THE PRESENT AND THE FUTURE OF BREAST CANCER BURDEN IN THE KINGDOM OF SAUDI ARABIA*

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Abstract

Background: Despite the low Cancer incidence in the Kingdom of Saudi Arabia (KSA), the country must be ready to face the challenge of foreseeable increase in Cancer burden attributed to growth and aging of population.

This work was designed to study Female Breast Cancer as a model to assess future Cancer burden and the impact on healthcare resources. Methods Cancer statistics for KSA were compared with that for USA. The Joinpoint regression program was used to identify changes in secular trends, while the GLOBOCAN 2002 software projected future incidence and mortality. Results In KSA, the age-standardized Cancer rate (ASR) is 61 per 100,000 population, while the median age at diagnosis is 54 and 49 years for men and women, respectively. Fitting the ASR for Breast Cancer did not show any significant trend over a 10-year calendar period (16.2–18.2 per 100,000), a pattern that was similar to that for USA in the prescreening mammography era. Considering the growth and aging of population and using conservative estimates for the annual percent change in incidence (increase) and mortality (decrease) by 2025, incidence and mortality cases are expected to increase by about 350% and 160%, respectively.

Conclusion: In developing countries, future Cancer rates could demonstrate a considerable increase and enormous demands on healthcare resources. The present work may provide an impetus to study other prevalent Cancer types particularly in developing countries.

Keywords: Breast Cancer in Saudi Arabia Incidence Developing Country.

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INTRODUCTION

The Kingdom of Saudi Arabia (KSA) has witnessed gigantic progress in socio-economic development over the last 30 years. The country has committed vast resources to improving medical care for its citizens, and it earned 26th place according to the WHO ranking of the world's healthcare systems [1]. World Cancer statistics Parkin et al. estimated that there were 10.9 million new cases, 6.7 million deaths, and 24.6 million persons living with Cancer in the year 2002 [2]. Rates could further increase by 50% to 15 million new cases in the year 2020. Comparisons of Cancer rates across time or region are complicated by variation in the age structures of different populations. To compensate for such variations, a statistical technique called age-standardized rate (ASR) is employed. ASR is a summary measure of the Cancer rate that a population would have if it had a standard age structure [3]. The most frequently used standard for international comparisons is the World Standard Population (WSP).

KSA Cancer statistics In 2007, the population of KSA was estimated to be 27 million including approximately 6 million resident expatriates. Currently, half the Saudi population is under the age of 20 [4].

The National Cancer Registry (NCR) is a populationbased registry commenced reporting Cancer since January 1994 [5]. In 2002 and according to the NCR, the total number of all Cancer cases reported among Saudis and expatriates was 5,876 and 1,700, respectively. In the same year, 52% of male and 34% of the female patients were diagnosed in the age group above 59 years, while that age group accounts for only 5.2% of the Saudi population.Among Saudi patients, the ASR was 61 per 100,000 population. The mean age at diagnosis was 54 and 49 years for men and women, respectively.

World Breast Cancer incidence Breast Cancer is by far the most frequent Cancer of women worldwide with an estimated 1.15 million new cases in 2002. Incidence rates are high in most of the developed areas, with the highest ASR in North America (99 per 100,000). The high incidence in the more affluent world areas is likely because of the presence of screening programs that detect early invasive Cancers [6]. After the implementation of screening mammography, there was an additional increase of tumors among older women [7, 8]. The rates are low (\30 per 100,000) in most of Africa and Asia. In the period 1975– 1990, the largest increases, greater than 1% and sometimes 5% per year, are exhibited by registries previously having low rates of disease. In contrast, the smallest increases are usually seen in places previously having high rates.

Since 1998, overall Breast Cancer incidence rates have decreased 9.8%, with a decrease of 12% among women age 50–69 years [9]. Recent declines in hormone replacement therapy (HRT) usage have likely accelerated this decreasing incidence trend among older women [10, 11].The change in Breast Cancer incidence in USA could have been also related to a major decrease in the rate of screening mammography [12].

KSA Breast Cancer incidence In KSA, there is no national Breast Cancer screening program. According to the 2002 NCR statistics, there were 932 cases of Breast Cancer among females (614 cases were Saudi women). The disease was the most frequent Cancer among females accounting for 21% of all Cancer sites. The ASR was 17 per 100,000 Saudi women [5]. While underreporting may be attributed to that low incidence, it is unlikely to be a major contributing factor. The NCR is a well-structured program that was established in 1994. The reported low ASR in the country is similar to that reported from other low-incidence countries in the same region [2, 3, 13]. Moreover, examining ASR among women younger than 50 years—a more uniform group among different societies—showed an even lower ASR (approximately 10 per 100,000).

World Breast Cancer mortality, Breast Cancer ranks less highly (fifth) as a cause of death because of the relatively favorable prognosis where mortality- to-incidence ratio is 0.35. That favorable prognosis of Breast Cancer explains its high prevalence rate of 17.9% [2]. The overall pattern of Breast Cancer mortality reveals high rates for Western, industrialized nations, and lower rates for less industrialized and Asian nations [14]. Recently, however, Breast Cancer mortality rates in selected countries have been falling [15, 16]. In KSA, while current Cancer Care programs are well established, enormous additional resources will be required to meet future increase in Cancer incidence. In this report, we considered Female Breast Cancer as a model that allows examining current and future Cancer burden.

METHODS

Age-standardized rates for Breast Cancer in KSA were calculated from the NCR database adjusted for the WSP 2000. ASRs' incidence per 100,000 USA woman-years was calculated with SEER*Stat 6.2.3 [17] using information from the SEER databases collected from nine Cancer registries covering a calendar period from 1973 through

2003 and adjusted according to the WSP 2000. SEER's Joinpoint regression program was used to identify changes in secular trend and to determine whether apparent changes in trend data are statistically significant, two-sided, P\0.05 [18]. The software takes the annual rate data and fits a series of joined straight lines on a log scale to the trends in rates. The tests of significance use a Monte Carlo Permutation method. In this report, the resultant trends of varying time periods were described by an annual percentage change (APC). To predict Female Breast Cancer incidence and mortality in KSA, we used the GLOBOCAN 2002 database software that estimates incidence and prevalence of, and mortality from 27

Cancers for all countries in the world in 2002 [19].

RESULTS

Table 1 and Fig. 1 show the ASR for Female Breast Cancer in KSA (1994–2003) and USA (1994–2003, 1984–1993, and 1974–1983). It appears that the ASR in KSA did not show any significant trend over a 10-year calendar period (16.2–18.2 per 100,000 women). That steady pattern is similar to that in USA prior to the implementation of screening mammography (1974–1983). On the other hand, ASR rates in USA during the 1980s and the 1990s showed steady increase. In KSA, the median age of Breast Cancer patients increased from about 40 years during the calendar period 1994–1998 to 45 yeas during 1999–2002. In 2003, the median age was up to 48 years.

Table 2 shows the summary statistics for the ASR fitting of trends by Joinpoint software for USA women during three different decades. From 1974 to 1983, the APC in the first line segment showed significant decrease that more likely represents early unstable data, besides the possible inclusion of some prevalent cases. The significant increase in the APC in first line segment of the subsequent decade (1984–1993) is the result of launching mammography screening. In the most recent decade, there was a significant increase in the APC of about 2% during the first line segment only. Fitting the ASR data for KSA cases (1994–2003) did
not demonstrate any significant trend in the APC (Table 3 and Fig. 2). That the pattern in KSA was similar to that for USA during the prescreening mammography era (1974–1983) again with a decreased–though not significant– in the APC during the first line segment. Future Breast Cancer burden in KSA According to the US Census Bureau International Database, by the year 2010, 2025, and 2050 the total female population of KSA is expected to be 14, 17, and 25 million, respectively [20]. Moreover, the median age of females in the country is projected to increase from the current 21 year to 24, 29, and 36 year in 2010, 2025, and 2050, respectively. Figure 3 shows the pattern of median age of females in KSA and USA from 1990 to 2050. While the difference in the median ages is currently 14 years, it would only be 10 and 4 years in 2025 and 2050, respectively. GLOBOCAN 2002 incidence data for KSA are slightly higher than those reported by the NCR as data were adjusted for under- and delayed-reporting, besides adjustment against rates in nearby regions. Predicting numbers were estimated using conservative estimates of APC of 0 to 3% increase or 0 to -1% decline for incidence and mortality rates, respectively. Table 4 demonstrates the expected increased incidence and mortality cases based on trends in future decades. In 2025, most of the affected women could be in the age group 45–54 years; however, in 2050 the disease would predominantly affect women above the age of 65 years. Table 4 also shows that incidence cases could increase by approximately 350% and 1600% in 2025 and 2050, respectively, as compared with 2002.
Furthermore, mortality cases could increase by 160% and 450% in 2025 and 2050, respectively. Notwithstanding, the projected future Breast Cancer burden was not modeled to account for any additional increase in incidence if the country embraced a national mammography screening program.

DISCUSSION

While the ASR for Female Breast Cancer in KSA is among the lowest in the world [5], our analyses predicted a significant increase in Breast Cancer burden in the coming decades. The natural growth and aging of the country population would be the main attributable factors for such increase. Moreover, it is expected that the fertility rates in the coming few decades would be only half of the current trends [20]. The latter factor together with the expected older age at first full-term pregnancy due to social development would lessen the protective effect of these reproductive variables [21–23]. A recently published survey clearly demonstrated a significant increase of age at first pregnancy and age at marriage, and a decrease in parity rate [24]. Also recently, it has been shown that the country is witnessing a high prevalence of physical inactivity [25] and an alarming increase in obesity [26, 27]. Furthermore, Saudis are embracing westernized nutritional habits than ever before [28, 29]. The prevalence of HRT use in postmenopausal women in KSA is not precisely known. A recent retrospective analysis showed that 47% of Saudis had taken HRT at some time after menopause [30]. On the other hand, in another cross-sectional study in a primary care setting, only 5% of women were using HRT [31]. With the release of the new warning data, we expect that the use of HRT in the country will be even lower. With the planned introduction of a nationwide health insurance program, it is also expected that Cancer rates would show additional increase. In KSA, the median age of Breast Cancer patients demonstrated an increase over a decade (1994–2003). On the other hand, in USA the median ages initially increased from 60 to 63 years, and then decreased over time to 60. During 2000 to 2003, the bimodal age distribution returned to predominantly younger ages at onset with a peak frequency near age 50 years [9]. That recent pattern is similar to current pattern in KSA. Meeting future demands in oncology practice in KSA, the healthcare personnels are approximately 180,000 and it is dominated by expatriates of various nationalities [32]. Saudis constituted 20% of the total
number of physicians and Saudi nurses, 27%. In 2002, the health-worker-per-population ratio was 15 physicians per 10,000 [33], which compares favorably with the World

Health Organization (WHO) minimum recommendation of one physician per 10,000 population for developing countries, and the WHO Eastern Mediterranean Region average of 9.4 physicians per 10,000 population [34]. However, the future expected increase in Cancer burden as demonstrated here for Breast Cancer mandates visionary strategic plans. Shortage in the supply of oncology manpower is a worldwide predicament. Aging and growing population, increasing numbers of Cancer survivors, and slower growth in the supply of oncologists will result in a significant shortage of medical and gynecologic oncologists in USA by 2020 [35]. Shortage in oncological surgeons, radiation oncologists, and nurses also exists [36–39]. In British Columbia, patients often wait 6–8 weeks for an initial assessment and up to 10 weeks after that for treatment [40]. Lack of resources and basic infrastructure worldwide means that millions of people worldwide have no access to Cancer screening, early diagnosis, treatment, or palliative care [41]. Reducing paperwork and regulations, and improving efficiency through information technology such as electronic medical records are highly recommended [35].

Facing the prospect of manpower shortages by training more physicians and nurses is not always easily attainable and cannot be recommended as the sole plausible strategy. Authorities in KSA should embrace the concept of training sufficient number of nurse practitioners and physician assistants. Cancer preventive programs must be carefully planned to meet the expected rise in incidence. Mammographic screening program would probably be cost effective considering that 14% and 50% of patients present with distant and regional stage, respectively [5].

According to the WHO recommendations, mammography should not be introduced for screening unless the resources are available to ensure effective and reliable screening of at least 70% of the target age group. Program to encourage breast self-examination alone would not reduce mortality from Breast Cancer [42].

For any early Cancer detection programs to be effective there must be adequate healthcare resources to facilitate delivery of appropriate care. While there are a handful of adequate Cancer Care Centers in the major cities equipped with recent facilities and run by qualified and trained staff, many remote areas lack necessary human and physical resources. Unfortunately, Cancer Care disparity do exist even in the industrialized nations with vast resources [43, 44]. It may be pragmatic to initiate pilot programs in certain defined catchment areas where high-risk patients may be targeted perhaps based on their age or family history.

The pilot programs must be supported with adequate resources such as health educators, trained family physicians, efficient media campaign, dedicated static or mobile mammography units, qualified radiologists, speedy referral systems for suspected patients, etc. The pilot programs will help in studying people's willingness to participate, cultural impact, required needs, staff performance, detection rate, etc. Moreover, the single greatest opportunity to improve health and reduce deaths lies in personal behavior. In fact, behavioral causes account for nearly 40% of all deaths in

USA [45]. Battling obesity, physical inactivity, smoking, and polluted air and water should be a top national priority in the war against Cancer and other health problems. Table 4 Predicting numbers of Female Breast Cancer incidence and mortality in the Kingdom of Saudi Arabia using GLOBOCAN database. Age, Number of patients for incidence. Number of patients for mortality GLOBOCAN, We believe that the present work should provide an impetus to study other prevalent Cancer types particularly in developing countries.

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DO NOT FORGET TO EXAMINEE THE BREASTS A PLEA TO MY GYNECOLOGISTS COLLEAGUES *

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"I had just returned from taking my children to lunch one day when, by absolute chance, I felt it. Whether through woman's intuition or because of my professional training , I knew at once what the lump in a woman breast could mean. I checked the lymph nodes under my arm. The swelling I felt there convinced me beyond any doubt. I had to face the terrifying truth . As a gynecologist who had felt many similar masses, I recognized the likelihood that this was a malignancy. Clinical tests confirmed the worst ; it was Breast Cancer and it was an advanced stage .As if that is not enough it was one of the most aggressive type, with poorly differentiated cells and Cerb-B2 : 2+ .

The statistics for late detection flashed through my mind with deadly clarity.....there could surely be only one outcome. As a woman, a mother and a physician, I began the journey. In this journey, I discovered many things.

I just hope, by sharing, some of what I have learned I may help my colleague Gynecologic doctors to appreciate our roles as Health Care providers dealing with women's, and Breast Cancer. According to the National Cancer Registry (NCR) of Saudi Arabia which is a population-based registry developed in 1992, Breast Cancer is the most common Cancer, ranked first among females and it accounted for 19.9% of all newly diagnosed Female with Cancers (2,741). The ASR (Age- Standardized Rate) was 11.8/100,000 for female population[1-3].

World wide statistics confirm that Cancer of the breast is the most common Cancer in the world among women. The estimated number of cases diagnosed in 2000 was 1,050,346. Fifty-five point tow percent (55.2%) were in more developed countries. The disease in Saudi Arabia is different from many industrialized countries in that it presents at an earlier age. Approximately more than a decade younger than their American counterparts, and in advanced stages[4,5].

The fact, a rather frustrating one, is that successful treatment i.e. the cure, of Breast Cancer depends heavily on early detection[6]. Paramount to early detection is an organized screening programme including self breast examination, Clinical Breast Exams (CBEs) and most importantly mammography.

In many countries particularly developing ones –such as in our country- gynecologists plays the role of the women "primary health care" physicians. They are in a unique position to deal with women throughout most of their life stages. Some, not many, women may seek premarital checkup, but a large proportion come for common gynecological problems of reproductive age. The majority however are seen when pregnant and after delivery for postnatal checkup. Problems of the premenopausal years

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and early menopause are another opportunity for health check up. Beyond that, in advanced postmenopausal years, few women may report for gynecological checkup. Hence it is Gynecologists – not family practitioners or surgeons – who can play a major role both in fashioning women's perceptions of screening Breast Cancer and particularly towards the importance of mammography check up. The real problem comes when women's fail to recognize the importance of early detection in improving chances of survival. Women sometimes fail to do the test even thought they might be of the high risk group, the reasons for not being screened is "no reason/never thought about it" or "didn't need/know that we need it" which shows that many are unaware of thier risk.

Another possibility is that health care providers- in such case the woman Gyncologist- may not recognize such risk, or perhaps inaccurately and often inconsistently address or consider risk factors for Breast Cancer[7,8]. Findings from a nationally representative dataset conservatively suggest an estimated 9.4million women ages 40 to 75 years recently seen by a health care provider have not had a mammogram within 2 years. Twelve percent of these women had increased Breast Cancer risk, and more than 70% regardless of risk, reported no screening recommendation[9].

In Saudi Arabia there are a variety of structural, organizational, psychological, and socio cultural barriers that may preclude women from using breast-screening services.

This places an even greater challenge upon the health care system to convince such patients to undergo screening[10]. Health education and early screening programmes are important to raise public awareness and modify behavior for early detection of Breast Cancer. In this respect our role as gynecologist can't be overemphasized. The Female Breast, being relevant primarily to reproduction, is a "Gynecologic" organ. Hence gynecologists are in the best position to affect early diagnosis of Breast Cancer at its early stage.

In conclusion as a woman, as a patient and most importantly as a Gynecologist I call upon all my collogues to value our important and critical role in the early detection of Breast Cancer. By our own awareness and education of our patients, we could play an effective role in substantiating a national program to fight forward beast Cancer. This is not only important because breasts are emblematic of women identity, or being the prime source of nourishment of our babies, but so not to loose life just because we did not care to spend few more minutes to examine the breasts.

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HER-2 POSITIVITY AND CORRELATIONS WITH OTHER HISTOPATHOLOGIC FEATURES IN BREAST CANCER PATIENTS - HOSPITAL BASED STUDY*

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ABSTRACT

Objective: To review HER-2 status and its correlation with all other prognostic histopathological features of all Breast Cancer (BC) patients diagnosed between January 2000 and December 2004 at King Abdul Aziz University Hospital (KAUH) in the western region of Saudi Arabia.

Methods: Histopathology specimens were examined by Immunohistochemistry (IHC) and labeled as HER-2/neu positive when Hercep Test score was three plus (3+).

Results: HER-2/neu was reported only in 145 patients out of 260. Out of 145 patients, it was positive in 41 patients (28.3%), negative in 104 patients (71.7%). Correlations between HER-2/neu status and age, race and other prognostic histopathologic features revealed: No correlation with age (or <40 Y vs >40 Y with a p-value of 0.552), race (Saudis vs Non-Saudis with a p-value of 0.133), histopathology subtype (p=0.980), tumor size (p=0.455), number of positive lymph nodes (p=0.660), tumor grade (p=0.062), lymphovascular invasion (p=0.055) and progesterone receptor (PR) status (p=0.069) but positive correlation only with estrogen receptor status (ER) (p=0.003).

Conclusion: HER-2/neu over expression was positive in 28.3% of the tested specimens of BC which is consistent with what was reported in literature. It was found to correlate inversely with ER status. Routine testing is mandatory because of its prognostic value and impact on further management (JPMA 56:65;2006).

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INTRODUCTION

Breast Cancer is the leading malignancy in females and it accounted for 20.6% of all newly diagnosed Female Cancers (5,617) in Saudi Arabia.1 The mean age at diagnosis is 49 years. Breast Cancer is a multifactorial disease.

Several hereditary and acquired genetic alterations are known to introduce genomic instability, resulting in a disbalance between cell proliferation and cell death, and ultimately in tumor growth development and progression. In the process of tumor growth and progression, a large number of hormones, growth factors, receptors, signal transduction pathways and proteases are involved, forming valuable targets for new (molecular) biological therapies.2 Several histological features have prognostic significance, such as histopathological subtypes, tumor grade, lymphovascular invasion, ER and PR status, Proliferation markers and DNA content, peptide hormones, growth factors and their receptors, oncogenes and tumor suppressor genes.3 HER2/neu is the human homologue of the neu gene, called HER2 or CerbB2, shares extensive homology with EGF-R (C-erbB1).

HER2/neu or its protein p185 is overexpressed in 10-35% of BC.4 It is considered one of the poor prognostic factors in Breast Cancer. The overall survival was significantly better for patients without HER2/neu receptor markers compared to patients with HER2/neu overexpression (p=0.007).5 This study presents the results of HER-2 status and its correlation with all other prognostic histopathological features of Breast Cancer (BC) patients at KAUH, Saudi Arabia.

MATERIALS AND METHODS

Histopathology reports of all patients diagnosed to have BC between January 2000 and December 2004 at KAUH were reviewed. All available data regarding demographic and prognostic histopathologic features were collected and analyzed. Histopathologic features were; histopathology subtype, tumor size, number of lymph nodes, tumor grade, lymphovascular invasion, ER and PR status and HER2/neu oncogene overexpression.

Histopathology specimens were examined by Immunohistochemistry (IHC) and labeled as HER-2/neu positive when Hercep Test score was three plus (3+) only and all other results were considered negative. All unknown cases were excluded from the study. Results of HER2/neu status were analyzed by using simple descriptive statistical analysis (frequency distribution, cross tabulation, chisquare and Fishers exact test) by SPSS statistical program and then correlated with age, race and all available prognostic features.

RESULTS

Two hundred and sixty histopathology reports of BC patients were reviewed. All characteristic features (sex, age, race, tumor site, histopathology subtype and HER2/neu status) are summarized in *(Table 1)*. Almost all were females and 3 (1.1%) were males. Age distribution ranged from 20 to 87 years with a mean age of 47 years. Two thirds (61.5%) were >40 years of age while 31.2% were equal or <40 years.

Correlation of HER2/neu status with age showed that HER2 was positive in 14 patients (34.1%) of the young age group (<40 years) versus 27 patients (65.9%) of >40 years (p=0.552). HER2/neu status was found positive in 41 patients (15.8%) of the total cases reviewed and 28.3% of the tested specimens, negative in 104 patients (40%) of the total cases and 71.7% of the tested specimens. One hundred and fifteen (44.2%) were excluded from the study because they were unknown. Correlation of HER2/neu status with all other prognostic features, are summarized in *(Table 2)*.

There were no significant correlation between HER2/neu status and the following features; Histopathology subtype (p=0.980), tumor size (p=0.455), number of positive lymph nodes (p=0.660), tumor grade (p=0.062), lymphovascular invasion (p=0.055) and PR status (p=0.069). The only positive significant correlation was found with ER status which is inversely correlated with HER2/neu oncogene over expression (p=0.003).

DISCUSSION

Multiple different oncogenes have been described previously to be amplified in BC including HER2, EGFR, MYC, CCND1, and MDM2. Gene amplification results in oncogene overexpression but may also serve as an indicator of genomic instability. As such, presence of one or several gene amplifications may have prognostic significance.6 In our study, only 41 out of 145 patients (28.3%) were positive for HER2/neu (3+) and 104 were negative (71.7%). This is similar to what was reported in literature. Regarding age, almost one third of our patients (31.2%) were equal or less than 40 years of age. Primary BC arising before age 40 are far more aggressive and likelier to metastasize and reduce patients survival than those arising in older patients, regardless of hormone receptor status.7 Only 40% of breast tumors arising before age 45 overexpress ER, but these ER positive younger age tumors appear more proliferative and genetically unstable (higher nuclear grade, more frequent p53 abnormalities) than the more prevalent ER positive tumors arising later in life.8 In literature, HER2 and EGFR overexpression tend to decline with age and the opposite with ER overexpression which tends to increase with age.7 In this study, correlation of HER2 overexpression with age showed that 14 patients (34.1%) were positive in the young age group and 27 patients (65.9%) were above 40 years. Regarding race, HER2 overexpression revealed no significant difference.

Correlation of HER-2/neu with all other prognostic features

revealed that it is inversely correlated with ER status (HER-2 was positive in only 19.5% of BC patients with positive ER status vs 80.5% positive in BC patients with negative ER status). Regarding HER-2/neu and PR status, HER-2 was positive in only 36.6% of BC patients with positive PR and 63.4% of patients with negative PR status which did not reach statistical significance. Eppenberger- Castori et al. reported that erbB2/HER2 overexpressing BC express much lower levels of both ER and PR protein as compared to breast tumors lacking erbB2/HER-2 overexpression.
9 The reported studies suggest that the magnitude of reductions in both ER and PR levels may in part explain the apparent clinical resistance of these tumors to selective estrogen receptor modulators like tamoxifen.10 HER-2 gene amplification was also found to be significantly associated with high tumor grade. HER-2 amplification was found to be an independent poor prognostic factor of tumor grade, tumor size and lymph node status.6 In our study, tumor grade III was higher in HER-2 positive patients (46.3%) than HER-2 negative ones (25%) but it did not reach statistical significance.

Assessment of HER2/neu overexpression in BC patients has an impact on prognosis and treatment modality. Trastuzumab is a recombinant humanized monoclonal antibody that targets the extracellular domain of the HER2 growth factor receptor. Addition of trastuzumab to chemotherapy for patients with metastatic BC who are HER-2 (3+) improves survival. In conclusion, HER-2/neu overexpression is positive in 28.3% of the tested specimens of BC patients at KAUH which is consistent with what was reported in literature. It was found to correlate inversely with ER status. Routine testing is mandatory either by IHC or by FISH method because of its prognostic value and impact on further management.

Table 1: Characteristics of 260 Breast Cancer patients.

Character	Frequency	%
Sex:		
Female	257	98.9
Male	3	1.1
Age:		
< or 40 Y	81	31.2
> 40 Y	179	68.8
Race:		
Saudi	100	38.5
Non Saudi	160	61.5
Tumour site:		
Right	135	51.9
Left	115	44.2
Bilateral	2	0.8
Unknown	8	3.1
Histopathology:		
Infiltrating Ductal Carcinoma	229	88.1
Lobular Carcinoma	12	4.6
Medullary Carcinoma	4	1.5
Papillary Carcinoma	4	1.5
Others	11	4.3
HER2/neu status:		
Positive (IHC 3+)	41	15.8
Negative	104	40.0
Unknown	115	44.2

Table 2: HER2/neu Oncogene (HER-2) overexpression analysis (excluding unknown cases) and its correlation with all other Histopathological features in Breast Cancer patients.

Histopathological features	HER2/neu Oncogene		
	3 + ve	-ve	
	No.(%)	No.(%)	p-value
Histopathology:			
Infiltrating Ductal Caricinoma	36 (87.8)	93 (89.4)	
Lobular Carcinoma	1 (2.4)	3 (2.9)	
Medullary Carcinoma	1 (2.4)	3 (2.9)	0.980
Papillary Carcinoma	1 (2.4)	2 (2.9)	
Others	2 (4.9)	3 (2.9)	
Tumor size:			
T1 (< 2 cm)	11 (26.8)	29 (27.9)	
T2 (2-5 cm)	21 (51.2)	39 (37.5)	
T3 (5-10 cm)	4 (9.8)	11 (10.6)	0.455
T4 (> 10 cm)	0 (0)	2 (1.9)	
Unknown	5 (12.2)	23 (22.1)	
Number of Lymph nodes:			
Negative	21 (51.2)	53 (51)	
1 - 3	8 (19.5)	21 (20.2)	
4 - 9	4 (9.8)	10 (9.6) 0.660	
10 or >	2 (4.9)	1 (1)	
Unknown	6 (14.6)	19 (18.3)	
Tumor grade:			
G.I	6 (14.6)	13 (12.5)	
G.II	15 (36.6)	60 (57.7)	
G.III	19 (46.3)	26 (25)	0.062
G.IV	0 (0)	0 (0)	
Unknown	1 (2.4)	5 (4.8)	
Lympho-vascular Invasion:			
Yes	12 (29.3)	13 (12.5)	
No	18 (43.9)	56 (53.8)	0.055
Unknown	11 (26.8)	35 (33.7)	
Estrogen Receptor status:			
Positive	8 (19.5)	47 (45.2)	
Negative	33 (80.5)	57 (54.8)	0.003
Unknown	0 (0)	0 (0)	
Progesterone Receptor status:			
Positive	15 (36.6)	54 (51.9)	
Negative	26 (63.4)	50 (48.1)	0.069
Unknown	0 (0)	0 (0)	

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BREAST CANCER AWARENESS AMONG HEALTH PROFESSIONALS*

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The prevalence of Breast Cancer in recent years has prompted women to seek medical advice randomly with minimal breast symptoms, but only a small number of women are aware of the proper methods of conducting breast self-examination (BSE) or the importance of radiological screening for Breast Cancer. In the Middle East, the incidence of Breast Cancer is rising and affecting a younger population compared to the West.[1] Breast Cancer awareness programs (BCAP) are meant to help in the prevention and early detection of Breast Cancer. In the Arab world, there are very few such programs. In an attempt to develop a structured BCAP in our community and to trigger wide-scale programs, 300 women from the medical field were interviewed to be recruited as future health education providers.

Subjects and Methods

This study was carried out at King Fahd University Hospital, Al Khobar, in the Eastern Province of Saudi Arabia. The 300 subjects were women working in the medical field, and comprised final-year medical students, interns, nurses, technicians, pharmacists, residents and consultants. The subjects were informed about the increased incidence of Breast Cancer in Saudi Arabia, especially among the young female population, and were requested to fill out a questionnaire, which was designed to capture the following information: 1) demographic data,2) family history of Breast Cancer, 3) performance of breast self-examination, 4) timing of breast self-examination, and 5) attitudes towards mammographic screening.

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Results

There was a 100% response rate, with all participants promptly filling in the questionnaires. The participants ranged in age from 21-58 years, with a mean age of 33.4 years. They were all aware of the gravity of Breast Cancer but had no background knowledge on the methods of conducting breast self-examintion, or the need for mammographic screening. Of the 300 women, 78% had previously performed BSE, however, only 17.3% had performed the monthly examination at the proper time, and only 42.7% had agreed to a mammographic screening. Rating the level of knowledge about Breast Cancer detection methods among the subjects was also disappointing in the high-risk group. Thirty-five of the subjects (11.6%) gave a positive family history of Breast Cancer, yet only 10 of these (28.5%) performed the regular monthly BSE, while 20 (57%) had agreed to a mammographic screening. Such results obtained from a highly educated sector are very disturbing, especially from people working in the medical field.

Discussion

Breast Cancer is the most common malignancy among women internationally.[2] Hormonal, environmental and genetic factors have been shown to play a role in the pathogenesis of Breast Cancer. It is known that the incidence of Breast Cancer varies in different ethnic groups, with high incidence rates being reported from North America and Europe, while figures from the Middle East have been significantly lower. However, Breast Cancer in this part of the world comprises the highest relative frequency rates of all Cancer types,[3] compared to data from Western Societies.1 Women from developing countries are diagnosed at a much younger age.[4] And the nature of health education and information is significantly different in developing countries compared to the developed ones.

Evaluation of public awareness, attitudes and misperceptions is of fundamental importance for the successful implementation of Cancer control activities.5 The scarcity of known proven means for Breast Cancer prevention prompts more reliance on the methods for early detection to improve patient outcomes.

The primary goal of Breast Cancer awareness programs is to promote and develop awareness about the importance of early detection and advanced treatment of Breast Canceramong medical professionals and society at large. This can be achieved by encouraging proper BSE, annual evaluation by medical professionals, quality-control screening mammography, and genetic testing, especially in high-risk groups. The rationale of the monthly BSE is for women to familiarize themselves with the consistency of the breast tissue, as they are best placed to detect any new changesthat occur.

An annual breast examination by medical professionals is a mandatory part of a complete physical check-up. Screening mammography, although not a perfect diagnostic tool, remains the best means of early detection of Breast Cancer. It is expensive and requires high-technology equipment, special films with dedicated processing, and highly trained radiologists. It detects only 95% of all Breast Cancers, but has proven its essential value in early Cancer detection.[6] A common fear and misconception in our community is that the screening mammography increases the risk of breast Cancer. It has been reported that exposure of the breast tissue to ionizing radiation is associated with increased risk of Breast Cancer, especially when exposure occurs at a young age. Existing barriers for obtaining mammography include lack of physician recommendation; the misconception that if there are no symptoms, then there is no need for a mammogram; lack of awareness about mammography; lack of access to a facility; and the fear of Cancer detection.

Another common misconception is that the majority of women develop Breast Cancer because of a genetic link. In fact, it has been estimated that only 5%-10% of all Breast Cancers may be hereditary, caused by a mutated predisposing gene. The inheritable type of Breast Cancer is characterized by early age of onset, bilaterality, an autosomal dominant mode of inheritance and association with other Cancers.[7] Treatment options for women at high risk include chemoprevention and prophylactic mastectomy. Results from a recent study showed that prophylactic mastectomy significantly reduces the incidence of Breast Cancer.[8] The level of education plays a role in the ease of delivering health education, however, it can also be an obstacle if some misconception exists. In a previous study, the participants, who were highly educated, had a higher erroneous response regarding the outcome of Breast Cancer, the potential risk factors, and the importance of mammography than the general population.[9] In the current study, it was expected that the results from the highly educated medical personnel would supersede those of the general population. On the contrary, the limited knowledge and misconception among these professionals was alarmingly disappointing, with only 17.3% performing the BSE at the proper time, and only 42.7% having agreed to a mamm graphic screening. Even the high-risk group (11.6%) ignored the potential risks and did not comply with the basic principles of early detection.

The need for Breast Cancer Awareness Programs cannot be overemphasized. Over 70% of the target population must accept the invitation to participate if a screening program is to significantly reduce mortality. High standards should be set to ensure quality assurance at each stage of the screening process.

To establish Cancer Health Education, Cancer Prevention or early detection programs, primary health physicians should be educated on the objectives of these programs. They are the main health service providers for the community at large and have to be equipped for this important task. This can be achieved through incorporation of appropriate topics in the curricula of the undergraduate medical students, and into continuing education for physicians, nurses and technicians. Professional training courses should be available for practicing physicians, and perhaps academic or financial rewards should be offered.[10] It is also essential to implement regular audit and reviews of these programs in order to achieve the set standards.

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MAMMOGRAPHIC PARENCHYMAL PATTERN IN 489 SAUDI PATIENTS*

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ABSTRACT

BACKGROUNDS: Mammographic parenchymal pattern has been proposed as a method of determining woman at high risk of developing Breast Cancer. a relative risk of Breast Cancer as high as 37:1 was determined for DY pattern as compared with N1 pattern the intermediate risk values determined for P1 pattern and P2 pattern were not uniformly confirmed by others. This study is aimed towards breast mammographic Parenchymal Pattern Among Saudi women.

Materials and methods: mammograms of Saudi women who presented to King Fahd hospital of the university AL KHOBAR Saudi Arabia between January 1994 and December 1997 were retrospectively reviewed assignment of mammographs to various reports.

RESULTS: five hundred fifty four mammograms were identified, of which 65 [11.7%] were for women with a definitive diagnosis of Breast Cancer that were excluded. the remaining 489 mammograms were analyzed. Their mean (SD) age was 38.8 (9.9) years. one hundred thirty eight mammograms [28.2%] 158 [32.3%], 138 [28.2%] and 55 [11.3%] showed N1, P1, P2, And DY pattern, respectively. there was no statistically significant difference in the mean age of women in any of the categories.

CONCLUSION: Saudi women demonstrate a relatively high prevalence of P2 and DY mammographic parynchemal patterns [39.5%] moreover, these potentially risky patterns were identified among younger women. These data in addition to providing emerging evidence from population- based Cancer registries in Saudi Arabia about Breast Cancer incidence, should provide input to assess the feasibility and cost- effectiveness of a nationwide mammography screening program.

Key words: mammography, parenchymal

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INTRODUCTION

Breast Cancer is the leading Cancer site and main cause of death among women in many countries worldwide[1]. in the kingdom of Saudi Arabia (KSA) hospital based statistics have shown that the disease has the highest crude frequency rates among Saudi women, with an average frequency of 18%[2][3]. Moreover population- based statistics accessible from some regions of KSA(4) and from the national Cancer registry (unpublished data) validated that higher rate, albeit relatively low age adjusted rates of 15 to 17 per 100,000 have been reported from KSA[4] and from similar neighboring countries like Kuwait[5].

Mammography has been shown to be the most effective method of finding small Breast Cancer and presumably will give a patient the best opportunity for cure or at least long–term survival[6].

In 1976, Wolfe[7] described four patterns of mammograms, varying with the amount of ductal and dysplastic elements present, and reported relative risks as great as 37:1 from the highest (DY) to the lowest class (N1) relative risks of 3.1 for DY to N1, 3.5 for P2 to N1 and 2.0 for P1 to N1 were determined, Wolfe's work received international attention and prompted over 50 articles, some of which supported his theory, while others did not the most cogent criticisms were advanced by Egan and Mosteller[8]. who suggested that Wolfe's results were due to a «masking effect» that elevated the risk rations of the P2 and PDY categories solely because of the difficulty of identifying Cancer in these dense breast. Mendell et[9] al suggested that Wolfe's methods introduced a bias by requiring a normal mammogram before a patient could be inclouded in a study.

In 1985 whitehead and his group[10] showed in their study of 221 prevalent and 706 incident Cancer followed for up to ten years that a masking effect does exist but that it operates in addition to a difference in risk of Breast Cancer within the four Wolfe classes, and Wolfe's hypothesis is found to be valid.

In this retrospective study, the author was prompted to study breast mammographic parenchymal patterns among Saudi women who were not diagnosed to have Breast Cancer.

Providing description of such patterns should shed Some light on the potential risk of developing Breast Cancer, furthermore, these date should contribute further support for any future national mammography screening program. however the low incidence of Breast Cancer may make a screening program not cost effective.

MATERIALS AND METHODS

The radiology logbook and the hospital computerized database at king Fahd university hospital, Al-Khobar, Saudi Arabia, were reviewed to identify Saudi women who had mammographic studies over a four–year period (January 1994 to December 1997). to eliminate any bias, patients with a definitive diagnosis of Breast Cancer were, subsequently excluded. for the purpose of the current analysis, all studies were reviewed by tow experienced radiologists without knowledge of the diagnosis and the finding that were initially reports. mammographic parenchymal pattern was determined based on Wolfe's classification[11], concordance was attained in most cases 495 (89.4%) and for 59 cases (10,6%) where there was a discrepancy an open discussion between the two radiologists was conducted to reach consensus.

A computerized database was constructed, and various variables were numerically coded using a personal computer. One-way analysis of variance (ANOV) was used to compare the age of women assigned to the four mammographic patterns and classified Wolfe's classes in different age groups adjustment for multiple comparisons was made using Bonferoni's technique. A P value < 0.05 was considered significant . All data analysis were performed using the BMDP statistical software[12].

RESULTS

Over a four–year period (January 1994 to December 1997) 554 Saudi women had mammographic studies at King Fahd Hospital of the University. of those, 65 (11.7%) were found to have a definitive diagnosis of Breast Cancer and were subsequently excluded from further analysis the remaining 489 mammographic studies constitute the basis of this report the mean age (SD) for the entire group was 38.8 (9.9) years with a range of 15.75 years the confidence intervals were 95% (CI 51 to 75). the main complaints were as follows: 44 (9%) with no breast complaints, 236 (48.3%) with breast pain, 201 (41.1%) with breast lump, 42 (8.6%) with nipple discharge, 3 (0.6%) with nipple retraction, and 19 (3.9%) with auxiliary lump.

The parenchymal pattern in 489 patient was 138 mammograms 32.2% for N1, 158 mammograms 32.3 for P1, 138 mammograms 28.2% for P2,and 55 mammograms 11.3% for DY. *(Table 1)* shows the distribution of women and their mean age grouped and 95% confidence intervals according to Wolfe's classification, further analysis of the number of patients in age bands of ten-year intervals revealed *(Table 2)* the distribution of woman in each age band according to Wolfe's classification. ANOVA did not show any statistically significant difference in the mean age of woman in any one of the four categories against the others (P= 0.21).

DISCUSSION

Breast Cancer is the leading Cancer type among women in Saudi Arabia[2]. Mammography has been shown to be the most effective method of finding small Breast Cancer and presumably will give a patient the best opportunity for cure or at least long–term survival[6]. The land mark study of the health insurance plan of New York Breast Cancer screen-

ing program in New York[13] demonstrated a 30% reduction in mortality in woman over the age of 50 years who were screening annually by mammography and physical examination, conclusively demonstrating the value of such screening. Mammography was also demonstrated as an effective method of finding non- palpable and minimal Breast Cancer detection demonstration project study of 270,00 self–referred women in 29 different centers[14]. In 1976, Wolf stated that the radiographic appearance of the parenchyma provides a method of predicting who will develop a Breast Cancer on basis of the radiographic appearance of the breast parenchyma patients were placed into four groups of risk for developing carcinoma of the breast.

N1 is the lowest risk category. In it, the parenchyma is composed primarily of fat with, at most, small amounts of «Dysplasia» without visible ducts. P1 is also a low risk pattern where the parenchyma is chiefly fat with prominent ducts in anterior portion up to one-fourth of volume of breast, also there may be a thin band of ducts extending into a quadrant. P2 is a high–risk pattern that represents a severe involvement with a prominent duct pattern, occupying more than one–fourth of volume of breast, on the other hand, DY is the highest risk pattern, that pattern shows severe involvement with «dysplasia,» which often obscures an underlying prominent duct pattern[11]. it is possible to predict with considerable accuracy which woman will develop Breast Cancer and, equally important, those who are less likely to develop it based solely on the parenchymal pattern as seen by mammography utilizing Wolfe's classification[7].

Over the period of January 1994 to December 1997, 554 Saudi patients presented to King Fahd Hospital with different breast complaints. Patients with definitive diagnosis of Breast Cancer were excluded (11.7%). analysis of the remaining 489 mammograms m revealed that there was a considerable proportion of Saudi women patients at higher risk to develop Breast Cancer (28.2% were P2, and 11.3% were DY). The proportion of women with P2 and DY pattern in this series was surprisingly higher than their percentages in the Wolfe's original report irrespective of age[11]. Women with P2 and DY patterns, particularly if symptomatic, required meticulous, periodic clinical examination supplemented with annual or biannual mammography. Systematic Breast Self-Examination for those high-risk groups cannot be overstated. The young age of women in this series adds more importance to the necessity of launching a well-designed screening program enriched with an intense public awareness protocol. The poor knowledge about Breast Cancer and the unsatisfactory attitude towards the disease in our community that we demonstrated in an earlier study[15] provide an indisputable plea for such preventive strategies, but the low incidence of Breast Cancer may make a screening program not cost effective.

Table 1: Distribution of women and their mean age (SD) AND 95% CI grouped according to Wolfe's classification

	N1	P1	P2	DY
No. (%) Of Women	28 137	32.3 158	28.6 140	11 54
Mean Age (SD)	12.3 39.9	8.6 39.2	9.2 38.0	8.1 37.0
(%95 CI)	41.9-37.8	37.7 - 40.4	39.8-36.8	40.1-35.2

Table 2: Distribution of women in each age band according to Wolfe's classification

Age band	N1 (%)	P1 (%)	P2 (%)	DY (%)
<31 years	5.52 72	4.9 24	6.3 31	1.64 8
40 -31 years	11.6 57	13.7 67	10.0 49	6.1 30
50-41 years	5.5 72	10.4 51	9.8 48	2.7 13
> 50 years	5.5 27	3.3 16	2.0 10	0.8 4
Total	28.2 138	32.3 158	28.2 138	11.3 55

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BREAST SELF-EXAMINATION AMONG SAUDI FEMALE NURSING STUDENTS IN SAUDI ARABIA*

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Abstract

Objective: The purpose of this study was to investigate the knowledge and practice of breast self-examination (BSE) among Saudi female nursing college students in Riyadh, Kingdom of Saudi Arabia (KSA).

Methods: A cross-sectional study was conducted between October and December 2003. Saudi female nursing students (149) from the College of Applied Medical Sciences, King Saud University, and from the College of Nursing, King Abdulaziz Medical City, National Guard, Riyadh, KSA, constituted the study population. The questionnaire contained items on the demographic characteristics of the respondents, knowledge of Breast Cancer, attitudes toward BSE and questions regarding the practice of BSE. The analysis included descriptive statistics and chi-squared tests to examine the association between BSE and demographic, medical history, knowledge of BSE and attitudes toward
BSE.

Results: The results of the study indicated that 66% of the sample performs BSE. Approximately 62% of those who perform BSE said they learned information regarding BSE in their college curricula. The significant relation was found between higher levels in nursing college and BSE practice. Except for age, no significant relation was found between the socio-demographic factors and BSE practice. The sample showed strong belief in nipple discharge as a causing factor of Breast Cancer and had significant correlation and BSE practice.

Conclusion: Positive correlations were found between nursing students BSE practice and their academic experience in nursing college. Studies like these can enhance the knowledge regarding BSE among nurses and other medical professionals.

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Introduction

Breast self-examination is a simple, very low cost, noninvasive adjuvant screening method for the detection of early Breast Cancer (BC) in women. Its purpose is 2 fold: to make women familiar with both the appearance and the feel of their breasts and to help women detect any changes in their breasts as early as possible. There is evidence that women who correctly practice BSE monthly are more likely to detect a lump in the early stage of its development, and early diagnosis has been reported to influence early treatment and to yield a better survival rate.[1] In a randomized, controlled assessment of the effectiveness of From the Department of Surgery, College of Medicine and King Khalid University Hospital, King Saud University, Riyadh, Kingdom of Saudi Arabia.

International screening programs for BC in Scandinavian countries, it was found that mortality had fallen by 31% after 7-years for women aged 40-70 at the beginning of the trial.[2] Unfortunately, despite the benefits of regular BSE, few women actually examine themselves; in fact, a majority does not even know how to do a BSE.[3,4] Although opinions conflict regarding the value of BSE,[5,6] the American Cancer Society continues to support the inclusion of BSE as an early detection behavior.[7] Research suggests that women who receive personal instruction on BSE from a health care professional demonstrate greater knowledge and confidence and are more likely to practice routine BSE than those who become aware of the method from other sources.[8,9] There is no published data on the practice with which BSE is performed by the female health care professionals (nurses) in Saudi Arabia. There is also little information regarding these Professionals knowledge of the procedure. The present study explores the level of knowledge among nursing students in the Department of Nursing at College of Applied Medical Sciences, King Saud University, and at the College of Nursing, King Abdulaziz Medical City, National Guard, Riyadh, KSA, regarding facts related to BC and BSE, and the practice of BSE by those nursing students. Information regarding such

a study population is important as [1]. They are women and, thus, at risk of getting BC, and 2. They study and train in settings where primary health care is offered and have, as part of their duty, to give instructions to other women on how to perform BSE competently.

Methods

A cross-sectional study was conducted between October and December 2003, to investigate the research problem. The study was designed to provide a description of the knowledge and practice of performance of BSE, the sociodemographic factors, medical history and the interrelationships among these variables. All female nursing students from College of Applied Medical Sciences, King Saud University, and from the College of Nursing, King Abdulaziz Medical City, National Guard, Riyadh area constituted the study population. The total sample consisted of 149 nursing students with a mean age of 21.60 (2.60 SD). The questionnaire contained items on the demographic characteristics of the respondents; knowledge of the signs, symptoms, risk factors, early detection, and prognosis of BC; attitudes toward BSE; and questions regarding the practice of BSE. The analysis included descriptive statistics and chi-squared tests to examine the association between demographic data (age, marital status, family income) body mass index (BMI), personal and family history of breast diseases and BSE. Statistical analysis. Data was entered using IBM compatible pc and Microsoft Excel software. Statistical analysis was performed using SPSS version [10].

Results

Participants in this study ranged in age from 18-32-years, with a mean of 21.6-years (SD =2.6) and their BMI was 22.30 (SD=4.5). Single women made up to 85% of the sample with 15% being married. Only 14% of the subjects had 3,000 SR per month, 43% of them had 3,000-7,000 SR, 27% of them had 7,000-14,000 SR and rest of them (16%) had more than 14,000 SR as per monthly family income. In the present study, 66% of the subjects are doing BSE regularly. Only 7% of the subjects were having positive family history of BC and 70% of them showed regular menstrual cycle.

Out of the total sample, 16 subjects reported pain in their breasts. However, more than 40% of the subjects learned facts regarding BSE in their college curriculum. *(Table 1)*. *(Table2)* presents the association between demographic variables and cues to action, and the practice of BSE. A chi-square was used to test the association of BSE practice with age, level in nursing college, BMI, marital status, family income and family history of BC, regular menstrual cycle and feeling pain in breasts. The variables, age (above 21-years) and higher level in nursing college (level 4 and higher) were significantly associated ($P<0.001$) with the practice of BSE. Table 3 presents the BSE beliefs and their significant correlation with the practice of BSE. Sixty to eighty percent of subjects believe that, presence of masses in the breasts, family history of BC, nipple discharge, frequent mammograms and smoking are the causing factors for BC. Thirty-five to 55% of subjects believe that, usage of contraceptives, wearing nylon bra, using breast creams, direct sun exposure, obesity and ovarian pain are the BC causing factors. In this present study sample, pregnancy at early age and breast feedings are the least believed to be causative factors of BC. The significant correlation was seen between nipple discharge and BSE practice. Table 4 displays the frequency, and percentage distribution of knowledge of the recommended BSE steps. The most frequently endorsed steps were examining breasts in front of a mirror or during bath,

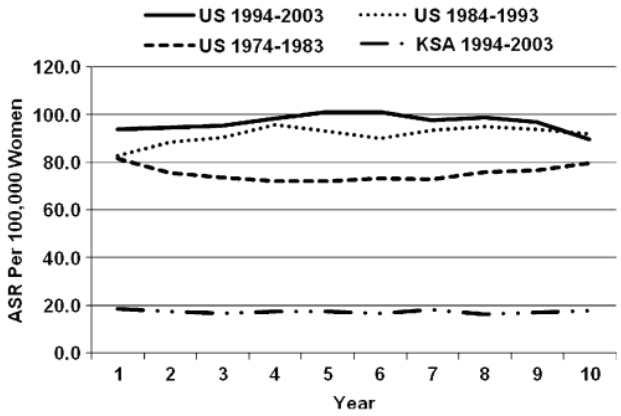

Fig. 1 The age-standardized rate (ASR) for female breast cancer over several decades in the Kingdom of Saudi Arabia (1994–2003), and USA (1994–2003, 1984–1993, and 1974–1983)

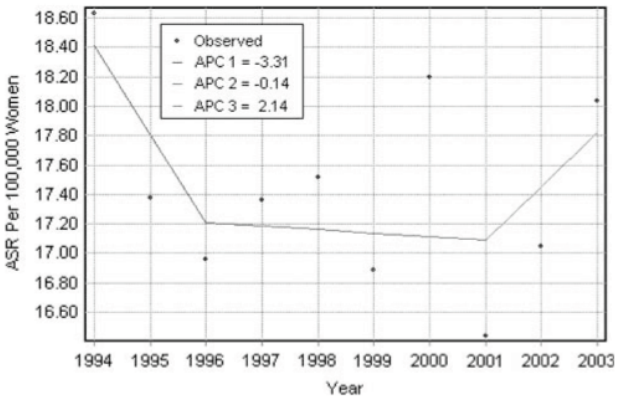

Fig. 2 Fitting the age-standardized rate for female breast cancer patients in the Kingdom of Saudi Arabia (1994–2003) according to the Joinpoint regression model

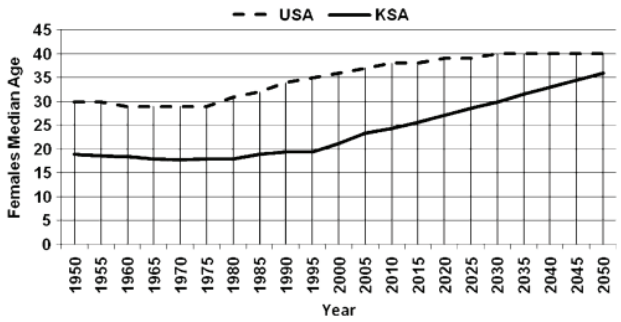

Fig. 3 The pattern of median age of females in the Kingdom of Saudi Arabia and the USA from 1990 to 2050

examining breasts while lying down, and feeling for lumps, hard knots, nipple discharge, or breast thickening. The least frequently endorsed step was looking at breasts in the mirror with hands on thighs. Overall, the majority of subjects knew most of the recommended steps.

Discussion

To date, the etiology of BC is uncertain and adequate primary prevention is not possible. Thus, early detection measures remain the first priority for national health promotion programmers. These measures include BSE, which is a screening behavior of relevance to women's health. It is a unique procedure in many ways: it is inexpensive, noninvasive, involves little time and physical energy, is simple and does not depend on professional help.[10] However, the effectiveness of BSE remains controversial. The American Cancer Society[11] continues to recommend monthly BSE to women, but the Canadian Task Force on Preventive Health Care has announced that physicians should no longer routinely teach BSE as a screening technique for Cancer to older women as it can do more harm than good.12 In contrast, it is argued that a significant number of women find masses when they are bathing or dressing, and BSE once a month may contribute to a women's heightened awareness of what is normal for her.[13] In a study of 1500 patients, it was shown that 81% of women first noticed symptoms themselves.[14] Thus one may argue that if women are finding most BC themselves, it is possible that by knowing how to do a more thorough BSE they could find BC of smaller sizes, which in turn may lead to an improved prognosis. Medical professionals have knowledge of the causes of diseases and have learned to recognize the warning signs of disease when present in their patients. It seems, however, that these professionals, do not always recognize the signs of their own illness.[15,16] Nursing profession is one of them, and it is very important for self carefulness to be able to recognize the signs of their own illness. Breast self-examination is an examination that should be perfect for nurses. They have the knowledge of the clinical signs of BC and of the examination technique, and they can do it themselves without consulting a physician. Furthermore, they are especially aware of the importance of the early detection of BC for a successful treatment. It has been shown that confidence in one's BSE ability is strongly correlated to BSE practice in the general population.[17,18] In the present study, 66% of the subjects are practicing BSE, and the significant correlation was seen between students' level of advancement in nursing curricullam and BSE practice. In a similar study, Budden19 reported that, 96% of the nursing
students performed BSE during a year but only 46% had practiced regularly as once per month.
Haji-Mahmoodi et al,20 reported from a cross-sectional study among female health care workers that, more than

70% of subjects had knowledge regarding BSE and also had strong belief on its beneficial affects but only 6% of them was performing BSE regularly. It is well documented that beliefs and behaviors surrounding BC vary with several factors such as ethnicity, age, education, and socioeconomic status.[21,22] In the present study, significant correlation was seen between age, nursing educational level, and nipple discharge. These findings are in-agreement with Budden,[23] that, the positive correlations were found between student's BSE practices and their nursing experience. However, marital status, family monthly income and family history of BC showed no significant association with BSE practice. Similar results were reported by Budden,24 that, no significant relation was found between a family history of BC and regular BSE practice. Self-efficacy theory and behavioral self-regulation theory suggest that the most important predictor of a highly specific behavior (such as BSE) is the individual's own confidence in performing the behavior.[25,26] Our findings of the predictors of BSE were consistent with self-efficacy theory.[25] However, our results were only partially consistent with behavioral self-regulation theory.[26] Other studies have demonstrated that optimists, who anticipate good outcomes, tend to engage in beneficial behaviors, including skin self-examination, more than do pessimists.[27-29] A more optimistic attitude would appear to increase the likelihood of greater self-efficacy in performing BSE. In other words, women who anticipated favorable outcomes in general were more confident in their breasts. This theory applies to the present study; our findings showed that there is a strong belief that nipple discharge is a causative factor of BC, which was reflected on its significant correlation with BSE practice. In conclusion, the results of this study suggest that, for nurses, if more emphasis of BSE occurs in the workplace and in undergraduate and postgraduate courses, nurses' teaching of BSE to clients may be increased. Also, the provision of BSE educational programs is necessary to increase nurses' knowledge, confidence, performance, and teaching of BSE.

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DECREASED AXILLARY LYMPH NODE RETRIEVAL IN PATIENTS AFTER NEOADJUVANT CHEMOTHERAPY*

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ABSTRACT

Background: The purpose of this study was to assess our clinical impression that fewer lymph nodes are retrieved after level I and II axillary dissection after neoadjuvant chemotherapy and whether there is a positive correlation between the total number of lymph nodes are retrieved and the number of diseased lymph nodes.

Method: Patient included those with stage IIB, IIIA, and IIIB Breast Cancer of whom 77 had neoadjuvant chemotherapy and 58 had initial surgery only. All had modified radical mastectomy with in continuity level I and II axillary dissection.

Results: patients after neoadjuvant chemotherapy had 14.3 + 6.7 lymph nodes detected versus 16.9 + 8.8 (mean + SD; P <0.057) for those with initial surgery only. The number of positive nodes were 3.7 + 4.7 versus 6.6 + 8.7 (mean + SD; P <0.033) respectively and the number of negative were 10.6 + 7.5 versus 10.4 + 8 (mean + SD; P <0.9). the correlation between the number of positive lymph nodes and the total number of lymph nodes was r = 0.58; P <0.001.

Conclusions: it appears that fewer lymph nodes are retrieved after level I and II axillary dissection after neoadjuvant chemotherapy. The total number of lymph nodes retrieved increases directly with the number of positive lymph nodes in patients not treated with chemotherapy.

Keywords: axillary lymph node retrieval; neoadjuvant chemotherapy; locally advanced Breast Cancer

We have had the clinical impression that we retrieve fewer lymph nodes after neoadjuvant chemotherapy and that there is an association between the total number of lymph nodes retrieved and the number of diseased lymph nodes. The aim of the present retrospective study was to test these clinical observations.

* The American Journal of Surgery 2002, Vol.184, 299-301

METHODS

From our database we collected patients treated during the 5 years from 1995 to 1999, excluding stages I and IV and patients who had any surgery outside king Faisal specialist hospital and research centre. We then had 77 patients who had neoadjuvant chemotherapy and 58 who had initial surgery. The neoadjuvant chemotherapy consisted of a regimen containing either anthracyclin or taxol [1] .all patients had modified radical mastectomy with a continuity level I and II maxillary dissection by the same surgical team post mastectomy specimens were examined as follows. multiple sections were taken from the tumor site . in addition to random sections from the nipple – areola complex and the Four quadrants. All grossly identified nodal tissue was sampled and the remaining fat was immersed in Carnoy>s solution for more lymph node sampling. For the postchemotherapy specimen, the extent of the therapeutic effect in the primary tumor and axillary nodes was examined. Descriptive statistics for the continuous variables are reported as mean +1 standard deviation. Comparisons between groups were made using students t test and the chi-square test or fisher>s exact test as appropriate.

RESULTS

The clinical response to neoadjuvant chemotherapy was complete in 21% (16 of 77), partial in 45% (35 of 77), and stable disease in 34% (26 of 77). No patents progressed on neoadjuvant treatment. Clinical data are available in *(table 1)* and pathology lymph node data are summarized in *(table 2)*.

The total number of lymph nodes retrieved after neoadjuvant chemotherapy was 14.3+6.7 versus 16.9+8.8: (P= 0.057) without neoadjuvant chemotherapy. After neoadjuvant chemotherapy the number of positive nodes was 3.7 + 4.7 versus 6.6 + 8.7 : P= 0.0003 without neoadjuvant chemotherapy. The number of negative nodes both with neoaduvant treatment and without, however, was of the same magnitude 10.6 + 7.5 versus 10.4 + 8.0; P= 0.9, respectively. The number of diseased lymph nodes and the total number retrieved after level II and ii dissection in the group treated with surgery initially were positively correlated (r= 0.58; P= 0.001; *Fig. 1*). After neoadjuvant chemotherapy there was no sush correlation (r= 0.17; P = 0.1).

COMMENTS

In this study we have found support for our observation that fewer lymph nodes are retrieved after neoadjuvant Chemotherapy. We have also confirmed previous studies [2-5] demonstrating significantly fewer positive lymph nodes after neoadjuvant chemotherapy. The number of negative nodes is the same in patients with and without neoadjuvant chemotherapy.

In this study, patients with similar stages have been compared and the surgery has been peen compared and the surgery has been performed in the same manner by only tow, very experienced breast surgeons. The pathology team has been the same throughout the study period. The most significant difference between the study groups was that patients treated with neoadjuvant chemotherapy had more advanced axillary disease and a higher overall stage *(table 1)*. The obvious disappearance of lymph nodes is yet to be explained. Chemotherapy-induced histologic and cytologic changes have been described [6,7]. Fibrosis and various cytologic changes such as increased cell size and cytoplasmic vacuolization of tumors treated with chemotherapy have been described [6,7]. In some cases. We have seen that a lymph node is completely filled and replaced by fat and in other cases replaced by fibrosis. Perhaps previously diseased lymph nodes become fragile and therefore fragment during our current way of processing? Have recently had 2 patients after high-dose sequential chemotherapy in whom no lymph nodes were found after routine level I and II dissection. Interestingly, both patients had locally advanced breast tumors measuring at maximum 10 cm and 12 cm, respectively, and both had large fixed lymph node conglomerates. After treatment, each had complete clinical response and no tumor was found in the breast or the axilla.

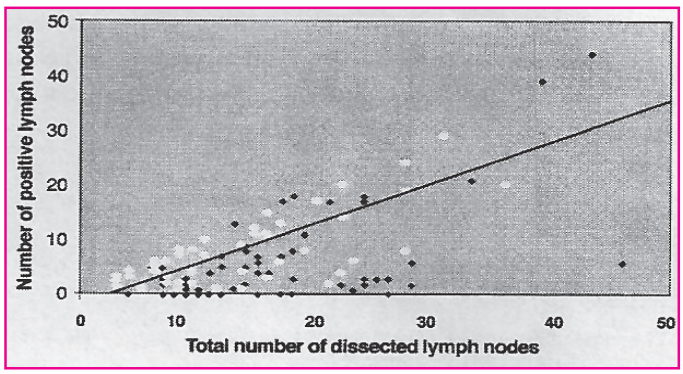

fig. 1. Correlation between number of positive nodes and the total number of dissected lymph nodes. (white dots) r= 0.58 (P= 0.001), current data

The strong correlation between the total number of lymph nodes in patients treated with surgery initially has previously been demonstrated by our group [8]. There is no such correlation in patients treated with neoadjuvant chemotherapy. If we assume a relatively fixed number of lymph nodes in the axilla, one possible explanation of our findings is that several are too small to be detected in individuals without disease [9]. Hypertrophy of lymph nodes is a well-recognized phenomenon and is frequently seen in advanced Breast Cancer. A second possibility, however never described would be hyperplasia, i.e. the multiplication of lymph nodes after stimulation.

In summary, our data demonstrate a variability in axillary lymph node disease and treatment with neoadjuvant chemotherapy. These findings support the idea that a more conservative surgical approach to the axill should be considered in patients with a significant response to neoadjuvant chemotherapy.

Table 1: clinical information

	Naoadjuvant therapy	No neoadjuvant therapy	P value*
Clinical tumor stage			
T2	3 (3.9%)	33%))19	<0.0001
T3	33 (42.9%)	20 (33%)	
T4	41 (53.2%)	20 (34%)	
Clinical axillary lymph			
Node stage			
N0	20 (26%)	17 (29%)	<0.005
N1	36 (46.8%)	39 (67%)	
N2	19 (24.6%)	2 (4%)	
N3	2 (2.6%)	0 (0%)	
Clinical stage			
IIB	15 (19.5%)	27 (46.5%)	<0.005
IIIA	20 (26%)	11 (19%)	
IIIB	42 (54.5:%)	20 (34.5%)	

* Chi-square or fishers test as appropriate.

Table 2: Lymph node pathology

	Naoadjuvant therapy	No neoadjuvant therapy	P value*
Total nodes removed			
Mean	14.3+6.7	16.9+8.8	0.057
Median	14	15	
Range	1+41	4+46	
Positive nodes removed			
Mean	3.7+4.7	6.6+8.7	0.003
Median	2	3	
Range	0-18	0-44	
Negative nodes removed			
Mean	10.6+7.5	10.4+8	ns
Pathologic lymph nodes stage			
N0	28 (36%)	13 (22%)	Ns
N1	49 (46%)	45 (78%)	Ns

* Unpaired t test, Chi-squre or Fishers exact test ad appropriate, Ns = not significant.

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THE ROLE OF MRI ON CANCER DETECTION AND MANAGEMENT: THE SAUDI ARABIAN EXPERIENCE*

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INTRODUCTION

MRI is increasingly being used as a problem solving tool; Examination timing, indications, and technique are critical to its success. It is particularly useful in mammographically-dense breasts, patients presenting with abnormal axillary nodes, the post-operated breast and to monitor neoadjuvant therapy response. It has also been recommended for screening high risk patients.

Disease Epidemiology

Breast Cancer in Saudi Arabia is the most common Cancer in women. National screening is as yet not implemented. Most women usually come because of symptoms. Many of the Cancers discovered are at an advanced stage.

SCREENING METHODS OVERVIEW

Although mammography remains the primary imaging modality for the detection and evaluation of Breast Cancer, additional imaging is usually required to further stage the disease so that preoperative or other management strategies are planned. MRI is superior to other modalities in the detection of occult disease in the same or contralateral breast. MRI is also superior than other breast imaging modalities in the evaluation of the post operative breasts, monitoring neoadjuvant chemotherapeutic response and in the assessment of high risk patients.

In our hospital, 1226 patients had breast MRI examinations. 406 patients were thought to have malignant lesions based on MRI findings. 298 cases were histopathologically proven malignancies. Of the proven malignant cases, 28 patients gave a family history of Breast Cancer. 71 patients continued their investigations elsewhere and histopathology results were not available. 35 cases were false positive. Only 2 cases were false negative. Breast Cancer recurrence was diagnosed by MRI in 42 patients, 8 of those were histopathologically negative for malignancy. Only a few patients were monitored by MRI during the course of their Neoadjuvant therapy.

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OUTCOME AND RECOMMENDATIONS

- Contrast-enhanced MRI has a high sensitivity and a high negative predictive value for the detection of invasive Breast Cancer.
- It is superior to mammography and sonography for the detection of recurrence.
- Breast MRI should be interpreted in conjunction with other breast imaging modalities.
- Patients' history with dates of previous treatments should be given.
- As with mammography, previous MRI studies availability is helpful.
- It is also logical that lesions found only on MRI are biopsied under MRI guidance, a situation which is difficult to undertake in most hospitals if a dedicated breast MRI unit is not available.
- MRI should be used to screen high risk patients.
- MRI has made a significant impact on Breast Cancer detection and management in our practice.

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CHALLENGES OF CANCER SCREENING PROGRAM*

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BACKGROUND

Cancer is a global public health problem. It is the second leading cause of death worldwide. It is often regarded as a disease cause of the developed world, but with improved living standards, incidence in low and middle income countries is on the rise. By the year 2030, seven out of every ten new cases will occur in the developing world.[1]

Survival outcomes vary dramatically throughout the world and variation in access to quality Cancer Care is a major cause of these discrepancies.[2] Over 40% of more than 7 million Cancer deaths can be prevented. Furthermore, Cancer is curable if detected early and treated adequately. This applies in particular to Breast Cancer, colon, prostate, and cervical Cancer as the technology for screening, diagnosis and treating is mature.

A recent publication about the future burden of Breast Cancer in Saudi Arabia which anticipated the incidence and mortality of cases will increase by about 350% and 160% respectively over a ten-year period.[3]

Saudi Society for Cancer recognized the importance of prevention and early detection. In an effort to combat Cancer through early detection, Abdulatif Charitable Screening Center was established as the first dedicated Cancer Screening Center in the Kingdom.

The objective of this manuscript is to address the challenges/barriers which were encountered. Data related, center related, personal related challenges were identified, different interventions were implemented for each barrier. Furthermore, we will review the planning strategies for such project. This information may be of benefit to health care providers, health care organizations and health care systems personnel when considering establishing public Cancer screening programs.

Readers are advised to review the World Health Organization (WHO) guide for effective programs which includes six modules that provide practical advice for program manager and policy makers on how to advocate, plan and implement effective Cancer control programs, prevention and early detection.

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