Breast Cancer in Iran: An Epidemiological Review

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Abstract: Breast cancer is one of the most frequent malignancies among Iranian women, however; the epidemiological aspects of breast cancer among Iranian patients are uncertain. A literature review of the published articles from January 1998 to December 2005 was conducted using different search engines: MEDLINE, Scientific information data base of Academic Center for Education, Culture and Research, and over 2000 issues of 94 Persian medical journals. The headings “Breast Cancer,” “Breast Tumor,” “Breast Malignancy,” and “Breast Carcinoma” were combined with the word “Iran” to execute the search. In all, 85 full papers were reviewed. These findings showed that participants ranged from 15 to 84 years old, with those 40–49 being the most prevalent. The incidence of breast cancer in women was 22 per 100,000. The prevalence in this same population was 120 per 100,000. Stage I was diagnosed in 18%, stage II in 57% and stage III in 25% of the cases. About 72% of the patients were diagnosed with a tumor over 2 cm. Sixty-three percent of the patients had lymph node involvement at the diagnostic time. Infiltrative ductal carcinoma was found to be the most common at 77% and lobular carcinoma the least at 5%. This review indicates that the epidemiological aspects of breast cancer in Iran are relatively well-studied. Shortcomings in study of its clinical aspects are evident and need to be a central part of upcoming investigations.

Key Words: breast cancer, epidemiology, Iran, review

BACKGROUND

Breast cancer is the most common cancer among women worldwide (1). Incidence rates increased rapidly predominantly in women 50 and older (2) in the 1980s due to the increased detection of smaller, earlier-stage cancers with the widespread adoption of the screening of mammography among asymptomatic women (3). A portion of this increase can be attributed to changes in reproductive patterns, such as delayed childbearing and having fewer children (increased life expectancy). Though at one of the lowest incidence rates in Iran as in other Asian countries, during last four decades, increasing its incidence rate has made breast cancer one of the most frequent malignancies among Iranian women (4) (Table 1).

Breast cancer affects Iranian women at least one decade younger than their counterparts in developed countries (5). The mortality rate of breast cancer was 5.8 per 100,000 women in Tehran in 1998 (6), 2.5 per 100,000 for female population, and 7762 years of life lost in the 18 provinces of Iran in 2001 (7). Developing countries hope to be on the threshold of eliminating breast cancer as a major public health threat (8). Early detection of breast cancer remains an important challenge to health professionals. According to the World Health Organization’s recommendations on implementing national cancer control programs (9), assessment of the magnitude of the cancer problem (i.e., incidence, prevalence, and mortality) is the first step in this process. There are many published studies about breast cancer in Iran, but the epidemiological aspects of Iranian breast cancer are uncertain. This paper reviews such studies to shed more light on the topics.

METHODS

A literature review of the published articles from January 1998 to December 2005 was conducted to...
assess the epidemiological aspects of breast cancer in Iran. The search strategy included all papers containing “Breast Cancer,” “Breast Tumor,” “Breast Malignancy,” and “Breast Carcinoma” were combined with the word “Iran” in their titles. Since 1998 breast cancer was publicized as a major public health problem in Iran and the results of numerous projects and screening programs were published after this year; this year was selected as starting point. Hindering efforts to gather all published articles, particularly those published in Persian medical journals was the fact that they did not have a citation index, much of the data was not available in articles to allow for appropriate classification and many laboratories did not have all the issues. Many of them were searched by hand. Several authors were asked to provide us copies of their published manuscripts. The databases of Tehran Cancer Registry and National Cancer Registry Program were used for this study. Different search engines were used including MEDLINE, ISI, and Scientific Information Database (SID) of the Academic Center for Education, Culture and Research. Over 2000 issues of 94 Persian medical journals were assessed manually from the Medical College Library of Tehran University and Iran University Reference Medical Library. The abstracts and unpublished information were not included in the study. There was no hypothesis to be tested, and assessment focused solely on breast cancer in females. We excluded studies relating to treatment modalities reviewing only the epidemiological findings, as information was lacking concerning surgical, chemotherapeutic, or radiotherapeutical protocols and there was no mean for accurate comparisons. The findings were classified into epidemiological, basic and clinical categories.

RESULTS

In all, there were 53 citations in MEDLINE, 27 in ISI, 51 in SID and 42 in Persian medical journals. Seven articles were published both in Persian and international journals. Duplicate citations were excluded. Of these 85 full text articles were reviewed.

Epidemiologic Aspects

Incidence and Prevalence Rate. Breast cancer accounted for 25.5% of all female cancers with a crude incidence rate of 22.4% in 100,000 in Tehran in 1998 (10). The National Cancer Registry reported 1,603 new cases of breast cancer in 2000, and 3946 new cases in 2003, and 4557 new cases in 2004 (4). Two screening programs and a cross-sectional study showed the prevalence rate of breast cancer was 352 per 100,000 women aged 30–65 in Bushehr in 1998 (11), 660 per 100,000 for women 35 years and older in Shiraz in 1997 (12), and 120 per 100,000 for women aged 30 years and over in Northwest of Tabriz (13).

Histology and Clinical Stage. Table 2 shows studies that dealt with histology, clinical stage, size of tumor, and lymph node involvement (14).

Risk Factors. Many studies reported the risk factors for breast cancer in Iranian women (15–25). These are shown in Table 3. The most significant findings from these studies are the point that Iranian breast cancer patients are younger than their western counterparts.

Screening and Diagnostic Modalities. Table 4 shows the results of two population-based breast cancer screening programs in Shiraz and Bushehr, and several diagnostic evaluation studies in Iran.

Knowledge, Attitude and Practice. Table 5 shows the knowledge, attitude and practice studies. A descriptive study in Tehran investigated how religion might contribute to breast self-examination (BSE) among Muslim women. Ninety percent indicated BSE is not against their religious beliefs, although only 6% of respondents stated they performed BSE consistently on a monthly basis. Fifty-eight percent preferred to be examined by a female physician though 47% said that a clinical breast examination by a male physician is not against their Islamic beliefs (26). Performing BSE was defined in 6% of the women regularly (27). A study evaluating the national breast cancer information services indicated that it was effective in providing information and support for patients, relatives and the general public. The real challenge appears to

Table 1. Changes in Occurrence of Cancers among Women in Iran From 1965–1998

| Type of cancer | 1965 % of total cancer | 1998 % of total cancer |
|---------------|------------------------|------------------------|
| Cervix        | 19.7                   | 5.5                    |
| Breast        | 12.6                   | 25.3                   |
| Esophagus     | 6.2                    | 3.9                    |
| Lymphoma      | 4.2                    | 3.2                    |
| Corpus Uteri  | 3.2                    | 2.2                    |
be making the service more widely available, especially to breast cancer patients (28).

Basic and Clinical Aspects

Survival. There were four published studies on breast cancer survival rate; 5-year survivals of 167 breast cancer cases were found to be 62% in a historical cohort study (29). There were other reports that indicated the survival rate for breast cancer in Iran stands between Eastern and Western Europe; that is a 5-year survival rate of 50–70% (30–32).

Estrogen Receptor, Progesterone Receptor. In a study involving three men and 111 women age 23–75 years evaluating hormone receptors: ER-positive and PR-positive was 62.3% and 51.8%, respectively in 111 Paraffin block of breast cancer in Tehran in 2000–2002 (33). Another study found ER-positive 57%, PR-positive 47% among breast cancer cases (29).

Molecular and Genetics. Chromosome 1 and 8 (34), epidermal growth factor (35), HER2 (36–38), Catapsin D (39), free prolactin receptor (40), Ag NOR (41), HLA-DRB1 (42), BRCA1 and BRCA2 genes (43–45), P53 gene mutation (46), and Stromal cell-Derived Factor-1 (SDF1-3′A) mutation (47) had been evaluated in Iranian breast cancer.

Case Report. Unusual presentations for breast cancer were reported such as right eye Uveal metastasis (48), and subacute peripheral neuropathy (49).

Delay Presentation. Delay presentation is a public health problem for breast cancer, many patients was diagnosed at a very late stage with little chance of being cured. It was reported to lie between 25% and 42.5% in women with breast cancer. Only 17.5% of patients presented immediately (12,50).

Prognosis. There were no published studies about the prognosis of breast cancer and its association factors with the exception of a case control study. The results were as follows: 100 breast cancer (tumor size under 2.5 cm and without axillary lymph node involvement), 100 breast cancer (tumor size over 2.5 cm and with axillary lymph node involvement) and 1,000 patients without breast cancer were compared. Blood group B was associated with breast cancer prognosis [OR: 1.8, 95% CI: 1.2–2.8] (51).

Mood Disorders in Iranian Breast Cancer. The prevalence of depression was 40% in Kerman city (52). A study defined a significant difference between patients with breast cancer and controls regarding depression, and anxiety (53). A prospective study found that 48%
## Table 3. Risk Factors of Breast cancer in Iran

| Name of Study | Year  | Setting | Type of study | Number of patients (case/ control) | Age of patients Min–Max | Positive family history of breast cancer | Mean age of first period Year ± SD (p-value) | Mean age of first pregnancy Year ± SD | Marital status (%) OR (CI: 95%) | Mean age of menopause Year ± SD OR (CI: 95: %) |
|---------------|-------|---------|---------------|------------------------------------|-------------------------|------------------------------------------|---------------------------------------------|-------------------------------------|--------------------------------|------------------------------------------|
| Yavari et al. (18) | 2004  | Tehran  | Case-control  | 303/303                            | 24–84 48.8 ± 9.8         | 14.7% cases 7.6% control OR: 2.09 CI: 95%(1.22–3.55) | NA (NS)                                    | Age at first live birth>=30 Years old 4.39 (1.80–10.73) p < 0.0001 | 94.7 1.0 (reference) 5.3 8.48 (1.94–37.10) p < 0.005 | Postmenopause 2.97 (2.09–4.20) p < 0.001 |
| Aminisani et al. (24) | 2001  | Mashhad | Case-control  | 105/105                            | NA NA                  | NA NA                                    | NA NA                                       | NA NA NA                                    | NA NA NA                                    | 46.5 case 43.9 control p-value =0.02 |
| Ebrahimi et al. (16) | 1997–1998  | Tehran  | Case-control  | 286/249                            | 24–81 47.5 ± 12.5        | 6.6 cases, 2.4 control, OR: 2.87 CI: 95%(1.13–7.30) | 13.4 (1.5) case 13.5 (1.7) Control NS | 20.7 case 18.6 control (p-value =0.0001) | 71.7 1.00 (ref.) 19.6 1.68 4.25 (1.05–2.68) (1.71–10.57) 1.60 (0.86–2.96) | |
| Fathinajafi et al. (19) | 2002  | Mashhad | Case-control  | 170/180                            | 15–49 41.5 ± 5.6        | 0.6 cases p-value=0.191                  | NA NA                                       | NA NA NA                                    | NA NA NA                                    | |
| Pesaran et al. (56) | 2003  | Shahrekord | Case-control  | 176/176                            | 49 ± 11.3               | 5.3% cases 0.8% control OR: 3.06 CI: 95%(1.12–8.34) | NA                                         | After 20 years OR: 2.40 CI: 95% (1.52–3.8) | NA NA NA                                    | After 50 years old: OR: 2.7 CI: 95% (1.26–5.8) |
Table 4. Screening and Diagnostic Modalities of Breast cancer in Iran

| Name of Study          | Year          | Setting       | Type of study     | Number of population | Setting Type | Age of women | Screening or diagnostic tests | Acting                  | Main result                                                                 |
|------------------------|---------------|---------------|-------------------|----------------------|--------------|--------------|-------------------------------|-------------------------|-----------------------------------------------------------------------------|
| Silanian et al. (68)   | 1993–2000     | Tehran        | Diagnostic evaluation | 516                  | Menopauses   | Mammography | NA                            | Sensitivity of mammography in menopauses with or without hormone replacement therapy were 67%, 79% respectively (p-value < 0.008) Sensitivity of mammography in menopauses with or without hormone replacement therapy were 32%, 84% respectively (p-value < 0.002) |
| Talei et al. (14)      | 1994–1995     | Shiraz        | Screening         | 12894–9,934 (77)     | >35          | BSE          | Health worker                | Prevalence rate: 6.6 per 1000 (95% Confidence Interval: 2.5–10.7 per 1000) |
| Assadi et al. (13)     | 1996–1997     | Bushehr       | Screening         | 2842–1253 (44.1)     | 30–65        | CBE          | General practitioner         | Prevalence rate: 10/2842 = 3.5/1000 T1: 25% – T2: 37% – T3: 37% – N0:50% – N1:50% |
| Sina et al. (69)       | 1997–1998     | Urmia         | Diagnostic evaluation | 1004                | NA          | Mammography | Radiologist                   | Sensitivity and specificity of mammography was 100% and 79% respectively p-value ? Sensitivity, specificity, and accuracy of FNA for detecting breast mass were 92%, 97%, 95%, 86%, 88% respectively (p-value ?) |
| Assadi et al. (70)     | 1997–1999     | Tehran        | Diagnostic evaluation | 101                  | NA          | FNA pathology of biopsy | Radiologist               | Sensitivity 100%, PPV 35%, p-value? Sensitivity and specificity of FNA for detecting breast mass were 78%, 91% respectively (p-value ?) |
| Mahbobi et al. (71)    | 1998–1999     | Babol         | Diagnostic evaluation | 100                  | 39.7 ± 11.02 | Mammography | Radiologist                  | Sensitivity 72.7%, specificity 81.6%, PPV: 64%, NPV: 87% Accuracy 78.88% CBE by health worker had sensitivity 99.18%, specificity 95.8%, p-value < 0.01 |
| Dabiri et al. (72)     | 1998–2000     | Kerman        | Diagnostic evaluation | 75                   | 50.5±?       | FNA pathology of biopsy or mastectomy | Radiologist               | Efficiency of axillary sonography before surgery for detecting metastatic lymph adenoma in breast cancer was: sensitivity 78%, specificity 79%, PPV: 85%, NPV: 70% Sensitivity 65%, specificity 100%, p-value? |
| Ahmadinegad et al. (73)| 1999–2000     | Tehran        | Diagnostic evaluation | 71                   | NA          | Doppler sonography and power Doppler with 7.5 MHz probe | NA                       | Sensitivity 72.7%, specificity 81.6%, PPV: 64%, NPV: 87% Accuracy 78.88% |
| Naderi et al. (74)     | 1999          | Kerman and Zand | Diagnostic evaluation | 2000                | 20–98      | CBE          | Health worker physician       | CBE by health worker had sensitivity 99.18%, specificity 95.8%, p-value < 0.01 |
| Omranpoor et al. (75)  | 2000–2001     | Tehran        | Diagnostic evaluation | 100                  | 29–76       | Axillary sonography surgery | Radiologist surgeon       | Efficacy of axillary sonography before surgery for detecting metastatic lymph adenoma in breast cancer was: sensitivity 78%, specificity 79%, PPV: 85%, NPV: 70% Sensitivity 65%, specificity 100%, p-value? |
| Modir et al. (76)      | 2001          | Tehran        | Diagnostic evaluation | 110                  | 19–64       | FNA          | NA                            | Sensitivity 90.6%, specificity 100%, PPV: 100%, NPV: 96% Prevalence rate: 120/100.000 Cl: 95% (100–140) |
| Hasaniesfahani et al. (77)| 2001       | Yazd          | Diagnostic evaluation | 110                  | 48.9 ± 10.4 | FNA          | NA                            | Sensitivity 90.6%, specificity 100%, PPV: 100%, NPV: 96% Prevalence rate: 120/100.000 Cl: 95% (100–140) |
| Abbasalizadeh et al. (15)| 2001         | Tabriz        | Cross-sectional   | 842                  | >30         | Risk assessment and CBE mammography biopsy | General practitioner        | Sensitivity: 92.3% p-value? Specificity: 71.4% p-value? PPV and NPV: 85.7%, 83.3% Sensitivity: 91% p-value <0.04 Specificity: 17% p-value <0.0001 (because of normal mammography had not been done) Accuracy 74.5% p-value <0.0001 |
| Zakavi et al. (78)     | 2002–2003     | Mashhad       | Diagnostic evaluation | 20                   | 20–79       | Breast scan with TC-MIBI    | NA                       | Sensitivity, specificity, PPV, NPV, and accuracy of FNA for detecting breast mass were 75.8%, 100%, 100%, 86%, 88% respectively (p-value ?) |
| Talei et al. (79)      | 2003          | Shiraz        | Diagnostic evaluation | 110                  | NA          | Mammography biopsy | Radiologist surgeon       | Sensitivity: 92.3% p-value? Specificity: 71.4% p-value? PPV and NPV: 85.7%, 83.3% Sensitivity: 91% p-value <0.04 Specificity: 17% p-value <0.0001 (because of normal mammography had not been done) Accuracy 74.5% p-value <0.0001 |
| Ziaeian et al. (80)    | 2003          | Zahedan       | Diagnostic evaluation | 92                   | NA          | FNA pathology of biopsy | NA                       | Sensitivity, specificity, PPV, NPV, and accuracy of FNA for detecting breast mass were 75.8%, 100%, 100%, 86%, 88% respectively (p-value ?) |
of the patients had severe symptoms of anxiety at both baseline and follow-up, more than 60% of patients had no symptoms of depressive illness at pre and postdiagnosis assessments (54). Another prospective study was conducted to assess the long-term impact of attending a support group on the prevalence of psychological morbidity in patients with breast cancer before and after 1-year participation in the Iranian breast cancer support group. Psychological morbidity was measured using Hospital Anxiety and Depression. While at baseline, 29% scored high on the anxiety subscale and 14% scored high on the depression subscale (55). The mean total fatigue score of the breast cancer was reported to be 18.7% (±13.5), severe anxiety 16% and depression 32% (56). Other studies reported the mood disorders in breast cancer (57,58).

**Treatment Modalities.** A cross-sectional study was conducted to evaluate general surgeons’ preference regarding breast cancer surgery (breast-conserving surgery versus mastectomy) and predicting factors. Only 19% of surgeons prefer breast-conserving surgery in their routine practice (59). A retrospective cross-sectional study of patients who underwent surgical therapy for breast cancer with either modified radical mastectomy (MRM) or breast preservation was carried out. Seventy-three percent underwent MRM and the remaining 27% received breast-preservation surgery. Seroma occurred in 35% of patients. In multivariate logistic regression analysis, an association of postoperative seroma formation was noted with MRM [OR: 2.83, 95% CI: 1.01–7.90] (60).

**DISCUSSION**

Participants ranged from 15 to 84 years old with those 40–49 being the most prevalent, over 30% of patients are under 30 years. The incidence rate of breast cancer in women over 30 in Iran is 22 per 100,000. The prevalence rate in this same population is 120 per 100,000. Stage I was diagnosed in 18%, stage II in 57% and stage III in 25% of the cases. Seventy-two percent of the patients were diagnosed with a tumor over 2 cm. Around 63% of the patients had lymph node involvement at diagnostic time. Infiltrative Ductal carcinoma was found to be the most common at 77% and lobular carcinoma the least at 5%. There are many controversies about risk factors of breast cancer because of the number of case and control, sampling methods, selecting the population and etc.

| Table 5. KAP Studies about Breast Cancer in Iran |
|---|
| **Name of Study** |
| Jokar et al. (81) |
| Danesh et al. (82) |
| Ramezani et al. (83) |
| Dadkhah et al. (84) |
| Abedzadeh et al. (85) |
| Haji-Mahmoodi et al. (86) |
| Mahori et al. (87) |
| **Year** |
| 1998 |
| 1998 |
| 2000 |
| 2001 |
| 2001 |
| 2001 |
| 2002 |
| **Setting** |
| Ilam |
| Shahrekord |
| National |
| Ardebil |
| Rasht |
| Tehran |
| Shiraz |
| **Type of study** |
| Case series |
| Cross-sectional |
| House hold survey |
| Case series |
| Case series |
| Cross-sectional |
| Cross-sectional |
| **Number of population** |
| 264 |
| 340 |
| 13325 |
| 150 |
| 400 |
| 1000 |
| **Mean ± SD Knowledge, Attitude, Practice** |
| 57.3 ± 64 |
| 41.8 ± 22 |
| 52.7 ± 22 |
| 42.9 ± 20 |
| 44.7 ± 18 |
| 43 ± 18 |
| **Other results Knowledge, attitude and practice of women about breast cancer associated with their age and education (p < 0.05)** |
| N/A |
| N/A |
| N/A |
| N/A |
| N/A |
| N/A |
| **Knowledge, attitude and practice of women about breast cancer associated with their age and level of education (p-value)** |
| 0.01 |
| 0.0001 |
| 0.0001 |
| 0.0001 |
| 0.0001 |
| 0.0001 |
| **Knowledge and practice of women about breast cancer screening associated with their level of education and past history of breast cancer in the family (p < 0.0001)** |
| 28.7 |
| 45 |
| 45 |
| 45 |
| 45 |
| 45 |

KAP, Knowledge, attitude and practice.
Sensitivity and Specificity of diagnostic tests are as follows: clinical breast exam by health worker (99.18%, 95.8%) mammography (91–100% and 79%), breast scan with TC-MIBI (92.3%, 71.4%), fine needle aspiration (65–90%, 97–100%), Doppler sonography and power Doppler with 7.5 MHz probe (72.7–81.6%). Illiteracy was seen 23–73% of all Iranian female breast cancer patients. The prevalence of depression was 40% in those patients. Other factors included knowledge (52%), attitude (42%) and practice (20%) of Iranian women about breast cancer self-exam. Five-year survival rate of breast cancer was 65–73%. ER-positive 57–62% and PR-positive 47–51% among breast cancer. Delay presentation was seen 68–73%. ER-negative 57–62% and PR-negative 47–51% among breast cancer. Survival rate of breast cancer in Iran are recommended to be defined as a reference to planning future studies. Policymakers can utilize it as a template to design and perfect a national cancer control program for breast cancer in Iran. Studies relating to surgical, chemotherapeutical and radiotherapeutical protocols, prognosis and the survival rate of breast cancer in Iran are recommended to be designed as common projects with neighboring countries in medical multicenter specialty studies not only to define its epidemiology but to develop the impact of screening, treatment, and the palliative therapy of breast cancer.

CONCLUSIONS

This was the first study focusing on a comprehensive breast cancer epidemiological review in Iran. The primary implication for clinicians is: it will serve as a reference to planning future studies. Policymakers can utilize it as a template to design and perfect a national cancer control program for breast cancer in Iran. Studies relating to surgical, chemotherapeutical and radiotherapeutical protocols, prognosis and the survival rate of breast cancer in Iran are recommended to be designed as common projects with neighboring countries in medical multicenter specialty studies not only to define its epidemiology but to develop the impact of screening, treatment, and the palliative therapy of breast cancer.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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