

Co Morbidity of HIV and Breast Cancer: A One Year Multicentric Pilot Study in Cameroon

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ABSTRACT

Background: Breast cancer is a common cancer in women worldwide and in Cameroon but the global number of breast cancers in WLWHA is not known. Although the disease is not AIDS-defining, and albeit the decrease in the national prevalence of HIV infection in the past few years in Cameroon, patients with HIV-related malignancies, especially breast cancer are frequent. There is enormous challenge in the management of these patients in our setting. Both diseases respectively and collectively, have a high morbidity and mortality. Few studies on the profile of patients with both HIV infection and breast cancer have been carried out in our setting, whereas their Knowledge is essential in the short and long term management strategies for both diseases.

Aim: This study was aimed at finding the factors associated with co morbidity of HIV and breast cancer.

Materials and methods: A one year prospective, cross-sectional, multi-centre pilot study in 5 hospitals across 3 regions of Cameroon. Vital data on the patients and data concerning both HIV infection and breast cancer respectively were assembled and analysed.

Results: We found 71 patients with malignant breast lesions and a concomitant co-infection of HIV. The Standardised Incidence Ratio (SIR) of breast cancer amongst HIV positive patients compared to breast cancer in the general population did not show any significant incidence of the disease in the latter group. The patients ranged in age between 14 and 72 years (median age = 40+ 12) and 45% were less than 40 years of age. About 3% were males, while 32% were unemployed and 55% were married. Majority (59%) had secondary education and beyond. The main breast lesion was an invasive duct carcinoma (56.3%), followed by a lobular carcinoma (11.27%). HIV serotype I was predominant (61%) and in 24% of cases there was type 1 and 2 co-infection. Majority (45%) had CD4 counts between 200 and 499 cells/mm3 and were diagnosed at advanced cancer stage (69%). The average HIV/cancer transition time was 2.7 years.

Conclusion: HIV breast cancer comorbidity is common and the relation between the diseases remains complex. Further studies are recommended to find out factors associated with and how they influence this relationship.

Keywords: Breast; cancer; HIV; Cameroon.

INTRODUCTION

The burden of disease in developing countries is being overwhelmed by known and emerging infections. It has also been shown by various studies that non-communicable diseases are becoming a public health problem in these communities [1]. Numerous viral infections have for long been associated with various types of cancers. Prominent amongst these is the cervical cancer [1-3]. The history of HIV and its link with cancer started with the first descriptions of AIDS [4]. People infected with HIV have a higher risk of some types of cancer than uninfected people.

Almost 4 decades after the apparition of the HIV/AIDS pandemic, new challenges to this disease are being faced by patients and the global health systems. Patients are living longer with HIV infection due to increase availability of HAART with increased chances of

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developing a cancer [5].

Breast cancer is the most common cancer in women both in the developed and less developed world. It is estimated that worldwide over 508 000 women died in 2011 due to breast cancer [6]. Although breast cancer is thought to be a disease of the developed world, almost 50% of breast cancer cases and 58% of deaths occur in less developed countries [7]. In Cameroon, with a cancer prevalence of 25.000 and an annual incidence of 15.000, an age-adjusted incidence of 107 new cases per 100 000 inhabitants, breast cancer is most prevalent and accounts for 18.5% of all cases [8].

Much controversy exist concerning the relationship between HIV and breast cancer, and breast cancer has no established viral associations, although several reports alleging a direct relationship have been suggested [9-11].

Although the oncologic relationship between HIV/AIDS and certain cancers is well understood, there is little evidence about breast cancer among individuals with HIV infection. The natural history of breast cancer in individuals with HIV is poorly understood, and it is unknown whether viral infection is a protective factor for breast cancer development, a risk factor for accelerated oncogenesis, or unrelated. A definitive link between these two disease processes is yet to be established. Some reports [12] indicate that breast cancer is not an acquired immunodeficiency syndrome (AIDS)-defining disease and its incidence is not increased in HIV patients.

Alternatively, the biology of breast cancer appears to be more aggressive in HIV-positive women suggesting a permissive role of the virus in the progression of the cancer [12]. The incidence of breast cancer is however increasing in Sub Saharan Africa [13] and has since overtaken invasive cervical cancer as the leading cause of cancer in South African women [14]. The coexistence of these two diseases in a single patient has become a reality [15], which significantly increases health challenges amongst women [16].

The national HIV infection rate in Cameroon has decreased from 12% in 1995 to 4.5% in 2014, yet there has been an upsurge of both AIDS-defining and other cancers in patients with the infection [17]. This is due to longer survival of HIV- infected patients which increases the risk of cancer amongst them. This occurs even though preventive actions against cervical cancer began two decades ago with screening for breast cancer amongst women. The shortcoming of this program is that it is limited to urban areas and is not regular and also restricted to breast palpation while mammography and biopsies are reserved for suspicious cases.[18].The advent of HIV/AIDS has caused a significant change in the epidemiology of cancer in Cameroon, reducing the average incidence age for cancer in the population by about 8 years [19].

In resource-stressed communities like ours, numerous difficulties are faced in the management of HIV/AIDS and cancer patients respectively, and the situation is worse in patients who have both diseases. The role of underlying genetics, co-infections, and lifestyle exposure to known/ unknown antigens can never be underestimated. It is imperative therefore those scientists should continue to investigate the interaction of HIV and its proteins with host machinery in the aetiology of cancer from a molecular to epidemiologic level. This study of the profile of patients with co morbidity of HIV and breast cancer in Cameroon is aimed at

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documenting basic epidemiologic and other findings that characterise patients with both diseases and serve as platform for further studies.

MATERIALS AND METHODS

For this prospective study, data on patients with both HIV infection and cancer from 5 pilot centres of an NCI-sponsored HIV malignancies project were assembled. The data collection began from January 1 to December 31 2015. It is from this cohort that we extracted data on patients who tested HIV positive and had a breast cancer. The vital statistics of the patient, data on HIV and cancer respectively were all assembled and analysed. The duration of both cancer occurrence and HIV infection were inferred from the respective dates of diagnoses of the diseases.

RESULTS

 Table 1: Age distribution of HIV+ /breast cancer patients in our study.

Age range (years)	Number	%
≤ 19	1	1.4
20-29	4	5.6
30-39	27	38
40-49	14	19.7
50-59	14	19.7
60-69	10	14.1
≥70	1	1.4
Total	71	100

Breast cancer in HIV+ patients predominates at the peak age group 30-39 years (38.0%). A high proportion of cases are below 40 years of age (45.0%).

DISCUSSION

In Cameroon, breast and cervical cancers are the leading causes of cancer-related morbidity and mortality [18]. Breast cancer is not an acquired immunodeficiency syndrome (AIDS)-defining disease and its incidence is not increased in HIV patients. The biology of breast cancer appears to be more aggressive in HIV-positive women suggesting a permissive role of the virus in the progression of the cancer [12].

The first case of breast cancer in an HIV-infected person was reported in the literature in 1988 and only 42 detailed patient reports were available until the early 2000s [19]. While two relatively small cohorts [20] reported a marginal increased incidence in breast cancer in PWLWHA; the vast majority document a statistically significant deficit [21].

We found an annual incidence of 71 patients with HIV/breast cancer in this multi-centre study in Cameroon, unlike Amir et al in a Tanzanian study that showed a statistically significant decrease in the incidence rate of breast cancer in both males and females after the appearance of HIV/AIDS [19].

Matching population based cancer registries with HIV/AIDS registries may provide the best level of evidence to verify the SIR trend [22]. Using this method, the majority of studies have shown significantly lower standardized incidence ratios (SIR) for breast cancer in WLWHA [23]. Using reports of the Yaounde Cancer Registry [24], in this study we found a SIR of breast cancer in HIV

positive patients compared to the general population to be 1.0.

This implies an equal prevalence of breast cancer in HIV patients compared to the general population. This observation is similar to a contemporary report of infected breast cancer patients in Soweto, South Africa, which constitutes the largest cohort to date, where Cubasch et al reported an equal prevalence of HIV in breast cancer patients compared to women in the source population [25]. However, more recent and updated cohort studies have clearly shown a shift towards increasing SIR that approaches that of the general population [26, 27], whereas some European cohorts have shown a drop in this ratio [28].

This study found a prevalence of breast cancer in HIV+ males to be about 3% (figure 1), a rate similar to that in the entire population as reported in a previous study on male breast cancer in this population [29]. Breast cancer patients with HIV receiving ART are reported to have a relevant metabolic syndrome significantly associated to patients with both diseases [30]. We did not investigate this assertion in our study.



Figure 1: sex distribution of cases.



Our patients ranged in age between 14 and 74 years (median age = 40+ 12) and 45% of them were less than 40 years of age (table I). This finding is similar to reports that patients with breast cancer in sub Saharan Africa generally present at a relatively younger age regardless of HIV status [31]. The overall mean age of presentation in West African women is between 35 and 45 years, 10 to 15 years earlier than women in high-income countries [32]. Similarly to our results, a 3-year retrospective review of 374 patients with breast cancer in Kenya showed a median age of 44 years [33], and the mean age in a Tanzanian cancer registry is 44.7 years [34]. A study in South Africa reported trends similar to the population in the high-income countries, with a median age at presentation of 56 years for patients without HIV compared with 42 years for patients with HIV (P < .001) [35].

Generally in SSA, a majority of patients present with advanced-stage disease, with 69%, 89.6% and 72.8% of patients with breast cancer in Cameroon, Kenya and Nigeria, respectively, presenting with advanced-stage disease [24,36,37]. Amongst about 57% of our patients with a known stage of disease, 26% were advanced (stage III and IV), while majority (31%) were at an early stage (I and II). The stage distribution was as follows: stage I 9%, II 22%, III 19% and IV 7% (figure 2).

Similar to our study, this finding of early disease stage of breast cancer among HIV + patients has been reported [38]. It has been earlier found that patients with breast cancer in high-income countries predominantly present with early-stage disease.

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Figure 2: Stage of cancer at diagnosis amongst HIV+ patients.

Patients with HIV and breast cancer in the United States present with stage distribution similar to their seronegative counterparts [38]: 60% of patients present with stage I disease, 33% with stage II or III disease, and 5% with stage IV disease [39]. Contrary to our finding, some earlier reports indicated no difference in stage at presentation of disease of the disease amongst HIV+ and HIVpatients [40].

The histologic type of breast cancer among our patients was similar to that of the general population (figure 3) [24] showing a preponderance of invasive duct carcinoma. This is similar to earlier reports that the distribution of histologic subtypes of breast cancers is independent of HIV status [35].



Figure 3: pathological diagnosis of breast cancer amongst patients (*ca=cancer).

In this study the median CD4 count amongst our patients was 414 cells/ μ L (figure 4), similar to what most past studies found in the University of Maryland (437.5 cells/ μ L) [41] and another on an Italian cohort (424 cells/ μ L) [42]. In 45% of our cases, the CD4 counts were between 200 and 499 cells/ μ L, a finding similar to 50% in a similar study in South Africa [25]. We found no correlation between CD4 count and breast cancer in our patients. This assertion is similar to reports that breast cancer in WLWHA is certainly not associated with a low CD4 count [43] implying that the degree of immune-compromise does not correlated with tumorigenesis [44]. CD4 count is also not associated with breast cancer stage at presentation, histological subtypes, or tumor grade in this study, lke in previous ones [45].



Figure 4: CD4 count amongst patients at diagnosis.

Up to 40.8 % of our patients had one or another form of cancer treatment (figure 5). This finding is higher than 9% by Suneja et al [46] which showed that for most cancers, a significantly higher proportion of individuals with HIV did not receive cancer treatment in their study. In our series 12 out of 29 known patients (41.4%) were treated by chemotherapy a rate lower than 60% reported by Parameswaran et al [47]. Other forms of treatment included radiotherapy, and surgery.



Figure 5: Cancer treatment options amongst HIV+/breast cancer patients.

Our study covered 3 out of 10 regions of the country (30%); a ratio likely to impact on the national incidence of this disease (table 2). Up to 55% of our patients were married (figure 2). In consideration of HIV versus marital status, this rate is higher than the report by Shisana [48] in South Africa who found an HIV prevalence among married people of 10.5% compared to 15.7% among unmarried people. They inferred in their work that the risk of HIV infection did not differ significantly between married and unmarried people; and concluded that the relationship between marital status and HIV is complex, depending on various demographic factors and sex behaviour practices. In a different study however, the author reported that those who were married living with their spouse had significantly reduced odds of being HIV-positive compared to all other marital spouses groups [49]. The relationship between breast cancer and marital status in our study showed a relative rarity of the disease in the unmarried (35.2%) and a higher incidence in married women (55%) (Figure 6). This is different from Sumedha et al [50] who found 74% prevalence amongst unmarried against 60% married HIV +/breast cancer women.



Figure 6: Bar chart illustration of marital status of patients.

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Table 2: Distribution of HIV+/breast cancer patients by region of origin.

Region of origin	Number of cases	%
Unknown	14	19.7
West	16	22.5
North West	10	14.1
South West	10	14.1
Centre	11	15.5
Littoral	4	5.6
south	4	5.6
North	2	2.8
All regions	71	100

Majority of patients are married (55%).

The HIV serotype was predominantly type 1 (61%) (figure 7). In the absence of data on HIV serotype in HIV + women with breast cancer, we compared this parameter with HIV + women having a similar (cervical) cancer. Our finding is higher than previous reports where an HIV-1 prevalence of 21.0% in a comparative study of HIV positive and negative women and concluded that HIV-1 infection is associated with invasive cancer of the cervix [51]. In 24% of our cases, infection was both by HIV serotypes 1 and 2. This is similar to an earlier report of 19.2% concurrent HIV-1/ HIV-2 infection in an earlier study in Cameroon [52].



Figure 7: HIV serotype among HIV+/breast cancer patients.

Up to 99% of our cases had cancer in only one breast while 1% had a bilateral cancer. This finding is similar to others [53] who found bilateral tumours in 0.8% of their series without predilection for the laterality as no significant difference was noted between the proportions of left vs. right breast cancers.

The most common histologic subtype (figure 8) was invasive ductal carcinoma (56.3%, 40/71). Second most common type was lobular carcinoma (11.3%, 8/71) followed by medullary (5.7%, 4/71) and 'mastitis carcinomatosa' (4.2%, 3/71). All of the 3 male breast cancers were invasive ductal carcinomas. These findings are common in trend and value and different in same aspects concerning the various histologic subtypes to earlier reports. They [53] found invasive ductal carcinoma (78.12%, 300/384), mucinous carcinoma (6.25%, 24.6/384) followed by medullary (4.6%, 18/384) and invasive papillary (2.34%, 9/384), with 4 of six male breast cancers being invasive ductal carcinomas.



Figure 8: HIV+ to breast cancer transition time in years.

In our study, majority (59%) of participants had a secondary education and beyond, while 41% had not gone beyond primary school (figure 9). This is in accordance with notion that unlike cervical cancer, breast cancer is a disease of the higher class [54], assuming that education level is directly proportional to a high socio-economic status. Our finding is similar to the trend though lower in value to Hailemariam [55] who in a study on a similar cancer in this cohort reported that the likelihood of cervical cancer among literate women was 6.1 times higher as compared to illiterate women at a value of 78.9% compared to the later.



Figure 9: distribution of patients by educational level.

In all cases (100%), the HIV infection preceded the apparition of breast cancer for periods ranging between 1-6 years. The average duration of the infection before diagnosis of cancer was 2.8 years (figure IX). Like in our study, some reports on cervical cancer patients indicated the time interval since HIV/AIDS diagnosis amongst cervical cancer patients ranged from 1 month to 10 years, with a mean of 2.5 ± 2.2 years [56].

CONCLUSION

HIV and breast cancer comorbidity prevalence is common in our community though the cancer does not show any particular predilection amongst these patients. Breast cancer occurs within few years following HIV infection. The risk factors of these comorbid conditions include infection by HIV serotype I, a low CD4 count, married women and a high educational level. A duct carcinoma is most predominant in these patients, who generally present at late stages of disease. Screening and treatment for breast cancer and appropriate HIV management strategies are recommended as soon as the infection is diagnosed as well as breast cancer surveillance in the first few years following the infection.

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