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Education-Family Physician Corner

Breast Cancer Prevention in Primary Health Care

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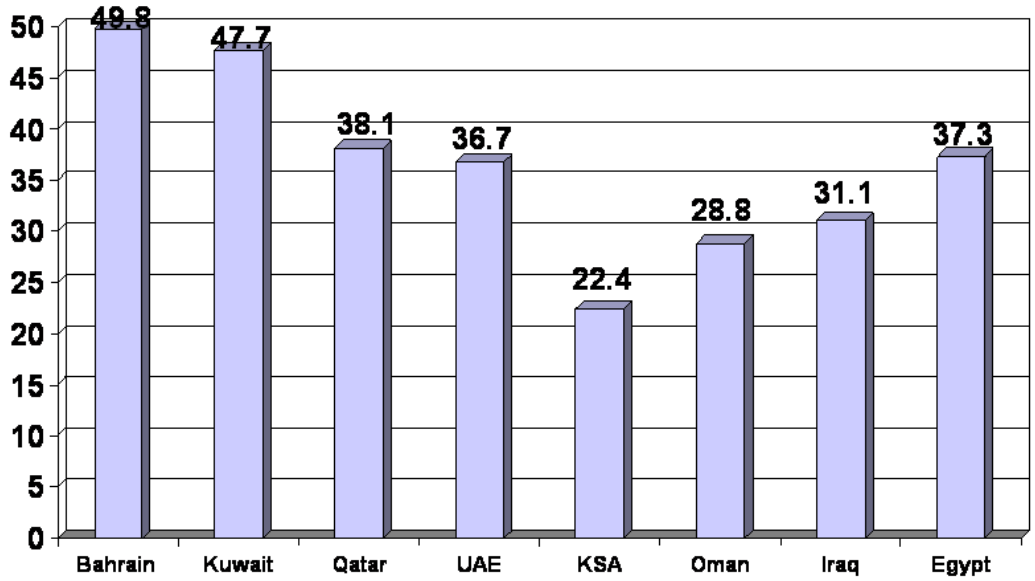
Breast cancer is the commonest invasive malignancy and the main cause of death from cancer among women globally[1]. The incidence however varies around the world, scoring the lowest in under-developed countries and the highest in developed countries[1-3].

In Bahrain, the estimated incidence of breast cancer is 117. The age-standardized rate (ASR) per 100,000 is 49.8, exceeding that for the rest of Middle Eastern countries, see figure 1[1]. A higher number of women are diagnosed each year worldwide, the mortality associated with breast cancer is on the decline, principally due to early diagnosis and prevention program.

Primary care physician plays a vital role in prevention, diagnosis and management of breast cancer. This article reviews breast cancer and focuses on the preventive measures the family physician should pay attention to.

Figure 1: Breast Cancer (ASR per 100,000) in Some of the Middle Eastern Countries[1]



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Prevention

Preventive measures can be divided into four levels, see Table 1. The government should play the major role in prevention by issuing laws for health damaging exposures and hazardous emissions. The government should generate subspecialties and health protective resources, to prevent the emergence of risk factors leading to cancer, specifically to breast cancer. A good example is to have strict laws regarding tobacco use especially among females[4]. Because multinational companies target and load our conservative societies with tons of unhealthy processed food products, our role as health-care providers is to ring the bell for the government and legislative bodies to interfere and restrict the expansion of these companies. Westernizing our lifestyle is probably one of the major factors that led to drastic rise in the incidence of breast cancer in our region particularly in Bahrain, a cohort study is needed to prove that; needless to say, the war pollutants, which spread in the region during the two Gulf wars?

Table 1: Levels of Prevention

Level of Prevention	Stage of the Disease	Target Population
Primordial	Underlying conditions Leading to causation	1. Total population 2. Selected group
Primary	Specific causal factors	1. Total population 2. Selected group 3. Healthy individuals
Secondary	Early stage of the disease	1. patients
Tertiary	Late stage of the disease	1. patients

*Taken from Sorin Ursoniu lectures' on primordial prevention with modification

Primary Prevention

The aim is reducing the risk factors of breast cancer. The commonest risk factors are listed in table 2.

Table 2: Risk Factors of Breast Cancer

Non-modifiable Risk Factors	Modifiable Risk Factors
Gender- Female	Increased Bodyweight
Increased Age	Physical Activity
Genetic Risk Factors and Positive Family History of Breast Cancer	Alcohol
Personal History of Breast Cancer	Ionizing Radiation
Race	Socio-economic Status
Early Age at Menarche	Oral Contraceptives
Older Age at First Birth	Smoking
Lower Parity	Environmental Estrogens
Not Breast Feeding	High Fat Diet
Late Menopause	Clomiphene Citrate

Proliferative Lesions of Benign Breast Disease	Hormone Replacement Therapy

Non-modifiable Risk Factors

Gender
Women are at a higher risk for developing breast cancer. This is because women have a higher number of breast cells compared to men, in addition to their constant exposure to stimulating hormones such as estrogen and progesterone. Males can develop breast cancer but the incidence is low. The male to female risk is 1:100. In countries where the incidence of breast cancer is lower than the rest of the world, this ratio reaches up to 1:7[5].

Age
Age is a strong risk factor for many types of malignancies including breast cancer. It is well known that the older the woman, the higher the risk of developing breast cancer[6], see table 3.

Table 3: Breast Cancer and Age among Females

Risk up to age 25	1 in 15,000
Risk up to age 30	1 in 1,900
Risk up to age 40	1 in 200
Risk up to age 50	1 in 50
Risk up to age 60	1 in 23
Risk up to age 70	1 in 15
Risk up to age 80	1 in 11
Risk up to age 85	1 in 10
Lifetime risk (all ages)	1 in 9

*Taken from Cancer research UK (2003)

Genetic Risk Factors and Positive Family History of Breast Cancer

In the past two decades, we have begun to learn about the genetic predisposition to breast cancer. It is estimated that around 7% of all cases can be attributed to inheriting autosomal dominant susceptibility alleles[7]. Two genes were strongly associated with increased risk of breast cancer, BRCA1 and BRCA2. One of the largest population based studies in the UK found that 2% of the cases presenting before the age of 55 years with breast cancer were associated with BRCA1 or BRCA2 mutations[8].

These genes are important for the repair of double-strand DNA breaks. If a woman inherits a BRCA1 or BRCA2 mutation, she will have up to 80% chance of developing breast cancer during her lifetime. She is also more likely to develop it at a younger age.

Although the genetic component has a considerable influence, a Nordic study on twins showed that environmental and lifestyle factors have great effects as well. This population-based study of 45,000 pairs of twins in three Nordic countries showed that hereditary factors

were estimated to contribute to around 25% and environmental and lifestyle factors to around 75% of the inter-individual differences in susceptibility to breast cancer[9].

Many studies show that for first-degree relatives (mothers, sisters, daughters) of affected patients the risk of breast cancer is about two-folds and for affected second-degree relatives (grandmothers, aunts, granddaughters), the risk is less[10].

There are many other genes, which are associated with an increased risk of breast cancer and other malignancies, such as the ATM, CHEK-2 and p53 tumor suppressor genes. Therefore, it is very important to obtain a detailed family history and ask specifically for individuals diagnosed with cancer. Table 4 illustrates some of the rare familiar cancer syndromes, which are linked to breast cancer.

Table 4: Familial Cancer Syndromes Associated with Breast Cancer

Gene	Cancer Syndrome	Associated Tumors
BRCA1	Breast/ovarian predisposition	Breast, ovarian, bowel, prostate
BRCA2	Breast/ovarian predisposition	Breast (including male), ovarian, prostate, pancreatic
TP53	Li Fraumeni syndrome	Childhood sarcoma, brain, Leukemia, adrenocortical, carcinoma, early-onset breast
PTEN	Cowden's syndrome	Breast, gastrointestinal, thyroid (benign and malignant)
STK11/LKB1	Peutz-Jeghers syndrome	Breast, gastrointestinal, pancreatic, ovarian
ATM	Ataxia telangiectasia	Non-Hodgkin lymphoma, ovarian, breast (in heterozygote carriers)

*Taken from Cancer research UK, 2003

Personal History of Breast Cancer

It is estimated that if a woman has had breast cancer in the past, her risk increases 2-6 times for developing another primary in the breast[11].

Race

Some races are at a higher risk of developing breast cancer, such as Ashkenazi Jews. This is probably because of inheriting the causative genes as mentioned earlier. Breast cancer has a slightly higher incidence among white women compared to African-American women[5]. Nevertheless, the mortality among African-American women tends to be higher. This is explained by the aggressive nature of cancer affecting African-American women. Asians seem to have a lower risk[12].

Reproductive History, Breast Feeding and Breast Cancer Risk

Age at Menarche

It has been established by several studies that the earlier age of menarche the higher the risk of developing breast cancer. The relative risk for premenopausal breast cancer is reduced by almost 7% for each year that menarche is delayed after the age of 12 years[6].

Age at First Birth

It is well known that early pregnancy is protective against breast cancer. It is estimated that for each year of delay there is an increase of 3% risk of breast cancer[13].

Parity
Parity is protective in reducing the risk of breast cancer. For each birth, there is a reduction of 7% if breast-feeding is excluded[13].

Breastfeeding
Breast-feeding is not only good for the infant; it reduces the breast cancer risk by 4.3% for each year a woman breastfeeds[13].

Age at Menopause
Late menopause subjects woman to longer periods of exposure to estrogen and progesterone hormones; therefore, increasing the risk of breast cancer[14]. The risk increases by 3% for each year delayed[15].

Benign Breast Disease and Mammographic Parenchymal Patterns
Benign breast disease can be classified as non-proliferative lesions, which do not increase the risk of cancer and proliferative lesions, which increase the risk 2-4 folds compared to women with no lesions[16]. Patients with radiodense mammographic parenchymal patterns are at increased risk of breast cancer compared to women with radiolucent mammographs[16].

Increased Bodyweight
A high body mass index (BMI) of > 28kg/m^2 compared to normal BMI in postmenopausal women was shown to increase the risk 30%[17]. BMI is calculated by dividing weight in kg by height in metres^2.

Physical Activity
Moderate exercise reduces the risk of breast cancer especially in the pre-menopausal period. Key et al suggested 30% reduction[16].

Alcohol
Alcohol consumption has been clearly associated with a moderate increase in the risk of breast cancer. There is about 10% increased risk per 10g alcohol (1 unit) consumed per day[16].

Other Significant Risk Factors

Ionizing Radiation
Exposure to radiation (including diagnostic X-rays) at a younger age increases the risk of developing breast cancer[18].

Smoking
Although smoking has a clear association with all types of cancers, there is no enough data or studies to support or mitigate the fact that it increases the risk of breast cancer[16].

Socio-economic Status
Many studies showed that the higher level of socio-economic status is the higher risk of breast cancer[5].

Oral Contraceptives

There is an increased risk of 25% for developing breast cancer among women taking combined oral contraceptives, but this risk falls after cessation[16].

Factors Having Less Clear Association

Environmental Estrogens
Some artificial compounds have a structural similarity to estrogen such as organochlorines, but so far, there is no clear association to breast cancer[16].

Diet
A high fat diet was suggested to increase the risk, but there is no hard evidence to support this hypothesis[16].

Clomiphene Citrate (Clomid)
There is a growing concern that the wide use of fertility drugs such as Clomid might increase the risk of breast cancer. Burkman et al support the association, but others showed no evidence to support it[19,20]. The latter is more subjective because it is a cohort study, which is known to be less influenced by methodological biases. Therefore, further studies are needed to confirm the association.

Hormone Replacement Therapy (HRT)
Many studies within the last few years have shown very controversial results regarding the use of HRT and the risk of breast cancer. However, it was noticed that as the decline in the use of HRT, a decline in breast cancer incidence was observed mainly in women over 50 years old and in women presenting estrogen-receptor positive tumors[21]. Despite this decrease in breast cancer incidence in the absence of HRT, it still is not possible to establish a definite association with HRT use.

Secondary Prevention
Secondary prevention aims at detecting breast cancer in its early stages. Therefore it is crucial for all primary care doctors to know about all available screening tests, when to order them and to whom, see table 5.

Table 5: Screening Tests for Breast Cancer[22,23]

Screening Test	Remarks
Clinical Breast Examination	Based on fair evidence, screening by clinical breast examination reduces breast cancer mortality.
Screening by Breast Self-examination	Based on fair evidence, teaching breast self-examination does not reduce breast cancer mortality.
Mammogram	Based on fair evidence, screening mammography in women aged 40 to 70 years decreases breast cancer mortality. The benefit is higher for older women, in part because their breast cancer risk is higher.
Ultrasound	Ultrasound can detect small, otherwise occult, breast cancers. However, it should not be used alone for screening.
Magnetic Resonance Imaging (MRI)	Breast MRI is superior to mammography and ultrasound for screening women at high risk for hereditary breast cancer.

While mammogram remains the gold standard test for screening breast cancer, one should not order it for a young lady with hyperdense breast tissue. MRI has the advantage of posing no radiation and has a higher sensitivity to detect small lesions but the higher cost reserves it for women at risk.
Blood tests, which include BRCA1 and BRCA2, are available to women with strong family history of breast cancer. The test is costly and it is not supported by governmental health services nor all insurance companies are willing to pay for it. Deciding on what screening test to order should always be based on the clinical picture, needless to mention, the importance of correctly informing the patient about potential benefits and risks.

Tertiary Prevention
Means treating and rehabilitating the patient diagnosed with breast cancer, it is a multidisciplinary task, mostly taken care by secondary care doctors. However, patients recovering from breast cancer may still visit her primary care doctor for continuing support.

CONCLUSION

Primary care doctors play an important role in preventing breast cancer. Early detection is the most important practical task. This can only happen if doctors start ringing the bell and take the responsibility.

Potential Conflicts of Interest: No

Competing Interest: None, **Sponsorship:** None

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