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Breast Cancer Risk Factors and Stage at Presentation

Suhair Khalifa Al Saad, MBCHB, CABS, FRCSI* Akbar A Jalal, MBBS**

Background: Breast cancer is the most common cancer in females all over the world. In American females, it is accounting for 32% of all cancers. It is well-known that there are major risk factors for cancer of the breast, such as, advanced age, positive family history and history of cancer in the same or other breast. Minor factors have been associated with breast cancer, such as, mammogram abnormalities, biopsy confirmed a typical hyperplasia, early menarche and late menopause ... etc… etc.

Not enough studies have concentrated on reviewing the risk factors in Bahrain; therefore, we have embarked on this study[1,2].

Objective: To review and assess the staging and risk factors of breast cancer.

Setting: Surgery Department, Salmaniya Medical Complex.

Design: Retrospective / Prospective study.

Method: It is a retrospective / prospective clinical review involving 52 breast cancer patients operated upon by the senior author over five years period (1999-2005). Presentation, diagnostic approach, and management were evaluated. Age at presentation, age of menarche and menopause were recorded. The risk factors, such as age at first delivery if any, lactation, hormonal therapy and if there were any past history or family history of breast or other related cancers. The stage of the disease at presentation was reviewed. Mortality and morbidity were recorded.

Result: All patients were females. Age at diagnosis was below 30 years in 2 patients (3.8%), between 30-39 years in 12 patients (23.1%), between 40-49 years in 21 patients (40.4%), 50 years or more in 17 patients (32.7%).

The mean age at menarche was 12 years of age. Sixteen patients (30.8%) were at menopause. The mean age at menopause was 48 years. Thirty-seven patients had child birth (71.2%), unmarried or nuliparous were 10 patients (19.2%). Age at first delivery was ranging between 16 and 40 years of age.

Number before percentage 59.6% of the patients breast fed their infants. Only 11 patients (22%) were using oral contraceptive pills (OCP). One patient was on hormonal replacement therapy. Family history of breast cancer was positive in 18 patients (34.6%).

Two patients had history of breast cancer of the other breast.

Thirty-seven patients (71.2%) had early breast cancer (T1, T2, N0, N1, M0) and 15 patients (28.8 %) had advanced breast cancer (T3, T4, N1, N2, M0 -1).

There was no local recurrence, and three mortalities to date.

Conclusion: More than half of our patients (67.3%) were below 50 years at presentation whereas internationally it is prevalent above fifty years (85%).

There was a significant high incidence of positive family history (35.3%) in comparison to international studies (5-15%).

In this study, breast cancer was still diagnosed late. In this study, locally-advanced breast cancer was 28.8%, which may improve as breast screening program is being implemented.

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* Consultant G. Surgeon
** Senior Surgical Resident
Salmaniya Medical Complex
Kingdom of Bahrain

It is also the leading cause of death in American women between the ages of 40-45 years. In USA 183000, and in UK 26000 new cases are diagnosed per year. Almost 1/15 (7%) of ladies in Western Europe, and 1/8 (12%) of ladies in USA will develop breast cancer during their life time. In USA 12% of ladies will develop breast cancer if they live to be 85 years old. The patient risk increases up to 50% after the age of 65. Breast cancer is internationally considered low in patients below age of 40 years (6.5%)[1,2].

Breast cancer is the most common non-skin malignancy among women. In American females, it is the second cancer to lung as a cause of cancer-related death. In 2001, an estimated 192,200 new cases of breast cancer were diagnosed in American women, and 40,200 women died of the disease. In Bahrain, 2002, Breast cancer accounted for 33.8% of all types of cancer in Bahraini females. The incidence rate was 26.1/100,000 of cancer cases in 2002[5]. There were 54 newly diagnosed breast cancer cases. About 68.5% were between 30-49 years of age[5]. In Bahrain in 1998, breast cancer accounted for 24.1% of all cancers diagnosed. The newly diagnosed cases were 39 patients. There were 24 cases below 45 years of age, and 15 cases above 45 years 0f age[5].

About 180,000 women in the United States will be diagnosed with breast cancer each year[6]. However, not all women have the same risk of developing breast cancer. Studies have shown that certain risk factors increase the likelihood that women will develop

cancer. Many of these factors are fixed, but some can be modified[6]. The presence of risk factors in a certain patient does not mean that cancer is inevitable. Instead, risks factors help identify women who may benefit most from screening.

It is important to know that breast cancer can develop in women with no identifiable risk factors but mostly at an older age group. Some risk factors increase a women's risk of breast cancer more than others. It is also possible to have more than one risk factor for breast cancer.

The primary and the major risk factor in most women is advancing age. The probability of developing invasive breast cancer over the next 10 years is 0.4% for women aged 30-39, 1.5% for women aged 40-49, 2.8% for women aged 50-59, and 3.6% for women aged 60-69. The second major factor is family history. Women who have first-degree relatives (a mother, daughter, or sister) with breast cancer before their menopause have an increased risk when compared to women who do not have any affected first degree relatives. This risk is sometimes related to BRCA1 and BRCA2 genes. The third major factor is history of cancer in the same or the other breast. There are other minor risk factors,1 such as, mammogram abnormalities, biopsy-confirmed atypical hyperplasia, or had exposure to high-dose radiation of the chest. Many other factors increases the risk but non are very powerful, and are related to exposure to estrogen[6]. These are early menarche and late menopause, age at first pregnancy and breast feeding, hormone replacement therapy, height and weight, and alcohol consumption. Also, the presence of other cancer of the endomertium, ovary, or colon increases the risk in the same patient[6]. One main factor decrease the risk of developing breast cancer, which is removal of the ovaries[6].

The early stage at which breast cancer is being diagnosed in for the last few decades has improved the survival rate. This early diagnosis has been improved by increased awareness, improvement in follow-up of high risk patients, and breast screening programs in general. These programs includes, breast self-examination, clinical breast examination and the most important of all screening mammography[7].

The American Medical Association, the American College of Radiology, and the American Cancer Society all support screening with mammography and clinical breast examination beginning at age 40[7].

Overall mortality due to breast cancer has decreased in recent years because of early detection[3-4].

Objective: The aim of this study is to review and assess the risk factors and epidemiology of breast cancer.

- To measure the stage at first presentation (early or advanced) in our group of patients.
- To emphasize the need to improve our early detection protocols by well established screening program.

METHOD

During the last five years (August 1999 to November 2005) fifty-two patients breast cancer were diagnosed and operated by the senior author: all were included in the study. Presentation, diagnostic approach, and management were evaluated. Age at presentation, age of menarche and menopause were recorded. The risk factors, such as the age at first delivery, lactation, hormonal therapy and past history or family history of breast or other related cancers. The stage of the disease at presentation was reviewed with the histopathology. The management included, the type of the operation performed, chemo radiotherapy, hormonal and other treatments if given. The form also includes information about recurrence local or systemic, morbidity, and last follow-up visit and mortality if any.

These data were recorded retrospectively for almost the first half of the patients. The other half of patients information was recorded prospectively. The patients were followed upon for three years.

Mortality and morbidity were recorded.

The data was entered into and analyzed on the SPSS system.

Result

All patients were females. Age at diagnosis was below 30 years in 2 patients (3.8%), between 30-39 years in 12 patients (23.1%), between 40-49 years in 21 patients (40.4%), more than 50 years in 17 patients (32.7%). (Table 1 & chart 1)

The mean age at menarche was 12 years of age (range between 9-18 years). Twelve patients (23%) were below 12 years of age (Table 2). Sixteen patients (30.8%) were at menopause during diagnosis. (Chart 2) The mean age at menopause was 48 years (range 38-59)(Table 3). Four patients had their menopause above 50 years(Chart 3). Thirty-seven patients (71.2%) had child birth were unmarried or nuliparous were 10 patients (19.2%).(Table3) Age at first delivery was ranging between 16 and 40 years of age.(Table 4) The mean was 24.3 years. In this study, the married patients had their first delivery at an early age.

Number before percentage 59.6% of patients breast fed their infants.(Chart 5). Eleven patients (22%) were using oral contraceptive pills (OCP).(Table 5) One patient was on hormonal replacement therapy due to premature ovulatory failure. Family history of breast cancer was positive in 18 patients (35.3 %) (Table 6, Chart 6).

Thirteen patients had breast cancer (72.2%), one patient had ovarian cancer (5.6%), and 4 patients had other types of cancer such as colon, and uterine (22.2%). (Table 7)

Two patients in this study had history of breast cancer in the other breast.

We found that 37 patients (71.2%) had early breast cancer (T1, T2, N0, N1, M0) and 15 patients (28.8 %) had advanced breast cancer (T3, T4, N1, N2, M0 -1).). (Table 8, chart 7)

There was no local recurrence, and three mortalities to date.

DISCUSSION

Unlike lung cancer, for which smoking is the principal and major risk factor, there is no single, most powerful factor that places women at risk for breast cancer. Nevertheless, three factors have been found to increase a woman's risk of developing breast cancer. These are advancing age, family history, and history of breast cancer[4].

The primary risk factor for breast cancer in most women is advancing age[4]. Only 5% of breast cancers occur in women in their 30s and younger, whereas 10% occur in women in their 40s, and 85% occur in women 50 years of age and older[4]. In this study, 2 patients (3.8%) were in their twenties, 12 patients (23.1%) were in their thirties, 21 patients (40.4%) were in their forties, 17 patients (32.7%) were at or above 50 years of age. In 2002 in Bahrain, 54 new breast cancer cases were diagnosed.

There was13 cases (24%) in their thirties, 21 cases (38.8%) in their forties, 9 cases (37%) in their fifties and above. Bar chart (1)

Our results indicate that most of our patients were in the younger age group, below the age of forty. This is not similar to the international figures, but almost similar to Bahraini result for breast cancer in 2002[5]. Breast cancer accounted for 33.8% of all types of cancer in Bahraini females in 2002[5]. The incidence rate was 26.1/100,000 0f cancer cases in 2002[5]. (Table 9,chart 8)

Two large studies found that patients younger than 35 years of age at diagnosis have a worse prognosis than older patients. However, other studies found there is no relation with age[8,9].

The second most important risk factors for developing breast cancer is positive family history of the disease. Internationally it was found that about 5 to 15 % of the patients with breast cancer have positive family history. In this study, we found a significant positive family history of breast cancer in 18 patients (35%)*. table

A critical issue is determining which patients are most likely to harbor clinically significant gene mutations (BRCA1 and BRCA2) that can be identified by genetic testing. There are still important questions unanswered regarding cancer risk, the benefits of genetic testing, and the efficacy of management options.

When compared to general population, BRCA1 and BRCA2 carriers have an earlier age of onset of breast cancer. Approximately 20% of BRCA1 carriers will have developed breast cancer before the age of 40, and one-half by the age of 50. BRCA2 carriers may have a slightly older age of breast cancer onset[11].

Management strategies for the affected women with BRCA1\ 2 mutations who are at risk for primary breast cancer include intensified surveillance strategies, chemoprevention with Tamoxifen, or prophylactic mastectomy[11].

With significantly high family history we would recommend genetic testing for them to be categorized in the high risk group and follow them regularly and intensively.

Early menarche and late menopause are considered to be significant risk factors affecting the incidence of breast cancer. As per the patients records in our review this rule was not applicable. The mean age of menarche was 12 (9 -18) years and mean age of menopause was 48 (38 – 59) years.

Some studies were indicating that females who are more than 25 years old at their first full-term pregnancy have 40 % increased risk versus females that have their first full term pregnancy below 20 years old.(5) Other studies concludes that women who have never given birth are more likely to develop breast cancer after menopause than women who have given birth multiple times[9]. The timing of the first pregnancy also appears to play a role: women who have a first full-term pregnancy at the age of 30 years or older have an increased risk of breast cancer[9]. The mean age of our group of patients at their first pregnancy was 24.3 (16 – 40) years. These results may indicate that this risk factor may not be significant in our group.

Lactation is associated with a slight reduction in risk of breast cancer among pre-menopausal women and the increasing cumulative duration of lactation was found to be associated with a decreased risk of cancer among premenopausal women. Also a younger age at 1st lactation was significantly associated with a reduction in risk of pre-menopausal breast cancer. However, no reduction in the risk of cancer occurred among post menopausal women with history of lactation[6-8]. In our review 59.6 % of the patients breast fed their children.

The subject of OCP use and the risk of developing breast cancer is controversial, some studies indicates that there is small risk increase of breast cancer when associated with long duration use particularly when started at an early age[13-15]. In our patients only 22% were taking OCP which is may not be significant.

There was only one patient in our group who was on hormonal replacement therapy (HRT) for premature ovulatory failure. Long-term use of HRT for 5 years or more increases a woman's risk of breast cancer[9].

Delayed presentation and unavailability of national screening program is probably the main cause of increased number of advanced breast cancer as it was noted in about half of the patients (48 %) presented after three months from the symptoms. table

There were three mortalities in our study population mainly due to distant metastasis, and there has been no local recurrence.

CONCLUSION

More than half of our patients (67.3%) were below 50 years of age at presentation where's in USA it was 85% in ages above fifty years. With younger age of breast cancer onset in Bahrain, we would recommend screening program at a younger age group possibly 40 years of age.
There was a significant high incidence of positive family history (35.3%) in comparison to international results (5-15%). This significant high result means that we would recommend genetic testing for our breast cancer patients and their relatives to categorize them if positive in the high risk group and follow them regularly and intensively.

In our study, breast cancer was still diagnosed late. There was high incidence of Advanced disease (28.8%), while in mammographically screened populations it is diagnosed only in 5%. This could be explained by the absence of National Screening Program.

All other moderate factors (early menarche, late menopause, lactation, age at first delivery etc) were not significant in our patients indicating that these factors may not be applicable in our part of the world, other factors should be looked for and more studies should look in this subject.

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Age at diagnosis (Table 1)

	Frequency	Percent
20 - 29	2	3.8
30 - 39	12	23.1
40 - 49	21	40.4
>= 50	17	32.7
Total	52	100.0

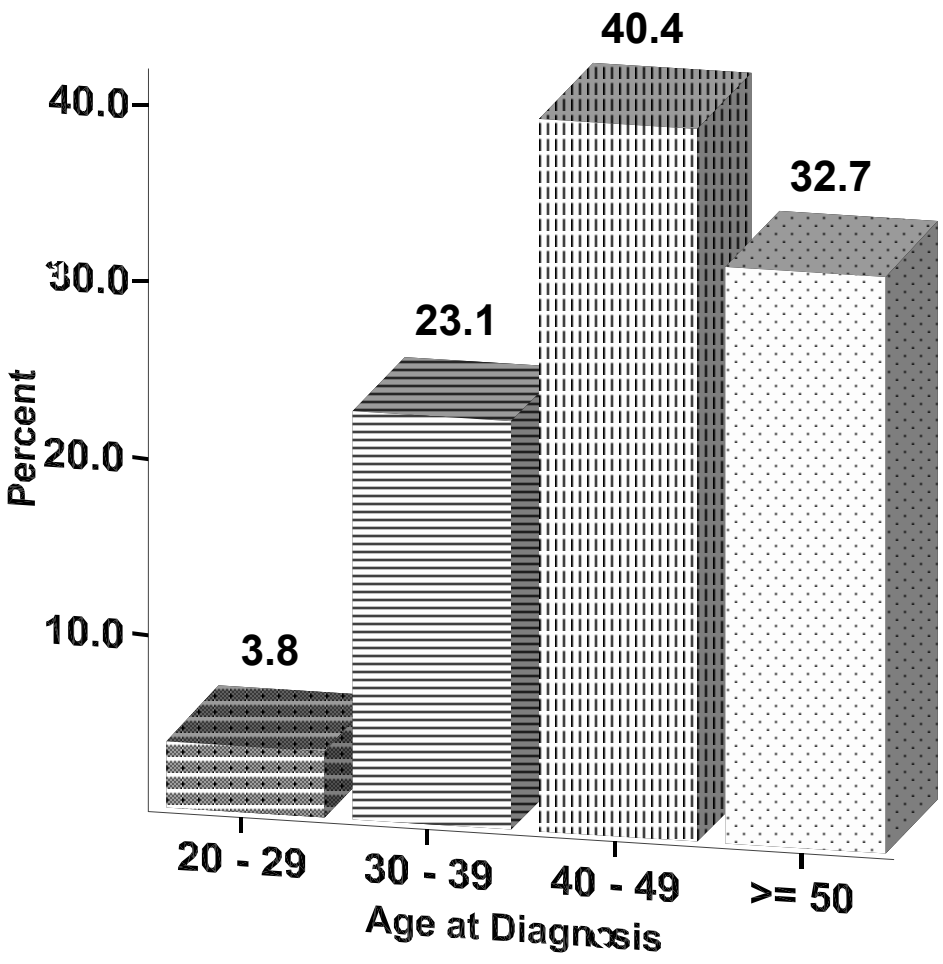
40.4
32.7
23.1
3.8
40.0
30.0
20.0
10.0
Percent
20 - 29
30 - 39
40 - 49
>= 50
Age at Diagnosis

Chart 1

	Number	Minimum	Maximum	Mean
Age of menarche	41	9	18	12.44

Table 2

Table 3

	N	Minimum	Maximum
Age of menopause	13	38	59

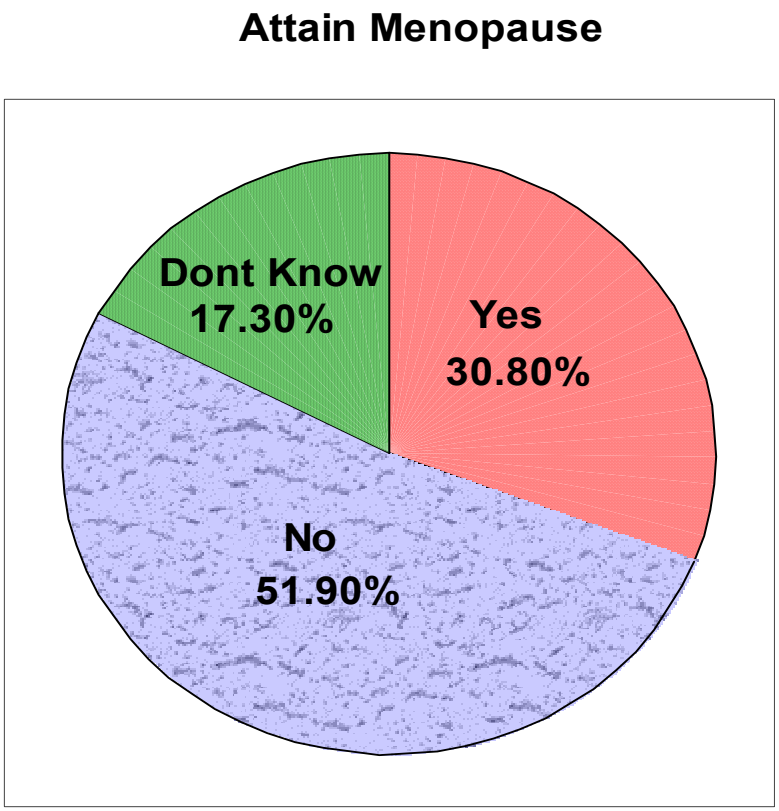

Chart 2

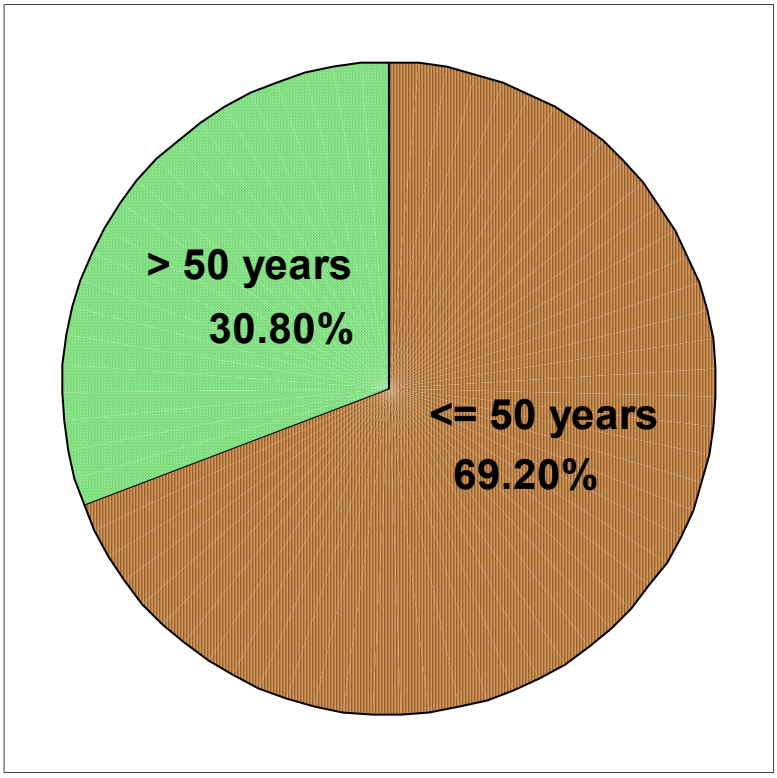

Chart 3

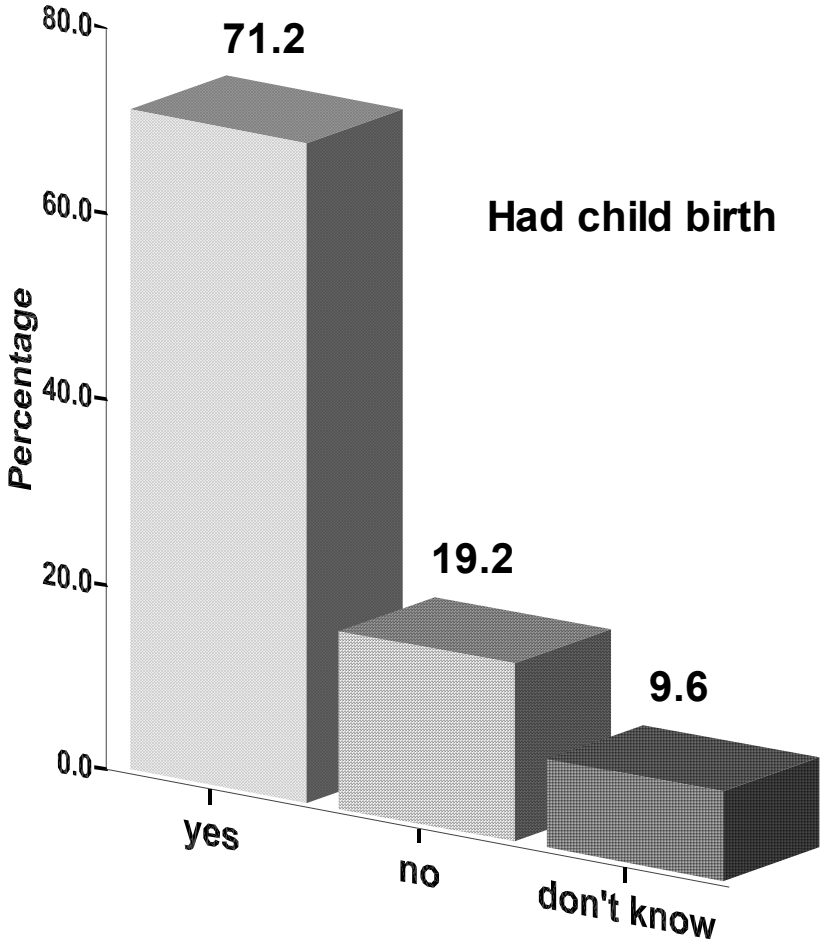
Had child birth
Percentage
80.0
60.0
40.0
20.0
0.0
71.2
19.2
9.6
yes
no
don't know

Chart 4

Had child birth (Table 3)

	Frequency	Percent
yes	37	71.2
no	10	19.2
don't know	5	9.6
Total	52	100.0

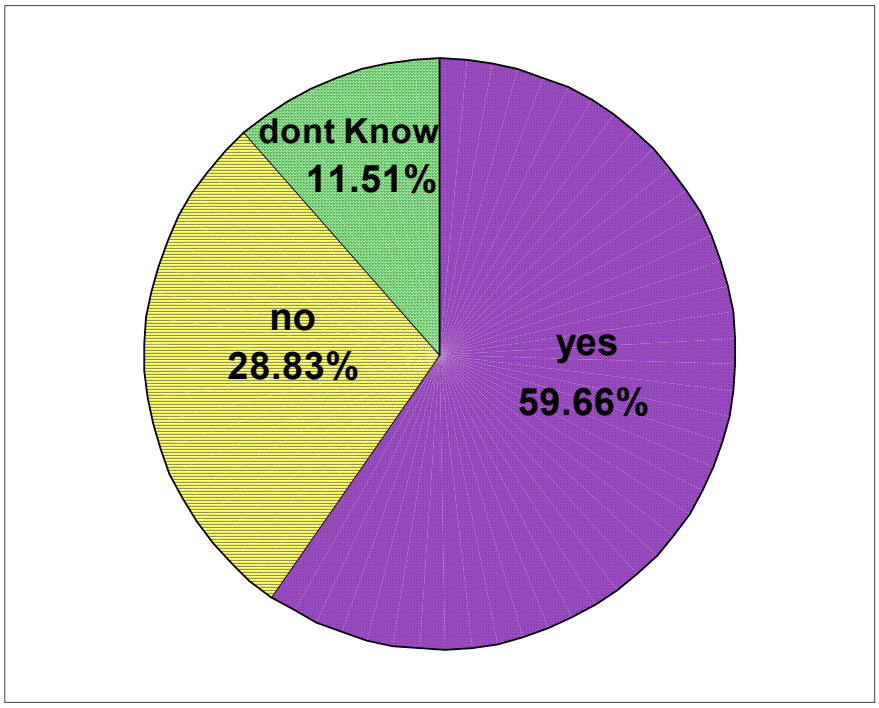

Chart 5

Tumor Stage (Table 8)

	Frequency	Percent
Early	37	71.2
Advanced	15	28.8
Total	52	100.0

Malignancy type in the family (Table 7)

		Frequency	Valid Percent
	breast	13	72.2
	ovarian	1	5.6
	others	4	22.2
	Total	18	100.0

Family history of malignancy (Table 6)

		Frequency	Percent	Valid Percer
	yes	18	34.6	35.3
	no	33	63.5	64.7
	Total	51	98.1	100.0
Missing	System	1	1.9	
Total		52	100.0	

Used OCP (Table 5)

		Frequency	Percent	Valid Percent	Cumulative Percent
	yes	11	21.2	22.0	22.0
	no	35	67.3	70.0	92.0
	don't know	4	7.7	8.0	100.0
	Total	50	96.2	100.0	
Missing	System	2	3.8		
Total		52	100.0		

Age at first delivery (Table 4)

	N	Minimum	Maximum	Mean
Age at 1st delivery	31	16	40	24.35

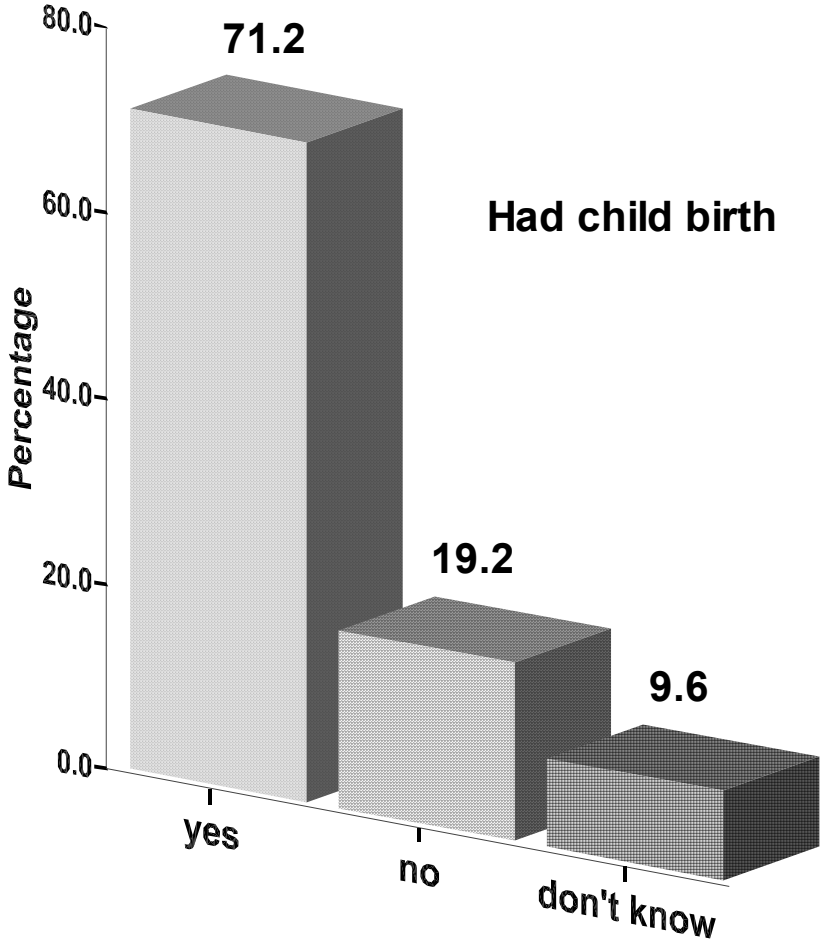
80.0
60.0
40.0
20.0
0.0
Percentage
71.2
19.2
9.6
Had child birth
yes
no
don't know

Chart 4

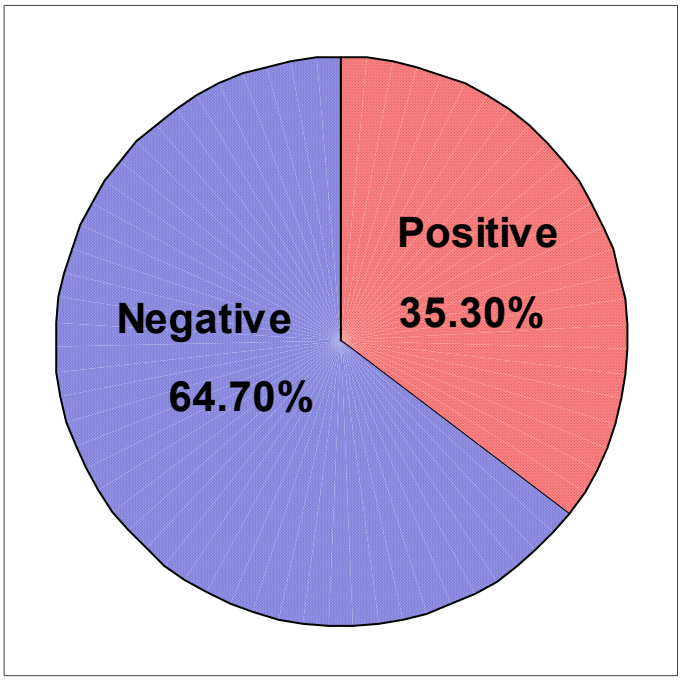

Chart 6

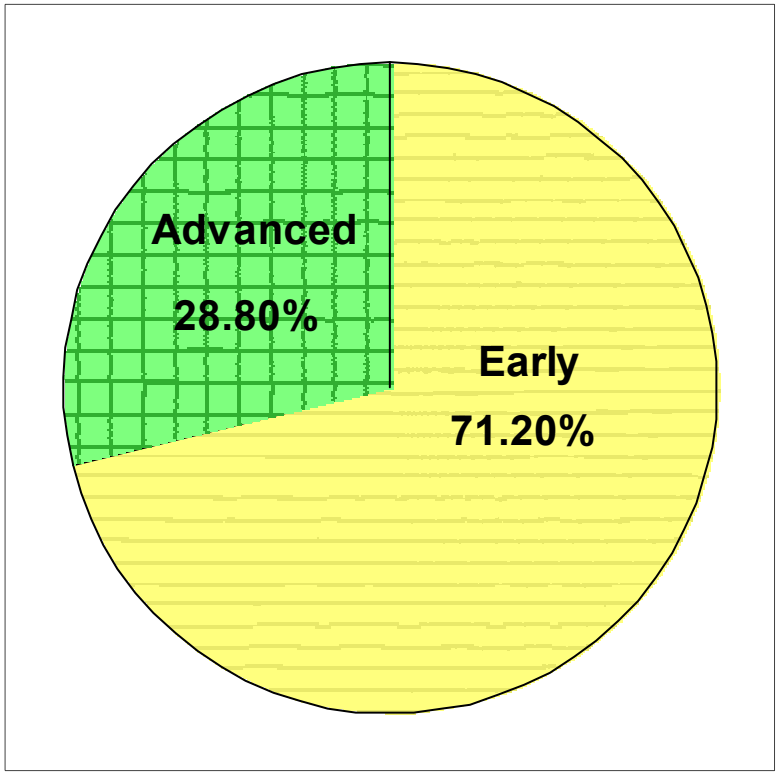

Chart 7

Age at diagnosis(Table 9)

	20 - 29	30 - 39	40 - 49	>= 50
Our Study	3.8	23.1	40.4	32.7
Bahrain 2002	.0	24.0	38.8	37.0
USA	.0	5.0	10.0	85.0

Age at Diagnosis in our study, Bahrain Cancer Registry 2002, and USA

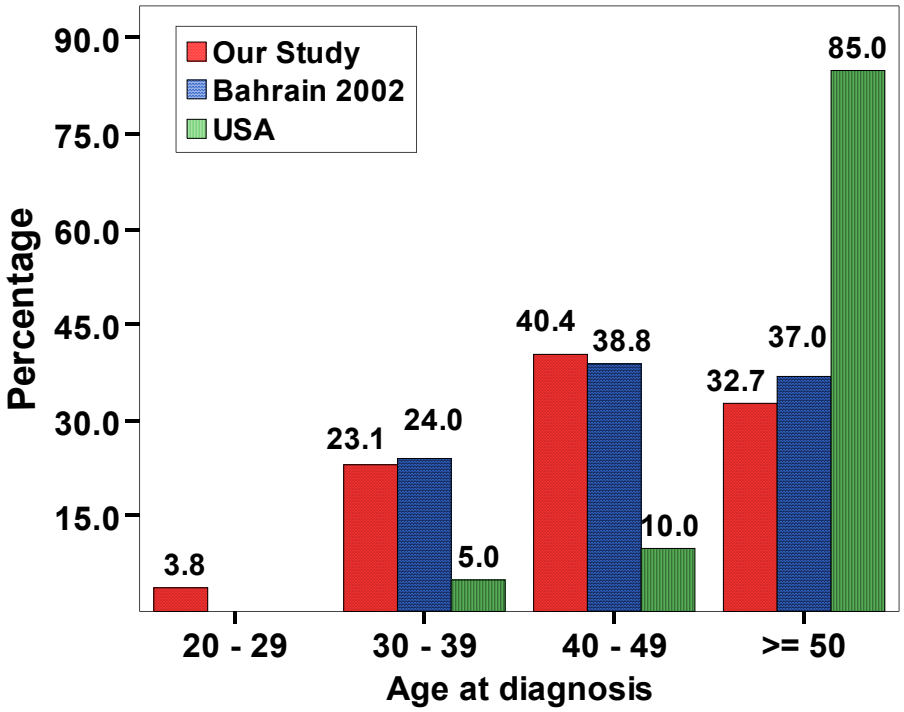

Chart 8