MEDICAL SCIENCE

# Breast cancer in Sudan, clinical, histopathological and receptors characteristics: A retrospective study

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## ABSTRACT

*Background:* Breast cancer is the leading cause of death globally, the tumor surpassed lung cancer in prevalence. Few studies assessed breast cancer in Sudan. *Objectives:* We aimed to assess breast cancer among women in Khartoum, Sudan. *Methods:* We reviewed 1395 specimens at a retiary pathology center in Khartoum, Sudan from June 2022 to March 2023. A data sheet (excel) was used to collect specimen type and nature of excision, the tumor grade, site and recurrent or multifocal carcinoma. In addition, tumor size, lymph node involvement and distant metastasis were evaluated for tumor classification and grade. Immunohistochemistry was conducted. *Results:* Out of 1395 specimens, 99.6% were invasive ductal carcinoma, more than half were grade II, and 50.5% were on the left. Breast biopsy was the commonest (79.1%) and mastectomy specimen (4.5%) and complete excision was done in 89% of cases. In the present study, stage tumor I (T I) was observed in 17.3 and tumor III (TII) in 54.8%. Estrogen receptor status, progesterone receptor, HER 2 Neu receptor and triple-negative cancer were positive in 47.8%, 32.4%, 26.1% and 32.3% respectively while Ki67 expression was >50% in 40.2%. *Conclusion:* The majority of breast cancer in Sudan was invasive ductal carcinoma with lower estrogen, progesterone and Human Epidermal Growth Factor Receptor 2 (HER 2 Neu receptor) positivity, while triple-negative and Ki67 were higher. The patients presented late to the healthcare system. Further retrospective studies focusing on genotyping are important for a proper management decision.

**Keywords:** Breast cancer, surgical, histopathological characteristics, Sudan.

## 1. INTRODUCTION

Breast cancer was the second cause of women suffering and premature death after bronchial carcinoma, genetic and environmental factors are to blame. However, recently breast cancer displaced bronchial cancer to the sidetrack. The causes can be nonmodifiable including family history, genes, race and ethnicity, in addition to modifiable risk factors like alcohol consumption,

female reproductive factors, exogenous hormones and lack of exercise (Coughlin, 2019; Cao et al., 2021). Through sex hormones: The young at menarche, parity and older age at the first pregnancy can substantially influence breast cancer incidence (De-Bono et al., 2018). Importantly, triple-negative breast cancer is considered a distinct variant according to recent studies (Derakhshan and Reis-Filho, 2022).

The global cancer statistics reported that there are 19 million new cases and 10 million died due to cancer in the year 2020 although breast cancer among women surpassed lung cancer in prevalence. However, lung cancer is the commonest among men (Sung et al., 2021). There are 2.3 million new Breast cancer and 685,000 deaths in the year 2020, the highest incidence was reported in New Zealand, The USA, Europe and Australia, while a lower report was observed in Africa and some Asian countries. There was no difference in mortality across the globe, but transitioning countries bear the greatest burden compared to transitioned countries (Arnold et al., 2022). The projection for new cases and death is three million new cases and one million deaths every year by the year 2040. Early diagnosis and timely treatment have been set as goals to reduce mortality from breast cancer (Anderson et al., 2021).

Cancer in Sudan is largely ignored despite the increasing rate; migration from rural areas to central cities and the adoption of an unhealthy lifestyle are plausible explanations, in addition to the increased aging population (Elamin et al., 2015). Breast cancer affects 3.9 cases per 100,000 women with invasive breast carcinoma of no special type being the commonest. North Sudan reported the highest incidence (Elbasheer et al., 2019). Although breast cancer is lower in Sub-Saharan Africa, death among women with breast cancer is higher compared to the developed world. Lack of awareness, poverty of screening methods and late presentations explained the high mortality (Elgaili et al., 2010).

Hormonal receptors are not routinely identified in developing countries due to cost and hormone therapy is usually prescribed without previous determination. In addition, most research from Africa reported negative progesterone and estrogen receptors in females with breast cancer (Nyagol et al., 2006; Mbonde et al., 2000). Therefore, this study aimed to assess carcinoma of the breast among women in Sudan, clinical and histopathological characteristics.

## 2. METHODS

This retrospective study was conducted at a central histopathology center in Khartoum State, Sudan. The center receives specimens from governmental and private clinics all over the country. All the female patients' records (number 1395) were approached during the period from June 2022 to March 2023. The privacy of the patients was strictly conserved according to Helsinki Declaration. The local ethical committee approved the research.

A data sheet (excel) was used to collect the tumor grade, site and recurrent or multifocal carcinoma. The specimen type and nature of excision (complete or partial) were reported. The tumor, lymph nodes or distant metastasis was recorded based on the tumor size, the extent of lymph node involvement and distant metastasis (TNM classification).

**Immunohistochemistry**

Avidin–biotin–peroxidase complex method was used. The specimen was fixed in formalin and paraffin-embedded and the Fisher Scientific Super frost slides (positively charged) were used. The specimens were deparaffinized and rehydrated in graded ethanol and steamed in 0.01 mol/L citrate buffer (pH 6.0) in a water bath at 95°C for 10 minutes to retrieve the antigens. Blocking for endogenous peroxidase in three percent hydrogen peroxide mixed with methanol. The non-specific binding in tris-buffered saline containing saponin (0.2), Triton X-100 (0.3%) and 0.5% blocking agent. The specimen was then incubated at 4 degrees centigrade overnight.

For this study, the following antisera were used:

Novocastra Ltd, Progesterone receptor antibody (IA6) at 1:40 dilution.

ID5, monoclonal mouse anti-human antibody (ER) at 1:25 dilution

Vector laboratories biotinylated horse anti-mouse.

Vector laboratories goat anti-rabbit secondary antibodies.

The slides were independently reviewed and the receptors were reported as negative or positive depending on immunostaining.

**Ethical consideration**

The records were approached in a confidential manner with strict adherence to the Declaration of Helsinki. No patient's identities were taken. The information collected was used only for this research. We obtained ethical approval from Elnoor Polyclinic; Omdurman, Sudan (ref. number E-2021-001, dated, April 21, 2021).

**Statistical analysis**

The excel datasheet was entered in the Statistical Package for Social Sciences (IBM, version 20, New York). The data were presented as numbers and percentages.

## 3. RESULTS

In the present study, 99.6% was invasive ductal carcinoma followed by micro-invasive ductal carcinoma in 0.2%, more than a half were grade II, no side preference was observed (50.5% on the left breast and 49.1% on the right, while only 0.3% were bilateral). Recurrent and multifocal carcinoma was very rare, 2.1% and 0.9% respectively (Table 1).

**Table 1** Diagnosis, grade, and location of breast cancer in Sudan

| Character | No% |
|---|---|
| Diagnosis | |
| Invasive ductal carcinoma | 1389 (99.6%) |
| Micro- Invasive ductal carcinoma | 03 (0.2%) |
| Metastatic-invasive ductal carcinoma | 02 (0.2%) |
| Mixed ductal and lobular carcinoma | 01 (0.1%) |
| Grade | |
| Grade one | 143 (12.1%) |
| Grade two | 601 (50.7%) |
| Grade three | 440 (37.1%) |
| Grade four | 001 (0.1%) |
| Tumor location | |
| Right | 602 (49.1%) |
| Left | 619 (50.5%) |
| Bilateral | 004 (0.3%) |
| Recurrent carcinoma | 029 (2.1%) |
| Multifocal carcinoma | 013 (0.9%) |

Regarding the mode of diagnosis, breast biopsy was the commonest (79.1%); followed by mastectomy specimens (18.6%), while mastectomy and axillary clearance specimens constituted 2.4%. Importantly complete excision was done in 89% of cases (Table 2). In the present study, stage T I was observed in 17.3 and TII in 54.8%. The different TNM stages were depicted (Table 3).

**Table 2** Diagnostic approach of breast cancer

| Character | No% |
|---|---|
| Diagnosis | |
| Breast biopsy | 1102 (79.1%) |
| Mastectomy specimen | 260 (18.6%) |
| Mastectomy and axillary clearance specimen | 33 (2.4%) |
| Specimen | |
| Breast | 1163 (83.4%) |
| Breast and lymph nodes | 232 (16.6%) |
| Completely excised | 1241 (89%) |

Estrogen receptor status was positive in 47.8%, followed by progesterone receptor in 32.4% and human epidermal growth factor receptor 2 (HER 2 Neu) statuses in 26.1%. In the current study, triple-negative cancer was found in 32.3% (Table 4). In this study, Ki67 expression was evenly distributed across grades (Table 5). In the present study, premenopausal dominance was obvious (72%) (Figure 1).

**Table 3** TNM classification of breast cancer in Sudan

| Classification | No % |
|---|---|
| T1N0Mx | 37 (5.8%) |
| T1N1Mx | 21 (3.3%) |
| T1N2Mx | 12 (1.9%) |
| T1N3Mx | 8 (1.3%) |
| T1NxMx | 32 (5.0%) |
| T2N0Mx | 69 (10.9%) |
| T2N1M0 | 1 (0.2%) |
| T2N1Mx | 85 (13.4%) |
| T2N2Mx | 65(10.3%) |
| T2N3Mx | 40 (6.3%) |
| T2NxMx | 68 (10.7%) |
| T3N0Mx | 23 (3.6%) |
| T3N1Mx | 30 (4.7%) |
| T3N2Mx | 18 (2.8%) |
| T3N3Mx | 28 (4.4%) |
| T3N6Mx | 1 (0.2%) |
| T3NxMx | 7 (1.1%) |
| T4N0Mx | 8 (1.3%) |
| T4N1Mx | 12 (1.9%) |
| T4N2Mx | 18 (2.8%) |
| T4N3Mx | 22 (3.5%) |
| T4NxM1 | 1 (0.2%) |
| T4NxMx | 20 (3.2%) |
| TxN0Mx | 5 (0.8%) |
| TxN2Mx | 1 (0.2%) |
| TxN3Mx | 2 (0.3%) |

**Table 4** Estrogen and progesterone receptors status among women with breast cancer in Sudan

| Character | No % |
|---|---|
| Estrogen receptor status | |
| Positive | 297 (47.8%) |
| Negative | 324 (52.2%) |
| Progesterone receptor status | |
| Positive | 203 (32.4%) |
| Negative | 424 (67.6%) |
| HER 2 neu receptor status | |
| Positive | 160 (26.1%) |
| Negative | 453 (73.9%) |
| Triple negative cancer | |
| Positive | 196 (32.3%) |
| Negative | 410 (67.7%) |

**Table 5** Ki67 expression among women with breast cancer in Sudan

| Ki67 expression | No % |
|---|---|
| 1.00 | 4 (5.3%) |
| 2.00 | 5 (6.6%) |
| 4.00 | 1 (1.3%) |
| 5.00 | 9 (11.8%) |
| 10.00 | 11 (14.5%) |
| 15.00 | 7 (9.2%) |
| 20.00 | 8 (10.5%) |
| 25.00 | 1 (1.3%) |
| 30.00 | 7 (9.2%) |
| 40.00 | 7 (9.2%) |
| 50.00 | 3 (3.9%) |
| 60.00 | 7(9.2%) |
| 70.00 | 2 (2.6%) |
| 80.00 | 2 (2.6%) |
| 90.00 | 2 (2.6%) |

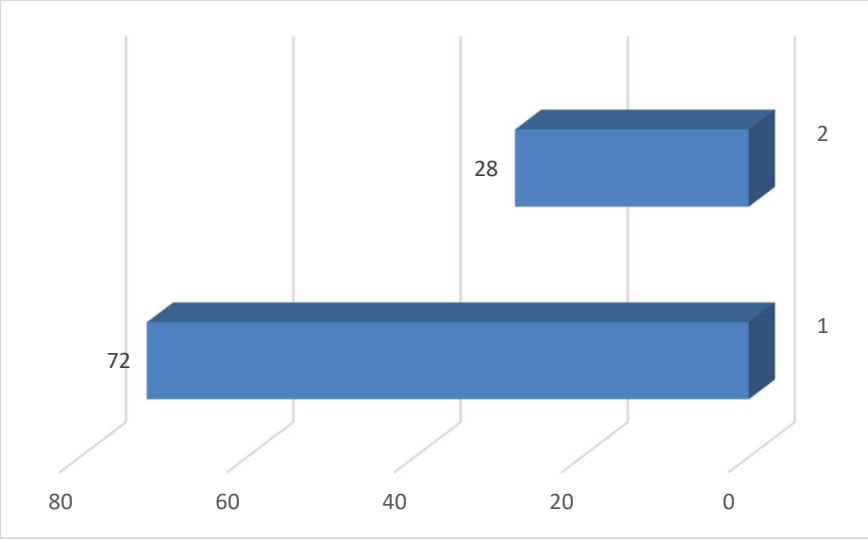


**Figure 1** Menopausal status among Sudanese women with breast cancer

## 4. DISCUSSION

In the present study, the majority were diagnosed with invasive ductal carcinoma and late presentation in line with a previous study conducted in Central Sudan (Elgaili et al., 2010). In the present study, 72% of women with breast cancer were premenopausal, similar previous studies among black women in Africa (Anyanwu, 2000) and America (Carey et al., 2006) observed that the majority of females with breast cancer presented before menopause (age <50 years). Bowen et al., (2008) conducted a study in the United Kingdom and found that breast cancer affects young African women; similarly, few American Women with breast cancer were younger than fifty years (Stringer-Reasor et al., 2021). Child bearing at an earlier age and multiparty might explain the findings (Pathak et al., 2000; Palmer et al., 2003).

Educational interventions are highly needed in terms of raising awareness about breast cancer and self-examination is highly needed. Patient navigation connected to the local community needs, integration of lay community workers into the healthcare system and free availability of screening programs is vital to reduce the breast cancer burden in Sudan (Stringer-Reasor et al., 2021). In the current study, 47.8% were estrogen receptor-positive and 32.4% were positive for progesterone receptors, the current findings were lower than a study conducted in Pakistan (Lateef et al., 2017) in which 61% and 55% were estrogen and progesterone receptors positive respectively.

However, the Hormone receptor and human epidermal growth factor receptor 2 (Her2neu) were similar in the two studies (26.1% versus 23%). Triple-negative cases were higher (32.3%) than the results observed among women in Pakistan (17%). The commonest histopathological type was ductal carcinoma (invasive variant) and 49.1% involved the right breast in line with the findings of Mutar et al., (2019) from Iraq. However, recurrence was lower in our sample (2.1% versus 12%) and all types of receptors were less positive in our findings. In the present study, 87.8% of women presented with class II and III, while stage IV was reported in only a minority, our findings were slightly better than Mutar et al., (2019) who found grade II & III in 70.3% and grade IV in 25%.

Lack of awareness and religious issues might explain the late presentation (Mutar et al., 2019). Importantly, triple-negative breast cancer constituted nearly one-third of breast cancer among women in Sudan. Triple-negative breast cancer had a poor prognosis and mortality is double compared to receptor-positive counterparts (Odongo et al., 2015). To complicate the matter further, triple-negative breast cancer affects germline including breast cancer gene (BRCA) mutations, genomic predictors and epidemiologic characteristics of molecular types are very difficult in a resource-limited country like Sudan. In addition, intratumor genetic heterogeneity and basal gene expression are greater among triple receptor-negative diseases (Howard and Olopade, 2021).

In the present study, Ki67 expression was <14% in 39.5% of specimens, 19.7% between 15 and 24%, another 19.7% were 25-50%, and the rest > 50 percentage. Ki67 expression and breast cancer were discussed controversially, in addition, no agreement about the cut-off values and inter-laboratory validity (Keenan et al., 2015). However, a meta-analysis included those randomized trials (Luporsi et al., 2012; Haroon et al., 2013) and observational studies (Petrelli et al., 2015; De-Azambuja et al., 2007) showed that using 25% as high cutoffs, Ki67 was associated with poor prognosis and tumor recurrence.

In the present study, 40.8% of Ki67 were above 25% indicating that women with breast cancer in Sudan are at higher risk of mortality. However, we did not assess prognosis, which was a major limitation of our study, other limitations were the retrospective nature and the study being conducted at a single central laboratory. Thus, the current result cannot be generalized for the whole country.

## 5. CONCLUSION

This study showed that women with breast cancer in Sudan were younger, presented with late invasive ductal carcinoma, low estrogen and estrogen receptors expression and higher triple negative receptors. Ki67 was relatively higher indicating a predisposition to poor prognosis and higher mortality. Further studies focusing on genomic characteristics are suggested.

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**Author Contributions**

KA and HM: Concept and design and introduction drafting. SA: Concept and drafted the Methods. AK: Data analysis and results drafting. HM: Discussed the results. All authors critically revised the manuscript and approved it before submission

**Informed consent**

Not applicable.

**Approval**

The study was approved by the Medical Ethics Committee of Elnoor Polyclinic, Omdurman, Sudan (Ethical approval code, E-2021-001).

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**Conflict of interest**

The authors declare that there are no conflicts of interests.

**Data and materials availability**

All data associated with this study will be available based on the reasonable request to corresponding author.

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