

Invasive Cervical Cancer in HIV-Infected Women in Low-Income Countries: Experience from Côte d'Ivoire.

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ABSTRACT

Aims: To assess experience in the management of invasive cervical cancer in HIV- infected women in a sub-medical setting.

Methods: Retrospective cohort study of patients with cervical cancer at the University Hospital of Treichville between 2012 and 2016. The association between HIV infection and epidemiological data was investigated using the chi-square test. Survival data were calculated according to the Kaplan-Meier method.

Results: A total of 99 women with cervical cancer were included in the study; 49 (49.5%) of whom were HIV positive. The average age of patients was 51.5 years. HIV testing was performed in 53.1% after the diagnosis of cancer. Virtually all (98%) of women living with HIV had received antiretroviral therapy. Their median CD4 was 382 elements / ml. HIV infected Women were significantly younger than HIV-negative women. The median survival rate for patients living with HIV was 9.6 months Versus 15 months for HIV-negative patients. HIV infection was associated with a significant increase in deaths and a shorter survival among patients with cervical cancer.

Conclusions: Cervical cancer is more aggressive in HIV infected women. Overall survival was significantly shorter when the patients were infected with HIV.

Keywords: cervical cancer, epidemiology, HIV infection, survival.

INTRODUCTION

Cervical cancer and HIV infection are two major public health problems, particularly in sub-Saharan Africa. Indeed, this region alone accounts for the vast majority of cases of cervical cancer and HIV infection reported each year.^{1,2} In these countries, cervical cancer is the second most common cancer of women after breast cancer and the leading cause of cancer deaths due to their generally late diagnosis and the inadequate technical facilities.^{3,4}

In addition, there is evidence of an increased burden of cervical cancer since the onset of the HIV epidemic. Thus, HIV-infected women present a higher risk of cervical cancer, making this cancer one of the criteria for entry into the AIDS stage.^{5,6}

In Côte d'Ivoire, a country that is under-medicalised and that has a high prevalence of HIV infection, few studies have focused on the comorbidity of invasive cervical cancer and HIV infection. This study was

carried out to assess our experience in the management of this comorbidity in a sub-medical setting.

METHODS

This is a retrospective cohort study carried out at the Gynecology and Cancer Department of the University Hospital of Treichville between January 2012 and December 2016. The update of the files was done in January 2017. The study focused on patients with histologically proven invasive cervical cancer. Among them, HIV-infected women were identified and compared to HIV-negative women. The criteria for non-inclusion were mainly patients whose HIV status was unknown. The data needed for our study were collected using a standardized questionnaire based on medical files. The variables studied were epidemiological data (age, parity, occupation, marital status, educational level, age of first sexual intercourse), related to HIV infection (time of HIV testing, CD4 count, antiretroviral treatment) and related to cervical cancer (FIGO classification,

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treatment, death, survival time).

Radiotherapy that was unavailable in the country during the study period, was not part of the therapeutic strategy for patients with cervical cancer. Thus, stage I to IIA patients were treated by surgery. From IIB, patients were treated with 6 monthly courses of chemotherapy with Cisplatin neo-adjuvant chemotherapy associated with Irinotecan or 5-FU. Complementary surgery was performed 6 to 8 weeks after the end of the chemotherapy in the case of a good response.

Regarding the treatment of HIV infection, antiretroviral treatment was systematically initiated for naive patients. The standard first-line treatment according to national guidelines is the Tenofovir / Emtricitabine / Efavirenz regimen for HIV1 infection and the Tenofovir / Lamivudine / Lopinavir / ritonavir regimen for HIV2 or dual HIV. Antiretroviral treatment was continued for those already on treatment. This antiretroviral treatment is provided free of charge in public hospitals in the country.

Data analysis was performed using SPSS.22 software. The association between HIV infection and epidemiological data was investigated using the chi-square test or Fischer's exact test (when recommended). A p-value <0.05 was used as the significance level. Overall survival was calculated using the Kaplan-Meier method, taking into account the time elapsed (in months) between the date of diagnosis of the cancer and the date of the last report. The survival curves were compared using the Logrank test.

The full protocol of the study was approved by the hospital's ethics committee.

RESULTS

A total of 104 records of patients followed during the study period for cervical cancer were found. Four patients whose HIV status was not specified were excluded. In the end, the analysis involved 99 patients, 49 (49.5%) of whom were HIV-infected and 50 (50.5%) of whom were HIV-negative. Among the HIV-infected patients, 26 (53.1%) had been screened after the diagnosis of the cervical cancer. They had a median CD4 of 382 elements / ml with extremes of 18 and 946 elements / ml [Table-1].

Table-1: Data related to HIV infection (n = 49)

Medical characteristics	n(%)
Time of HIV testing	
Before cancer diagnosis	23(46.9)
After cancer diagnosis	26(53.1)
CD4 counts (cellules/ml)	

< 350	20(40.8)
350-500	16(32.7)
≥ 500	13(26.5)
Antiretroviral therapy	
Yes	49(97.9)
No	1(2.1)

The epidemiological and prognostic data of all patients with cervical cancer are summarized [Table-2].

Table-2: Epidemiological characteristics of patients by HIV status (n = 99)

Characteristics	HIV status		P
	Positive (n=49)	Negative (n=50)	
Age (years)			
< 40	17	3	
≥ 40	32	47	0.02
Parity			
≥ 4	33	45	
< 4	16	5	0.005
Occupation with an income			
No	30	43	
Yes	19	7	0.003
Level of education			
None and primary	46	49	
Secondary and higher	3	1	0.34
Marital status			
Single woman	38	37	
With a partner	11	13	0.41
Age of the beginning of sexual intercourse (in year)			
≤ 17	48	49	
> 17	1	1	0.75
FIGO stage of cervical cancer			
III - IV	33	38	
I - II	16	12	0.2
Treatment performed			
Surgery	2	0	
Chemotherapy	21	17	
Palliative Treatment	26	33	0.14
State at the assessment date			
Dead	40	23	
Living	9	37	<0.004

They had an average age of 51.4 ± 13 years and a median parity of 6 (interquartile range: 4 to 9 years). Among the 99 patients, 71 (71.7%) had been diagnosed at a locally advanced stage.

The group of patients living with HIV had

significantly more patients under 40 ($p = 0.02$) and had a median age of 41 years [IQR, 37 to 49 years] Versus 60 years [IQR 50.7 to 69.2 years] for the control group. In addition, multiparous women ($p = 0.005$) and patients with no income ($p = 0.003$) were significantly more numerous among HIV infected women. The treatment of cancer has been palliative for the majority of patients. Patients had a median follow-up of 11 months (extremes at 1 and 4 years).

Prognostically, there were significantly more deaths ($p < 0.004$) in HIV-infected patients than in HIV-negative patients.

The median survival of patients living with HIV was 9.6 months versus 15 months for HIV-negative women. Overall survival was significantly shorter when the patients were infected with HIV [Figures-1].

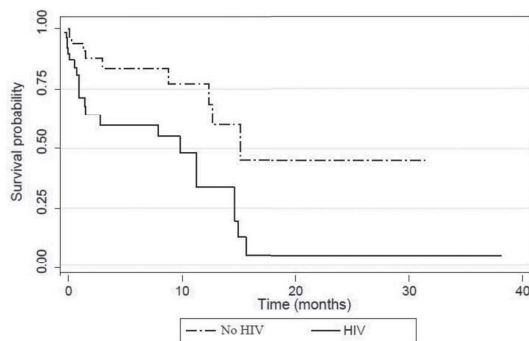


Figure-1: Kaplan-Meier estimated survival by HIV status ($p < 0.001$).

DISCUSSION

In the present study, almost half (49.5%) of patients with invasive cervical cancer were HIV-infected. Our observation is in agreement with data from the literature that show the existence of a strong association between cervical cancer and HIV infection.⁷⁻⁹ Moreover, epidemiological data show that of all AIDS defining cancers, cervical cancer is the one whose incidence has not really decreased with the advent of HAART.^{10,11} In fact, HIV-infected women are more likely to have a persistent infection with high-risk HPV which is the major risk factor for precancerous lesions and cervical cancer. This explains the low incidence of cervical cancer among women living with HIV in countries with organized

precancerous lesions screening programs.^{12,13}

Our study also found that women with invasive cervical cancer who were infected with HIV were significantly younger than HIV-negative patients. This earlier onset of invasive cervical cancer in women living with HIV was also demonstrated in other African series.^{14,15}

As in most studies in resource-limited countries, our study noted that irrespective of the HIV status of patients, invasive cervical cancer was of poor prognosis.^{16,17} The factors that explain the poor prognosis of this cancer in our countries with limited resources are mainly the lack of qualified human resources and the inadequacy or even the absence of technical facilities.¹⁸ These different factors constantly lead to a diagnostic delay or to inappropriate therapeutic choices which darken the prognosis of the disease.

In addition, the results of our study show that invasive cervical cancer is more aggressive in case of comorbidity with HIV infection since HIV-infected patients have a higher death rate and shorter survival. In a prospective series on 348 women with invasive cervical cancer in Botswana, Dryden-Peterson et al¹⁹ also showed that HIV-infected patients had a higher risk of death and poorer survival. On the other hand, in the series of Grabar et al⁹ in France, five-year survival among women living with HIV with invasive cervical cancer was similar to that of HIV-negative women. The difference is due to barriers to achieving optimal cervical cancer treatment in resource-limited countries due to lack of radiation therapy or low completion rate of treatment.

CONCLUSIONS

Aggressiveness of cervical cancer among HIV-infected women calls for increased screening for precancerous cervical lesions in women living with HIV as well as its prevention. Survival from cervical cancer is shorter if there is coexistence of HIV infection.

Conflict of Interest: No

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