

Breast Cancer in Iraq: A Review

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Abstract:

Globally, breast cancer is the most common cancer among women, comprising 23% of the 1.1 million female cancers that are newly diagnosed each year. In Iraq, breast cancer is the commonest type of female malignancy, accounting for approximately one-third of the registered female cancers according to the latest Iraqi Cancer Registry [4]. This shows that the breast is the leading cancer site among the Iraqi population in general, surpassing even bronchogenic cancer. As proposed by the World Health Organization, early detection and screening, especially when combined with adequate therapy, offers the most immediate hope for a reduction in breast cancer mortality. The incidence of breast cancer increased in Iraq in recent years, indicating a significant health problem. Actions are needed on the national level for better estimate of the problem.

Introduction

Globally, breast cancer is the most common cancer among women, comprising 23% of the 1.1 million female cancers that are newly diagnosed each year [1, 2]. It is also the leading cause of cancer-related deaths worldwide; case fatality rates being highest in low resource countries [3]. Approximately 4.4 million women diagnosed with breast cancer in the last 5 years are still alive, making breast cancer the most prevalent cancer worldwide [1].

In Iraq, breast cancer is the commonest type of female malignancy, accounting for approximately one-third of the registered female cancers according to the latest Iraqi Cancer Registry [4]. This shows that the breast is the leading cancer site among the Iraqi population in general, surpassing even bronchogenic cancer. As proposed by the World Health Organization, early detection and screening, especially when combined with adequate therapy, offers the most immediate hope for a reduction in breast cancer mortality [5]. This was the basis of the Iraqi national program for early detection of breast cancer, which was initiated in 2001, in an attempt to down-stage this disease at the time of presentation. Since then, specialized centers and clinics for early detection of breast tumors have been established in the major hospitals in all Iraqi provinces [6].

Recently, different biomarkers were evaluated for their association with breast cancer. The mean serum and positivity frequencies of CMV IgG, EBV VCA IgG, EBV EBNA-1 IgG and heterophile antibodies were significantly higher in women with breast cancer as compared to controls. Odd ratio and area under ROC curve confirmed an association between breast cancer and CMV and EBV infections. CMV detected in 20% of breast cancer tissue, while EBV detected in 26.7%. Thus, CMV and EBV infection may play a role in development and prognosis of breast cancer [7]. Breast cancer continues to rise in Iraq, and scientists have established the Iraqi National Cancer Research Program to better understand the underlying molecular and environmental causes in an effort to curb the incidence of cancer. "Breast cancer is the most common type of malignancy recorded in the cancer registries of almost all countries within the Eastern Mediterranean Region. In Iraq, the continuous rise in the incidence rate is

associated with an obvious trend to affect premenopausal women [6]. A "project includes within its objectives comprehensive epidemiologic studies on risk factors of the main encountered cancers in Iraq, with a focus on the characteristics and behaviors of cancer in patients inhabiting different geographic areas," Despite these facts, regarding breast cancer, there is no comprehensive collaborative study that encompasses national registrations of breast cancer in all Iraqi governorates, to give a more illustrative and representative overview about the problem. And, the real magnitude of this disease problem is not yet fully evaluated and reported in Iraq. Moreover, most of the studies carried out in various parts of Iraq addressed the histopathological, Immuno-histochemical, and hormonal features of breast cancer rather than the epidemiological and demographical characteristics; this is because of the small number of cases included in these studies, which do not reflect the real size of the problem. The aim of this paper is to shed light on breast cancer in Iraq through reviewing the studies published by various centers in Iraq.

Because of sporadic nature of the studies on breast cancer in Iraq, our approach to give more realistic view of the problem was to divide Iraq into three major geographic zones: north, middle, and south zones. The north zone included reports from Dohuk, Erbil, Kirkuk, and Sulaymanya. The middle zone included; Mosul, Tikrit, Baghdad, Al-Anbar, Babel, Karbala, Al-Najaf, Al-Qadissya, and Wasit. The southern zone included; Maisan, Al-Muthana, ThiQar, and Al Basrah.

The North of Iraq

Studies on patients from the three governorates of the north of Iraq, showed that the average age of breast cancer patients was 47.4 ± 11.0 years with a median age of 46 and the 25th and 75th percentiles being 39 and 55 years old respectively [8]. The proportion of patients reported that they were menstruating at the time of diagnosis and those who were designated as pre-menopausal were 59.5%. There were no significant differences between breast cancer patients and controls in BMI, marital status, and number of pregnancies. The average BMI was in the overweight category, but the median BMI was just above normal weight at 26.7 kg/m^2 and the 25th and 75th percentiles were 24.4 and 30.3 kg/m^2 respectively.

Breast cancer patients ≥ 50 years old had significantly fewer children than the same aged control subjects ($P = 0.001$), and breast cancer patients ≥ 50 years old were more often nulligravida than controls, with this difference tending toward but not being significant. By conditional logistic regression, the independent variables of marital status ($P = 0.76$) and number of children ($P = 0.08$) were not significant predictors of breast cancer, although the number of children approached significance. The regression coefficient suggests a trend for fewer children being related to breast cancer ($r = -0.063$, 95%CI: -0.132 to 0.006) with this effect being seen in subjects ≥ 50 years old ($P = 0.03$, $r = -0.111$, 95%CI: -0.210 to -0.012) but not < 50 years of age ($P = 0.77$, $r = -0.015$, 95%CI: -0.114 to 0.084).

The Kurdish incidence rates for breast cancer exceeded those for Israeli Arab and Jordanian women and were similar to Egyptian women; [7], beginning at age 35-39. Kurdish rates reached a peak of 168.9 per 100,000 at 55-59 and then declined markedly to where they were less than half that for Jordanian, Israeli

Arab, and Egyptian women at age 70-74 and approximately one-third of the rates for those regions at 75 years of age and above.

Breast Cancer in Kurdish women of Sulaymanyia Iraq is currently diagnosed at advanced clinical stages with 60% of patients being under 50 years of age [8]. Until approximately age 45, age specific incidence rates were similar to those of Egypt and the United States and were higher than reported for Israeli Arabs and Jordanians. These findings suggest that breast cancer risk for pre-menopausal Iraqi Kurds may be unusually high for a Middle-Eastern country. The cause of these seemingly higher pre-menopausal breast cancer rates could not be related to parity or to an excessive familial risk. Interventional programs need to be directed toward methods that will reduce clinical stage of disease in younger women, but the best approach to cost effective screening is not readily apparent.

In another study [9] carried on 526 cases of breast cancer, the age range was 20–82 years. The mean age at diagnosis was 49.42 ± 11.66 years compared to control 46.7 ± 10.2 ($p < 0.001$, 95% CI: 1.7–3.7). The age-standardized rate was 17.9/100,000 Kurdish women population/year. Five –year- age-specific rates show the peak incidence for the age group 45–49 years (79.3/100,000). A significant percentage of patients were premenopausal at the time of diagnosis, which is 55.52% of cases compared to control 59.67% ($p = 0.53$). About 13.49% of cases have family history of breast cancer compared to control 3.2% ($p = 0.02$). This study concluded that, among Kurdish women in Iraq, the incidence of breast cancer is less than Middle-East and Western countries, with higher incidence in younger age group than western society, but similar to Middle-East countries. More than half of Kurdish women with breast cancer are premenopausal.

In Kirkuk, [10], 100 patients diagnosed as with breast cancer patients were included in a study. They were recruited from women attending Breast Clinic in Azadi Hospital in Kirkuk during the period from December 2012 till the end of May 2013. All patients were female, their ages ranged from 35-74 years. Apparently healthy 100 women were selected as control group. Serum mean values of prolactin, progesterone receptor, estrogen receptor, glucose, HBA1C, and calcium were significantly higher in women with breast cancer than in controls. While circulating estrogen, progesterone, IGF-1, PTH, and vit D means values were significantly lower in breast cancer than in controls. OR confirm the association between the tested markers and breast cancer. This study indicated a significant association between breast cancer and serum levels of prolactin, progesterone, estrogen, progesterone receptor, estrogen receptor, sugar, HBA1C, insulin growth factor, Ca^{+2} , Vit. D and PTH. However, AUC of ROC indicated the low predictive value of estrogen and progesterone. Additionally [11], serum mean values of CA 15-3, CA 27-29, CEA, BRCA1 and BRCA2 were significantly higher in women with breast cancer than in controls. OR and relative risk confirm the association between serum increase of the five markers to breast cancer. AUC of ROC indicated the high sensitivity of their determination in breast cancer. This data suggest evidence that serum CA15-3, CA27-29 and CEA simultaneous determination are potential markers for early diagnosis of breast cancer metastasis and treatment monitoring.

Recent study in Erbil, Iraq [12] which included a total of 148 breast cancer cases and the analysis of variables performed with stratification of 10 years age interval. Age distribution of breast cancer indicated that 20.3% of cases were with age of ≤ 20 years and 14.9% were with age of 16-18 years. In addition more than half of cases [52.7%] were with age of less than 30 years. Furthermore, 79.7% of breast

cancer cases were in women ≤ 40 years of age. Only 5.4% of cases were with age of > 45 years. Odd ratio confirmed a significant association between age and breast cancer development in their study cohort. The highest frequency was in women with age of 21-30 years, followed by those with age of 31-40 years. Age of women with breast cancer significantly influences the CEA and ER mean serum values whether the analysis performed on group or individual stratification. In addition, P53 mean serum level in women with breast cancer was significantly different when the analysis performed on individual stratification, however, non-significant differences was achieved between age group. The same pattern was demonstrated for CA 27-29 and PR. Thus this study suggested that age at diagnosis was with two decades earlier than that in Western countries.

The middle zone of Iraq

More informative data on incidence and clinic-pathological features of breast cancer in Iraq came from reports on patients from Baghdad [13], Ramadi-Falluja [14], Mosul [15], and middle Euphrates area [16]. AlAlwan [13] report presents a review on the main demographic characteristics and clinico-pathological parameters in Iraqi patients diagnosed with breast cancer. The study was carried out on 721 out of a total of 5044 patients (14.3%) who complained of palpable breast lumps that were diagnosed as cancer. The procedure for tumor nuclear DNA Ploidy assessment was performed by means of Image Cytometry. Immuno-cytochemical and histochemical assays were applied for the determination of Estrogen and Progesterone receptor (ER/PR) contents and Her-2/neu expression of the tumor tissues.

It was found that: "Approximately one third of the breast cancer patients were diagnosed in the age period (40-49 years), 71.9% came from urban areas and 75% were married. History of lactation and hormonal therapy was reported in 63.1% and 29% respectively, while positive family history was recorded in 16.2%. Although the lump was detected by the patient herself in 90.6%, yet only 32% sought medical advice within the first month. Accordingly 47% of these patients presented in advanced stages (III and IV). The main histological type was invasive ductal carcinoma; in which pathological changes of grade II and III were observed in 56.6% and 39.9% respectively. Cytophotometric DNA analysis showed that 80.3% of Iraqi mammary carcinomas were aneuploidy. ER and PR positive tumor contents were demonstrated in 65.1% and 45.1% of the examined specimens respectively while Her-2/neu over expression was displayed in 46.4%" the author concluded that the afore mentioned data justifies increasing efforts for establishing comprehensive breast cancer control programs in our country. And recommended that further interventional research studies using molecular biomarkers should be promoted to address the factors contributing to the illustrated aggressive tumor behavioral form [13]. In another report [14], a descriptive study based on collecting of all cancer cases above 10 years old in Fallujah district of Al-Anbar Governorate during the period between 1st of January 2011-31st of December 2011, new cases of males and females who were diagnosed with any type of cancer excluding leukemia which was referred and treated in different centers outside of Al- Anbar Governorate. Results: The incidence of cancer in Fallujah is 96 per 100,000. The most common cancers in the whole population irrespective of sex were carcinoma of the breast, lung, stomach and colorectal cancers. The most common cancers in females were those

of breast, ovary and uterus, comparative finding in males were lung, stomach and bladder cancers. The incidence of cancer in Fallujah appears to be higher than the other regions in Iraq and other Middle East countries the leading cancers are in Fallujah [14]. The overall pattern of cancer is however similar to the finding in other countries, carcinoma of the breast, lung, stomach and colorectal

In middle Euphrates [15] it was found that despite the three-fold increase of all types of breast cancer in Iraq due to long-term exposure to depleted uranium, this heightened exposure does not appear to be correlated with HER-2/neu over expression. Differences may become evident with time and as mutations are passed to future generations. Further longitudinal studies and the use of techniques such as microarrays are required to investigate whether any effect of depleted uranium does manifest in the pathology of breast cancer.

South zone of Iraq

Reports from south Iraq from Maisan and Basrah. [16, 17], in a study from Maisan [16], south of Iraq, comprised 144 patients were collected by direct interview with breast cancer patients and from the records and registrations of the oncologist and pathologist. Patient's age, sex, social state, proper history of disease and investigations results was recorded. The diagnosis is confirmed by cytology (Fine Needle Aspiration Cytology) and or tissue biopsy inform of core or excisional biopsy. Breast cancer was staged according to the TNM classification (T tumor size, N nodes M metastasis). The TNM classification is based on clinical & histological assessment following definitive surgery. Liver ultra-sound, chest x ray, full blood count and CT scan used in assessment of the staging system. We exclude the patients with incomplete records, registrations and follow up. The results showed that breast cancer is a common problem presenting at middle and old age patients. The majority of our patients in this study were presented at late stage due to lack of proper screening programs and low socio-economic state of the patients, which demand more effort for early detection of breast cancer.

Reports from Basrah, [17] showed that breast cancer is the most frequent cancer in females. Its incidence is higher in developed countries than in developing ones partly due to variation in risk exposure and partly due to better detection methods. Scattered evidence in Basrah, Iraq, suggests that breast cancer has been increasing at a significant pace in recent years. This study aimed to measure the current level of risk of breast cancer among females in Basrah and to describe the time trend over almost a decade of years. Data on breast cancer cases from all sources of cancer registration in Basrah governorate were compiled for the years 2005-2012. The data for each year were first checked separately for duplicate reporting of cases among various sources. Then the eight files were pooled together and checked again for any duplicate cases among years of registration. The final set of data contained 2,284 cases of breast cancer (2,213 female cases and 71 male cases). All patients were inhabitants of Basrah governorate at the time of diagnosis. Figures on the Basrah population were obtained from various sources including the Ministry of Health, Ministry of Planning and Developmental Collaboration and local household surveys. It was possible to have total population estimates for each year and by age and sex. Age specific and year specific incidence rates were calculated. The age standardized incidence rate was also calculated using world population as the standard

population to be 34.9 per 100,000 females. Age-wise, no case was reported among children aged less than 15 years and the incidence increased with advancing age reaching a peak of 123.8/100,000 females at the age range of 50-54 years. The time trend of the crude incidence rate showed only modest increased risk with passage of years and no age shift could be documented in this study. Breast cancer in females in Basrah is a significant health problem. The current incidence rate (crude, 23.7/100,000, age-standardized, 34.9/100,000) is high and justifies intensive efforts to improve early detection of cases, provide better treatment amenities and introduce long term preventive measures. Using to put the risk in Basrah within a regional and international context.

In conclusion, the incidence of breast cancer increased in Iraq in recent years, indication a significant health problem. Actions are needed on the national level for better estimate of the problem.

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