Prevalence of HIV/AIDS among Breast Cancer Patients and the associated Clinico-pathological features

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Abstract

Introduction: There is uncertainty as to the exact interaction between HIV and Breast Cancer. Available studies are inconclusive about any relation whether causal or protective and the number of patients in these studies small.

Objective: To determine the prevalence of HIV among confirmed incident breast cancer cases and to describe the associated clinico-pathological features.

Design: Analytical cross sectional study

Methods: Over a period of 6 months consecutively eligible patients were recruited from the Mulago Hospital breast clinic. Breast lesions were biopsied and blood withdrawn for HIV sero-survey. Collected data was double entered into Epidata version v 3.1.1, exported to STATA 10.0 for analysis.

Results: Sixty two breast cancer patients consented to participate in the study and of these, 22(35.48%) were positive for HIV compared to HIV prevalence in the general population of 6-7%. All the participants were female. The mean age of HIV negative subjects was 45 years (range: 21-80 years) and for HIV positive subjects was 32.4 years (range 18-52 years). There was a significant association between HIV status and age, BMI and CD4 Counts as well as for histological grade and stage (P< 0.024).

Conclusion: The prevalence of HIV among the studied breast cancer group was significantly higher than that in the general population. HIV was associated with poor prognostic factors. A high index of suspicion of the co-existence of these two diseases in a context of high HIV prevalence is warranted. Future studies should explore for a causal association.

Introduction

Global statistics demonstrate that almost one third (32%) of all cancers diagnosed in women are breast cancer (1).

In Uganda, the incidence of breast cancer has risen from 11:100,000 in the 1960s to 31:100,000 in 2006 (2). It is second to Kaposi sarcoma in cancers affecting women in the HIV/AIDS (3). The breast tumors seen in Sub Saharan Africa present in relatively younger women and mostly in late stage (III and IV), run an aggressive course and carry a low 5 year survival rate (56%) (4, 5) .

Sub-Saharan Africa still remains the region most heavily affected by HIV worldwide, accounting for over two thirds (67%) of all people living with HIV and for nearly three quarters (72%) of AIDS-related deaths in 2008. An estimated 1.9 million [1.6 million–2.2 million] people were newly infected with HIV in sub-Saharan Africa in 2008, bringing to 22.4 million [20.8 million–24.1 million] the number of people living with HIV (6). Non-AIDS-defining cancers that have shown increased inci-

dence in studies of population-based registries of people with HIV/AIDS include multiple myeloma, lip cancer and lung cancer [7], but data about Breast cancer as an AIDS or Non AIDS defining cancer is limited and conflicting (8) and the association of HIV infection with breast carcinoma is still unclear (9). The longer patient survival of HIV patients is expected to result in higher prevalence of breast cancer in these patients (10).

Patients with HIV and breast cancer present two distinct challenges to the clinician: to confirm the diagnosis and accurately stage breast cancer, and to evaluate the safety and timing of surgery and adjuvant treatment in the setting of immunosuppression (11, 12).

There is no clear data about the clinicopathological correlation of breast cancer in HIV-positive patients and their current prevalence is not known in our setting.

This study was conducted to determine the prevalence of HIV in breast Ca patients and determine if the clinico-pathological features of the disease are different in HIV+ versus HIV- patients

Methodology

Study Design: An analytical cross sectional study

Study Duration: The study was conducted over a period of six months from January 2011 to June 2011 inclusive.

Study Setting: Mulago hospital is the National Referral and Teaching hospital for Makerere University in central Uganda. It has a bed capacity of about 1700. Incident cases were recorded from Mulago hospital surgical outpatient department (breast clinic) and ward 3C (in-patient ward).

Study participants

All patients with histologically confirmed breast cancer who were able to give relevant information and consent to participate in the study were included.

The sample size (n) was calculated using the modified simple random sampling formula by Wayne [17], seeking to establish the prevalence of subjects. Ethical approval was sought and all participants consented.

Laboratory Procedures

HIV diagnosis was made using a standard diagnostic method. The blood was tested once using the ELISA method which is 99.3% to 99.7% sensitive and 99.7% specific (Statpak test kit) [18]. The participants underwent pre and post HIV/AIDS screening counseling by a trained counselor.

Core breast biopsies, fixed in 10% formalin solution were processed for paraffin embedding for Heamatoxylin and Eosin staining at the Pathology Department of Mulago Hospital. The slides were reported according to Evans Histological classification and Nottingham grading of tumors (19).

Data Collection and Analysis

Data were entered, verified and analyzed using the Epidata and SPSS computer program. The confidence interval was set at 95%. The level of significance as $p < 0.05$.

Results

A total of 62 participants with histological diagnoses of breast cancer were studied. Of these, 22 participants were positive for HIV (35.5%). There was a significant relationship between HIV status and the socio-demographic plus clinic pathological characteristics except tribe among the 62 Breast cancer participants (Table 1).

Discussion

Prevalence

The study findings demonstrated a 35.5% prevalence of HIV among this group of patients with breast cancer. This is similar to a study done 10 years earlier at the same facility that found the HIV prevalence to be 35.7% (16). Given that the HIV prevalence in the general population is 6.7% (17), a 7-fold difference in prevalence in this breast cancer patients group may suggest a link between breast cancer and HIV infection even though this study wasn't designed to confirm a causal relationship. We would have anticipated a corresponding drop in prevalence of HIV among breast cancer patients since HIV in the general population has dropped over the years among the age group that tested positive (18).

Age

Our findings demonstrate a mean age of 32.4 years among the HIV positives. This finding also suggests that breast cancer is affecting the younger population compared to earlier studies which found the mean age for breast cancer to be 41.7years and 47 years (4, 5, 13). While breast cancer seems to be more common in age group of 30-39years, participants that had both HIV and breast cancer were mostly observed among the 18-29years group. The predominance among pre menopausal women begs the question whether HIV infection may indeed be a risk factor.

BMI, CD4 count and stage

The proportions of subjects with normal Body Mass Index (BMI) were almost equally distributed by HIV status. However high BMI was most observed among the non-reactive (83.87%). Perhaps the comorbid conditions that come with HIV infection are likely to have reduced the patient weights. Among the 22 reactive participants, 8 (36%) were on treatment with anti-retroviral drugs (ART). Among those who never had ART (64%), 3 (21.4%) were only prophylactic treatment as recommended by Ministry of Health (MoH) guidelines which state that; Cotrimoxazole prophylaxis should be given to all HIV-infected adults and children in Uganda regardless of whether they are on antiretroviral therapy (ART) or not. The low use of prophylaxis may be explained either by the delay in HIV diagnosis or limited access to

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Variables	HIV -ve	HIV +ve	Mean diff (95% CI)	p-value
	N=40	N=22		
	Mean(SD)	Mean(SD)		
Continuous				
Age	45.0(12.6)	32.4(9.5)	12.6(6.4,18.7)	0.0001!
BMI	25.2(2.28)	22.3(2.19)	2.9(1.7,4.1)	<0.001!
CD4+	666(130)	320(80)	346(285,407)	<0.001!
Categorical	N (%)	N (%)	X2 (df)	
Sex Female	40(100)	22(100)		
Age				
Young(18-39)	15(37.5)	16(72.7)	7.4(2)	0.025x
Middle(40-64)	23(57.5)	6(27.3)		
Old(65+)	2(5.0)	0(0.0)		
Tribe				
Ganda	23(57.5)	10(45.5)	0.8(1)	0.362x
Others	17(42.5)	12(54.5)		
BMI				
Normal(18-24)	14(35.0)	17(77.3)	10.1(1)	0.001x
Overweight(25+)	26(65.0)	5(22.7)		
ART				
Yes		8(36.4)	16.7(1)	<0.001x
No		14(63.6)		
CD4+				
<250	0(0.0)	3(13.6)	5.7(1)	0.017x
>250	40(100)	19(86.4)		
Clinical:				
Stage of Br Ca				
I	1(2.5)	0(0.0)	7.4(3)	0.024xx
II	21(52.5)	5(22.7)		
III	18(45.0)	16(72,7)		
IV	0(0.0)	1(4.6)		
Histology Type				
Ductal (NOS)	35(87.5)	12(54.5)	10.2(3)	0.017x
Lobular	3(7.5)	3(13.6)		
Medullary	2(5.0)	5(22.7)		
Scirrhous	0(0.0)	2(9.1)		
Histology Grade				
Low	6(15.0)	0(0.0)	6.1(2)	0.048x
Intermediate	21(52.5)	9(40.9)		
High	13(32.5)	13(59.1)		

Table 1: Distribution of social demographics & clinico-pathology by HIV status of the 62 Breast Cancer participants

Others* Basoga 5, Ankole 7, Acholi 3, Mukiga 3, Itesot 3, Batoro2, Alur 2, Lugbara2, Langi 1, Mukonjo 1
! t-test used to calculate the p value, xxFisher's exact test used to calculate p value
xChi test square used to calculate p-value

care. These subjects were however referred to HIV care centres for the prophylaxis and further treatment.

Among the HIV positives, 3(13.6%) had their CD4 less than 250cells/mm³. Nineteen (86.4%) respondents and all those who were HIV negative had their CD4+ counts greater than 250cell/mm³. The finding that all negative participants had CD4+ count greater than 250cell/mm³ may be difficult to interpret and may require in-depth exploration.

Most of the HIV positive participants were observed to be in clinical stage III of breast cancer (47.06%) whereas those without HIV were mainly in clinical stage II of breast cancer (80.77%). One patient had stage IV disease and this patient also tested positive for HIV. (P-value =0.024[fisher's exact test]) This may suggest that HIV probably accelerates the natural progression of breast cancer to advanced disease (12), and therefore a poor prognostic indicator.

Histopathology

Invasive ductal carcinoma (NOS) was the most common type of breast cancer observed in the study of which 12 (25.53%) were HIV positive making up 54.5% of the HIV reactive participants. This is in agreement with an earlier case series report (9). Medullary carcinoma was observed in 7 individuals of which 5 (71.4%) were reactive. Both participants who had scirrhous carcinoma were also positive with HIV. This supports the fact that breast cancer in the face of HIV presents with unusual forms (8).

Histological grading of breast cancer in the setting of HIV was also significant with the majority of HIV positive individuals (n=13, 50%) having high grade cancer and 9(30%) having intermediate grade disease with none of them exhibiting low grade breast cancer. Among the non-reactive participants, 13(50%) of them had high grade cancer, 21(70%) had intermediate grade and 6(100%) had low grade breast cancer. This suggests that HIV is associated with poor grades. A similar suggestion was published by El-Rayes et al, 2002 in a 5 patient case report series (12).

Limitations of the study

A single sample was collected and analysed once for HIV infection. The "window period" could affect the results of the true prevalence of HIV in breast cancer patients.
It is possible that there could have been referral bais

based on the premise that HIV positive patient health managers promptly refer their patients to further care. However a significant proportion of the patients in this study only knew of their HIV status during the study. It is also conceivable that if there was referral bias they should present at earlier stages than the HIV negative ones but this wasn't the case.

Conclusions

The prevalence of HIV among breast cancer patients was higher than in the general adult population. Breast cancer is occurring more in the younger population than observed before and seems to impact negatively on the progression of breast cancer.

A high index of suspicion regarding breast cancer and HIV co-existence is warranted. A further in-depth study for a causal association recommended.

Acknowledgments

References

1. American Cancer Society, Breast Cancer Facts and Figures 2009-2010. http://www.cancer.org/downloads/STT/F861009 final%209-08-09

2. Parkin DM, Nambooze S, Wabwire-Mangen F, et al. Changing Cancer Incidence in Kampala, Uganda, 1991-2006. Int J Cancer 2009; 126(5):1187-1195

3. The Uganda Breast Cancer Working Group, Breast cancer guidelines for Uganda Afr Health Sci 2008; 3(1):47-50

4. Gakwaya A, Kigula MJ, Kavuma A, et al.. Cancer of the breast: 5 – year survival in a tertiary hospital in Uganda. Br J Cancer 2008; 99(1):63-67

5. Gondos A.B.H, Wabinga H, Parkins D.M. Cancer survival in Kampala, Uganda. Brit J of Cancer 2005; (92):1808-1812

6. AIDS epidemic up date: November 2009. UNAIDS/09.36E / JC1700E".

7. Chiao EY, Krown SE. Update on non-acquired immunodeficiency syndrome defining malignancies. Curr Opin Oncol 2003; 15: 389-397.

8. Naeem L, Fauzia R, Troy G. Breast Cancer and HIV in the Era of HAART: A case Report and Review of the Literature. 2010; 61(3): 6-40

9. Soji Fo, Ayoola OA, Zahara S, et al. Breast Cancer in Women With HIV/AIDS: Report of Five Cases With a Review of the

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Literature. Journal of Surgical Oncology 2005; 89; 23-27.

10. Guiget M, Curie M. "Effect of immunodeficiency, HIV viral load, and antiretroviral therapy on the risk of individual malignancies (FDH-ANRS CO4): A prospective cohort study" Lancet Oncol 2009; DOI: 10.1016/S1470-2045(09)70282-7.

11. Voutsadakis IA, Silverman LR. Breast cancer in HIV-positive women: a report of four cases and review of the literature. Cancer Invest 2002; 20: 452-457.

12. El-Rayes BF, Barenji K, Schuman P, et al. Breast cancer in women with human immunodeficiency virus infection: implications for diagnosis and therapy: five case reports and a review of literature. Breast Cancer Res Treat. 2002; 76: 111-116.

13. Amir H, Kaaya EE, Kwesigabo G Kiitinya JN. Breast cancer before and during the AIDS epidemic in women and men: a study of Tanzanian cancer registry data 1968 to 1996. J Natl Med Assoc. 2001; 92:301-305.

14. Wayne D.W: Biostatics; A foundation for Analysis in Health Science: 5th edition. John Wiley and Sons; 1987. p157.

15. http://www.livestrong.com/article/133176-accuracy-elisa-hiv-test/#ixzz14zICgP1H

16. David JBA. Evans Histological Appearance of Tumors. Fourth Edition 1990. 424; 441-450..

17. Najjuka JL (SR). Is there any association between Breast Cancer and HIV-AIDS in women in Uganda? 2000.

18. Hladik W, Musinguzi J, Kirungi W, et al. The estimated burden of HIV/AIDS in Uganda, 2005-2010. AIDS Feb 2008; 22(4): 503-510.doi:10.1079/QAD. Obo 13e3282f470be