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## ORIGINAL ARTICLE

# Breast Cancer in Iran, from Epidemiology, Clinicopathological and Biomarker Feature

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### ABSTRACT

*Breast cancer is the most prevalent cancer among females in the world. This cancer is a major medical and public health problem. This study describes the epidemiology, risk factors, clinical staging, clinical pathology, biological markers, clinical subtypes and survival of breast cancer in Iran. All the data were gathered from cancer registration system of ministry of health and medical education (MOHME) and also Cancer research Center of Shahid Beheshti Medical University of Iran (CRC- SBMU). Some data was also added from other published Iranian articles to increase the accuracy of incidence, prevalence, burden of the disease, risk factors, clinical staging, clinical pathology, biological markers, clinical subtypes and survival rate of breast cancer in the last decade and compare the epidemiological data with other part of the world. Breast cancer is the most common cancer in Iran overall. ASR of breast cancer is 33.21 in 100.000according to latest national databases. The mortality rate of breast cancer has not changed in the past 30 years in Iran. ASR for mortality is 14.2 in 100.000 and the mean age is 49.84 years. The most common cancer in Iran is invasive ductal carcinoma. In our last review 65.5-70.5% of cases are in the early stages (2/3) and less than 30% are in the advanced stages. Five-year overall survival rate is estimated to be 72% in women and 60% in men. This survival rate is significantly affected by the stage and number of positive lymph nodes. Our study shows that cancer prevalence is multi-dimension and needs multi-center involvement including the governmental authorities, clinicians and scientist.*
*Keywords: MOHME, Breast Cancer, ductal carcinoma*

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## INTRODUCTION

Breast cancer is the most common diagnosed cancer among women in the world. According to GLOBOCAN report about 1.38 million new cases were diagnosed in 2008 .and it was 1.67 million in 2012 [1]. It means 23% of all female cancers include breast cancer [2].

Among females worldwide the most common cancer sites were either breast or cervical cancer, with the exception of China (lung), South Korea (thyroid), Mongolia and Vietnam (liver) [3].

Female breast cancer incidence rates varied internationally by more than 13-fold in 2008 between different countries, ranging from 8.0 cases per 100,000 in Mongolia and Bhutan to 109.4 per 100,000 in Belgium, the highest age-standardized incidence rates are observed in North America, Northern Europe and the lowest rates in Asia and Africa [3, 4].

The incidence of breast cancer has increased by 3.1% annually in the world, between years 1980 and 2010 [5]. An estimated 1 in 8 women in the United States will develop this disease in their life [4, 6].

The rate is very high in east Europe by 93.1 per 100,000 and 89.7 per 100,000in west Europe according to GLOBOCAN report (Tab 1) [2].

**Table 1:** Difference of ASR for incidence according to GLOBOCAN 2014 result & national data base [1,7]

| ASR for Incidence | IRAN National Data base | IRAN GLOBO CAN | EMRO | European Union | Australia New Zealand | Canada | USA |
|---|---|---|---|---|---|---|---|
| **2012** | 33.21 | 28.1 | 41.9 | 82.1 | 85.8 | 79.8 | 92.9 |

The incidence of breast cancer by age and geographic distribution in the world shows that in developing countries the incidence of breast cancer is 23% in young adults (15- 49yr) versus 10% in developed countries and in menopause female ( > 50 yr) the incidence is 28% in developing countries versus 39% in developed countries [8]. It means in developed countries the most cancer females are old age.
According to GLOBOCAN database 2014 the incidence, mortality and prevalence of breast cancer in Iran was compared with database of the world and there was no significant difference between their percentages (Tab 2) [1].

**Table 2:** Difference of incidence, mortality and 5 years. prevalence between Iran and globe [1].

| Breast Cancer | Number | Incidence % | ASR(W) | Number | Mortality % | ASR(W) | Number | 5 year Prevalence % | Prop |
|---|---|---|---|---|---|---|---|---|---|
| **world** | 1676633 | 25.2 | 43.3 | 521817 | 14.7 | 12.9 | 6255391 | 36.4 | 240.8 |
| **Iran** | 9795 | 24.5 | 28.1 | 3304 | 14.2 | 9.9 | 34105 | 37.7 | 118.1 |

According to national developing database the cumulative probability of breast cancer incidence for individuals aged 15–79 years in Iran was increased in the last 30 years.: in 1980, 1.4 (0.9-2.9); in 1990, 1.8 (1.1-2.8); in 2000, 2.1 (1.9-2.4) and in 2010, 2.2 (1.8-2.7) [8]. As in figure 1 illustrates incidence rate of breast cancer rose from 2005-2008 in Iran.
Based on the Iranian Cancer Registry Report in 2008, the total number of women diagnosed with breast cancer was 8,616 cases with Age Standardized incidence Rate (ASR) of 33.21 per 100,000 female populations [7]. Table 3 shows age-specific incidence of breast cancer in Iran in 2005-2006 from national cancer registry system.

**Table 3:** Age-specific incidence rate of breast cancer in Iran in 2005–2006 (n = 5981) [9]



Incidence rate

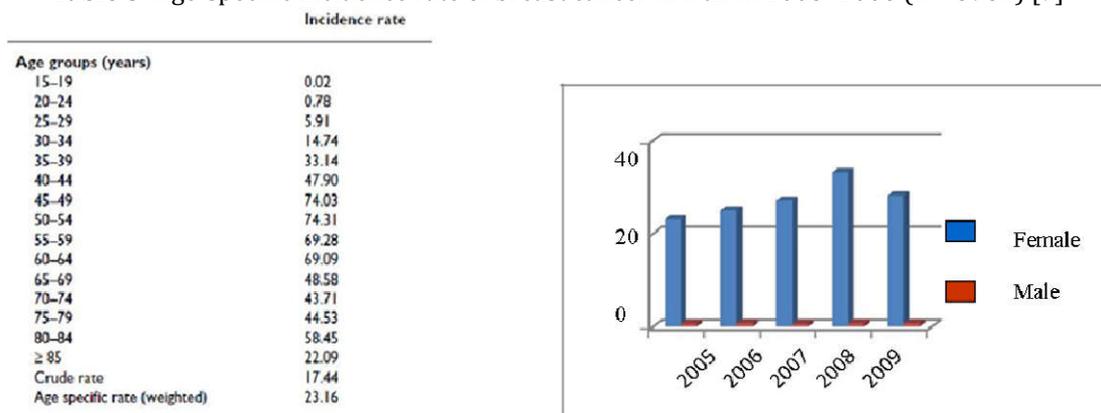| Age groups (years) | |
|---|---|
| 15–19 | 0.02 |
| 20–24 | 0.78 |
| 25–29 | 5.91 |
| 30–34 | 14.74 |
| 35–39 | 33.14 |
| 40–44 | 47.90 |
| 45–49 | 74.03 |
| 50–54 | 74.31 |
| 55–59 | 69.28 |
| 60–64 | 69.09 |
| 65–69 | 48.58 |
| 70–74 | 43.71 |
| 75–79 | 44.53 |
| 80–84 | 58.45 |
| ≥ 85 | 22.09 |
| Crude rate | 17.44 |
| Age specific rate (weighted) | 23.16 |

**Figure 1:** Trend of ASR of breast cancer from 2005 to 2009 in Iran

Prevalence of breast cancer is increased by 3.1% per year in the world [5]. The 5 years prevalence of breast cancer means the estimated number and proportion of peoples alive with breast cancer in previous 5 years that was 6,255,391 in the world and 34,175 in Iran [1].
According to data pool from cancer research center of Iran the 5 years prevalence of breast cancer is 28,750.
The mean age of breast cancer in Iran is 5 years earlier in Iranian women in comparison to developed countries according to Akbari *et al* study (Tab 4). According to national data base more than half of breast cancer cases (%57.6) are less than 50 years [10,11].

**Table 4:** Age distribution of the breast cancer patients [7, 10] Age of diagnosis (years)

| Age group | Count | percent |
|---|---|---|
| **<30** | 39 | %6.4 |
| **30-34** | 42 | % 6.9 |
| **35-39** | 89 | % 14.5 |
| **40-44** | 114 | 18.6% |
| **45-49** | 125 | 20.4% |
| **50-54** | 83 | 13.5% |
| **55-59** | 59 | 9.6% |
| **60-64** | 23 | 3.8% |
| **65-69** | 22 | 3.6% |
| **70-74** | 17 | 2.8% |

Breast cancer is the second leading cause of cancer death in developed countries 15.4% after lung cancer and in Iran it is the fifth leading cause of cancer death like overall part of the world and it is 14.2% [1, 11, 12].

The global total number of deaths from breast cancer has increased from 250 000 (95% CI: 239 000–296 000) in 1980 to 425 000 (359000– 453000) in 2010—an annual rate of increase of 1.8% [5].

From 1980 to 2010, deaths in reproductive-aged women from breast cancer increased 1.8% per year. The proportion of breast and cervical cancer deaths in women younger than 50 years varies from 0.13 in central Europe to 0.37 in the Middle East [5].

The cumulative probability of breast cancer death for individuals aged 15–79 years in the last 30 years. In Iran is illustrated in table 5 [5].

**Table 5:** The cumulative probability of breast cancer death in Iran

| Years | Death Rate | Confidence Interval |
|---|---|---|
| **1980** | 0.6 | (0.3-1.1) |
| **1990** | 0.7 | (0.4-1.1) |
| **2000** | 0.7 | (0.7-0.8) |
| **2010** | 0.7 | (0.5-0.8) |

It means the mortality rate isn't change a lot in last 30 years and this rate in Iran is similar to developed countries in the world and is less than other countries in our region (EMRO) (Tab 6).

**Table 6:** Age standardized rate for mortality according to GLOBOCAN 2014 REPORT [1]

| ASR For Mortality | Iran | EMRO | European Union | Australia | Canada | USA |
|---|---|---|---|---|---|---|
| | | | | New Zealand | | |
| **2012** | 14.2 | 18.6 | 15.4 | 14.5 | 13.9 | 14.9 |

**MATERIAL AND METHOD**

There are many published data about breast cancer status in Iran in Cancer research center (CRC), SBMU. These data cover epidemiological, clinical, pathological, radiological, economical, geographical distribution, ethnicity and efficacy/beneficial of diagnostic and therapeutic intervention about breast cancer in the Islamic Republic of Iran.

We decided to collect and organize these data to introduce the real status of breast cancer in Iran.

The main source of data was based on cancer registry department of health ministry and the other data that was extracted from published articles and data provided in CRC, SBMU.

There were some published data from other institutes in Iran, which we have yet to compare and compile with our data.

We tried to compare the different status of this disease in Iran with other parts of the world, using the international data from IARC, GLOBOCAN, APC and other sources.

**RESULTS**

**Age & Gender**

Mean age of breast cancer diagnosis in Iran, according to different published articles is reported between 47.95-54.6 years, and it is 49.84 years according to National data base [11]. Half of patients were 48 years old and younger. The most common age group of patients was 41- 49 years (34.5%) [10,11, 13-17]. The rate of breast cancer in men was reported 2.8%, which is much higher than the other parts of the

world [18]**.**

**Risk & protective factors**

The most common risk factors of breast cancer in Iran are similar to other studies, but some protective factors are bolded: young age at the first full term pregnancy and multiparty are protective against cancer , the best results were found with 1-3 parity [12, 16, 19, 20].

In two studies the role of long term breast feeding between 18-24 months per child had significant protective effects.

Effects were seen in cases with breast-feeding duration not less than 18 months, with best results being achieved with 24 months per child. In one study that was done in Cancer Research Center,70% of cases with breast cancer and 86% of controls have ever breastfed, and 29.5% of cases and 14% of controls had never breastfed).

It means in comparison of case and control groups breast cancer patients had less breast feeding time and less breast fed to their children [Fig 2] [12, 20].
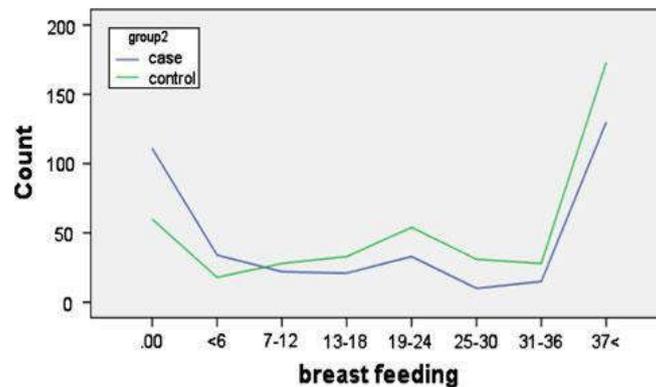


**Fig.2:**Trend of breastfeeding in the case and control group(12)

According to WHO report: Breast feeding, moderate or vigorous physical activity and maintaining a healthy body weight are all associated with a lower risk of breast cancer [3].

Tobacco consumption and fatty diet and being overweight, increased the risk of breast cancer (p = 0.02 and 0.04, respectively). Increased body mass index as risk factor was calculated in one study and show significant difference: Mean BMI (SD) in cases was 27.9 (3.9) and in control group was 26.3 (4.3) (p=0.004) [17].

Use of hormones (estrogen, progesterone) as contraceptive did not increase the risk of disease [12, 17, 19, 20].

Positive family history for breast cancer was 22.8% in cases and 16.9% in the community portion of controls, which shows that it is significant difference in cases and the community portion of controls [12, 19, 20].

**Pathologic feature**

Statistical analysis of 5 studies show: Invasive ductal carcinoma with 89.5-93% is the most frequent cancer and invasive lobular carcinoma as second one is 2.8-5.9%. Frequency of In-situ carcinoma is 1.2-3.2% and other types of cancer are less than 7%. Table 7 shows these percentages [9, 11, 14, 21, 22].

Table 7 : The analysis of data pool of 2224 cases of Cancer Research Center

| PATHOLOGY | PERCENT |
|---|---|
| **DCIS** | 4.0 |
| **IDC** | 79.3 |
| **IDC+DCIS** | 1 |
| **ILC** | 9.1 |
| **MIXED IDC+ILC** | 2.9 |
| **IDC+PAGET** | 0.4 |
| **PAGET** | 0.3 |
| **OTHER** | 0.4 |

**Clinical staging**

The clinical stages of the tumor, in a 20-years period study from 1985 to 2005, shows that the situation has improved in that the tumor has been down staged both in tumor size and number of lymph nodes positive [14]. The published data (table 7) show that, in a ten year study (1985-1995) early stage cancer

was 30%. In the 2001-2005 it was improved to 65% [9]. Several studies have been conducted from 2006-2011, in Iran, on breast cancers. These studies included more than 1606 patients in which 65.5% with early breast cancer and 34.5% with advanced cancer [22, 23]. The information from data pool of Cancer Research Center which include 1812 cases, early breast cancer is 70.5% and advanced cancer is 29.5% from 2007-2013 .

Comparing the 2001-2005 report with 65.5% early stage cancer finding , not much change have been observed in 2005-2011. One would expect much more improvement in the staging since medical practice has improved in the past decade. This should be good sign for implementation of health responsibility system in Iran [7, 10, 13, 14, 2-24]

**Table 8:** Clinical Staging of breast cancer in Iran in 5 published articles & data pool of CRC during 1985-2013

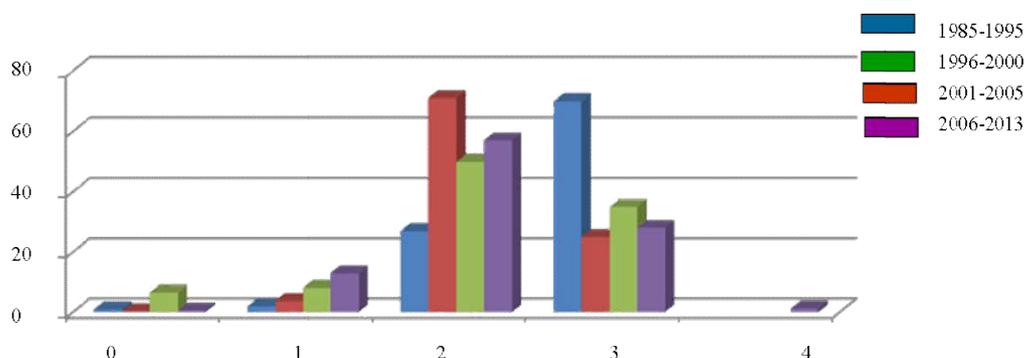| Stage | 1985-1995 N=903 | | 1996 -2000 N=778 | | 2001- 2005 N=1265 | | 2006-2011 N=1250 | | 2007-2013 N=1812 | |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 9 | 1% | 2 | 0.4% | 43 | 6.6% | 17 | 1.36% | 10 | 0.6% |
| **1** | 18 | 2% | 21 | 3.8% | 53 | 8.2% | 194 | 15.52% | 234 | 12.8% |
| **2** | 244 | 27% | 392 | 71.1% | 326 | 50.2% | 634 | 50.74% | 1034 | 57.1% |
| **3** | 632 | 69.6% | 136 | 24.7% | 220 | 35% | 309 | 24.72% | 511 | 28.2% |
| **4** | - | - | - | - | - | - | 54 | 4.34% | 23 | 1.26% |



**Figure 3:** Trend clinical stage of diagnosed breast cancer from 1985 to 2013

There were no significant difference in proportion of patients diagnosed in stage 0 and 1 between the first and last time periods from 1985-1995 and 2007-2013 (p=0.24 &0.1), respectively but the proportion of patients in stages 2 & 3 were different significantly (p<0.001 &<0.001) so the patients were diagnosed in earlier stages in the recent years (Tab 8 & Fig 3).

According to our result from data pool of CRC 70.5% of breast cancers were diagnosed in early stages and 29.5% were diagnosed in late stages.

In study from north east of Iran with 797 patients, 48.4% are early breast cancer and 51.6% are advanced breast cancer, and it is similar to our last result that early cancer was %54.5 and advanced cancer was %45.5 in CRC [10].

According to the frequency of advanced stage in Iran it seems health system notification for increasing early detection program has to improve.

**Biologic markers**:

In addition to some clinic-pathologic characteristics such as tumor size, grade, histological feature and lymph node status in breast cancer prognosis, some of biological Biomarkers provide information on disease outcome.

Pathological and biomarker features of breast cancer such as steroids receptors, C-erb (HER2) may play a key role in evaluating the clinical course, prognosis and planning the type of treatment.

Because of the key role of biomarkers in correct management of disease, the importance of further investigations and standard evaluation of biomarkers has to be focused on, in different regions of the country.

Hereby is a brief introduction to biomarkers in Iranian patients:

According to studies in the last 10 years, Estrogen, Progesterone receptor and p53 are available and C-erb oncogene for last 5 years is available in patient's data. Only Estrogen receptor is related to age, meaning that in old patients the degree of ER positivity is increased. This is one of the reasons for better

prognosis with increase age [18, 22, 25].

There is no significant relation between tumor size and biologic markers in studies, only PR negativity has showed to be related to more positive lymph nodes. Positive P53 is associated with more metastasis in one study, without any relation with steroid receptors. In this study overall survival and disease- free survival had significant difference in metastatic patients with P53 positive and P53 negative groups [18, 25]. Two studies in 2005 and 2009 showed no relationship between Biomarkers and tumor recurrence has been observed [22, 25]. But in a study that was done by Akbari and colleagues, it has been shown that in the absence of ER and having Lymphovascular invasion, probability of tumor recurrence is increased, but not other receptors are associated with the recurrence. It means ER negativity along with the other proliferative indexes can increase the risk of recurrence [24].

The following table 9 shows the amount of positive receptors in five different studies that have been reported ,as it is evident ,there is a huge difference in HER2 reports of 14% to71%, which seems to be difference because of how it is measured and what's the quality of test.

**Table 9 :** Percentage of positive biomarkers in 5 published articles& data pool of Cancer research center.

| Biomarker | Range | Percent in 1788 case of CRC |
|---|---|---|
| ER | 45.5-67% | 72.2% |
| PR | 43 -65.5% | 65% |
| P53 | 18.7-35% | 36% |
| HER2 | 14 - 71. 5% | 24.3% |

In the established study of cancer Research Center, this figure was %20.5 for HER2 positivity which was roughly based on global statistics and it doesn't have any significant difference with new data pool analysis of CRC.(11, 13,HYPERLINK  \l "page14"  20). Because of the difference of laboratory set up for assessing Her2 positivity, we checked out the same result at least in two separate laboratories by FISH test for validation of HER2 result ,in this study 30% of results were not comparable to FISH test.

This is important because specific treatment for patients with HER2 –positive is needed.

It seems that national policy should be designed to homogenize the laboratories to evaluate the HER2 receptor, in order to unify the results that are to be obtained in future studies.

**Recurrence and Survival**

Early stage breast cancer had operation at first and locally advanced cancer had neoadjuvent chemotherapy then surgery, for first group all cases who were less than 70 years with tumor size more than one centimeter or lymph node positive take adjuvant chemotherapy and all cases with hormone receptor positive take hormone therapy, regarding to surgical type, all cases of lymph node positive take radiotherapy. In a study on overall survival, Disease free survival and recurrence only two factors correlated with recurrence: absence of two steroid receptor and lymphovascular invasion, tumor size and lymph node involvement were not affecting the recurrence rates [24].

This means that not only the early detection (no lymph node involvement) and small size of tumor is important in patients with breast cancer but also the type of bio-marker being involved should be considered when survival is investigated.

5 years overall survival rate isn't related to type of surgery [10, 24]. It is estimated %72 in women and %60 in men. It means survival rates in men is less than global [11].
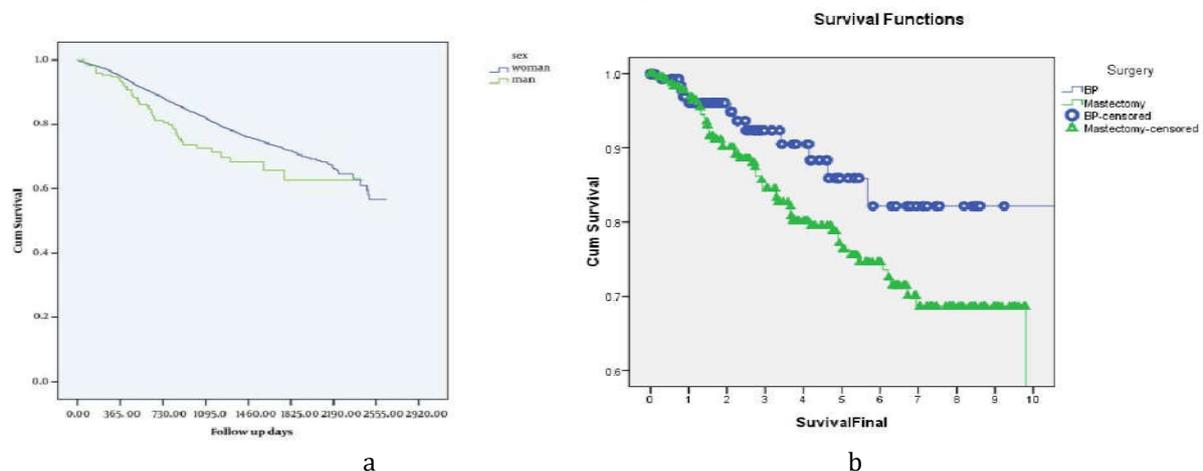


a                                          b

**Figure 4:** Survival curve according to a) gender, b) type of surgery

Overall survival is significant different by stages, also it has significant relation with number of positive lymph nodes (Fig 5).
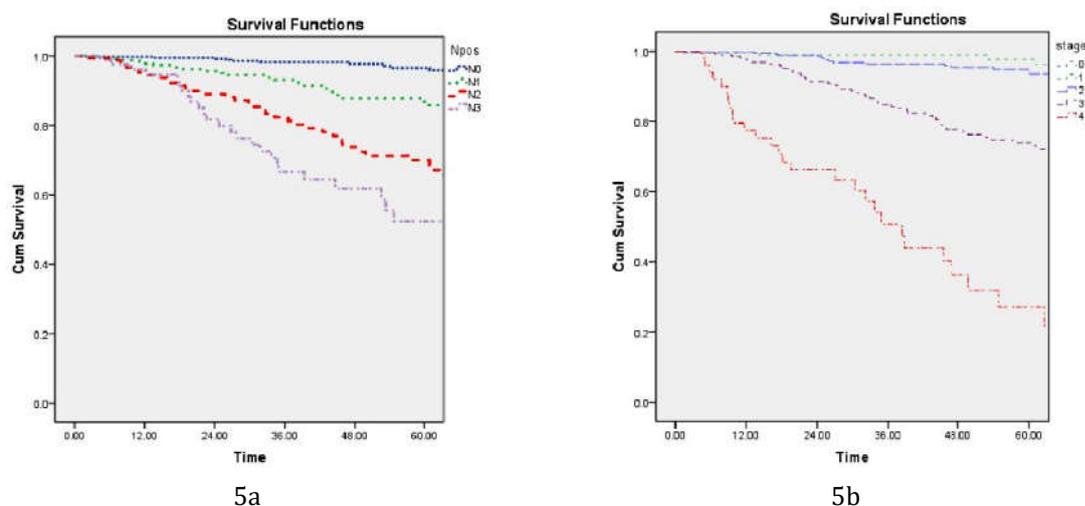


5a        5b

**Figure 5:** Survival according to number of a) positive nodes b) stages; data pool of CRC

5-year survival rate of 81-88% and ten-year survival rates 77-81%have been reported. A National study conducted in 2010 in over 6147 patients has reported 5-year survival rate of 71% (fig 6) [7, 20].
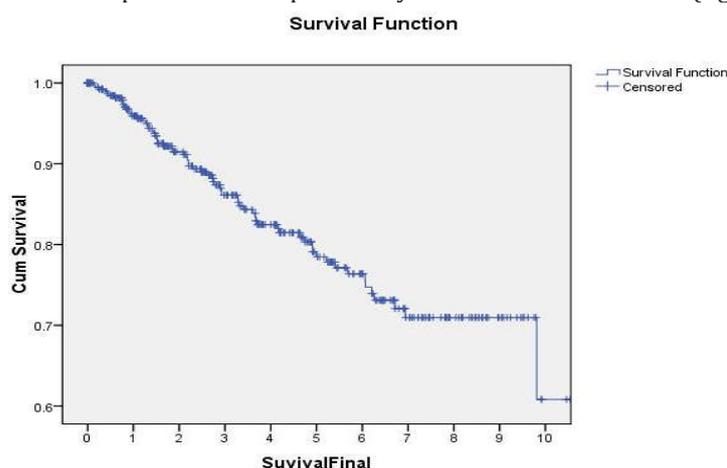


**Figure 6:** Overall Survival for Breast Cancer Patients (national data)

According the standardized mortality ratio (SMR), the mortality of 5-years period was 6/74, 10 years period was 6/55 and 15 years period was 1/26.Total mortality in a population of Iranian women of all ages, is %0.13-1.9. The 15 years period SMR is similar in breast cancer patients and normal population [7].

Due to the effectiveness of socio-economic and cultural issues on survival, a dramatic difference was found in term of the geographical distribution of cancer: The lowest survival rate was in the North West and the highest survival rate was in the northern part of the South West of the country. This study showed that high family income, smoking, tumor size and grade, and number of involved nodes were significantly related to survival rate (Tab 10) [11].

**Table 10:** Survival Rate of Breast Cancer by Place of Residence

| Place of | No. (%) | | One year | Two year | Three year | Four year | Five year |
|---|---|---|---|---|---|---|---|
| residence (Region) | | | Survival (%) | Survival (%) | Survival (%) | Survival (%) | Survival |
| | | | ± SE | ± SE | ± SE | ± SE | (%) ± SE |
| West South (Upper part) | 728 | (11.8%) | 94.4 ± 0.009 | 87.5± 0.013 | 82.9± 0.016 | 78.3 ±0.021 | 76.2 ± 0 .025 |
| Central (North part) | 625 | (10.2%) | 95.2 ± 0.005 | 88.5± 0.007 | 82.8± 0.009 | 77.9 ±0.012 | 75.3 ±0.015 |
| Central (Center part) | 359 | (5.8%) | 94.8 ± 0.007 | 88.3 ± 0.01 | 82.7± 0.013 | 76.4 ±0.016 | 73.3 ±0.018 |

| Region | Count | % | | | | | |
|---|---|---|---|---|---|---|---|
| Middle West | 437 | (7.1%) | 91.9 ± 0.014 | 86.5±0 .018 | 76.3± 0.026 | 73.6 ±0.029 | 69.6± 0.036 |
| North | 294 | (4.8%) | 96.3 ± 0.007 | 88.1± 0.012 | 80.6± 0.017 | 75.7 ±0.021 | 69.3± 0.028 |
| South West (Lower part) | 1974 | (32.1%) | 95.2 ± 0.01 | 88.2± 0.016 | 82.8 ± 0.02 | 76.1 ±0.025 | 68.9 ±0.032 |
| Central (South part) | 221 | (3.6%) | 96.4± 0.013 | 90.9± 0.016 | 81.9± 0.029 | 74.1 ± 0.040 | 67.4 ±0.052 |
| East | 430 | (7.0%) | 95.3 ± 0.01 | 87.6 ± 0.016 | 80.4 ± 0.021 | 72 ± 0.032 | 65.7 ±0.046 |
| North West | 1078 | (17.6%) | 92.5 ± 0.015 | 84.2 ± 0.02 | 76.0 ± 0.028 | 65.5 ± 0.038 | 62.1 ± 0.043 |

High survival rate in the upper part of South West may be due to a screening program which was initiated in 1994. This led to a downstage for breast cancer. It is noteworthy that this region has the highest income.

This study also showed that Northwest with minimum survival rate is ranking as third in economy and income of community in the country [11]. But this study didn't want to show that monthly income can change the survival rate alone because a lot of other risk factors are related to this difference .

Moreover, North West with the lowest survival rate had the lowest mean age of patients at diagnosis and the highest prevalence of invasive ductal carcinoma. This decline in younger age is associated with decreased survival rate and has been demonstrated in many studies.

Comparing the mean age of patients, pathology type, literacy and employment there were no statistically significant difference between areas with maximum and minimum survival rates [11].

**CONCLUSION**
In light of breast cancer being the most prevalent cancer in female Iranian, critical investigation on its prevalence seemed necessary. Our study shows that cancer prevalence is multi-dimension and needs multi-center involvement including the governmental authorities, clinicians, scientist, etc.

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Not declared

**REFERENCES**
1. GLOBOCAN (2012). Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx.
2. Ferlay J, Shin H, Bray F, Forman D, Mathers C, Parkin D. GLOBOCAN (2008). Cancer incidence and mortality worldwide: IARC CancerBase No. 10. Lyon, France: International Agency for Research on Cancer.29-34
3. Melissa Center, Rebecca S, Ahmedin J. (2011). Global Cancer Facts & Figures. Atlanta, Georgia: American Cancer Society.
4. Kelsey JL, Bernstein L. (1996). Epidemiology and prevention of breast cancer. Annual review of public health.17(1):47-67.
5. Ferlay J, Forman D, Mathers C, Bray F. (2010). Breast and cervical cancer in 187 countries between 1980 and 2010. The Lancet. 379(9824):1390-1.
6. http://www.cancer.org/cancer/breastcancer/overviewguide/breast-cancer-overview-key-statistics.Last Revised: 01/31/2014.
7. Haghighat S, Akbari M, Ghaffari S, Yavari P. (2012). Standardized breast cancer mortality rate compared to the general female population of Iran. Asian Pacific Journal of Cancer Prevention. 13(11):5525-8.
8. Forouzanfar MH, Foreman KJ, Delossantos AM, Lozano R, Lopez AD, Murray CJ, et al. (2011). Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. The Lancet. 378 (9801):1461-84.
9. Montazeri A, Vahdaninia M, Harirchi I, Harirchi AM, Sajadian A, Khaleghi F, et al. (2008). Breast cancer in Iran: need for greater women awareness of warning signs and effective screening methods. Asia Pac Fam Med. 7(1):6.
10. Akbari M, Khayamzadeh M, Khoshnevis S, Nafisi N, Akbari A. (2012). Five and ten years survival in breast cancer patients mastectomies vs. breast conserving surgeries personal experience. Iranian Journal of Cancer Prevention. 1(2):53-6.
11. Movahedi M, Haghighat S, Khayamzadeh M, Moradi A, Ghanbari-Motlagh A, Mirzaei H, *et al.* (2012). Survival Rate of Breast Cancer Based on Geographical Variation in Iran, a National Study. Iranian Red Crescent Medical Journal. 14 (12):798.
12. Akbari A, Razzaghi Z, Homaee F, Khayamzadeh M, Movahedi M, Akbari ME. (2011). Parity and breastfeeding are preventive measures against breast cancer in Iranian women. Breast Cancer. 18(1):51-5.
13. Khadivi R, Harrirchi I, Akbari M. (2012). Ten year breast cancer screening and follow up in 52200 women in Shahre-Kord, Iran (1997-2006). Iranian Journal of Cancer Prevention. 1(2):73-7.
14. Harirchi I, Kolahdoozan S, Karbakhsh M, Chegini N, Mohseni S, Montazeri A, *et al.*(2011). Twenty years of breast cancer in Iran: down staging without a formal screening program. Annals of oncology. 22(1):93-7.

15. Ghavamnasiri M, Shahidsales S, Ahmadi Simab S. (2013). The importance of Prognostic factors (ER, PR, P53) in breast cancer. 6th BCRC Breast Cancer Congress- Abstract Book; Tehran, Iran.
16. Rezaianzadeh A, Heydari S, Hosseini H, Haghdoost A, Barooti E, Lankarani K. (2011). Prevalence of breast cancer in a defined population of iran. Iranian Red Crescent Medical Journal.13(9):647.
17. Montazeri A, Sadighi J, Farzadi F, Maftoon F, Vahdaninia M, Ansari M, *et al*.(2008). Weight, height, body mass index and risk of breast cancer in postmenopausal women: a case-control study. BMC cancer.  8(1):278.
18. Sirati F, Ghahari A. (2007). Detection of Prognostic factors in breast cancer and their relation with menopause and age. Iranian Journal of Surgery.15 (3).38-45.
19. Lotfi M, Shobairi SCS. (2008). Breast cancer risk factors in an urban area of Yazd city-Iran 2006. Acta Medica Iranica. 46(3).
20. Zare N, Haem E, Lankarani KB, Heydari ST, Barooti E. (2013). Breast cancer risk factors in a defined population: weighted logistic regression approach for rare events. Journal of breast cancer. ;16(2):214-9.
21. Akbari M, Mirzaei H, Soori H. (2006). 5 year survival of breast cancer in Shohada-e-Tajrish and Jorjani hospitals. Hakim. 9(2):39-44.
22. Moradi-Marjaneh M, Homaei-Shandiz F, Shamsian SAA, Eftekhar-ZadehMashhadin I , Hedayati-Moghadam MR. (2008). Correlation of HER2/neu Over Expression, p53 Protein Accumulation and Steroid Receptor Status with Tumor Characteristics: An Iranian Study of Breast Cancer Patients. Iranian J Publ Health,;37(3):19-28.
23. Harirchi I, Karbakhsh M, Kashefi A, Momtahen AJ. (2004). Breast cancer in Iran: results of a multi-center study. Asian pacific journal of cancer prevention.;5(1):24-7.
24. Akbari ME, Mozaffar M, Heidari A, Zirakzadeh H, Akbari A, Akbari M, et al. (2011). Recurrence and Survival Effect in Breast Conserving Surgery: What are the Predictive and/or Prognostic Factors? Iranian Journal of Cancer Prevention. 4(2):49-54.
25. Hashemi E, Montazeri A, Akbari ME, Najafi M, Haghighat S, A. K. (2006). Role of Tumor Markers in Breast Cancer Recurrence. Journal of Guilan University of Medical Sciences. 15 (57) :28-32