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ORIGINAL ARTICLE

Breast Cancer Co-Morbidity Among People Living with HIV infection in Southern Nigeria

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Abstract

Introduction: Breast cancer is witnessing increasing detection in Nigeria following more awareness and access to medical care. It is predominantly observed in the same group (women of reproductive age) with the highest prevalence of human immunodeficiency virus infection. This study focused on breast cancer and HIV infection co-morbidity with regards to cytopenia during a follow-up period.

Methods: This follow-up study enrolled 50 persons living with HIV (PLWH) and accessing care at the University of Calabar Teaching Hospital at Calabar, Southern Nigeria. Breast cancer co-morbidity and other clinical information were retrieved from patients' folders. Blood sample was appropriately obtained from each subject at intervals of six months starting from the time of diagnosis and analysed by automation for blood cell and CD4 counts. Frequencies, student T-test was used for analysis of data. Statistical significance was drawn at a $p \leq 0.05$.

Results: Mean values of haemoglobin concentration, CD4 count and platelet count were significantly lower among PLWH compared to control subjects. The prevalence of HIV infection and breast cancer co-morbidity was observed to be 6%. There was reduction in the prevalence of cytopenia as duration of therapy progressed. Anaemia and immunosuppression were not completely addressed after one year of therapy.

Conclusion: The study observed 6% of breast cancer co-morbidity in HIV infection among women of reproductive age. Unresolved cytopenia remains a challenge in HIV infection, particularly with breast cancer co-morbidity, even after a year of adhering to antiretroviral therapy.

Key words: HIV infection, breast cancer, cytopenia, co-morbidity

Introduction

The medical management of human immunodeficiency virus (HIV) infection has improved tremendously since its recognition as a distinct infectious condition. Advancement in its treatment occasioned by the emergence of highly active antiretroviral therapy (HAART) has to a great extent stabilized the infection epidemiologically and clinically(1-3). This progress notwithstanding, persisting morbidity indicators have been reported among infected persons on therapy(4-7). In fact, haematological complications of HIV which include cytopenia of all major cell lines were recognized shortly after the first description of AIDS cases, and are still being reported despite advancement in therapy(8-11). Among several reported derangements, anaemia has been observed to greatly influence quality of life, disease progression and survival(12-14). Other aspects of cytopenia such as leukopenia and thrombocytopenia are reportedly often asymptomatic(8,10). Generally, disease progression associates with increasing severity and prevalence of these derangements.

So far, antiretroviral therapy has greatly altered the course of HIV infection from a global pandemic to a manageable health condition by arresting viral replication but reversal of associated morbidities remains a great concern. Several perspectives have been explored towards resolving this challenge, including investigations on potential adverse effects of some antiretroviral agents as well as the issue of comorbidity. While the former cuts across the different categories of infected persons using an identified antiretroviral agent or combination, comorbidity may differ according to sub-groups and settings. In sub-Saharan Africa for instance, tuberculosis has been reported as a common comorbidity to HIV infection with greater degree of haematological derangements (15,16). Such an observation has generated the interest to investigate other comorbidities in the Nigerian setting.

At a national prevalence of 1.4% among persons of reproductive age and an observed female preponderance, adult females constitute a vulnerable group with regards to HIV infection (2). The vulnerability of adult females with regards to health remains an issue of concern particularly within the study setting. Maternal healthcare in Southern Nigeria is yet to attain optimal coverage even at basic medical care level (17,18). In addition, breast cancer has been recognized an important maternal health challenge owing to its significant morbidity and mortality rates(19,20). Its detection in Nigeria has been increasing following more awareness and access to medical care(21,22). Although breast cancer is not an acquired immune deficiency syndrome (AIDS) – defining cancer, cancer-related morbidity and mortality in HIV infection is an area of interest(23-27, 7)[,]. Thus, having two medically important conditions occurring more in an identified group calls for research interest even if neither condition has been reported to be predisposed to the other. The effort is to appreciate in comparative terms the proportion of subjects with cytopenia and the degree to which therapy impacts on these proportions.

Materials and methods

This follow-up study enrolled 50 females of reproductive age living with HIV and accessing care at the University of Calabar Teaching Hospital at Calabar, Southern Nigeria. Ethical approval was obtained from the Health Research and Ethics Committee (HREC) of University of Calabar Teaching Hospital. Informed consent was obtained from each participant enrolled in the research and confidentiality was maintained. Breast cancer co-morbidity and other clinical information were retrieved from patients' folders. Participants were recruited at diagnosis and followed up through a one-year period. They were on Tenofovir/ Lamivudine backbone in combination with either Efavirenz or

Dolutegravir. Adherence to therapy was encouraged and ascertained during the study period. Subjects with co-morbidities other than breast cancer were not part of the study. Equal number of age-matched sero-negative apparently healthy females were also recruited to serve as normal control group for the initial assessment of derangements.

Blood sample was appropriately obtained from each subject at intervals of six months starting from the time of diagnosis for testing of blood cell and CD4 counts. These were respectively determined by automation using Sysmex Kx-21N and Cyflow Counter (Sysmex Corporation, Japan). Data generated were entered into Microsoft excel spreadsheet and analysed using Statistical Package for Social Sciences (SPSS) software version 22.0. Frequencies, student T-test was used for analysis of data. Statistical significance was drawn at a $p \leq 0.05$.

Results

The study enrolled fifty participants at their respective time of diagnosis. At the end of the follow-up period of one year for each participant, only 39 persons could be assessed. Details of this distribution and the factors that contributed to it are shown in Table 1. The measures of cytopenia at diagnosis between PLWH and control subjects are shown on Table 2. Mean values of red cell parameters, as well as lymphocyte, CD4 and platelet counts were significantly lower among PLWH compared to control subjects while platelet distribution width was higher in PLWH compared to controls.

The prevalence of HIV infection and breast cancer co-morbidity was observed to be 6% (Figure 1). Table 3 shows reduction in the prevalence of cytopenia as duration of therapy progressed. Persisting proportions of anaemia (42.1%) and to a lesser degree immunosuppression (10.5%) were recorded even though both were observed to be high at diagnosis (91.5% for anaemia and 89.4% for immunosuppression). The mortality rate after one year of management was observed to be higher among those with breast cancer co-morbidity than those with HIV infection alone (Figure 2).

Table 1: Distribution of participants during the study period

Variables	HIV infection alone	HIV infection and Breast cancer co-morbidity	Total
Number of participants			
Enrolment at diagnosis	47	3	50
Participants after 6months of therapy	44	1	45
Participants after 1year of therapy	38	1	39
Reasons for discontinuation			
Discontinuation due to death	3	2	5
Discontinuation due to missing of appointments	6	0	6

Table 2: Blood cell parameters and CD4 count at diagnosis between PLWH and control subjects

Parameter	PLWH n = 50	Controls n = 50	p-Value
Red Blood Cell count	4.30±0.69	5.63±0.55	0.001
Haematocrit	0.34±0.06	0.40±0.03	0.001
Haemoglobin conc.	97.02±16.64	119.80±6.64	0.001
White Blood Cell count	5.44±1.48	5.91±1.30	0.093
Neutrophil count	2.29±1.04	2.46±0.93	0.385
Lymphocyte count	2.46±0.82	2.89±0.71	0.006
Mixed cell count	0.62±0.31	0.56±0.18	0.198
Platelet count	226.18±63.26	250.52±59.55	0.05
Mean Platelet Volume	9.41±0.98	9.16±0.61	0.137
Platelet Distribution Width	15.16±0.67	14.80±0.36	0.001
CD4 cell count	350.10±137.33	857.20±228.20	0.001

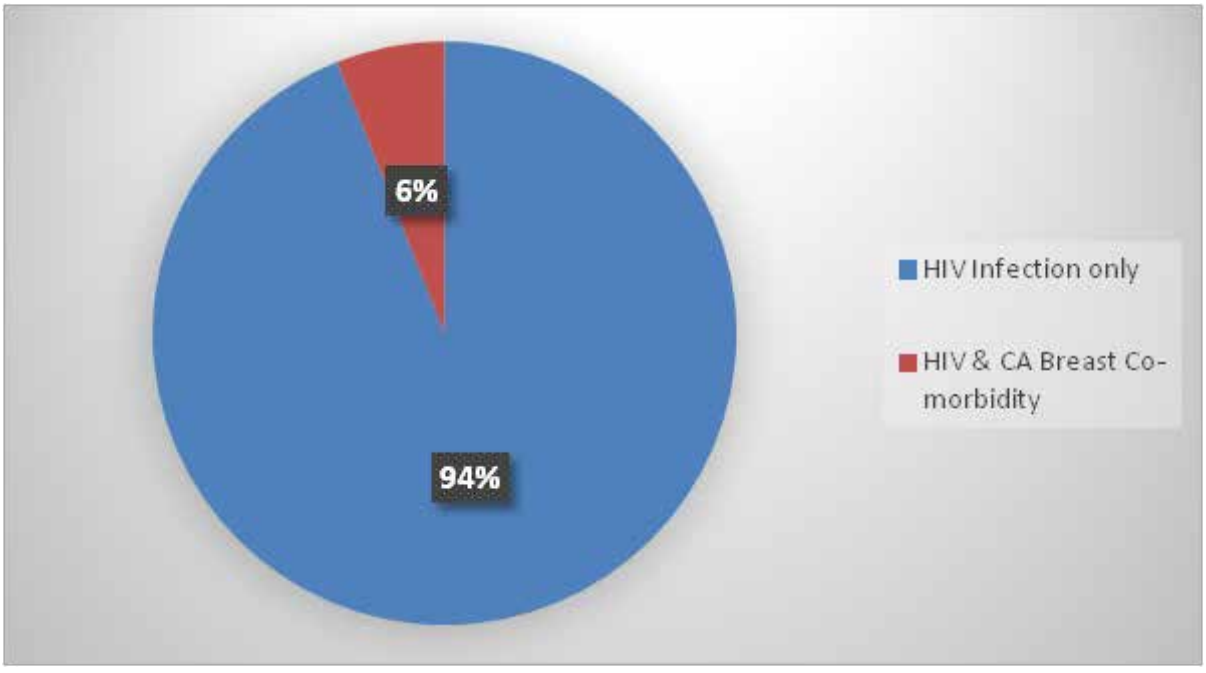

Fig 1. Prevalence of breast cancer among PLWH

Table 3. Prevalence of cytopenia during one year of therapy

Parameter	At diagnosis	6 months of therapy	I year of therapy
HIV Infection alone	**n = 47 (100%)**	**n = 44 (100%)**	**n = 38 (100%)**
Anaemia (Hb <120g/L)	43(91.5)	28(63.6)	16(42.1)
Leucopenia (WBC <4.0x10^9/L)	6(12.8)	2(4.5)	0
Neutropenia (Neutrophils <1.2x10^9/l)	5(10.6)	2(4.5)	0
Lymphopenia (Lymphocytes <1.0x10^9/l)	2(4.3)	0	0
Thrombocytopenia (Platelets <150x10^9/L)	4(8.5)	1(2.3)	0
Immunosuppression (CD4 <500 cell/L)	42(89.4)	12(27.3)	4(10.5)
HIV Infection & CA Breast	**n = 3(100%)**	**n = 1(100%)**	**n = 1(100%)**
Anaemia (Hb <120g/L)	3(100%)	1(100)	1(100)
Leucopenia (WBC <4.0x10^9/L)	0	1(100)	1(100)
Neutropenia (Neutrophils <1.2x10^9/l)	0	1(100)	1(100)
Lymphopenia (Lymphocytes <1.0x10^9/l)	0	1(100)	1(100)
Thrombocytopenia (Platelets <150x10^9/L)	0	0	0
Immunosuppression (CD4 <500 cell/L)	1(33.3)	0	0

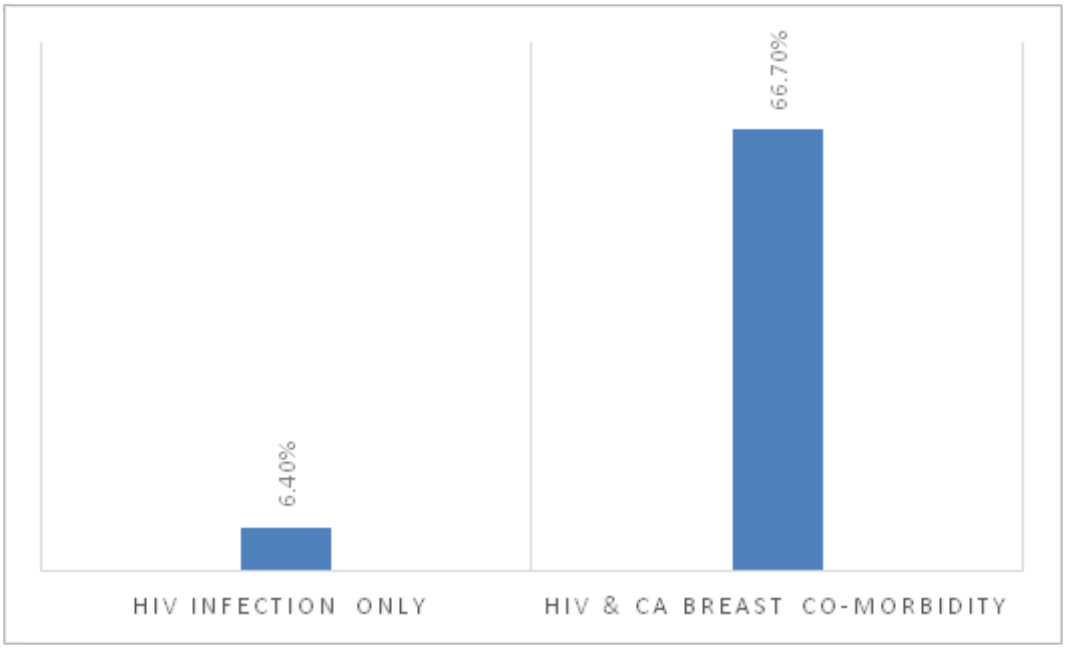

Fig 2. Mortality rates during the study period

Discussion

Improving the quality of life as well as reduction of transmission risks are at the heart of HIV infection management, and are achievable by targeting early detection and prompt commencement of antiretroviral therapy(1). The expectation from this approach is the ultimate reversal of morbidities. However, derangement in blood cell counts otherwise known as cytopenia remains a challenge in the management of HIV infection, although reports of amelioration as treatment progresses abound in literature (8-11). At diagnosis, anaemia, lymphopenia, thrombocytosis and immunosuppression were evident as observed in the significant reduction of the representing parameters when compared to mean values from the control group. Beyond this known direction of findings, is the need to evaluate the proportions of these derangements through a follow-up period.

The present study recorded decline mostly in the cytopenia among subjects with HIV infection alone. The Tenofovir/ Lamivudine backbone in combination with either Efavirenz or Dolutegravir completely resolved leucopenia and thrombocytopenia. While an 8.5 times reduction (89.4%: 10.5%) was achieved for immunosuppression, the occurrence of anaemia reduced to a lesser degree of 2.2 times (91.5%: 42.1%) during the one-year study period. However, anaemia and leucopenia persisted in HIV infection comorbidity with breast cancer while thrombocytopenia and immunosuppression were resolved. It is important to appreciate that treatment protocol for breast cancer involves surgery, chemotherapy and radiotherapy, while cytopenia is among the adverse effects of these treatment strategies in addition to the effect from the tumour (22,28). Comorbidity apparently exacts greater derangement in the frequency of cytopenia. Thus, targeted efforts towards addressing cytopenia is imperative for better management of PLWH who have

been diagnosed with breast cancer.

The CD4 count remains useful at indicating immune response to the invasive debilitating mechanism of the HIV virus. While antiretroviral therapy improves this biomarker of immunosuppression, overall improvement of other morbidity indicators such as cytopenia as well as survival appear to be dependent on other factors such as co-morbidity. Within the first 6 months of the study period, 6.4% mortality (3 out of 47) was recorded for the subjects with HIV infection alone while a much higher rate of 66.7% (2 out of 3) was observed among those with breast cancer comorbidity. The subject of HIV infection and breast cancer co-morbidity suffers from paucity of research output probably due to small sample size. However, a more aggressive manifestation of breast cancer has been previously reported with regards to HIV infection co-morbidity(29). It is the finding of this study that cytopenia and mortality are issues of concern in the co-morbidity condition, while anaemia remains a major challenge in HIV infection even after a year of adhering to antiretroviral therapy.

Conflict of Interest

The authors declare no conflict of interest.

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