


## Original Research

# Exploration and Assessment of Breast Cancer Awareness in the Saudi Population: A Cross-Sectional Study

Dalia A. Elmaghraby<sup>1,\*</sup>, Ahmad Mohammed Al ben Hamad<sup>1</sup>,  
Khalid Mohammed Alhunfoosh<sup>1</sup>, Hamzah Redha Alturifi<sup>1</sup>, Mohammed Abdullah Albahrani<sup>1</sup>,  
Ahmed Ali Alshalla<sup>1</sup>, Anas Alyahyan<sup>1</sup>, Muntathir Altaweel<sup>1</sup>

<sup>1</sup>Department of Pharmacy Practice, College of Clinical Pharmacy, King Faisal University, 31982 Al Ahsa, Saudi Arabia

\*Correspondence: [delmaghraby@kfu.edu.sa](mailto:delmaghraby@kfu.edu.sa) (Dalia A. Elmaghraby)

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## Abstract

**Background:** Breast cancer represents a considerable health burden and is a leading cause of mortality among women. Despite the availability of screening methods, many women remain unaware of their importance, leading to delayed diagnoses and poorer outcomes. Increased awareness of breast cancer symptoms and screening modalities may improve early detection and ultimately reduce breast cancer mortality. This study aimed to evaluate the level of awareness, practices, and attitudes regarding breast cancer and its screening methods in the general population, males and females, in Saudi Arabia. **Methods:** This cross-sectional study was conducted using an online questionnaire to collect data on personal information, medical and family history of breast cancer, participation in breast cancer awareness programs, knowledge of breast cancer and screening methods, and attitudes and practices related to breast cancer and breast self-examination. The questionnaire was distributed via social media platforms. **Results:** A total of 714 individuals completed the study questionnaire. The age range of the participants was 18 to 70 years, with a mean age of  $29.9 \pm 11.5$  years. Among the participants, 60.1% were female. The most commonly reported risk factors for breast cancer were female sex (38.8%), smoking (35.8%), obesity (25.6%), consumption of fat-rich foods (23.9%), and alcohol intake (23.6%). The most widely recognized warning signs of breast cancer among participants were the presence of a hard, painless lump or nodule in the breast or armpit (79.7%), breast swelling (62%), and discharge from the breast (59.5%). Among female study participants in Saudi Arabia, 36.4% reported practicing breast self-examination (BSE). **Conclusions:** In conclusion, this study revealed that the participants demonstrated a low level of knowledge and awareness regarding breast cancer and its associated screening methods, particularly mammography. Furthermore, the practice of breast self-examination, which is especially important for women under 40 years of age, was below average, with only one out of every three female participants performing it. Educational programs and health campaigns are essential to increase awareness about breast cancer and the importance of early detection to improve the rates of mortality and morbidity.

**Keywords:** breast cancer; awareness; breast self-examination; screening; disease prevention; public health

## 1. Introduction

Breast cancer is a leading cause of morbidity and mortality among women worldwide [1]. Early detection through screening is essential for improving outcomes and reducing mortality rates [2,3]. Various screening methods, including mammography, clinical breast examination, and breast self-examination (BSE), are available [4–6]. Mammography is considered the gold standard for breast cancer screening and has been shown to reduce mortality by detecting cancer at an early stage [6–8]. However, access to mammography may be limited in some populations, highlighting the importance of other screening methods, such as BSE that could be done at home and do not need hospital visits or medical equipment [9–13]. Guidelines recommend starting mammography by the age of 40 for average-risk women, while for younger women, BSE is an option for breast cancer screening [3–6]. Regular performance of BSE can aid in the early detection of breast abnormalities and

prompt further evaluation [11–13]. Despite the availability of these screening methods, many women remain unaware of their importance or do not regularly participate in screening [13,14]. Increased awareness and utilization of breast cancer screening methods are essential for improving early detection and ultimately reducing breast cancer mortality [4,15]. In Saudi Arabia, breast cancer is the most prevalent form of cancer among women over the age of 40 [16]. However, more than half of all cases are diagnosed at an advanced stage, in contrast to only 20% in developed countries [1–3,16,17]. This leads to a higher mortality rate, lower chances of successful treatment, and increased healthcare costs [17–19]. Early detection through screening techniques such as mammography can greatly improve the likelihood of successful treatment and survival [2,20]. Therefore, initiatives to raise awareness and promote the use of breast cancer screening methods are crucial in mitigating the impact of this disease in Saudi Arabia [21,22].



Published studies investigating awareness in males in Saudi Arabia are scarce [23,24]. The majority of the published studies investigated the awareness of breast cancer among Saudi females only [21,22]. The current study aimed to assess awareness levels, attitudes, and practices regarding breast cancer and its screening methods in the general population (males and females) in Saudi Arabia using a validated reliable questionnaire. We believe that increasing awareness of the whole population will increase health awareness regarding breast cancer, rather than choosing only the target affected population, females.

## 2. Materials and Methods

### 2.1 Study Design

This cross-sectional study was conducted to evaluate the awareness, attitudes, and practices regarding breast cancer and its screening methods among adults in Saudi Arabia.

### 2.2 Participants

Individuals aged 18 years or older. Participants under the age of 18 and those who declined to complete the questionnaire were excluded from this study.

### 2.3 Setting

The majority of the responses were collected using an online questionnaire, which was disseminated to the general population of accessible adults until no further responses were received. In order to reach older people and those who do not use the internet, some of the responses, approximately 5%, were collected during face-to-face interviews. The questionnaire was developed by researchers following an extensive review of the literature and consultation with experts in the field [25].

### 2.4 Data Sources

The researchers and their relatives and friends disseminated the questionnaire online using social media platforms from January to June 2022.

### 2.5 Data Analysis

The validity of the study questionnaire was assessed by a panel of three experts, and all confirmed modifications were applied. Reliability and clarity were also assessed using a pilot study of 30 individuals, who were subsequently excluded from the main study. The Cronbach's  $\alpha$  for the questionnaire was 0.71, confirming its internal reliability.

The questionnaire included questions on participants' personal data, medical and family history of breast cancer, attendance at training programs for breast cancer awareness, knowledge regarding breast cancer and screening methods, attitudes and practices regarding breast cancer, and performance of BSE.

After data extraction, the data were revised, coded, and entered into SPSS Version 22.0 (IBM Corporation, Chicago, IL, USA) for statistical analysis. All analyses

were performed using two-tailed tests, with a  $p$  value of less than 0.05 considered statistically significant. For knowledge items, each correct answer was assigned a score of one point, and the total summation of the discrete scores for the different items was calculated. Participants with a score of less than 60% of the total score were considered to have poor awareness, while those with a score of 60% or higher were considered to have good awareness. Descriptive analysis, based on frequency and percent distributions, was performed for all variables, including participants' age, sex, education level, personal and family history of breast cancer, and attendance at health education sessions for breast cancer. Additionally, participants' knowledge items regarding breast cancer, screening methods, attitudes, and BSE practices were displayed and graphed. Crosstabulation was used to assess the distribution of knowledge levels according to participants' personal data and the distribution of their practices according to their knowledge levels. Relationships were tested using Pearson's chi-square test and Fisher's exact test for small frequencies.

### 2.6 Study Size

Utilizing an online sample size calculator provided by Raosoft® software (Raosoft Inc., Seattle, WA, USA) available on their website (<http://www.raosoft.com/samplesize.html>), we determined the sample size under a 5% margin of error and a 95% confidence interval. The calculated desirable sample size was 341 participants. However, the actual sample size that was achieved for this study was 714 participants.

The sample size  $n$  and margin of error  $E$  are given by:

$$x = Z(c/100)2r(100 - r)$$

$$n = Nx / ((N - 1)E^2 + x)$$

$$E = \text{Sqrt}[(N - n)x / n(N - 1)]$$

Where  $N$  is the population size,  $r$  is the fraction of responses, and  $Z(c/100)$  is the critical value for the confidence level  $c$ .

## 3. Results

A total of 714 participants completed the study questionnaire. The age range of the participants was 18–70 years, with a mean age of  $29.9 \pm 11.5$  years. The majority of participants were female (60.1%,  $n = 429$ ) and Saudi nationals (96.5%,  $n = 689$ ). In terms of marital status, 44.8% ( $n = 320$ ) were married, and 53.4% ( $n = 381$ ) were single. With regard to education, the majority of participants were university graduates (73.8%,  $n = 527$ ), while 24.1% ( $n = 172$ ) had a secondary school education. A total of 26.1% ( $n = 186$ ) of participants reported having a family history of breast cancer, while 3.5% ( $n = 25$ ) had a personal history of the disease and 8.8% ( $n = 63$ ) reported having a breast mass. Of the participants surveyed, 39.2% ( $n = 280$ ) reported having attended a breast cancer awareness program or activity and derived benefit from it, while 7.8% ( $n = 56$ ) reported attending but did not perceive any benefit (Table 1).

**Table 1. Biodemographic data of study participants, Saudi Arabia.**

Biodemographic data	No.	%
Age in years		
18–24	347	48.6%
25–34	149	20.9%
35–49	164	23.0%
50+	54	7.6%
Sex		
Male	285	39.9%
Female	429	60.1%
Nationality		
Saudi	689	96.5%
Non-Saudi	25	3.5%
Marital status		
Single	381	53.4%
Married	320	44.8%
Divorced/widowed	13	1.8%
Educational level		
Below secondary	15	2.1%
Secondary	172	24.1%
University/above	527	73.8%
Personal history of breast cancer		
Yes	25	3.5%
No	630	88.4%
Do not know	58	8.1%
Family history of breast cancer		
Yes	186	26.1%
No	473	66.2%
Do not know	55	7.7%
Personal history of breast mass		
Yes	63	8.8%
No	549	76.9%
Do not know	102	14.3%
Have you ever attended any program or activity related to breast cancer awareness?		
Yes, with no benefit	56	7.8%
Yes	280	39.2%
No	378	52.9%

In terms of risk factors for breast cancer, the most commonly reported risk factors among study participants were female sex (38.8%), smoking (35.8%), obesity (25.6%), intake of fat-rich food (23.9%), alcohol consumption (23.6%), sedentary lifestyle (21.6%), vitamin D deficiency (8.4%), and exposure to high doses of radiation (6.2%). With regard to awareness of warning signs of breast cancer, the most commonly known among study participants were the presence of a hard, painless lump or nodule in the breast or armpit (79.7%), breast swelling (62%), discharge from the breast (59.5%), changes in the size and shape of the breast or wrinkling of the skin (58.8%), changes in the nipple (58.3%), and breast pain (51.5%). The least known warning signs were itching, crusty sores, or a rash around the breast (36.1%), with 11.5% of participants reporting no knowledge of the warning signs of breast cancer (Table 2).

A total of 75.8% of participants reported that physical examination by a physician was one screening method, followed by BSE (70%), mammography (67.5%), and ultrasound (32.5%). Of the participants, 36% reported having good or excellent knowledge regarding BSE, compared to 23.6% for physical breast examination and 23.8% for mammography. Approximately 80% of participants were aware that BSE can help detect the presence of lumps in the breast, and 47.3% reported that it can help detect masses in the lymph nodes under the armpits. Of the participants, 37.7% reported that BSE should be performed monthly after menstruation, while 56% were aware that mammography should begin at the age of 40 years. Additionally, 59.9% knew that mammography should be performed annually, while 45.7% were aware that it is not painful, and 25.4% believed that a mammogram should only be performed when there are symptoms of breast cancer (Table 3).

**Table 2. Participants' awareness and knowledge regarding breast cancer in Saudi Arabia.**

Breast cancer awareness		No. of correct answers	%
Risk factors for breast cancer	Female sex	276	38.8%
	Smoking	255	35.8%
	Obesity	182	25.6%
	Consumption of fat-rich food	170	23.9%
	Alcohol intake	168	23.6%
	Sedentary lifestyle	154	21.6%
	Vitamin D deficiency	60	8.4%
	Exposure to high doses of radiation	44	6.2%
	Family history of BC	18	2.5%
	No breastfeeding	14	2.0%
	Radio and hormonal therapy	11	1.5%
	Older age	11	1.5%
	Previous history of BC	10	1.4%
	Delayed menopause	8	1.1%
	Early menarche	7	1.0%
	Do not know	52	7.3%
Breast cancer warning signs and symptoms	A hard, painless lump or nodule in the breast or armpit	569	79.7%
	Breast swelling	443	62.0%
	Discharge from the breast	425	59.5%
	A change in the size and shape of the breast or wrinkling of the skin	420	58.8%
	Changes in the nipple	416	58.3%
	Breast pain	368	51.5%
	Change in skin color	284	39.8%
	Itching, crusty sores, or a rash around the breast	258	36.1%
	Do not know	82	11.5%

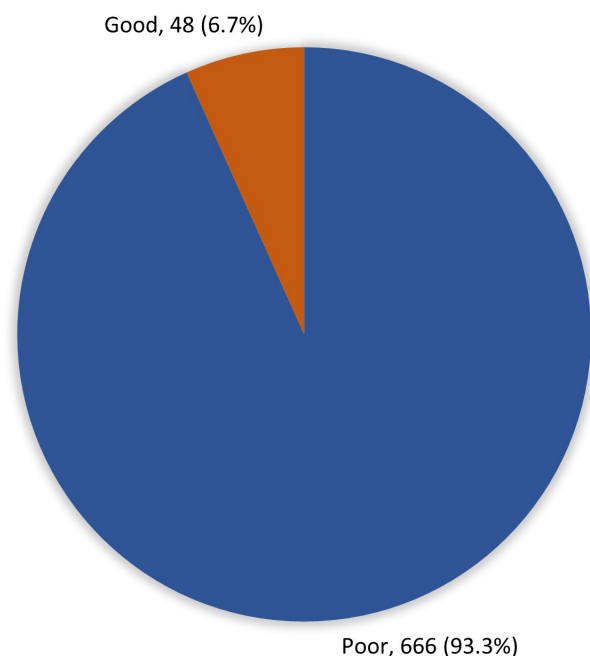
BC, breast cancer.

Of the participants, 158 (36.4%) reported having performed BSE, with 109 (69%) performing it weekly and 6 (3.8%) performing it monthly. The most commonly reported reasons for not performing BSE were forgetfulness (41.5%), being below the age of 40 years (33.8%), lack of concern (30.9%), doubt about its efficacy (21.7%), and fear of discovering a mass (13.2%) (Table 4).

In terms of participants' attitudes toward breast cancer and its screening methods in Saudi Arabia, 304 (42.6%) believed that there was sufficient awareness of breast cancer in their area. Of the participants, 30.1% reported confidence in their ability to notice changes in the breast area, while 53.1% reported having a good or excellent attitude toward the importance of early detection of breast cancer (Table 5).

Data on overall knowledge and awareness regarding breast cancer and its screening methods in the study population is presented in Fig. 1. Of the participants, 48 (6.7%) demonstrated a good level of knowledge, while 666 (93.3%) had poor knowledge regarding breast cancer and its screening methods.

Regarding factors associated with participants' knowledge regarding breast cancer and its screening methods. Good knowledge was detected among 8.5% of university-educated participants, compared to none of

**Fig. 1. Overall knowledge and awareness regarding breast cancer and screening methods in the study population.**

**Table 3. Breast cancer screening knowledge and awareness among study participants in Saudi Arabia.**

BC screening knowledge		No.	%
Methods of breast examination	Clinical examination by a physician	541	75.8%
	Breast self-examination	500	70.0%
	Mammogram	482	67.5%
	Ultrasound	232	32.5%
	Do not know	65	9.1%
How much do you know about BSE?	Excellent	73	10.2%
	Good	184	25.8%
	Low/intermediate	271	38.0%
	No knowledge	186	26.1%
How much do you know about clinical breast examination?	Excellent	43	6.0%
	Good	126	17.6%
	Low/intermediate	267	37.4%
	No knowledge	278	38.9%
How much do you know about mammography?	Excellent	54	7.6%
	Good	116	16.2%
	Low/intermediate	213	29.8%
	No knowledge	331	46.4%
What is the importance of BSE?	To detect the presence of lumps in the breast	571	80.0%
	To detect a mass in the lymph nodes under the armpits	338	47.3%
	Do not know	82	11.5%
What is the best time to perform BSE?	Weekly	15	2.1%
	Monthly after period	269	37.7%
	Monthly before period	70	9.8%
	Annually	174	24.4%
	Do not know	186	26.1%
What is the suitable age to start undergoing mammography?	40 years	400	56.0%
	After menopause	41	5.7%
	20 years	158	22.1%
	During puberty	115	16.1%
What is the frequency of undergoing mammography?	Weekly	5	0.7%
	Monthly	71	9.9%
	Annually	428	59.9%
	Do not know	210	29.4%
Do you think mammograms are painful?	Yes	147	20.6%
	No	326	45.7%
	Do not know	241	33.8%
Do you think a mammogram should be performed only when there are symptoms of breast cancer?	Yes	181	25.4%
	No	368	51.5%
	Do not know	165	23.1%

BC, breast cancer; BSE, breast self-examination.

those with below a secondary education, with a statistically significant difference ( $p = 0.005$ ). Similarly, 10.2% of participants with a family history of breast cancer had good knowledge about the disease, compared to 1.8% of those without such a history ( $p = 0.045$ ). Of the participants with a personal history of breast cancer, 14.3% had good knowledge about the disease, compared to 1% of those without such a history ( $p = 0.004$ ). Additionally, 11.8% of those who reported having benefited from attending a

program or activity related to breast cancer awareness had good knowledge, compared to 4% of those who did not attend ( $p = 0.001$ ). Furthermore, 14.6% of participants who performed BSE had a good level of knowledge, compared to 4.3% of those who did not ( $p = 0.001$ ) (Table 6).

#### 4. Discussion

In Saudi Arabia, breast cancer is frequently diagnosed at advanced stages and has more cases among young pre-

**Table 4. Breast self-examination practices among study participants in Saudi Arabia.**

BSE	No.	%
Do you perform BSE?		
Yes	158	36.4%
No	276	63.6%
Frequency of performing BSE		
Rarely	43	27.2%
Weekly	109	69.0%
Monthly	6	3.8%
If not, what are the reasons for not doing it?		
Forgetfulness	113	41.5%
Still below the age of 40	92	33.8%
Do not care	84	30.9%
Not sure of its efficacy	59	21.7%
Fear of discovering mass	36	13.2%
No need as I have no symptoms	6	2.2%
Do not know how to	2	0.7%

BSE, breast self-examination.

**Table 5. Participants' attitudes toward breast cancer and screening methods, Saudi Arabia.**

Attitude	No.	%
Do you think that there is enough awareness of breast cancer in your area?		
Yes	304	42.6%
No	257	36.0%
Do not know	153	21.4%
How confident are you in your ability to notice a change in the breast area?		
Totally uncertain	21	2.9%
Uncertain	69	9.7%
Do not know	409	57.3%
Certain	157	22.0%
Totally certain	58	8.1%
To what extent are you aware of the importance of early detection in the context of breast cancer?		
Excellent	112	15.7%
Good	267	37.4%
Low/intermediate	273	38.2%
No knowledge	62	8.7%

menopausal women than in Western countries [26–30]. The Saudi Health Council [31] reported that the incidence of new cases of breast cancer in 2018 was 2814, which represents 17.9% of all cancers. In the United States, half of new breast cancers are detected in women above 65 years of age, while in Saudi Arabia, breast cancer mostly occurs among women aged 30–44 years [8,29,30]. Furthermore, developed countries assess breast cancer mainly in the early stages compared with developing countries where there are large numbers diagnosed at advanced stages [2,32]. The awareness of breast cancer has an important role in the early detection and prevention of the disease [2,33].

The current study aimed to assess public knowledge regarding breast cancer and screening methods. In terms of awareness and knowledge of breast cancer, this study revealed that the most commonly recognized risk factors were female sex, smoking, obesity, consumption of high-fat

foods, and alcohol consumption while the rest of the stated risk factors were recognized by a small percentage of the participants. This could be attributed to the low breast cancer (BC) awareness programs attended by the study participants. With regard to the warning signs and symptoms of breast cancer, the most commonly recognized signs among study participants were the presence of a hard, painless lump or nodule in the breast or armpit, breast swelling, discharge from the breast, changes in the size and shape of the breast or wrinkling of the skin, changes in the nipple, and breast pain. A smaller percentage of the participants (36.1%) knew that changes that happened to breast skin are considered signs of breast cancer as the least known warning signs were itching, crusty sores, or a rash around the breast. The correct technique of BSE could detect a lump in the breast as well as lumps in the axilla due to lymph node invasion [2–4]. there is a trend towards good knowl-

**Table 6. Factors associated with participants' knowledge regarding breast cancer and screening methods.**

Factors	Knowledge level				<i>p</i> value
	Poor		Good		
	No.	%	No.	%	
Age in years					
18–24	325	93.7%	22	6.3%	0.519
25–34	141	94.6%	8	5.4%	
35–49	152	92.7%	12	7.3%	
50+	48	88.9%	6	11.1%	
Sex					
Male	272	95.4%	13	4.6%	0.060
Female	394	91.8%	35	8.2%	
Marital status					
Single	357	93.7%	24	6.3%	0.887\$
Married	297	92.8%	23	7.2%	
Divorced/widowed	12	92.3%	1	7.7%	
Educational level					
Below secondary	15	100.0%	0	0.0%	0.005*
Secondary	169	98.3%	3	1.7%	
University/above	482	91.5%	45	8.5%	
Personal history of breast cancer					
Yes	23	92.0%	2	8.0%	0.279\$
No	585	92.9%	45	7.1%	
Do not know	57	98.3%	1	1.7%	
Family history of breast cancer					
Yes	167	89.8%	19	10.2%	0.045*
No	445	94.1%	28	5.9%	
Do not know	54	98.2%	1	1.8%	
Personal history of breast mass					
Yes	54	85.7%	9	14.3%	0.004*
No	511	93.1%	38	6.9%	
Do not know	101	99.0%	1	1.0%	
Have you ever attended any program or activity related to breast cancer awareness?					
Yes, with no benefit	56	100.0%	0	0.0%	0.001*
Yes	247	88.2%	33	11.8%	
No	363	96.0%	15	4.0%	
Do you perform BSE?					
Yes	135	85.4%	23	14.6%	0.001*\$
No	264	95.7%	12	4.3%	

*p* value, Pearson  $\chi^2$  test is used unless otherwise stated; \$, exact probability test; \*,  $p < 0.05$  (significant).

edge regarding breast cancer screening modalities. When we asked the participants about screening methods, approximately 70% were aware that BES can help detect lumps in the breast, but only 47% reported that it can also help detect masses in the lymph nodes under the armpits. This could indicate the deficient knowledge and improper way applied by the participants to perform BSE. Overall, the level of knowledge regarding breast cancer and its screening methods was very low. Higher levels of knowledge

were reported among participants with higher levels of education, those with a personal or family history of breast cancer, those who had attended health education sessions, and those who performed BSE. This highlights the importance of health education in improving the knowledge of the population. Women who have less knowledge about the risk factors and screening methods for breast cancer tend to check their breasts less frequently or not at all.

Our findings on the low level of knowledge are far greater than those reported by Naqvi *et al.* [34] from Pakistan where 446 individuals, representing 34.2% of the study population, exhibited a low level of knowledge concerning breast cancer. Likewise, in Cameroon, Halmata *et al.* [35] concluded that the knowledge and practice of breast cancer screening were low among women in Douala city. In contrast to previous findings, a systematic review conducted in Nigeria demonstrated a high level of awareness regarding breast cancer (80.6%), BSE (60.1%), knowledge of associated mortality, and the benefits of early detection (73.2% and 73.9%, respectively). However, knowledge of symptoms and signs was lower (45.1%). Furthermore, both perceived susceptibility and the performance of BSE were low, at 26.8% and 22.9%, respectively. Overall, the rate of screening performance did not vary with changes in the level of awareness or knowledge [36]. In Saudi Arabia, previous studies examining knowledge, attitudes, and practices related to breast cancer have revealed low levels of awareness [23,24,37–39]. Based on a study conducted in Makkah among female teachers, the level of knowledge about BC was low and differed significantly by age and marital status. Those aged 46–55 and those who were married had more knowledge about breast cancer than others [37].

With respect to the practice of BSE, the current study revealed that approximately one-third of the participants performed BSE. The most commonly reported reasons for not performing BSE included forgetfulness (41.5%), being under 40 years of age (33.8%), lack of concern (30.9%), doubt regarding its efficacy (21.7%), and fear of discovering a mass (13.2%). A higher rate of BSE practice was reported by Alsaif *et al.* [40], with their study indicating that 66% of participants performed BSE. Of those who performed BSE, approximately 62% reported having learned about it through their college curricula. This underscores the importance of proper education about breast cancer and its influence on BSE practice [40]. It is crucial to highlight that the incidence of breast cancer in Arab Gulf countries occurs at a younger age compared to Western countries [41]. This phenomenon may be attributed to several factors, including consanguineous marriage, which may result in the accumulation of homozygous recessive mutations, in addition to the adoption of a high-fat Western diet that increases obesity rates [42,43]. The American and European guidelines recommend starting mammography by the age of 40 because the majority of their breast cancer patients are above 60 and starting BSE by the age of 20 [4–7,44]. Consequently, we recommend implementing local guidelines regarding the age at which breast cancer screening using mammography should commence. In the meantime, BSE remains an important tool, particularly for women under 40 years of age, to increase awareness of changes that may occur in the breast due to cancer.

The current study has some limitations. First, Data obtained by a self-administered questionnaire may be sub-

jected to reporting bias. Second, the method of distributing the questionnaire did not allow for enough participants who did not use mobile devices. We tried to overcome this limitation by conducting face-to-face interviews to collect responses from different age groups and areas in Saudi Arabia.

## 5. Conclusions

In conclusion, this study revealed that the participants demonstrated a low level of knowledge and awareness regarding breast cancer and its associated screening methods, particularly mammography. Furthermore, the practice of breast self-examination, which is especially important for women under 40 years of age, was below average, with only one out of every three female participants performing it. Educational programs and health campaigns are essential to increase awareness about breast cancer and the importance of early detection to improve the rates of mortality and morbidity.

## Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Author Contributions

DAE, AA, MAA, and AMAH designed the research study. AA, MAA, AMAH, KMA, and HRA performed the research. AA, MAA, AMAH, KMA and HRA analyzed the results. DAE was responsible for Funding acquisition. AAA, AMAH, AA, KMA, HRA, and MA collected the data. DAE supervised the research. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of King Faisal University (protocol code KFU-REC-2022-MAR-EA000474 and date of approval 1/03/2022). All participants provided written informed consent.

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## Conflict of Interest

The authors declare no conflict of interest.

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