REASONS OF PATIENT-RELATED DELAY IN DIAGNOSIS OF BREAST CANCER AMONG WOMEN FROM A DEVELOPING COUNTRY: A MULTI-CENTRE COMPARATIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Background and Objective: Breast cancer (BC) is the most commonly diagnosed cancer among women globally, with developing countries like Pakistan facing significant challenges related to late diagnosis and high mortality rates. A large proportion of Pakistani women present with late-stage BC due to a lack of awareness, cultural barriers, and healthcare accessibility issues. This study aimed to identify patient-related factors contributing to delays in BC diagnosis among women in Lahore, Pakistan.

Methods: A multi-centre comparative cross-sectional study was conducted at two hospitals in Lahore, including public and private healthcare facilities. A total of 208 female BC patients were enrolled using non-probability convenience sampling from June 2023 to December 2023. Data were collected through structured interviews assessing socio-demographic factors, medical history, and healthcare-seeking behaviors. Statistical analyses, including binary logistic regression, were performed to identify predictors of delayed diagnosis, with a p-value of <0.05 considered statistically significant.

Results: The study found that 58.2% of participants experienced a delay in diagnosis of more than three months. Significant predictors of delayed diagnosis included a preference for alternative therapies (AOR=2.49, 95% CI: 1.17–5.29, p=0.018), fear of biopsy spreading cancer (AOR=5.99, 95% CI: 2.70–13.32, p<0.001), and social stigma associated with cancer (AOR=3.67, 95% CI: 1.58–8.48, p=0.002). Additionally, lack of awareness regarding breast self-examinations and screening programs was prevalent among delayed cases.

Conclusion: Patient-related factors such as fear, misconceptions, and cultural stigma play a significant role in delayed BC diagnosis in Pakistan. Targeted public health interventions, awareness campaigns, and culturally sensitive educational programs are critical to promoting early detection and improving BC outcomes in developing countries.

Key Words: Breast Cancer, Diagnostic Delay, Predictors of Delay, Cultural stigma, Misconceptions.

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B reast Cancer (BC) –defined as the abnormal growth of cells in the breast stemming from the milk-producing lobules or milk ducts – is the most common cancer in the world presenting in 12.5% of all cancer diagnoses, and among females specifically, presenting in 25.8% of all cancer diagnoses.¹ Developing countries, such as Pakistan, often unknowingly face the grim effects of breast cancer with these countries having overall lower rates of diagnosis, delayed diagnosis when identified (defined as the patient presenting with stage III/IV at time of diagnosis), and higher incidences of death related to BC.² In consideration of Asia, Pakistan has

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the highest rates of BC with one in every nine females expected to be diagnosed at one point in their lifetime, and among those diagnosed, 59% presented with late-stage BC.^{3,4} Due to insufficient screening techniques in Pakistan as well as an extreme lack of general awareness regarding BC and the respective screening tests, a large majority of the BC cases in Pakistan present with late diagnosis which can contribute to the higher rates of mortality.³ Numerous potential factors have been suggested to be associated with delayed diagnosis of breast cancer including socioeconomic factors, cultural factors, and hospital system relevant factors.⁵ However, this study focuses on the specific patient related factors that contribute to the overwhelming percentage of delayed diagnosis. Patient related delay encompasses both awareness and detection of potential symptoms as well as patient initiative to seek professional healthcare.⁶ Patients often are unable to discern whether or not their symptoms are due to cancer or other external factors such as stress, aging, physical exertion, or other changes and most ignore symptoms such as the initial lump.⁷ Furthermore, concerns regarding potential treatment, shame due to the location of the cancer, fear of being diagnosed with cancer, and other disease related anxieties may prove to discourage the patient from seeking help.⁷ Studies have been conducted regarding the possible reasons for delayed diagnosis among patients in Pakistan, however a majority of said studies have been conducted using data from large for-profit hospitals in populated, urban areas.^{5,8-11} To cover any discrepancies that may arise from data being collected from a certain type of hospital, this study was conducted in three hospitals: government sector, for-profit, Jinnah Hospital and Mayo Hospital, and private sector, non-profit, Hijaz Hospital. This study aims to pinpoint the specific, recurring patient related factors that prevent women in Lahore from obtaining a BC diagnosis timely, regardless of what type of hospital they visit, and the necessary steps that must be taken to relieve the burden of such delays.

METHODS

A cross-sectional study design was utilized for this

study to examine specific factors contributing to late BC presentation at Jinnah Hospital, Lahore, and Hijaz Hospital, Lahore after taking approval from ERB of Allama Iqbal Medical College.. A sample of 208 female patients with BC visiting these hospitals was taken using non-probability convenience sampling from June 2023-December 2023 with a 95% confidence interval, 5% margin of error, and an anticipated frequency of delayed diagnosis of 83.7%. Inclusion criteria was female patients age>18 years presenting with primary BC, confirmed by histopathology. Patients were excluded from study with unreliable data (i.e. those who could not recall accurate information regarding date of presentation to a physician), patients who had not agreed/given consent to participate, patients who could not understand Urdu, Punjabi, or English, patients presenting with co-morbid psychiatric illnesses, patients in the Intensive Care Unit or other high dependency units, and patients with a recurring history of breast cancer. Data collection was done through a standard questionnaire assessing patient demographics as well as medical attention seeking history and tendencies. Patients were selected on the basis of the aforementioned specifications, and, after obtaining written informed consent, were interviewed in person according to the developed questionnaire to assess the various factors that contributed to late diagnosis. The time between the first symptoms noticed by the patient to the first doctor visit was noted. If this time was within three months, no delay was noted; if the time exceeded three months, then delay was noted. The data collected included, the disease profile, patient fears and awareness and socio-demographic features including income and area of residence.

For each categorical variable, frequency distributions with percentages were calculated. Responses on nominal data were tabulated. Numerical data was checked for normality assumption and mean standard deviation was calculated, and difference of means was analyzed using student t-test. We used binary logistic regression method to identify the association between potential factors which may be responsible for patient-related delay in diagnosis. Mostly, we used lowest value as reference for comparison, however, in some variables -- awareness about selfexamination, awareness about screening of cancer, choice for medical consultation-- highest values were used in model. Models were mutually adjusted and Daggity software was used to draw a Directed Acyclic Graph (DAG) to identify potential confounding factors. Models were adjusted for age, educational status, area of residence, consultation choice, health facility type and various fears regarding the disease, such as fear of side effects, fear of social labelling, fear of marriage breakdown, fear of financial burden, and fear of cancer spread by surgery. Adjusted odds ratios with 95% confidence intervals were used to describe predictors of delayed diagnosis. We used omnibus models of coefficients to assess whether models with predictors were improved compared to null model and we found our model to be statistically significant (<0.001). Hosmer-Lameshow test (0.55) indicated that this model has improved predictive ability. Negelkerke R square value of 0.53 showed that our model has the ability to explain 53% of the variation in the delayeddiagnosis variable (dependent variable) based on the independent variables in the model. Our predictor model has the sensitivity and specificity of 84.3% and 70.1% respectively with an accuracy of 78.4%. Chi-Squared analysis was used to assess statistical significance. We used a p-value of <0.05 to describe statistical significance and to judge the null hypotheses.

RESULTS

A total of 233 patients were approached for this study; 19 of which declined to participate, 6 were excluded due to inconsistent or absent data, leaving the remaining 208 as the study population.

Table 1 demonstrates the sociodemographic features of the participants. A large majority of participants presented to public sector hospitals (78.4%) as compared to a private hospital (21.6%). Patients aged over 50 years were less likely to experience delays (47.9%) compared to those aged 50 years or younger (52.1%) (p=0.021). Divorced/Widowed women had a larger percentage of delayed cases (26.4%) as compared to non-delayed cases (13.8%), while married women had a decreased percentage of delayed cases (73.6%) compared to non-delayed Table 2 illustrates clinical characteristics along with medical concerns and perceptions about breast cancer amongst participants.

A substantial difference was observed in the cancer stage at the time of diagnosis between the those presenting with delayed diagnosis and non-delayed diagnosis (p < 0.001). Of the patients presenting with Stage III breast cancer, 55.4% had a delayed diagnosis, and the same pattern was observed for patients presenting with Stage IV with a majority presenting with delay (16.5%) (p<0.001). However, this phenomenon was not seen in patients with Stage I or Stage II breast cancer, as the percentage of delayed cases was less than the percentage of nondelayed cases in both presentations (p<0.001). A majority of patients without delay (77.0%) presented with a painless breast lump as the first symptom, while only 9.1% of those with a delay reported the same (p < 0.001). In contrast, 52.1% of patients with delayed diagnosis reported a lump in both the breast and axilla and only 2.3% of patients without a delayed diagnosis reported the same (p<0.001). Awareness of breast self-examination was significantly higher among those without delays (27.6% vs. 14.9%, p = 0.024), but practice of breast self-examination did not differ significantly between the groups (p = 0.272). A lack of awareness of breast cancer screening was found in those with delayed cases (86.0%, p=0.015); conversely, those aware of breast cancer screening demonstrated fewer delayed cases (27.6% vs 14.0%, p=0.015) Fear of biopsy due to concerns about cancer spreading was significantly higher in the delayed diagnosis group (52.9% vs. 20.7%, p<0.001). Additionally, fear of social stigma related to cancer labeling was notably higher among patients with delayed diagnosis (80.2% vs. 50.6%, p = 0.001). More participants chose alternate therapy as their first choice of medical consultation in delayed cases than non-delayed (41.3% vs 23.0%, p=0.006).

Table 3 showcases the predictors of delay in

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diagnosis among the participants of this study. Patients opting for alternative therapies exhibited a significantly higher likelihood of delay (AOR = 2.49, 95% CI: 1.17-5.29, p = 0.018) compared to those who consulted allopathic medical practitioners. The fear that a biopsy might spread the cancer was found to be a major cause of delay (AOR=5.99, 95% CI: 2.70–13.32, p < 0.001). Fear of social labeling also emerged as a significant factor, with an AOR of 3.67 (95% CI: 1.58–8.48, p = 0.002).

Table 1: Socio-demographic characteristics of breastcancer patients in public and private hospital	ıls
of Lahore, Pakistan (n=208)	

	(<3 r	<u>in diagnosis</u> nonths) 1=87	<u>Delay in</u> <u>diagnosis</u> (≥3 months) n=121		Total n=208			
Characteristics	f	%	f	%	f	%	P *	
Consulting hospital							0.187	
Private sector	13	14.90%	32	26.40%	45	21.60%		
Public sector	74	85.10%	89	73.60%	163	78.40%		
Age							0.021	
\leq 50 years	59	67.80%	63	52.10%	122	58.70%		
>50 years	28	32.20%	58	47.90%	86	41.30%		
Employment status							0.124	
Not Employed	65	74.70%	101	83.50%	166	79.80%		
Employed	22	25.30%	20	16.50%	42	20.20%		
Area of residence								
Rural	35	40.20%	55	45.50%	90	43.30%	0.459	
Urban	52	59.80%	66	54.50%	118	56.70%		
Marital status							0.028	
Married	75	86.20%	89	73.60%	164	78.80%		
Widowed/ Divorced	12	13.80%	32	26.40%	44	21.20%		
Educational Status							0.079	
No formal Schooling	25	28.70%	51	42.10%	76	36.50%		
Completed school	37	42.50%	48	39.70%	85	40.90%		
Completed College/ Uni	25	28.70%	22	18.20%	47	22.60%		
Monthly Income (Rs)							0.178	
\leq 50 K	58	66.70%	91	75.20%	149	71.60%		
>50K	29	33.30%	30	24.80%	59	28.40%		
vistance to nearest health facility							0.02	
\leq 5 km	39	44.80%	74	61.20%	113	54.30%		
>5 km	48	55.20%	47	38.80%	95	45.70%		
Mode of transport available							0.069	
Public	30	34.50%	57	47.10%	87	41.80%		
Private	57	65.50%	64	52.90%	121	58.20%		

Abbreviations: f, frequency; %, Percentage; Uni, University; k, thousands; Rs, Pakistani rupees.

Footnotes: Column percentages are used. P-value was computed using Pearson Chi-square test (χ 2). Provided the cell number below 5, Fisher's exact test was used

	N <u>o Delay i</u>	in diagnosis	De	lay in	Т	otal	
		nonths) =87	(≥3 n	gnosis nonths)		=208	
Characteristics	f	%	f	=121	f	-208 %	Р*
Cancer stage at diagnosis	J	/0	J	70	J	/0	<0.001
Stage 1	10	11.50%	2	1.70%	12	5.80%	01001
Stage 2	42	48.30%	32	26.40%	74	35.60%	
Stage 3	26	29.90%	67	55.40%	93	44.70%	
Stage 4	9	10.30%	20	16.50%	29	13.90%	
First symptoms/signs							< 0.001
Painless breast lump	67	77.00%	11	9.10%	78	37.50%	
Axillary area lump	1	1.10%	43	35.50%	44	21.20%	
Nipple discharge/changes	17	19.50%	4	3.30%	21	10.10%	
Lump in breast and axilla	2	2.30%	63	52.10%	65	31.30%	
Breast cancer in family							0.951
Yes	32	36.80%	44	36.40%	76	36.50%	
No	55	63.20%	77	63.60%	132	63.50%	
First consultation choice							0.006
Allopathic/medical doctors	67	77.00%	71	58.70%	138	66.30%	
Alternative therapy ^a	20	23.00%	50	41.30%	70	33.70%	
Perceived cancer incurable disease							0.116
Yes	22	25.30%	43	35.50%	65	31.30%	
No	65	74.70%	78	64.50%	143	68.80%	
Perceived cancer as from God							0.764
Yes	18	20.70%	23	19.00%	41	19.70%	
No	69	79.30%	98	81.00%	167	80.30%	
Aware of breast self-examination							0.024
Yes	24	27.60%	18	14.90%	42	20.20%	
No	63	72.40%	103	85.10%	166	79.80%	
Practice breast self-examination							0.272
Yes	13	14.90%	12	9.90%	25	12.00%	
No	74	85.10%	109	90.10%	183	88.00%	
Aware of breast cancer screening							0.015
Yes	24	27.60%	17	14.00%	41	19.70%	
No	63	72.40%	104	86.00%	167	80.30%	
Preference for female doctor							0.519
Yes	53	60.90%	79	65.30%	132	63.50%	
No	34	39.10%	42	34.70%	76	36.50%	

Table 2: Clinical characteristics, perception about the disease and health seeking concerns among breast cancer patients attending public and private hospitals of Lahore, Pakistan (n=208)

Characteristics	f	%	f	%	f	%	P *
Female doctor available nearby							0.19
Yes	49	56.30%	79	65.30%	128	61.50%	
No	38	43.70%	42	34.70%	80	38.50%	
Medical appointment difficulty							0.009
Yes	33	37.90%	26	21.50%	59	28.40%	
No	54	62.10%	95	78.50%	149	71.60%	
Fear of biopsy (will spread cancer)							< 0.001
Yes	18	20.70%	64	52.90%	82	39.40%	
No	69	79.30%	57	47.10%	126	60.60%	
Fear of social cancer labelling/taboo							0.001
Yes	44	50.60%	97	80.20%	141	67.80%	
No	43	49.40%	24	19.80%	67	32.20%	
Fear of losing breast (surgery)							0.215
Yes	50	57.50%	59	48.80%	109	52.40%	
No	37	42.50%	62	51.20%	99	47.60%	
Fear of chemotherapy/ Alopecia							0.003
Yes	47	54.00%	89	73.60%	136	65.40%	
No	40	46.00%	32	26.40%	72	34.60%	
Financial fear of treatment							0.818
Yes	51	58.60%	69	57.00%	120	57.70%	
No	36	41.40%	52	43.00%	88	42.30%	
Fear of marital issues/divorce							0.002
Yes	22	25.30%	11	9.10%	33	15.90%	
No	65	74.70%	110	90.90%	175	84.10%	

Abbreviations: f, Frequency; %, Percentage. Footnotes: Column percentages are used. P-value was computed using Pearson Chi-square test

(χ 2). Provided the cell number below 5, then Fisher's exact test Alternative therapies include homeopathy, Herbal and Chinese medicine, faith/spiritual therapy

DISCUSSION

This study allowed the identification of significant patient-related factors that greatly contribute to the delay in breast cancer diagnosis among women in urban and peri-urban areas of Lahore, Pakistan.

The findings of this study found a delay in diagnosis in more than half of the cases presented (58.2%). Of these cases, most were primarily associated with patients receiving care in public hospitals (78.3%) and a majority of patients presented with advancedstage diagnoses (Stage III/IV) (72%). These findings are supported by previous studies that make the overall same consensus that a majority of delayed diagnoses are at advanced stages of the disease.⁴ Moreover, an interesting correlation can be made from a previous study conducted in Lahore that found that the microbiological profile of BC in Pakistan is distinct in that it is more aggressive in its presentation and affects younger women; furthermore, this study found late-stage diagnoses to be correlated with a more aggressive tumor profile.¹² As our study found delayed diagnosis to be associated with late-stage BC, and given the unique profile of BC in Pakistan and the subsequent consequences, it is evident that there is a critical need for earlier detection interventions through screening in order to minimize the burden of cancer among patients and to prevent morbidity of tumors.

Moreover, our study found that most patients with a delayed diagnosis are severely lacking awareness of BC screening tests (86.0%) and self-examination (85.1%), however these factors were, interestingly, not found to be significant predictors of patient-related delay which does deviate from similar

Predictors	Adjusted Estimate (<i>B</i>)	v	95% Confidence interval of AOR	р
Age				
\leq 50 years	Reference	1	Reference	
>50 years	0.43	1.54	0.75-3.14	0.238
Area of residence				
Rural	0.708	2.03	0.96-4.27	0.063
Urban	Reference	1	Reference	
Education				
No formal schooling	Reference	1	Reference	
Attended School/College	0.111	1.12	0.52-2.37	0.774
Choice of consultation				
Allopathic Medical practice	Reference	1	Reference	
Alternative therapies	0.912	2.49	1.17-5.29	0.018
Health facility access (distance)				
\leq 5 km	Reference	1	Reference	
>5km	-0.443	0.64	0.31-1.34	0.236
Health facility type				
Public sector	Reference	1	Reference	
Private sector	-0.17	0.84	0.30-2.34	0.745
Aware of breast self-examination				
Yes	Reference	1	Reference	
No	0.535	1.71	0.72-4.06	0.227
Aware of cancer screening				
Yes	Reference	1	Reference	
No	0.482	1.62	0.68-3.84	0.275
Preference for female doctor				
Yes	0.54	1.71	0.81-3.64	0.159
No	Reference	1	Reference	
Biopsy will spread cancer				
Yes	1.791	5.99	2.70-13.32	<0.00
No	Reference	1	Reference	
Fear of Social cancer labelling				
Yes	1.299	3.67	1.58-8.48	0.002
No	Reference	1	Reference	
Fear of side effects/alopecia				
Yes	0.159	1.17	0.56-2.46	0.674
No	Reference	1	Reference	

Table 3: Predictors of patient-related delay in diagnosis of breast cancer among patients attending public and private hospitals in a developing country (n=208)

Footnote: Binary logistic regression method was used to compute odds ratio and its 95% confidence intervals using the lowest category as reference. Models were adjusted for socio-demographic characteristics, clinical factors, perception and health seeking concerns.

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studies.One of the most prominent predictors of delayed diagnosis was the preference for alternative therapies, with 41.3% of women initially opting for unorthodox treatments. This supports previous research indicating how alternative medicine is frequently chosen due to cultural beliefs, misinformation, or financial burdens in developing countries.^{13–15} The significant association between this choice and diagnosis delay reiterates the importance of public health campaigns to promote evidence-based treatments that address these cultural concerns, and guide patients towards taking beneficial steps towards a more evidence-based practice.

We also found social stigma regarding BC to be a significant predictor of delay. Previous studies too have pointed to social stigmatization of cancer as a deterrent to treatment, especially among the South Asian population where conversations regarding the breast as an organ are considered culturally taboo.^{9,16} Patients are hesitant to seek help due to prevailing social conditions that cause them to self-isolate in fear of being sympathized or labelled in a negative connotation.⁹ Lack of proper social support for BC patients can cause further harm to patient psyche that can manifest in unfavorable ways.

Furthermore, misconceptions about diagnostic treatments (i.e. cancer spreading through biopsy) was found to be significantly associated with patient-delay in this study. These results are uniform with a previous study conducted in Pakistan which illustrated that fear of cancer spreading through biopsy is a common myth that is more commonly found among participants lacking a proper education.¹⁷ Fears regarding BC treatment methods and screening due to misinformation or a lack of general awareness cause reluctancy among patients to seek professional help, contributing to the overwhelming percentage of delayed diagnoses. Thus, it is imperative that these misconceptions regarding diagnostic procedures be cleared.

This study highlights many key factors that contribute to the delay in breast cancer diagnose, such as fear of biopsy, social stigma, and the preference for alternative therapies. We can address these social barriers via culturally sensitive education programs to aid in normalizing discussions around these topics. The recurrent justification that arises behind the aforementioned patient-related factors of delay is a lack of proper education surrounding BC and its diagnostic procedures. Pakistan is severely lacking robust, accessible BC awareness campaigns that address cultural taboo and societal misinformation,

as mentioned in a study that evaluated the current BC campaigns in Pakistan.¹⁸ One study found that mammography to be an incredibly effective screening method in reducing morbidity and mortality of late diagnoses in developing countries.² Rivera-Franco et al. pointed out that as BC diagnosis in developing countries are present in younger women at a higher proportion than developed countries, mammography screening programs should include younger populations.¹⁹ Effective screening programs that target relevant age populations and the fears that patients in Pakistan hold are crucial in alleviating the burden of delayed diagnoses. Another key point that Shamsi et. al. found in a recent study conducted in Karachi details how that even if patients do identify symptoms, the gravity of the situation is often undermined due to a lack of education regarding the potential manifestations of these symptoms.¹⁰ This corroborates numerus studies conducted in various developing countries that point to a lack of education or a weak understanding of the severity of potential symptoms to be the critical influence that gives rise to specific delay factors.²⁰⁻²⁴

The depth of education regarding BC often is discussed to the limit of identifying symptoms and screening/treatment options, however this education must be taken further in order to accentuate the impact and severity of BC should it manifest to advanced stages. Patients should be encouraged to seek professional help even when they are unsure of their symptoms in order to detect BC early in its progression. Social stigma regarding discussion of BC as well as seeking help from healthcare providers must be addressed in potential programs in order to initiate the process of prevention or to gain a timely diagnosis. Addressing the root cause of these predictors can potentially improve the rate and time of detection and has the possibility of improving survival outcomes for women in Pakistan.

Future research around this topic should explore the effectiveness of such interventions on the patient-related factors of delay and the broader impact of healthcare education for timely cancer diagnosis in similar settings.

CONCLUSION

Targeted public health interventions, awareness campaigns, and culturally sensitive educational programs are critical to promoting early detection and improving Breast Cancer outcomes in developing countries.

ETHICALAPPROVAL

The study was conducted after obtaining ethical

approval from the Ethical Review Board (ERB) of Allama Iqbal Medical College and with permission from authorities of all hospitals involved (reference number: ERB130/8/03-11-2022/S1 ERB).

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Conceptualization and study design	GQ, HN, AA
Data Acquisition	GQ, HN, LA, SSN, AZ, MA
Data Analysis/ interpretation	GQ, HN, AA, AZ, AF
Manuscript drafting	GQ, HN, AA, LA, MWI, AF
Manuscript review	GQ, HN, LA, MWI

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