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Original article

Clinicopathological characteristics of gene-positive breast cancer in the United Arab Emirates

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ABSTRACT

Introduction: Breast cancer is the most prevalent cancer in the United Arab Emirates (UAE). This is the first study to provide data on predisposition of breast cancer susceptibility genes with associated clinical and pathological aspects in the UAE.
Material & methods: A retrospective chart review for breast cancer patients undergoing genetic testing from 2016 to 2018. According to National Comprehensive Cancer Network (NCCN) guidelines genetic testing was offered. The analyzed data included; age, ethnicity, family cancer history, pathogenic variant, histopathology, stage, molecular subtype and proliferation.
Results: 309 patients underwent genetic testing with a positive result in 130 patients (11.9%) over a period of 36 months. In 34.6% pathogenic and likely pathogenic variants were identified. BRCA2 was the most common gene identified. The mean age was 42.9 years (±9.01). Positive family history was identified in 66 patients (50.7%). Majority had stage 1 or 2 disease (66.2%), invasive ductal carcinoma (81.5%) and hormone receptor positive cancer (45.3%).
Conclusions: This is the first study in the UAE to describe the clinical and pathological characteristics of hereditary breast cancer in a mixed ethnic group with dominant Arabic population. Further genetic studies will be required in the UAE population, as the prevalence of breast cancer continues to rise.

Introduction

A genetic predisposition to breast cancer significantly influences screening, management, and follow-up for women at high risk of developing breast cancer. However, a specific gene is identified in approximately 5%–10% of cases in patients with a positive family history [1].

The population of the United Arab Emirates (UAE) continues to rise with 9.54 million living across the seven emirates. Demographically, 28% are females aged 25–54 years. Local Emiratis comprise only 11.27% of the total population [2]. Expatriates clearly outnumber the local Emirati population in the UAE, with a mixed variety of Indian (27.49%), Pakistani (12.69%), Filipinos (5.56%), Egyptians (4.23%), and other nationalities (38.55%) [2].

Internationally in 2018, breast cancer was the second most common cancer after lung cancer with an incidence of 11.6% (2,088,849) [3]. In the UAE, according to the World Health Organization data 2018, breast cancer is the most prevalent cancer in the UAE [3], with an incidence of 22.6% (1,054) [4]. In all newly diagnosed cancers in females, breast cancer was diagnosed in almost 40% of all new cancer cases. Age standardized incidence rates are between 56.7 and 72.9 per 100,000 people. The Ministry of Health and Prevention of the UAE operates a breast cancer screening program in the form of a mammogram every 2 years for females aged 40 years and older [5].

The Breast Care Center at Tawam Hospital, Al Ain, UAE, is the national center with the largest referrals for breast cancer. It is a dedicated unit providing comprehensive service from screening and diagnostic imaging to delicate surgical and post-surgical care.

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Annually, over 3000 screening and diagnostic mammograms are performed with an average of 4000 patients and over 200 cases requiring breast surgery.

There is no data available on breast cancer susceptible genes and their clinical and pathological aspects in the UAE. This study was undertaken to provide this information about UAE with its Arabic dominant mixed ethnic population.

Materials & methods

This is a retrospective chart review of prospectively compiled data from Electronic Medical Documents from January 2016 to December 2018. The study is performed in the Breast Care Center, Tawam Hospital, Al Ain, UAE. Genetic testing is performed on breast cancer patients to identify breast cancer susceptibility genes.

The criteria for genetic testing is according to National Comprehensive Cancer Network (NCCN) breast cancer guidelines and includes: known mutations in the family, age of onset below 50 years, bilateral breast cancer, triple negative in below 60 years of age, ovarian cancer, male breast cancer or other cancers involved in genetic syndromes related to breast cancer. Genes that are included in this study have an association with breast cancer. Exclusion criteria are patients with benign breast disease and positive results for non-breast cancer susceptible genes, mutations that are not known to cause breast cancer.

All patients that fulfilled the criteria were offered genetic testing after breast cancer diagnosis. Consent was taken and genetic testing was explained with the possible consequences for positive results. Three different gene panels were used for testing and samples were sent to a laboratory in an outside facility. BRCA1/2 panel analysis was only done for a few patients during 2016 after which other 2 panels were used for more germ-line mutation identification. Gene panel with 13 genes associated with breast and ovarian cancer, including ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, NBN, PALB2, PTEN, RAD51C, STK11, and TP53. Multi-gene panel with 49 genes for common cancers, including genes from panels above, CDKN2A, MUTYH, PMS2, PTCH1, MSH2, MSH6 and others. The panel of choice was decided according to personal and family history of cancers for each patient by the ordering physician. All patients with a positive test were referred to genetic counseling for further management.

Data is analyzed according to susceptible genes and ethnic group. Clinical variables that are analyzed includes: age, family history of cancer, previous breast cancer and other cancer history. Pathological variables analyzed includes: genetic sequence variants, stage at diagnosis, histopathology type, molecular subtypes, grade, lymph node invasion, distant metastasis and the Ki67 proliferative status. All variables are presented as numbers and percentages.

The age variable analyzed is the age of onset of initial breast cancer diagnosis. Ethnicities are categorized as Emiratis (local population from United Arab Emirates), Middle Eastern (all Arabic-speaking countries and Iranians), South Asians (Indian subcontinent and South Eastern Asians), Africans, and Westerns (Europeans and North and South Americans). Family history is divided into first-degree and second-degree family members with breast cancer, ovarian cancer, and strong family history of cancer (more than three first- and second-degree family members with any cancer). Other cancer history included cancers that were related to the affected gene.

Genetic sequence variants is classified according to International Agency for Research on Cancer (IARC) which classifies each gene into pathogenic (class 5), likely pathogenic (class4), variant of uncertainty (VUS) (class 3), likely benign (class 2) and benign (class 1). Significant mutation was defined as class 4 and 5 variant. Stage of breast cancer at diagnosis is classified according to the American Joint Committee on Cancer staging scheme [6]. Pathology type is classified as invasive ductal, invasive lobular, ductal carcinoma in situ (DCIS), and metaplastic cancer. Grade of tumor included low (grade 1), intermediate (grade 2) and high (grade 3). Molecular subtypes are classified into the estrogen receptor/progesterone receptor (ER/PR)-positive, triple-positive, triple-negative, and Her2-enriched. Cellular proliferation status of Ki67 is determined according to percentage, with <6% considered as low, 6%–8% considered as intermediate, >10% considered as high.

This study is approved by an Investigational Review Board (IRB) in our institute's ethical committee.

Results

A total of 1092 new breast cancer patients presented to our institute from January 2016 to December 2018. During 2018 there were a total of 1054 new breast cancer cases in the country out of which 378 (35.9%) cases were managed at our institute. Genetic testing was offered to 309 (28.3%) new breast cancer patients who fulfilled the criteria in the three-year period. No patient declined genetic testing.

In 130 (11.9%) patients 19 positive susceptibility genes were identified. No large deletion, duplication or rearrangements were encountered in the data. In 58 genes of 45 cases (34.6% of 130) there were pathogenic and likely pathogenic variant. Two genes were simultaneously identified in 16 cases (12.3%) with pathogenic variant seen in 5 cases (3.8%). One patient had three different genes with pathogenic variant. There were 129 females and one male. Male breast cancer case was associated with BRCA2 with pathogenic variant. The mean age of our patients was 42.9±9.01 from a range of 25–80 years and a median of 42 years of age. There were five major ethnic groups with a positive genetic test. Emiratis were 55(42.3%), Middle Eastern were 51 (39.2%), South Asian were 17 (13.1%), African were 3 (2.3%) and Western were 4 (3.1%).

BRCA2 was the most common gene identified in 29 cases (19% of the 130) followed by BRCA1 in 25 cases (17%). Fifty-one cases (38.5%) had pathogenic variant and 89 cases (68.5%) had a variant of uncertain significance (Table 1). Among Emirati patients, a significant mutation was seen in 22 (16.9%), and 33 (25.4%) had VUS results. Middle Eastern patients; 23 (17.7%) had significant variant, and 28 (21.5%) had VUS results. South Asian patients; 7 (5.4%) had a pathogenic variant and 10 (7.7%) had VUS results. African patients; 3 (2.3%) had VUS results. Western patients; 3 (2.3%) had a pathogenic variant and one had VUS.

Table 2 plotted all genes according to the ethnic group. Patients' characteristics including personal and family history were described according to ethnic group (Table 3) and gene (Table 4). Twenty cases (15.4%) had previous history of ipsilateral or contralateral breast cancer. Five cases (3.8%) had other cancer history that was associated with susceptibility gene. Presence of phenotypic features for all patients were identified prior to genetic testing.

In 66 cases (50.7%) a positive family history of cancer was identified. Thirty-five cases (53% of 66 cases) had first-degree relatives with breast cancer and 21 cases (13.8%) had second degree relatives with breast cancer. First and/or second degree ovarian cancer was found in 6 cases (9%). Breast and ovarian cancer together in one family was found in 3 cases (4.5%). Fourteen cases (21%) had strong family history. Among those with strong family history; BRCA1 was identified in 4 cases, BRCA2 in 5 cases, Tp53 in 2 cases, ATM in 2 cases and CHEK2 in 1 case. A positive family history in BRCA1/2 mutations was found in 29 cases (53.7%). Only one patient with CHEK2 mutation had family history of male breast cancer.

All patients had unilateral breast cancer. At initial breast cancer

Table 1
Positive breast cancer susceptible genes and classification of sequence variants (IARC).

Genes	Total no. of cases	Class 1 Benign	Class 2 Likely Benign	Class 3 Variant of Uncertain Significance	Class 4 Likely Pathogenic Variant	Class 5 Pathogenic Variant
BRCA1	25	–	–	11	2	12
BRCA2	29	–	–	12	3	14
TP53	3	–	–	1	–	2
PTEN	5	–	–	4	–	1
CDH1	9	–	–	9	–	–
STK11	4	–	–	3	–	1
ATM	18	–	–	13	2	3
CHEK2	14	–	–	9	–	5
PALB2	10	–	–	7	–	3
RAD51C	8	–	–	5	–	3
BARD1	5	–	–	4	–	1
PMS2	2	–	–	1	–	1
MSH2	2	–	–	1	–	1
MSH6	1	–	–	1	–	–
BRIP1	4	–	–	3	–	1
NBN	2	–	–	1	–	1
PTCH1	1	–	–	–	–	1
MUTYH	3	–	–	2	–	1
CDKN2A′	3	–	–	3	–	–

Table 2
Positive susceptible breast cancer genes in ethnic groups according to class 4 and 5 pathogenic variants.

Genes	Emiratis	Middle Eastern	South Asian	African	Western
BRCA1	7 (4)	4 (2)	2 (2)	0 (2)	1 (1)
BRCA2	5 (3)	11 (7)	1 (2)	–	–
TP53	1 (1)	1	–	–	–
PTEN	0 (3)	1 (1)	–	–	–
CDH1	0 (4)	0 (1)	0 (3)	0 (1)	–
STK11	1 (1)	0 (1)	0 (1)	–	–
ATM	2 (7)	2 (5)	1 (1)	–	–
CHEK2	3 (2)	4 (2)	1	–	0 (2)
PALB2	2 (6)	0 (1)	1	–	–
RAD51C	3 (2)	2 (1)	–	–	–
BARD1	0 (1)	1 (1)	0 (2)	–	–
PMS2	1 (1)	–	–	–	–
MSH2	0 (1)	1	–	–	–
MSH6	0 (1)	–	–	–	–
BRIP1	1 (1)	0 (2)	–	–	–
NBN	1 (1)	–	–	–	–
PTCH1	–	1	–	–	–
MUTYH	–	0 (2)	1	–	–
CDKN2A′	–	0 (1)	0 (2)	–	–

( ) = number having VUS (class 3).

diagnosis; 30 cases (23%) had stage 1, 56 cases (43%) had stage 2, 19 cases (14.8%) had stage 3, 16 (12.3%) had stage 4 and in-situ disease in 9 cases (6.9%). In 73 cases (56.2%) lymph node involvement was detected. Low grade tumors were identified in 12 cases (9.2%), intermediate grade tumors in 56 cases (43%) and high-grade tumors in 62 cases (47.7%). Fifty-nine cases (45.3%) had ER/PR-positive cancer, 21 cases (16.2%) had Her2/neu receptor-positive, 24 cases (18.5%) had triple-positive and 26 cases (20%) had triple-negative. Classical “Luminal A” (ER/PR positive, Her2/neu negative and low Ki67) breast cancer was detected in 9 cases (6.9%) and “Luminal B” (ER/PR positive, Her2/neu positive and high ki67) in 21 cases (16.2%). Ki67 proliferative status was interpreted as low in 11 cases (8.4%), intermediate in 15 cases (11.6%), and high in 104 cases (80%). Pathological characteristics were described for each ethnic group (Table 5) and gene (Table 6).

Discussion

The data reveals that a variety of genes are involved in breast cancer in a mixed ethnic population with Arabic predominance in the UAE. BRCA2 is the most prevalent among all genes, followed by BRCA1. In 44.6% a significant mutation was detected.

BRCA1/2 and many other genes are involved in hereditary breast cancer. Genetic testing is currently recommended for individuals with high index of suspicion concerning the risk of breast cancer. Up to 25% of the hereditary cases are due to a mutation in one highly penetrant gene, such as BRCA1, BRCA2, PTEN, TP53, CDH1, and STK11, which confers up to an 80% lifetime risk of breast cancer [7,8]. The most common genetic mutation can be found in BRCA1/2, which carries a very high risk of breast and ovarian cancer. Women harboring this mutation can benefit from a prophylactic bilateral mastectomy and salpingo-oophorectomy [9]. Nevertheless, negative BRCA1 and BRCA2 test results often remain suspicious for another hereditary cancer syndrome due to the family history of cancer. In more recent years, additional rare, moderate-penetrance genes and common, low-penetrance alleles have also been identified [10]. Moderate-penetrance genes associated with breast are

Table 3
Clinical characteristics of breast cancer in ethnic groups according to class 4 and 5 pathogenic variants.

Ethnicities	Age 20–29 years	Age 30–39 years	Age 40–49 years	Age > 50 years	Previous History of cancer	Other Cancer History related to the gene	Positive family history
Emiratis	1	10 (10)	6 (17)	5 (6)	4 (1)	2	17 (11)
Middle Eastern	2	8 (7)	11 (13)	2 (8)	7 (6)	2	15 (12)
South Asian	2	4 (5)	1 (5)	–	1 (1)	1	4 (5)
African	–	0 (2)	0 (1)	–	–	–	0 (2)
Western	–	1 (1)	0 (2)	–	–	–	1 (1)

( ) = number having VUS (class 3).

Table 4
Clinical characteristics of susceptible genes according to class 4 and 5 pathogenic variants.

Genes	Age 20–29 years	Age 30–39 years	Age 40–49 years	Age > 50 years	Previous History of cancer	Other Cancer History related to the gene	Positive family history
BRCA1	2	7 (8)	3 (3)	2	3 (1)	1	10 (2)
BRCA2	1	7 (2)	5 (10)	4	4	2	15 (2)
TP53	–	1	–	1 (1)	–	1	2 (1)
PTEN	–	1	0 (1)	0 (3)	1	–	1 (1)
CDH1	–	0 (4)	0 (3)	0 (2)	–	–	0 (7)
STK11	–	0 (1)	1 (2)	–	–	–	0 (1)
ATM	1	1 (2)	3 (6)	0 (7)	0 (2)	1	3 (6)
CHEK2	–	2 (3)	2 (5)	1 (1)	1 (2)	–	0 (12)
PALB2	–	2 (3)	1 (2)	0 (2)	1 (1)	–	3 (4)
RAD51C	1	1	1 (3)	0 (2)	1 (1)	–	3 (1)
BARD1	–	0 (2)	1 (2)	–	–	–	1 (1)
PMS2	–	–	1	0 (1)	–	–	0 (1)
MSH2	–	0 (1)	1	–	1	–	–
MSH6	–	–	0 (1)	–	–	–	–
BRIP1	–	1 (1)	0 (2)	–	–	–	1
NBN	–	–	1	0 (1)	–	–	1
PTCH1	–	–	1	–	–	–	–
MUTYH	–	–	1 (2)	–	–	–	–
CDKN2A′	–	0 (1)	0 (2)	–	0 (1)	–	0 (2)

( ) = number having VUS (class 3).

Table 5
Pathological characteristics of breast cancer in ethnic groups according to class 4 and 5 pathogenic variants.

Ethnicities	Invasive Ductal Carcinoma	Invasive Lobular Carcinoma	Ductal Carcinoma Insitu	Metaplastic Cancer	Axillary Lymphadenopathy	Distant Metastasis
Emiratis	17 (24)	2 (4)	1 (5)	2	15 (10)	1 (1)
Middle Eastern	20 (24)	3 (3)	0 (1)	–	18 (18)	5 (6)
South Asian	7 (8)	–	0 (2)	–	5 (4)	1
African	0 (3)	–	–	–	0 (2)	0 (2)
Western	1 (2)	0 (1)	–	–	1	–

( ) = number having VUS (class 3).

ATM, BRIP, PALB2 and CHEK2 [11–14].

All patients with a positive genetic test result were referred to genetic counseling regardless of sequence variance. Patients with pathogenic variant especially in BRCA1/2 were advised to undergo bilateral mastectomy with optional reconstruction regardless of age. All our patients with pathogenic BRCA1/2 mutation underwent bilateral mastectomy with or without reconstruction as patients were already diagnosed with unilateral breast cancer. Advice was given for screening of other cancers associated with susceptible gene mutation. Gynecology referral for bilateral salpingo-oopherectomy was given to BRCA1/2 patients. Patients with variant of uncertain significance (class 3) results were for

Table 6
Pathological characteristics of susceptible genes according to class 4 and 5 pathogenic variants.

Genes	ER/PR positive	Triple Positive	Triple Negative	Her2/neu positive	Invasive Ductal Carcinoma	Invasive Lobular Carcinoma	Ductal Carcinoma Insitu	Metaplastic Cancer	Axillary Lymphadenopathy
BRCA1	4 (5)	1 (2)	8 (2)	1 (2)	14 (7)	–	0 (2)	2	10 (3)
BRCA2	8 (5)	3 (5)	3 (2)	2 (1)	14 (20)	2 (1)	1 (1)	–	14 (4)
TP53	1	1 (1)	–	–	2	–	0 (1)	–	1
PTEN	1 (2)	–	0 (1)	0 (1)	1 (3)	0 (1)	–	–	1 (1)
CDH1	0 (3)	0 (1)	0 (2)	0 (3)	0 (7)	0 (2)	–	–	0 (2)
STK11	1 (2)	–	–	0 (1)	1 (1)	–	–	–	0 (1)
ATM	3 (8)	1 (2)	0 (1)	1 (2)	4 (13)	1	–	–	4 (6)
CHEK2	3 (4)	1 (4)	1 (1)	–	4 (6)	1 (1)	0 (2)	–	3 (3)
PALB2	1	0 (3)	1 (2)	1 (2)	2 (7)	–	1	–	2 (2)
RAD51C	1 (1)	1 (2)	0 (1)	1 (1)	2 (4)	1	0 (1)	–	2 (4)
BARD1	1 (1)	0 (3)	–	–	1 (4)	–	–	–	1 (1)
PMS2	–	0 (1)	1	–	1 (1)	–	–	–	1
MSH2	0 (1)	1	–	–	1 (1)	–	–	–	0 (1)
MSH6	–	–	–	0 (1)	–	–	0 (1)	–	–
BRIP1	0 (2)	1 (1)	–	–	1 (3)	–	–	–	1 (1)
NBN	0 (1)	–	1	–	1 (1)	–	–	–	–
PTCH1	1	–	–	–	–	1	–	–	–
MUTYH	1 (1)	–	–	0 (1)	1 (1)	0 (1)	–	–	1 (2)
CDKN2A′	0 (2)	0 (1)	–	–	0 (2)	–	0 (1)	–	0 (2)

( ) = number having VUS (class 3).

discussion with genetic counselor and advised to repeat genetic testing to confirm if the gene is truely benign or pathogenic.

More than 50 different genes were identified in association with breast cancer in Saudi Arabia [15]. Most frequent mutations seen in Arabic countries were BRCA1/2 and Tp53 [16]. In Arabic population, breast cancer occurred at younger age between 30 and 40 years, advanced stage, higher axillary lymph node invasion and higher receptor negativity compared to other ethnicities [17–19]. In the present study, Arabic populations was predominant, with a similar age group but at lower stage at diagnosis, possibly due to compliance of screening program at our institute. Arab women were diagnosed with breast cancer a decade earlier than Western women, which indicates a different genetic predisposition among the Arab population [20]. One in five women with hereditary breast cancer among Arabs have a BRCA mutation with BRCA2 mutations being most common [21].

Younes et al. in a systematic review of BRCA1/2 of ovarian cancer among patients in Arabic countries demonstrated that BRCA1 mutations is more prevalent and 8 variants were unique to Arab population [22]. In Saudi Arabia and Oman TP53 gene mutations were detected in 40% of the breast cancer cases [23]. Significant mutations in PTEN gene was documented in breast cancer patients in Saudi Arabia [24]. Bujassoum et al. demonstrated a variant of uncertain significance was more common than pathogenic variety in a mixed ethnic population similar to ours [25].

In the Jones et al study, 683 mixed ethnic women underwent genetic testing; African ethnic women had majority of gene mutation with pathogenic variant in BRCA1/2, CHEK2 and ATM [26]. Asians were the next population with gene mutations, followed by Hispanics and lastly Caucasian. In the Asian population variant of uncertain significance was higher compared to other ethnic groups [26]. Despite these results African women were less likely to undergo genetic counseling compared to Caucasian women [27]. A study of BRCA mutations in different races showed that all races with genetic mutations were diagnosed prior to 50 years-of-age [28]. The same authors reported that BRCA1 gene mutations were more common than BRCA2 mutations among all races, except Asians.

A strong family history, including more than 3 family members with cancer history and at least one having breast cancer, was the greatest predictor in our study. In our institute all patients with a strong family history had pathogenic variant gene positive result. Among patients with strong family histories of cancer and negative BRCA1/2, approximately 12% carry a mutation in one of the other genes associated with breast cancer, and approximately 5% may carry a mutation in CHEK2 or TP53 [29].

Pathological features were similar to the present study with majority of patients having invasive ductal carcinoma and hormone receptor positive cancers [30,31]. Lymph node involvement was present in more than 50% of cases [30]. The majority of tumors diagnosed were intermediate and high grade tumors [30,31]. A substantial majority of the triple-negative breast cancers are of the molecularly classified triple negative type, similar to that of the BRCA1 mutation carriers [32]. Cancers with Her2/neu positive status were based on Immunohistochemistry test and In Situ Hybridization test in equivocal cases in our study.

The main limitations of our study are being a retrospective study, not all patients had the same gene panel testing that could rest in a risk of missing other genes associated with their type of breast cancer. In addition, gene panel testing has higher rates of mutations of unknown significance. Finally, it cannot be conclude that our positive genetic test results are similar to other institutions in the country, as there are no data available from these other institutes.

There is still a further need to do more germ-line testing in our community. As for now testing is only done for patients diagnosed with cancer. Our findings could give more understanding of the importance of identifying pathogenic germ-line mutations throughout the country for earlier management as in the form of screening. Offering patients prophylactic measures before cancer can occur.

Conclusions

This is the first study in the UAE describing clinical and pathological characteristic of hereditary breast cancer patients in a mixed ethnic with Arabic dominant population. Further genetic studies will be required in the UAE given the rising prevalence of breast cancer.

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Ethical approval

Ethical approval by the Investigational Review Board in Tawam Hospital, Al Ain, UAE.

Declaration of competing interest

No conflict of interest to declare.

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References

[1] Couch FJ, Shimelis H, Hu C, Hart SN, Polley EC, Na J, Hallberg E, Moore R, Thomas A, Lilyquist J, Feng B, McFarland R, Pesaran T, Huether R, LaDuca H, Chao EC, Goldgar DE, Dolinsky JS. Associations between cancer predisposition testing panel genes and breast cancer. JAMA Oncol 2017;3(9):1190.
[2] UAE population statistics 2019 (infographics). Global; media insight. https://www.globalmediainsight.com/blog/uae-population-statistics/. [Accessed September 2019].
[3] Breast - Global Cancer Observatory. International agency for Research on cancer. 2018. . [Accessed March 2019].
[4] United Arab Emirates - Global Cancer Observatory. International agency for Research on cancer. https://gco.iarc.fr/today/data/factsheets/populations/784-united-arab-emirates-fact-sheets.pdf. [Accessed March 2019].
[5] Cancer. The official portal of the UAE government. https://government.ae/en/information-and-services/health-and-fitness/chronic-diseases-and-natural-disorders/cancer/. [Accessed November 2019].
[6] Giuliano AE, Edge SB, Hortobagyi GN. Eighth edition of the AJCC cancer staging manual: breast cancer. Ann Surg Oncol 2018;7(25):1783–5.
[7] Antoniou AC, Easton DF. Models of genetic susceptibility to breast cancer. Oncogene 2006;25:5898–905.
[8] Walsh T, Casadei S, Coats KH, et al. Spectrum of mutations in BRCA1, BRCA2, CHEK2, and TP53 in families at high risk of breast cancer. J Am Med Assoc 2006;295:1379–88.
[9] Ludwig KK, Neuner J, Butler A, Geurts JL, Kong AL. Risk reduction and survival benefit of prophylactic surgery in BRCA mutation carriers, a systematic review. Am J Surg 2016 Oct;212(4):660–9.
[10] Shiovitz S, Korde LA. Genetics of breast cancer: a topic in evolution. Ann Oncol 2015;26(7):1291–9.
[11] Meijers-Heijboer H, van den Ouweland A, Klijn J, et al. Low-penetrance susceptibility to breast cancer due to CHEK2(*)1100delC in noncarriers of BRCA1 or BRCA2 mutations. Nat Genet 2002;31:55–9.
[12] Seal S, Thompson D, Renwick A, et al. Truncating mutations in the Fanconi anemia J gene BRIP1 are low-penetrance breast cancer susceptibility alleles. Nat Genet 2006;38:1239–41.
[13] Renwick A, Thompson D, Seal S, et al. ATM mutations that cause ataxia-telangiectasia are breast cancer susceptibility alleles. Nat Genet 2006;38:873–5.
[14] Rahman N, Seal S, Thompson D, et al. PALB2, which encodes a BRCA2-interacting protein, is a breast cancer susceptibility gene. Nat Genet 2007;39:165–7.
[15] Amemiya Y, Bacopulos S, Al-Shawarby M, Al-Tamimi D, Naser W, Ahmed A,

Khalifa M, Slodkowska E, Seth AA. Comparative analysis of breast and ovarian cancer-related gene mutations in Canadian and Saudi Arabian patients with breast cancer. Anticancer Res 2015;35:2601–10.
[16] Tadmouri GO, Sastry KS, Chouchane L. Arab gene geography: from population diversities to personalized medical genomics. Glob Cardiol Sci Pract 2014;2014(4):394–408.
[17] Alhuqail A, Alzahrani A, Almubarak H, Al-Qadheeb S, Alghofaili L, Almoghrabi N, et al. High prevalence of deleterious BRCA1 and BRCA2 germline mutations in Arab breast and ovarian cancer patients. Breast Canc Res Treat 2018;168(3):695–702.
[18] Chouchane L, Boussen H, Sastry KS. Breast cancer in Arab populations: molecular characteristics and disease management implications. Lancet Oncol 2013 Sep;14(10):e417–24.
[19] AlHarthi FS, Qari A, Edress A, Abedalthagafi M. Familial/inherited cancer syndrome: a focus on the highly consanguineous Arab population. NPJ Genom Med 2020 Feb 3;5:3.
[20] Ezzat AA, Ibrahim EM, Raja MA, Al-Sobhi S, Rostom A, Stuart RK. Locally advanced breast cancer in Saudi Arabia: high frequency of stage III in a young population. Med Oncol 1999;16:95–103.
[21] Abdulrashid K, AlHussaini N, Ahmed W, Thalib L. Prevalence of BRCA mutations among hereditary breast and/or ovarian cancer patients in Arab countries: systematic review and meta-analysis. BMC Canc 2019;19:256.
[22] Younes N, Zayed H. Genetic epidemiology of ovarian cancer in the 22 Arab countries: a systematic review. Gene 2019 Feb 5;684:154–64.
[23] Al-Qasem AJ, Toulimat M, Eldali AM, Tulbah A, Al-Yousef N, Al-Daihan SK, et al. TP53 genetic alterations in Arab breast cancer patients: novel mutations, pattern and distribution. Oncol Lett 2011;(2):363–9.
[24] Alam MS, Jerah ABA, Ashraf JM, Kumaresan K, Eisa ZM, Mikhail NT. Promoter methylation and loss of expression of PTEN gene in breast cancer patients from Saudi population. J Clin Exp Oncol 2017;6:6–11.
[25] Bujassoum Al-Bader S, Alsulaiman R, Bugrein H, Ben Omran T, Abbaszadeh F, Bakheet N, Kusasi SA, Abdou N, Solomon BD, Ghazouani H. Cancer genetics program: follow-up on clinical genetics and genomic medicine in Qatar. Mol Genet Genomic Med 2018 Nov;6(6):865–72.
[26] Jones T, Trivedi MS, Jiang X, et al. Racial and ethnic differences in BRCA1/2 and multigene panel testing among young breast cancer patients. J Canc Educ 2019 Dec 4.
[27] Armstrong K, Micco E, Carney A, Stopfer J, Putt M. Racial differences in the use of BRCA1/2 testing among women with a family history of breast or ovarian cancer. J Am Med Assoc 2005 Apr;13;293(14):1729–36.
[28] Hall MJ, Reid JE, Stat M, Burbidge LA, Pruss D, Deffenbaugh AM, Frye C, Wenstrup RJ, Ward B, Scholl TA, Noll WW. BRCA1 and BRCA2 mutations in women of different ethnicities undergoing testing for hereditary breast-ovarian cancer. Cancer 2009;115(10):2222–33.
[29] Walsh T, Casadei S, Coats KH, Swisher E, Stray SM, Higgins J, King MC. Spectrum of mutations in BRCA1, BRCA2, CHEK2, and TP53 in families at high risk of breast cancer. J Am Med Assoc 2006;295(12):1379.
[30] Bakkach J, Mansouri M, Derkaoui T, Loudiyi A, Fihri M, Hassani S, Barakat A, Nourouti NG, Mechita MB. Clinicopathologic and prognostic features of breast cancer in young women: a series from North of Morocco. BMC Wom Health 2017 Nov;9(160).
[31] Larsen MJ, Thomassen M, Gerdes AM, Kruse TA. Hereditary breast cancer: clinical, pathological and molecular characteristics. Breast Cancer (Auckl) 2014;8:145–55.
[32] Walsh T, King MC. Ten genes for inherited breast cancer. Canc Cell 2007;11(2):103–5.