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\(^1\).\(^2\)\(^3\).

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. 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

<table>
<thead>
<tr>
<th>Level of Prevention</th>
<th>Stage of the Disease</th>
<th>Target Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primordial</td>
<td>Underlying conditions Leading to causation</td>
<td>1. Total population 2. Selected group</td>
</tr>
<tr>
<td>Primary</td>
<td>Specific causal factors</td>
<td>1. Total population 2. Selected group 3. Healthy individuals</td>
</tr>
<tr>
<td>Secondary</td>
<td>Early stage of the disease</td>
<td>1. patients</td>
</tr>
<tr>
<td>Tertiary</td>
<td>Late stage of the disease</td>
<td>1. patients</td>
</tr>
</tbody>
</table>

*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

<table>
<thead>
<tr>
<th>Non-modifiable Risk Factors</th>
<th>Modifiable Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender- Female</td>
<td>Increased Bodyweight</td>
</tr>
<tr>
<td>Increased Age</td>
<td>Physical Activity</td>
</tr>
<tr>
<td>Genetic Risk Factors and Positive Family History of Breast Cancer</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Personal History of Breast Cancer</td>
<td>Ionizing Radiation</td>
</tr>
<tr>
<td>Race</td>
<td>Socio-economic Status</td>
</tr>
<tr>
<td>Early Age at Menarche</td>
<td>Oral Contraceptives</td>
</tr>
<tr>
<td>Older Age at First Birth</td>
<td>Smoking</td>
</tr>
<tr>
<td>Lower Parity</td>
<td>Environmental Estrogens</td>
</tr>
<tr>
<td>Not Breast Feeding</td>
<td>High Fat Diet</td>
</tr>
<tr>
<td>Late Menopause</td>
<td>Clomiphene Citrate</td>
</tr>
</tbody>
</table>
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 1:75.

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, see table 3.

Table 3: Breast Cancer and Age among Females

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk up to age 25</td>
<td>1 in 15,000</td>
</tr>
<tr>
<td>Risk up to age 30</td>
<td>1 in 1,900</td>
</tr>
<tr>
<td>Risk up to age 40</td>
<td>1 in 200</td>
</tr>
<tr>
<td>Risk up to age 50</td>
<td>1 in 50</td>
</tr>
<tr>
<td>Risk up to age 60</td>
<td>1 in 23</td>
</tr>
<tr>
<td>Risk up to age 70</td>
<td>1 in 15</td>
</tr>
<tr>
<td>Risk up to age 80</td>
<td>1 in 11</td>
</tr>
<tr>
<td>Risk up to age 85</td>
<td>1 in 10</td>
</tr>
<tr>
<td>Lifetime risk (all ages)</td>
<td>1 in 9</td>
</tr>
</tbody>
</table>

*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. 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.

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**

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

*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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{14}. The risk increases by 3% for each year delayed\textsuperscript{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\textsuperscript{16}. Patients with radiodense mammographic parenchymal patterns are at increased risk of breast cancer compared to women with radiolucent mammographs\textsuperscript{16}.

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

**Physical Activity**
Moderate exercise reduces the risk of breast cancer especially in the pre-menopausal period. Key et al suggested 30% reduction\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{16}.

**Socio-economic Status**
Many studies showed that the higher level of socio-economic status is the higher risk of breast cancer\textsuperscript{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\textsuperscript{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\textsuperscript{16}.

**Diet**
A high fat diet was suggested to increase the risk, but there is no hard evidence to support this hypothesis\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{22,23}**

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Breast Examination</td>
<td>Based on fair evidence, screening by clinical breast examination reduces breast cancer mortality.</td>
</tr>
<tr>
<td>Screening by Breast Self-examination</td>
<td>Based on fair evidence, teaching breast self-examination does not reduce breast cancer mortality.</td>
</tr>
<tr>
<td>Mammogram</td>
<td>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.</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Ultrasound can detect small, otherwise occult, breast cancers. However, it should not be used alone for screening.</td>
</tr>
<tr>
<td>Magnetic Resonance Imaging (MRI)</td>
<td>Breast MRI is superior to mammography and ultrasound for screening women at high risk for hereditary breast cancer.</td>
</tr>
</tbody>
</table>
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.

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

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**REFERENCES**