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HIV prevalence in patients with cervical carcinoma

A cohort study at a secondary hospital in South Africa

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Abstract

The Human Immunodeficiency Virus (HIV) seropositive prevalence among women with cervical cancer varies in different parts of the world and even within a country. This study aimed to document the prevalence of HIV infection in women with newly diagnosed cervical cancer at a secondary hospital in South Africa.

This study is a retrospective review of records of 89 women who were newly diagnosed with cervical cancer between 01 June 2010 and 31 May 2013 at Pelonomi Hospital, Mangaung, South Africa. Data such as age, parity, gravidity, marital status, occupation, HIV status, CD4 count, on anti-retroviral treatment, clinical stage of disease were retrieved from the case files, the Meditech-patient record and Disa laboratory system. Data analysis was done using the SAS statistical package.

HIV-seropositive prevalence was 52.4%, with the highest prevalence (91.3%) in the age group 40 years and younger. In HIV-positive women, the mean CD4 cell count was 280 cell/mm^3 and 43% of them were not on anti-retroviral treatment. The majority (86%) of all patients presented with late stage disease (International Federation of Gynecology and Obstetrics Stage III and IV) when newly diagnosed with cervical cancer.

This study highlights high HIV-seropositive prevalence; severe immunosuppression and late presentation of the disease in women newly diagnosed with cervical cancer. Cervical cancer screening programs need to be fully reinforced into existing HIV health care services to allow for ideal prevention and early detection of the disease. Anti-retroviral treatment needs to be prioritized for HIV-positive women.

Abbreviations: ART = anti-retroviral treatment, FIGO = International Federation of Gynecology and Obstetrics, HIV = human immunodeficiency virus, HPV = Human Papilloma Virus.

Keywords: cervical cancer, HIV, prevalence

1. Introduction

Cancer of the cervix remains a major cause of morbidity and mortality among women, especially in the developing world.[1,2] Progress has been made in both screening, prevention and treatment, but there still remain many challenges in low-resource settings. These include lack of proper epidemiological data, differing Human Immunodeficiency Virus (HIV) infection prevalence rates reported in women with cervical cancer, and inadequate health care services, which all hamper the progress to reduce morbidity and mortality of cancer of the cervix.[3]

HIV and Acquired Immunodeficiency Syndrome have resulted in high cervical cancer incidence, and therefore, cervical cancer has been classified as an Acquired Immunodeficiency Syndrome-defining disease.[4–6] HIV-seropositive women have been found to be at higher risk of Human Papilloma Virus (HPV) infection due to their immune-compromised status and that they are more likely to develop cervical precancerous lesions that lead to cervical cancer than HIV-negative women.[4,5] Globally, 1% to 2% of HIV-negative women develop high-grade Cervical Intraepithelial Neoplasia annually while HIV-positive women are 10% more prone to develop high-grade Cervical Intra-epithelial Neoplasia lesions.[7] A systematic review by Mapanga and colleagues found that lower economic status, multiple sexual partners, early sexual debut, and smoking may also be confounding factors in cervical cancer and therefore, makes prevention of cervical cancer very important.[3] Denny reported that in South Africa during the year 1998/1999, the highest age specific rate of cervical cancer for all race and age groups occurred among black women aged 66 to 69 years with a rate of 152.5/100,000.[1]

Due to lack of data from low-income settings and in particular the rural Provinces in South Africa, it was decided in 2013 to review the clinical case records and HIV status of newly diagnosed cervical cancer patients attending the Pelonomi Hospital in South Africa. The Pelonomi Hospital is a public

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. All data generated or analyzed during this study are included in this published article [and its supplementary information files]. The datasets generated during and/or analyzed during the current study are publicly available.

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sector facility which renders health services to the low or no-income communities. Results from this retrospective cohort study can serve as baseline data for the developing countries and to be compared with future studies looking at special prevention and treatment programs for cervical cancer patients. It can also assist in improving cervical cancer screening guidelines for HIV-positive women in the low-income settings as HIV-seropositive women are a high-risk group for developing cervical cancer. Identifying the ideal cervical cancer screening methodology for these women in low-income settings will assist in reducing premature mortality among these women.[4]

The results of this study will enhance the education of clinicians and other health care workers on the association of HIV infection and cervical cancer.

2. Methods

This is a retrospective descriptive study and permission to conduct the study was obtained from the Ethics Committee of the Faculty of Health Sciences, University of Free State, and the Head of Clinical at the Pelonomi Hospital. The study was carried out in accordance Declaration of Helsinki, and local guidelines for conducting research. Case records were reviewed from 89 women who were newly diagnosed with cervical cancer between 01 June 2010 and 31 May 2013 at the Gynecologic Unit of the Pelonomi Hospital, Mangaung, South Africa. A structured data form to collect information on each patient was used. Data such as age, parity, gravidity, marital status, occupation, HIV status, CD4 cell count, on anti-retroviral treatment (ART), clinical stage of disease, tumor histological type were retrieved from the case files including the MEDITECH-patient record and Disa laboratory system. The International Federation of Gynecology and Obstetrics (FIGO-2009) cervical cancer clinical staging was used to stage the disease and was extracted from case records.[8]

Patients accessing the Gynecologic Unit of the Pelonomi Hospital were all referred patients from primary health care clinics and primary hospitals in the Mangaung district. HIV testing and CD4 cell counts have previously been done as part of implementing anti-retroviral treatment on relevant HIV-positive women. These HIV test results were done through the referring centers and their laboratories and the results were available on the Disa Laboratory System. HIV tests were all confirmed by Enzyme-linked immunosorbent assay (ELISA – 10283020 Centaur CHIV) in the Pelonomi hospital laboratory. CD4 lymphocyte counts were done using flow cytometry. For known HIV-positive women, a new CD4 cell count was requested after cervical cancer diagnosis was made on histology to obtain their recent CD4 cell count. The CD4 cell counts were done at the Pelonomi hospital laboratory.

The information collected was entered on a structured form and each patient was decoded to protect confidentiality. The FREQ and MEAN procedures of the SAS statistical package were performed to analyze the data and results presented in frequencies, percentages, and charts for graph presentation.

3. Results

Records from 89 women attending Pelonomi Hospital and who were newly diagnosed with cancer of the cervix during 01 June 2010 and 31 May 2013 were reviewed. Table 1 shows selected characteristics and HIV infection prevalence in these patients.

Table 1

Demographic, selected characteristics, and HIV infection prevalence of newly diagnosed cervical cancer patients (n = 89).

Variable	Cases n (%)
Age ≤ 40	23/89 (25.8)
Gravidity ≥ 3	52/89 (58.4)
Unmarried	39/89 (43.8)
Unemployed	76/89 (85.3)
HIV positive	44/84 (52.4)
HIV negative	40/84 (47.6)
Unknown HIV status	5/89 (5.6)
CD4 ≤ 200 cells/mm^3	20/44 (45.5)
CD4 201–500 cells/mm^3	19/44 (43.2)
CD4 501–660 cells/mm^3	5/44 (11.3)
On anti-retroviral treatment	25/44 (56.8)
Not on anti-retroviral treatment	19/44 (43.2)

HIV = Human Immunodeficiency Virus.

In this cohort, 23 (25.8%) of the women were 40 years of age and younger. The mean age calculated was 49.7 years ranging from as young as 25 and up to 79 years old. Fifty-two (58.4%) had 3 or more children, 43.8% were unmarried, and unemployment was high at 85.3%.

Among the total of 89 women, 44 were HIV-positive, 40 were seronegative, and 5 had unknown HIV status, the latter was most likely due to declining HIV testing or unable to provide consent. The HIV prevalence was 52.4% (44/84) with a 95% CI of 41.2 to 63.4. In the HIV-positive cohort, 19 women (43.2%) were not on ART. CD4 cell counts were only conducted and available for the HIV-positive women. Overall, 45.5% (20/44) of the newly diagnosed cervical cancer patients with HIV infection had CD4 cell count ≤200 cells/mm^3 and 43.2% (19/44) had a count between 201 and 500 cells/mm^3. The majority (88.6%) therefore, had a CD4 cell count of less than 500 cells/mm^3. The mean CD4 cell count in HIV-positive women was 280 cells/mm^3.

In this study, the HIV infection was further analyzed per age group. Figure 1 shows that women 40 years of age and younger had the highest HIV infection prevalence of 91.3% (21/23) followed by 52.4% (22/42) in the age group 41 to 60 and only 5.3% (1/19) in the age group older than 60 years.

All 89 patients were clinically staged and Table 2 shows the cancer characteristics.

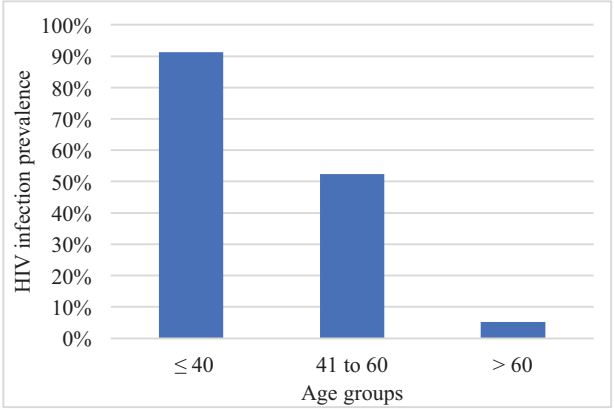

Figure 1. HIV infection prevalence per age group in newly diagnosed cervical cancer patients (n-84). HIV = Human Immunodeficiency Virus.

Table 2

Cervical cancer FIGO-2009 clinical stages and histological types (n = 89).

Variable	No-cases (%)
Clinical stage (FIGO-2009)	
I	3 (3.4)
II	10 (11.2)
III	48 (53.9)
IV	28 (31.5)
Histological types	
Squamous cell carcinoma	84 (94.4)
Adenocarcinoma	4 (4.5)
Adenosquamous	1 (1.1)

FIGO = International Federation of Gynecology and Obstetrics.

Overall, 3.4% were in FIGO-2009 clinical stage I, 11.2% stage II, 53.9% stage III, and 31.5% stage IV. The majority of patients irrespective of HIV status, presented with late stage (III and IV) disease. Squamous cell histological type was the most common accounting for 94.4% (84/89) of the patients.

4. Discussion

During the 3-year period, 89 patients were referred by the primary hospitals and health care clinics to Pelonomi Hospital and on presentation were newly diagnosed with cervical carcinoma. Their ages ranged between 25 and 75 years with a mean age of 49.7. The majority of patients (85%) presented with late stage disease.

The HIV infection prevalence among the newly diagnosed women with cervical cancer was 52.4% (44/84). The high HIV infection prevalence in this cohort of women within the Free State Province in South Africa is in contrast to a much lower HIV prevalence reported by a number of other studies conducted in South Africa including studies from other African countries,[9–16] see Table 3. Lomalisa et al found a HIV prevalence of 7.2% in women who presented with cervical cancer during Jan 1997 to June 1998 in Gauteng Province.[9] In KwaZulu Natal Province, a prevalence of HIV infection among women with cervical carcinoma was reported by Moodley M over 2 time periods of 1999 and 2003 as 21% and 21.8%, respectively.[10] Within Kenya, 2 studies among cervical carcinoma patients also reported different HIV infection prevalence rates.[11–12] Rogo and Kavoo-Linge in 1990 reported a HIV prevalence of 1.5% among cervical cancer patients from Nairobi[11] and Gighangi et al in 2003 found a HIV-seropositive prevalence of 15% among women with cervical cancer referred to the National Kenyatta Teaching Hospital in Nairobi.[12] Newton et al in 2001 reported a 32% HIV prevalence among cervical cancer patients in Uganda[13] and in 2007 Sekirime and Gray reported a HIV prevalence of 18% from case records reviewed between 1993 and 1995.[14] More recently (2018) a study was undertaken in BUTH, Zaria, North-Western Nigeria using data retrieved from case files and reported a 4% HIV seropositivity among patients with cervical cancer.[15] Also in 2018, Simonds et al in Western Cape Province of South Africa reported in their study a HIV infection prevalence rate of 14.4% among patients with cervical cancer.[16] Different background of HIV prevalence rates may account for the differences, as shown by 3 South African studies from sites with different HIV prevalence rates.[9,10,16] The South African National HIV Prevalence Survey-2012 demonstrated different general population background of HIV prevalence rates in different provinces, where KwaZulu Natal-eThekwini Metro had the highest HIV prevalence rate of 14.5%; followed by Gauteng-City of Johannesburg Metro (11.1%); Free State-Mangaung Metro (7.9%); and Western Cape-City of Cape Town (5.2%).[17]

A number of studies reported that HIV-positive patients present with cervical cancer at a younger age compared to HIV-negative patients.[9–16] In this study, the HIV infection was further analyzed per age group and data showed that women 40 years old and younger had the highest HIV prevalence of 91.3% followed by 52.4% in the age group 41 to 60 and only 5.3% in the age group 61 and older, confirming reports by others.

In this study, clinical staging of cervical cancer among the women (89) was evaluated at the time of presentation. The majority of women presented with FIGO (2009) advanced stage III and IV disease. Limited access to health care facilities and poor implementation of cervical cancer screening programs are most likely contributing factors towards late stage disease presentation. Maiman et al demonstrated that HIV-positive women presented with more advanced stages of cervical cancer than HIV-negative women[18] and the high prevalence of HIV infection (52.4%) in this study might also be a contributing factor to the advanced cervical cancer stages at presentation.

It is historically well established that the most common histological type of cervical cancer is squamous cell carcinoma followed by adenocarcinoma. In this study, squamous cell carcinoma was observed in 94% of the women; adenocarcinoma in 5% and adenosquamous formed 1%. A similar pattern was observed by Maiman et al.[18]

The mean CD4 cell count in this cohort was 280 cells/mm^3 and immunosuppression status might be due to the high prevalence of HIV infection as well as the advanced stages of disease. Lomalisa et al reported that HIV-seropositive patients with CD4 cell counts less than 200 cells/mm^3 had significantly more advanced stage cervical carcinoma than HIV seronegative patients.[9] The severe immunosuppression status found in this cohort of women might influence their overall disease progression and response to future treatment.

In the HIV-positive women with newly diagnosed cervical cancer, 43.2% were not on anti-retroviral treatment. This is

Table 3

The Prevalence of HIV infection in cervical cancer patients in different African countries.

African Country	Author	Study period (Year)	Prevalence of HIV infection in patients with cervical carcinoma (%)
South Africa	Moodley M	2003	21.8%
Kenya	Gichangi et al	2000–2002	15%
Uganda	Newton et al	1994–1998	32%
Nigeria	Abdullahi et al	2012–2016	4%

HIV = Human Immunodeficiency Virus.

despite of their low CD4 cell counts with 45.5% having CD4 cell count $\leq$200 cells/mm^3 and 43.2% between 201 and 500 cells/mm^3. The majority (88.6%) had a CD4 cell count of less than 500 cells /mm^3. It has been shown that women living with HIV infection and demonstrating low CD4 cell counts were more likely to acquire oncogenic HPV and less likely to clear HPV infection, but these risks can be mitigated once women are on ART.[19]

Good clinical management of patients with both HIV infection and cervical cancer requires integrated screening, prevention and treatment services. South Africa's current cervical cancer screening policy in the public health sector is offering asymptomatic women 3 free cervical smears, which begin at age of 30 years and are repeated every 10 years. For women with HIV infection, cervical cancer screening is done at 3 yearly intervals for the duration of the woman's life. And only when the screening test is positive for the disease, then the annual screening is recommended for the duration of the woman's life.[20] Screening programs in resource-poor areas remain challenging.[21] For HIV screening in South Africa, Human immunodeficiency virus Counselling and Testing was launched in the year 2000. And the South African department of health national Human immunodeficiency virus Testing Services: Policy, 2010 (updated 2016) renders HIV counselling and testing services to all members of the public. The service delivery platforms are available in the settings of health facilities (hospitals, clinics, mobile clinics) and community sites (home-based, workplace, schools, and higher learning institutions). Any person aged 12 years and older with sufficient maturity and mental capacity to understand the benefits, risks, social, and other implications of HIV testing, may give consent for HIV Testing Service in South Africa.[22] Intensive execution of cervical cancer prevention and treatment programs is strongly advocated for women living with HIV infection.

5. Conclusion

This study highlights a high HIV infection prevalence in younger women newly diagnosed with cancer of the cervix, severe immunosuppression in these women and late presentation of the disease. It further highlights that close to half (42%) of the HIV-positive women were not receiving ART at the time of their diagnosis with cervical cancer. These study results can be used for

(1) the improvement of screening and treatment guidelines for cervical cancer in HIV infected women,
(2) monitoring the effect of scaling up ART in HIV infected women,
(3) educating health care workers on the importance of HIV infection and cervical cancer as dual disease.

Cervical cancer screening programs need to be fully reinforced into the existing HIV health care services, this will allow for ideal prevention and early detection of the disease in the low-resource settings with high HIV prevalence.

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