Breast Cancer in the Arabian Gulf Countries

Subjects: Oncology

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Breast cancer stands as the prevailing malignancy across all six Gulf Cooperation Council (GCC) nations. Most of the studies reported a consistent increase in breast cancer incidence over the past decades, which was particularly attributed to the adoption of a Westernized lifestyle in the region and the implications of emerging risk factors and other environmental and societal factors, the increase in screening uptake, as well as the improvement in data collection and reporting in the GCC. The data on breast cancer risk factors in the GCC were limited. In this geographic region, breast cancer frequently manifests with distinctive characteristics, including an early onset, typically occurring before the age of 50; an advanced stage at presentation; and a higher pathological grade.

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1. Introduction

Recently, breast cancer (BC) has surpassed lung cancer to become the most diagnosed cancer in the world, with approximately 2.3 million new cases diagnosed in 2020, while still globally contributing to the top five leading causes of cancer mortality [1]. It is commonly known that BC incidence rates in Gulf Cooperation Council (GCC) countries are lower than in Westernized countries; nevertheless, it is postulated that the anticipated demographic shift from a younger to an older population, increasing life expectancy, and the unique and evolving combination of lifestyle factors in the GCC would lead to a substantial increase in cancer incidence and mortality, including BC, over the next two decades [2].

Breast cancer is the most common cancer among women. In light of the anticipated increase, proper planning and decision making require reliable, up-to-date, and accurate data to ensure effective cancer control and the provision of optimal care for patients with BC.

2. Epidemiology of BC in the GCC

2.1. Incidence

Most of the studies reported a consistent increase in BC incidence over the past decades, which was particularly attributed to the adoption of a Westernized lifestyle in the region and the implications of emerging risk factors and other environmental and societal factors, as well as to the increase in screening uptake [3]. Both citizens and non-citizens of the GCC region experienced breast cancer earlier than women in comparable high-income nations [4].

Data from the Kuwait Cancer Registry showed that the annual number of new cases remarkably increased from 212 cases in 2012 to 608 cases in 2017 [5][6]. The age-standardized rate (ASR) was 61.0 and 41.3 cases per 100,000 populations for Kuwaiti and non-Kuwaiti females, respectively. Breast cancer among males represents <1.0% of breast cancer cases [5]. As for Kuwaiti females, BC had the highest incidence; it increased by three-fold over the last 44 years (18.5 to 63.5 cases per 100,000 people per year). The trend of the ASR of Kuwaiti female breast cancer cases over the time period of 2013–2017 was 64.6 per 100,000, where the crude rate was 47.85 per 100,000, while the trend of non-Kuwaiti female breast cancer cases over the time period was 45.2 per 100,000, and the crude rate was 29.06 per 100,000 [5].

2.2. Risk Factors

A study from Qatar describing the use of BC risk assessment to better guide the clinician's decision about screening and clinical management. The study used the Gail model to evaluate the BC risk among 1338 women aged 35 years and older selected from 12 primary healthcare centers in Qatar between July 2012 and June 2014. The study reported mean 5-year and lifetime BC risks of 1.12 ± 0.52 and 10.57 ± 3.1, respectively, among the women of Qatar. A linear regression analysis identified significant predictors of the 5-year and lifetime risks, such as age, age at menarche, age at first birth, family history, and age at menopause. Overall, the Gail model was found to be an appropriate risk assessment tool in the Gulf. Nevertheless, one of its limitations, as reported by the authors, is that it does not take into consideration BC among second-degree relatives as a risk factor, and it may incorrectly estimate the risk of BC as reported in previous studies given that risk factors differ between ethnicities [7]. A systematic review looking at the association between obesity, physical inactivity, and BC incidence in the GCC did not report any association between BC and neither obesity nor physical inactivity in the five countries of interest between 1999 and 2019 [8]. One study looked at the association between serum 25-hydroxyvitamin D [25(OH)D] levels and BC risk and found that women with serum 25(OH)D levels lower than 20 ng/mL were at higher risk of BC (odds ratio, 4.63; 95% CI, 2.61–8.23) after adjusting for age, body mass index, and menopause status [9].

2.3. Financial Burden

In terms of financial burden, a review looking at the economic costs associated with non-communicable diseases (NCDs), including BC in the GCC, concluded that only 0.5% of the annual total direct medical costs of selected NCDs, which were estimated at USD 16.7 billion, were due to BC, implicating that BC was less common compared with other NCDs such as type 2 diabetes mellitus and coronary heart disease [10].

3. BC Presentation in the Region

3.1. Age at Diagnosis

In Oman, a study reported that more than half of the 14,109 cancer cases (53.5%) diagnosed between 1996 and 2010 were diagnosed below 50 years of age, and the highest age-specific incidence rates were between 50 and 54 years (57.1 per 100,000) and 45 and 49 years (46.7 per 100,000) [11]. Through Oman Cancer registry sources, the highest frequency of incident cases among Omani female nationals was at the age of 35 (*n* = 56) [12]. In the UAE, the average age at diagnosis among the 988 patients diagnosed with BC at Tawam Hospital between January 2008 and December 2012 was 48 years [13]. Another, more recent study from Sharjah Breast Care Centre reported a mean age at diagnosis of 51 ± 12 years in 94 patients diagnosed with BC between March 2016 and July 2018 [9]. Data from Bahrain from the periods 2000–2010 and 2017–2019 reported a mean age at diagnosis of 50.9 and 51.8 in 1005 [14] and 216 BC patients, respectively [15]. The median age at diagnosis of female breast cancer among the Saudi female population was 50 years (ranged between 14 and 108 years), and the number of BC incident cases peaked in the age group of 45–49 (*n* = 356) [16].

The GCCR recorded that 25.5% of all BC cases occurred in women less than 40 years old in the GCC [17], and a review reported an overall mean age at BC diagnosis of 50.6 years in the GCC countries compared with 60 years in Western countries [3]. Another review from the Arab countries mentioned that the median age at diagnosis in the Arab population was about 48 years and that about two thirds of women with BC were younger than 50 years [18].

3.2. Prognosis and Survival

To our knowledge, a single-institutional retrospective analysis analyzing 988 patients with a follow-up of 35 months was the only study examining BC survival in the UAE. The predicted 2-year and 5-year survival rates for the same period were 97% and 89%, respectively, and were within the normal ranges when compared to countries in the Western world such as Australia (89.5%) and Canada (88.2%). Comparing Kuwait (75.2%) and Qatar (71.95%), two countries in the same region, the 5-year survival rate is also high [13][19][20]. According to the 2017 annual report of the Kuwait Cancer Registry, the overall 5-year survival rate of Kuwaiti BC patients was 90.5% [5].

Breast cancer represents the commonest cancer in Saudi females and in the Saudi population in general. Despite a 5-year observed survival of 72%, this represents a slightly lower value than western countries, though most of them report relative 5-year survival [19][21][22]. Reasons behind a lower survival are likely related to a relatively high percentage of presentation in advanced stage (12.5%) and a low rate of screening [22][23]. Screening for breast cancer has developed in several phases yet has not materialized into a national screening program [22][24][25][26][27].

3.3. Stage and Grade

The GCCR reports that up to 58% of the patients present at a late stage with regional or distant metastases [17]. A review of data from the Kuwait Cancer Registry showed that there was an overall decreasing trend in localized and regional stages between 2000 and 2004, 2005 and 2009, and 2010 and 2013, and an increasing trend in distant and unknown stages [28]. About 39.3% of all breast cancers presented with regional extension, 13.9% presented with distant metastasis, and an unknown extent of disease was observed in about 22.7%. Stage II was the most

frequent presentation at diagnosis: 28.0% [5]. A report from the Kuwait Cancer Registry shows the following stage distribution for breast cancer cases diagnosed in 2017 among Kuwaiti nationals, stage I: 17.0%, II: 29.0%, III: 20.0%, IV: 12.0%, unknown: 21%, and Tis: 1%, whereas that among non-Kuwaiti nationals was stage I: 10%, II: 27%, III: 28%, IV: 16%, Unknown: 16%, and Tis: 3% [5]. Although the UAE Cancer Registry does not have complete data for the stage at presentation, it is evident that there is a relative decline in stage IV disease, with the percentage of localized disease increasing from 10% in 2011 to 25% in 2017 [29]. This may reflect improvements in mammography screening and uptake because of public awareness [30].

3.4. Histology

In terms of histological subtypes, all the reviewed studies confirmed the data from the national registries' reports [12][29][31][32] with infiltrating ductal carcinoma being the most common BC histology [3][9][14][18][33][34]. Among the respective recent national cancer registries of Qatar, Bahrain, Oman, and Saudi Arabia, Oman has the highest rate of infiltrating duct carcinoma at 90.3% [12][16][31][32].

3.5. Molecular Subtypes

In Oman, the luminal A subtype was the most common among 542 cases of BC diagnosed between 2006 and 2010 [11]. Similarly, luminal A was the most common in Bahrain (60.2% of 216 patients), followed by luminal B (19%), TN (13.4%), and HER2+ (7.4%) [33]. In the UAE, a short letter to the editor reported an overall incidence of estrogen-receptor-positive (ER+), progesterone-receptor-positive (PR+), HER2+, and TN tumors of 59.3%, 51.0%, 39.1%, and 20.8%, respectively, among the 192 patients diagnosed with BC between April 2008 and May 2009 [35]. More recently, a study reported positive hormone receptor (HR) status in 62 out of 94 patients with BC (66.0%) between 2016 and 2018 [9].

3.6. Association of Clinicopathologic Features with Selected Factors

Several studies looked at the association between clinicopathologic characteristics and selected factors. The most consistent finding across these studies was the observation that younger patients were more likely to have HER2+, TN, or basal-like cancers as compared with older patients [9][15][35][36]. Additionally, younger patients were more likely to have tumors of a higher stage ($p = 0.012$) and grade ($p = 0.031$) and were more likely to have lymph node metastases (88.6% versus 56.1%) ($p = 0.0004$) and distant metastases (26.7% versus 6.8%) ($p = 0.005$), leading to a worse prognosis [15]. Conversely, a study from Bahrain ($n = 1005$) did not find any association between age at diagnosis and tumor grade, metastasis, or stage of cancer [14]. One study from Oman observed that high-grade tumors were most common in the basal-like subtype (41.0%) and lowest in the luminal A subtype (19.0%), while a higher stage at presentation (stages III and IV) was more common in HER2+ tumors (59.0%) [36].

4. Genetic and Molecular Profiling

4.1. BRCA1/2 and Other Genes

The involvement of BRCA mutations in familial and sporadic BC has been fairly explored in the GCC, but findings have been inconclusive across studies, and other genes have been suspected to be implicated in the onset or progression of BC, of which BRIP1 was the most reported.

A study looked at the frequency of BRCA1/2 mutations in high-risk affected and unaffected patients referred to the hereditary and high-risk clinic in Qatar between March 2013 and December 2016 based on either a personal or family history of breast and/or ovarian cancers. Of the 167 subjects who underwent genetic testing, 38.0% had BRCA mutations, 41 of whom had BC [37].

In contrast, other studies only found a minimal to no role for BRCA mutations in BC, with the involvement of a variety of other genes. A study from Oman looking at 50 BC patients and 30 healthy individuals and/or carriers of benign tumors undergoing biopsy and BC surgery between January 2012 and April 2014 found that the majority of patients (84.0%) did not have a family history of BC and did not exhibit any BRCA1/2 mutations, indicating that such mutations are unlikely to play a key role in sporadic BCs [38]. An earlier study did not detect any significant mutational rates in BRCA1/2 either [39], which led to the investigation of other genes linked to BRCA1/2 that could be involved in the onset of BC, such as BRIP1. BRIP1 was found to potentially interact with BRCA1/2 as an oncogene, albeit previously demonstrated as a tumor suppressor gene. It was expressed five times more in breast tumors as compared to normal tissue.

4.2. Value of Genetic Profiling

Two studies from the UAE and Kuwait looking at the value of Oncotype DX testing in clinical practice and treatment decisions. One study looked particularly at the value of Oncotype DX testing on adjuvant treatment decisions based on a retrospective analysis of data for 50 female node-negative ER+ early BC patients who underwent Oncotype DX between October 2009 and June 2012 in the UAE. The test was successful in 47 patients, and the proportion of patients with low, intermediate, and high recurrence scores was 53.2%, 40.4%, and 6.4%, respectively. The risk assessment based on the St. Gallen criteria and Oncotype DX testing were concordant in approximately half of the patients. Treatment decisions were changed (pre-testing vs. post-testing) in 28% of patients, mostly from chemoendocrine therapy to endocrine therapy alone, with a statistically significant change in the low recurrence group (from 56.0 to 8.0%; $p = 0.0005$) [40].

4.3. Other Biomarkers

Several studies from the GCC looking at the significance of specific markers in the presentation and prognosis of BC. A study from Oman found a strong association between metastasis and younger age (women ≤ 40 years), lymphovascular invasion, and epithelial–mesenchymal transition (EMT) expression, indicating that EMT could possibly predict a higher metastatic potential in tumors and suggesting EMT expression as a surrogate marker for predicting metastasis [41]. In addition, EMT was found to be associated with Ki67 PI and basal-like tumors [41]. Further, the expression of nucleostemin was found to be higher in less differentiated, more advanced stage, larger, and lymph-node-positive tumors, as well as in more aggressive molecular subtypes (HER2+ and TN) when evaluated in 51 patient archival specimens from the UAE, although none of these associations reached statistical

significance [42]. A study from Oman observed a statistically significant relationship between high elastosis and ER positivity (p = 0.015) and HER2-status (p = 0.045) in 80 female patients who were not treated with neoadjuvant therapy from 2009 to 2019, suggesting that elastosis may be used as a surrogate marker for ER positivity and HER2 negativity in BC [43]. A study from the UAE found that A20 expression evaluated through immunohistochemistry (IHC) was associated with early grade 1 BC (p < 0.001) in all molecular subtypes, suggesting its use as a biomarker for early cancer. A20 overexpression was also associated with a lower OS rate in patients treated with endocrine therapy [44]. Another study found that insulin-like growth factor 1 receptor (IGF1R) membranous and mixed (membranous and cytoplasmic) expression in BC cells was evident in HR + HER2− cases in contrast with HR−HER2+ cases, which showed cytoplasmic or diminished IGF1R expression, suggesting that luminal subtypes may benefit from targeted IGFR therapy [45]. Trefoil factor 3 (TFF3) expression was found to be associated with residual breast carcinoma following neoadjuvant chemotherapy in 133 cases from the UAE, suggesting that its expression is associated with increased resistance to chemotherapy. Moreover, there was a significant co-expression of TFF3 with antiapoptotic proteins AKT1 (p = 0.0365), BCl2 (p = 0.0152), and NF Kappa-B (p = 0.0243) in breast carcinoma cases with residual carcinoma following neoadjuvant therapy, which reinforces the role of TFF3 in chemoresistance [46]. Vitamin D receptor (VDR) was also assessed using IHC in 120 Kuwaiti female BC fixed tissues and was found altered in BC, with its absence being associated with high-grade differentiated tumors (p = 0.01) and its cytoplasmic expression being associated with lymph-node-positive tumors (p = 0.03) [47].

5. Management and Outcomes

5.1. Management Trends

Data on BC management trends in the region were very scarce and far from representative of current practice. In the 2018 QNCR, 319 (89%) of the total cases were reported with treatment information. Among them, the top five treatment modalities were Chemotherapy/Surgery (23.20%); Surgery (19.12%); Chemotherapy/Radiation Therapy/Surgery (15.67%); Chemotherapy/Hormonal Therapy/Radiation Therapy/Surgery (12.23%); and Hormonal Therapy/Radiation Therapy/Surgery (8.78%) [31], while data from the KCCC reported the treatment type for 359 patients with TNBC between 1999 and 2009 [48]. Recently, KCCC reported the type of treatment among Kuwaiti and non-Kuwaiti for the year 2017, where 82.3% of Kuwaiti nationals had surgery; 60.8% had chemotherapy; 65.8% had radiotherapy; and 74.0% had hormonal-based treatment. On the other hand, 77.6% of non-Kuwaitis had surgery, 70.5% had chemotherapy; 65.9% had radiotherapy; and 67.5% had hormonal-based treatment [5].

The TRIPOLI study possibly provides a more valid description of current treatment strategies as it reports on more recent data collected between 2017 and 2019; it describes that out of the 387 TNBC cases from Oman, Kuwait, and Qatar, among other Arab countries, with non-metastatic disease who started treatment during that period, 217 patients (56.1%) had upfront surgery and 170 patients (43.9%) started with neoadjuvant chemotherapy [34].

5.2. Outcomes

Data on outcomes from the GCC were also scarce. Besides data from the GLOBOCAN database [49], only the UAE's and Bahrain's national registries [29][32] reported BC deaths. Looking at original papers published from the five countries between 2011 and 2021, most analyzed datasets were of patients diagnosed before 2000 and up to the year 2012 [3][15][48][50][51][52][53][54][55], and one meta-analysis looking at survival rates in patients with BC from the Eastern Mediterranean region included data within the same timeframe [56]. Only a couple papers reported outcome data up to year 2015 [57][58] with the absence of any outcome data from the region thereafter.

References

1. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 2021, 71, 209–249.
2. Cheema, S.; Maisonneuve, P.; Lowenfels, A.B.; Abraham, A.; Doraiswamy, S.; Mamtani, R. Influence of Age on 2040 Cancer Burden in the Older Population of the Gulf Cooperation Council (GCC) Countries: Public Health Implications. Cancer Control. 2021, 28, 10732748211027158.
3. Albeshan, S.M.; Mackey, M.G.; Hossain, S.Z.; Alfuraih, A.A.; Brennan, P.C. Breast cancer epidemiology in Gulf Cooperation Council Countries: A regional and international comparison. Clin. Breast Cancer 2018, 18, e381–e392.
4. Chaabna, K.; Ladumor, H.; Cheema, S. Ecological study of breast cancer incidence among nationals and nonnationals in the Gulf Cooperation Council countries. East. Mediterr. Health J. 2023, 29, 40–48.
5. Kuwait Cancer Registry; Kuwait Cancer Control Center (JCCC). Annual Report 2017; Kuwait Cancer Control Center: Kuwait City, Kuwait, 2017.
6. Zahedi, R.; Molavi Vardanjani, H.; Baneshi, M.R.; Haghdoost, A.A.; Malekpour Afshar, R.; Ershad Sarabi, R.; Tavakoli, F.; Zolala, F. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: A systematic review and meta-analysis. BMC Women's Health 2020, 20, 53.
7. Bener, A.; Çatan, F.; El Ayoubi, H.R.; Acar, A.; Ibrahim, W.H. Assessing breast cancer risk estimates based on the gail model and its predictors in qatari women. J. Prim. Care Community Health 2017, 8, 180–187.
8. Tanner, L.T.A.; Cheung, K.L. Correlation between breast cancer and lifestyle within the Gulf Cooperation Council countries: A systematic review. World J. Clin. Oncol. 2020, 12, 217–242.
9. Bendardaf, R.; Sharif-Askari, F.S.; Sharif-Askari, N.S.; Guraya, S.Y.; Almadhi, S.A.; Abusnana, S. Incidence and clinicopathological features of breast cancer in the Northern Emirates: Experience from Sharjah breast care center. Int. J. Women's Health 2020, 12, 893–899.

10. Finkelstein, E.A.; Malkin, J.D.; Baid, D.; Alqunaibet, A.; Mahdi, K.; Al-Thani, M.B.H.; Abdulla Bin Belaila, B.; Al Nawakhtha, E.; Alqahtani, S.; El-Saharty, S.; et al. The impact of seven major noncommunicable diseases on direct medical costs, absenteeism, and presenteeism in Gulf Cooperation Council countries. J. Med. Econ. 2021, 24, 828–834.
11. Mehdi, I.; Monem, E.A.; Al Bahrani, B.J.; Al Kharusi, S.; Nada, A.M.; Al Lawati, J.; Al Lawati, N. Age at diagnosis of female breast cancer in Oman: Issues and implications. South Asian J. Cancer 2014, 3, 101–106.
12. Ministry of Health Sultanate of Oman. Cancer Incidence in Oman; Ministry of Health Sultanate of Oman: Sultanate, Oman, 2019.
13. Elobaid, Y.; Aamir, M.; Grivna, M.; Suliman, A.; Attoub, S.; Mousa, H.; Ahmed, L.A.; Oulhaj, A. Breast cancer survival and its prognostic factors in the United Arab Emirates: A retrospective study. PLoS ONE 2021, 16, e0251118.
14. Hamadeh, R.R.; Abulfatih, N.M.; Fekri, M.A.; Al-Mehza, H.E. Epidemiology of breast cancer among Bahraini women data from the Bahrain Cancer Registry. Sultan Qaboos Univ. Med. J. 2014, 14, 176–182.
15. Alzaman, A.S.; Mughal, S.A.; Alzaman, Y.S.; Alzaman, E.S. Correlation between hormone receptor status and age, and its prognostic implications in breast cancer patients in Bahrain. Saudi Med. J. 2016, 37, 37–42.
16. Kingdom of Saudi Arabia; Saudi Health Council; National Health Information Center; Saudi Cancer Registry. Cancer Incidence Report Saudi Arabia; Saudi Health Council: Riyadh, Saudi Arabia, 2015.
17. Al-Othman, S.; Haoudi, A.; Alhomoud, S.; Alkhenizan, A.; Khoja, T.; Al-Zahrani, A. Tackling cancer control in the Gulf Cooperation Council Countries. Lancet Oncol. 2015, 16, e246–e257.
18. Chouchane, L.; Boussen, H.; Sastry, K.S.R. Breast cancer in arab populations: Molecular characteristics and disease management implications. Lancet Oncol. 2013, 14, e417–e424.
19. Allemani, C.; Weir, H.K.; Carreira, H.; Harewood, R.; Spika, D.; Wang, X.-S.; Bannon, F.; Ahn, J.V.; Johnson, C.J.; Bonaveture, A.; et al. Global surveillance of cancer survival 1995–2009: Analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet 2015, 385, 977–1010.
20. Al-Shamsi, H.O.; Abdelwahed, N.; Al-Awadhi, A.; Albashir, M.; Abyad, A.M.; Rafii, S.; Afrit, M.; Al Lababidi, B.; Abu-Gheida, I.; Sonawane, Y.P.; et al. Breast Cancer in the United Arab Emirates. JCO Glob. Oncol. 2023, 9, e2200247.
21. Chirlaque, M.D.; Salmerón, D.; Galceran, J.; Ameijide, A.; Mateos, A.; Torrella, A.; Jiménez, R.; Larrañaga, N.; Marcos-Gragera, R.; Ardanaz, E. Cancer survival in adult patients in Spain. Results from nine population-based cancer registries. Clin. Transl. Oncol. 2018, 20, 201–211.

22. Aseafan, M.; Devol, E.; AlAhwal, M.; Souissi, R.; Sindi, R.; AlEid, H.; Bazarbashi, S. Population-based survival for cancer patients in Saudi Arabia for the years 2005–2009. Sci. Rep. 2022, 12, 235.
23. El Bcheraoui, C.; Basulaiman, M.; Wilson, S.; Daoud, F.; Tuffaha, M.; AlMazroa, M.A.; Memish, Z.A.; Al Saeedi, M.; Mokdad, A.H. Breast cancer screening in Saudi Arabia: Free but almost no takers. PLoS ONE 2015, 10, e0119051.
24. Al Mulhim, F.A.; Al Mulhim, F.A.; Syed, A.; Bagatadah, W.A.; Al Muhanna, A.F. Breast cancer screening programme: Experience from Eastern province, Saudi Arabia. East. Mediterr. Health J. 2015, 21, 111–119.
25. Abulkhair, O.A.; Al Tahan, F.M.; Young, S.E.; Musaad, S.M.; Jazieh, A.R. The first national public breast cancer screening program in Saudi Arabia. Ann. Saudi Med. 2010, 30, 350–357.
26. Akhtar, S.S.; Nadrah, H.M.; Al-Habdan, M.A.; El Gabbani, S.A.; El Farouk, G.M.; Abdelgadir, M.H.; Al-Saigul, A.M. First organized screening mammography programme in Saudi Arabia: Preliminary analysis of pilot round. East. Mediterr. Health J. 2010, 16, 1025–1031.
27. Gosadi, I.M. National screening programs in Saudi Arabia: Overview, outcomes, and effectiveness. J. Infect. Public Health 2019, 12, 608–614.
28. Alawadhi, E.; Al-Awadi, A.; Elbasmi, A.; Coleman, M.P.; Allemani, C. Cancer survival by stage at diagnosis in Kuwait: A population-based study. J. Oncol. 2019, 2019, 8463195.
29. United Arab Emirates Ministry of Health and Prevention. Cancer Incidence in United Arab Emirates. Annual Report of the UAE National Cancer Registry; 2017 and 2019. Available online: https://www.mohap.gov.ae (accessed on 7 October 2023).
30. Abu Awwad, D.; Hossain, S.Z.; Mackey, M.; Brennan, P.; Adam, S. Women's breast cancer knowledge and health communication in the United Arab Emirates. Healthcare 2020, 8, 495.
31. Qatar National Cancer Registry Ministry of Public Health. Qatar Cancer Incidence Report, 2018. 2018. Available online: https://www.nhsq.info (accessed on 7 October 2023).
32. Kingdom of Bahrain Ministry of Health. Cancer Incidence and Mortality in the Kingdom of Bahrain; Kingdom of Bahrain Ministry of Health: Manama, Bahrain, 2018.
33. AlZaman, A.; Ali, E.; Mohamad, B.; Islam, M.; AlZaman, E.; AlZaman, Y. The association between clinicopathological features and molecular markers in Bahraini women with breast cancer. Gulf J. Oncolog. 2020, 1, 19–25.
34. Azim, H.A.; Kandil, A.; El Zawahry, H.; Abdel-Razeq, H.; Elghazaly, H.; Kharusi, S.A.; Abdelwahab, M.M.; Fayaz, S.; Saadeddin, A.; Alabdulkarim, H.A.; et al. Abstract PS7-65: Triple negative breast cancer prospective registry in middle East and Africa (TRIPOLI) study:interim

analysis of the patients' characteristics. In San Antonio Breast Cancer Virtual Symposium; American Association for Cancer Research (AACR): Philadelphia, PA, USA, 2020.

35. Al Bashir, M.; Al Ali, N.; Shaban, S.; Hassouneh, G.; Al Ashari, M.; Jaloudi, M. Young women in the UAE have higher incidence of HER2 positive breast cancer. Breast J. 2012, 18, 637–638.
36. Mehdi, I.; Monem, A.A.; Al Bahrani, B.; Ramadhan, F.A. Breast cancer molecular subtypes in oman: Correlation with age, histology, and stage distribution—Analysis of 542 cases. Gulf J. Oncol. 2014, 1, 38–48.
37. Bujassoum, S.M.; Bugrein, H.; Al-Sulaiman, R.J.; Ghazouani, H. Qatar's experience with hereditary breast and ovarian cancer and high risk clinic: A retrospective study 2013–2016. Int. J. Res. Granthaalayah 2017, 5, 184–196.
38. Gupta, I.; Ouhtit, A.; Al-Ajmi, A.; Rizvi, S.G.A.; Al-Riyami, H.; Al-Riyami, M.; Tamimi, Y. BRIP1 overexpression is correlated with clinical features and survival outcome of luminal breast cancer subtypes. Endocr. Connect. 2018, 7, 65–77.
39. Al-Moundhri, M.S.; Al-Ansari, A.; Al-Mawali, K.; Al-Bahrani, B. BRCA1 gene Molecular Alterations in Omani Breast Cancer Patients. Gulf J. Oncol. 2013, 1, 45–51.
40. Jaafar, H.; Al Bashir, M.; Taher, A.; Qawasmeh, K.; Jaloudi, M. Impact of Oncotype DX testing on adjuvant treatment decisions in patients with early breast cancer: A single-center study in the United Arab Emirates. Asia Pac. J. Clin. Oncol. 2014, 10, 354–360.
41. Lakhtakia, R.; Aljarrah, A.; Furrukh, M.; Ganguly, S.S. Epithelial Mesenchymal Transition (EMT) in Metastatic Breast Cancer in Omani Women. Cancer Microenviron. 2017, 10, 25–37.
42. Sami, M.M.; Hachim, M.Y.; Hachim, I.Y.; Elbarkouky, A.H.; López-Ozuna, V.M. Nucleostemin expression in breast cancer is a marker of more aggressive phenotype and unfavorable patients' outcome: A STROBE-compliant article. Medicine 2019, 98, e14744.
43. Al Abri, S.; Al Rawahi, A.; Rao, L. Elastosis in breast cancer as a surrogate marker for estrogen receptor positivity. Oman Med. J. 2020, 36, e247.
44. Sharif-Askari, F.S.; Al-Khayyal, N.; Talaat, I.; Sharif-Askari, N.S.; Rawat, S.; Jundi, M.; SyrjÄnen, K.; Hamoudi, R.; Bendardaf, R. Immunohistochemical assessment of TNFAIP3/A20 expression correlates with early tumorigenesis in breast cancer. Anticancer Res. 2021, 41, 739–745.
45. Alkhayyal, N.; Talaat, I.; Vinodnadat, A.; Maghazachi, A.; Abusnana, S.; Syrjänen, K.; Bendardaf, R. Correlation of insulin-like growth factor 1 receptor expression with different molecular subtypes of breast cancer in the UAE. Anticancer Res. 2020, 40, 1555–1561.
46. Al-Salam, S.; Sudhadevi, M.; Awwad, A.; Al Bashir, M. Trefoil factors peptide-3 is associated with residual invasive breast carcinoma following neoadjuvant chemotherapy. BMC Cancer 2019, 19, 135.

47. Francis, I.; AlAbdali, N.; Kapila, K.; John, B.; Al-Temaimi, R.A. Vitamin D pathway related polymorphisms and vitamin D receptor expression in breast cancer. Int. J. Vitam. Nutr. Res. 2021, 91, 124–132.
48. Fayaz, S.; Demian, G.A.; El-Sherify, M.; Eissa, H.; Aziz, M.; Abuzallouf, S. Triple Negative Breast Cancer: 10-Year Survival Update of the Applied Treatment Strategy in Kuwait. Gulf J. Oncol. 2019, 1, 53–59. Available online: https://pubmed.ncbi.nlm.nih.gov/30957764/ (accessed on 7 October 2023).
49. World Health Organization International Agency for Research on Cancer (IARC). GLOBOCAN 2020: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2020. 2021. Available online: https://gco.iarc.fr/ (accessed on 8 November 2021).
50. Radwan, H.; Hasan, H.; Ballout, R.A.; Rizk, R. The epidemiology of cancer in the United Arab Emirates: A systematic review. Medicine 2018, 97, e13618.
51. Fayaz, M.S.; El-Sherify, M.S.; El-Basmy, A.; Zlouf, S.A.; Nazmy, N.; George, T.; Samir, S.; Attia, G.; Eissa, H. Clinicopathological features and prognosis of triple negative breast cancer in Kuwait: A comparative/perspective analysis. Rep. Pract. Oncol. Radiother. 2014, 19, 173–181.
52. Al Ayyan, M.; Ali, O.B.; Al Sharri, S.; Kassis, A.; Hussain, S.; Al-Bashir, M. Negative axillary ultrasonography with biopsy may predict non-involvement of the non-sentinel lymph nodes in operable breast cancer patients. Asia Pac. J. Clin. Oncol. 2014, 10, e86–e89.
53. Al Ramadhan, M.A. Eradicating breast cancer: Longevity impact on Kuwaiti women. Asian Pac. J. Cancer Prev. 2017, 18, 803–809.
54. Krishnan, Y.; Alawadhi, S.A.; Sreedharan, P.S.; Gopal, M.; Thuruthel, S. Pathological responses and long-term outcome analysis after neoadjuvant chemotheraphy in breast cancer patients from Kuwait over a period of 15 years. Ann. Saudi Med. 2013, 33, 443–450.
55. Krishnan, Y.; Al Awadi, S.; Sreedharan, P.S.; Nair, S.S.; Thuruthel, S. Analysis of neoadjuvant therapies in breast cancer with respect to pathological complete response, disease-free survival and overall survival: 15 years follow-up data from Kuwait. Asia Pac. J. Clin. Oncol. 2016, 12, e30–e37.
56. Hassanipour, S.; Maghsoudi, A.; Rezaeian, S.; Arab-Zozani, M.; Mokhtari, A.M.; Abdzadeh, E.; Riahi, S.; Mohseni, S.; Salehiniya, H. Survival rate of breast cancer in eastern mediterranean region countries: A systematic review and meta-analysis. Ann. Glob. Health 2019, 85, 138.
57. Zahid, K.F.; Kumar, S.; Al-Bimani, K.; Ahmed, T.; Al-Ajmi, A.; Burney, I.A.; Al-Moundhri, M. Outcome of omani women with breast cancer-associated brain metastases experience from a university hospital. Oman Med. J. 2019, 34, 412–419.
58. Kumar, S.; Sinha, S.; Bharti, A.; Meena, L.P.; Gupta, V.; Shukla, J. A study to determine the prevalence, clinical profile and incidence of formation of inhibitors in patients of hemophilia in

north eastern part of India. J. Fam. Med. Prim. Care 2019, 8, 2463–2467.