

## Original paper

# How the Prevalence of Breast Carcinoma in Women Changed over 2009-2017, It's Stage and Grade in Young Females in Iraqi City, Kerbala

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## Abstract

**Background:** Breast cancer is the most common malignancy in females in general and it constitutes about one fourth of cancer cases in Iraq.

**Aim:** the goal of this study is to follow the trends in breast cancer prevalence over the last nine years in Kerbala, to make a focus on the percentage of cases that occur in young and its characters.

**Materials and methods:** The prevalence of breast cancer among general population and young females ( $\leq 40$ ) over 2009-2017 was interpreted using descriptive statistics while staging and grading characters and their relation to the age was analyzed using Chi square program and p value.

**Results:** annual increase in the number of cases was found over 2009-2017 with highest prevalence in 2016 (91 case). The mean for age was 50.7 and SD of 13.7. There was no significant difference in the percentage of young female carcinoma cases over the years (24%). Both grade III and stage III present at higher percentage in young female than old (23% vs. 5.9% for grade III and 50% vs. 30.5 for stage III), the results were near but did not reach the significant level statistically (p value 0.06, 0.07 respectively).

**Conclusion:** the prevalence of breast carcinoma is increasing in Kerbala over the` years 2009-2017 with higher percentage is noted in young females than other developed countries and breast cancer in young female present at somewhat higher grade and stage.

**Keywords:** breast carcinoma, prevalence, young women, stage and grade.

## Introduction

Breast cancer is the most common malignancy in females worldwide. It constitutes about one fourth of the registered cancer cases among the Iraqi population<sup>(1)</sup> and it is an important leading cause of death among Iraqi women<sup>(2)</sup>. The overall incidence of breast cancer worldwide has been doubled between 1975 and 2000<sup>(3)</sup>. This thought to be related to increase in life expectancy in some countries and to change in lifestyle in others<sup>(3)</sup>. Incidence of breast cancer was estimated to be 6.6 - 7% in women below the age of 40 years in many studies<sup>(4,5)</sup>, however incidence of breast cancer in young women showed little variation among different countries, which can be

attributed to the differences in risk factors in different countries<sup>(6)</sup>. In Iraq, It has a tendency to affect middle aged women in whom it is usually diagnosed in advanced stages with a likely prevalence of aggressive behavior yielding high mortality incidence ratio<sup>(7,8)</sup>. The definition of a 'young woman' in the context of breast oncology varies, with most articles referring to women under age 35 or 40 years as 'young'<sup>(9)</sup>. Although uncommon, breast cancer in young women need a special attention to the specific challenges associated with it such as preservation of fertility, bone health, and psychosocial impact<sup>(9)</sup>. In addition, breast carcinoma in young females usually present in later stages, high grade, hormone receptor negativity, and with high proliferation rate.

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This necessitate more aggressive treatment, careful monitoring and follow up<sup>(10)</sup>.

The differences in breast cancer between young and old age group regarding risk factors, tumor characteristics, behavior and clinical outcome suggest that breast cancer in young women may be a unique entity.<sup>(11)</sup> About one-third of breast carcinoma in *TP53* mutation positive cases occur prior to age 30 years<sup>(12)</sup>.

The incidence rate for all breast cancer for all age group in Iraq was increased from 26.6 per 100.000 in 2000 to 31.5 per 100.000 in 2009<sup>(13)</sup>. This increase in breast cancer prevalence specifically and cancer in general may necessity a search for the changes in environment regarding pollutions and carcinogenic chemicals increase that occur after a series of war our country pass through. Animal studies showed a link between industrial chemical exposure and mammary cancer<sup>(14)</sup>.

Late onset childbirth (first child after age 30 years) is suggested to be a risk factor for breast cancer in women older than 35. On the other hand, early childbearing could be a risk factor for breast cancer before the age of 35<sup>(15)</sup>. This discrepancy could possibly be explained by the transient increase in breast cancer risk that occurs around 2 to 7 years following a pregnancy, but more information is needed about this association<sup>(15)</sup>. Others well known risk factors are family history (there is 3-4 times increase risk if the first degree relative had a breast cancer), early menarche and late menopause, exogenous estrogen and contraceptive agents, and fibrocystic disease<sup>(16)</sup>.

## Materials and Methods

The data for this study had been collected from histopathology lab unit in Al- Hussein Teaching Hospital in Iraqi city (Kerbala) over the period from 2009 through 2017. The reason to choose this period is that there was no computerized data in the hospital before 2009. The total number of collected cases was 395. The hematoxyline

& eosin stained histopathological sections had been reviewed by microscopical examination for diagnosis of breast carcinoma, grade and stage (when present). All cases of breast carcinoma had been taken regardless the type of the biopsy (core biopsy, excisional biopsy and mastectomy) and for all ages. The number of breast carcinoma cases was calculated for every year and for all age groups then the percentage of breast carcinoma in young women ( $\leq 40$  year old) was calculated for every year using descriptive statistics. Nottingham modification of Bloom Richardson system was used for grading (considering tubule formation, atypia and mitotic activity) and American joint committee on cancer system which depend TNM staging system (T tumor size, N number of involved lymph nodes, M metastasis) for staging. For grading and staging the data had been grouped into two groups (young women ( $\leq 40$  years) and old women ( $> 40$  years). The data had been analyzed by Chi square and p value was calculated.

## Results

The trends in breast carcinoma prevalence over 2009-2017 was as follow( 16 cases in 2009, 16 cases in 2010, 21 case in 2011, 36 case in 2012, 34 case in 2013, 57 case in 2014, 54 case in 2015, 91 case in 2016, and 70 case in 2017) . As shown in table (1) and Fig (1) there is parallel increase in the prevalence of breast carcinoma over the studied years (2009- 2017), when all the patients are considered regardless of the age, with the highest incidence was reported in 2016. There was approximation in number of every 2 succeeding years and the mean age was 50.7 with SD of 13.7. While the prevalence of breast carcinoma in young female (equal or less than 40 years) over 2009- 2017 show similar progressive increase in the number, there was no significant difference over the studied years, with highest percentage was reported in 2010 and lowest percentage in

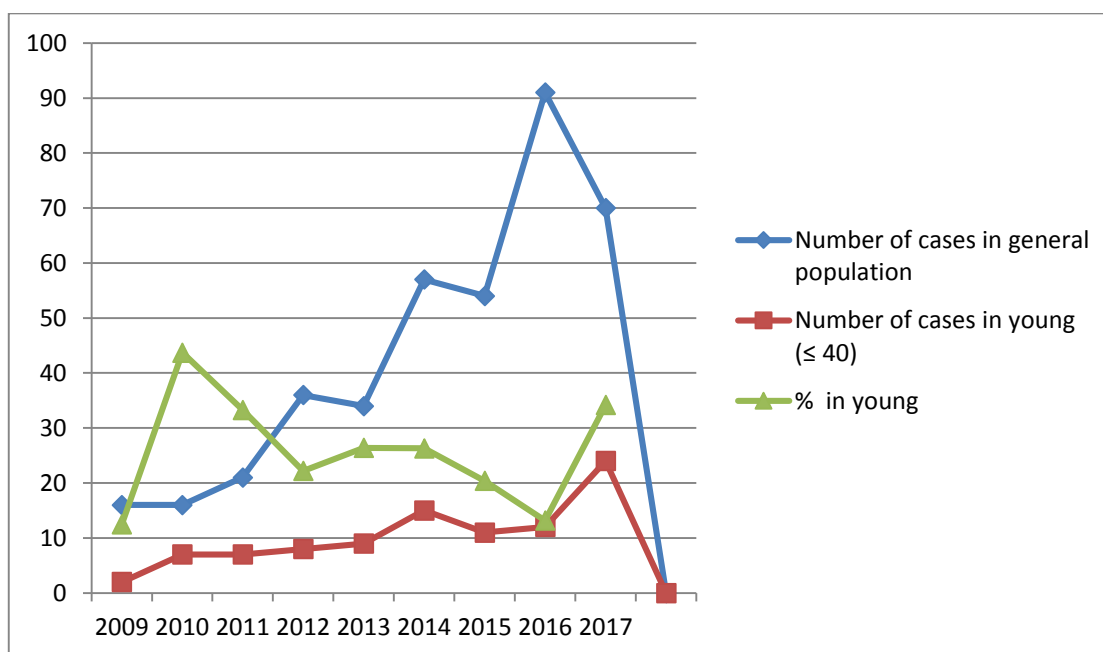
2009 otherwise there was fluctuation in the percentage among the studied years. The total number of cases in nine years was 395 and young female cases represent 24% of them (95 case).

Regarding grading, 135 case had been graded in women over 40 years with 3 cases was grade I, 114 case grade II, and 18 case for grade III. Results showed that grade II account for 92.5 % of cases in old women while grade III account for 5.9%. In young women ( $\leq 40$ ), 65 cases had been graded and grade II account for 76% while grade III was 23% of the cases and grade I 0% (Fig 2). There was a noticed increase in the percentage of grade III cases from 5.9% in old women to 23% in young, however this

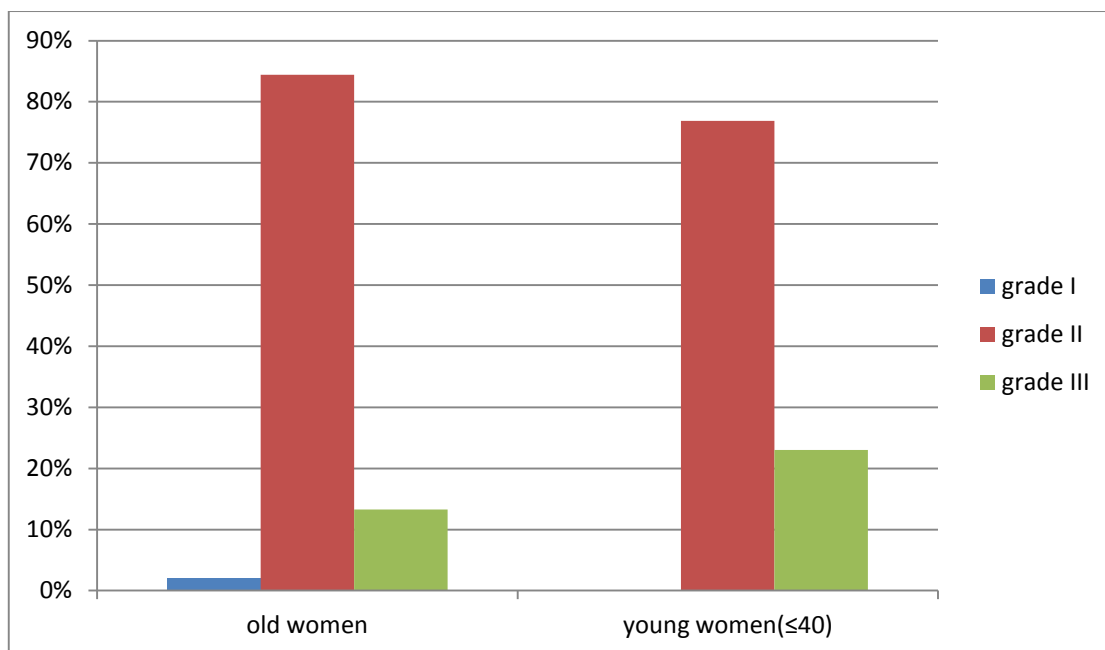
increase does not reach a statistically significant difference with a p value (0.06). Regarding staging, 72 cases had been staged in old women ( $>40$  years) with stage I account for 11.11% (8 cases), stage II 58.33% (42 case), and stage III 30.5 % (22 case), as illustrated in Fig (3). Stage II made the highest percentage in old women. In young women 40 cases had been staged and stage I cases form 10% (4 cases), stage II cases 40% (16 case), and stage III 50% (20 case). These data showed that stage III cases account for the highest percentage in young women ( $\leq 40$ ). As for grade, there is an increase in the stage III cases from 30.5 % in old women to 50% in young but this increase was near but yet insignificant with a p value of (0.07) .

**Table 1.** Prevalence of female breast carcinoma over 2009-2017 in Kerbala

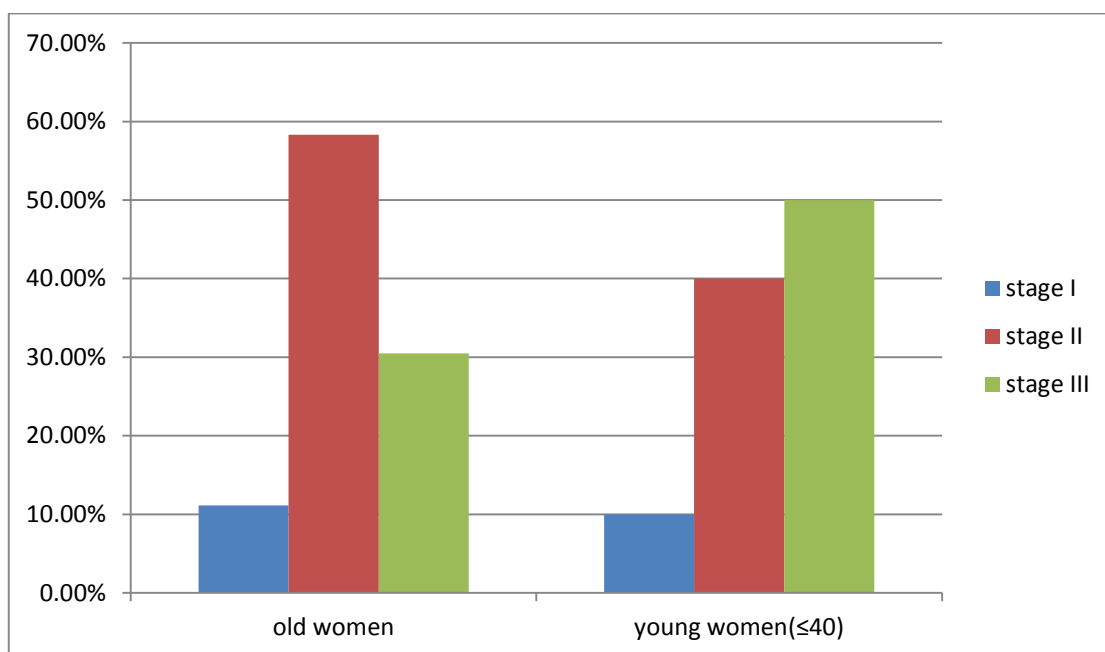
| year  | frequency of cases in general population | frequency of cases in young ( $\leq 40$ ) |
|-------|--|---|
| 2009  | 16                                       | 2 (12.5%)                                 |
| 2010  | 16                                       | 7 (43.7 %)                                |
| 2011  | 21                                       | 7 (33.3%)                                 |
| 2012  | 36                                       | 8 (22.2 %)                                |
| 2013  | 34                                       | 9 (26.4 %)                                |
| 2014  | 57                                       | 15 (26.3 %)                               |
| 2015  | 54                                       | 11 (20.4 %)                               |
| 2016  | 91                                       | 12 (13.18%)                               |
| 2017  | 70                                       | 24 (34.2%)                                |
| total | 395                                      | 95 (24%)                                  |



**Figure 1.** Prevalence and of female breast carcinoma over (2009-2017) in Kerbala



**Figure 2.** Grading of breast carcinoma among women in kerbala over the period (2009-2017).



**Figure 3.** distribution of breast carcinoma stages among women in Kerbala over (2009-2017).

### Discussion

The study showed progressive increase in the incidence of breast carcinoma among women in Iraqi city/ Kerbala, regardless of the age, over the period 2009-2017 with highest prevalence was documented in 2016. This increase may be related to the

series of wars that happen in Iraq in the last two decades in addition to large number of chemical pollutants in the environment<sup>(17)</sup>, as cancer and birth defects are the most common adverse outcome of these conflicts, according to the accumulative low dose carcinogenic effect hypothesis.<sup>(18)</sup> A similar marked increase in the annual

number of breast cancer among Iraqi women between 2000 and 2009 had been reported by (Muzahem MY Al-Hashimi and XiangJun Wang)<sup>(13)</sup>, as they related this increase to the improved awareness in connection with the Iraqi National Breast Cancer Research Program that began in 2000, better data collection by Iraqi national cancer research center, opening of new breast cancer screening mammograms from 2000 onward.

Low-dose exposures have previously been defined by the National Toxicology Program (NTP) as those occurring within the range of typical human exposures (Melnick et al. 2002)<sup>(19)</sup>. The results of the Halifax Project (Goodson et al. 2015) suggest that exposure to chemicals that are seemingly non carcinogenic individually may have combined effects that will result in cancer as a disease end point<sup>(20)</sup>. The low-dose mixture hypothesis of carcinogenesis was established using the hallmarks of cancer outlined by Hanahan and Weinberg (2011) as an organizing framework. The incidence of cancers tend to rise following migration from low to high incidence countries, especially if it occurs early in life<sup>(21)</sup>.

The results show no significant difference in prevalence of breast carcinoma in young women in Kerbala and the proportion was fluctuating among years, these results are supported by (Narods SA), in his study trends are not seen in early onset breast cancer, as the rates have been more or less stable in most countries in the past 20 years<sup>(22)</sup>. (Runnak A. Majid et al) found that the modest increase in age standardized incidence of breast cancer in Iraq is being seen specifically in older women and may be better attributed to a trend for care in urban cancer centers rather than changing tumor characteristics<sup>(23)</sup>.

The overall percentage of breast carcinoma over the nine years that involved in the study was 24%. This result is higher than those reported in the developed countries<sup>(4)</sup>. Although grade II represent the most common grade in women under 40 year in

our study, the occurrence of grade III was much higher in young than in old women (23% vs 5.9 %). It might be hypothesized that germ-line mutations could partially explain the more aggressive breast cancer in young patients<sup>(24)</sup>. Women diagnosed with breast cancer at the age of <35 years are likely to have germ-line BRCA1 or BRCA2 mutations in up to 15–30% of cases<sup>(25,26)</sup>. Runnak A Majid et al found that Luminal B/HER2+ tumors (ER +ve and/or PR +ve, HER2+ grade 3 tumors) had a significantly earlier peak than luminal A tumors (ER and PR +ve, HER2 –ve, grade 1 or 2 tumors)<sup>(23)</sup>. Despite the fact that high grade is a controversial prognostic factor for invasive breast carcinoma<sup>(27,28)</sup>, it is usually used in the decision for offering adjuvant treatments, and its role in this context was recently specified<sup>(29)</sup>.

In our study, stage III represent the peak in breast cancer staging in young (50% in young vs. 30.5% in old) so breast carcinoma in young present at an advanced stage, either because of its biological aggressive subtype or because of a low index of suspicion and delayed diagnosis<sup>(6)</sup>. A study of 732 non-metastatic breast cancer patients performed at Mount Sinai Medical Center, New York showed that women younger than 36 years had larger tumors (median 2.0 vs. 1.5 cm,  $P < 0.001$ ), more nodal involvement (50% vs. 37%,  $P = 0.022$ ), and were more likely to be present with stage II or III cancer (60% vs. 43%,  $P < 0.001$ ) than patients above 36 years<sup>(30)</sup> while other study performed at the European institute of oncology on the characteristics of stage at presentation for 'very young' patients as opposed to the 'less young' group found that no statistically significant difference was observed for stage of disease at diagnosis [according to the TNM (tumour–node–metastasis), for pathological tumor size and for the number of nodes involved<sup>(31)</sup>].

## Conclusion

There is an increase in the prevalence of female breast carcinoma in Kerbala over the last decade and this result may reflect an increase in the breast cancer in the region in general. The percentage of young women with breast carcinoma was higher than those reported in the western countries. Breast carcinoma in young women is more likely to be present with high grade and stage than old women but the difference still not reach statistical significance in Kerbala.

## Recommendation

We recommend more studies about the causes of breast cancer dissemination in the population and to start screening program for breast cancer at an earlier age (<40 year). Specific attention and study should be given to environmental and chemical carcinogens.

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