

# Age at diagnosis of female breast cancer in Oman: Issues and implications

Itrat Mehdi, Essam Abdul Monem, Bassim Jaffar Al Bahrani, Suad Al Kharusi, Ayman Mohammad Nada, Jawad Al Lawati, Najla Al Lawati<sup>1</sup>

## Abstract

**Introduction:** Female breast cancer (BC) is the most frequent malignancy diagnosed globally, about 23% of the diagnosed cancers. BC incidence varies geographically, highest in Western Europe and lowest in Africa. BC in females is strongly correlated to age, the highest incidence rate amongst older women reinforcing the importance of hormonal status. BC in young females has an aggressive phenotype. There is a shared observation amongst practicing oncologists that BC in Middle East and the developing world presents at an earlier age. **Aim and Objective:** The aims of this study are to evaluate the age at presentation of female BC in Oman, and to compare our data with international and regional published data. It discusses the impact of young age Breast Cancer. **Materials and Methods:** All diagnosed female BC cases registered from 1996-2010 all over the country, were retrieved from the National Cancer Registry, Ministry of Health. BC cases were analyzed with respect to age at presentation. The data were compared with regional and international data. **Results:** A total of 14,109 cancer cases were recorded during the period of study. BC was the leading malignancy as 1,294 cases (9.1%). Female BC patients were 1,230; denoting 19.2% of all female cancers. 53.5% of female BC presented below 50 years of age. Male BC constituted 5% of total, with 67% of male BC occurring over 50 years of age. Compared with data from Oman, the highest rates in UK and other Western countries are above 50 years of age. These rates are four to 10 times higher than local in different age groups. Interestingly, these rates increase with increasing age in UK from 40-45 to up to 85+, keep on increasing and go up to four times higher with higher age. This phenomenon, of increasing incidence rates with age, is not observed in our local population. **Discussion:** BC is significantly correlated to age as reported from Western population. BC is reported at a younger age from developing and Arab World, which need to be further studied and validated. This phenomenon of BC in younger age may have significant implications and effects ranging from screening, diagnosis, management, prognosis, and cost of treatment. **Conclusion:** The impact on young women diagnosed with BC is enormous, ranging from psychosocial to healthcare services and economics. There is a need to study it further in depth in developing World.

**Key words:** Breast cancer, breast cancer in Oman, young age, young breast cancer

## Introduction

Breast cancer (BC) is the most frequent malignancy diagnosed globally, about 11% of all malignancies and 23% of the female malignancies.<sup>[1]</sup> The incidence rates vary geographically, being highest in Western Europe and lowest in Eastern and Middle Africa.<sup>[1,2]</sup> The BC incidence has shown an alarming increasing trend in recent years.<sup>[3,4]</sup> An estimated 1.7 million women will be diagnosed with BC in 2020, mostly in developing countries, which is about 26% higher than the current figure.<sup>[5]</sup> The low and middle income countries will contribute 45% new cases and 55% of mortality associated with BC.<sup>[6]</sup> The challenges in these countries are lack of awareness, social barriers, access to

imaging, stage at presentation, adequacy of management, availability of latest management options, low priority for health, healthcare standards, healthcare infrastructure, and poor follow-up data.<sup>[6-11]</sup>

Cancer is a known disease of aging. With the exception of pediatric malignancies, the risk of cancer increases with age.<sup>[12]</sup> The correlation of age and BC is more pronounced, with higher incidence rates reported amongst older women reinforcing a hormonal association and patients' reproductive status. BC in younger age has rather poor clinic-pathologic variables with larger tumor size, more lymph node positivity, poorly differentiated grade, high ER and PR negativity, and higher human epidermal growth factor receptor (HER-2) overexpression. All of these translate into a more aggressive biological behavior, metastatic potential, and a rather poor outcome.<sup>[6,13-15]</sup>

Our country is in the Arabian Peninsula, with an area of 309,500 km<sup>2</sup> and a population of 2,749,734 (70.3% locals and 29.7% nonlocals). The National Oncology Center is the main institute caring for cancer patients. It started functioning in December 2004 providing state of the art services including chemotherapy, radiotherapy, and palliative care. National Cancer Registry was established in 1996 under the Ministry of Health. It keeps a validated and updated record of all cancer cases reported from all over the country as an electronic

Department of Medical Oncology, National Oncology Center, Royal Hospital, <sup>1</sup>Directorate of Non-infectious Diseases, Ministry of Health, Muscat, Sultanate of Oman

**Correspondence to:** Dr. Itrat Mehdi,

E-mail: [itrat\\_mehdi@yahoo.com](mailto:itrat_mehdi@yahoo.com)

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retrievable database. Additionally, annual reports are published as hard copies and on CDs. BC is the most frequent malignant tumor diagnosed in females, parallel to established global data. On an average, 100-150 new cases are reported annually.<sup>[19,16,17]</sup>

There is a well-known and shared observation amongst practicing oncologists that BC in Middle East and developing world presents at an early age compared to Western population.<sup>[5,7,15,18-23]</sup> However, the validated statistical data to support this clinical impression is rather scanty.

## Aims and Objectives

The aims and objectives of this study/analysis were:

- To evaluate the age at presentation of female BC in the country
- To compare our data with known and published international and regional data.

## Materials and Methods

All cancer cases registered from 1996-2010 (15 years) were retrieved from the National Cancer Registry, Ministry of Health. BC cases were analyzed retrospectively with respect to age at initial presentation.

Data about the age at diagnosis of BC from some regional and international reports were reviewed and compared to our data.

The ethical approval for the study was obtained by the Institutional Medical Ethics and Scientific Research Committee.

Microsoft Office Excel 2007 was used for data collection and analysis.

The data was presented as graphs, tables, diagrams, and as descriptive results.

## Results

A total of 14,109 cancer cases were registered during the 15 years period of study. Omani patients were 12,989 (92%) and 1,120 cases were non-Omanis. Omanis are locals who were born in Oman and have Omani nationality and Arab ethnicity. Non-Omanis are non-locals, economic migrants mostly of South East Asian origin. Of the Omanis; 7,016 cases were male (54%) and 5973 were female (46%). BC was the leading malignancy in 1,594 cases (11.3%) combined in both males and females. About 1,312 cases were Omanis (82.3%), and 282 were Non-Omanis (17.7%). Among Omanis patients; 1,248 cases were female (95.1%) and 64 cases were male (4.9%). BC represented 20.9% of all female cancers.

Among female Omanis BC cases, mean age at diagnosis was 49.05 years, and median age was 48 years (range 17-99 years). Two cases (0.1%) diagnosed at age younger than 20 years, 78 cases (6.2%) between 20 and 29 years of age, 237 cases (19%) between 30 and 39, 345 cases (27.6%) between 40 and 49, 316 cases (25.3%) between 50 and 59, 150 cases (12%) between 60 and 69, 77 cases (6.1%) between 70 and 79, and 42 cases (3.3%) were

diagnosed at age of 80 years and above. Non-Omanis female BC cases were 282 (17.6%), with median age at diagnosis 45.5 years and mean age as 45 years (range 23-99 years). Male BC cases recorded were 64, with mean age at diagnosis of 56.1 years and median age of 56 years (range 26-90 years). Sixty-seven percent of male BC diagnosed was over 50 years of age.

Table 1 compares age-specific incidence rates between UK and this country. The highest rates in UK are above 50 years of age. These rates are four to 10 times higher than Omanis in different age groups. Interestingly, these rates increase with increasing age in UK from 40-45 years to up to 85+, keep on increasing and go up to four times higher with higher age. This phenomenon, of increasing incidence rates with age, is not observed in our local population. These observations are not seen in male BC, as evident by Table 2. This may indicate something intrinsic and specific to female BC only.

**Table 1: Comparison between age-specific incidence rates of female breast cancer per 100,000 population, UK (2007-2009) and our country (1996-2010)**

Age group (years)	Average number of new cases per year and age-specific incidence rates UK (2007-2009)		Age-specific incidence rates from our country (1996-2010)	
	No.	Rates (number of cases per 100000 population)	No.	Rates (number of cases per 100000 population)
15-19	4	0.2	2	0.1
20-24	28	1.4	18	1.1
25-29	178	8.9	60	5.4
30-34	510	26.6	98	14.4
35-39	1,363	60.9	138	24.6
40-44	2,883	121.4	154	32.6
45-49	4,267	193.1	188	46.7
50-54	5,245	272.2	191	57.1
55-59	5,258	282.7	117	41.3
60-64	6,599	357.1	97	43.7
65-69	5,744	400.1	50	41.7
70-74	4,074	319.1	55	46
75-79	4,164	374.9	52	31.7
80-84	3,492	397.7	NA	NA
85+	3,989	437	NA	NA

NA: Not available

**Table 2: The median age at diagnosis of breast cancer in some Arab countries**

Country	Year of publication	Median age at diagnosis (years)
Jordan	2002	46
Bahrain	2006	50
Emirates	2005	49
Saudi Arabia	2007	45
Egypt	2004	43
Sudan	2007	52
Qatar	2003	48
Oman	2004	48

Age-standardized incidence rates of female BC from 1998 to 2009 observed a significant and persistent increase from 2004 onwards (National Cancer Registry of Oman, Ministry of Health data Table 3).

Figure 1 shows comparison of incidence rates from around the world. Saudi Arabia and Oman seem to have the lowest, while Europe and Australia have the highest rates. The American and Asian population incidence rates are in between. Table 2 shows median age at BC diagnosis. In the Arab world it is between 43 and 52 years, while the median age of BC diagnosis in the UK population is approximately 63 years.<sup>[18]</sup>

Figure 2 shows that over 81% BC cases in UK are above 50 years of age, while in our country only 53.5% are above 50 years of age. Figure 3 shows population pyramids

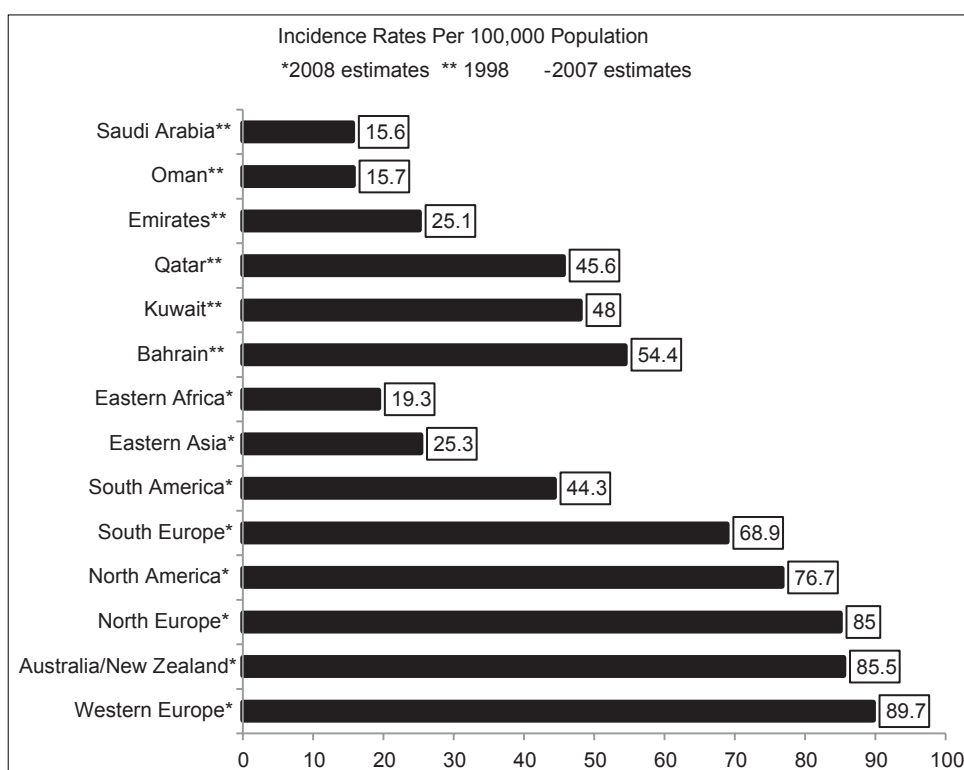
of our country and UK. The population of our country is a relatively young population, while that of UK is predominantly middle to old age population.

### Discussion

Our study demonstrated that nearly half of BC patients in Oman are diagnosed before their 50<sup>th</sup> birthday, and the highest age-specific incidence rates are between 50-54 years (57.1) and 45-49 years (46.7) [Table 1 and Figure 2]. A data review of BC in Arab countries showed that the median age at diagnosis is generally below 50 years, and on an average is 48 years [Table 2].<sup>[1,7]</sup> The age-standardized incidence rates of BC in our region are much lower than that seen in Western countries with the lowest incidence being reported from Oman and Saudi Arabia [Figure 1].<sup>[1,7,8,10,17]</sup> Al-Moundhri *et al.*, in 2004 reported that the mean age of BC locally was 48.5 years, consistent with other developing countries but significantly lower than the developed world.<sup>[17]</sup> They also reported a higher disease stage at diagnosis, lower survival rates, and a younger age at diagnosis. Al Bahrani *et al.*, again demonstrated similar results from Oman and the region.<sup>[16]</sup> The data from the United Kingdom (UK) revealed that 45% of BC were diagnosed in women over 65 years of age [Figure 2]. Age-specific incidence rates showed highest incidence rates among the age groups 65-69 years (400.1) and above 85 years (437) [Table 1]. In Australia, the average age of BC diagnosis was 60 years in 2008, about 51% in women aged 50-69 years. In Canada, 80% of new BC cases occur over 50 years of age. In USA (2005-2009) the median age at diagnosis for BC was 61 years.<sup>[2-4,12,18]</sup>

**Table 3: Age standardised breast cancer incidence rate in females (per 100, 000) in Oman 1998-2009**

Year	Age standardised incidence rate per 100, 000
1998-1999	13.4
2000	13.8
2001	16.5
2002	16
2003	14.8
2004	13.6
2005	22.9
2006	21.8
2007	22.6
2008	22
2009	22.1



**Figure 1: Age-standardized incidence rates of breast cancer per 100,000 population in Gulf countries and other world regions**

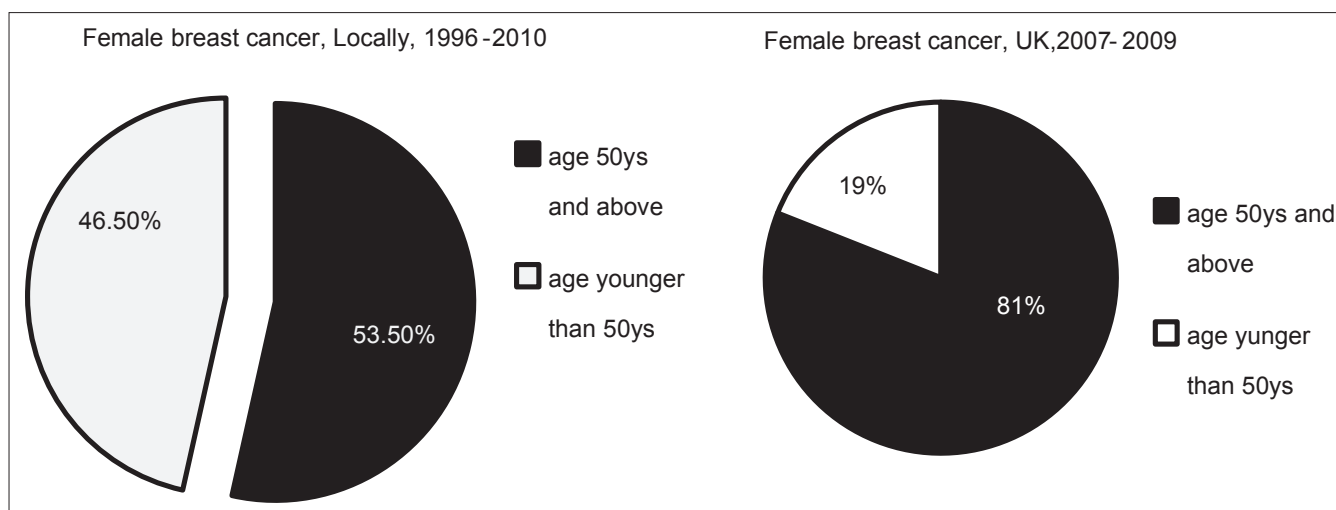


Figure 2: Comparison of age at diagnosis of female breast cancer in Oman and UK

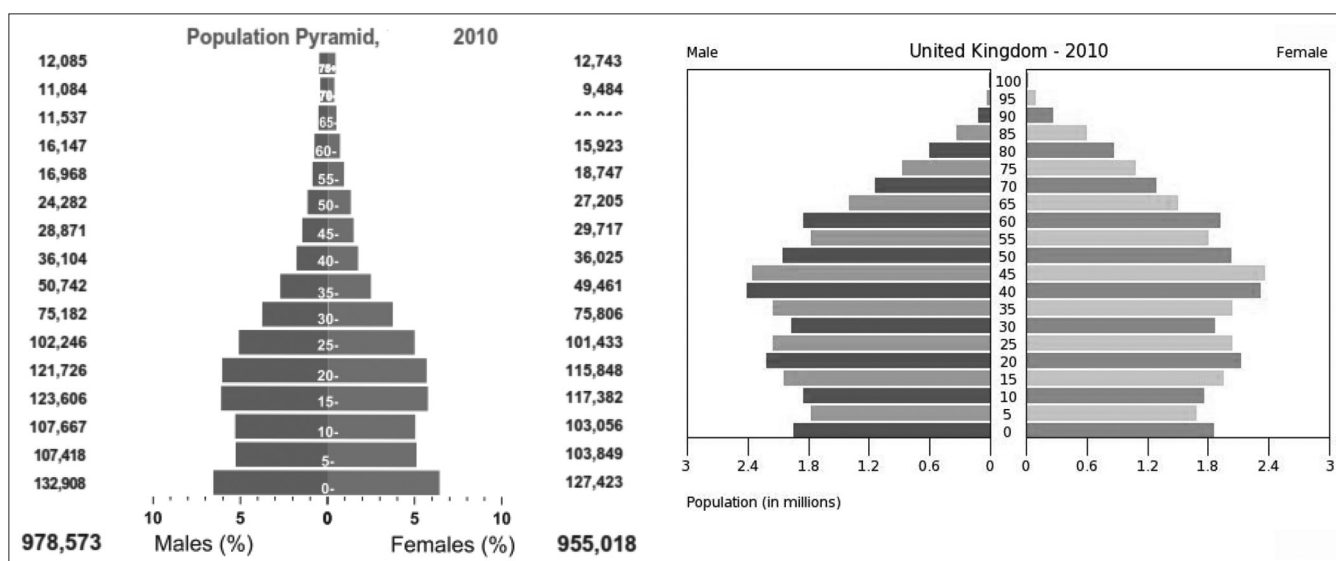


Figure 3: Population pyramid, Local 2010 and UK, 2010 (www.significancemagazine.uk)

The population pyramid in Oman and most developing countries shows concentration at the base with more population at young age [Figure 3]. The pyramid in developed countries is rather inverse showing predominantly an older population [Figure 3]. Ethnicity, environmental factors, genetic aspects, hormonal status, and other yet unknown factors can influence the age at diagnosis for BC. It was reported from UK that the median age at diagnosis was younger in black population, 50 years compared with 62 years for the white population.<sup>[3,4,16-18,23]</sup>

Young age BC is more aggressive and have a worse prognosis. Evaluation of clinical outcome was beyond the scope of our study; however there is sufficient data in the literature. Aziz *et al.*, reported from Pakistan a comparative local data with SEER showing young age at incidence, larger T size, higher grade, more receptor negative, and advanced stage at presentation of BC.<sup>[23]</sup> Younger patients present at advanced stage (20 vs. 13%), and are more

likely to undergo mastectomy than conservative surgery (47.7 vs. 37.7%).<sup>[24]</sup> The incidence of BC is rising in India as well, more significantly in the younger age group, with half being premenopausal.<sup>[5,6]</sup> Similar trends have been reported from Mexico, Africa, and the Arab world.<sup>[6,22]</sup> Clinical data and observational surveys from Arab countries have shown comparatively young age at diagnosis of BC.<sup>[1,6,21]</sup> Young women even with an early stage node negative BC, have a worse outcome in terms of overall survival, progression free survival, local recurrence, and distant metastasis.<sup>[19,25]</sup> Fear of losing husband due to physical impairment (separation and/or second marriage by the husband), social taboos, a male dominated society (treatment decision is made by the males even in the treatment of females) are contributors to late diagnosis in young age. Higher parity in the developing world with poor socioeconomic status, lack of health education, and ineffective population control programs are challenges in BC prevention<sup>[1,4,6,22-23]</sup>, because breast evaluation is

difficult in pregnant/lactating women<sup>[1,4,6]</sup>. There are definite issues and implications of BC in young age, distinct in our population.<sup>[1,6]</sup> These issues and differences vary and include environmental factors, genetic makeup, screening, diagnosis, pathology, treatment, and prognosis. There are definite overwhelming implications on health economics, health policy, social issues, reproductive health, and psychological impact on society.<sup>[1,24]</sup> There is a need to study the cancer incidence versus age using other common malignant tumors as a reference (prostate or colorectal), to validate the observation of BC at younger age. It is also imperative to validate whether the BC is really occurring at young age as observed, or we are merely seeing it at younger age in a relatively young local population.<sup>[6,20,23-26]</sup> The correlation of age and BC is more significant and distinct<sup>[1]</sup>. A woman, on an average, has a one in eight chance of developing invasive BC in her lifetime<sup>[18,21]</sup>. It was not the objective of our analysis but it is already established that BC in young age is reportedly associated with poor prognostic indices like larger tumor size, more lymph node positivity, higher grade, lower ER and PR positivity, and higher HER-2 overexpression.<sup>[5-6,9,13]</sup> We see advanced stage at presentation in most Arab countries.<sup>[6,17]</sup> Mastectomy rates are also higher in Arab World between 68 and 87%<sup>[6,19]</sup> due to advanced stage and lack of radiation facility.<sup>[24-26]</sup> All of these translate into a more hostile biological behavior, greater metastatic potential, and a relatively dismal outcome.<sup>[1,18,19,24-26]</sup>

The “Westernization of the developing world” is quoted as the prime cause of global increment in BC. There has been a significant increase reported from Japan, Korea, Singapore, and China.<sup>[6]</sup> The prominent reasons are obesity, lack of exercise, high caloric diet, early menarche, delayed parity, and reduction in breast feeding.<sup>[3,6,15,18,24]</sup>

The overall incidence rate of BC is reported relatively low from our country, the Arab world, and the developing world. This could be the direct effect of having a higher proportion of young population relatively less vulnerable to malignancy. In the younger age it may be explained by marriage at a younger age, higher ratio of married to unmarried women, frequent multiparity, less frequent use of contraceptive pills, no consumption of alcohol or tobacco smoking, younger age at first pregnancy, more frequent and longer period of breast feeding, more physical activities, and less frequent obesity.<sup>[1,15,19]</sup> There may well be further effects of undetermined environmental and genetic factors. It is interesting to note that the cumulative incidence of BC in developed countries would have been reduced by half, if woman had higher average number of child births and higher lifetime duration of breast feeding.<sup>[1,10,15,20,21]</sup>

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Some cases of BC were obviously missed in early years of cancer registration in the country due to an evolving system of registration, lack of experience and expertise, many cases getting treatment abroad, and other logistical factors.<sup>[17]</sup> The overall incidence is recorded as low correlating with the relatively lower ratio of old age population.<sup>[15]</sup> An obvious increase in local incidence rates was however noticed after 2004, with the availability of better established state of the art oncology care facilities within the country. These include the establishment of National Oncology Center in 2004 and the National Association of Cancer Awareness (NACA) in 2005. We expect to witness a surge in BC cases in the future as the noncancerous mortality (infections, cardiac, accidental, and maternal) is becoming low, the life expectancy and survival rates from other ailments are improving.<sup>[16,17]</sup>

A young age at diagnosis for non-Omani female BC cases could be explained as selection bias because majority of Non-Omani are essentially in the middle age working class living and working in the country. It is, however, rather unclear as to why nearly half of Omani female BC cases are younger than 50 years. It is evident from the data of National Cancer Registry of Oman over the last 10 years that age at diagnosis for other malignancies in female like colon and gastric cancer, contrary to BC are above the age of 50 years (65% of colorectal cancer and 76% for gastric cancer).

The western guidelines should not always be extrapolated and applied to Omani BC, as such. BC may well be a different disease locally in many respects. There is a need to develop evidence based local guidelines supported by local large scale multicenter studies, clinical data, and local experience. Western screening guidelines suggest a 2 yearly mammogram starting from age of 50 (US Task force recommendation, and UK guidelines). We see significantly higher proportion of BC at a relatively younger age, where screening mammogram often is not very effective.<sup>[6]</sup> Screening, therefore, has to be considered more frequently and may need to be started at an earlier age: Which needs further study. There is similarly issues of upper age cut off limit in a predominantly young population with a different life expectancy, and the recommended mode of screening. Mammogram at a younger age is not as specific and sensitive, due to dense and nodular breast undergoing cyclical hormonal changes.<sup>[6]</sup> There is debate where to place magnetic resonance imaging (MRI) in the screening protocol locally. It may well be expensive, but larger studies are required to validate cost effectiveness. Breast Health Global Initiative (BHGI) was founded to overcome these issues, and an effective program was thus developed initially in Lebanon.<sup>[5,6,14,21,22]</sup> The question of conservative breast surgery needs further exploration in terms of its efficacy in local population. There is a need to study the failure rates of breast conservative surgery, so as to justify it in our young local population with a more aggressive disease.<sup>[19,23-24]</sup> The genetic make-up of women

with BC in Oman was not analyzed and the proportion of genetic BC in local population is unknown. We do not have true customized and individualized tailored treatment strategy; as drug chemosensitivity assays or predictive markers are not available. Therefore the cost of treatment is high, often with a poor outcome and an unimaginable burden on health resources. The young population is the productive asset, so the work time lost is also an enormous burden on health economics. We must also not forget the psychological and psychiatric morbidity, not just for the patient but family and generation as well.<sup>[1,6,9,11,13-14]</sup>

## Conclusions

The study highlight the observation that BC is probably more frequently seen in younger age in our population, consistent with observation from Arab and developing World. This BC in young population may have clinical, social, psychological, and economic implications which need to be studied in depth. The data focusing on BC in young women will allow researchers, advocacy groups, public health officials, and individuals to monitor cancer rates and trends. It will help identifying the causes and effects of age differences and whether these age differences are truly translated into differences in pathobiology, treatment options, diagnostic policies and prognosis.

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