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# Characteristics of Breast Cancer at First Presentation in Sudanese Patients Attending the National Cancer Institute–University of Gezira (NCI–UG)

Muna Ahmed Eltayeb[a], Areeg Faggad[b], Osama Sharafeldin Abbadi[c], Moawia Mohammed Ali Elhassan*[d]

[a] *Department of biochemistry, Faculty of Medicine, Gezira University, Sudan*
[b] *Department of molecular biology, National Cancer Institute, University of Gezira, Sudan*
[c] *Department of biochemistry, Faculty of Medicine, Omdurman Islamic University, Sudan*
[c] *Department of Radiation Oncology, National Cancer Institute, University of Gezira, Sudan*

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ABSTRACT

**Background:** Little information is available about breast cancer (BC) in Sudan. Therefore, the present study aimed to provide baseline information about the demographic features and tumor characteristics, and also to investigate the associations between demographic variables and presentation stage in BC patients attending the National Cancer Institute-University of Gezira (NCI-UG), Sudan.

**Methods:** In this cross-sectional study, we included all BC patients treated at the NCI-UG from January to December 2013. Patients' demographic, clinical and pathological data were retrieved from the hospital records and analyzed using SPSS version 20, and associations between these factors were tested as well.

**Results:** A total of 232 cases were included in this research. The majority (97.8%) of subjects were females and 2.2% were males. The median age at diagnosis was 50 years (range, 22-90). The mean time between identification of symptoms and diagnosis was 13 months (SD=16.1). Clinical stages I, II, III, and IV represented 6.9%, 37.0%, 40.9% and 15.2%, respectively. Advanced stage at diagnosis was associated with longer duration between identifying the symptoms to diagnosis (P=0.006). Also the level of education of BC patients was significantly associated with clinical stage at presentation (P = 0.01).

**Conclusions:** Sudanese patients with BC present at a younger age and with more advanced stage at diagnosis than those in developed countries. Patients' education level and duration from identification of BC symptoms to diagnosis significantly impact the stage at the time of presentation. In limited resource setting, early diagnosis of symptomatic BC is crucial in reducing the disease burden.

## Introduction

Breast cancer (BC) is the most commonly reported cancer among women worldwide.[1] According to Globocan (2018), the age at which BC occurs worldwide was 43.1/100,000.[1] However, there are marked geographical variations in incidence rates, with BC being highest in the high-income countries (HICs) and lowest in the low- and middle-income countries (LMICs). The actual incidence of BC in Sudan is unknown because of the lack of a national cancer registry. Data from hospital-based registry revealed that BC is the most common cancer in Sudan.[2] A report by the Khartoum Cancer Registry showed that the incidence of BC in Khartoum state was 25.1 per 100,000.[3]

In Sub-Saharan Africa, BC occurs at young age at presentation and is diagnosed at advanced stage.[4]

**Address for correspondence:**
*Moawia Mohammed Ali Elhassan, MD*
*Associate Professor of Oncology*
*Address: Clinical and Radiation Oncologist, National Cancer I nstitute-University of Gezira, Wad Madani, Sudan PO Box 20*
*Tel: +24 9121262156*
*E-mail: moawia2@gmail.com*

Women in this region may be aware of a breast lump for many months and not to seek medical advice until they observe complications like pain, ulcer, foul-smelling purulent discharge or symptoms of metastatic disease. Delayed presentation has been attributed to lack of early detection programs, low levels of community awareness and poor health care systems infrastructure. Undue delay is sometimes ascribed to physicians who misdiagnose the symptoms.[5] The majority of Sudanese women with BC present with locally advanced disease (stage III) or worse metastatic disease (stage IV) that is difficult to treat resulting in death.[6-8] It has been reported that approximately two-thirds of Sudanese women noticed symptoms of their cancer for at least 12 months prior to diagnosis which is typical in many countries in Sub-Saharan Africa.[5,7]

In Sudan, data on the epidemiology of BC is limited.[2,6-8] Therefore, we conducted this study to provide baseline information about the demographic features, tumor characteristics, and the associations between various demographic variable and stage at presentations in BC patients treated at the National Cancer Institute-University of Gezira (NCI-UG), Sudan.

## Methods

*Setting*

Sudan is a low-income country with approximately 40 million inhabitants. Health care in Sudan is delivered at three levels: Primary care is provided through primary health care unit, dressing stations and family health centers; the rural hospitals provide the secondary health care; and the tertiary care level is provided through teaching, general and specialized hospitals. The NCI-UG, located in Gezirastate, central Sudan, serves approximately 5 million people in Gezira and other patients from nearby states. Treatmens available at the NCI include radiotherapy, chemotherapy, and palliative care. Cancer diagnosis and treatments are available to patients for free at public cancer centers.

*Study design*

We performed a one-year cross-sectional study to investigate the demographic features, tumor characteristics and associations between various demographic variable and stage at presentations in all BC patients treated at the NCI-UG from January to December 2013. The patients with incomplete records (missing information on stage, or histopathology) were excluded.

*Data collection*

A pre-designed data form was used for data collection. The data regarding demographics, clinical characteristics, pathology, background medical history (diabetes mellitus, hypertension, and ischemic heart diseases), family history (FH) of BC, and disease clinical stage were obtained from patient medical files. The patients with first or second degree relatives with BC were considered positive for FH of BC. Tumor characteristics including histological types, grade, lymphovascular invasion (LVI), estrogen receptor (ER) and progesterone receptor (PR) status in addition to human epidermal growth factor receptor 2 (HER2) were obtained from histopathology reports attached to patients' folders. All records were retrieved from the NCI-UG Records, Statistical and information Unit.

*Statistical analysis*

The data was coded and analyzed by SPSS, version 20. Patient characteristics were described as frequencies and percentages for categorical variables or as median (range) and mean (SD) for numerical variables. Chi-square test and ANOVA test were used for comparisons and statistical analysis of association. A P value of 0.05 or less was assumed to be statistically significant.

*Ethical considerations*

Ethical approval was obtained from the Ethics Committee at the NCI-UG. Subsequently, the proposal was reviewed by the Oncology Research Committee at the Sudan Medical Specialization Board.

## Results

*Patient Characteristics*

A total of 232 patients were included in the study. The median age at diagnosis was 50 years (range, 22-90). The vast majority (97.4%) of the patients were females. The majority of the patients were unemployed (85%). More than half (59%) of women with BC were postmenopausal while 41% were premenopausal. The median age of menarche was 14 years (range, 10-18). Approximately 20% (45 cases) of patients had background medical history of diabetes mellitus (21 cases), hypertension (21 cases), and ischemic heart diseases (3 cases). 55% of our patients were from rural areas and only 15% had family history of BC. Table 1 illustrates the main demographic characteristics of the study population according to patients' residence.

*Tumor characteristics*

Histopathology examination of tumors revealed invasive ductal carcinoma as the most common type (70.3%) followed by infiltrating lobular carcinoma (12.9%) and malignant phyllode tumors (5.2%). Other subtypes represented a small percentage of the cases. Tumor characteristics are presented in Table 2. Tumor tissues were found to be hormone receptors (HR) positive i.e. ER positive and/or PR positive in 102 (44%) cases while 89 (38.8%) cases presented as HR negative i.e. both ER-negative and PR-negative. Information on ER and PR status was not available in 40 (17%) cases. Only few (67/232; 28.9%) patients

**Table 1.** Demographic characteristics of breast cancer patients according to residence

| Characteristics | | Rural N (%) | Urban N (%) | Total N (%) | P Value |
|---|---|---|---|---|---|
| Sex | Female | 122 (54.0%) | 104 (46.0%) | 226 (100%) | 0.24 |
| | Male | 4 (80.0%) | 1 (20.0%) | 5 (100%) | |
| | Total | 126(54.5%) | 105 (45.5%) | 231 (100%) | |
| Age | Mean | 50.1 | 51.6 | | 0.37 |
| | SD | 14.4 | 12.3 | | |
| Duration of symptoms | Mean | 13.5 | 12.5 | | 0.71 |
| | SD | 14.3 | 18.2 | | |
| Menopausal Status | Pre-menopausal | 52 (56.9%) | 41 (44.1%) | 93 (100%) | 0.64 |
| | Post-menopausal | 70 (52.6%) | 63(46.4%) | 133 (100%) | |
| | Total | 122 (54.0%) | 104 (46.0%) | 226 (100%) | |
| F/H of Breast cancer | Yes | 18 (43.9%) | 23 (56.1%) | 41 (100%) | 0.07 |
| | No | 104(58.1%) | 75 (41.9%) | 179 (100%) | |
| | Total | 122 (55.5%) | 98 (44.5%) | 220 (100%) | |
| Education level | Illiterate | 55 (73.3%) | 20 (26.7%) | 75 (100%) | 0.001 |
| | Primary | 50 (56.0%) | 30 (43.2%) | 88 (100%) | |
| | Secondary | 16 (35.6%) | 29 (64.4%) | 45 (100%) | |
| | High | 5 (22.7%) | 17 (77.3%) | 22 (100%) | |
| | Total | 126 (54.8%) | 104 (45.2%) | 230 (100%) | |

- N; number, F/H, Family history; SD, Standard deviation
- Missing data not included in the analysis

were tested for HER2 status as shown in Table 2.

*Presenting symptoms*

Breast mass was the most frequently reported clinical presentation (86%). Less frequent symptoms included breast pain (6%), nipple discharge (5%) and axillary mass (3%). Only 30 patients were diagnosed with tumors less than 2 cm (T1), 84 patients had tumor size 2-5cm (T2) and 67 patients with tumor bigger than 5 cm. Approximately, 30% (n= 68) of our patients presented with ulcerated tumor and/or fixed to skin or chest wall. The tumor size was not documented in 18 patients. At time of diagnosis, 58% of cases had palpable regional lymph node and 37(16%) patients had metastatic disease. Mammography as part of triple assessment was conducted for about 36.2% of the patients. Data on the time interval between identification of symptoms by the patients and diagnosis was available for 220 patients (Figure 1). The mean time between identifying the symptoms by BC patients and diagnosis was 13 months (SD=16.1). Only 15 (6.8%) out of 220 patients had less than one-month duration

**Table 2.** Pathological characteristics of breast cancer patients (232 cases)

| Characteristics | | Frequency | Percentage |
|---|---|---|---|
| Histopathology | Invasive Ductal Carcinoma | 163 | 70.3% |
| | Invasive Lobular carcinoma | 30 | 12.9% |
| | Malignant phyllodes tumor | 12 | 5.2% |
| | Others | 27 | 11.6% |
| Grade | I | 19 | 8.2% |
| | II | 97 | 41.8% |
| | III | 87 | 37.5% |
| | Unknown | 29 | 12.5% |
| Presence of LVI | Yes | 46 | 19.8% |
| | No | 91 | 39.3% |
| | Unknown | 95 | 40.9% |
| Presence of DCIS | Yes | 13 | 5.6% |
| | No | 28 | 12.1% |
| | Unknown | 191 | 82.3% |
| HR status | Positive (ER +ve and/or PR +ve) | 102 | 44.0% |
| | Negative (ER –ve and PR –ve) | 90 | 38.8% |
| | Unknown | 40 | 17.2% |
| HER2 status | Positive | 32 | 13.8% |
| | Negative | 35 | 15.1% |
| | Unknown | 165 | 71.1% |

LVI: lymphovascular invasion; DCIS: ductal carcinoma in situ; HR: hormone receptor; ER: estrogen receptor; PR: progesterone receptor; HER2: Human epidermal growth factor receptor 2

**Table3.** Comparison of different characteristics amongst disease stage at presentation

| Characteristics | | Stage I | Stage II | Stage III | Stage IV | Total | P value |
|---|---|---|---|---|---|---|---|
| Age | Mean | 48.8 | 49.0 | 52.1 | 52.4 | | 0.37 |
| | SD | 12.2 | 12.8 | 13.7 | 14.8 | | |
| Sex | | | | | | | |
| | Female | 15 (6.6%) | 82 (36.1%) | 93 (41.0%) | 37 (16.3%) | 227 (100%) | 059 |
| | Male | 0 | 3 (60.0%) | 2 (40.0%) | 0 | 5 (100%) | |
| Level of Education | Total | 15 (6.5%) | 85 (36.6%) | 95 (41.0%) | 37 (15.9%) | 232(100%) | |
| | illiterate | 2 (2.7%) | 16 (21.3%) | 42 (56.0%) | 15 (20.0 %) | 75 (100%) | 0.01 |
| | Primary | 6 (6.8%) | 35 (39.8%) | 31 (35.2%) | 16 (18.2%) | 88 (100%) | |
| | Secondary | 6 (12.8%) | 23 (48.9%) | 13 (27.7%) | 5 (10.6%) | 47 (100%) | |
| Residence | Higher | 1 (4.8%) | 11 (52.4%) | 8 (38.1%) | 1 (4.8%) | 21 (100%) | |
| | Total | 15 (6.5%) | 85 (36.6%) | 94(40.7) | 37 (16.0%) | 231(100%) | |
| Marital Status | Rural | 6 (4.7%) | 45 (35.7%) | 55 (43.7%) | 20 (15.9%) | 126 (100%) | 0.61 |
| | Urban | 9 (8.6%) | 40 (38.1%) | 39 (37.1%) | 17 (16.2%) | 105 (100%) | |
| | Total | 15 (6.5%) | 85 (36.6%) | 94 (40.7%) | 37 (16.0%) | 231 (100%) | |
| Symptoms duration | Married | 12 (7.5%) | 60 (37.5%) | 65 (40.6%) | 23 (14.4) | 160 (100%) | 0.32 |
| | Single | 2 (8%) | 12 (48.0%) | 6 (24.0%) | 5 (20.0%) | 25 (100%) | |
| Parity | Widowed/Divorced | 1 (2.2%) | 13 (28.3%) | 23 (50.0%) | 9 (20.0%) | 46 (100%) | |
| | Total | 15(6.5%) | 85(36.8) | 94(40.7%) | 37(16%) | 231(100%) | |
| F/H of breast cancer | Mean | 6.7 | 9.9 | 13.8 | 20.5 | | 0.006 |
| | SD | 6.5 | 13.2 | 17.5 | 18.2 | | |
| Menopausal Status | Nulliparous | 3 (6.2%) | 20 (41.7%) | 19 (39.6%) | 6 (12.5%) | 48 (100%) | 0.82 |
| | Parous | 9 (5.6%) | 56 (34.8%) | 71 (44.1%) | 25 (15.5%) | 161(100%) | |
| | Total | 12 (5.7%) | 76 (36.4%) | 90 (43.1%) | 31 (14.8%) | 209 (100%) | |
| | Yes | 3 (7.3) | 17 (41.5%) | 14 (34.1%) | 7 (17.1%) | 41 (100%) | 0.77 |
| | No | 10 (5.6) | 64 (35.6%) | 77 (42.8%) | 29 (16.1%) | 180 (100%) | |
| | Total | 13 (5.9%) | 81 (36.7%) | 91 (41.2%) | 36 (16.3%) | 221 (100%) | |
| | Premenopausal | 7 (7.5%) | 35 (37.6%) | 36 (38.7%) | 15 (16.0%) | 93(100%) | 0.11 |
| | Postmenopausal | 8 (6.0%) | 48 (35.8%) | 56 (41.8%) | 22 (16.4%) | 134 (100%) | |
| | Total | 15 (6.6%) | 83 (36.7%) | 92 (40.5%) | 37 (16.2%) | 227 (100%) | |

of symptoms before diagnosis.

*Clinical stage*

Slightly more than half of cases had locally advanced BC i.e. Stage III (40.9%) or metastatic disease i.e. Stage IV (15.9%). Stage I and II were seen in 6.5% and 36.6% of our cases, respectively. Higher stage at diagnosis was associated with longer duration between identifying the symptoms by patients and diagnosis (P=0.006) as shown in Table 3 and Figure 2. Level of education was significantly associated with clinical stage at presentation (P= 0.01) as seen in Table 3.

## Discussion

Worldwide, BC accounts for 24.2% of female cancer burden.[1] In Central Sudan, BC is the most common cancer representing 34% of all female cancers.[9] Epidemiological characteristics of BC appear to be different in LMICs compared to HICs, with notably large proportions of young patients and aggressive forms of the disease.[8,10-12] In the present study, the average age at diagnosis (50 years) is consistent with previous reports from Sub-Saharan Africa including Sudan, but approximately 10 years earlier than women in HICs.[13] The low frequency of grade 1 tumors observed in the current study is consistent with a previous report from Sudan.[13]

Male breast cancer accounted for 2.2% of our

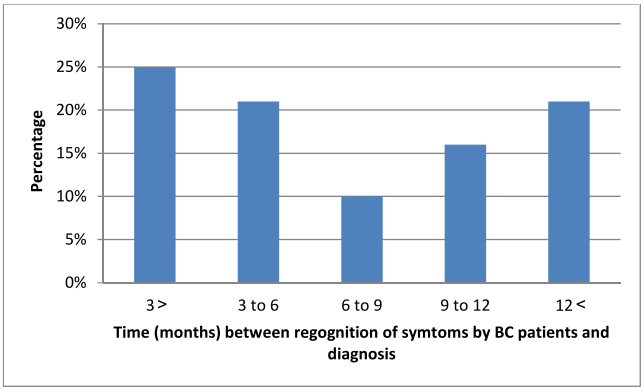


**Figure 1.** Distribution of BC Patients (220 cases) According to Time between Recognition of Symptoms and Diagnosis

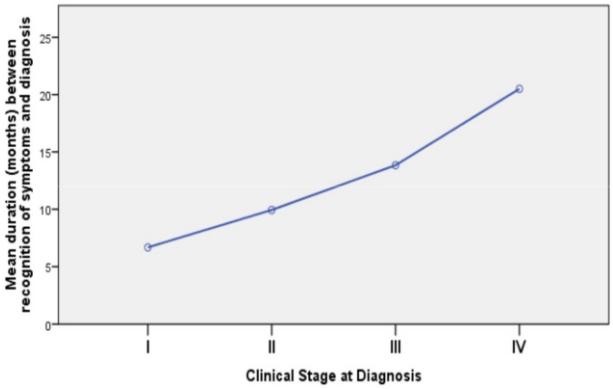


**Figure 2.** Distribution of mean duration between identification of symptoms by patients and diagnosis according to stage at diagnosis

study population. This finding is within the range that was reported previously for patients from Sudan and other African countries,[11, 14] but higher than populations in HICs.[15,1] Considering that blacks living in the United States had higher male-to-female ratio than their white counterparts, it is plausible to suggest that genetic background plays an important role in this phenomenon. The significant role of BRCA1/2 as an etiological factor of male BC in central Sudan was highlighted in a previous study.[16]

In this study, more than half of the patients presented with locally advanced (Stage III) or metastatic tumors (Stage IV). This has also been observed in other African countries.[4,12] This is largely attributed to modifiable factors such as poor BC knowledge, illiteracy, and limited health care infrastructure with no screening program for BC.[4] The level of education in the current study was able to demonstrate significant association with clinical stage at presentation. Several other studies have previously reported that education has a significant impact on stage at diagnosis and the prognosis of this devastating disease.[4,17] A possible explanation for the result in the current study is that well educated women are more likely to live in more developed cities and subsequently have a better access to health care services.

It has been reported that African women living in the rural areas are particularly vulnerable to late-stage diagnosis, partially due to the high cost of transportation and time taken to reach a secondary or a tertiary health care facility.[6] In the current study, women from rural areas presented more often with stage III or IV disease than women from urban areas. In our limited resources setting, the reason for the high rate of late-stage diagnosis among BC patients from rural areas is not well understood and needs further studies.

Mammography screening increases the detection of early-stage BC. In this study, only 40% of our patients had access to mammography. This is because, during the study period, there was no functioning mammography machine outside the capital, Khartoum. The impact of screening mammography in BC stage at diagnosis has been examined in several studies.[18,19]Taplin and colleagues used data that included 1.5 million women aged 50 years or older to examine differences in screening implementation among women with late-stage and early-stage breast cancer. They found that late-stage cancers were higher among women with an absence of screening.[18] A study conducted in Sudan showed that implementation of BC awareness and breast examination program that uses local volunteer women could increase the early detection of BC in rural areas.[20] In our limited resource setting, lack of national program for BC screening as well as shortage of health educational programs on BC could be contributing factors to the advanced stages at presentation.

The earlier BC is identified, the better chance in reducing the mortality from this disease. Studies have shown that a shorter time between the recognition of BC symptoms and the first medical consultation is associated with early-stage disease.[21,22] Yet, delayed presentation of BC patients is typical of many African countries, including Sudan.[5, 7, 23] We found the average duration between recognition of symptoms to diagnosis was 13 months, which is almost similar to previous studies from Sudan.[7,23]In our study, higher stage at diagnosis was significantly associated with longer duration between identification of symptoms by the patients and diagnosis. It has been reported that late stage diagnoses could be avoided if all patients with BC symptoms would present to a doctor within 1 month.[22] In the current study, a small number of patients (6.8%) identified the symptoms less than one month before diagnosis.

In Africa, there are considerable uncertainties regarding the frequency of ER/PR subtypes.[24] In previous BC series from Sudan considering the rate of ER/PR status, researchers reported inconsistent findings, although recent studies have suggested increased ER/PR positivity.[6, 8, 13, 25,26] This difference probably reflects enhanced quality control procedures in our setting. In this study, 44% were ER and/or PR positive while 38.8% were ER-negative and PR-negative. Information on ER and PR status was not available in 40 (17%) cases.

Our study suffers from several limitations including its retrospective nature and reliance on medical records. Moreover, it is a single institution's data; we therefore cannot make conclusions for all parts of Sudan. However, the NCI-UG is one of the only two referral oncology hospitals in central Sudan; therefore, the current data provide a background for the epidemiology of BC within this region.

In conclusion, we found that BC patients tend to be younger and present with more advanced stages at diagnosis than those in HICs. This study shows that the level of patient education and the duration from recognition of BC symptoms by the patients to diagnosis have a significant impact on stage at which the patients present. Our study showed that achieving earlier diagnosis of symptomatic BC is an important step in reducing the morbidity and mortality from this devastating disease.

**Conflict of interest**

The authors have no conflicts of interest to declare.

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