

Cancer Incidence in Patients Diagnosed with Acquired Immunodeficiency Syndrome (AIDS) in Colombia

Daniel Uribe Parra*, Diana Pulido, Gilberto Lopes, Patricia Sánchez Quintero, Lizbeth Acuna Merchan, Omaira Valencia Estupinan, Luis Soler and Jaime Gonzalez

Fondo Colombiano de Enfermedades de Alto Costo, Bogotá, Colombia

Abstract

Background: AIDS is associated with a number of malignancies, which in turn carry a high burden of mortality and morbidity in affected patients. This article was developed as an initiative of the High-Cost Diseases Office (CAC in Spanish) to provide the Colombian health system with evidence on the incidence of Cancer in patients diagnosed with AIDS in the country.

Methods: The CAC compiled the National Cancer and Human Immunodeficiency Virus (HIV) administrative registries, which identify unique patients diagnosed with both Cancer and AIDS from 1983 to 2015. For the 736 cases found, we considered only those diagnosed with Cancer five years before a diagnosis of AIDS and all cases after the diagnosis. A final sample of 238 individuals, with age ranging from 17 to 84 years, diagnosed with AIDS between 1998 and 2015, was analyzed using Stata Software to compute Standardized Incidence Ratio (SIR) of cancers.

Results: Results show that patients with AIDS display an elevated risk of developing the following specific types of cancer: Kaposi's sarcoma's (male SIR 301.12; female SIR 252.67) Invasive cervical cancer (female SIR 5.09); Non-Hodgkin Lymphoma (male SIR 20.65; female SIR 9.10). The following non-AIDS-defining cancers were also more common in patients with the disease: in men, anal cancer (SIR 51.52), eye and related malignancies (SIR 27.24), and Hodgkin's Lymphoma (SIR 20.96); in women: anal (SIR 24.82); vaginal and vulvar (SIR 10.36); and *in situ* cervical cancer (SIR 5.83).

Conclusion: There is an increased incidence of specific types of cancers in a population of patients diagnosed with AIDS in Colombia, in accordance with data from other regions of the world. The National Cancer and AIDS registries provide local information, which can be used for health care policy planning.

Keywords: AIDS; Cancer; Standard incidence ratio; AIDS-related cancer; AIDS non-related cancers

Introduction

Clinical trial cohorts and case series from Africa, Europe, and the Americas have explored the relationship between the Acquired Immunodeficiency Syndrome (AIDS) and cancer [1-5].

In spite of the fact that we have information about Kaposi's Sarcoma in Human Immunodeficiency Virus (HIV)/AIDS patients from a registry in Cali, Colombia [6,7], there are no other data available on cancer incidence in patients diagnosed with AIDS in our country.

The immunosuppression caused by HIV infection increases the risk of AIDS-defining malignancies such as Kaposi's Sarcoma's, Non-Hodgkin's Lymphoma and Invasive Cervical Cancer [6,8-10], as well as that of certain non-AIDS-defining cancers such as Hodgkin's Lymphoma, vulvar and anal cancers [3,11].

In Colombia, HIV infection is a major public health concern: 61174 people were living with HIV in 2015, 34076 of whom were diagnosed with AIDS [12]. Late detection of HIV leads to worse outcomes, including decreased survival and worse quality of life, and significantly increases health system expenditures in human resources [13], hospitalization, inpatient and ambulatory care [14]. Additionally, quality of life also severely diminishes, and mortality increases [15].

About 95% of patients in Colombia are eventually treated with antiretroviral therapy [12], but late diagnosis continues to be an issue. The improvement of results with available therapies and the increase in access to medicines have increased survival and consequently, the incidence of AIDS-defining malignancies and non-defining cancers [16-18] in patients with HIV infection.

This article was developed as an initiative of the High-Cost Diseases Office (CAC in Spanish) to provide the Colombian health system with evidence on the incidence of Cancer in patients diagnosed with AIDS in the country to optimize policy planning.

Materials and Methods

To evaluate the risk of cancer among AIDS patients in Colombia, we used the general administrative CAC population-based National Cancer Registry of 2015 [19], matched with the National HIV Registry of the same year [20], to create a database of unique patients using STATA software.

For analysis, we considered cases with a diagnosis of cancer and AIDS between 1983 and 2015, of which 1325 HIV patients matched with the national cancer database. Neoplasms were established in clusters by using International Classification of Diseases, Tenth Version codes. 213 different ICD10 codes were clustered into the most common and relevant pathologies into groups to make the analysis comprehensible and useful.

***Corresponding author:** Daniel Uribe Parra, Knowledge management, Fondo Colombiano de Enfermedades de Alto Costo, Carrera 45#10334, Bogotá, 110111, Colombia; Tel: 573144720888; E-mail: d.urbie11@uniandes.edu.co

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We used the classification and definitions of the Centers for Disease Control and Prevention to determine AIDS and non-AIDS-defining cancers [21]. Non-invasive neoplasms (ICD10, codes D00-D09) are also showed. However, invasive and *in-situ* neoplasms may be underreported to the CAC cancer registry, attenuating the results.

Data Analysis

This paper was limited to neoplasms diagnosed between 60 months before and any date after a diagnosis of AIDS. This time interval was established, on the one hand, to make our results comparable with other similar studies, and, on the other hand, because there is evidence to support that AIDS tends to occur within the first 60 months after HIV infection [9,22]. A diagnosis of a non-AIDS-defining neoplasm did not change the status of HIV-infected patients into AIDS, therefore counting them as in pre-AIDS period. Besides, patients that were diagnosed with AIDS and after that were diagnosed with cancer have no limit of incidence date and were counted as in post-AIDS period.

Applying the criteria described above we obtained a sample of 238 patients with AIDS and cancer. Age ranged from 17 to 84 years. Patients were diagnosed between 1998 and 2015. We estimated the individual incidence of cancer until five years before 1998, which is consistent with the first identified case of AIDS and cancer according to the matched data.

We compared the observed number of cancers cases among people with AIDS with the incidence of cancer in the Colombian population. We used the National Statistics Department (DANE in Spanish) registry to calculate cancer incidence (expected number of cases by -SIR).

Among the 238 patients in the final sample, we found that four died between September 2014 and October 2014. However, all patients included survived at least until they were diagnosed with AIDS. We cannot adjust results by survival rate because we currently do not have access to the corresponding information.

We first calculated the probability of developing a certain type of cancer using the National Cancer Registry Database by a group of age and diagnosis date, to determine the expected number of cases within the population with AIDS reported in the National HIV Registry Database for the same group ages and diagnosis date.

Thereafter we computed the odds ratio (OR) for the patients in the Post-AIDS period, obtaining a total sample of 183 of cases diagnosed with AIDS, that also developed specific neoplasms (both related and non-related cancers) between 2008 and 2015 (Figure 1).

Results

The National HIV Registry Database developed by the CAC displays a total of 61174 people living with HIV, from which 34076 have AIDS [12,20]. Additionally, the National Cancer Registry Database contains a total of 172879 patients with cancer [19,23]. By merging these two databases, we found that 736 patients were diagnosed with Cancer and HIV between 1983 and 2015.

From the 736 matches, 25 patients were diagnosed with HIV stage I, 103 patients were in stage II, 603 in stage III (AIDS) and five patients were in the process of being classified. 450 matches had no valid dates in both databases and 44 patients were in non-AIDS stage or were in date out of range.

The 238 patients included in the analysis developed Cancer up to 60 months before the diagnosis of AIDS, and the last case reported occurred 84 months after the diagnosis of AIDS. The majority of cases took place in the most populated departments of Colombia: Bogotá, D.C. and Antioquia with 50.84% of cases, followed by Valle del Cauca with 14.70% and the remaining 34.45% of cases corresponding to the rest of the country. Such characteristics are shown in Table 1.

Of the 238 identified patients (Figure 1), 77.31 % were men and 22.68% were women. Among the men, 91% were diagnosed with AIDS and cancer between the ages of 20 and 59 years old. Among women, 94.44% cases were between 25 and 64 years old.

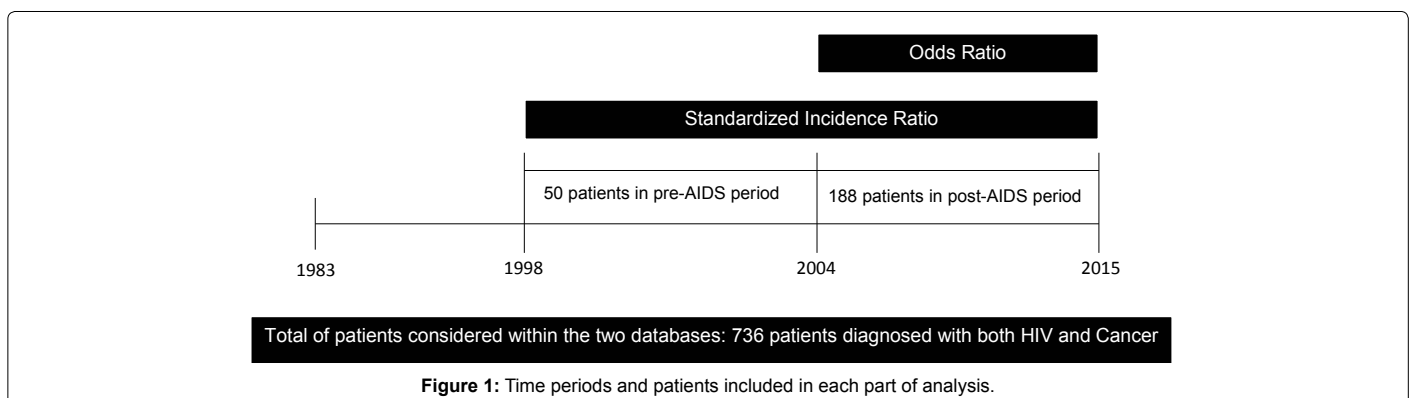
AIDS-defining cancers and SIR

The incidence of Kaposi's Sarcomas increased 301-fold in men and 252-fold in women in AIDS patients as compared to the general Colombian population. Similarly, the SIR for NHL was higher by 20.65-fold in men and 9.1-fold in women. Invasive cervical cancer was increased by 5.09-fold (Tables 2 and 3).

Non-AIDS-defining cancers and overall SIRs

The SIR was elevated for several types of cancer depending on gender. In men, patients with AIDS had a higher incidence of anal cancer (SIR 51.52); eye cancer and related malignancies (SIR 27.24); Hodgkin Lymphoma (SIR 20.96); connective tissue cancers (SIR 8.81); Penis and testicular cancer (SIR 3.6), and non-melanoma skin cancer (SIR 2.56). For women higher SIRs were found for vaginal and vulvar cancer (17.31), and *in-situ* cervical cancer (10.66). Results are summarized in Tables 2 and 3.

In Table 2, Observed and expected cancer cases and standardized incidence ratios of specific types of cancer among Colombian men with a diagnosis of Acquired Immunodeficiency Syndrome 15 years and



Department	Men		Women		
	n=	%	n=	%	
Antioquia	54	22.68	Bogotá	11	4.62
Bogotá	49	20.58	Antioquia	7	2.94
Valle	29	12.18	Valle	6	2.52
Risaralda	9	3.78	Cesar	4	1.68
Atlántico	7	2.94	Atlántico	3	1.26
Cundinamarca	5	2.10	Cauca	3	1.26
Santander	5	2.10	Risaralda	3	1.26
Boyacá	4	1.68	Bolívar	2	0.84
Quindío	4	1.68	Magdalena	2	0.84
Caldas	3	1.26	Nariño	2	0.84
Huila	3	1.26	Santander	2	0.84
Bolívar	2	0.84	Sucre	2	0.84
Cauca	2	0.84	Boyacá	1	0.42
Cesar	2	0.84	Caldas	1	0.42
Casanare	1	0.42	Casanare	1	0.42
Córdoba	1	0.42	Córdoba	1	0.42
Meta	1	0.42	Cundinamarca	1	0.42
Norte de Santander	1	0.42	Huila	1	0.42
Sucre	1	0.42	Quindío	1	0.42
Tolima	1	0.42			
Actual age		0			
	n=	%	n=	%	
15-19 years	1	0.42	0	0.00	
20-24 years	10	4.20	1	0.42	
25-29 years	19	7.98	5	2.10	
30-34 years	16	6.72	6	2.52	
35-39 years	33	13.87	6	2.52	
40-44 years	26	10.92	9	3.78	
45-49 years	19	7.98	6	2.52	
50-54 years	26	10.92	9	3.78	
55-59 years	19	7.98	5	2.10	
60-64 years	9	3.78	5	2.10	
65-69 years	0	0.00	1	0.42	
70-74 years	2	0.84	1	0.42	
75-79 years	3	1.26	0	0.00	
80 and older	1	0.42	0	0.00	
Mechanism of HIV transmission					
	n=	%	n=	%	
Unknown	39	21.20	6	11.11	
Sexual assault	0	0.00	1	1.85	
Sexual transmission	145	78.80	47	87.04	

Table 1: Socio-demographic characteristics of patients between matched registries of HIV and cancer in Colombian population.

older in the Acquired Immunodeficiency Syndrome/Cancer matched administrative record, Colombia, diagnosed between 1998 and 2015.

In Table 3, Observed and expected cancer cases and standardized incidence ratios of specific types of cancer among Colombian women with Acquired Immunodeficiency Syndrome aged 15 and older in the acquired immunodeficiency/cancer matched administrative record, Colombia, diagnosed between 1998 and 2015.

AIDS-defining cancers in post-AIDS cohort

In our cohort, 188 patients developed cancer after a diagnosis of AIDS. A total of 5 patients were excluded because of inconsistencies in diagnosis. The odds ratio (OR) for Kaposi's sarcoma increased to

390.24-fold in the AIDS population ($p < 0.05$) as compared to the average population. The OR for NHL was 12.37 in the AIDS population as compared to the general population ($p < 0.05$). The OR in cervical cancer was 17.07 ($p < 0.05$) (Table 4).

AIDS non-related cancers in post-AIDS odds ratio

Odds were elevated for several types of cancer: Anal cancer (OR=17.62 $p < 0.05$); Hodgkin's Lymphoma (OR=16.10 $p < 0.05$); Vaginal and vulvar cancer (OR 15.61 $p < 0.05$); Cervical *in situ* (OR=12.85 $p < 0.05$); eye and related cancers (OR=11.93 $p < 0.05$); Spine cancer (OR=11.01 $p < 0.05$); non-specified cancer (OR=6.23 $p < 0.05$) and connective tissue (OR=5.57 $p < 0.05$).

Type of cancer	Observed cases, AIDS with cancer	Expected cases	SIR	95% CI
Kaposi's Sarcoma	59	0.20	301.12	[229.15-388.56]
Non-Hodgkin's Lymphoma	49	2.37	20.65	[15.27-27.31]
Non-AIDS defining cancers				
Lip tongue and oropharynx	3	1.03	2.92	[0.60-8.53]
Stomach cancer	2	3.07	0.65	[0.07-2.35]
Colorectal cancer	7	4.16	1.68	[0.67-3.46]
Urinary tract cancer	2	1.13	1.77	[0.21-6.39]
Penis and testicles cancer	4	1.09	3.68	[1.00-9.41]
Connective tissue cancers	5	0.57	8.72	[2.83-20.34]
Skin non-melanoma related	13	5.07	2.56	[1.36-4.38]
Bone cancer	1	0.31	3.25	[0.08-18.12]
Anus cancer	7	0.14	51.52	[20.71-106.16]
Eye and related cancers	3	0.11	27.24	[5.61-79.62]
Brain cancer	1	0.70	1.44	[0.03-8.00]
Spine cancer	1	0.07	15.20	[0.38-84.69]
Prostate cancer	7	13.22	0.53	[0.21-1.09]
Cancer, site not specified	6	1.55	3.88	[1.42-8.44]
Hodgkin's Lymphoma	14	0.67	20.96	[11.45-35.17]

Table 2: Incidence ratios of specific types of cancer among Colombian men with a diagnosis of acquired immunodeficiency syndrome.

Type of cancer	Observed cases, AIDS with cancer	Expected cases	SIR	95% CI
Kaposi's Sarcoma	6	0.024	252.68	[92.69-550.22]
No Hodgkin's Lymphoma	13	1.428	9.11	[4.34-14.69]
Invasive cervical cancer	11	2.160	5.09	[2.54-9.11]
Non-AIDS-defining cancers				
Vagina and vulva cancer	5	0.29	17.32	[5.62-40.42]
Thyroid cancer	4	1.90	2.11	[0.57-5.39]
Breast cancer	5	9.29	0.54	[0.11-1.10]
Skin non-melanoma related	4	1.85	2.16	[0.33-4.73]
<i>In situ</i> cervical cancer	5	0.47	10.66	[3.46-24.89]
Anus cancer	1	0.04	24.82	[0.62-138.35]

Table 3: Incidence ratios of specific types of cancer among Colombian women with acquired immunodeficiency.

Type of cancer*	AIDS and Cancer	Patients with cancer without AIDS	OR	CI
Kaposi's Sarcoma	56	133	390.24	[285.5-533.3]
Non-Hodgkin's Lymphoma	41	3070	12.37	[9.08-16.81]
Cervical cancer	9	1087	17.07	[8.85-32.85]
Non-AIDS-related cancers				
Anus cancer	6	315	17.63	[7.85-39.52]
Hodgkin's Lymphoma	11	721	16.10	[8.87-29.19]
Vagina and Vulva cancer	5	660	15.61	[6.47-37.6]
<i>In situ</i> Cervical Cancer	6	1090	12.85	[5.76-28.65]
Eye and related cancer	2	155	11.94	[2.96-48.16]
Spine cancer	1	84	11.02	[1.53-79.11]
Non-specified cancer	5	742	6.24	[2.58-15.02]
Connective tissue cancers	5	830	5.57	[2.31-13.43]
Penis and testicles cancer	2	705	1.65	[0.41-6.62]
Urinary tract cancer	2	1289	1.64	[0.40-6.55]
Skin non-melanoma	13	7829	1.54	[0.89-2.64]
Lip and Oropharynx cancer	2	1370	1.35	[0.33-5.40]
Brain cancer	1	869	1.06	[0.14-7.56]
Thyroid gland cancer	3	5045	0.55	[0.17-1.70]
Colorectal cancer	3	6109	0.52	[0.16-1.60]
Breast cancer	4	21172	0.39	[0.14-1.03]
Prostate cancer	5	8977	0.32	[0.13-0.77]
Gastric cancer	1	3594	0.29	[0.04-2.08]

*Five cases were excluded from observations for uncertain in diagnosis timing of AIDS

Table 4: Odds ratio of specific types of cancer after acquired immunodeficiency, aged 20 and older.

In Table 4, Observed cancer cases in patients with AIDS, and odds ratio of specific types of cancer after acquired immunodeficiency, aged 20 and older, in the acquired immunodeficiency/cancer matched administrative record, Colombia, diagnosed between 2004-2015.

Discussion

In this paper, we assessed the association between AIDS and neoplasms in the Colombian population. Our data come from the national administrative cancer and HIV registries [19,20], gathered from all types of insurance within the Colombian health care system. We describe the results of matched data of cancer and HIV national administrative registries, making subsets of interest pathologies for analysis.

In Colombia, one prior study published on Kaposi's Sarcoma in patients diagnosed with HIV/AIDS [6]. However, our paper is the first study to evaluate the incidence and association of AIDS and cancer in Colombia. As expected, this article shows that Kaposi's sarcoma and non-Hodgkin's Lymphoma represent the vast majority of cases within the matched database.

We also showed elevated SIR in men for non-AIDS-defining cancers such as those of the anal canal, eye and related types of cancer, Hodgkin's Lymphoma, and connective tissue neoplasms. These results are relevant in our context, as anal cancer that could be effectively prevented through HPV vaccination of men in Colombia, challenging the current programs, which only provide vaccine to girls in school age [24].

Interestingly, data for women was scarce in the matched database, suggesting that there is a lower incidence of cancer in women with AIDS in Colombia. However, the SIR for non-AIDS-defining cancers was elevated for neoplasms of the vagina and vulva as well as for cervical cancer *in situ*. These findings provide evidence to the Colombian Health Care System that we should promote routine HIV screening in women with any findings suggestive of vulvar and vaginal cancer or *in situ* carcinoma in cervicovaginal cytology [24].

Limitations

Our study does have limitations. First, data were reviewed in a retrospective manner, even if collected prospectively and now continuously. As such there are cases which might have been missed, especially if not diagnosed. Second, the SIRs calculated were estimated based on registries within the health care system and not from population-based registries.

Conclusion

These shortcomings notwithstanding, our paper represents the full spectrum of patients diagnosed with cancer and AIDS in the country and significantly contributes to the understanding of AIDS and neoplasms in Colombia. Our findings have clear implications for policy makers and providers, for improving the quality of care in patients with AIDS and cancer in Colombia. Of special significance is the conclusion that we should increase HIV screening for women presenting with Human Papilloma Virus (HPV)-related cancers and should vaccinate men for HPV as well.

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