio-demographic and clinical factors with the diagnostic delay in breast cancer among Iranian patients.

This study was conducted on 505 newly diagnosed patients with breast cancer from southern part of Iran. Medical files of the patients who were admitted to the hospital from November 2013 to May 2015 were examined and clinical and demographic information were extracted.

According to the results, illiterate patients were diagnosed on average 87.42 days later compared with those with a college degree (95%CI: 29.68–145.16, $P=0.003$) and those from rural area were diagnosed on average 72.48 days later (95%CI: 35.94–109.03, $P=0.001$) compared with urban residences. Single women were diagnosed 65.99 days later (95%CI: 7.37–124.61, $P=0.02$) compared with those married. Lobular or medullary types of cancer were diagnosed 65.19 days later (95%CI: 2.67–127.70, $P=0.04$) compared with ductal type. On the other hand, those who were able to perform breast self-exam were diagnosed 49.07 days earlier compared with others (95%CI: 18.69–79.45, $P=0.002$). Those felt lump as the initiating symptom were diagnosed 62.01 days earlier, (95%CI: 8.17–115.85, $P=0.02$) compared with those with other initial symptoms. The only factor associated with doctors diagnosis delay was the place of residence as rural residences were diagnosed on average 87.42 days later compared with urban residences, (95%CI: 53.82–121.92, $P=0.001$).

Higher education, living in cities, ductal type of tumor, and noticing lump in breast were the most important demographic and clinical factors associated with shorter breast cancer diagnosis delay. Informing women and doctors, especially general physicians who are practicing in rural areas, of the common symptoms of breast cancer as well as training women to perform breast self-examination are effective measures in reducing breast cancer diagnosis delay. Providing accessible and effective diagnosis services to rural women reduces diagnosis delay in rural patients.

Abbreviations: BC = breast cancer, 95%CI = 95% confidence interval, OR = odds ratio, SD = standard deviation, TNM = tumor node metastasis.

Keywords: breast cancer, diagnostic delay, related factors

1. Introduction

Although the mortality of breast cancer is generally decreasing in both developed and developing countries, the disease is still the

most common cause of death due to cancer among women.^[1] In Iran, breast cancer is the most common malignancy among women and is relatively more common among Iranian women at younger age.^[2,3] One of the reasons for high mortality of breast cancer in developed and developing countries is long delay in seeking medical care.^[4] In addition to the lack of routine population-based screening programs, poor awareness about the symptoms, high cost, and limited access to diagnosis or treatment services are also among factors contributing to the longer delay in the diagnosis of breast cancer in women especially in low and middle-income countries.^[5,6] As the result, the World Health Organization has recommended routine mammography screening for women and early detection of symptoms among symptomatic patients as two major strategies for on time diagnosis and better prognosis of the patients.^[7] Despite all efforts, the delay in the diagnosis of breast cancer remains considerable.^[8]

Breast cancer diagnostic delay is defined as the interval between the date that patients noticed the first symptom attributable to the disease until the date that histological diagnosis is made.^[9] The diagnostic delay in breast cancer is associated with clinically important issues including late-stage of disease, bigger size of tumor, more aggressive interventions and, as the result, a reduced chance of survival.^[10,11] A clinically

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significant delay in breast cancer is defined as 3 months or longer delay in diagnosis which is associated with deteriorated prognosis.^[7] The delay in diagnosis is divided into patient's delay and medical services provider's delay (doctor delay).^[12] Patient's delay is defined as the time interval between the appearance of first symptom and seeking the first medical visit. The provider delay is defined as the interval between the first medical visit and the final diagnosis of the disease.^[13] Studies of legal cases suggested that patients with breast cancer who took legal actions against their doctor due to the delay in the diagnosis of their disease, were generally younger, more often had normal results of mammography and were diagnosed at stage II or above.^[13] The problem with the delay in diagnosis is so serious that nearly one-third of the patients with breast cancer are diagnosed so late that at the time of diagnosis the cancer has reached to regional or distant stage.^[9] In Iran, not only no systematic screening or mass education programs are implemented to achieve early detection of breast cancer, but also no defined plan has been yet approved in this regard.^[14] As a result, about 70% of Iranian women with breast cancer are diagnosed at late-stage.^[15]

It is believed that several demographic, social, and clinical factors (e.g., age, education, job, and medical care) affect diagnostic delay in breast cancer.^[16,17] As the above factors and their associations with diagnosis delay are highly culture and region dependent, better understanding the causal action of the factors and reducing diagnostic delay need studying a wider range of possible contributing factors with a regional view.

The aim of this study was to measure the association of a significant number of objective and perceptual factors with the diagnostic delay among Iranian patients with breast cancer.

2. Material and methods

2.1. Settings

This cross-sectional study was conducted on 505 patients with breast cancer from November 2014 to May 2015. The participants were newly diagnosed at Namazi Educational hospital, a referral diagnosis and treatment center for all types of cancer in southern of Iran.

The data were obtained partly from the patients' hospital records and partly from an interview administered questionnaire which was completed during the study period while the patients were visiting the center. Literate patients read and signed informed consent. Verbal consent was obtained from illiterate patients. Ethical approval was obtained from Shiraz University of Medical Sciences ethical committee.

2.2. Sampling:

The study participants included all women who were (newly) diagnosed with breast cancer at Namazi hospital from November 2013 to May 2015. The patients undergone an initial interview to see whether they fulfill the inclusion criteria. A priori sample size calculation was performed in order to detect 15 days difference in diagnosis delay between income groups with a significant level at 5% and 80% power.

2.3. Inclusion and exclusion criteria:

Since this study considered new cases, participants who came with relapse and recurrence of the disease were not included. Patients who could not remember the approximate date of onset of symptoms were also excluded.

2.4. Data collection:

All participants were interviewed by a trained female nurse in a quiet and private place. The questionnaire and interview procedures were evaluated and revised during a pilot study on 50 patients. Accordingly, using test-retest method, the questioner's reliability was estimated to be good (Cronbach alpha=0.76).

Data on age, education, income and marital status, place of residence, self-reported date and type of initial sign and symptom of breast cancer noticed by the patients, family history of breast cancer, age at first childbirth, previous breast problems, and the status of knowledge and regular practice of breast self-examination were obtained during an interview using a face-to-face questionnaire. Information on the date of pathology report and type of tumor were obtained from the medical file of the patients. A pathologist defined the stage of cancer based on tumor-node-metastasis (TNM) category. Type of tumor was categorized as ductal or lobular-medullary carcinoma.

Patient and her husband's occupation, education, and income status were also defined during the interview.

Delay time (day) was the primary outcome which was defined as the interval between the date that patient noticed the first symptom attributable to breast cancer until the date that pathology report was issued. The main reason for the delay in diagnosis was also reported by the participants. The reasons for delay, reported by the patients, were divided into two categories: patient delay (defined as the time between the date at which the first symptom of breast cancer was noticed to the date at which the patient sought medical care) which included reasons such as ignorance or non-affordable costs of medical services; and doctor delay (defined as the time between the date at which the first visit to a doctor was established to the date at which the pathology report was issued) which included reasons such as misdiagnosis or other related problems caused by medical service providers.

2.5. Statistical analysis:

To impose the clinical importance of diagnostic delay in bivariate analysis, the delay time was categorized to less or equal (no diagnostic delay) or longer (diagnostic delay) than 3 months.^[17] The analysis was first conducted to measure un-adjusted associations of all study variables with the diagnostic delay (as a binary variable using Chi-square test). Multivariate linear regression with stepwise forward selection strategy was applied as the main approach to measure adjusted associations of diagnostic delay (as a scale variable) with other study variables. The assumptions of normality of the residuals distribution and multicollinearity were assessed during the model fitting process after excluding those diagnosed via self-referral mammography screening and those with residual outliers. Multivariate logistic regression was performed with stepwise forward selection strategy to identify factors associated with the chance of longer than 3 months delay in the diagnosis of breast cancer. Statistical analysis was conducted assuming two-sided 5% level of significance. STATA (STATA Corp. version 12) package was used for analysis the data.

3. Results

Among 505 women with breast cancer who participated in this study, 135 (26.7%) were younger than 40 years of age. The patients were on average 47.77 (SD=10.65) years old. Overall, 187 (37.0%) of patients had minimal or no formal education, 465 (92.1%) were married and 191 (37.8%) had poor economic

status. Of all patients, 118 (23.4%) had more than 90 days delay in the diagnosis of breast cancer. Among the respondents who answered the question: “what was the main reason for delay in the diagnosis of your disease”, 36.2% reported misdiagnosis by their physician as the main reason.

The mean time of delay for those reported themselves or their physicians as responsible for delay were 146 (SD=188.08) and 120 (SD=190.55) days, respectively.

Table 1 shows the distribution of the study variables according to diagnosis delay.

Table 2 shows the results of multiple regression analysis. It is to be noted that those patients who were diagnosed through self-referral mammography were not included in the analysis ($n=35$). Results from multiple regression analysis suggested that after controlling for the effect of other study variables, place of residence (patients from rural area were diagnosed on average 72.48 days later compared with those from urban areas, 95%CI: 35.94–109.03, $P=0.001$), educational status (illiterate patients were diagnosed on average 87.42 days later compared with those with a college degree, 95%CI: 29.68–145.16, $P=0.003$), type of tumor (those diagnosed with medullary-lobular type of tumor were diagnosed 65.19 days later compared with those with ductal tumor, 95%CI: 2.67–127.70, $P=0.04$). Also single participants were diagnosed on average 65.99 days later compared with married patients (95%CI: 7.37–124.61, $P=0.02$).

Multiple regression analysis also suggested that, among those who put the blame of delay on themselves, those from rural areas were diagnosed 49.47 days later compared with those who were living in cities (95%CI: 15.77–83.16, $P=0.004$). Moreover, illiterate and single patients were diagnosed on average 43.45 and 66.46 days later than those with a college degree (95%CI: 0.41–96.12, $P=0.04$) or those married (CI: 16.62–116.30, 95%, $P=0.009$), respectively. Compared with other symptoms, feeling lump as the initial symptom of the disease was associated with 62.01 days longer delay (95%CI: 8.17–115.85, $P=0.02$). On the other hand, compared with those without knowledge, those with knowledge about breast self-examination were diagnosed 49.07 days earlier (95%CI: 18.69–79.45, $P=0.002$).

Among those who blamed their physician, the only factor associated with delay was the place of residence. Accordingly, patients from rural areas were diagnosed with breast cancer 87.42 days later compared with those from urban areas (95%CI: 53.82–121.92, $P=0.001$).

The results of logistic regression analysis on delay as a binomial outcome variable (less or equal to 3 months or more than 3 months) are presented in Table 3. Multivariate analysis indicates that place of residence ($OR_{\text{rural/urban}}=1.20$, 95%CI: 1.11–1.37, $P=0.001$), age at first childbirth ($OR_{\text{over30/less than 20}}=3.41$, 95%CI: 1.58–7.34, $P=0.002$), and history of breast problem ($OR_{\text{yes/no}}=2.37$, 95%CI: 1.21–4.65, $P=0.01$) are possible predictors of clinically significant delay in the diagnosis of breast cancer.

4. Discussion

As was mentioned in the results section, about 36% of patients who provided the main reason for the delay in the diagnosis of their disease, reported misdiagnosis as the main reason and about 23% of the patients reported a significant delay (>3 months) in the diagnosis of breast cancer. The diagnosis delay in the study population is longer than those reported from the UK (19%), Thailand (17%), and Germany (17.4%).^[17–19] These findings represent significant differences in the medical, cultural, or economic issues among women from the above countries and

Iran. Few studies reported a significant and direct association between delay in diagnosis and age of the patients.^[19,20] Present study found suggestive but non-significant longer diagnosis delay among older women. It is suggested that older women may attribute early symptoms of breast cancer to the impairs caused by ageing and menopause.^[21] Place of residence, education, type of tumor, and marital status, seems to be other predictors of delay in diagnosis of breast cancer. The longer delay in doctor's diagnosis among patients from rural area is remarkable as it may suggest ruralism discrimination in medical services. Moreover, although in cities required services for cancer diagnosis and treatment are being provided by specialized public and private medical centers, in rural areas only basic health and medical cares are provided by the Iranian ministry of health.^[22–24] As a result, in order to receive the specialized services, that is, mammography or pathology, rural residences have to go to the medical and pathology centers in cities, with a complicated, expensive, and time consuming process. Therefore, rural residences only seek specialized medical services when they are severely ill.^[25] The longer elapse from onset of symptoms to the final diagnosis among those who blamed themselves for the delay in rural area is also justifiable in term of limited geographic access to medical services.^[26] It seems that inequity in the access to specialized medical services in Iran and high cost of the services are important reasons for the delay of diagnosis in the rural women.^[4] Few other studies reported the same results.^[27,28] Studies also suggested that lower income is related to a longer delay in diagnosis of several types of cancer.^[28,29] This means, people who have less income consult their doctor later than others. In the present study, 16% of the participants reported the high cost of diagnosis and medical cares as the main reason for the delay in the diagnosis of their disease. Despite these, no significant association between the delay and family's income was found, suggesting economic status has no significant effect on the timeliness of diagnosis and medical procedures in the study population.

According to the results, higher education is related to less delay.^[16,29] It seems that educated people take more effective and on-time measures toward their health problems in comparison with less-educated individuals.^[30]

The other factor which is related to the delay in diagnosis, is employment.^[31] This study found no significant association between employment and the delay in diagnosis of cancer. This is in contrast to the studies that suggested employment as barrier to delay in the diagnosis of breast cancer.^[17] Employed women, due to their social interaction and higher education, have less cultural barriers to mammography and breast clinical examination.^[16] Employed women also have more knowledge about the symptoms of breast cancer in comparison with unemployed women.^[12] On the other hand, due to the time constraints and fear of diagnosis based on their knowledge, employed women may seek medical help later compared with housekeepers.^[16]

The association between marital status and delay in diagnosis of breast cancer is not universally accepted.^[4,20] In current study, single women experienced more delay in comparison to the married ones. Cultural barriers including being ashamed of breast examination and possibility of more opportunities for lumps in married women to be found (by chance) by their husbands are among reasons which may explain the association; though more data on the issue is needed to make more informed judgment.^[26]

According to the results, tumor type (lobular-medullary or ductal) was the other factor related to overall delay. Women with

Table 1**Characteristics of the study participants (n = 505).**

Factors	<3 months	≥3months	Total (%)	P [*]
	n (%)	n (%)		
Age				
<40	111 (27.8)	24 (22.6)	135 (26.7)	
40–50	118 (29.6)	33 (31.1)	151 (29.9)	
50–60	120 (30.1)	35 (33.1)	155 (30.7)	
>60	50 (12.5)	14 (13.2)	64 (12.7)	0.36
Place of residence				
Rural	77 (19.3)	59 (55.7)	136 (26.9)	
Urban	322 (80.7)	47 (44.3)	369 (73.1)	0.001
Education				
Primary or illiterate	142 (35.6)	45 (42.5)	187 (37.0)	
Middle school	67 (16.8)	32 (30.2)	99 (19.6)	
High school	125 (31.3)	28 (26.4)	153 (30.3)	
College	65 (16.3)	1 (0.9)	66 (13.1)	0.001
Family income				
Poor	142 (35.6)	49 (46.2)	191 (37.8)	
Moderate	141 (35.3)	40 (37.7)	181 (35.9)	
High	116 (29.1)	17 (16.1)	133 (26.3)	0.21
Job				
Household	292 (73.2)	83 (78.3)	375 (74.3)	
Employed	107 (26.8)	23 (21.7)	130 (25.7)	0.28
Marriage status				
Married	375 (94.0)	90 (84.9)	465 (92.1)	
Single	24 (6.0)	16 (15.1)	40 (7.9)	0.002
Age at first childbirth				
<20	177 (44.4)	35 (33.0)	212 (42.0)	
20–30	141 (35.3)	34 (32.1)	175 (34.6)	
>30	34 (8.5)	11 (10.4)	45 (8.9)	
Never married or have no child	47 (11.8)	26 (24.5)	73 (14.5)	0.08
Family history of BC				
No	299 (74.9)	78 (73.6)	377 (74.7)	
Close relative	41 (10.3)	8 (7.5)	49 (9.7)	
Other relative	59 (14.8)	20 (18.9)	79 (15.6)	0.22
History of breast problem				
No	349 (87.5)	80 (75.5)	429 (84.9)	
Yes	50 (12.5)	26 (24.5)	76 (15.1)	0.002
Length of delay in diagnosis (day)				
<30	NA	NA	220 (43.6)	NA
30–89			167 (33.0)	
>90			118 (23.4)	
Type of tumor				
Ductal	337 (84.5)	88 (83.0)	425 (84.2)	
Lobular and medullary	16 (4.0)	13 (12.3)	29 (5.7)	
Missing	46 (11.5)	5 (4.7)	51 (10.1)	0.003 [†]
Aware of self-examination				
No	192 (48.1)	51 (48.1)	243 (48.1)	
Yes	207 (51.9)	55 (51.9)	262 (51.9)	0.012
Practice self-examination				
No	256 (64.2)	67 (63.2)	323 (64.0)	
Yes	143 (35.8)	39 (36.8)	182 (36.0)	0.69
Nature of initial BC symptom [‡]				
Lump	285 (71.4)	72 (67.9)	357 (76.0)	
Discharge—pain	50 (12.5)	19 (17.9)	69 (14.7)	
Other [‡]	64 (16.1)	15 (14.2)	79 (9.3)	0.002
The main reason for delay [†]				
Misdiagnosis by doctor	141 (35.4)	42 (39.6)	183 (36.2)	
My ignorance	61 (15.3)	37 (34.9)	98 (19.0)	
Costs of medical care	52 (13.0)	27 (25.5)	79 (15.7)	
I had no delay	145 (36.3)	0	145 (29.1)	0.02 [§]

BC = breast cancer, NA = not applicable.

^{*} Chi-Square test.[†] According to patient's statement.[‡] Included redness 13 (2.6%), swelling of breast, 17 (3.4%), change in breast shape 26 (5.1%), or size 23 (4.6%).[§] The "I had no delay" group is excluded.

Table 2
Results of multiple linear regression analyses on the delay (day) of diagnosis (N=419).

Variable	Delay all			Patient delay			Doctor delay		
	b	95%CI	P	b	95%CI	P	b	95%CI	P
Place of residence									
Urban	Ref	—	—	Ref	—	—	Ref	—	—
Rural	72.48	35.94, 109.03	0.001	49.47	15.77, 83.16	0.004	87.42	53.82, 121.92	0.001
Educational status									
College	Ref	—	—	Ref	—	—	—	—	—
High school	52.93	-2.59, 108.47	0.06	29.04	-19.03, 77.11	0.23	—	—	—
Secondary	137.03	76.80, 197.26	0.001	56.46	2.56, 110.35	0.02	—	—	—
Primary and illiterate	87.42	29.68, 145.16	0.003	43.45	0.41, 96.12	0.04	—	—	—
Type of tumor									
Ductal	Ref	—	—	Ref	—	—	Ref	—	—
Lobular and medullary	65.19	2.67, 127.70	0.04	28.56	-27.48, 84.61	0.31	40.66	-24.22, 105.54	0.21
Knowledge about self-examination									
No	Ref	—	—	Ref	—	—	—	—	—
Yes	18.87	-15.18, 52.93	0.27	-49.07	-79.45, -18.69	0.002	—	—	—
Marriage status									
Ever married	Ref	—	—	Ref	—	—	Ref	—	—
Single (never married)	65.99	7.37, 124.61	0.02	66.46	16.62, 116.30	0.009	-5.66	-72.58, 61.25	0.86
Type of first symptom									
Lump	Ref	—	—	Ref	—	—	Ref	—	—
Discharge and pain	36.57	-8.35, 81.51	0.11	-27.21	-72.77, 18.33	0.24	45.28	-0.24, 89.93	0.05
Other	-1.68	-57.50, 54.12	0.95	-62.01	-115.85, -8.17	0.02	12.33	-42.62, 67.28	0.65

Thirty five patients were excluded because they were diagnosed with breast cancer after self-referral mammography screening.
 CI=confidence interval.

medullary and lobular tumors in comparison with those with ductal tumors had longer delay. One possible explanation for this finding is the more notifiable signs and symptoms.^[18] Some also believe that the difference in the diagnosis delay of breast cancer between ductal and lobular carcinoma is due to the fact that the latter is more difficult to diagnose.^[19] Moreover, medullary and lobular tumors (because of their nature) have slower rate of growth which can cause more delay as patients don't pay enough and on time attention to the symptoms.^[27,32]

In this study, the awareness about breast self-examination is the other factor related to the delay caused by the patients. In fact women who knew how to conduct breast self-examination, consulted their doctor earlier in comparison to those who not. Our findings are consistent with the results of other studies^[12,28] highlighted the importance of informing women and enabling them at younger age to self-exam their breast.^[26] Noticeably,

among the participants in the present study, only 35 patients were diagnosed following self-referral mammography and about 27% of the participants were below 40 years of age.

Results also suggested that having a history of benign disease of breast is a barrier to faster diagnosis^[12,33] as women who had a history of benign breast problem had longer delay in diagnosis compared with the others. Those with a history of breast problem may think that their current breast problem is also benign and do not require fast response.^[34]

5. Conclusions

The results suggest that patient's education and place of residence are the most important demographic factors affecting delay in diagnosis of breast cancer not only because of cultural issues but also due to medical care disparities. Improving knowledge of women at younger age about the common warning signs and initial symptoms of breast cancer seems to be effective approach to reduce delay in the diagnosis of breast cancer. This can be achieved via training and involving physicians and other health staff, especially general practitioners and providers of primary health care in rural areas. General and specialized practitioners need to be trained to provide more effective and on time diagnosis services to the patients. It also seems beneficial to establish a national breast cancer screening program and to support women in self-referral screening at younger age than what is currently suggested by the Iranian ministry of health (40 years or older).

5.1. Strengths and Limitations

The present study used a wide range of factors that might influence the timeliness of the diagnosis of breast cancer. Looking simultaneously at socio-economic status, knowledge about and performance of breast self-examination and some clinical factors in a relatively large sample of newly diagnosed patients is

Table 3
Summary of the logistic model of the determinants of diagnosis delay (>3 months).

Variable	OR	95%CI	P
Residence			
Urban	1	—	—
Rural	1.2	1.11-1.37	0.001
Age at first childbirth			
<20	1	—	—
20-30	1.86	0.99-3.05	0.051
>30	3.41	1.58-7.34	0.002
History of breast problem			
No	1	—	—
Yes	2.37	1.21-4.65	0.01

N=470, 35 cases were excluded because they were diagnosed with breast cancer after self-referral mammography.
 CI=confidence interval, OR=odds ratio.

remarkable. Recruiting participants visited the biggest referral center in the southern part of Iran makes the results generalizable to the population. Also, in this study we considered patient's perception on why such a delay took place.

The possibility of error in self-reported information is to be noticed as some women may have wrongly reported reason of delay or the type of symptoms or the time which first symptom was noticed. However, previous studies suggested that the information regarding recall and report of delay time and symptoms of breast cancer seem to be fairly precise.^[16,35]

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