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EDITORIAL

What are our Options in the Fight against Breast Cancer?

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ما هي خياراتنا في حربنا ضد معدلات وقوع سرطان الثدي المتزايدة؟

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In this issue of SQUMJ, Hamadeh *et al.* report on the epidemiology of female breast cancer in the Bahraini population with a total of 1,005 cases diagnosed over an 11-year period.[1] The authors report the age-standardised incidence rate of 58.2 per 100,000 population in 2000 and 44.4 per 100,000 in 2010. The median age at diagnosis was 49 years and the five-year survival rate was 63%. This article raises a number of important issues. The incidence in Bahrain is midway between that of developed and less-developed countries, while the mean age at diagnosis is lower than Western countries, and survival is somewhat inferior to that reported from most developed countries.

The incidence of cancer is rising across the globe. The International Agency for Research on Cancer (IARC) publishes data in a series of reports called GLOBOCAN. A comparison of the latest two versions (2008 and 2012) shows that the number of new cancer cases increased from 12.7 million in 2008 to 14.1 million in 2012.[2,3] Breast cancer remains the most common cancer among females and the second most common cancer overall, with an estimated 1.7 million new cases diagnosed in 2012. These account for more than a quarter of all the cases of cancer diagnosed in women. The incidence has increased by more than 20% since 2008.[4] Subsequent publication of the 2014 World Cancer Report confirmed that, regrettably, the earlier forecasts correspond to the actual numbers.[5] If this trend were to continue, the total number of new cancers would increase to an alarming 22 million by the year 2025. The mortality is expected to increase to 13 million at that stage. A catastrophe is looming and urgent action is required.

What is even more alarming is the fact that there is a palpable divide between regions with a high incidence or a low incidence of cancer, and this generally corresponds to their affluence. The age-standardised incidence rate of 268 cases per 100,000 population in the more developed regions, compares to 148 cases per 100,000 in the less developed regions.[4] However, in terms of actual numbers, 43% of all cancers develop in resource-rich developed regions and 57% in resource-strapped less developed regions. While the increasing incidence of cancer in developed countries roughly corresponds to the increasing median age of population, the increasing numbers simply outgrow the median age in the less developed regions. This is also reflected in cancer-associated mortality. About 70% of cancer-associated deaths occur in less developed regions.[4,5]

The incidence of breast cancer reflects the overall cancer situation. In women, the overall age-standardised rate for breast cancer is 43.3 per 100,000, with 74.1 cases per 100,000 in developed countries, and 31.3 cases per 100,000 population in less developed countries.[3] Compared to the incidence rate of around 90 cases per 100,000 female population in the USA, Hamadeh *et al.* reported an incidence rate of 44.4–58.2 cases per 100,000 women in Bahrain.[1] The current incidence rate in Oman is 25.5 cases per 100,000 population.[6]

Although the current incidence rate in Oman is towards the lower end of the spectrum in the Gulf Cooperation Council (GCC) countries, it is the increase in the incidence and the total number of cases which is of concern. For example, in Oman, the age-standardised incidence rate of breast cancer has progressively increased from 13.8 in 1999, to 21.8 in 2005 and then to 25.5 in 2011. In 2011 alone, a total of 147 cases of breast cancer were diagnosed out of 573 new cases (25.6%). This is in comparison with 38/389 (14.9%) in 1999 and 95/422 (22.5%) in 2005.[6] The reason for the increasing incidence remains unexplained. It could be either due to better detection and registration, e.g. the use of screening mammography, or an actual

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increase in incidence. A total of 17 cases were detected using mammography over a four-year period between 2009 and 2012 in Oman (personal communication with Hon. Ms. Yuthar Al-Rawahia, Chairperson, Oman Cancer Association); however, it is not clear how many of these patients already had a palpable lump and used the mobile mammography unit for diagnosis. Conversely, it is also not known how many patients may have travelled abroad for treatment and whose data therefore may not been captured by the National Tumour Registry. Clearly, this small number of cases does not explain the increased number of breast cancer cases diagnosed in the last few years.

The data from Bahrain is in many ways similar to that reported from Oman. Hamadeh *et al*. reported a median age at diagnosis of 49 years, compared to 48.5 years reported by Al Moundhri *et al*.[7] and 47.4 years reported by Kumar *et al*.[8] It should be noted that in the two studies from Oman 50.7% and 60.4% patients presented with stage III/IV disease, respectively.[7,8] The problem of countries in the region is more or less similar: younger age, advanced stage, and hence compromised overall survival.

So what can we do? Like many other cancers, breast cancer can be tackled along the continuum of care at different stages—by the application of effective strategies for treatment and cure, early detection and prevention.[9]

The role of chemotherapy and hormone therapy (in the case of estrogen-receptor-positive tumours) is well established and the standard of care. However, a significant number of cancers still relapse. Over the last decade, important advances have led to better cure rates with the use of monoclonal antibodies, tyrosine kinase inhibitors and more recently chemo-immunoconjugates. However, the treatment has become extremely expensive and out of reach for the vast majority of patients, especially in less developed countries. Even in developed countries, the exploding cost of new agents is now causing problems. Economists have questioned the sustainability of the model of evaluating and marketing new cancer drugs.

Early detection programmes using mammography have been in place for more than three decades. Although an earlier meta-analysis of randomised controlled trials showed a relative reduction in death from breast cancer,[10] more recently, the role of screening mammography has been questioned.[11] While, a significantly higher number of early-stage breast cancers are diagnosed by this method, the advantage is offset by over-diagnosis and, in several instances, over-treatment. Over-diagnosis may account for 20–30% of cancers detected,[12] while screening has not been shown to decrease the rate of detection of advanced cancers.[13] A recently concluded randomised trial showed that screening did not reduce mortality from breast cancer.[11] Furthermore, the cost-benefit ratio of screening mammography in low incidence countries augurs against its routine use.[14] As a result, there has been a strong motion amongst the oncology community to reassess the need for breast cancer screening.

Overcoming the increasing incidence and subsequent mortality of breast cancer by prevention is a possible option. Primary prevention by lifestyle modification is an attractive and, in many cases, an achievable target. The three major initiatives in this regard have been the European Prospective Investigation into Cancer and Nutrition (EPIC) study,[15] the ViTamins And Lifestyle (VITAL) study[16] and the recommendations of the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR).[17] The EPIC is an ongoing prospective cohort study, initiated in 1992 in 10 European countries. Dietary assessment is mainly carried out through a self-administered, semi-quantitative food frequency questionnaire and information on a wide range of lifestyle factors and anthropometric measurements are collected. In the VITAL study, the participants complete a detailed questionnaire on supplement use, diet and risk factors for cancers, and the cohort is prospectively followed-up for the incidence of cancers. In 2007, the WCRF/AICR released a set of recommendations on diet, physical activity and weight management for cancer prevention on the basis of the then available evidence.[16]

Risk factors for breast cancer are different for the pre and postmenopausal population.[4] For premenopausal breast cancer, there is convincing evidence that consuming alcohol increases the risk, whereas lactation protects against it. For postmenopausal breast cancer, there is convincing evidence that the consumption of alcohol, body fatness and adult-attained height increase the risk, whereas, lactation and physical activity protects against it. Many of these factors are modifiable. However, the question is whether lifestyle modifications actually lead to a reduction in the incidence of breast cancer. More recently, answers have begun to emerge. The EPIC investigators have reported that a greater concordance with the WCRF/AICR recommendations (for example: weight loss, physical activity and avoidance of sugar, salt, alcohol and red meat) was significantly associated with a decreased risk of cancer. A one-point increment was associated with a 5% risk reduction for all cancers.[18] In the VITAL study, the breast cancer risk was found to be reduced by 60% in women who met at least

five of the recommendations, compared with those who met only one.[19] The reduction in mortality was demonstrated by the EPIC investigators, who reported that participants with maximum adherence to the WCRF recommendations had a 34% reduced risk of death compared with those who had least adherence to them.[20]

In conclusion, the incidence of breast cancer is on the increase worldwide. Although the incidence is lower in less developed countries, it is rapidly increasing and so is mortality. Early detection through screening is not widely available in many countries or may not be relevant. Genetic studies may help to identify families with increased risk, who could then be offered early detection. However, these remain a small sub-set and account for no more than 5% of all breast cancer cases. The cost of the treatment has increased spectacularly and many patients or governments cannot or would not be able to afford it. Primary prevention through lifestyle modification is an attractive cost-effective option. However, if primary prevention measures were to be adopted to combat the rising incidence and mortality, this would require a coordinated campaign. At the moment, cancer is not considered a major problem in less developed countries. There is an urgent need to remedy this opinion. Future breast cancer outcomes will be determined by recognition of the problem; creating awareness not only by the advocacy groups, but also by the physicians; widespread dissemination of information through both print and electronic media, and the will of the policy-makers.

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