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CLINICAL & BASIC RESEARCH

Epidemiology of Breast Cancer among Bahraini Women

Data from the Bahrain Cancer Registry

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وبائيات سرطان الثدي عند النساء البحرينيات

معطيات سجل السرطان البحريني

رنده حماده، نجاة ابوالفاتح، ماجده فكري، هاله المهزه

ABSTRACT: ***Objectives:*** The aim of this study was to describe the epidemiology of breast cancer among the Bahraini female population in the years 2000–2010 and examine its health policy implications. ***Methods:*** All breast cancer cases in the Bahrain Cancer Registry from 1st January 2000 to 31st December 2010 were included. ***Results:*** There were 1,005 cases, 12.7% of which were detected by screening. The overall mean age at diagnosis was 50.9 years (95% confidence interval 50.1–51.6). The age-standardised incidence rate declined from 58.2 per 100,000 in 2000 to 44.4 per 100,000 in 2010. The majority of cases were infiltrating ductal carcinoma (76.9%). Of the registered cases, 44.1% and 48.1% had an unknown grade and stage, respectively. The five-year survival rate was 63 ± 2%. ***Conclusion:*** The low percentage of cases detected by screening merits further evaluation of Bahrain's screening programme. More effort should be made to reduce the proportion of unknown stage and grade breast cancers. Future research has to be directed towards understanding the reasons for Bahrain having the highest incidence rate of breast cancer in the Gulf Cooperation Council countries.

Keywords: Breast Cancer; Epidemiology; Incidence; Cancer Screening; Survival; Bahrain; Middle East.

الملخص: الهدف: وصف وبائيات سرطان الثدي بين السكان البحرينيات الإناث خلال الفترة بين 2000–2010م ودراسة السياسات المترتبة عليها. **الطريقة:** تم إدراج جميع حالات سرطان الثدي المسجلة في سجل السرطان البحريني من الأول من يناير 2000م إلى الواحد والثلاثين من ديسمبر 2010م. **النتائج:** تم تسجيل 1,005 حالة، منها 12.7% اكتشفت بواسطة الفحص الدوري. وكان متوسط العمر العام عند التشخيص 50.9 عام (95% CI 50.1، 51.6). وقد انخفض معدل الإصابة الموحد للعمر من 58.2/100000 في عام 2000 إلى 44.4/100,000 في عام 2010. وقد كانت معظم الحالات من نوع سرطان الأقنية المتسلل (76.9%). لم يتم التعرف على درجة ومرحلة السرطان لدى 44.1% و 48.1% من النساء على التوالي. وكان معدل نسبة البقاء لمدة خمسة أعوام على قيد الحياة 63 ± 2%. **الخلاصة:** إن انخفاض نسبة الحالات المكتشفة عن طريق الفرز الدوري تستحق المزيد من التقييم لهذا البرنامج. وينبغي بذل المزيد من الجهود للحد من نسب الحالات غير المعروفة الدرجة والمرحلة. يجب على الأبحاث المستقبلية التركيز على فهم أسباب ارتفاع نسبة الإصابة بسرطان الثدي في البحرين مقارنة بدول مجلس التعاون الخليجي.

مفتاح الكلمات: سرطان الثدي؛ علم الوبائيات؛ نسبة الانتشار؛ الفحص الدوري؛ نسبة البقاء؛ البحرين؛ دول مجلس التعاون الخليجي.

Advances in Knowledge

- *There is a lack of concrete data about the epidemiology of breast cancer in Arab nations. This study reports on the incidence of breast cancer in Bahrain over an 11-year period and describes cancer registration in Bahrain.*
- *This study also identifies deficiencies in cancer registration and areas for improvement in the registry and breast screening programmes in the country.*

Application to Patient Care

- *This study has implications for the evaluation and modification of Bahrain's on going breast screening programme and guidelines.*

Worldwide, breast cancer is the commonest cancer among females. It is estimated that more than 1.6 million new cases of breast cancer occurred among women globally in 2010.[1] There is great variation between the incidence rates of breast cancer in developed countries in comparison to developing countries. In 2008, incidence rates ranged from 19.3 per 100,000 women in Eastern Africa to 89.9 per 100,000 women in Western Europe. The rates were high (>80 per 100,000) in developed countries, except for Japan, and low (<40 per 100,000) in most developing regions.[2]

Breast cancer occupies the first rank among

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all female cancers in all Arab countries despite the fact that some rates are relatively low (20–30 per 100,000).[3,4] Patients tend to be young with an average age at presentation of 48 ± 2.8 years, which is a decade earlier than in Western countries.[5,6] In the six Gulf Cooperation Council (GCC) countries, breast cancer is the commonest female cancer. Compared to all female cancers, the proportion of breast cancer ranged from 15.7% in Oman to 54.4% in Bahrain.[7] Bahrain, Kuwait and Qatar were classified as high-incidence countries while the United Arab Emirates, Saudi Arabia and Oman were low-incidence. A comparison of the age-standardised rate (ASR) of breast cancer from high-incidence GCC countries with other countries shows that the GCC rates are similar to those of some European countries, meaning that the rates are higher than in Japan, but still lower than those of high-incidence countries like the USA [Figure 1]. Most international and interethnic differences in the incidence of breast cancer have been attributed to the varying environmental factors and lifestyles of the populations.[8] However, the disparities observed within the GCC region have been explained partly by the differences in fertility rates and the duration of breastfeeding.[8]

Cancer is the second leading cause of death in Bahrain (10%), following cardiovascular diseases.[9] However, the proportional mortality rate of cancer has been underestimated due to the high percentage of ill-defined causes of death.[10] In a Ministerial Decree in 1994, cancer notification became mandatory. Thus, all physicians in Bahrain became obliged to report all cancer cases to the Bahrain Cancer Registry (BCR) at the Medical Review Office of the Ministry of Health (MOH).[12] Compared to other GCC states, Bahrain has a higher incidence of cancers of the breast, lung, bladder, thyroid, uterus and ovary among females. A rising trend in cancer incidence is likely to continue for years or even decades to come. In Bahraini females, breast cancer remains the leading type of cancer.[13,14]

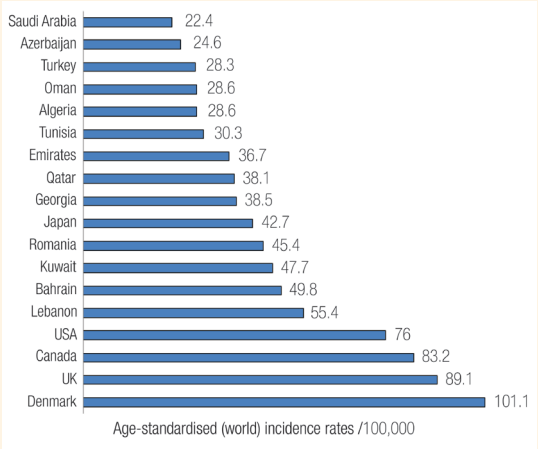

Figure 1: Age-standardised world incidence rates in Bahrain and selected countries calculated per 100,000 cases of breast cancer.

Figure reproduced with blanket permission: International Agency for Research on Cancer and World Health Organization. GLOBOCAN: Estimated Cancer Incidence, Mortality and Prevalence Worldwide.[11]

Breast cancer screening in Bahrain started in December 1992 for women aged 30–64 years old and included educational activities on clinical breast examination (CBE) and breast self-examination.[15] Screening by mammography was only performed for suspected and high-risk cases after referral. Between 2008–2010, the primary healthcare centres in Bahrain reported a CBE coverage rate of 6.6%, 7.1% and 6.9%, respectively, in women 30 years and above.[9] Mammography screening of Bahraini women 40 years and over was started in September 2005 with a recommendation for it to be performed every two years.[16]

Methods

The breast cancer cases included in the study were those in Bahraini patients registered in the BCR between 1st January 2000 and 31st December 2010. Incidence rates were calculated using CanReg4 software (Descriptive Epidemiology Unit, International Association of Cancer Registries, Lyon, France), in which the yearly crude incidence rate, age-specific incidence rates (ASPIRs) and age-standardised incidence rates (ASIRs) were computed. Incidence rates were standardised for age and sex by the direct standardisation method using the world standard population. Women were considered premenopausal if they were below 50 years and postmenopausal if they were 50 years old or above.

Data analysis was performed using the Statistical Package for the Social Sciences, Version 20.0 (IBM, Corp., Chicago, Illinois, USA). Analysis of variance (ANOVA) and least significant difference tests were performed to detect differences in age means. Pearson's chi-squared test was used to detect differences between premenopausal and postmenopausal age groups by type, grade, laterality and detection modality. Survival analysis was done using the life table technique. The probability of patient survival in each interval was calculated by taking account of the census observations in that interval. The survival proportion included only the overall survival—not the relapse-free survival. Breast cancer patients diagnosed with only a death certificate were excluded from the survival analysis due to the lack of a diagnosis date. The Wilcoxon-Gehan statistic was utilised to determine the five-year survival differences by age group, grade,

Table 1: Characteristics of breast cancer patients (N = 1,005)

Characteristics	n	%
Age at diagnosis in years		
20–24	5	0.5
25–29	18	1.8
30–34	42	4.2
35–39	117	11.6
40–44	153	15.1
45–49	180	17.9
50–54	156	15.5
55–59	94	9.4
60–64	84	8.4
65–69	72	7.2
≥70	84	8.4
Source of notification		
Salmaniya Medical Complex	833	82.9
Bahrain Defense Force Hospital	85	8.5
Private hospitals	8	0.8
Private clinics	11	1.0
Primary healthcare	34	3.4
Breast cancer screening programme	15	1.5
Unknown	19	1.9
Basis of diagnosis		
Death certificate only	12	1.2
Clinical only	1	0.1
Clinical investigation/ultrasound	6	0.6
Cytology/haematology	384	38.2
Histology of metastasis	10	1.0
Histology of primary cancer	586	58.3
Unknown	6	0.6

stage and detection modality. Ethical approval was obtained from the Research & Ethics Committee of the MOH in Bahrain.

Results

Between 2000–2010, 1,005 breast cancer cases were registered in the BCR, of which 28.7% were still alive by the end of the study period. The annual average number of cases was 91, with 2007 having the highest reported number (120) and 2002 the lowest (66). About three-quarters of the women were

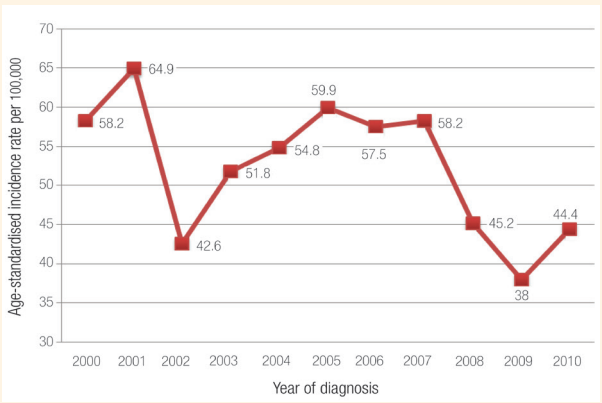

Figure 2: Age-standardised incidence rates of breast cancer by year of diagnosis.

married (74.7%) with 12.5% single, 2.3% divorced, 6.1% widowed and the rest unknown (4.4%). The proportion of premenopausal women diagnosed was 51.2% while 48.8% were postmenopausal [Table 1]. The median age at diagnosis during the 11-year period was 49 years while the average age was 50.9 years (95% confidence interval [CI] 50.1–51.6). There was a statistically significant difference (P <0.05) in mean age, with an increase in the mean age from the year 2000 to 2010. The lowest mean ages at diagnosis were 48.5 in 2000 and 48.0 in 2001 while the highest mean age at diagnosis was 53.9 in 2006.

The majority of the reported cases were from the Salmaniya Medical Complex and the Bahrain Defence Force Hospital (91.4%) which are the main governmental general hospitals. The screening programme contributed to the diagnosis in 1.5% of the cases. Over half of the patients were diagnosed based on a primary histological diagnosis [Table 1].

The average breast cancer ASIR in Bahrain was 52.3 per 100,000. The ASIRs declined from 58.2 per 100,000 in 2000 to 44.4 per 100,000 in 2010 [Figure 2]. The ASPIRs of the postmenopausal women

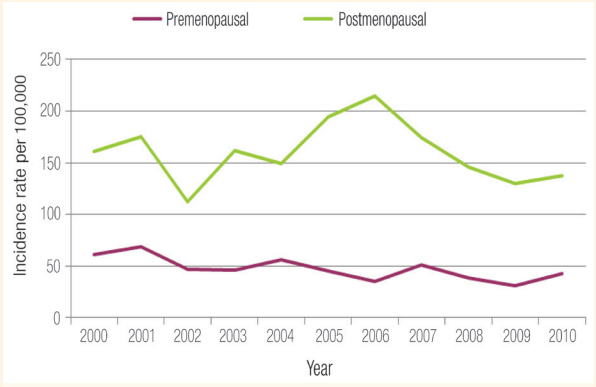

Figure 3: Incidence rates in premenopausal and postmenopausal women by year.

were generally higher than those of premenopausal women throughout the period. There was a noticeable variation in the rates of the postmenopausal women with a peak in 2006 while the rates of the premenopausal women had little variation [Figure 3]. Analysis by five-year age group showed that the age groups 65–69 and 50–54 had the highest overall average ASPIR during the 11-year period (184 per 100,000 and 179.8 per 100,00, respectively) and those of the 20–24 age group (2.4 per 100,000) and 25–29 age group (8.7 per 100,000) had the lowest.

Table 2 shows that the majority of breast cancer cases were infiltrating ductal carcinoma (76.9%) and grade 2 moderately differentiated tumours (28.6%) with regional and distant metastasis (35.1%). Both breasts were found to be equally affected. High proportions of cancers of unknown grade (44.1%) and stage (48.1%) were noted.

Although only 15 cases were notified through the breast cancer screening project, 113 more were detected by the tumour registrar while reviewing medical records, yielding 12.7% of the total cases through screening and 87.3% through routine notification [Table 2]. There was a statistically significant difference (P = 0.0043) among premenopausal and postmenopausal women whereby a higher proportion of the latter was detected by screening. Further analysis by year showed a statistically significant decline in the proportion of cases detected by screening (P <0.0001) reaching 13.0%, in 2010.

It was found that 57 patients (5.7%) did not undergo any treatment while 31 (3.1%) had an unknown modality of treatment. Surgery (84.7%) was the commonest modality performed for breast cancer patients, followed by chemotherapy (63.0%), radiotherapy (50.2%) and hormonal therapy (8.7%).

There was a progressive decline in the proportion of breast cancer patients' cumulative survival by year. After one year, 84.0% ± 1.0% survived in contrast to 63.0% ± 2.0% and 49.0% ± 3.0% respectively, for the five- and ten-year intervals. Table 3 shows the cumulative proportion surviving at the end of the five-year interval by age, grade, stage and detection modality. Women diagnosed at the age of 35 years or younger had a 73.0% ± 5.0% survival rate compared to 51.0% ± 5.0% in those 65 years old and over. There was an inverse relationship between grade and five-year survival whereby it reached 50.0% ± 35.0% in grade four (undifferentiated anaplastic) compared to 78.0% ± 8.0% in grade one (well-differentiated). Patients with unknown grades of cancer had a 58.0% ± 3.0% survival.

A similar inverse relationship was noted with respect to stage; however, those with an unknown stage of cancer had a higher five-year survival rate (62%). Further, those detected by screening had a 4% higher survival rate (65%) than those detected via routine examination (61%). There were significant differences (P <0.009) in the five-year survival rate with respect to age, stage and detection modality. A lower cumulative survival rate at five years was found among older women, patients with cancers that had advanced to a higher grade or advanced stage, and cancers detected through a routine check-up.

Discussion

The BCR is a reliable national population-based registry covering all residents (Bahraini and non-Bahraini) in the country; it gathers information on epidemiological, clinical and pathological aspects of the disease. Bahrain's cancer data is entered into the CanReg4 software and doctors started reporting this data to the *Cancer Incidence in Five Continents* publication in 2007.[13] Only five other countries (Kuwait, Oman, Algeria, Egypt and Tunisia) appeared in that volume; however, Jordan, Palestine, Saudi Arabia and Qatar also have population-based registries.[3]

Breast cancer is the commonest cancer among females in Bahrain.[14] The average breast cancer ASIR in Bahrain (52.3 per 100,000) is the highest among all GCC states.[7] All other Eastern Mediterranean countries, except for Lebanon (55.4 per 100,000), have rates that are higher than the world average (39.0 per 100,000) and that of less developed regions (27.3 per 100,000), but lower than that of more developed regions (66.4 per 100,000).[2] The rates declined from 58.2 per 100,000 in 2000 to 44.4 per 100,000 in 2010. This is in contrast to the trends of other GCC countries but in accord with those of some developed countries.[7,17] Similar to other studies, breast cancer risk in Bahrain increases with age.[18] The highest overall average ASPIR was 184 per 100,000 in patients between 65–69 years followed by 179.8 per 100,000 in those between 50–54 years. Those aged 65–69 years had the highest rate, as was also seen in Kuwait.[7]

The mean age at presentation for breast cancer in Arab countries is reported to be a decade earlier than Western countries.[3,6] This difference could be attributed to social, economic and population differences in the age at diagnosis between Arab and Western populations.[6] The median age at diagnosis (49 years) is similar to what has been reported from other Arab countries (48.5 years) but lower than the age at diagnosis in industrialised countries (63 years).[6] The overall mean age at diagnosis (50.9; 95% CI: 50.1–51.6 years) is slightly lower than that reported for Kuwaiti

Table 2: Type, grade, stage, laterality and detection modality of cases (N = 1,005)

	Premenopausal		Postmenopausal		Total		*P* value
	n	%	n	%	n	%	
Type							
Infiltrating ductal carcinoma	413	80.2	360	73.5	773	76.9	
NOS lobular carcinoma	25	4.9	24	4.9	49	4.9	
Unclassified neoplasm	18	3.5	31	6.3	49	4.9	
NOS carcinoma	19	3.7	23	4.7	42	4.2	0.010
Infiltrating ductal and lobular carcinoma	8	1.6	5	1.0	13	1.3	
NOS adenocarcinoma	8	1.6	14	2.9	22	2.2	
Other	24	4.7	33	6.7	57	5.6	
Grade							
1 Well-differentiated	15	2.9	35	7.1	50	5.0	
2 Moderately differentiated	145	28.2	142	29.0	287	145	
3 Poorly differentiated	131	25.4	91	18.6	222	22.1	0.005
4 Undifferentiated and anaplastic	2	0.4	1	0.2	3	0.3	
Unknown	222	43.1	221	45.1	443	44.1	
Stage							
In situ	12	2.3	12	2.4	24	2.4	
Localised	71	13.8	74	15.1	145	14.4	
Regional direct extension	11	2.1	17	3.5	28	2.8	
Regional lymph nodes	93	18.1	82	16.7	175	17.4	0.713
Regional direct extension and lymph nodes	8	1.6	8	1.6	16	1.6	
Distant metastasis	63	12.2	71	14.6	134	13.3	
Unknown	257	49.9	226	46.1	483	48.1	
Laterality							
Right	260	50.5	214	43.7	474	47.1	
Left	231	44.9	250	51.0	481	47.9	0.193
Bilateral	9	1.7	9	1.8	18	1.8	
Paired lateral unknown	15	2.9	17	3.5	32	3.2	
Detection modality							
Routine	465	90.3	412	84.1	877	87.3	0.004
Screening	50	9.7	78	15.9	128	12.7	
Total	**515**	**100.0**	**490**	**100.0**	**1,005**	**100.0**	

NOS = non-specific.

females (52.3; 95% CI: 51.7–52.9 years).[19] However, it is higher than that reported for Bahrain between 1998–2002 (49.0 ± 12.5 years)[5] and for Iran (46 ± 12.5 years).[20] The increase in mean age at diagnosis can be partially explained by the older population targeted by the screening programme. The results of the current study have shown that a higher proportion of postmenopausal (15.9%) cancers were detected by screening than those in premenopausal women (9.7%).

The commonest type of breast cancer found in Bahrain in this study was infiltrating ductal carcinoma (76.9%), a similar result to that reported for all GCC states combined (76.8%).[7] As was found in Kuwaiti and Saudi Arabian studies, in Bahrain both breasts were equally affected.[19,21] The fact that there was a considerable number of cases with an unknown grade

Table 3: Five-year survival by age, grade, stage and detection modality

Variables	Cumulative proportion surviving at five years by interval ± SD	Wilcoxon-Gehan statisic	*P* value
Age in years			
<35	0.73 ± 0.05	21.315	<0.0001
35–49	0.63 ± 0.03		
50–64	0.67 ± 0.03		
≥65	0.51 ± 0.05		
Grade			
1	0.78 ± 0.08	25.903	<0.0001
2	0.68 ± 0.04		
3	0.66 ± 0.04		
4	0.50 ± 0.35		
Unknown	0.58 ± 0.03		
Stage			
In situ	1.0 ± 0.0	76.294	<0.0001
Localised	0.91 ± 0.03		
Regional direct extension	0.83 ± 0.08		
Regional lymph nodes	0.77 ± 0.06		
Regional direct extension and lymph nodes	0.50 ± 0.19		
Distant metastasis	0.31 ± 0.05		
Unkown	0.63 ± 0.02		
Detection modality			
Routine	0.61 ± 0.02	14.537	<0.0001
Screening	0.65 ± 0.22		
Overall	0.63 ± 0.02		

SD = standard deviation; Grade 1 = well-differentiated; Grade 2 = moderately differentiated; Grade 3 = poorly differentiated; Grade 4 = undifferentiated and anaplastic.

(44.1%) and stage (48.1%) of cancer is disappointing. Having three cases of undifferentiated anaplastic grade could have been an underestimate due to the high percentage of cases with an unknown grade. This reflects the incompleteness of the data and underestimates the true grades and stages. However, the proportion with regional and distant metastasis doubled when the unknown grade cases were excluded and became similar to that of Kuwait (68%) but higher than that of Saudi Arabia (58.9%).[19,21] The BCR does not include full details on the types of treatment. Surgery was the commonest modality in Bahrain, as has also been reported in Kuwait.[22]

The cumulative five-year survival rate among Bahraini breast cancer patients (63% ± 2%) was slightly lower than that reported in an earlier study (68.8%) that was based on patients from the Salmaniya Medical Complex prior to the establishment of the BCR. In contrast, the 10-year survival rate found in that study was higher (49% ± 3%) than the current study's findings (36.4%).[23] The five-year survival rate in the current study lies midway between the lowest rate reported among developing countries (45%) and the highest rate among developed countries (89%).[8] It is also lower than that previously reported for Iran (72%) but is similar to the rate found in Saudi Arabia (63.1%) for 2000–2004.[20,24] Further, the fact that there were high proportions of breast cancer cases with unknown stage and grade might have affected the survival results among premenopausal and postmenopausal women.

Female breast cancer risk factors in the Arab world are similar to those of Western countries.[3] Globally, high breast cancer incidence rates are associated with a high prevalence of reproductive risk factors.[17] The decline in total fertility rates, the delay in the age of having one's first child, the shorter mean duration of breastfeeding and the increased early detection through screening underlie the high rates in Bahrain.[8,13,14] Further, early menarche (mean age 12.7 ± 1.7 years) was reported among breast cancer patients in Bahrain.[25] Lifestyle changes, including sedentary lifestyles, physical inactivity, Westernised diets, high-calorie diets and obesity, contribute to the high incidence rates of breast cancer in Bahrain.[26–28] In addition, the possibility of certain genetic dispositions may explain the higher Bahraini incidence rate compared to other GCC states.[4,14]

Breast cancer is a major public health burden in Bahrain that should be addressed by a multidisciplinary collaborative approach and an understanding of the unique risk factors.[29] There is an ongoing debate over the benefits and harm of breast screening and new approaches should be considered.[30,31] The fact that patients whose cancers had been detected by screening had higher survival rates is reassuring. The marked decrease in case detection with time can be partially explained by the possible inconsistency in the screening awareness programme campaigns and a lack of awareness among physicians and the public. Moreover, there is no comprehensive evaluation of the screening programme.[29] Further, the low percentage (12.7%) of cases detected by screening merits further evaluation of the Bahraini cancer prevention programme.

Conclusion

Breast cancer is a major public health burden which warrants the attention of health policy-makers. An evaluation of the Bahraini breast cancer screening programme, including the ideal age to start screening, and a re-evaluation of the national guidelines is urgently needed. More effort should be made to reduce the proportion of cancers of unknown stage and grade. Data on breast cancer risk factors, such as early menarche, hormonal receptors, age at the birth of the first child and oral contraceptive and hormone replacement therapy use are characteristics that should be further considered in breast cancer epidemiology research in Bahrain. Future research should be directed towards collaborative regional analytical studies to understand the multifaceted role of the interactive risk factors of breast cancer. Such research should also clarify the reasons why Bahrain has the highest breast cancer incidence rate among the GCC states and one of the highest rates in the Eastern Mediterranean region.

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