LETTER TO THE EDITOR

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High Number of Familial Breast Cancer Cases in the Arabian Gulf Countries: Investigating the Reasons

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Dear Editor,

The Global Burden of Disease Cancer Collaboration (GBDCC) published the global incidence of breast cancer (BC) in 2019 as 1 961 000 (1 938 000 females and 23 000 males). BC was declared as the fifth most prevalent cause of absolute years of life lost (YLLs) among both sexes between 2007 and 2017,[1] making it one of the most serious problems facing the medical field.

As someone new to the field of genetics oncology, I started wondering why there are so many families with BC in the Arabian Gulf countries (AGC; Kuwait, Saudi Arabia [SA], United Arab Emirates [UAE] Qatar, Oman, and Bahrain), especially those with no identifiable germ-line pathogenic variants of the known BC genes. So, I started browsing NCBI PubMed and Google Scholar for an answer. It turned out that the number of BC patients with positive germ-line pathogenic variants was fairly low: in the United State only 5.03%,[2] in Japan only 5.7%,[3] and in China only 11%.[4] Interestingly, smaller communities and endogamous communities had higher frequencies of the pathogenic variants in the risk genes (Bahamas [Caribbean], 14.2%[5]; Brazil, 23.4%[6]; Israel, 16%[7]; SA, 16%[8]; Greece, 31.5%[9]; and Poland, 50%).[10]

Slavin et al[11] showed that only 8.2% of US women with familial BC have the mutations which are statistically associated with BC in their genes. Maxwell et al[12] reported that in a group of 404 individual belonging to 253 families with hereditary BC, 11% had pathogenic/likely pathogenic mutations in BC susceptibility genes; 0.8% had mutations in autosomal-dominant cancer susceptibility genes; 3.9% had incidental pathogenic/likely pathogenic mutations in 32 non-cancer-associated genes; 9% were monoallelic carriers of a rare likely pathogenic or pathogenic mutation in 39 genes associated with autosomal-recessive cancer susceptibility; and almost 95% were carrier of at least one variant of unknown significance. Rahman and Zayed[13] in their review claimed that BRCA1/2 mutations do not significantly affect the inheritance of BC in the AGC. Hawsawi et al[14] said that though BRCA1/2 cannot be linked to hereditary or familial BC, the screening of BRCA is still limited in SA.

Abedalthagafi[15] said that the increasing numbers of cancer diseases among SA residents is strongly affected by the conventional consanguineous marriage system in the culture, which makes homozygous recessive mutations to accumulate to be visualized as a dominant trait. Consanguineous marriage in AGC has been there for centuries, with time more recessive mutations can accumulate, even those with minor effect on cell cycle can by time affect disease outcome. Rahman and Zayed found that the best way to address the possible recessive traits responsible for increased incidence of familial BC in Arab countries is the introduction of the Arab Genome Project. In their report, they claimed Arab, or specifically AGC, residents present advanced stages of cancer and its onset at younger ages compared with other Western countries.[13] AlHarthi et al[16] said that BC in Arab countries has increased in the last few decades due to the introduction of Western diets, which caused obesity, consanguineous marriages, and the lack of awareness toward screening programs for hereditary cancers.

In fact, Shetty and Sreedharan reported a significant correlation between increased total fat consumption and increased risk of BC after studying data from 88 countries across 5 continents.[17] In 2020, Althumiri et al reported prevalence of obesity as 24.7% across 13 regions of SA,[18] while it was 42.4% for the United States in 2017-2018,[19] and 27.2% and 10.6% among men and women, respectively, of Kobe, Japan, for 2020.[20] However, according to Tanner and Cheung,[21] though prevalence of obesity and physical inactivity is high in AGC, no positive correlation can be found between obesity or physical inactivity and BC risk.

Makhnoon et al[22] reported that only 41.6% of the patients—with positive pathogenic variants in BC genes—who visited the University of Texas MD Anderson Cancer for genetic counseling were eager to disclose their results to family members. Would Arab population have similar problem? Do they too do not disclose their results to their families and thus decrease the number of early detections of BC? AlHarthi et al[16] mentioned that familial genetic diseases in Arab culture are considered as a stigma, making counseling even harder. Ormond et al[23] discussed thoroughly the obstacles that stand in the way of genetics counseling, which include cultural, linguistic, and religious issues, among others. Such obstacles can be easily attributable to the Arabs. AlHarthi et al discussed the culturally pervasive belief in SA that cancer is not genetic. They also discussed the cultural stigma of familial diseases, the unfamiliarity with the term "counseling," and the distress researchers face in questioning about family history related to cancer.[16] In culture where cancer can be described as stigma, less families will be eager for genetics counseling and testing and thus the disease will keep growing especially in population with high consanguineous marriages.

Saeed et al[24] in 2014 reported that only 43.1% of women in Kuwait who participated in a survey related to BC awareness had overall good knowledge of BC with regard to symptoms, risk factors, and breast examination. Al Ramadhan[25] found that nearly 2.5% of Kuwaiti female live births are expected to die

from BC if no intervention is made by the government. Alkhawari et al[26] reported that only 7.8% of the target population of women between the age of 40 and 69 years participated in screening mammography in Kuwait between 2014 and 2019. Farsi et al[27] reported that the general knowledge among men and women regarding BC in SA is around 60% and 50%, respectively; knowledge of breast screening practices (self-examination, clinical examination, and mammography) is around 24% and 19%, respectively.

Al-Khamis found that around 94% of SA women face barriers in getting an early diagnosis of BC. The difficulty of getting a doctor's appointment was 39%; anxiety about the possibility of being diagnosed with BC was 31%; and being too busy to seek medical help was 26%.[28] Donnelly et al[29] described that only 28.9% of the Arab females in Qatar are aware of BC screening practices, and less than one-third of them actually practiced BC screening. Al-Ismaili et al[30] found only 60.5% of Omani teachers to possess a good overall knowledge about BC, and only 57% practicing breast screening examination.

Chattu et al[31] found that around 80% of the 2-day health exhibit attendees in the event held at a polyclinic in Al-Buraimi, Oman, had knowledge of BC, but only 43% of them practiced breast screening examination. Kharaba et al[32] found that 41% to 87% of UAE females were familiar with BC signs/symptoms, but only 46% did self-examination and 28% underwent a clinical examination. The lack of BC screening practices was attributed to the lack of a doctor's recommendation, fear, and embarrassment.[33-35] El Hajj and Hamid[36] in 2013 pointed out that 88% of pharmacies in Qatar fail to provide education programs for BC, though 60% were eager to participate in the promotion for BC awareness.

In 2015, Donnelly and Hwang[37] suggested several strategies to raise the awareness regarding BC in Arabic populations: (1) a language-appropriate and culturally sensitive educational program, (2) multi-level interventions that target both women and men as well as health care professionals and/or larger health care system, and (3) more vigorous, personal and cognitive interventions that address psychosocial factors. Interestingly, Alanzi et al conducted an experiment using Snapchat as an awareness tool for BC in the Dammam region, SA. They found a significant improvement in the overall awareness ($P = .001$) in the intervention group in relation to a control group.[38]

In 2022, Jaffar Al Bahrani et al[39] reported 41% decrease in the number of stage IV and 86.15% increase in the number of stages 0-1 BC discovery after the introduction of the Oman national screening program. Although one may argue that awareness programs only affect the time of diagnosis and the severity of the disease, I would argue that awareness can affect even the incidence of diseases in populations or at least in a specific family. Kuwaiti government several years ago introduced a pre-marriage genetic counseling program that aimed mostly to decrease the number of new inborn with hematological disorders. If such program was implemented for all type of genetic/inherited diseases including cancers, less birth will be expected to hold genetic diseases in the future and thus will affect the incidence of such. Another point that I may rise is that awareness programs may help in decreasing the number of consanguineous marriages and decreasing the inheritance of the recessive traits and thus the incidence of diseases as of BC.

Overall, the increase in familial BC in AGC can be attributed to several factors: (1) consanguineous marriage that may result in the accumulation of homozygous recessive mutations, (2) cultural stigma associated with familial cancer diseases that affect counseling and early detection, (3) lack of cancer awareness programs implemented by the governments.

Author Contributions

EMM alone is responsible for the content and writing of this paper. The author has read and approved the final manuscript.

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