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SHORT COMMUNICATION

Cervical intraepithelial neoplasia and invasive cancer risks in women infected with HIV in the French West Indies

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Objective

The aim of the study was to assess whether HIV infection is associated with a higher risk of invasive cervical cancer (ICC).

Methods

We conducted a region-wide, population-based observational cohort study of 1232 HIV-infected women over the age of 15 years in Guadeloupe, a French Caribbean archipelago, during the period 1999–2006. The observed numbers of incident cases of cervical intraepithelial neoplasia (CIN) and ICC were compared with the expected numbers of cases based on the incidence rates for the general population, and the standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) were calculated.

Results

The incidence rate of CIN was higher in the HIV-infected women than in the general population for all grades (SIR 10.1, 95% CI 6.8–14.6 for CIN grade 1; SIR 9.9, 95% CI 6.1–15.3 for CIN grade 2; and SIR 5.2, 95% CI 3.4–7.7 for CIN grade 3). However, no increase in the risk of ICC was observed (SIR 1.7, 95% CI 0.3–4.9).

Conclusions

Despite an increase in the occurrence of cervical cancer precursors, no increase in the risk of cervical cancer was found in a population of HIV-infected women who receive treatment for their infection and have access to ICC prevention services.

Keywords: Caribbean population, cervical intraepithelial neoplasia, cervical screening, HIV, uterine cervical neoplasms

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Introduction

Invasive cervical cancer (ICC) has been included among the conditions defining AIDS in adolescents and adults [1]. The prevalence of cervical cancer precursors [cervical intraepithelial neoplasia (CIN)] has been reported to be high in HIV-infected women [2,3], suggesting that HIV may favour the progression of CIN to ICC. Moreover, HIV is now recognized as a first-class carcinogen according to the World Health Organization [4]. However, although some studies have reported a higher risk of ICC in cohorts of HIV-infected women or in populations severely affected by HIV infection [5–8], others have not [9–11]. Such discrepancies have been explained by geographical differences, the choice of reference population or the efficiency of cervical cancer screening programmes [12].

ICC has not reached epidemic levels among HIV-infected women as initially feared in some areas [9,13], but the debate about the true impact of HIV infection on the incidence of ICC remains open because there is a need to address the question of the utility of intensive/aggressive surgical treatment for CIN in HIV-infected women who may be pregnant.

The incidence of ICC and the prevalence of HIV infection in the Caribbean are among the highest in the world [14]. We report here the incidence of the three grades of CIN and

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ICC in HIV-infected women in Guadeloupe (in the French West Indies), comparing the figures obtained with data for the general population.

Methods

This study was carried out in Guadeloupe, a French Caribbean archipelago with 405,000 inhabitants. The risk of CIN and ICC was investigated longitudinally in 1232 HIV-infected women aged 15 years and over, regardless of the route of infection, who were followed up between 1 January 1999 and 31 December 2006 at the Guadeloupian HIV Survey Health Centre. Each woman was resident in Guadeloupe and provided written consent. Follow-up visits were scheduled at intervals of no more than 6 months, although the precise timing of these visits varied with the patient's immunological status.

Cervical lesions (ICC or CIN) were diagnosed by histological procedures. We conducted a person-year analysis. Person-years at risk were calculated from the first visit to the date of death, the date of ICC or CIN diagnosis or the last follow-up visit, whichever occurred first. Women reporting a history of ICC at baseline or in whom ICC was diagnosed on evaluation at the entry visit were excluded from the study. The expected numbers of cases of ICC and CIN were calculated on the basis of ICC and CIN incidence rates for the period 1999 to 2006 in women aged 15 years and older for the general population of Guadeloupe. In the absence of a cancer registry for Guadeloupe, incidence rates were calculated from data collected from all the pathology laboratories in the archipelago, as previously described [15]. Mean annual age-standardized ICC or CIN incidence rates were multiplied by the number of person-years of observation, to obtain the expected numbers of ICC and CIN, respectively. The observed number of cases was then divided by the expected number, to obtain standardized incidence ratios (SIRs). Confidence intervals (CIs) were determined for these SIRs, assuming a Poisson distribution for the observed cases.

Results

In total, 7738 person-years of observation were accumulated during the study period for the population of HIV-infected women. Median age at inclusion was 37.2 (range 15 to 89) years. All HIV infections were caused by HIV-1. At inclusion, baseline CD4 cell count was ≥ 500 cells/μL in 31.4% of the women, 200–499 cells/μL in 43.6% of the women and <200 cells/μL in 25% of the women. Antiretroviral treatment was required in 78% of the women, and 63% of the women were treated with highly active antiretroviral therapy (HAART). The annual screening coverage rate for cervical cancer in women (Papanicolaou test) was 28%. The median duration of HIV disease since diagnosis was 6.8 years.

Table 1 Standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) for cervical intraepithelial neoplasia (CIN) and invasive cervical cancer (ICC) in Guadeloupe from 1999 to 2006

Lesions	Observed (*n*)	Expected (*n*)	SIR (95% CI)
CIN (all grades)	75	9.9	7.6 (6.0–9.5)
CIN 1	29	2.9	10.1 (6.8–14.6)
CIN 2	20	2.0	9.9 (6.1–15.3)
CIN 3	26	5.0	5.2 (3.4–7.7)
ICC	3	1.8	1.7 (0.3–5.0)

Seventy-five cases of CIN (29 of CIN 1, 20 of CIN 2 and 26 of CIN 3) were diagnosed in HIV-infected women during the study period, whereas only 9.9 were expected (2.9 of CIN 1, 2.0 of CIN 2, and 5.0 of CIN 3) (Table 1). Thus, HIV-infected women had a significantly higher risk of CIN than women of the general population of Guadeloupe, taking all grades into account (SIR 7.6, 95% CI 6.0–9.5). If the different grades of CIN were considered separately, the risk was higher than that for the general population for all grades, but this difference was smaller for CIN 3 than for CIN 1 and 2.

Three cases of ICC were diagnosed in HIV-infected women during the study period, whereas 1.8 were expected (Table 1). Thus, the HIV-infected women did not have a significantly higher risk of ICC than women in the general population of Guadeloupe (SIR 1.7, 95% CI 0.3–5.0).

Discussion

We report here incidence data for individual CIN grades and ICC in HIV-infected women in the Caribbean. We found that HIV infection in women was not associated with a significant increase in the incidence of ICC. This finding is consistent with those of previous studies in which no significant difference in ICC incidence was observed between HIV-infected women and women not infected with HIV [11] or the general population [9,10]. However, HIV-infected women had a significantly higher risk of presenting CIN lesions, whatever the grade considered. Several cross-sectional studies have reported the risk of CIN to be higher in HIV-infected women [2–4]. Goedert *et al.* [9] reported a higher risk of carcinoma *in situ*, a lesion included in grade 3 of the CIN classification, in HIV-infected women than in the general population.

Several explanations may be put forward for our observations relating to CIN. The coverage of annual screening for cervical cancer in HIV-infected women (28%)

was higher than in the general population in Guadeloupe (16%) [16]. Consequently, this may account for the higher frequency of CIN lesion discovery. In addition, it has been reported that, in women with high-grade squamous intraepithelial lesions (HSILs), corresponding to grades 2 and 3 of the CIN classification, the prevalence of human papillomavirus 16 (HPV-16) is lower in HIV-infected women than in women not infected with HIV, whereas the prevalence of other HPV serotypes considered less oncogenic than HPV-16 is higher in HIV-infected women [17]. This would result in a higher incidence of all grades of CIN, but this increase would be greater for CIN 1 and 2 than for CIN 3.

Despite the higher incidence of CIN in our population, no increase in the risk of ICC was observed. There may be several reasons for this. Firstly, the most oncogenic human papillomavirus, HPV-16, which has been reported to be involved in more than half of all ICC cases [18], is underrepresented in HIV-infected women with HSIL [17]. Other reasons probably relate to the treatments for CIN, such as cervical vaporization or conization, or medical treatment for HIV infection, such as HAART, which maintains a sufficiently high level of residual immunocompetence. This appears to be particularly important in our population, which benefits from the provision of health care and drugs paid for by the French national health insurance scheme. During the period covered by this study (1999–2006), the proposed guidelines recommended treating CIN 1 by cervical ablation (vaporization in our cases) or conization and CIN 2 or 3 by conization [19], and HIV infection by HAART when symptoms were present and/or when CD4 cell counts were <350 cells/μL and/or when the viral load was $>55\,000$ HIV-1 RNA copies/mL [20].

To our knowledge, this study is the first to explore the incidence of ICC and CIN in a Caribbean population of HIV-infected women. The strengths of this study are its regionally representative estimates and its exploration of individual CIN grades. This study also has some limitations. The small number of women with ICC in our cohort precluded the assessment of interactions with other risk factors (CD4 cell counts, parity, use of oral contraceptives, smoking and other sexually transmitted diseases). Furthermore, no information on HPV serotypes was available.

In conclusion, this study shows that, in a population in which HIV-infected women receive treatment for their infection and have access to ICC prevention services, there was no increase in the risk of cervical cancer, despite an increase in the occurrence of cervical cancer precursors. Therefore, our data support the statement that there is little evidence to support the designation of ICC as an AIDS-defining cancer [21], especially for populations which have a high level of medical care and access to HAART.

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