

Comparative demographic and clinicopathological study on the behavior of mammary carcinoma in three Iraqi governorates (Baghdad, Hilla and Karbala)

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Summary:

Background: Breast cancer is the most common malignant tumor in women worldwide. In Iraq, there is a tendency for this disease to be diagnosed in younger ages, at advanced stages with a prevalence of more aggressive tumor behavior.

Patients and Methods: The study included a total of 216 women with breast lumps and proven breast cancer who visited the Main Referral Training Center for Early Detection of Breast Tumors in the Medical City Teaching Hospital in Baghdad (85 patients) and the Specialized Clinics belonging to the major hospitals of Hilla (62 patients) and Karbala (69 patients) complaining of apparent breast lumps.

Results: 31% of patients was in the age category (40-49 years), 38.4% of patients whose highest education within the primary school level, 36.4% of patients had history of lactation, 52.3% of total had started menstruation at the age (10-12 years), 85% of patients had negative history of oral contraceptive pills consumption, Ki-67 tumor marker was demonstrated in 62.5% of total with highest frequency of expression was displayed in Baghdad and in relation with grade II.

Conclusion: Significant differences among the three Iraqi governorates were noted with respect to patient's age, educational status, history of breast feeding, age at menarche and history of oral contraceptive pills consumption. Higher Ki-67 nuclear expressions were demonstrated among patients from Baghdad. There was a direct significant relationship between Ki-67 nuclear expression and the nuclear staining intensity with tumor grades.

Key words: Breast Cancer

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Introduction:

Breast cancer incidence rates vary considerably, with the highest rates in the developed world and the lowest rates in Africa and Asia.(1)It is proposed that it is the outcome of multiple environmental and hereditary factors and that there are three factors which strongly increase a woman's risk of developing this disease: advanced age, family history of the disease, and a personal history of breast cancer.(2) A striking feature of breast cancer epidemiology is its geographic variation in occurrence, with differences in invasive breast cancer incidence as high as 10-fold internationally (3) and two-fold among countries within the United State.(4)

Patients and Methods:

The study included a total of 216 women who visited the Main Referral Training Center for Early Detection of Breast Tumors in the Medical City Teaching Hospital in Baghdad (85 patients) and the Specialized Clinics belonging to the major hospitals of Hilla (62 patients) and Karbala (69 patients) complaining of apparent breast lumps and proven breast cancer.

The age of the women ranged between (20-83 years). Only those in whom pathological examination revealed ductal carcinomas were included in this study. Those cases were selected from the total population visiting the center and/or clinics during the period (January 2008-February 2009). All patients were subjected to the triple assessment technique and all relevant data recorded within the patient's case sheet file questionnaire were included in the study. Paraffin embedded tissue blocks belonging to 40 patients diagnosed as having breast carcinoma were selected randomly and assessed for immunohistochemical expression of Ki-67 tumor marker.

Statistical analysis

All data collected from the patients and the results obtained from the immuno-histochemical staining for Ki-67, were statistically tested utilizing Chi-square tests to judge whether a relation existed between the variables by using SPSS program (Version: 17) and Harvad Graphic (Version: 4.0) application.

The Results

The peak age frequency in the total group studied was in the age category of (40-49 years) accounting for 67

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patients (31%). In Baghdad (32.9%) and Hilla (35.5%), the peak frequencies were demonstrated in the same age category while in Karbala (27.5%), the peak frequency was recorded equally in the age categories 20-39 and 60+ years (Figure 1). The highest number of patients was demonstrated in those whose highest education within the primary school level was 83 patients (38.4 %). In Karbala (3, 55%), the peak frequency was recorded in the same category while in Baghdad (29, 34%) and Hilla (25, 40%), the peak frequencies were displayed in the illiterate category (Figure 2). History of lactation was recorded in 137 patients (63.4%). Highest frequency was displayed in Baghdad as 65 (76.5%) patients were lactating (Figure 3). 52.3% of total had started menstruation at the age (10-12 years) versus 47.7% who had menarche at (13-17years). In Karbala and Hilla, the peak frequencies of those who had menarche at the age of (10-12 years) were 52 (75.4%) and 38 (61.3%) respectively versus 23 (27.1%) from Baghdad. The majority (85% of total=184 patients) had negative history of oral contraceptive pills consumption. The recorded figures were 60 patients (70.6%), 67 (97.1%) and 57 (91.9%) in Baghdad, Karbala and Hilla respectively. It was possible to compare the results of cytological (McKee); and histological (Nottingham) grading systems in the pathological specimens belonging to 40 patients. McKee's grade I was recorded in two patients (5% of total), while the same grade was reported histologically in 4 patients (10%), The corresponding frequencies for grade II in both cytological and histological systems were 62.5% and 57.5% respectively while grade III was recorded equally in both (32.5%). The total number of specimens which showed Ki-67 positive expression was 25 (62.5%), the recorded frequencies of Ki-67 expression in three governorates were 14 (56%), 5(20%) and 6 (24%) in Baghdad, Karbala and Hilla respectively. The peak frequency of Ki-67 expression was 13 (50% of total positive Ki-67 expression) and recorded in specimens belonged to patients diagnosed with grade II mammary carcinoma accounting for 57.5% of total tumor grades (Figure 4). The highest frequency (9, 52.9%) was displayed in specimens with moderate nuclear staining and belonged to patients with grade II mammary carcinoma.

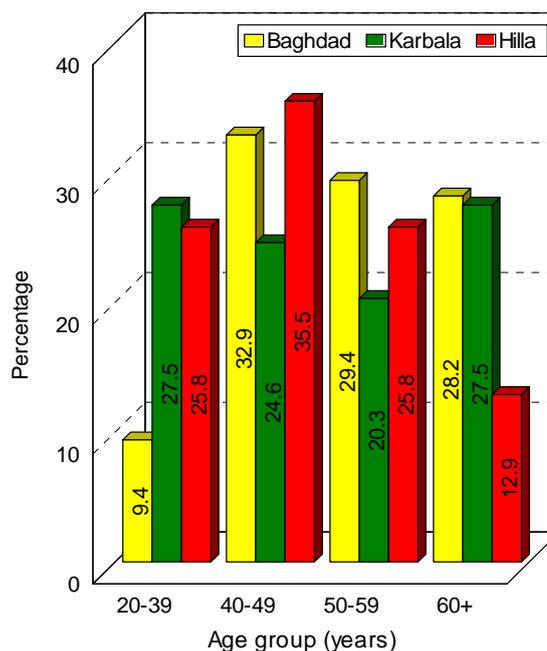


Figure (1): Age distribution of studied

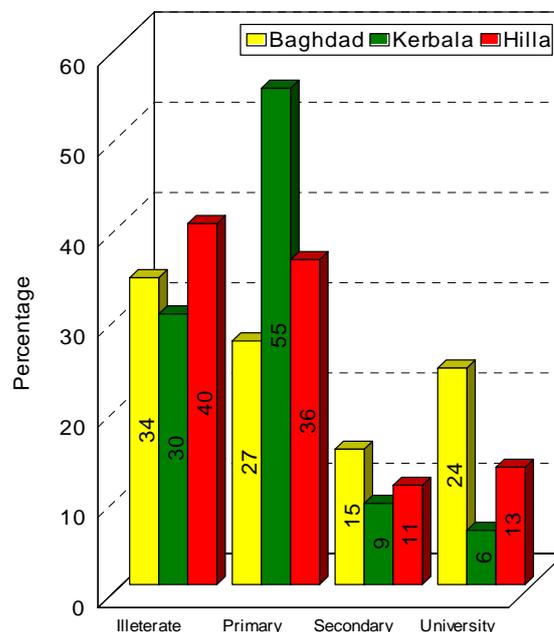


Figure (2): Educational status of population of breast cancer patients

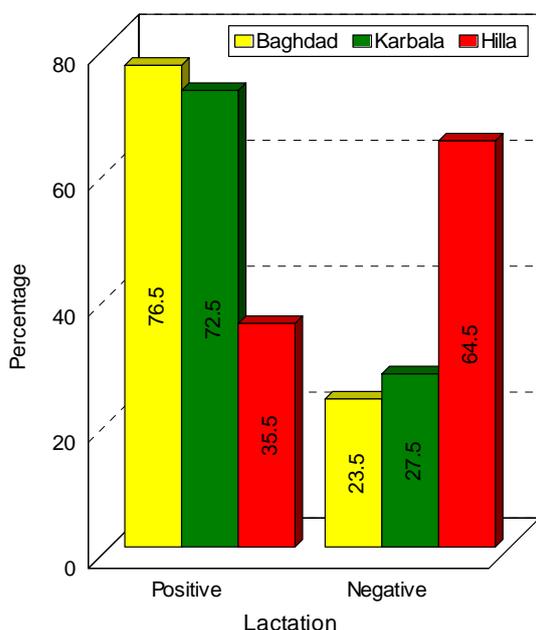


Figure (3): History of breast feeding.

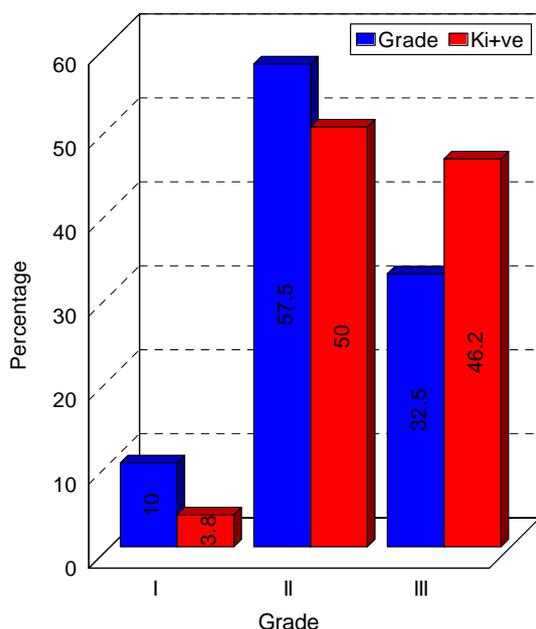


Figure (4): The correlation between in breast cancer patients Ki-67 expression and tumor Grade.

Discussion:

Most of the Iraqi patients are diagnosed in young age groups with late stage at presentation and a prevalence of more aggressive tumors.(5,6) In the present study, the peak age frequency of breast cancer occurred in the fifth decade of life (i.e., 40-49 years). In Karbala, the

peak frequency was recorded equally in the age categories 20-39 years and 60 and over; this could be attributed to a positive family history of breast cancer and high risk populations. Similar peak age frequencies were recorded in other reports from our country (Iraqi Cancer Registry, 2004; Al-Alwan, 1998 and 2004; Al-Anbari, 2009; Hasoon, 2007 and Ameen, 2009). (7, 8, 9, 10, 11, 12) In addition to Ahmad, 2004⁽¹³⁾ from the north of Iraq. Controversy still exists as well regarding the relationship between the educational status and breast cancer risk. Higher educational level was found to reduce the risk of breast cancer by 34.6% compared to low educational status. (14) In contrast another study showed that level of education had no association with risk of breast cancer.(15) Our study showed that the highest frequency of patients was observed in patients who reached primary school level (38.4 %); while in Baghdad and Hilla, the peak frequencies were 29 (34%) and 25 (40%) respectively and displayed in the illiterate category. However, the highest frequency of patients who reached the university level was observed in Baghdad (24%) then in Hilla (13%) and Karbala (6%). These differences may be attributed to a better socio-economic status in the population of the capital than other governorates. Ameen, 2009 (12) from Iraq on the other hand, observed that the highest frequency of his patients was 185(45% of total) and fell into illiterate category. History of lactation was demonstrated in 63.4% of total with highest frequency in patients from Baghdad. This might be attributed to a better awareness of the protective effect of lactation among the population of the capital. In a previous study, Ameen, 2009 (12) showed that 69.8% of his patients were lactating during their life. Al-Anbari (10) reported lower frequency (48.83%) while Hasoon(11) recorded that 80% of his breast cancer patients had history of lactation. Earlier studies had suggested that the alkaline milieu of unsuckled breast milk surrounding the epithelial cells plays an important role in the carcinogenesis of epithelial surfaces.(16,17) Evidence suggests that life-long exposure to estrogens plays an important role in determining breast cancer risk through their influence on cell proliferation and DNA damage, as well as their promoting effects on cancer growth.(18,19) It has been found that women who experience menarche at an early age, or late menopause have a higher risk of breast cancer. In the current study, 52.3% of patients had started menstruation at the age group (10-12 years) and a highest frequency was observed among Karbala and Hilla which might be attributable to racial effect rather than better nourishment. Earlier age at menstruation among breast cancer patients was also observed in other studies. (20, 21) There has been some concern about the possible effects of oral contraceptive pills on breast cancer risk, especially after long use. Many of

the risk factors for breast cancer are related to natural hormones and oral contraceptive pills work by manipulating these hormones by inhibiting the pituitary gland and thus follicular stimulating hormone and leutenizing hormone.(22) In the present study, 85% of patients had no history of oral contraceptive pills use and only 14.8% of total had used oral contraceptive pills with the highest frequency observed among patients from Baghdad; this might be attributable to easier access to the family planning health care clinics. An earlier study from Iraq by (Hasoon, 2007) (11) showed a comparable frequency (18%). Similarly Al-Saad et al showed that 20% of Bahrainian patients had history of oral contraceptive pills consumption.(23) Pathologically, there was a fairly good concordance between the cytological and histological grades of mammary ductal carcinomas in our study; reinforcing the findings recorded in other studies from Iraq (9,10,11) and endorsing the value of cytopathology in the assessment of breast pathology. The highest frequency of positive Ki-67 expression was 14 (56%) and recorded in Baghdad; this may be attributed to more proliferative potential and aggressiveness of breast cancer in Baghdad compared to other two governorates. A significant correlation between Ki-67 expression and histological grade of ductal carcinomas was displayed in the present study. The highest Ki-67 expression (50%) was demonstrated in patients with grade II. The same correlation was observed by (Nadoushan et al, 2007) from Iran. (24) Ding et al, 2004 from China (25) concluded that ki-67 was the only important marker that significantly and independently associated with tumor grade. These findings suggest that ki-67 might be involved indistinctly in the pathological and molecular features during breast cancer development.

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