Published in final edited form as:

Cancer Epidemiol. 2015 December ; 39(6): 1060–1065. doi:10.1016/j.canep.2015.09.002.

Cancer and HIV infection in referral hospitals from four West African countries

Antoine Jaquet^{1,2,*}, Michael Odutola³, Didier K Ekouevi^{1,2,4}, Aristophane Tanon^{5,*}, Emmanuel Oga³, Jocelyn Akakpo⁶, Manhattan Charurat³, Marcel D Zannou⁶, Serge P Eholie⁵, Annie J Sasco^{1,2}, Emmanuel Bissagnene⁵, Clement Adebamowo³, and Francois Dabis^{1,2} for the leDEA West Africa collaboration

¹Université Bordeaux, ISPED, Centre INSERM U897- Epidémiologie-Biostatistique, F-33000 Bordeaux, France

²INSERM, ISPED, Centre INSERM U897- Epidémiologie-Biostatistique, F-33000 Bordeaux, France

³Institute of Human Virology in Nigeria (IHVN), Abuja, Nigeria

⁴Département de Santé Publique, Faculté des Sciences de la Santé, Université de Lomé, Lomé, Togo

⁵Service de Maladies Infectieuses et Tropicales (SMIT), CHU de Treichville, Abidjan, Côte d'Ivoire

⁶Centre de Prise en Charge des Personnes vivant avec le VIH, CHNU de Cotonou, Cotonou, Bénin

Abstract

The consequences of the HIV epidemic on cancer epidemiology are sparsely documented in Africa. We aimed to estimate the association between HIV infection and selected types of cancers among patients hospitalized for cancer in four West African countries. A case-referent study was conducted in referral hospitals of Benin, Côte d'Ivoire, Nigeria and Togo. Each participating clinical ward included all adult patients seeking care with a confirmed diagnosis of cancer. All patients were systematically screened for HIV infection. HIV prevalence of AIDS-defining and some non-AIDS defining cancers (Hodgkin lymphoma, leukaemia, liver, lung, skin, pharynx, larynx, oral cavity and anogenital cancers) were compared to a referent group of cancers reported in the literature as not associated with HIV. Odds ratios adjusted on age, gender and lifetime number of sexual partners (aOR) and their 95% confidence intervals (CI) were estimated. Among

*Corresponding author: Antoine Jaquet, MD, PhD, Centre de Recherche INSERM U. 897, Institut de Santé Publique, Epidémiologie et Développement (ISPED), Université de Bordeaux, Tel: 33 (0)5 57 57 95 37, Fax: 33 (0)5. 57.57.45.28, antoine.jaquet@isped.u-bordeaux2.fr.

Funding and financial disclosure: This work was funded by the following institutes: the National Cancer Institute (NCI), the Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD), the National Institute of Allergy and Infectious Diseases (NIAID) (grant n° 5U01AI069919).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

the 1,644 cancer patients enrolled, 184 (11.2%) were identified as HIV-infected. The HIV prevalence in the referent group (n=792) was 4.4% [CI 3.0–5.8]. HIV infection was associated with Kaposi sarcoma (aOR 34.6 [CI: 17.3–69.0]), non-Hodgkin lymphoma (aOR 3.6 [CI 1.9–6.8]), cervical cancer (aOR 4.3 [CI 2.2–8.3]), anogenital cancer (aOR 17.7 [CI 6.9–45.2]) and squamous cell skin carcinoma (aOR 5.2 [CI 2.0–14.4]). A strong association is now reported between HIV infection and Human Papillomavirus (HPV)-related cancers including cervical cancer and anogenital cancer. As these cancers are amenable to prevention strategies, screening of HPV-related cancers among HIV-infected persons is of paramount importance in this African context.

Keywords

Cancer; Cervical cancer; anal cancer; skin cancer; Epidemiology; HIV; Human papillomavirus; Africa

Introduction

In sub-Saharan Africa, mortality and morbidity of people living with the human immunodeficiency virus (HIV) are mainly mediated by opportunistic infections [1]. However, with the scale-up of antiretroviral therapy (ART), chronic conditions such as cancer will soon substantially contribute to disease burden in this part of the world as already observed in high-resource countries [2,3]. HIV infection has been historically associated with malignancies such as Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL) and invasive cervical cancer (ICC) thus contributing to the definition of the AIDS stage according to the US Centers for Disease Control classification [4]. Since then, population-based record linkage studies have enabled the identification of a higher risk of several non AIDS-defining cancers in HIV-infected persons, thus questioning the relevance of such a classification initially designed for clinical care purposes [5]. Mechanisms leading to a higher risk of malignancies is still debated, and they are probably multiple and cancer type-specific. Nevertheless, it is commonly agreed that immunodeficiency and oncogenic virus co-infections such as human papillomaviruses (HPV) play a major role in the occurrence of malignancies in HIV-infected people. In sub-Saharan Africa, the distribution of etiologic factors such as oncogenic viruses interacting with HIV is quite different from what has been previously described in high-resource countries. The paucity of functional cancer registries as well as the absence of national death registries severely limits the ability to conduct population-based record linkage studies on this continent. Several case-referent studies on HIV and malignancies have been conducted in a time of no or limited access to ART and mainly in East and Southern Africa [6,7]. Our aim was to estimate the association between HIV infection and selected types of cancers among patients hospitalized for a malignant condition in four West African countries and in a time of wider access to ART.

Materials and Methods

A case-referent study was initially conducted in three referral hospitals of Abidjan (the economic capital of Côte d'Ivoire) and one referral hospital of Cotonou (the economic

capital of Benin) in 2009-2010. The study was subsequently extended to four referral hospitals in Nigeria: two in Abuja (federal capital), one in Benin city (Edo state), one in Ile-ife (Osun State) and one referral hospital in Lome (the economic capital of Togo) in 2011-2012. Details of the study methodology have been previously reported in a preliminary analysis restricted to data from Côte d'Ivoire and Benin [8]. In brief, during a 24-month period, clinical wards likely to manage patients with cancer were asked to pre-include all adult patients attending with a suspected or confirmed diagnosis of cancer. Pre-included patients were administered a structured questionnaire to collect socio-demographic characteristics including age, gender, marital status, formal education, income, lifetime number of sexual partners, place of living. For diagnostic purposes, clinical, biological, radiological and surgical data leading to the diagnosis of cancer were systematically collected. A cytological and/or histological examination, if indicated, was systematically proposed and financially supported by the research project. Cancer diagnoses were reviewed by local medical staff and confirmed according to available diagnostic resources. Cancers were then classified according to their primary anatomical site (topography) and histological morphology where available using the world health organization third edition of the international classification of diseases for oncology (ICD-O-3) [9]. A rapid HIV test (Determine®, Abbott Diagnostics) was systematically performed by collecting capillary blood by a finger prick test at the time of interview. In case of positive result, a venous blood sample was collected for confirmation purposes, according to the respective national algorithms. Cases were defined as selected types of cancer thought or known to be positively associated with HIV infection including KS, NHL, ICC, cancers of the anogenital organs, oral cavity, pharynx and larynx, Hodgkin lymphoma, squamous cell skin carcinoma, lung cancer, primary liver cancer and leukaemia. A referent group was constituted with a mixture of cancer cases reported in the current literature as not associated with HIV infection [6,7]. The study was approved by the national ethic committees of Benin, Côte d'Ivoire, Nigeria and Togo.

Statistical analysis

Patient characteristics were compared according to the presence or absence of HIV infection using Pearson's χ^2 test or Fisher's exact test when appropriate for categorical variables and Kruskal-Wallis test for continuous variables. An unconditional logistic regression model was used to estimate the association between selected cancers cases and HIV infection. Odds ratio (OR) estimates were reported with their 95% confidence interval (95%CI). In multivariate analysis, ORs were adjusted on age taken as continuous variable, gender (except for ICC), lifetime number of sexual partners (<5 *versus* 5 partners) and country (referent country=Côte d'Ivoire) for cancer types sufficiently represented (n>50 cancer cases). All statistical analyses were performed using SAS software, version 9.2 (SAS Institute Inc, Cary, NC, USA).

Results

A total of 1,913 adults with a suspected diagnosis of cancer were pre-included to participate. Of these, 269 (14.1%) were secondarily excluded for a wrong cancer diagnosis (n=221) or a lack of confirmation of the HIV diagnosis (n=48). Overall, 1,644 patients with a confirmed

diagnosis of cancer and HIV serostatus were included: 60.3% were women and the median age was 49 years [inter quartile range (IQR) 38 – 60]. HIV infection was diagnosed in 184 (11.2%) patients of whom 58 (31.7%) did not know they were HIV-infected prior to the study. HIV-infected patients were significantly younger and more likely to be women compared to the HIV-uninfected ones (Table 1). Of the 126 patients who were aware of their HIV infection at the time of the cancer diagnosis, 72 had a documented ART status. Of these 72 patients, 46 (64%) were on ART.

The most common cancers reported in the 184 HIV-infected patients were ICC (26.0%), KS (20.0%), NHL (12.0%), breast cancer (9.0%) and cancer of the anogenital organs (5.0%). In the 1,460 HIV-negative patients, the most frequently reported cancers were breast cancer (19.0%), ICC (14.0%), prostate cancer (9.0%), NHL (8.0%) and leukaemia (7.0%) (Figure 1).

The prevalence of HIV infection was 4.4% (95%CI 3.0 – 5.8) in the referent group of 792 patients with cancer types considered as not HIV-related including breast (n=288), prostate (n=130), colorectal (n=90), ovary (n=44), myeloma (n=43), stomach (n=38), sarcomas other than KS (n=42), pancreas (n=29), endometrium (n=19), oesophagus (n=14), bladder (n=13), kidney (n=10), endocrine tumours (n=15), gallbladder and biliary ducts (n=8), melanoma (n=8) and mesothelioma (n=1).

HPV-related cancers

The prevalence of HIV infection in the 258 women with ICC was 18.2% (95%CI 13.5 – 22.9). In multivariate analysis, ICC was significantly associated with HIV infection with an adjusted OR of 4.3 [95%CI 2.2 – 8.3] (table 2). Cancers of the anogenital organs included 17 (68%) vulvovaginal cancers and eight (32.0%) anal cancers of which five occurred in women. Altogether, anogenital cancers were associated with HIV infection with an adjusted OR of 17.7 [95%CI 6.9 – 45.2]. Overall, 72.0% of ICC and anogenital cancers had histological confirmation. When restricting our analysis to cancers with pathological confirmation a significant association remained for ICC (adjusted OR=4.4 [95%CI 2.3 – 8.5]) and cancers of the anogenital organs (adjusted OR=13.9 [95%CI 4.5 – 42.2]).

Other cancers

HIV infection was documented in six (20.0%) of the 30 patients diagnosed with a squamous cell skin carcinoma, all confirmed by pathological examination. A significant association with HIV infection was reported with an adjusted OR of 5.2 [95%CI 2.0 – 14.4].

A total of 41 cancers of the oral cavity, 17 cancers of the larynx and 24 cancers of the pharynx were diagnosed. Of these 82 cancers, 63 (76.8%) were confirmed by histological examination of which 57 (90.5%) were squamous cell carcinoma. Altogether, cancers of the oral cavity, larynx and pharynx were not significantly associated with HIV infection (OR=1.6 [95%CI 0.6 – 4.4]). When restricting our analysis to cancer diagnoses with documented squamous cell carcinoma, a similar association was found with an OR of 1.4 [95%CI 0.4 – 4.0].

Of the 58 patients diagnosed with KS, 37 (63.8%) were HIV-infected. KS was associated with HIV infection with an adjusted OR of 34.6 [95%CI 17.3 – 69.0]. Twenty two (16.5%) of the 133 patients diagnosed with an NHL were HIV-infected. Of the 133 NHL cases diagnosed, 83 (62.4%) had a documented morphological type and 86.7% of them were mature B-cell NHL. Marginal zone B-cell (16.9%), diffuse large B-cell (15.7%), small B-cell lymphocytic (14.5%) and Burkitt lymphoma (12.0%) were the four most commonly reported types of NHL with specified morphological type. In multivariate analysis, NHL was significantly associated with HIV infection with an adjusted OR of 3.6 [95%CI 1.9 – 6.8]. When restricting our analysis to AIDS-defining NHL subtypes (diffuse large B-cell lymphoma [n=20], Burkitt lymphoma [n=16] and primary lymphomas arising in the central nervous system [n=1]) the association remained with an adjusted OR of 4.7 [95%CI 1.4 – 15.9]. Primary liver cancer was diagnosed in 69 patients and seven (10.1%) were HIV-infected. A significant association between HIV infection and primary liver cancer was reported with an adjusted OR of 2.2 [95%CI 1.0 – 5.8]. No significant associations were reported between other cancers and HIV infection including Hodgkin lymphoma (adjusted OR=3.4 [95%CI 0.9 – 13.5]) and lungcancers (adjusted OR=2.0 [95%CI 0.4 – 8.9]).

Discussion

AIDS-defining cancers were strongly associated with HIV infection and remain leading causes of cancer in West Africa, irrespective of HIV-infection in the ART era. The magnitude of the association between KS, NHL and HIV was quite similar to what has already been reported in our preliminary report as well as previous studies from Uganda and South Africa [6,7,10]. In a context of increasing access to ART, the proportion of HIV-infected patients presenting with a KS and to a certain extent NHL, should decline as already reported in high-resource countries [11]. Indeed, a report from the Ugandan cancer registry showed a decline in the incidence of both KS and NHL in the past decade [12]. In South Africa, observational cohorts suggest a significant reduction in the incidence of KS in HIV-infected patients accessing ART versus non ART users [13]. These two studies also showed that a significant proportion of KS cases still occur despite effective ART use. In sub-Saharan Africa, the scale-up of ART is the best prevention strategy against KS and NHL. However, access to efficient and adapted chemotherapy will still be needed for these two HIV-related neoplasms.

ICC was the most frequent cancer in HIV-infected patients. The significant association with HIV was consistent with the five-fold increased risk previously described in record-linkage studies from high-resource countries [14]. This association between ICC and HIV is also consistent with previous dedicated case-referent studies conducted in Côte d'Ivoire en Senegal a decade ago (i.e. before the ART era) reporting adjusted ORs of 3.4 [95%CI 1.1-10.8] and 6.5 [95%CI 2.1 – 19.8], respectively [15,16]. Unlike KS and certain subtypes of NHL, no clear decline has been reported in the occurrence of ICC since the advent of ART [11]. The integration of efficient cervical screening programs in HIV-infected women as well as HPV vaccination of HIV-infected adolescents remains a priority in sub-Saharan Africa to prevent ICC.

The large-scale of our case-referent study enabled the identification of significant associations between HIV infection and some non-AIDS defining cancers including cancer of the anogenital organs and squamous cell skin carcinoma. These findings are concordant with a previous report from South Africa using the same methodological approach. In their case-referent study, Stein *et al* had indeed reported for the first time a significant association between anogenital cancers (adjusted OR=2.2 [95%CI 1.4–3.3]), squamous cell skin carcinoma (adjusted OR=2.6 [95%CI 1.4–4.9]) and HIV infection [7].

Cancers of the anogenital organs were particularly frequent among HIV-infected patients representing the second most frequent non-AIDS defining cancer after breast cancer. The association reported here between anogenital cancers and HIV infection is slightly lower than the 20-fold to 80-fold increased risk associated with HIV infection reported in previous record linkage studies from high-resource countries [5,17]. However, in these settings, the risk of anogenital cancers associated with HIV infection was mainly driven by the high proportion of men who have sex with men which tends to be less important among HIV-infected populations in sub-Saharan Africa. In the present study, the majority of anogenital cancers occurred in women. Although sharing the same risk factor, less emphasis has been put on these cancers compared to ICC in sub-Saharan Africa so far. Like ICC, previous reports have shown that ART use has limited or no effect in reducing the incidence of anogenital cancers [18]. There are currently no recommendations for anal cancer screening in high-risk populations of sub-Saharan Africa. Nevertheless, using preexisting cervical cancer programs represent a great opportunity to sensitize participating women and healthcare providers to the risk of other HPV-related cancers such as anal cancers in a context of endemic HIV and HPV infections. In addition, pilot projects assessing the feasibility and acceptability of anal cancer screening in high-risk populations such as HIV-positive women could be implemented relying on preexisting cervical cancer screening programs.

Skin cancers are the most common cancers affecting Caucasian individuals worldwide. While being less common in persons with skin of color, it is associated with greater mortality [19]. A cohort study comparing HIV-infected and HIV-uninfected adult Caucasians showed that the incidence of squamous cell skin carcinoma was higher in HIV-infected participants (adjusted rate ratio of 2.6 [95%CI 2.1 – 3.2]). Moreover, a significant trend of higher rate ratios with lower CD4 counts was also identified [20]. The impact of immunodeficiency on the occurrence of squamous cell skin carcinoma was also reported in solid transplant recipients [14,21]. Therefore, the high association between squamous cell skin carcinoma and HIV infection might be related to the more profound immunodeficiency experienced by HIV-infected patients in West Africa compared to Caucasians HIV-infected patients. The implication of HPV infection in the occurrence of squamous cell skin carcinoma is less clear compared to ICC or anogenital cancers. Nevertheless, the impact of immunodeficiency on squamous cell skin carcinoma in HIV-infected persons suggests the implication of an infectious agent as most cancers linked to immunodeficiency have a known viral etiology [14]. Furthermore, an increasing literature reports an association between squamous cell skin carcinoma and the presence of HPV DNA of β -papillomavirus species 2 [22–24]. Primary liver cancer has been reported as associated with HIV infection in

our preliminary report, in accordance to what has been observed in industrialized countries [8]. Indeed, a meta-analysis reported an increased standardized incidence ratio of 5.6 [95%CI 4.0-7.7] for primary liver cancer in HIV-infected persons who are at higher risk of chronic viral hepatitis [5]. In this updated analysis, the limited number of additional cases of primary liver cancer provided from Nigeria and Togo did not allow us to measure this specific association with sufficient statistical power. Therefore, the exact role of HIV infection in the occurrence of primary liver cancer in the specific context of Sub-Saharan Africa needs to be explored further. Indeed, in West Africa, HBV infection is endemic and usually acquired during childhood. The prevalence of HBV infection seems not influenced by HIV status and immunodeficiency might play a major role in the occurrence of this cancer as suggested by its higher incidence in transplant patients compared to the general population [14].

Limitations

The cross-sectional nature of the study prevents from drawing any causal relation between HIV infection and cancer. However, in a context where the collection of prospective cancer cases is particularly challenging, this approach enabled us to study the association of HIV and relatively rare cancer such as cancers of the ano-genital organs or skin cancer. Our study population might not reflect the exact distribution of cancers occurring in these countries. Indeed, these cancer cases are only representative of patients attending the participating referral hospital during the study period as we disregarded patients with cancers attending exclusively the private health sector or other referral hospitals in these countries. However, the pattern of cancers reported was quite similar to the distribution of cancers reported from most recent incidence estimates data reported by the Globocan program in West Africa [25]. Potential selection biases might have distorted the estimated prevalence of HIV infection in the different groups of cancers. These biases might explain some heterogeneity between countries in terms of strength of association with HIV infection for selected cancer types. Nevertheless, regarding the referent group, reported HIV prevalence figures in Côte d'Ivoire and Nigeria are quite similar (see. supplementary table) and consistent with the estimated HIV prevalence in the adult general population of both countries. Finally, this present extension of our preliminary report failed to include a significant number of additional cases for several important cancer types including hepatocellular carcinoma or lymphomas. Dedicated case-control studies exploring the full spectrum of etiologic factors for important cancers are needed. For this purpose, international epidemiologic networks represent a unique opportunity to gather information on specific malignant conditions in Sub-Saharan Africa.

Conclusion

Our study provided a rather representative and precise picture of the association between AIDS-defining cancers and HIV infection in West Africa. Several non AIDS-defining malignant conditions including cancers of the anogenital organs and squamous cell skin carcinoma were reported to be linked with HIV. HPV-related cancers are reported here as leading causes of malignancies in people living with HIV in the ART era. As these cancers

are amenable to prevention strategies, adapted screening programs among persons living with HIV are of paramount importance in sub-Saharan Africa.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We are indebted to all of the patients who agreed to participate in this present study as well as to the medical referents of the clinical wards where the study was conducted. We are also indebted to clinical monitors who ensured the data collection. We want to thank Mr Benjamin Kariyare (CaResP, Lome), Mr Jesse James (IHVN, Abuja), Mr Jules Mahan and Mr Jean-Claude Azani (PACCI, Abidjan) for their implication in data entry and data management process. Special thanks to Rosemary Mc Kaig (NIAID) and Geraldina Dominguez (NCI) for encouraging the study.

References

1. Lewden C, Drabo YJ, Zannou DM, Maiga MY, Minta DK, et al. Disease patterns and causes of death of hospitalized HIV-positive adults in West Africa: a multicountry survey in the antiretroviral treatment era. *J Int AIDS Soc.* 2014; 17:18797. [PubMed: 24713375]
2. Morlat P, Roussillon C, Henard S, Salmon D, Bonnet F, et al. Causes of death among HIV-infected patients in France in 2010 (national survey): trends since 2000. *AIDS.* 2014; 28:1181–1191. [PubMed: 24901259]
3. Smith CJ, Ryom L, Weber R, Morlat P, Pradier C, et al. Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration. *Lancet.* 2014; 384:241–248. [PubMed: 25042234]
4. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR Recomm Rep.* 1992; 41:1–19.
5. Shiels MS, Cole SR, Kirk GD, Poole C. A meta-analysis of the incidence of non-AIDS cancers in HIV-infected individuals. *J Acquir Immune Defic Syndr.* 2009; 52:611–622. [PubMed: 19770804]
6. Newton R, Ziegler J, Beral V, Mbidde E, Carpenter L, et al. A case-control study of human immunodeficiency virus infection and cancer in adults and children residing in Kampala, Uganda. *Int J Cancer.* 2001; 92:622–627. [PubMed: 11340563]
7. Stein L, Urban MI, O'Connell D, Yu XQ, Beral V, et al. The spectrum of human immunodeficiency virus-associated cancers in a South African black population: results from a case-control study, 1995–2004. *Int J Cancer.* 2008; 122:2260–2265. [PubMed: 18241034]
8. Tanon A, Jaquet A, Ekouevi DK, Akakpo J, Adoubi I, et al. The spectrum of cancers in West Africa: associations with human immunodeficiency virus. *PLoS One.* 2012; 7:e48108. [PubMed: 23144732]
9. Fritz, A.; Percy, C.; Lang, A.; Shanmugaratnam, K.; Sobin, L., et al. International classification of diseases for oncology. 3rd. Geneva: World Health Organisation; 2000.
10. Mbulaiteye SM, Katabira ET, Wabinga H, Parkin DM, Virgo P, et al. Spectrum of cancers among HIV-infected persons in Africa: the Uganda AIDS-Cancer Registry Match Study. *Int J Cancer.* 2006; 118:985–990. [PubMed: 16106415]
11. Shiels MS, Pfeiffer RM, Hall HI, Li J, Goedert JJ, et al. Proportions of Kaposi sarcoma, selected non-Hodgkin lymphomas, and cervical cancer in the United States occurring in persons with AIDS, 1980–2007. *JAMA.* 2011; 305:1450–1459. [PubMed: 21486978]
12. Wabinga HR, Namboozee S, Amulen PM, Okello C, Mbus L, et al. Trends in the incidence of cancer in Kampala, Uganda 1991–2010. *Int J Cancer.* 2014; 135:432–439. [PubMed: 24615279]
13. Bohlius J, Valeri F, Maskew M, Prozesky H, Garone D, et al. Kaposi's Sarcoma in HIV-infected patients in South Africa: Multicohort study in the antiretroviral therapy era. *Int J Cancer.* 2014; 135:2644–2652. [PubMed: 24729433]

14. Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. *Lancet*. 2007; 370:59–67. [PubMed: 17617273]
15. Adjorlolo-Johnson G, Unger ER, Boni-Ouattara E, Toure-Coulibaly K, Maurice C, et al. Assessing the relationship between HIV infection and cervical cancer in Cote d'Ivoire: a case-control study. *BMC Infect Dis*. 2010; 10:242. [PubMed: 20716343]
16. Holmes RS, Hawes SE, Toure P, Dem A, Feng Q, et al. HIV infection as a risk factor for cervical cancer and cervical intraepithelial neoplasia in Senegal. *Cancer Epidemiol Biomarkers Prev*. 2009; 18:2442–2446. [PubMed: 19690181]
17. Silverberg MJ, Lau B, Justice AC, Engels E, Gill MJ, et al. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. *Clin Infect Dis*. 2012; 54:1026–1034. [PubMed: 22291097]
18. Piketty C, Selinger-Leneman H, Bouvier AM, Belot A, Mary-Krause M, et al. Incidence of HIV-related anal cancer remains increased despite long-term combined antiretroviral treatment: results from the french hospital database on HIV. *J Clin Oncol*. 2012; 30:4360–4366. [PubMed: 23091098]
19. Gloster HM Jr, Neal K. Skin cancer in skin of color. *J Am Acad Dermatol*. 2006; 55:741–760. quiz 761-744. [PubMed: 17052479]
20. Silverberg MJ, Leyden W, Warton EM, Quesenberry CP Jr, Engels EA, et al. HIV infection status, immunodeficiency, and the incidence of non-melanoma skin cancer. *J Natl Cancer Inst*. 2013; 105:350–360. [PubMed: 23291375]
21. Euvrard S, Kanitakis J, Claudy A. Skin cancers after organ transplantation. *N Engl J Med*. 2003; 348:1681–1691. [PubMed: 12711744]
22. Andersson K, Michael KM, Luostarinen T, Waterboer T, Gislefoss R, et al. Prospective study of human papillomavirus seropositivity and risk of nonmelanoma skin cancer. *Am J Epidemiol*. 2012; 175:685–695. [PubMed: 22419740]
23. Bouwes Bavinck JN, Neale RE, Abeni D, Euvrard S, Green AC, et al. Multicenter study of the association between betapapillomavirus infection and cutaneous squamous cell carcinoma. *Cancer Res*. 2010; 70:9777–9786. [PubMed: 21098702]
24. Wang J, Aldabagh B, Yu J, Arron ST. Role of human papillomavirus in cutaneous squamous cell carcinoma: a meta-analysis. *J Am Acad Dermatol*. 2014; 70:621–629. [PubMed: 24629358]
25. Ferlay, J.; Soerjomataram, I.; Ervik, M.; Dikshit, R.; Eser, S., et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No 11. Internet
26. [accessed on 02/03/2015] Lyon, France: International Agency for Research on Cancer. 2013. Available from: <http://globocan.iarc.fr>

Highlights

- The study assessed the association between HIV and several cancers in West Africa
- A strong association was reported between HIV infection and HPV-related cancers
- Significant association between HIV infection and anogenital cancers
- Significant association between HIV infection and squamous cell skin carcinoma

Figure 1. Most reported cancers sites or morphological types according to their HIV status in Benin, Côte d'Ivoire, Nigeria and Togo (N=1,644), 2009-2012

Table 1
Characteristics of patients with a confirmed diagnosis of cancer according to HIV status (N=1,644), 2009-2012

		HIV-infected patients diagnosed with cancer (n=184) n (%) [*]	HIV-uninfected patients diagnosed with cancer (n=1,460) n (%) [*]	P	Total number of patients diagnosed with cancer (N=1,644) n (%)
Age, median [inter quartile range]		41 [35 – 48]	50 [38 – 61]	<10 ⁻⁴	49 [38 – 60]
Gender					
	Men	57 (31.0)	596 (40.8)	0.01	653 (39.7)
	Women	127 (69.0)	864 (59.2)		991 (60.3)
Marital status^{**}				<10 ⁻³	
	Single	52 (28.4)	273 (18.9)		325 (20.0)
	Married/cohabitant	99 (54.1)	1009 (69.8)		1108 (68.0)
	Widowed/divorced	32 (17.5)	164 (11.3)		196 (12.0)
Formal education[†]				0.11	
	No school	33 (18.3)	361 (25.0)		394 (24.3)
	Primary school	43 (23.9)	297 (20.6)		340 (21.0)
	Secondary and over	104 (57.8)	782 (54.4)		886 (54.7)
Place of living				0.52	
	Rural	92 (50.0)	767 (52.5)		859 (52.2)
	Urban	92 (50.0)	693 (47.5)		785 (47.8)
Country				0.05	
	Benin	12 (6.5)	79 (5.4)		91 (5.5)
	Côte d'Ivoire	116 (63.0)	809 (55.4)		925 (56.3)
	Nigeria	46 (25.0)	513 (35.1)		559 (34.0)
	Togo	10 (5.5)	59 (4.1)		69 (4.2)
Tobacco use	Former or current smoker	19 (10.3)	130 (8.9)	0.52	149 (9.1)
Alcohol use	During the last 12 months	51 (28.6)	343 (24.2)	0.19	394 (24.7)
Number of lifetime sexual partners[‡]				<10 ⁻²	
	0 to 2	87 (49.4)	824 (58.5)		911 (57.5)
	2 to 4	49 (27.8)	393 (27.9)		442 (27.9)
	5	40 (22.7)	191 (13.6)		231 (14.6)
Cancers with histological diagnosis		124 (71.3)	916 (68.6)	0.47	1040 (70.0)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Absolute number and percentage for baseline characteristics of patients according to their HIV status

*
15 missing values,
24 missing values,
61 missing values

Table 2
Association between selected cancers and HIV infection in referral hospitals of Benin, Côte d'Ivoire, Nigeria and Togo, 2009-2012

Cancer site or morphological type (and ICD-O-3 code)	Univariate			Multivariate*		
	n/N** (%)	OR	95% CI	P	OR	95% CI
Control group [†]						
Total	35/792 (4.4)	1			1	
Women (for ICC)	21/483 (4.3)	1			1	
HPV-related cancers						
Invasive cervical cancer (C53)	47/258 (18.2)	4.7	2.7 – 7.9	<10 ⁻⁴	4.3	2.2 – 8.3
Anogenital organs (C21, C51, C52, C60)	10/25 (40.0)	14.0	5.9 – 33.3	<10 ⁻⁴	17.7	6.9 – 45.2
Other cancers						
Oral cavity, pharynx and larynx (C00-10, C32)	6/82 (7.3)	1.6	0.7 – 3.9	0.29	1.6	0.6 – 4.4
Squamous cell skin carcinoma (C44, M8050-8080)	6/30 (20.0)	5.3	2.0 – 13.7	<10 ⁻³	5.2	2.0 – 14.4
Kaposi sarcoma (M9140)	37/58 (63.8)	37.0	19.7 – 69.5	<10 ⁻⁴	34.6	17.3 – 69.0
Non Hodgkin lymphoma (M9591, 9670-9727)	22/133 (16.5)	4.2	2.4 – 7.3	<10 ⁻⁴	3.6	1.9 – 6.8
Hodgkin lymphoma (M9650-9667)	3/23 (13.0)	3.1	1.0 – 11.1	0.05	3.4	0.9 – 13.5
Primary liver cancer (C22)	7/69 (10.1)	2.4	1.1 – 5.5	0.04	2.2	1.0 – 5.8
Lung cancer (C34)	2/26 (7.7)	1.7	0.4 – 7.7	0.46	2.0	0.4 – 8.9
Leukemia (C42, M9800-9891)	4/102 (3.9)	0.9	0.3 – 2.5	0.77	0.7	0.2 – 2.4

* Adjusted on age taken as a continuous variable, gender (except for invasive cervical cancer [ICC]), lifetime number of sexual partners (<5 versus ≥5) and country (referent country= Côte d'Ivoire) for sufficiently represented cancer types (n>50 cancer cases).

** n/N: number of HIV+ patients/number of patients with cancer

[†] Control group of cancers not known to be related with HIV infection from the existing literature: prostate, breast, colon/rectum, oesophagus, stomach, pancreas, endometrium, ovary, endocrine, sarcomas other than Kaposi sarcoma.

Abbreviations: OR Odd Ratio, CI Confidence Interval