

Knowledge of Non-Invasive Biomarkers of Breast Cancer, Risk Factors, and BSE Practices Among Nursing Undergraduates in Farasan Island, KSA

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Abstract

Background of the Study: Mammograms are sometimes met with issues of overdiagnosis and underdiagnosis; therefore, they are less reliable in identifying cancer in women with dense breasts. As a result, it is critical to be aware of other sensitive screening techniques for the early diagnosis of breast cancer.

Aim: The ultimate objective of this study was to assess the knowledge of nursing undergraduates regarding non-invasive biomarkers, such as volatile organic compounds in breath, nipple aspirate fluid, sweat, urine, and tears, for the early detection of breast cancer to help improve patient care, determine the risk factors, and encourage practice of breast self-examination.

Methods: Cross-sectional research was done in the Department of Nursing at Farasan campus using a self-structured questionnaire as the study tool. A total of 260 students willingly participated. The study tool had evaluation questions focused on the non-invasive biomarkers of breast cancer, risk factors, and breast self-examination practices to collect data. The data were subjected to descriptive and inferential statistics. The statistical significance was calculated at $P < .05$. Data analyses were done using Microsoft Excel (2013).

Results: A significant knowledge gap existed among the study participants about the non-invasive biomarkers of breast cancer. A lesser percentage of students (25%) stated that they do breast self-examination on a monthly basis. The most common reasons for not doing the breast self-examination were “not knowing how to do the breast self-examination” (77.3%), fear of a positive diagnosis (53.9%), thinking that they are not at risk as all were in their teens and hence not required (44.7%), and lack of time (48.7%). Age and frequency of breast self-examination were significantly associated ($P < .05$) as those few students (22.7%) who were doing breast self-examination practices every 2–4 months belonged to a higher study year. Furthermore, knowledge regarding incidence rates and health care expenditure by the government on breast cancer was also significantly low ($P < .05$).

Conclusions: Outcomes would help prioritize actions to help future nurses better understand breast cancer, allowing them to extend patient care in the best way possible.

Keywords

breast cancer, non-invasive biomarkers, nursing undergraduates, BSE, risk factors

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Introduction

After lung cancer, breast cancer (BC) is the most common malignancy in women worldwide and the second-leading cause of cancer-related mortality in developed countries (WHO, 2012). In 2020, approximately 68,500 people died from breast cancer globally, and approximately 2.3 million women received diagnoses. By the end of 2020, BC had become the most common disease in the world, with 7.8 million women staying alive after being diagnosed with breast cancer in the preceding 5 years (WHO, 2021).

Breast cancer is very common, thereby putting a lot of strain on healthcare resources and significantly raising prices (Cocco et al., 2022). The financial burden of managing breast cancer in Saudi Arabia is high and dramatically escalates as the disease progresses. In 2018, an estimated \$13.345 million USD was spent to treat breast cancer in Saudi Arabia, with Stage I patients paying an average of \$14,249 USD and Stage IV patients paying an average of \$81,489 USD. One of the major factors influencing the total healthcare costs was the price of medications, hospitalization, and diagnostic testing. The majority of trastuzumab-based regimens accounted for 67% of the overall cost of medications in the targeted therapy category (Alghamdi et al., 2021).

Early BC diagnosis programs, assessment of costly interventions, and consideration of non-invasive biomarkers of BC and biosimilars are some of the ways that could lead to cost savings (Cesarec et al., 2007). According to estimates, there were 3,629 cases of breast cancer in Saudi Arabia in 2018. By 2040, that number is expected to rise to 6,886 (Alghamdi et al., 2021). Additionally, it has been noted that the bulk of Saudi Arabian patients with breast cancer receives a diagnosis at an advanced stage, which could significantly raise resource consumption and cost (Alghamdi et al., 2021; Bcheraoui et al., 2015; Cesarec & Likić, 2017; Cocco et al., 2022; WHO, 2021). Age, family history of the disease, hormone problems, alcoholism, stress, and other factors are established risk factors for breast cancer development. However, it's crucial to remember that 75% of breast cancer cases in women have an unknown cause. Breast density genes may possibly be linked to an increased risk of breast cancer.

Breast cancer could happen to any woman, irrespective of her education, social, and cultural background. Therefore, a woman's awareness of breast cancer is crucial. The ability to identify the difference between normal and abnormal breasts, to know what to look for during breast self-examination (BSE) practices, and identify the appropriate time for breast cancer screening may help detect the early stage of breast cancer (Almuhlim et al., 2018; Yousuf, 2010). BSE increases women's awareness of their breast health, potentially resulting in the early diagnosis of breast cancer. BSE and adherence to this practice, at least on a monthly basis, are gateways to health promotion behaviors.

Mammograms have been one of the most effective screening methods and a crucial component of early breast cancer identification in recent years (Guide to Mammography and Breast Imaging, 2012; Ponraj et al., 2011). They also expose the breast to substantially lower radiation doses than previous devices (Rangayyan et al., 2006). However, mammography does not always offer a conclusive diagnosis regarding the existence or absence of cancer, particularly in situations with dense breast tissue, which is defined as the quantity of fibro-glandular tissue in the breast that is radiologically dense (Boyd et al., 2007; Johns, 1987). Therefore, mammographic screening is frequently unreliable in differentiating between people with breast cancer and healthy individuals, in addition to being costly, uncomfortable, and sometimes hazardous for sensitive patients.

The search for disease markers in unconventional bodily fluids is becoming increasingly popular as biomarker identification methods continue to progress. Breast cancer-associated biomarkers have been identified in urine (Beretov et al., 2015), nipple fluid aspirate (Shaheed et al., 2018), and breast milk (Aslebagh et al., 2022). The knowledge of breast cancer markers in fluids other than those traditionally associated with cancer diagnosis could improve nurses' ability to identify the disease and create community awareness for diagnosis. Tears also contain hundreds of proteins/peptides, lipids, glycoproteins, hormones, and small-molecule metabolites (Barmada & Shippy, 2020). The changing expression levels of ocular proteins in response to systemic disease have been well established in the literature. In a study conducted by Daily et al. (2022), ocular proteomes were examined to identify protein biomarkers with altered expression levels in women diagnosed with breast cancer.

Tears, sweat, urine, nipple aspirates, and exhaled breath are examples of circulatory, non-invasive biomarkers that may be used to detect therapeutically relevant mutations and tumor features. These non-invasive biomarkers may also offer important insights regarding the course of the disease and its response to treatment (Barmada and Shippy, 2020; Bohm et al., 2012; Chen et al., 2016; Deutscher et al., 2010; Erbes et al., 2015; Hanna et al., 2019; Hermann et al., 2018; Li et al., 2020; Patel & Shah, 2022). Compared to imaging or tissue samples, these non-invasive biomarkers can be gathered at a higher frequency, which may enable more intelligent early diagnoses and management of the disease (Barmada and Shippy, 2020; Bohm et al., 2012; Chen et al., 2016; Deutscher et al., 2010; Erbes et al., 2015; Hanna et al., 2019; Hermann et al., 2018; Li et al., 2020; Patel & Shah, 2022).

Literature Review

Global Incidence

The patterns and trends of breast cancer vary in different countries. There were approximately 2.3 million new breast

cancer cases and 685,000 breast cancer deaths worldwide in 2020 (Lei et al., 2021). Its incidence and mortality vary among countries, with the age-standardized incidence ranging from the highest of 112.3 per 100,000 of the population in Belgium to the lowest of 35.8 per 100,000 of the population in Iran and the age-standardized mortality from the highest of 41.0 per 100,000 of the population in Fiji to the lowest of 6.4 per 100,000 of the population in South Korea. Breast cancer is the most common type of cancer in women in the United States (Yıldırım et al., 2022). As per the estimates of the American Cancer Society, approximately 4 million women in the country had a history of breast cancer as of early 2019 (DeSantis et al., 2019). Additionally, approximately 50,000 women in the US receive a diagnosis of breast ductal carcinoma in situ (DCIS), one of the most common precancers in all tissues (American Cancer Society, Breast Cancer Facts & Figures, 2019). In several Asian and African nations, the peak age of breast cancer is more than 10 years younger than in European or American nations (Sung et al., 2021).

The incidence of breast cancer is significantly higher in developed countries than in developing nations. This is because of a long-standing higher prevalence of risk factors, including decreased fertility rates, a high percentage of oral contraceptive or hormonal menopausal therapy use, shorter breastfeeding durations, and higher body weights (Cancer CGoHFIB, 2002; Hu et al., 2013; Kim et al., 2019; Møller et al., 2002; Nguyen et al., 2020; Pfeiffer et al., 2018; Zhang et al., 2012).

National Incidence

In 2018, breast cancer was the most commonly diagnosed type of cancer and the second-leading cause of death after leukemia in Saudi Arabia (Alqahtani et al., 2020). In recent years, the KSA has seen an increase in the incidence of breast cancer, with instances rising from 1,152 per 100,000 people in 2008 to 1,473 per 100,000 people in 2010 and 1,826 per 100,000 people in 2014 (Alothaibi, 2018; Basudan, 2022). According to the KSA Health Council's 2014 cancer registry, breast cancer accounts for 28.7% of all cancer cases in women. However, a different study found that breast cancer causes 13.08% of all cancer-related fatalities, with 98% of cases affecting women and 12% affecting males (Alothaibi, 2018). Scientific studies from different regions in the KSA have reported the prevalence of breast cancer among females (Alothaibi et al., 2018; Heena et al., 2019; Yakout et al., 2014), with three to eight confirmed cases of breast cancer per 1,000 patients from 2010 to 2017. Moreover, the highest incidence rates of breast cancer were reported in 2017.

Two distinct patterns of breast cancer were also observed, with the most common type being ductal carcinoma with an incidence percentage of 81.80%, followed by lobular carcinoma with a 3.40% incidence rate (Asiri et al., 2020).

These data indicate that further steps are still needed to identify breast cancer at an early stage.

Opportunities for Control and Intervention

One of the most successful programs that have been implemented by the Saudi government is the breast cancer screening program that offers mammography, which is provided for free at all government facilities, and malls. Despite this, the incidence remains high. Sometimes, extensive mammogram use may also lead to high incidence rates of breast cancer. Mammography screening is the best way to discover breast cancer early, but it can also lead to overdiagnosis, which can increase the incidence of breast cancer. The rate of overdiagnosis varies from 5% to 50% (Srivastava et al., 2019).

The Center for Disease Control stated that early detection is the best defense against the morbidity and mortality of breast cancer (Srivastava et al., 2019). In line with this, the best way to reduce incidence is to know the non-invasive biomarkers of breast cancer, identify the risk factors, and encourage the practice of breast self-examination (BSE) that may help in the early detection of breast cancer.

Significance of the Study

Nurses comprise the largest proportion of the Saudi health care system (MOH, 2014). Female nurses can positively impact the attitudes and beliefs of female patients. They are also the first point of contact for female patients and their families/friends. In order to do this, it would be crucial to make sure that these young nurses have the necessary knowledge to share with their patients, family members, and friends.

Breast cancer awareness includes knowledge of the risk factors, signs, symptoms, and screening methods for breast cancer. Knowledge and awareness play a vital role in the early detection and optimal treatment of breast cancer. Creating awareness among female health workers could go a long way in enhancing awareness and early diagnosis of breast cancer. Identification of breast cancer at an early stage is the best way to prevent it and is of utmost importance in saving lives and improving the quality of life. These non-invasive methods of breast cancer detection using tears, sweat, and nipple aspirates are relatively convenient, simple, inexpensive, and free from risk or harm; hence, nurses should have the relevant knowledge and skills, such that they may create awareness at the community level. Studies on the knowledge of non-invasive breast cancer biomarkers, risk factors, and BSE practice in future nursing professionals in the age group of 18 to 23 years old are not yet available, despite the fact that numerous studies about breast cancer knowledge and BSE practice in female university students have already been presented (Hadi et al., 2010;

Nemenqani et al., 2014; Yousuf, 2010). To assess the level of knowledge and skills among nursing students, KAP studies are required. The present study was conducted to assess KAP of nursing undergraduates about the non-invasive biomarkers of breast cancer in view of the increasing incidence of breast cancer in KSA.

The knowledge of nurses on the non-invasive biomarkers of breast cancer, such as nipple aspirates, breath, tears, and urine, are important determinants for the early diagnosis of breast cancer and for the reduction of the economic burden of the disease on the health care system.

Overdiagnosis leads to overtreatment due to mammographic screening in the case of dense breasts and inflicts considerable physical, psychological, and economic harm on many women (Autier & Boniol, 2018). The dense breast tissue is linked to a markedly reduced mammographic sensitivity and a higher interval cancer rate (Boyd et al., 2007; Bodewes, 2022; Kerlikowski 2007; Mandelson et al., 2000); thus, an increased understanding of breast cancer with relation to knowledge on non-invasive biomarkers, risk factors, and breast self-examination (BSE) practices is important to enable future nurses to extend better patient care and disease management by helping them in the early diagnosis of breast cancer and may reduce the mortality rate globally. To the best of our knowledge and based on a PubMed search, this is the first study dealing with the above mentioned issue in the XXX and XXX provinces in Saudi Arabia. Therefore, the present study was undertaken to assess the knowledge of non-invasive biomarkers of breast cancer, associated risk factors, and attitudes toward BSE among nursing undergraduates.

Methodology

Setting. Department of Nursing, Farasan Island.

Study design. A descriptive cross-sectional study.

Study sample. Female nursing undergraduates of the Department of Nursing.

Sampling procedure. Simple random sampling.

Study tool. A questionnaire was used as the research tool for data collection from the study participants.

There were nine sections in the questionnaire:

Section 1: *Demographic Information*. It included eight items (i.e., age, gender, marital status, residence, living with parents, study year, family's educational background, and family history of breast cancer)

Section 2: The *Knowledge Evaluation Questions* included 16 items.

Section 3: The domain for knowledge *regarding non-invasive biomarkers of breast cancer* had seven evaluation items.

Section 4: The domain for *Awareness of Risk Factors* had 12 items.

Section 5: *Source of Information on Breast Cancer* had six evaluation questions

Section 6: BSE practices and barriers to breast self-examination had three evaluation questions.

Section 7: Lifestyle *characteristics* had eight items.

Section 8 had six evaluation questions on the *Knowledge of Treatment*.

Section 9 had three items on knowledge *regarding incidence rates and expenditures on breast cancer in KSA*.

Ethical considerations. Sufficient research information was provided to the participants with the help of full informed consent. This was achieved via a consent form attached to the questionnaire. Full confidentiality was ensured. The rights of the participants were protected by the Helsinki Code of Ethics. The study was approved by the Head of Ethics Committee of the College (No. 1/1/1444H, 2022).

Data collection procedure. Formal approval was used to conduct this research. Consent was obtained from all the participants, and a free hand was given to the participants to participate in the study or refuse to participate.

Study timeline. Data collection was conducted from February to March 2022.

Inclusion and exclusion criteria. Regular students enrolled with a university during the academic year 2021–2022, and those who were not willing to participate, were excluded from the study.

Definitions

Breast self-examination. One's self-examination of her breasts to identify any changes.

Breast self-Examination performed. BSE done at least once within the duration of 12 months.

Sample size and sampling procedure. A sample size of 260 students was determined using Cochran's formula (1964): $n = z^2 pq / e^2$, where p is the proportion of knowledge on breast cancer among female students (22%); e is the desired level of precision (5%); and $z = 1.95$ at CI 95% (Cochran, 1963). The calculation also included a 5% non-response rate. Simple random sampling was done. Reliability was calculated to check the internal consistency among items of the questionnaire using Cronbach's alpha (α) and was 0.875, which was considered within the acceptable range.

Data analyses. Data analyses were done using Microsoft Excel software. Descriptive statistics were used to summarize

the data, which were then displayed in the tables and figures. The study's hypothesis was either accepted or rejected using inferential analysis and the *t*-test. Based on prior research on breast cancer risk factors, the most important risk factors for breast cancer were found to be breast density, obesity, age, menarche and menopause at different times, lifestyle, and diet (Engin, 2017). The current study used these risk factors to determine the participants' knowledge of breast cancer and the risk factors. Correct responses were summed up to get the total knowledge scores for each participant. The connections between the sociodemographic characteristics of the participants and their understanding of the most significant risk factors for breast cancer were examined using Pearson's Chi-squared test. The threshold for significance was established at a *P*-value < .05.

Results

Demographic Features of the Study Participants

The participants were first- to fourth-year female nursing undergraduates, the majority of which constituted third-year study groups, followed by fourth-year study groups. The participants' mean age was 21 years (SD = 21.3 ± 3.2; ranging from 18 to 25 years). Eighty seven percent of the study participants were unmarried, and 1% reported having a family history of breast cancer (Table 1).

General Knowledge of Breast Cancer

General knowledge of breast cancer was significantly high (*P* < .05) among the respondents. Table 2 shows a comparison of the knowledge regarding the signs and symptoms of breast cancer among the participants. The participants belonging to higher study years were found to have more knowledge of breast cancer symptoms than those in the lower study years. The participants were found to be well-aware of the breast pain symptom (63.1%). A higher number of the study participants also recognized change in breast shape (88.8%) and painless lumps (55.8%) as breast cancer symptoms. However, some respondents were still unaware of nipple discharge (42.1%) and inverted nipples (16.9%) as breast cancer symptoms (Table 2). There was a strong correlation among the knowledge, study year, and marital status of the study participants (Table 3).

General Breast Density Knowledge and Importance

Most participants were unaware that having dense breasts raises a woman's risk of breast cancer and can conceal tumors on mammograms (65%). The other risk factors mostly recognized by the study participants were advanced age (76.2%), genetic mutation (66.9%), smoking (86.9%), alcoholism (88.1%), stress (69%), obesity (47.7%), and early or late onset of menstruation and menopause (48.1%).

Table 1. Study Samples' Distribution According to Their Demography, Knowledge, Lifestyle, and Dietary Habits (N = 260).

Parameters	Frequency (N)	Percentage (%)	*P-value
<i>Section 1: Demographic information</i>			
Mean age (21.3 ± 3.2 years)			<i>P</i> < .04
≤20 years	44	17.1	
>20 years	216	82.9	
Gender			<i>P</i> < .07
Female	260	100	
Male	–	–	
Marital status			<i>P</i> < .06
Married	34	13	
Unmarried	226	87	
Residence			<i>P</i> < .02
Farasan	147	56.6	
Jazan	96	36.8	
Other cities	17	6.6	
Living with parents			<i>P</i> < .04
Yes	171	65.8	
No	89	34.2	
Study year			<i>P</i> < .02
First year	32	12.3	
Second year	59	22.7	
Third year	74	28.5	
Fourth year	95	36.5	
Family's educational background			<i>P</i> < .01
Educated in school/ college	244	94	
Educated at home	16	6	
Family history of breast cancer			<i>P</i> < .04
Yes	3	1	
No	231	89	
Don't know	26	10	
<i>Section 2: Knowledge evaluation questions</i>			
Have you heard about breast cancer before?			<i>P</i> < .04
Yes	209	80.3	
No	51	19.7	
When does the signs and symptoms of breast cancer start?			<i>P</i> < .01
Before puberty	68	26.3	
After puberty	113	43.4	
After child birth	17	6.6	
After menopause	62	23.7	
Does breast cancer change the size and shape of the breast?			<i>P</i> < .04
Yes	229	88.2	
No	31	11.8	
What is the level of pain in breast in case of breast cancer?			<i>P</i> < .01
0–2	24	9.2	
2–4	89	34.2	
5	51	19.7	
None	96	36.8	
Early detection of breast cancer helps in treatment protocol			<i>P</i> < .07
Yes	233	89.5	
No	27	10.5	

(continued)

Table 1. Continued.

Parameters	Frequency (N)	Percentage (%)	*P-value
<i>Section 1: Demographic information</i>			
Do you know about mammograms?			
Yes	209	80.3	$P < .02$
No	51	19.7	
Where can you do mammogram?			
Hospitals	178	68.4	$P < .05$
Shopping malls	17	6.6	
Schools	21	7.9	
Don't know	44	17.1	
Is it free at all government centres?			
Yes	202	77.6	$P < .04$
No	58	22.4	
Do you know women with dense breast tissue are at higher risk of developing breast cancer?			
Yes	89	34.3	$P < .01$
No	84	32.3	
Maybe	85	32.7	
Do you know about the severity of breast cancer if developed at young age?			
Yes	32	12.3	$P < .03$
No	65	25	
Maybe	163	62.7	
Do you think that if women have the knowledge of their breast density, it would help in early diagnosis of disease and could be useful to prevent mortality?			
Yes	77	29.6	$P < .09$
No	90	34.6	
Maybe	93	35.8	
Do you know about the signs and symptoms related to breast cancer?			
Yes	211	81.6	$P < .01$
No	48	18.4	
Maybe	–	–	
Does breast cancer change your dietary habits?			
Yes	112.3	43.4	$P < .04$
No	62	23.7	
Maybe	86	32.9	
Does there occur some nipple discharges in breast cancer?			
Yes	109	42.0	$P < .03$
No	100	38.5	
Maybe	49	18.9	
Is there palpable painless lump?			
Yes	145	55.77	$P < .01$
No	50	19.2	
Maybe	65	25.0	
Is there palpable auxiliary lymph nodes?			
Yes	98	37.7	$P < .05$
No	35	13.5	
Maybe	127	48.9	
Are there deviated/inverted nipples in breast cancer?			
Yes	44	16.9	$P < .02$
No	59	22.7	

(continued)

Table 1. Continued.

Parameters	Frequency (N)	Percentage (%)	*P-value
<i>Section 1: Demographic information</i>			
Maybe	157	60.4	
Does breast cancer affect male as well?			
Yes	89	34.2	
No	51	19.7	
Maybe	117	44.8	
Section 3: Knowledge regarding non-invasive biomarkers of breast cancer			
Do you think breast cancer could be diagnosed by sweat/apocrine sweat?			
Yes	133	51.1	$P < .03$
No	39	15	
Maybe	87	33.5	
Do you think breast cancer could be diagnosed by nipple aspirate?			
Yes	29	11.1	$P < .02$
No	57	21.9	
Maybe	174	66.9	
Do you think urine could be a biomarker for breast cancer?			
Yes	49	18.8	$P < .04$
No	98	37.7	
Maybe	113	43.5	
Do you think tears can serve as ideal diagnostic fluid for breast cancer?			
Yes	35	13.5	$P < .02$
No	100	38.5	
Maybe	125	48.1	
Do you think there could be a typical change in exhaled breath odor in breast cancer?			
Yes	54	20.8	$P < .01$
No	98	37.7	
Maybe	108	41.5	
Do you think saliva could be potential biomarkers for breast cancer?			
Yes	133	51.1	$P < .03$
No	8	3.1	
Maybe	117	45	
Do you think circulating cell-free tumor DNA and other metabolites as lipids, etc., could be biomarkers for breast cancer?			
Yes	24	9.2	$P < .02$
No	59	22.7	
Maybe	177	68.1	
Section 4: Awareness of risk factors			
Early or late onset of menstruation and menopause			
Yes	125	48.1	$P < .05$
No	12	4.6	
Maybe	123	43.3	
Advanced age			
Yes	198	76.2	$P < .02$
No	62	23.9	
Maybe	–	–	
High breast density			
Yes	56	21.5	$P < .053$
No	145	55.8	

(continued)

Table 1. Continued.

Parameters	Frequency (N)	Percentage (%)	*P-value
<i>Section 1: Demographic information</i>			
Maybe	59	22.7	
Genetic mutations or positive family history of breast cancer			
Yes	174	66.9	<i>P</i> < .061
No	22	8.5	
Maybe	64	24.61	
High fat diet			
Yes	135	51.9	<i>P</i> < .03
No	68	26.2	
Maybe	57	21.9	
Smoking			
Yes	226	86.9	<i>P</i> < .01
No	15	5.8	
Maybe	19	7.3	
Alcoholism			
Yes	229	88.1	<i>P</i> < .02
No	3	1.2	
Maybe	28	10.7	
Stress			
Yes	179	69.0	<i>P</i> < .01
No	56	21.5	
Maybe	26	9.6	
Do you think obesity could be a risk factor for breast cancer?			
Yes	124	47.7	<i>P</i> < .04
No	77	29.61	
Maybe	59	22.7	
Endocrine/Hormones. Do you think it is related to a certain hormone?			
Yes	177	68.1	<i>P</i> < .02
No	45	17.4	
Maybe	36	13.9	
Could exposure to plastic pollutants make hormonal issues that may cause breast cancer?			
Yes	137	52.9	<i>P</i> < .01
No	41	15.8	
Maybe	81	31.2	
Do you think alcohol containing perfumes may cause hormonal issues related to breast cancer?			
Yes	232	89.1	<i>P</i> < 0.03
No	12	4.5	
Maybe	14	5.2	
Section 5: Source of information on breast cancer			
What is the source of information for breast cancer?			
Internet	85	32.7	<i>P</i> < .03
Government awareness Program regarding breast cancer	51	19.6	
Family and friends	48	18.5	
Lecture sessions in college	35	13.5	

(continued)

Table 1. Continued.

Parameters	Frequency (N)	Percentage (%)	*P-value
<i>Section 1: Demographic information</i>			
Course/curricula	17	6.5	
Primary health care center	23	8.9	
Section 6: Breast self-examination practices and barriers to BSE			
Do you know how to do breast self-examination?			
Yes	59	22.7	<i>P</i> < .05
No	147	56.5	
Maybe	54	20.8	
If yes then how frequently you do the BSE?			
Monthly	13	5.0	<i>P</i> < .02
Every 2–3 months	25	9.6	
Every 4 months	9	3.46	
Once in 6 months	19	7.3	
Once in year	57	21.9	
Never practiced	137	52.7	
Barriers to self-examination of breast			
Lack of time	30	11.54	<i>P</i> < .01
Thinking that not at risk and hence not required	71	27.3	
Do not know how to perform BSE	118	45.4	
Fear of positive diagnosis	71	27.3	
Section 7: Lifestyle characteristics			
Do you have an active lifestyle?			
Yes	181	69.7	<i>P</i> < .02
No	78	30.3	
Do you have a regular breakfast?			
Yes	90	34.7	<i>P</i> < .073
No	155	59.7	
Sometimes	14.0	5.5	
Do you prefer junk food?			
Yes	185	71.1	<i>P</i> < .09
No	75	28.9	
Do you take energy drinks?			
Yes	241	92.7	<i>P</i> < .06
No	19	7.3	
If yes, then how frequently?			
Once/day	85	32.7	<i>P</i> < .03
Twice/day	108	41.5	
After every meal	39	15.0	
More than 3 times/day	25	9.6	
Do you wear tight clothing?			
Yes	38	14.6	<i>P</i> < .04
No	197	75.8	
Maybe	22	8.5	
Do you prefer non-veg?			
Yes	252	96.8	<i>P</i> < .03
No	8	3.1	

(continued)

Table 1. Continued.

Parameters	Frequency (N)	Percentage (%)	*P-value
<i>Section 1: Demographic information</i>			
Do you think good hygiene practices may reduce the risk of breast cancer?			
Yes	232	89.3	$P < .01$
No	19	7.1	
Maybe	8	3.2	
Section 8: Knowledge of treatment			
BC could be treated by:			
Surgery	120	46.1	$P < .05$
Chemotherapy	58	22.4	
Medicines	34	13.2	
Radiotherapy	17	6.6	
Hormone therapy	14	5.3	
Biological treatment	16	6.1	
Section 9: Knowledge regarding incidence rates and expenditure on breast cancer in KSA			
Had knowledge about the incidence of breast cancer all over the world?			
Yes	44	16.92	$P < .01$
No	194	74.61	
Maybe	22	8.46	
Had knowledge about the incidence of breast cancer in Saudi Arabia?			
Yes	39	15	$P < .04$
No	117	45	
Maybe	104	40	
Did you have any knowledge about the percentage of government expenditure on breast cancer in Saudi Arabia?			
Yes	13		$P < .02$
No	215	82.69	
Maybe	32	12.31	

Significant at P value $< .05$; *Significant at P value $< .05$ based on Chi-squared test.

The participants were unaware that breast cancer can happen at a young age and has the worst prognosis (12.3%).

Knowledge Regarding Non-Invasive Biomarkers

The knowledge of the study participants about non-invasive biomarkers was significantly low ($P < .05$) as a very low percentage of the study participants (27%) responded that they were aware of these non-invasive biomarkers (Figure 1). The majority of the participants marked this as 'No' and were found to be confused. They marked it 'Maybe' as a response to these evaluation questions.

Knowledge Regarding Risk Factors

The majority of the participants (78.5%) were not aware of breast density as a risk factor for breast cancer. However,

Table 2. Participants' Responses in Relation to Signs and Symptoms of Breast Cancer ($n = 260$).

Breast cancer signs and symptoms	Frequency	Percentage	*P-value
Palpable, painless lump	145	55.8	0.01
Changes in breast shape	229	88.2	0.04
Palpable axillary lymph nodes	23	8.85	0.05
Deviated nipples	44	16.9	0.02
Nipple discharge	109	42.0	0.03

Significant at P value $< .05$; *Significant at P value < 0.05 based on Chi-squared test.

Table 3. Correlation Between Study Years in the Program, Age, Marital Status, and Level of Knowledge of Study Participants ($n = 260$).

Variables	Correlation coefficient	*P-value
First year	.894	.321
Mid year	.837	.045
Final year	.859	.001
Age	.789	.021
Marital status	.009	.064

Significant at P value $< .05$; *Significant at P value $< .05$ based on the Chi-squared test.

the study participants identified alcohol containing perfumes (89.1%), excessive alcohol consumption (88.1%), genetic mutation and positive family history of breast cancer (66.9%), and waist circumference/obesity (61.2%) as established and most important risk factors of breast cancer. The participants also identified stress, poor dietary habits, and fewer physical activities as the major modifiable risk factors. Accordingly, 47.7% of the participants identified no breastfeeding as one of the significant risk factors for breast cancer. However, their knowledge of the other associated risk factors of breast cancer was poor.

Majority of the study participants (69.7%) identified age as the major non-modifiable risk factor for breast cancer. However, very few participants were aware of the risk of breast cancer due to disruption in biological clock like early menarche, late menopause, and hormonal therapy. It was also found that their knowledge of the modifiable and non-modifiable risk factors was unsatisfactory.

Knowledge of BSE Practices

The study participants had less knowledge about BSE practices, with the majority responding that they did not know how to perform BSE (77.3%). In fact, 52.7% of the participants responded that they had never done BSE (Table 4). There was a significant correlation between breast self-examination practice and age ($P < .05$) as those few

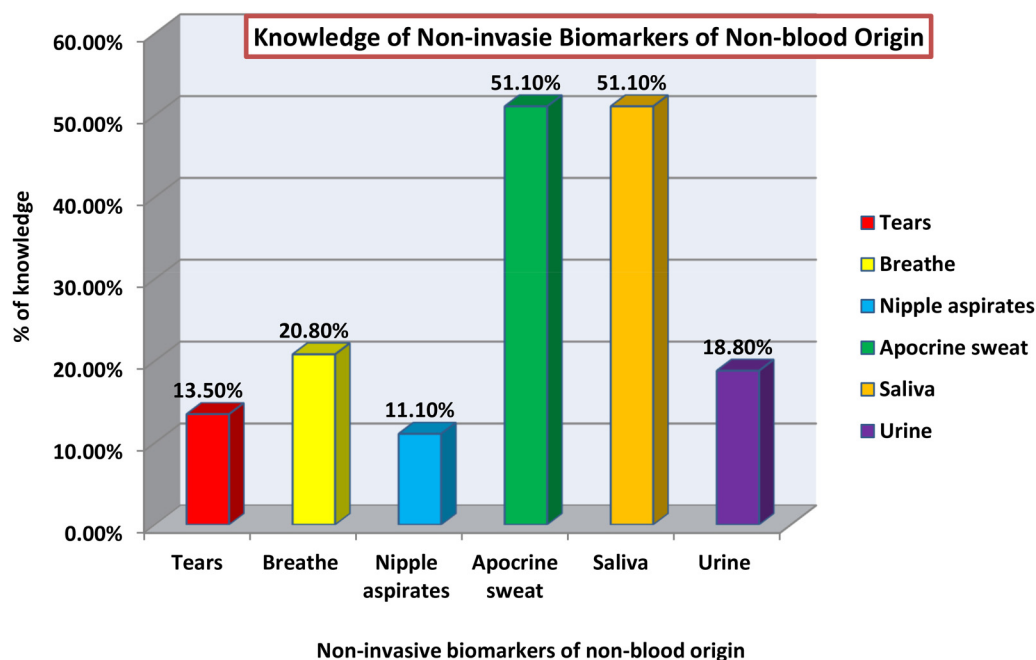


Figure 1. Participant for Knowledge of Non-invasive biomarkers of Non-blood origin.

Table 4. Examination Practice Among Study Participants (n = 260).

	Frequencies of BSE (N)	Percentage of BSE (%)
Monthly	13	5.0
Every 2–3 months	25	9.6
Every 4 months	9	3.46
Once in 6 months	19	7.3
Once in a year	57	21.9
Never practiced	137	52.7

students (22.7%) who were doing breast self-examination practices every 2–4 months belonged to a higher study year.

Barriers of BSE Practices

The study participants cited “Not knowing how to perform breast self-examination” as the most common reason for not performing the breast self-examination (45.4%, Table 1), fear of a positive diagnosis (27.3%), thinking they were not at risk as all were in their teens and hence not required (27.3%), and lack of time (11.54%).

Knowledge of Source of Information Regarding Breast Cancer

Regarding the source of information, the majority of the participants identified the internet as the major source of information, followed by government health programs.

Table 5. Knowledge Regarding Incidence Rates and Expenditure on Breast Cancer in the KSA (n = 260).

Variables	Frequency	Percentages	*P-value
Did you have knowledge about the incidence of breast cancer all over the world?	44	16.92	.01
Did you have knowledge about the incidence of breast cancer in Saudi Arabia?	39	15.0	.04
Did you have knowledge about the percentage of government expenditure on breast cancer in Saudi Arabia?	13	05.0	.02

Significant at P value < .05; *Significant at P value < .05 based on the Chi-squared test.

Knowledge of Global and National Incidence Rates and Epidemiology of BC

The majority of the participants did not have sufficient knowledge regarding the epidemiology, incidence, and current trends of breast cancer at the global and national levels (Table 5). Furthermore, knowledge regarding the incidence rates and health care expenditure by the government on breast cancer was also significantly low (P < .05).

Discussion

The high incidence rates of breast cancer could be caused by a number of factors, including an aging population, an increase in risk factors, the widespread use of mammography screening (Srivastava et al., 2019) for detection, age (Britt et al., 2020; NCD, 2017), and changes in population and epidemiology (Blüher, 2019; Hu et al., 2013; Møller et al., 2002; NCD, 2017; Zhang et al., 2012). The most crucial steps to reducing breast cancer-related mortality are acquiring knowledge and performing skill-based interventions required for early diagnosis.

Nevertheless, mammography has certain drawbacks, one of which is its inability to identify breast cancer. The range of mammographic sensitivity for identifying breast cancer in a randomized, controlled mammography screening experiment was 71% to 96% (Humphrey et al., 2002). Mammographic sensitivity decreased even further in patients with dense breast tissue, that is, from 48% to 70% (Humphrey et al., 2002; Pisano et al., 2005). For women with thick breasts, ultrasonography is more sensitive than mammography in identifying lesions (Skaane, 1999; Zonderland et al., 1999). Nevertheless, the majority of microcalcifications, which are characteristic findings in ductal carcinoma in situ, are also missed by ultrasonography. Ductal carcinoma in situ accounts for 75% of the tumors that ultrasonography misses, while invasive carcinomas account for 25% (Nemec et al., 2007).

In the KSA, despite the healthcare facilities being free of charge with widespread screening services, even in shopping malls, as community service activities, the utilization of breast cancer screening methods, including mammography, and screening rates is not optimal and are very low, respectively, with one study reporting that for women 50 years of age or older, 89% reported not having a clinical breast examination, and 92% reported never having a mammogram in the past year (Bcheraoui et al., 2015).

Studies have reported that ease of collection, high protein concentration, and lower complexity of the tear fluid compared to blood make tears an ideal diagnostic fluid (Ponzini et al., 2022; Ravishankar & Daily, 2022; Zhou & Beuerman, 2017). Additionally, low-molecular weight proteins are easily accessible in tear fluids and can aid in identifying crucial cancer biomarkers (Hagan et al., 2016). The study conducted by Leemans et al. (2022) demonstrated that volatile organic compounds in sweat differ between healthy individuals and breast cancer patients, suggesting the possibility of using these compounds as novel breast cancer biomarkers in non-invasive screening tools.

Phillips et al. (2003), Peng et al. (2010), Phillips et al. (2010), and Patterson et al. (2011) reported that breath analysis exhibits potential in cancer screening and early diagnosis because it is an easy, safe, painless, and non-invasive procedure that poses no risks to patients. Increased oxidative stress and the induction of cytochrome P450 enzymes are

associated with BC. This leads to the lipid peroxidation of polyunsaturated fatty acids in cell membranes, which increases the production of volatile alkanes and alkane derivatives in the breath and ultimately affects the amount of volatile organic compounds in exhaled breath (Patterson et al., 2011; Peng et al., 2010; Phillips et al., 2003, 2010). Peng et al. (2010) also demonstrated that women with breast cancer have increased levels of 3,3-dimethyl pentane in their breath. However, the participants of this study had very little knowledge about the typical changes in breath odor in breast cancer patients.

Human urine is also one of the most useful biofluids of non-blood origin, which serves as an important biomarker of various diseases, including breast cancer. Studies have demonstrated increases in phosphatidylcholine and phosphatidylethanolamine in the urine samples of breast cancer patients (Beretov et al., 2015). Fifty-nine urinary proteins were differentially detected in breast cancer patients (Beretov et al., 2015). Furthermore, the biomarkers in nipple aspirate fluids could also be a better source for the identification of breast cancer as they contain exfoliated breast epithelial cells from which breast cancer originates (Sauter et al., 1997).

However, the study participants, who are future nursing professionals, had almost negligible knowledge regarding these noninvasive biomarkers that could be utilized as sensitive tools for creating awareness, which could help in early diagnosis and reduce the severity and mortality due to knowledge gaps.

Moreover, the participants reported breast cancer risk factors that were almost similar to those reported in various previous studies, such as older age, high body mass index or obesity, exposure to tobacco, physical inactivity, high-fat diets, early-age menarche, late age at first full-term pregnancy, shorter breastfeeding periods, use of hormonal menopausal therapy or oral contraceptives, breast density, and family history of breast cancer (Kushi et al., 2012).

Most of the research participants were unaware that dense breasts have a masking effect on mammographic screening, increasing their intrinsic risk of developing breast cancer. Therefore, more work has to be done to increase the students' understanding of the various types of breast tissue and the increased risks of breast cancer.

The study participants were also almost unaware of the severity of breast cancer at such a young age. Several studies have shown that breast cancer arising at a young age is linked with a worse prognosis. Various studies have suggested that BC at a young stage is enriched with more aggressive breast cancer subtypes, particularly triple-negative or basal-like tumors (Azim & Partridge, 2014; Azim et al., 2020). In the study of Heena et al. (2019) among health professionals, the study participants were also found to have less knowledge and awareness about breast cancer, screening, and attitude.

The inadequate breast cancer knowledge determined in this study is in line with the results obtained for a study

conducted among female university students in Saudi Arabia, which reported that only 4.2% of the study participants have adequate knowledge about BSEs (Albeshan et al., 2023). In another study conducted among Palestinian females by Jobran et al. (2023), the majority of females (68.7%) scored poorly on their knowledge of BC considering possible risk, methods of detection, methods of diagnosis, methods of treatment, signs and symptoms, information about mammography, and other knowledge questions. Only 31.7% scored well.

In contrast to this, the study conducted on female university students in Gambia by Kinteh et al. (2023) revealed that they had good knowledge regarding breast cancer screening. Abo Al-Shiekh et al. (2021), in their study on female university students in Gaza, found that the majority of students (80.2%) had acquired previous information about breast cancer from different sources, including university studies (57%), the internet (45%), and social media (41%). Findings showed good scores ($\geq 70\%$) for the signs and symptoms and risk factors of breast cancer. Roughly, all students (96.5%) have heard about BSE, and 69.8% knew the time to do BSE; however, only 31.4% of them practice it regularly.

Similar to our study, the work of Abo Al-Shiekh et al. (2021) also reported that the three main barriers to BSE practice were students who do not have a breast problem (39.7%), do not know how to do it (37.9%), and are busy (31%). More than three-quarters (76.6%) of the respondents had never practiced any form of breast cancer screening. Kinteh et al. (2023) revealed almost similar results, where more than three-quarters (76.6%) of the respondents had never practiced any form of breast cancer screening. Alotaibi et al. (2018) reported that most of the participating students had never performed BSE (82%). Other researchers, however, who investigated the reasons for not practicing BSE, found that a lack of knowledge was the main reason. Alzabadi et al. (2017), Birhane et al. (2017), and Hassan et al. (2017), for example, reported that most students did not perform BSE because of insufficient information and skills about its steps. Findings of our study on reasons for the majority of the study participants not doing BSE practices also corresponded to the results of these studies.

None of the studies investigated the specific knowledge of the non-invasive biomarkers of breast cancer among female nursing undergraduates. The results of the present study revealed inadequate knowledge of the non-invasive biomarkers of BC, such as sweat, urine, breath odor, and nipple aspirates, for breast cancer detection.

The study findings confirmed that the study population had inadequate knowledge of the non-invasive biomarkers of breast cancer at baseline. A training program should be implemented to increase the level of knowledge about the non-invasive biomarkers of BC and BSE practice because, when educated youth are well aware of the disease and its early diagnosis procedures, they can create community

awareness about the easy and early diagnosis of breast cancer using breath, sweat, and other non-invasive biomarkers discussed in this study. The outcomes of this study could be useful for policymakers to chalk out policies by focusing more on knowledge-building measures about the non-invasive biomarkers of breast cancer and knowledge of the breast self-examination technique, which would help in controlling the incidence of the disease and preventing its adverse outcomes on the quality of life.

Conclusion and Recommendations

In summary, there appears to be a broad general awareness about breast cancer among the study participants. However, only a small portion have a thorough understanding and knowledge of breast cancer, despite the fact that most of them have heard of the disease. Programs for educating nursing professionals about breast cancer symptoms, non-invasive biomarkers, and prevention should be launched, especially at the university level.

Knowledge- and skill-based interventions are required for early diagnosis using sensitive non-invasive biomarkers, such as changes in the smell of sweat, breath, or discharge from the nipples. This would help in better managing the disease, reducing the psychological load, and improving the quality of life of affected people. In view of the lesser percentage of study participants with knowledge of BSE practice, it is advisable that BSE knowledge and practice be incorporated into the nursing program.

Limitations

The main limitation of the study was the small sample size. A cross-sectional study sample should be large so as to get accurate findings from the study participants.

The self-report questions for the young nurses were another limitation of this study because of their bias.

Strength

The published data on breast cancer knowledge among nursing undergraduates are totally lacking from this very important island, which is now registered under UNESCO for its immense underwater wealth; hence, the study outcomes will advance our understanding of the existing knowledge on breast cancer and will add to the global efforts of the WHO to better understand and manage the disease.

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Authors' Contributions

Dr. Shabihul Fatma Sayed conceptualized and designed the study and performed sampling and analyses, statistical analyses of the data, and manuscript writing. Dr. Hamad G. Dailah and Dr. Sumathi Nagarajan participated in data analyses and manuscript reviews. Dr. Siddig Ibrahim Abdelwahab and Dr. Shaived Shabeehul Hasan Abadi took part of the statistical analyses and manuscript writing. The manuscript was critically reviewed by Dr. Shabihul Fatma Sayed. All authors have given final approval of the manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Considerations

The study has been conducted in full accordance with the ethical guidelines of Jazan University, and has been approved by the College Ethical Committee (No. 1/1/1444H, 2022). Sufficient research information was provided to the participants with the help of full informed consent, and this was achieved via a consent form attached to the questionnaire. Full confidentiality was ensured. The rights of the participants, were protected by the Helsinki Code of Ethics.

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