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ORIGINAL RESEARCH

The prevalence of macroscopic cervical cancer in women on antiretroviral therapy in the Pietermaritzburg metropolitan area

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Background: Women living with HIV (WLWH) are screened for cervical cancer at diagnosis or within a year of sexual debut. Our study looked at the prevalence of macroscopic invasive cervical cancer in WLWH on antiretroviral treatment (ART).

Methods: This was a descriptive retrospective chart review of WLWH on ART. The women were referred with invasive cervical cancer to the Gynaecological Oncology Unit of Greys Tertiary Hospital from January 2018 to December 2019.

Results: We reviewed 220 records. The prevalence of macroscopic invasive cervical cancer was 95%. Of these women, 151 (68.64%) did not have an initial screening test. Of all patients with cervical cancer, 129 (58.64%) were not screened in the previous three years prior to the diagnosis of cervical cancer. There were 212 (96.4%) patients on ART for more than six months. Squamous cell carcinoma made up 212 (96.36%) of the cases, five (2.27%) adenocarcinoma, and two (0.91%) adenosquamous carcinoma. Only 5% of cases were FIGO stage 1A, while the majority were locally advanced disease FIGO stage 2B and 3B (23.2% and 52.3% respectively).

Conclusion: The prevalence of macroscopic and locally advanced cervical cancer is still unacceptably high in WLWH on ART. We need to strengthen cervical cancer screening practices at all healthcare centres that are caring for WLWH in line with national guidelines.

Keywords: macroscopic cervical cancer, antiretroviral therapy, WLWH

Introduction

Cervical cancer is the fourth most common cancer in women worldwide, and the second most common in low- and middle-income countries (LMICs) according to the latest data from the global cancer incidence, mortality, and prevalence report for 2020.[1] There are approximately 604 000 new cases of cervical cancer, with 342 000 deaths annually. The majority of new cases, approximately 85%, as well as 90% of deaths, occur in LMICs.[2]

In 1993, the Centers for Disease Control and Prevention (CDC) declared invasive cervical cancer an AIDS-defining illness in women living with HIV (WLWH). WLWH are six times more likely to develop cervical cancer compared to women without HIV, and it is estimated that 5% of all cervical cancer cases are attributable to HIV.[3,4] The South African National Guidelines for Cervical Cancer Control and Management recommend that the target age for screening low-risk asymptomatic women is 30–50 years of age at a 10-year interval. Asymptomatic women under the age of 30 or above 50 years should not be screened unless upon request. Women who are found to have an abnormality during routine screening should subsequently be screened at three-year intervals until the screen result is negative. When the result is negative, the woman can return to the 10-year schedule. Women should be screened for cervical cancer at diagnosis of HIV, or within a year of sexual debut for vertically transmitted HIV, and subsequently every three years if the screening test is negative. Annual intervals should be used if the screening test is positive for LSIL or ASC-US until the test returns to normal. If the screening test is positive for ASC-H, HSIL, or carcinoma, she should be referred to a cervical evaluation centre for further management. Cervical cytology screening tests are currently a readily available option, but HPV DNA testing is the preferred option due to its sensitivity and cost-effectiveness.[5] These recommendations should drastically reduce or eliminate the diagnosis of macroscopic invasive cervical cancer in WLWH who are on the antiretroviral treatment (ART) programme, especially those who have had multiple visits to healthcare facilities.

Cervical cancer screening uptake is low in LMICs. A meta-analysis of seven studies showed an 18.17% of pooled prevalence of cervical cancer screening uptake among WLWH in Ethiopia.[6] In Malawi, cervical cancer screening for WLWH aged 30–45 years increased from 9.3% in 2011 to 26.5% in 2015.[7] The overall cervical cancer screening coverage is below 20% in South Africa.[8] A local study showed that while healthcare workers are aware of cervical cancer screening protocols in WLWH, there are deficiencies in knowledge and practice.[9] Given the high burden of HIV and cervical cancer in South Africa, our study objectives were to look at the prevalence of macroscopic invasive cervical cancer in WLWH on ART, and to determine the frequency of cervical cytology screening prior to the diagnosis of invasive cervical cancer in HIV-positive women. That way, we could indirectly determine if HIV-positive women on ARVs are routinely screened for cervical cancer according to national guidelines.

Materials and methods

This was a retrospective, chart review study of WLWH on ART who were referred to our tertiary gynaecological oncology unit of the Department of Obstetrics and Gynaecology at Greys Hospital in KwaZulu-Natal Province, South Africa, with invasive cervical cancer from January 2018 to December 2019. Inclusion criteria were WLWH while on ARVs for more than three months. We excluded all HIV-negative and WLWH on ART for less than three months, or not on ART.

Statistical analysis

A total of 267 case records were retrieved; 220 records were included in the study and 47 were excluded (three HIV-negative, 45 ART for less than three months). Descriptive statistics were used to analyse data. Frequencies and percentages were used for categorical data, such as referral sites and previous cervical cytology. Sub-group comparisons between women with and without previous cervical cytology, or between different histological diagnoses, were done using chi-square or Fisher's exact tests. A *p*-value = 0.05 was considered statistically significant.

Results

The prevalence of macroscopic cervical cancer was 95% of all cervical cancer stages in the study. Of the patients diagnosed with invasive cervical cancer, 218 (99.09%) were of black African ancestry. The majority were parous women, and 94 (42.73%) were between the ages of 41 and 50. Regional hospitals referred 150 (68.2%) of the patients. There were 212 (96.4%) patients on first-line fixed dose regime, while 218 (99.09%) were on ART for more than six months. Virally suppressed patients totalled 161 (73.18%), and 178 (89.91%) had a CD4 count greater than 200 µl/ml. Results are shown in Table I.

With regards to cervical cancer screening patterns, only 69 (31.36%) patients had been screened prior to being diagnosed with invasive cervical cancer. Seven (3.18%) patients were screened less than six months before invasive cervical cancer diagnosis, and all those patients had smear results suggestive of squamous cell carcinoma. Before the diagnosis of invasive cervical cancer, 84 (38.2%) patients had subsequent cervical cancer screening between six and 36 months. Squamous cell carcinoma histological type of cervical cancer was diagnosed in 212 (96.36%) patients, and the majority had locally advanced cervical cancer FIGO stage 3B (115 patients, 53%). Results are shown in Table II.

Ten (5.6%) patients with microscopic disease and 168 (94%) with macroscopic invasive cervical cancer had a CD4 count above 200 cells/µl.

There was a significant association in the interval of time between cervical cancer screening and the diagnosis of micro- and macro-invasive cervical cancer ($p < 0.001$). All patients with microscopic invasive cervical cancer were screened within 36 months before the diagnosis of cancer, and 129 (61%) patients with macroscopic invasive cervical cancer were not screened for a period of 36 months or more before the diagnosis of invasive cervical cancer.

Table I: Demographic characteristics of WLWH with invasive cervical cancer

Race	Frequency	Percentage
Black	218	99.09
Indian	1	0.45
Coloured	1	0.45
Total	220	100
Age		
< 30	4	1.82
31–40	50	22.73
41–50	94	42.73
> 51	72	32.73
Total	220	100
Parity		
0	15	6.82
1–3	133	60.45
4–5	30	13.64
> 5	42	19.09
Total	220	100
Referral site		
District hospital	66	30
Regional hospital	150	68.2
General practitioner	4	1.8
Total	220	100
Viral load		
> 200	4	1.82
< 200	161	73.18
Not done	2	0.91
No results	53	24.09
Total	220	100
CD4⁺		
> 200	178	80.90
< 200	12	5.45
Not done	1	0.45
No results	29	13.2
Total	220	100
ARVS regime		
First line	212	96.4
Second line	8	3.6
Total	220	100

Discussion

The aim of the study was to determine the prevalence of macroscopic disease in WLWH on ART. We found the prevalence of macroscopic disease to be 95% in our study population. This prevalence is extremely high for this group of the population, given that the national guidelines in place are aimed at ensuring that women are frequently screened compared to the low-risk population.[5] Only 14 (6.4%) of the study population were

Table II: Cervical cancer screening patterns

Initial cervical cytology	Frequency	Percentage
NILM	58	84
ASC-US/LSIL	7	10
ASC-H	1	1.4
HSIL	3	4.3
Total	69	100
Last cervical cytology prior to cancer diagnosis		
< 6/12 months	7	3.18
6–12 months	7	3.18
12–24 months	23	10.45
24–36 months	54	24.54
Not done	129	58.64
Total	220	100
FIGO staging		
1A (1A1 and 1A2)	11	5
1B1	18	8.18
1B2	5	2.27
1B3	1	0.45
2A	1	0.45
2B	51	23.18
3A	9	4.09
3B	115	52.27
4	9	4.09
Total	220	100

screened within a 12-month period before the diagnosis of cervical cancer. This implies that most patients were either not screened at the time of HIV-positive status diagnosis as per guideline recommendation,[5] or at some point of their ART programme. Table II demonstrates that the wider the screening interval, the higher the FIGO stage at the diagnosis of the disease. Therefore it was not surprising to find that 83.6% of patients referred to our gynae-oncology unit were at least FIGO stage 2B and above.

A local study looking at healthcare worker compliance with cervical cancer screening guidelines found that while most healthcare workers were aware of the guidelines, there were significant deficiencies in both knowledge and practices.[9] Our findings appeared to confirm those gaps that highlight the need for remedial action to correct and improve compliance with the guidelines.

The most common FIGO stage of macroscopic invasive cervical cancer was stage 3B in our study at 52.3%, which is consistent with the findings of a local study from another province in South Africa.[10] Although there were similarities in FIGO stage findings, we noted that the data from the other study was between 2010 and 2013. With the introduction of the universal test and treat policy on 1 September 2016, which made ARV available to all HIV-infected persons regardless of CD4 count, we expected better findings in our study as more WLWH were supposedly visiting healthcare facilities.[11]

Strengths and limitations

Being retrospective, this study may be subject to bias and a cautious interpretation of the results is recommended. Some patients may indeed have been screened, but their information was stored under a different name or hospital number. Although the sample was small, it does highlight a lack of adherence to the cervical cancer screening programme.

Conclusion

The prevalence of macroscopic invasive cervical cancer is still unacceptably high in WLWH on ART. Factors contributing to poor adherence to cervical cancer screening guidelines for WLWH need to be identified and addressed urgently. A stringent clinical governance approach is needed to reduce advanced cervical cancer in WLWH. We need to strengthen cervical cancer screening at all healthcare centres, especially those caring for WLWH. Our findings may not only assist our catchment area, but may also motivate other institutions to audit the screening for cervical cancer in WLWH in their catchment areas. This could help reduce the burden of cervical cancer in WLWH in South Africa.

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Conflict of interest

The authors have no conflict of interest to declare.

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Ethical approval

Ethical approval for the study was granted by the University of KwaZulu-Natal (UKZN) Biomedical Research Ethics Committee (Reference number: BREC/00002921/2021). The study was registered with the National Health Research Database (NHRD) of South Africa (KZ_202107_006).

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