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Profile and Features of Breast Cancer in HIV Positive and Negative Patients at Mankweng Academic Hospital, Limpopo Province, South Africa

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ABSTRACT

Background: HIV and breast cancer are a major global burden of disease for women. There were 35 million people infected with HIV in 2013, over 70% of whom lived in sub-Saharan Africa. Breast cancer is the leading form of cancer affecting South African women. The main aim of this study was to better understand the profile and features of breast cancer in HIV-positive and negative patients in the Limpopo province, South Africa.

Methods: This is a retrospective cross-sectional descriptive quantitative study designed to analyse the profile of patients with breast cancer who attended Mankweng Breast Oncology Clinic from July 2020 to December 2021.

Results: From a total of 205 patients, the HIV-positive group consisted of 43 patients and the HIV-negative group of 162 patients. The age range was 20-90 years, the mean age was 51, the mean age of HIV-positive group was 46.6(30-79) years and HIV-negative 52.4 (20-90) years. Early-stage cases (0, I & II) included 46 patients and late stage cases (III & IV) included 159 patients. In the HIV-negative group (162), 36 patients (22%) presented with early stages and 126 (78%) in the late stages. The HIV-positive group (43) consisted of 10 (23%) patients in the early stage and 33 (77%) in the late stage.

Conclusion: In this study, the mean age of HIV-positive patients was lower than the mean age of HIV-negative patients (46.6 vs 52.4). Triple negative molecular subtype breast cancer was more frequently present in HIV-positive patients than in HIV-negative patients (24.2% vs14.4%). HIV-positive patients demonstrated a higher grade 3(47%), while HIV-negative patients had a higher grade 2(62%).

INTRODUCTION

HIV and breast cancer are a major global burden of disease for women.[1,2] There were 35 million people infected with HIV in 2013 and over 70% of them lived in sub-Saharan Africa (SSA).[3] In South Africa (SA) in 2021, the prevalence of HIV was 19.5% in the adult population (15 - 49 years old) and 8.2 million (13,7%) people were living with HIV.[4] Lifetime risk of developing cancer in patients with HIV is higher, when compared with HIV-negative patients.[5,6] Breast cancer remains the most common cancer in many parts of the world,[7,8] and it is also the leading type of cancer affecting SSA women.[9] In SA in 2019, breast cancer was on the top list (23.22%) among all female cancers.[8] Breast cancer occurs usually in elderly white ethnic groups.[10] However, in SA, breast cancer displays itself in the younger age group in an advanced stage.[1] A South-Western Nigerian study found that most affected patients with breast cancer were aged 50-59 years.[11] A study done in Limpopo,

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in SA, showed that 38% of breast cancer patients were younger than 50 years.[12] Tygerberg Academic Hospital in SA reported a median age at presentation of 56 years for patients without HIV compared with 42 years for patients with HIV (P<001).[13] Edge *et al*. found that patients with breast cancer in SSA usually appear to be at a younger age, irrespective of HIV infection.[14] Conversely, another study in Sub-Saharan Africa found no association between breast cancer and HIV infection.[15] In African countries, over 70% of breast cancer patients usually present in an advanced stage.[1,15,16] In Limpopo province, SA, the majority of patients (76%) presented with a late stage disease.[17] There are no proven conclusive relations established between HIV, tumor stages and grades, tumor markers or molecular subtypes of breast cancer, and further research is required.[1,15,18] There has been no study on the profile of breast cancer patients with HIV in the Limpopo province. Our study is the first to study the profile and features of breast cancer (stage, hormonal status, grading and molecular subtype) in HIV positive and negative patients in Limpopo province, and to identify any differences between these two groups.

METHODS

This is a retrospective cross-sectional descriptive quantitative study designed to analyse the profile of patients with breast cancer who attended Mankweng Breast Oncology Clinic for 18 months from July 2020 to December 2021. All patients with histologically confirmed breast cancer were included in this study. Patients with missing information and cases in which HIV (human immunodeficiency virus) status was not known were excluded. Immunohistochemistry estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 and Ki67 index were not considered in some cases, because tissue specimens appeared insufficient, or histology investigations were done in private laboratories. The analysis of immunohistochemistry was performed for all those patients whose histology reports provided their immunohistochemistry status. The Mankweng Breast Oncology Clinic registers were used as a starting point for data collection. Patients' files and histology reports were retrieved from the hospital archive to compile the data sheets. Data collection sheets comprised gender, age (age was categorized into two groups: <50 and >50 years in addition to actual age), histological type of breast cancer, estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), Ki67 index, grading (according to the Nottingham modification of the Bloom-Richardson system),[19] molecular subtype, stage of cancer, and HIV status. Stages at presentation were grouped into early (0, I & II) and late (III & IV) stages. Molecular subtypes of breast cancer were classified based on immunohistochemistry into Luminal A (ER+/PR+/HER2-/low Ki-67), Luminal B (ER+/PR+/HER2-/+/high Ki-67), HER2-overexpression (ER-/PR-/HER2+) and triple-negative breast cancers (TNBCs; ER-/PR-/HER2-).[20]

Statistical analysis

Continuous variables were expressed as mean and standard deviation. Categorical variables were described as proportions and frequency. The comparison between normally distributed variables was made by performing one-way Analysis of Variance (ANOVA) to compare the means between more than two groups. The association between categorical variables was done using the Chi-square test. P-value of less than 0.05 was considered as statistically significant. The statistical software package IBM SPSS version 28 was used for data analysis.

Study setting

Mankweng Hospital Breast Oncology unit is situated in Turfloop/Sovenga, Limpopo Province, South Africa. It is a tertiary hospital providing breast oncology services among other services, to all the population of the Limpopo Province.

RESULTS

A total of 205 patients met the inclusion criteria of this study. The HIV-positive group consisted of 43 patients and the HIV-negative group of 162 patients. There were 201 female and 4 male patients. The age range was 20-90 years, the mean age was 51, the mean age of HIV-positive group was 46.6 (30-79) years and the age of HIV-negative was 52.4 (20-90) years.

Stages

Early-stage cases (0, I &II) comprised 46 patients, and late stage cases (III & IV) 159 patients. In the HIV-negative group (162), 36 patients (22%) presented with early stage disease and 126 patients (78%) presented with late-stage disease. The HIV-positive group (43) consisted of 10 (23%) patients in the early stage and 33 (77%) in the late stage. The details are presented in Table 1.

DISCUSSION

This study evaluated 205 breast cancer patients, among whom 43 (21%) were HIV-positive, in keeping with the national estimated adult population.[4] The age range of investigated patients was 20-90 years (mean age = 51 years). HIV-negative group

Table 1. Summary of the results by HIV status in patients diagnosed with breast cancer

		HIV Negative	HIV Positive	Total
	Description	Freq.	Freq.	Freq.
Gender	Female	160	41	201
	Male	2	2	4
	Total	162	43	205
Age<50 & >50	<50	81	28	109
	>50	81	15	96
	Total	162	43	205
Stage	0	1	1	2
	I	2	1	3
	II	33	8	41
	III	120	33	153
	IV	6	0	6
	Total	162	43	205
Type of cancer	Ductal carcinoma in situ	1	1	2
	Invasive carcinoma (NST)*	157	41	198
	Lobular carcinoma	1	1	2
	Papillary carcinoma	3	0	3
	Total	162	43	205
Grading	1	5	7	12
	2	84	11	95
	3	46	16	62
	Not done	27	9	36
	Total	162	43	205
Hormone ER**	Negative	42	16	58
	Positive	99	18	117
	Not done	21	9	30
	Total	162	43	205
Hormone PR***	Negative	45	16	61
	Positive	96	18	114
	Not done	21	9	30
	Total	162	43	205
HER 2****	Borderline	31	8	39
	Negative	58	14	72
	Positive	49	12	61
	Not done	24	9	33
	Total	162	43	205
Molecular type	Her2+	10	4	14
	Luminal A	36	7	43
	Luminal B	73	14	87
	Triple negative	20	8	28
	Not done	23	10	33
	Total	162	43	205

*NST:(No special type: **ER: estrogen Receptor: ***PR: Progesterone receptor, HER 2: Human Epidermal growth factor receptor 2. In the HIV-negative group patients, there are equal numbers of patients (n 81; 50%) below and above 50-year age. On the other hand, HIV-positive group patients are 65% below the age of 50 and 35% above the age of 50. HIV-positive patients with breast cancer are younger (mean of 46.65 years) compared to HIV-negative patients (mean of 52.38 years). There is a significant difference between the age of HIV-positive and negative patients diagnosed with breast cancer (P=0.0181<0.05).

patients had an equal number of patients (n = 81; 50%) below and above 50 years of age.

On the other hand, HIV-positive group patients showed 65% below the age of 50 and 35% above the age of 50 (Figure 1).

HIV-positive patients with breast cancer are younger (mean of 46.65 years) compared to HIV-negative patients (mean = 52.38 years). There was a significant difference between the age of HIV-positive and negative patients diagnosed with breast cancer (P=0.0181<0.05). Nikoli van Zyl *et. al.* mentioned a similar finding in Dr. George Mukhari Academic Hospital, Breast Clinic, Ga-Rankuwa, South Africa. [21] Reddy *et al.* also stated that HIV-positive patients with breast cancer were statistically younger than HIV-negative patients (P < 0.001).[6] Rohini K *et al.* found in their study that HIV-infected individuals tended to present at a younger age at

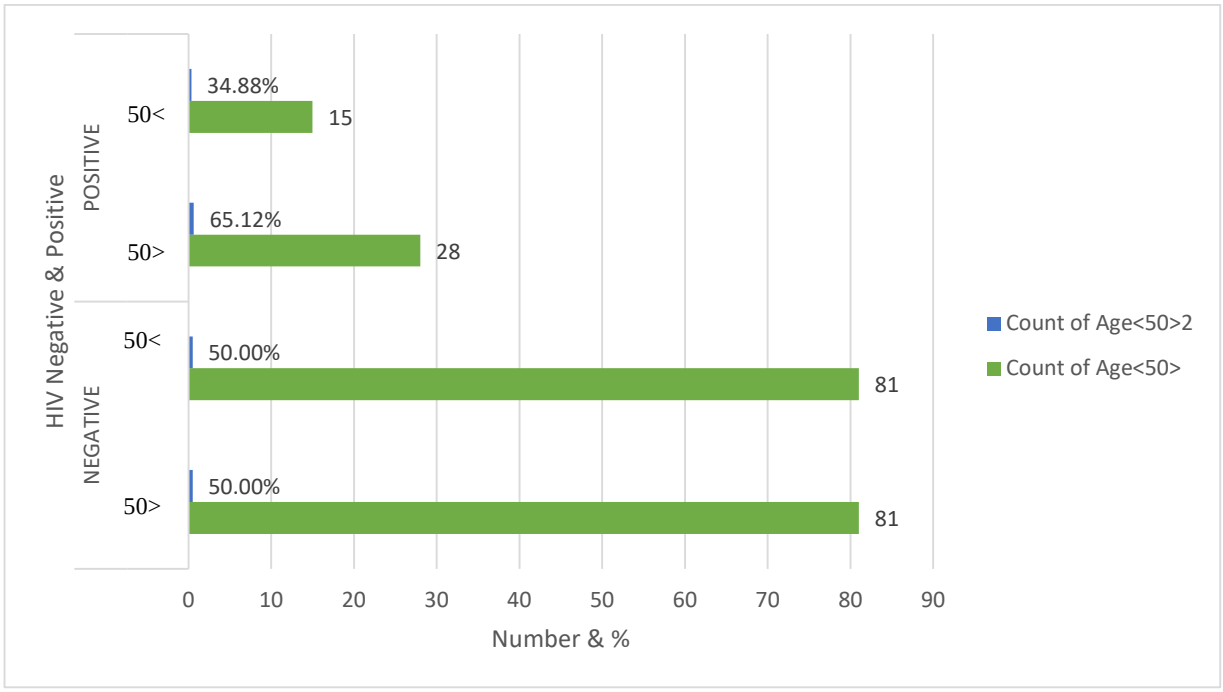

Figure 1. Age<50 & >50 of HIV negative & positive group patients

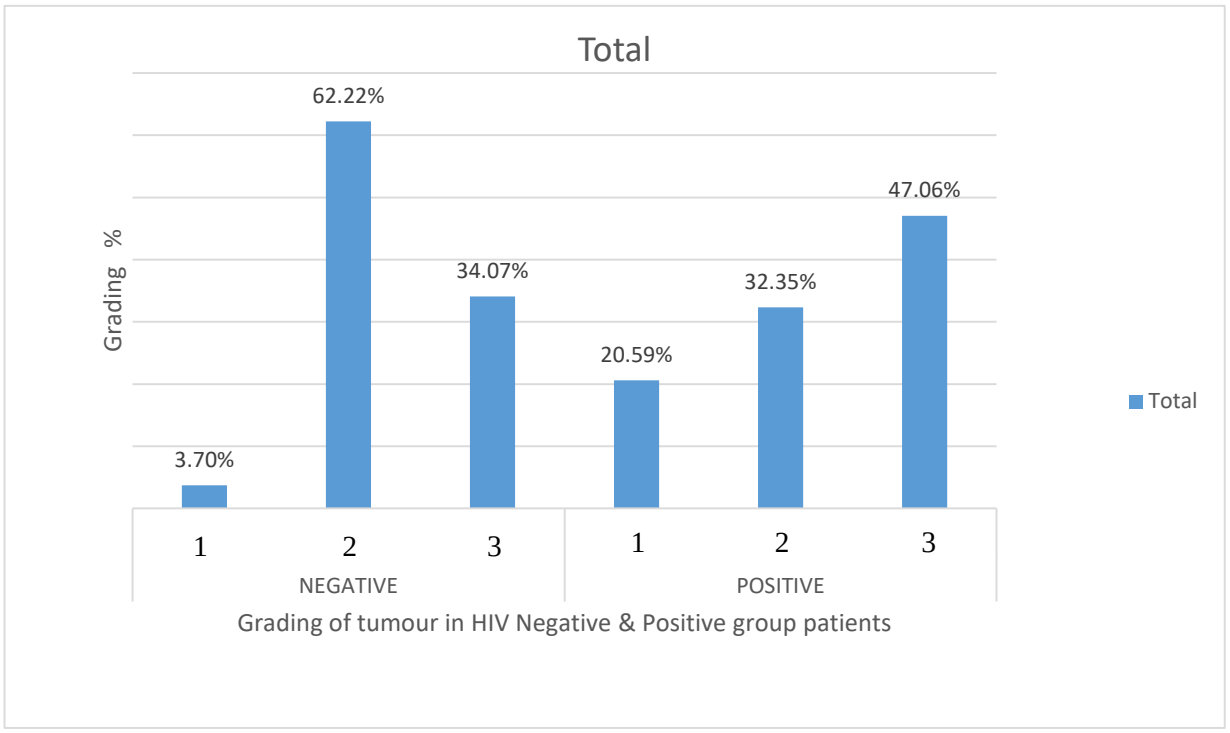

Figure 2. Grading the tumor in HIV negative & positive patients

initial diagnosis compared to HIV uninfected individuals.[22] A few other studies confirmed also that breast cancers occur earlier among HIV-positive patients in comparison to their HIV-negative counterparts.[23,24,25]

Invasive ductal carcinoma (no special type) is the most common histological type of breast cancer in this study 197;(96.1%). In many parts of sub-Saharan Africa, invasive ductal carcinoma (IDC) is more common. Kohler *et al*. reported that IDC was the most common (86%) histological type in Malawi. [26] Another study in south western Nigeria found 88.9% invasive ductal carcinoma of no special type from a 10-year retrospective study.[11] A similar trend was found among the women in Limpopo, South Africa.[12] No significant difference in the histological subtype of breast cancer was found between HIV-positive & HIV-negative patients.

In our study, most (33) of HIV-positive patients presented with breast cancer in stage III (76.7%) and 8 patients (18.6%) with stage II. Also, 20.4% of HIV-negative patients were in stage II and 120 (74.1%) patients in stage III. Fewer patients were in stages I and 0 (2.3%). Therefore, in our study, there were no significant associations between the stage and HIV status. Other studies showed similar results with regards to the stage of the disease.[1,7,15] A few studies in the literature have reported that HIV does not affect the stage, grade, tumor sub-type, and survival of patients with breast cancer.[1,18]

Concerning tumour biology with grading in our study, HIV-positive patients were mostly grade 3 (47%) cases, while HIV-negative patients more often were of grade 2 (62%) (Figure 2).

Some other studies have reported that breast cancers among HIV-positive patients in comparison to their HIV-negative counterparts were more aggressive in tumor biology.[24,25,26]

Regarding receptor status in this study, 57% breast cancer patients showed the presence of oestrogen receptor (ER), which was similar to the finding in Botswana.[22] In our study, HIV-positive patients had a much lower oestrogen receptor (42%) compared to HIV-negative patients (61%). With regard to molecular classification in our research finding (Figure 3), Luminal B Molecular subtype was more frequent in both HIV-positive and HIV-negative patients in this study.

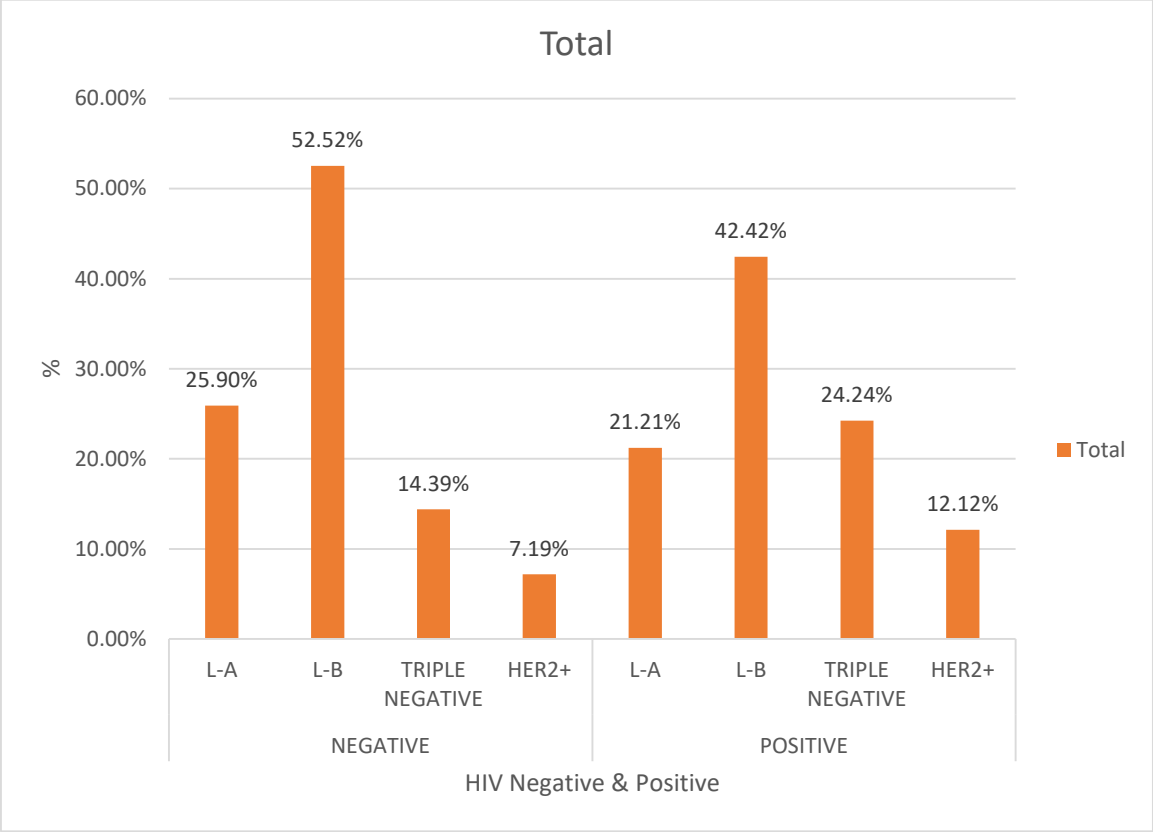

Figure 3. Molecular type in HIV negative & Positive patients

However, triple negative was more frequent in HIV-positive group patients (24.2%) than in HIV-negative patients (14.4%). HER 2 overexpression was 12.1% in HIV positive patients and 7.2% in HIV negative patients. Triple negative (TN) breast cancer was found in 28 patients in this study. The majority of these TN patients presented with grade 3 cancer at 67.9%, grade 2 at 32.1% and no patient presented with triple negative grade 1 breast cancer. This indicates the aggressive nature of this histological subtype. Fragomeni *et al.* stated that triple negative subtype breast cancers were revealed in younger women with the age range of 40 - 60 years.[27] The prevalence of TN in Botswana was reported to be 21.3%.[22] and patients presented usually in an advanced stage of the disease.[28]

CONCLUSION

In this study, the mean age of HIV-positive patients was lower than the mean age of HIV-negative patients (46.6 vs 52.4). Triple negative molecular subtype breast cancer was more present in HIV-positive patients than in HIV-negative patients (24.2% vs 14.4%). HIV-positive patients

demonstrated a higher grade 3 (47%), while HIV-negative patients had a higher grade 2 (62%). Both HIV-positive and negative group patients presented in more advanced stages. Screening for breast cancer is required to be commenced in the earlier age of younger patients, particularly for HIV-positive female patients.

CONFLICT OF INTEREST

None declared.

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