Clinico-pathological features of breast cancer in patients below 50 years of age in Khartoum

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Abstract

Background: The burden of breast cancer is high among all age groups but younger age groups have recently shown a distinct pattern of presentation.

Objective: This study describes the clinicopathological features of breast cancer among Sudanese patients below the age of fifty who presented with breast cancer to the University Of Khartoum Surgical Unit (USU) in Khartoum Teaching Hospital (KTH).

Patients and Methods: This is a descriptive analytical hospital-based study. Data was collected by reviewing medical records of a total number of 292 female patients who presented to USU with breast cancer from January 2010 to December 2014.

Results: A total number of 292 patients of breast cancers were included. Of these 177(60.6%) were below the age of fifty. Analysis of below fifty years group showed that the majority of them were multiparous (78%). The lag time between the initial complaint and presentation was 3-6 months in 55%. Ninety nine (56%) presented with locally advanced breast cancer (stage III), while 17% had metastatic cancer at the time of presentation, and 27% presented with early breast cancer (stage I&II). Histopathological results showed invasive ductal carcinoma in 161(91.5%) patients, and the majority 14481.5%)) were poorly differentiated tumors. Estrogen receptor (ER) status was negative in 106 (60%) patients.

Conclusion: Breast cancer amongst Sudanese patients who are younger than 50 years is characterized by a triad of longer lag time (>3 months) between the initial complaint and presentation, advanced clinical stages at the time of presentation (stages III&IV) and aggressive histopathological features (poor differentiation and negative ER). The majority of patients are multiparous and premenopausal.

Introduction:

Breast cancer is the most common malignancy in females, accounting for nearly one in three cancers diagnosed among women in the United States, and the second leading cause of cancer death worldwide.[1] In Africa breast cancer is the commonest malignancy affecting females and is most commonly observed among patients who are younger than 50 years old.[2, 3] In Sudan, in 2006, the incidence of breast cancer was 34.5% of all female cancers.[4] and 74% of patients were below the age of 50 years.[5]

While mortality rates due to breast cancer are declining in the developed world as a result of early diagnosis, screening, and improved cancer treatment programmes, the reverse is largely true in the developing world.[6] Several factors contribute to this higher mortality rates in developing countries but the clinical stage at the time of presentation is an important determinant of the outcome.[6] In developing countries patients usually present with advanced stages.[6, 7] In Sudan, a study showed that 60%of breast cancer patients presented with

late clinical stages (stages III & IV).[5] This delay may be caused partially by the patients themselves, as they are often less concerned about and/or less aware of breast cancer, and also by some physicians who have low suspicion of this disease particularly among young women.[8, 9] So, advanced clinical stages of the disease, lack of adequate screening and higher mortality are common features of breast cancer in developing countries.[10] Furthermore, in African women, the diagnosis of breast cancer is often made between 35 and 45 years of age which is 10–15 years earlier than the peak incidence for western countries[7]. However; the reasons for this earlier onset are poorly understood.[7, 11] The current study assessed the clinical and histopathological features of breast cancer among Sudanese patients who were below fifty years of age who presented with breast cancer to the University of Khartoum Surgical Unit (USU) in Khartoum teaching hospital (KTH).

Patients and methods:

This was a descriptive analytical cross-sectional hospital-based study. Data was collected by reviewing medical records of a total number of 292 patients who presented with breast cancer to the University of Khartoum Surgical Unit (USU) at Khartoum Teaching Hospital (KTH) from January 2010 to December 2014.University of Khartoum Surgical Unit (USU) is the largest surgical unit in KTH which is one of the central referral hospitals in Khartoum city with a capacity of 40 Surgical beds. The inclusion criteria were patients who presented to the USU during the period of the study and were diagnosed with breast cancer using triple assessment [12- 14]. Patients who were 50 years old or more, male patients and those with incompletely filled medical records were excluded from study. A predesigned questionnaire was used to collect epidemiological and clinical data. Data was analyzed using the SPSS software package (version 21 windows). Pearson test was used and probability test (*P* value) to determine the statistical significance of differences with $P< 0.05$ considered as significant at 95% confidence interval.

Results:

One hundred seventy seven patients with breast cancer were below 50 years old and they constituted about 60.6% of the total number of patients (292) who presented to USU during the study period. All were females. The median age of the patients at the time of diagnosis was 44±5 years. The majority 143(81%) were pre-menopausal and 78% were multiparous. Duration of the initial complaint before seeking medical advice ranged between 1-29 months, the lag time between the initial complaint and presentation was 3-6 months in more than half of the patients (55%) and more than 6 months in 32% and only 13% had a lag time less than three months. The cause of delay in seeking medical advice was investigated (Table 1). No significant association was found between the educational level of the patients and the earlier presentation to the hospital as our study didn't show significant differences between patient's educational level and the lag time between initial complaint and the presentation (*P=0.15*).

Ninety patients (51%) presented with a breast lump, thirty five (19.7%) patients had nipple discharge as the most frequent complaint, whereas 33 (19.0%) presented initially with skin changes and ulcers and 17(10.2%) patients presented primarily with an axillary lump. Significant association was found between the clinical stage at time of presentation and the lag time before presentation (*P=0.004*). Patients who presented with skin ulceration and nipple changes (late clinical stages) had a longer lag time between initial complaint and the presentation, in contrast to those who presented with early clinical stages who had relatively a shorter duration between initial complaints and presentation.

The upper outer quadrant was the most commonly involved site (66%) either as a single lesion or as a part of multifocal disease. Half of patients (51%) had lesions in the right breast, whereas 46% had left breast lesions and 3% had bilateral breast disease. Tumor, Nodes and Meatstasis (TNM) stage of breast cancer is summarized in Table 2. Patients with tumor size more than 5 cm had significant association with

nodal involvement (*P<0.001*). Clinical stages are summarized in Table 3. Significant association was found between the lag time and clinical stage at the time of presentation (*P=0.014*)**.** Most common sites of metastasis were the lungs (56%) followed by the liver (23%) then the dorsal vertebrae (11%), the proximal femur and humerus (7%) and least frequent the brain (3%). One hundred sixty two (91.5%) patients had invasive ductal carcinoma (IDC), while twelve (6.7%) patients had invasive lobular carcinoma, two (1.3%) had mucinous carcinoma and undifferentiated histopathology was reported in one (0.56%) patient.

Regarding histopathological grading; only nine patients (5.4%) had grade I (well differentiated tumors), 24 (13.6%) had grade II (moderately differentiated tumors) and the majority 144 (81.9%) had grade III (poorly differentiated tumors). Estrogen receptors were negative in 60% of patients.

Discussion:

Early onset breast cancer has a variable prevalence all over the world [3]. In this study we report a series of 177 (66%) patients who were below fifty years old, which is quite comparable to a previous report from Sudan which found that 74% of breast cancer patients in Sudan were below the age of fifty years. [5]

The mean age at the time of presentation was forty four years which is fairly comparable to the regional literature that reported earlier age of presentation of breast cancer in the developing countries in Africa [7, 15]. However, this is remarkably lower than that reported in the Western countries in which the majority of patients (65%) were in the sixth decade of life at the time of presentation.[16] The reasons for this earlier presentation in African countries are not fully understood.[7] Nevertheless; the aggressive nature of the disease in African patients could partially explain this pattern of earlier onset of this disease.[15] Furthermore, this earlier age may suggest a strong genetic component of this disease in Sudanese patients.[9] Unfortunately, breast cancer at younger age is associated with poor prognosis.[16- 18] We report a high prevalence of breast cancer among multiparous patients (78%), supporting findings from Sudan and Africa[7, 9], but contradicting findings from Western countries which have lower prevalence among multiparous patients.[10, 16] Nevertheless, there is a well known association of reduction of the risk of breast cancer and higher parity, it is based on the assumed protective role of Progestrone.[7] However; our findings disagree with that association.

More than half of our patients (55%) presented with a lag time of more than 3 months and one third (32%) presented after 6 months, these findings are in agreement with other local and regional reports in developing countries.[9, 20, 21] This could be attributable to decreased awareness of patients and limited availability of trained medical staff in the vast peripheries of Sudan leading to a delay in diagnosis.

No association was found between patient's educational level and the lag time between the initial complaint and presentation (*P=0.15*), contradicting previous reports that showed a high educational level is associated with raised awareness and earlier presentation.[2, 7, 22]

In agreement with previous reports[7, 9, 15], a significant association (*P=0.002*) was found between the lag time before presentation and clinical stage, as patients who presented late (>3 months) had advanced clinical stages (stages III and IV). Furthermore; patients with larger tumor size (>5 cm) had nodal diseases (*P<0.001*) which is similar to other reports [7, 15]. Thirty (17%) patients had metastatic breast disease at the time of presentation which is in keeping with regional reports [7, 9], but far higher than figures mentioned in other reports from Western countries [20]. The pattern of metastatic disease is quite similar to that found in previous reports.[7, 15]

Invasive ductal carcinoma (IDC) was the commonest histopathological variant (91.5%) which is in agreement with local, regional and international literature.[2, 7, 9, 14, 22, 23] On the other hand, Invasive lobular carcinoma (ILC) was reported in 6.7% of

patients which is quite similar to other reports.[7,9,14] The reason for this low prevalence of ILC could be explainable by the fact that ILC is a relatively more common among older patients so this finding is quite consistent with younger ages in our series.[9] Most of histopathological reports showed poorly differentiated tumors (grade III), which is in keeping with other reports.[7, 9, 16]

Estrogen receptors (ER) were predominately negative (60%) which is fairly consistent with similar reports[7, 9]. This could be attributable to multiparity which is linked with reduced positivity of Estrogen receptors.[9] Moreover; the positivity of ER is strongly associated with increasing age, being more prevalent in older postmenopausal women.[24] Therefore, we can also explain the predominance of the negativity of ER in our series by the fact that our patients were relatively young.

Conclusion:

Breast cancer amongst Sudanese patients who are younger than 50 years is characterized by a triad of longer lag time (>3 months) between the initial complaint and presentation (87% presented after three months), advanced clinical stages at the time of presentation (73% were in stages III& IV at presentation) and aggressive histopathological features (poor differentiation (81%) and negative ER status (60%). The majority of patients were multiparous and premenopausal.

Table 1. Causes of delayed presentation of patients with breast cancer (n=177)

Cause of delayed presentation	Number of patients
Lack of health centers/poor accessibility	71 (40.1%)
Lack of awareness	60 (33.9%)
Self-reassurance	23 (12.9%)
Reassurance by medical personnel	12 (6.8%)
Missed data	11 (6.3%)
Total	177(100%)

Table 2. Tumor, Node and Metastasis (TNM) stage of breast cancer (n=177)

Tumor, Node and Metastasis (TNM) stage		Number of patients
Tumor stage (T)	T1	12 (6.8%)
	T2	35 (19.7%)
	T3	49 (28.4%)
	T4	81 (45.4%)
Node stage (N)	N0	37 (20.9%)
	N1	44 (24.9%)
	N2	56 (31.7%)
	N3	40 (22.5%)
Metastasis stage (M)	M0	147 (83%)
	M1	30 (17%)

Table 3. Clinical stages of breast cancer (n=177)

Clinical stage	Number of patients
Early breast cancer	49 (27.7%)
Locally advanced breast cancer	98 (55.3%)
Metastatic breast cancer	30 (17%)
Total	177(100%)

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