Review Article

Breast cancer in Africa, are we dealing with a different disease

Omer EL Faroug H Salim, FRCSI*, Samah IA Mukhtar, MSc**, Babikier I Mohammed, MD***, Nada Salih, MSc****, Kamal Hamad, FFRCSI, DMRT, DSN*****

Associate Professor of Surgery, Department of Surgery, Medical Officer**, University of Khartoum, Soba University Hospital, Sudan, Consultant Oncologist***, Laboratory Histopathology and Cytology Technician****, Associate Professor of Oncology, Faculty of Medicine, University of Khartoum ***** Radiation and Isotope Centre Khartoum, Sudan

Breast cancer in Africa, are we dealing with a different disease

Abstract

**Background**

The burden of breast cancer is high among individuals of all races and ethnicities. Despite its lower incidence in Africa, the mortality from breast cancer is higher in African women than in Caucasians. The present study was conducted to investigate the clinicopathologic features of breast cancer in Sudanese women and compared them with similar studies in other populations of native African, African American and European origin.

**Methods**

This is a hospital-based study. Data was obtained for breast cancer cases from the Radiation and Isotope Centre of Khartoum (RICK) from the period 2009-2011. A total of 497 women aged diagnosed with breast cancer were eligible for inclusion in the study.

Nada Salih, MSc

Department of Surgery, Soba University Hospital, Sudan, Soba University Hospital, Sudan, Consultant Oncologist, Consultant Oncologist

Corresponding author

Email: omersalim9@hotmail.com

Sudan Med J 2014 April;50(1)
Results
Seventy percent of patients were ≤50 year of age. The majority of patients were diagnosed at late stages (III & IV) with a high tumour grade (grade II & III) and Invasive ductal carcinoma was the most frequent histotype. More than half of cases had nodal involvement at presentation. Estrogen and progesterone receptor status was found to be predominately negative whereas almost half of patients were HER-2 positive. A triple negative tumor status was observed in 35.4% of women.

Conclusion
Breast cancer amongst Sudanese women is characterized by an early peak age of onset, advanced stage and more aggressive biological characteristics compared to Caucasian women. Strategies to address modifiable risk factors and improve breast cancer awareness together with implementation of a screening program are essential, especially among younger age groups.

Keywords: Breast, stage, grade, hormonal receptors

Introduction
Most of what we know about the epidemiology and management of breast cancer stems from studies carried out in economically developed countries. As breast cancer awareness rises globally, there is a pressing need to better investigate the characteristics of the disease in other populations. This current study, performed in the Sudan, partly addresses this need.

Sudan is one of the largest countries in Africa, lies in eastern north Africa. It is considered as microcosm of the continent due to its large ethnic diversity. Reported breast cancer incidence and mortality figures in Sudan are presumed to be an underestimate due to the absence of an adequate nationwide cancer registry. This situation is likely to improve as a new registry was established in 2010. Breast cancer is the most frequent hospital treated malignancy in Sudan, constituting 34.5% of all females’ cancers. In 2002, breast cancer accounted for 16.6 per 100,000 Sudanese female mortalities.

Breast cancer in Sudan is commonly diagnosed in young multiparous women at a late stage. Awadelkarim et al (2007) reported that 76% of breast cancer diagnoses in Sudan are made in multiparous women. A study of tumour biology in 1,255 Sudanese women with breast cancer in central Sudan reported that 74% of patients were younger than 50 years at diagnosis and the majority presented at stage III & IV (60.7%). Unfortunately, due to the cost of investigations, the information regarding receptor status was only available for 50 patients; 68% and 70% were Estrogen receptors (ER) and Progesterone receptors (PR) negative respectively. In addition, there was no data on tumor grade and HER-2/neu which are important prognostic variables as these services were not available at the time of study.

The younger age at diagnosis suggests a higher inherited susceptibility to breast cancer. Data from central Sudan also revealed that mutations in the breast cancer susceptibility protein (BRCA1/2) form an important risk factor for premenopausal women. Awadelkarim et al (2007) observed BRCA1/2 mutations in 35 breast cancer patients (1 male and 34 females) selected by diagnosis for a women under age of 40 or male gender. Thirty-three patients were found to carry 60 BRCA/2 variants. The detected variants incorporated 5 truncating mutations and 55 non truncating mutations. As BRCA1 mutations are associated with a higher risk of triple negative disease (ER, PR, Her2 negative), this could play a role in accounting for the high incidence of receptor negative disease in the country.

Methods
This is a retrospective, single-center hospital-based study carried out at Radiation and Isotope Centre of Khartoum (RICK), in
capital of Sudan. The center receives referrals from all over the country and sees 6,000-7,000 cancer patients per annum. Therefore, it will be the most representative sample available in the country. The study procedures were approved by the Institutional Ethical Committees at RICK. A total number of 3,042 patients with breast cancer were referred and treated at RICK from Jan 2009 to Dec 2011. All native Sudanese patients for whom medical records were available were enrolled in the study. Only 497 patients were eligible for this study.

The exclusion criteria were as follows:
- Male patients
- Secondary - recurrent tumors.
- Cases in which problems of histological processing were reported (e.g. fixation problems).
- Cases with inadequate sampling for microscopic examination.
- Patients whose slides were no longer available for revision.

Data on tumor characteristics (histological type, grading, lymph nodes involvement and receptor status) of breast cancer patients were collected from a hard copy of original reports at histopathology and immunohistochemistry labs. Breast cancer specimens were fixed in 10% formalin, embedded in paraffin wax and all sections were stained by haematoxylin and eosin (H&E) stain for microscopic examination. Histological grading was performed using the Bloom–Richardson system.

To assess receptors status, Immunohistochemical staining for ER, PR receptors and HER-2/neu was performed. Antigen retrieval was achieved by heat retrieval and slides were stained using Dako reagents. Binding of antibodies was detected by incubation for 20 minutes with the flex secondary system (dextran polymers from Dako) and immunostaining was scored (0=no staining, 1=weak staining 2=focal staining, 3=strong staining). A score of ≥1 was considered positive. Microscopic examination was performed by three different consultant pathologists. As this could add variability, all of slides included in the study were reviewed by single consultant pathologist blinded to tumor status.

Data on age at diagnosis and stage at presentation were obtained from patient’s medical file. Patients underwent a thorough clinical examination, investigations and were staged in accordance with the American Joint Committee on Cancer (AJCC) guidelines. Data was collected using standardized questionnaire.

Statistical Package for Social Sciences (SPSS) software 18 was used for statistical analysis and the association between age and different study variables was evaluated by chi-square test. p <0.05 was considered significant.

Results
A total of 497 women diagnosed with breast cancer fulfilled all eligibility criteria.
- Age at presentation ranged from 20 to 90 years, but the majority of cases 70% (348/297) were ≤ 50 years, while only 30% (149) of women were >50 years. The frequency of breast cancer is highest among women aged between 41-50 years old.
- The mean age at diagnosis was 44.7 years ± 12 and the median age was 49.6 years.
- According to AJCC guidelines, the majority of patients (63.2%) were diagnosed at late stages with tumors that had metastasized either locally (stage III) or to distant areas (stage IV). Locally advanced disease (stage III) constituted the highest percentage (37%) followed by distant metastasis disease (stage IV) which was seen in 26.2% of women. Stages 0, I, II were the least common forming 1.4%, 7.6%, 23.5% respectively. Unstaged cancers represented approximately 4.2% of cases.
- The tumour characteristics of cancer
patients are summarized in Table 1. Invasive ductal carcinoma was the most frequent histotype among RICK’s patients (86.7%) with the other subtypes present at lower frequencies. Almost two-thirds of cases had nodal involvement at presentation (317/497), 145 patients had ≥ 4 positive lymph nodes. Unfortunately there were a significant number of patients in which this assessment was not performed (64 women). 41.9% of women had tumour size ≥ 5cm.

- Eighty six percent of tumours were classified as high grade (grades II or III) and thereby more aggressive with a higher probability of spreading.

Table 1: Tumour characteristics of Sudanese women with breast cancer

<table>
<thead>
<tr>
<th>Tumour characteristics</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histological type</strong></td>
<td></td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
<td>431 (86.7)</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>25 (5)</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>10 (2)</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>9 (1.8)</td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td>8 (1.6)</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>8 (1.6)</td>
</tr>
<tr>
<td>Tubular carcinoma</td>
<td>3 (0.6)</td>
</tr>
<tr>
<td>Scirrhous carcinoma</td>
<td>3 (0.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lymph node</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with nodal involvement</td>
<td>317 (63.8)</td>
</tr>
<tr>
<td>Patients without nodal involvement</td>
<td>116 (23.3)</td>
</tr>
<tr>
<td>Missing /unknown</td>
<td>64 (12.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lymph nodes (LN) numbers</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (no LN.)</td>
<td>116 (23.3)</td>
</tr>
<tr>
<td>1-3 positive LNs.</td>
<td>111 (22.3)</td>
</tr>
<tr>
<td>≥4 positive LNs.</td>
<td>145 (29.1)</td>
</tr>
<tr>
<td>LN. are involved but were not counted</td>
<td>61 (12.3)</td>
</tr>
<tr>
<td>Missing/unknown</td>
<td>64 (12.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumour size</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T is carcinoma in situ</td>
<td>7 (1.4)</td>
</tr>
<tr>
<td>T1 tumour size &lt; 2cm</td>
<td>45 (9.1)</td>
</tr>
<tr>
<td>T2 tumour size 2-5cm</td>
<td>134 (27)</td>
</tr>
<tr>
<td>T3 tumour size &gt; 5cm</td>
<td>208 (41.9)</td>
</tr>
<tr>
<td>T4 skin extension</td>
<td>82 (16.5)</td>
</tr>
<tr>
<td>Missing/unknown</td>
<td>21 (4.2)</td>
</tr>
</tbody>
</table>

Estrogen and progesterone receptors status were negative in 72% and 75.7% of patients respectively (Table 2).

Table 2: Biological markers

<table>
<thead>
<tr>
<th>Biological markers</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER Status</td>
<td></td>
</tr>
<tr>
<td>ER positive</td>
<td>139 (28)</td>
</tr>
<tr>
<td>ER negative</td>
<td>358 (72)</td>
</tr>
<tr>
<td>PR Status</td>
<td></td>
</tr>
<tr>
<td>PR Positive</td>
<td>121 (24.3)</td>
</tr>
<tr>
<td>PR negative</td>
<td>376 (75.7)</td>
</tr>
<tr>
<td>Her-2/neus status</td>
<td></td>
</tr>
<tr>
<td>Her-2/neu positive</td>
<td>132 (26.6)</td>
</tr>
<tr>
<td>Her-2/neu negative</td>
<td>147 (29.6)</td>
</tr>
<tr>
<td>Missed/not done</td>
<td>218 (43.9)</td>
</tr>
</tbody>
</table>

The majority of patients (64.5%) were ER-/PR-, 16.9% were ER+/PR+, 11% were ER+/PR- and 7.4% were ER-/PR+ (Table 3).

Table 3: ER/PR Status

<table>
<thead>
<tr>
<th>Biological markers</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER-/PR-</td>
<td>321(64.5)</td>
</tr>
<tr>
<td>ER+/PR+</td>
<td>84 (16.9)</td>
</tr>
<tr>
<td>ER+/PR-</td>
<td>55 (11.00)</td>
</tr>
<tr>
<td>ER-/PR+</td>
<td>37 (7.4)</td>
</tr>
</tbody>
</table>

Due to availability of reagents together with the cost of the investigation, HER-2/neu status was available for only 279 women. When comparing the prevalence of HER-2/Neu over-expression in women whose expression status is known, we could see 47.3% (132/279) were HER-2/neu positive versus 52.6% (147/279) who were HER-2/Neu negative (Table 2). Thirty-five point four percent (99/279) of women had triple negative tumours.

Age specific analysis in relation to different clinicopathological variables (stage, grade, lymph nodes status and biological markers) was not significant except for histological type (P= 0.000). Most of the women with invasive ductal carcinoma were presented at younger age group (71.6% of invasive ductal carcinoma (IDC) cases were <50 years).
Discussion

Registry studies have provided valuable information on the epidemiology of breast cancer, thereby forming a basis for many national treatment initiatives. Such information has been lacking in the Sudan and so, in our current study we investigated multiple breast cancer characteristics in over 450 Sudanese women. Our results demonstrate an aggressive Immunohistochemical phenotype and advanced stage in younger women, which is consistent with similar studies in women of African origin. The epidemiology of breast cancer among native African women is similar to that of African-American women as both have a lower time risk of breast cancer, but comparatively higher mortality rates after diagnosis (7,8,9).

Breast cancer among Sudanese women is most commonly observed within a younger age group with a peak age incidence between 41-50 years. This finding is in line with previous studies in the region (4,5). A similar retrospective study carried out in Ugandan women showed that 73% were ≤ 50 years old (7,4). The mean age diagnosis in our series was 44.7 years which also agrees with the findings by researchers in Nigeria, Kenya and Tanzania in which the mean age was ranged between 43-51 years (10-13). Also, a comparable result of mean age of onset was noted in African Americans. Interestingly, Sudanese women present approximately 15 years earlier than Caucasians (44.7 years versus 60 years) (14,15). The underlying reasons for this difference in the mean age for occurrence of breast cancer worldwide are not known, but are likely to be multifactorial reflecting both intrinsic predisposition and external factors. However, such genetic, environmental, socioeconomic factors and cultural practices need further evaluation in future studies. Nevertheless, the trend of early age of onset of breast cancer seen native African and African American signifies a strong possibility of an inherited component in the causation of the disease.

Most of the patients (63.2%) seen was when their cancers were at advanced stages (III, IV) with a predominance of stage III (37%). It is likely that our figures were underestimation as lack of proper diagnostic facilities meant that many patients were unstaged. This is in accordance with a report done in Africa by Amir et al (1997) who observed that 67% of Tanzanian women with breast cancer presented at stage III, 10% with metastatic disease (16). Chen et al (1994) studied the histological characteristics of breast carcinoma in Caucasians and African Americans in the United States and reported a higher stage III incidence in African Americans (21.9% vs. 13.4%) (17). Elmore et al (1998) carried out a cohort study comparing 100 African American with 300 Caucasian patients diagnosed with breast cancer and found a statistically significant racial difference, as African American women were more likely to have an overall higher advanced stage (14). The same trends of racial differences were seen between Nigerian and English populations, most of the Nigerian cancers (61.8%) were stage III and IV compared with 11.4% of British cancers (18). Similarly only 7.4% of Sudanese women in our series presented with stage I breast cancer which contrasts with data from Furberg et al (2001) who found that 46.6% of Caucasian women in US were diagnosed at stage I (19). The advanced stage distribution in our series could be due to delayed seeking of medical advice, lack of availability and access to adequate medical care, absence of a screening program or the poor socioeconomic and educational status of women in the Sudan. In addition, the majority of mammography machines are available only at private centers in Sudan’s capital so the financial cost of traveling, investigation and treatment may prolong a patient’s decision to seek medical advice. However, an innate aggressive
biological behavior of the tumour in young African women cannot be ruled out\textsuperscript{(20)}. Several investigators evaluated aspects of tumour pathology and found tumours in African Americans were larger in size, more likely to have lympho-vascular invasion and necrotic areas than Caucasian women\textsuperscript{(14,17)}. The dominant histopathological type was IDC. This is similar to histopathologic predominance observed in native African, African American and Caucasians\textsuperscript{(9,14,21-25)}. Whilst 86.7\% of our patients presented with IDC only 1.6\% had intraductal type. There was a large difference between the proportions of cases with invasive (86.7\%) versus intraductal disease (1.6\%) which is likely to reflect a high rate of late presentation. A study by Page et al (1995) demonstrated that the majority of invasive ductal carcinoma cases start out as intraductal disease and this progression typically occurs over a long time period. Although the natural history of intraductal carcinoma will vary depending on tumour grade, the authors conclude that the natural history is over 15-25 years\textsuperscript{(26)}.

Classically, Invasive lobular carcinoma (ILC) is diagnosed in older women and is more likely to be estrogen and progesterone receptor positive than invasive ductal cancers\textsuperscript{(27,28)}. Thus, in this study the low percentage of ILC (5\%) observed among RICK’s patients is consistent with younger age and increased receptor negative disease at diagnosis. Other histological subtypes represented a small fraction of sampled population. This could be in part due to the fact that many women present at advanced stages of disease with poorly differentiated carcinomas which may mask distinguishing characteristics of tumour type\textsuperscript{(29)}.

In general, the absence of lymph node involvement suggests that the cancer is very unlikely to have spread systemically and therefore predicts a more favorable long term prognosis. Unfortunately, in line with other evidence of more advanced disease at presentation, the majority of patients (317/497, 63.8\%) in this study had axillary lymph node spread on diagnosis. Almost one third of them were found to have ≥4 lymph nodes involved which is associated with a worse prognosis. However, our figures for axillary involvement are likely to be a lower boundary as the technique for nodal assessment and counting is very poor in the country and assessment of nodal status was not performed in many women. Unfortunately, less effort has been made in earlier studies to assess the number of positive axillary nodes in native Africans women, but one similar study in Nigeria also reported high rates of nodal involvement (78.7\%)\textsuperscript{(12)}. In contrast, Caucasian women exhibit a low rate of nodal metastasis (24\%)\textsuperscript{(14)}. In the United States Furberg et al (2001) have found that Caucasian women were more likely to present with node negative disease (65.1\%) than African Americans (56.7\%)\textsuperscript{(19)}. The highest frequency of breast cancer cases (29.1\%) in our series were presented with ≥4 positive lymph nodes compared to African American (18\%) and white Caucasian (11\%)\textsuperscript{(19)}. There have been several studies investigating predictors of lymph nodes metastasis. Larger tumour size was found to be an independent predictor for node positive disease in many studies\textsuperscript{(30-32)}, but in our study a larger tumour size was highly associated with nodal metastasis (P = 0.000). Lauria et al (1995) has reported a positive correlation between lympho-vascular tumour invasion and axillary lymph node spread\textsuperscript{(33)} and an interesting study by Ficher CJ and colleagues in the UK noted a clear decrease in the incidence of lymph node metastasis with increasing age\textsuperscript{(34)}. These predictive factors fit the aggressive tumour biology in patients of African origin as they are more prone to have larger tumour size, younger age at presentation and lympho-vascular tumour invasion.

Analysis of the tumour size revealed that a primary tumour of >5cm was the most
Breast cancer in Africa Omer EL Faroug H Salim

common (41.9%). In contrast to my report a study in Caucasian women demonstrated that 58% were diagnosed with a tumour size <2cm while only 4.5% presented with tumour size >5cm.19 Again, it is difficult to establish whether this is due biological factors or socio-economic limitations leading to delayed presentation but a study of American women of African descent revealed that they were 2.37 times more likely to present with larger tumour size (>5cm) than Caucasians. A large tumour size together with lymph node involvement has a negative effect on the 5-year survival rate. Carter et al (1989) reported that in breast cancer patients who have a tumour size <2cm in diameter with no lymph node involvement the 5 years survival rate is 96.3% and this declined to 82.2% for patients with 1-3 axillary lymph nodes and 66% for patients with ≥4 positive nodes. The lowest 5-year survival rate of 45.5% was observed in those who had tumours >5cm in diameter along with ≥4 positive nodes.

The extent of cellular differentiation, as assessed by the grading system, was heavily biased towards intermediate or poorly differentiated (86%). This is in line with the previous studies on native Africans from Kenya, Tanzania and Uganda as 80-85% presented with higher grades tumours (II&III) on diagnosis. In addition, Stead et al (2009) reported that African American women also tended to have higher grade tumours on presentation (grade II: 44% and grade III: 48%) only 14.1% of Sudanese women presented with low grade tumours compared to 30.3% in Caucasians. Breast cancer screening programs have been very successful in detecting tumours while they are still of relatively low malignant potential and before they develop more aggressive characteristics that lead to metastasis. This could explain to some extent the high proportion of grade 1 disease in Caucasian women in Western countries. Furthermore, the low incidence of grade 1 observed in our series could be due to factors outlined above e.g. delayed presentation and an absence of screening mammography leading to a progression to a more advanced phenotype prior to detection.

There is also evidence to support an aggressive biological behavior. Ikpatt et al (2002) examined 285 specimens from Nigerian women with breast cancer and compared them to 300 specimens from Finnish women. Nigerian women had multiple features of a poorly differentiated tumour e.g. higher proliferative rate, less tubular differentiation, necrosis, nuclear atypia and high mean apoptotic index compared to Finnish women. The poorly differentiated tumours among African American women were found to be associated with over-expression of cell cycle regulatory genes (cyclin E, p53 and p16) and high mitotic activity, consistent with advanced stage at diagnosis being a consequence of rapid tumour growth rather than just simple delay. The higher tumor grades in our series were found to be significantly associated with larger tumor sizes which may be attributed to the rapid tumor doubling time seen with poorly differentiated tumors (P = 0.000). Estrogen receptor negative (ER-) and progesterone receptor negative (PR-) disease constituted the majority of cases, (72% and 75.7% respectively). This could be explained by factors related to age and reproductive style. Estrogen positive receptor is strongly associated with age, being more prevalent in older postmenopausal women whereas most breast cancer cases in our series were within a young age group. Multiparty, early age at first birth and late menarche are linked with reduced estrogen positive disease which is consistent with the reproductive pattern in Sudanese women who are typically multiparous (average number of children: 4.6 years) and have their first birth at a young age (median: 20.5 years).

A high incidence of ER- and PR- disease was
Mbonde et al (2000) reviewed tumour markers in 60 Tanzanian women with breast cancer: 67% of patients were ER- and 82% were PR-. Similar results were found in Nigerian women by Ikpatt et al (2003). In contrast to my study and previous studies\(^{(21)}\), Adebamowo et al (2008) reported that 67% of Nigerian women who are <50 years of age were ER+ and 62% PR+ while 77% of women who are older than 50 years had ER+ and 65% PR+\(^{(46)}\).

African American women tend to have a little bit low incidence of ER- and PR- 53.5% and 69% respectively compared to our result but overall higher incidence compared to Caucasian women\(^{(47)}\). A high prevalence of ER+ tumours was reported among Caucasians (80%) which contrasts with the 28% observed in this study\(^{(37)}\).

The Surveillance, Epidemiology and End Result Program (SEER) collected data from breast cancer cases across nine geographic regions of the United States. Joslyn et al (2000) evaluated the hormone receptor status of African American and European Americans. In that study 40.1% of African American women had ER- disease compared with 22.9% of European American patients, whereas 47.2% of African American had PR-tumours compared with 32.3 % of European American women\(^{(24)}\). Gukas et al (2008) compared the immunhistrochemical profiles of Nigerian and British women with breast cancer. British women showed higher expression of estrogen receptor than Nigerian women (58.8% vs. 26.5%) but there was no significant difference in progesterone receptor expression between the two populations. In addition to that there were no differences in \(p53\) and \(HER2\) expressions between the two groups\(^{(18)}\). This is supported by another study done by Elledge et al (1994) who found that African American women had more ER-disease than Caucasians, but there were no differences in \(HER2\) and \(p53\) expression between the two populations\(^{(48)}\).

The combined ER-/PR- subset has been widely demonstrated among Sudanese patients, constituting 64.5% of cases while only 16.9% had ER+/PR+. This in line with the previous study done in Kenya where 66% of women with breast cancer had ER-/PR-tumours\(^{(10)}\). Burson et al 2010 found 49% of Tanzanian women had ER-/PR- tumours\(^{(49)}\). In contrast the majority of tumours diagnosed among Caucasian women were ER+/PR+ tumours (54.8%) while only 27% had ER-/PR- tumours\(^{(19)}\). Furberg et al (2001) reported that African American women have a twofold increased risk of ER-/ER- tumours\(^{(19)}\). ER-/PR+ tumours constitute 7.4% of studied cases. This is a biologically unexplained state, and has been considered as false negative ER test due to poor processing and fixation or may due to ER variants that cannot demonstrated by immunohistochemistry test because of an absence of a ligand binding domain. A trial of hormonal therapy may be successful in such patients.

In 2009, a better understanding of breast cancer biology in Sudanese women has provided additional technique for evaluating Her-2 using immunohistochemistry, however the test is still prohibitively expensive and due to an absence of reagents it is available only in a few laboratories and cannot be provided for all breast cancer patients. Fluorescent in situ hybridization (FISH) is the best technique for evaluating HER-2 status because of its reliability and reproducibility, but it is more expensive than immunohistochemistry and routinely not feasible in low resource environment\(^{(50)}\).

As mentioned before, HER-2 is a protein that is encoded by a proto-oncogene located in chromosome 17. The prevalence of HER-2+ status in women whose expression status is known is 47.3%. HER-2 status was tested in 279 women and over a third had triple negative (TN) disease.

The prevalence of HER-2+ cases in my study is extremely high compared to the reviewed
studies while the TN prevalence is within the prevalence range in Africa. Recently, Ugiagbe et al (2012) carried out a 5 years retrospective study to observe the occurrence of HER2 over-expression in histologically confirmed breast cancer in Nigerian patients. Of 81 women diagnosed with breast cancer, 9 (10.8%) showed positive expression of Her-2. Roy et al (2011) from Uganda assessed the HER-2 status in 44 cases of breast cancer and found that 11% of patients had HER-2+ disease with most of the positive cases being grade III invasive ductal carcinomas that were weakly positive for estrogen receptor. Also, the author found that 36% of Ugandan women were TN and 69% of this group were ≤50 years of age. Bird et al (2008) and Nyagol et al (2006) reported two different incidence rates for Kenyan women with TN tumours which were 44% and 28% respectively. However, whilst Stead et al (2009) found that the proportion of HER-2+ disease is higher among African Americans compared to Caucasians, other studies by Elledge et al (1994) and Jones et al (2004) found no statistical significant difference in HER-2 expression between African American and European-American women. This disparity is difficult to explain and suggests that a larger more comprehensive study of racial variations in HER2 status is needed. Further targeted studies are needed to tease apart the contribution of intrinsic versus extrinsic factors in accounting for the breast cancer characteristics demonstrated in this series. For example, it would be informative to have a thorough assessment of multiple risk factors for each woman including family history, reproductive history and BRCA mutation status. This could then be correlated with age, stage and grade at presentation. In the longer term, such information could also be related to mortality to establish how the prognostic outcomes compare with current studies across different ethnic groups. As already mentioned, the Sudan is highly ethnically diverse, particularly in the capital. Therefore, knowledge of whether there are subpopulations at higher or lower risk would be valuable. Data from our study will be used to increase awareness of the more aggressive breast cancer features in Sudanese women at presentation and it is now critical to investigate the impact of early detection and treatment via screening on these characteristics.

References
9. Roy I, Othieno E. Breast carcinoma in Uganda microscopic study and receptor
Review Article
Breast cancer in Africa Omer EL Faroug H Salim


Review Article
Breast cancer in Africa Omer EL Faroug H Salim