

HUMAN IMMUNODEFICIENCY VIRUS IN CERVICAL CANCER PATIENTS TREATED WITH RADIOTHERAPY IN IBADAN, NIGERIA; A REVISIT

A.A. Abdus-Salam^{1,2}, S.A. Yusuf², E.C.G Ehiedu², O.K. Adeleke²

1. Department of Radiation Oncology, University of Ibadan, Ibadan.

2. Department of Radiation Oncology, University College Hospital, Ibadan.

Correspondence:

Dr. S.Y. Akanni

Dept. of Radiation Oncology,
University of Ibadan,
Ibadan.

Email: skrysf@yahoo.com

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ABSTRACT

Background: Cervical cancer and human immunodeficiency virus are diseases of public health concern as they both have debilitating effects on human health. Human immunodeficiency virus worsens the carcinogenicity of HPV, thereby elevating the risk of cervical cancer. A previous study conducted at our center two decades ago reported a low prevalence of HIV among cervical cancer patients. **Objective:** This study is aimed at determining the current prevalence of HIV among patients with cervical cancer presenting for radiation treatment and comparing it with our previous findings 20 years earlier in order to assess changes in epidemiological trends.

Methods: A retrospective analysis of patients with histologic diagnosis of cervical cancer seen between 2017 and 2019 was carried out. HIV statuses were determined using the Determine test kit for screening and Western blot for confirmation, and data was analyzed using appropriate statistical methods including the chi-square test for categorical variables and t-tests for continuous variables. P-values < 0.05 were considered statistically significant.

Results: A total of 156 patients were seen with a mean age of 54.9 ± 11.4 years (range from 33-90 years). The prevalence of HIV was found to be 6.4%, slightly higher than our previous finding with prevalence of 2.7%. The HIV positive patients were younger (mean age 44.7 ± 6 years) than the HIV negative patients (55.14 ± 10.84 years) by about 10 years which was statistically significant ($p=0.003$). Most of the patients presented with an advanced disease, with 50% of the patients presenting with stage III disease, while 10% had stage IV disease. The HIV positive patients presented with more early stage (Stages I and II) diseases (60%). Squamous cell carcinoma was the most common histological type accounting for 89.7%.

Conclusion: As a follow up study, it appears that not much has changed from our previous findings as there is a slight increase in prevalence of HIV amongst cervical cancer patients compared to data from two decades ago, though overall burden is relatively still low in our study population. The earlier age of diagnosis observed in HIV-positive individuals suggests evolving epidemiological pattern that warrants public health attention.

Keywords: AIDS; Cervical cancer; HIV Prevalence.

INTRODUCTION

Cervical cancer and human immunodeficiency virus (HIV) are diseases of public health concern as they both have a debilitating effect on human health.

Cervical cancer is the fourth commonest cancer among women, both in incidence and mortality globally¹. It accounted for about 660,000 new cases and 350,000 deaths in 2022.¹ Cervical Cancer is the leading cancer type among women in 25 countries of the world and a leading cause of cancer mortality in 37 countries.^{1,2}

Incidence and mortality rates of cervical cancer vary globally, with the highest rates observed in Eastern

and Southern Africa, while the lowest rates are seen in North America, Australia, New Zealand, and Western Asia.¹ There is a rising incidence and mortality in low- and middle-income countries as against declining incidence and mortality in the developed countries.^{1,3} Human papilloma virus (HPV) infection is an important etiological agent of cervical cancer. However, the reduced immunity caused by the Human Immunodeficiency Virus (HIV) infection has been shown to increase the incidence of cervical cancer. HIV-attributable cervical cancer burden varies widely among countries and regions; however, 85% of cases are seen in Sub-Saharan Africa alone. Southern Africa especially

bears the brunt of the HIV-related cervical cancer epidemic, accounting for over half of all cervical cancer cases attributed to HIV in 2018.³

In Nigeria, cervical cancer is the second most frequently diagnosed cancer among women and the second leading cause of mortality.¹ It accounts for about 12,075 new cases and 7968 number of cancer deaths per year.¹

Although human papilloma virus is a mandatory causal factor for cervical cancer,⁴ however important co-factor such as human immunodeficiency virus worsens the carcinogenicity of HPV thereby elevating risk of cervical cancer.⁵ This is possibly through chronic antigenic stimulation, inflammation and dysregulation of cytokines which contributes to cancer development.⁶ HIV epidemic has led to a significant increase in cervical cancer cases leading to its classification as an AIDS-defining disease.⁷ This elevated risk has been substantiated in a study aimed to investigate cervical cancer risk among women living with HIV across four continents; Africa, Asia, Europe and North America and revealed that women living with HIV were at higher risk of developing cervical cancer compared to those without HIV by 6 fold.⁸

However, a previous study conducted 20 years ago among our cervical cancer patients who presented with HIV did not show a significant role for HIV in our cohort of patients as only 6 of the 221 recruited patients between 2005-2007 were HIV seropositive accounted for 2.7% of the cohort. This current study is aimed at reviewing the current prevalence of HIV among patients with cervical cancer presenting for radiation treatment and comparing it with our previous findings 20 years earlier in order to assess changes in epidemiological trends.

MATERIALS AND METHODS

We conducted a retrospective analysis of patients with histologically confirmed cervical cancer who were treated at the Radiation Oncology clinic, University College Hospital, Ibadan, Nigeria, between 2017 and 2019, building upon a previous retrospective study of patients seen at the same clinic between 2005 and 2007. Patients' Socio-demographic and clinicopathological data along with HIV status were extracted from case notes. Patients were made to undergo voluntary HIV test as part of their baseline work-up before commencement of treatment. The screening was done using determine test kit, while those that were positive had Western Blot test for confirmation.

Data was analyzed using the Statistical Package for Social Sciences (SPSS), version 25.0. Association

between categorical variables was determined using Chi-square. Association between quantitative variables was determined using students t-test. P-values < 0.05 were considered statistically significant.

RESULTS

Between January 2017 and December 2019, a total of 156 women with histologically confirmed cases of cervical cancer were enrolled in the study. The age of the participants ranged from 33 to 90 years with a mean age of 54.9 ± 11.4 years. Many of the patients (57%) were between 41 to 60 years, followed by those in the 61 to 80 year group (29.5%). Very few patients (less than 1%) were above 80 years. Significantly, however 11% of the patients were below 40 years. (Figure 1)

A majority of the patients (51.9%) were from the Yoruba speaking South West part of Nigeria where our hospital is located. The rest were from the other parts of Nigeria with ethnic Igbos from South East and South South geopolitical zones accounting for about half of them. (Table 1)

Disease stages

Most of the patients presented with advanced stages of the disease. Half of the patients (50%) presented with stage III disease while 10% had stage IV disease.

Table 1: Socio-demographic characteristics of the participants

Variable (N = 156)	Frequency	Percent (%)
Tribe		
Yoruba	81	51.9
Igbo	32	20.5
Urhobo	9	5.8
Ijaw	5	3.2
Hausa	4	2.6
Others	25	16
Residential zone		
South West	74	47.5
South East	25	16.02
South South	41	26.28
North Central	7	4.5
North West	3	1.92
North East	1	0.64
Marital Status		
Married	103	82.7
Single	5	3.2
Widowed	32	20.5
Divorced	4	2.6
Religion		
Christian	129	82.7
Islam	27	17.3

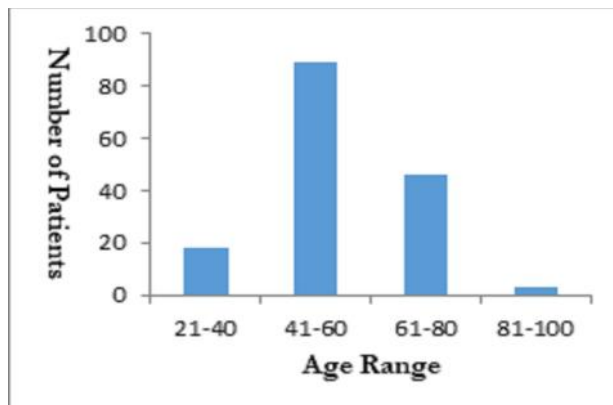


Fig. 1: Age range of cervical cancer patients seen between 2017 and 2019.

Only two patients (less than 1%) had stage I disease while the remaining cases (32%) had stages II disease with slightly more of them having locally advanced stage IIb disease. (Figure 2)

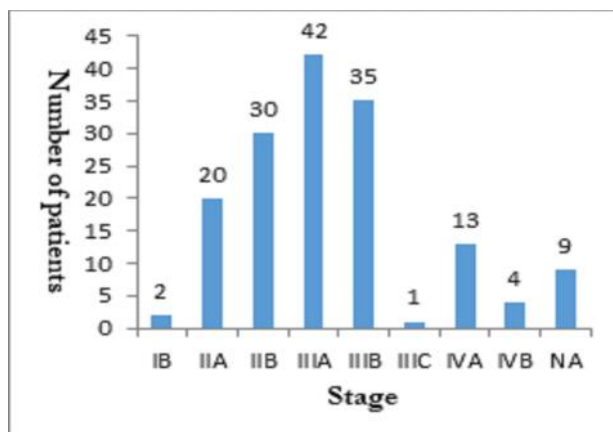


Fig. 2: Distribution of patients by disease stages

Histological Types

Squamous cell carcinoma accounted 89.7% of the cases with the rest distributed among Adenocarcinoma (4.5%), Adenosquamous Carcinoma (1.9%) and Sarcomas (1.3%). The histology type of four patients could not be ascertained. (Table 2)

Table 2: Distribution of patients by histological types

Histological types	No-case (%)
Squamous cell carcinoma	140 (89.7)
Adenocarcinoma	7 (4.5)
Adenosquamous	3 (1.9)
Sarcoma	2(1.3)
N/A	4 (2.5)

HIV status

Of the 156 patients seen during the study period 146 (93.6%) tested negative to HIV while the remaining 10 (6.4%) tested positive.

The HIV positive patients were younger (mean age 44.7 ± 6 years) than the HIV negative patients (55.14

± 10.84 years) by about 10 years. This age difference was found to be statistically significant ($p=0.003$).

The HIV positive patients also presented with a greater proportion of early stage (Stages I and II) diseases (60%) compared to HIV negative patients of which only 34.1% presented with early stage disease.

DISCUSSION

The observed mean age of 54.9 years in this study aligns with local and global data indicating that cervical cancer is primarily a disease of middle-aged and older women. This was consistent with a study by Awolude *et al.* which found a mean age of 55.4 years.⁹ and a time trend study by Wu *et al.* which reported peak cases 50-54 age group in China and India.¹⁰

The ethnic and geographic characteristics of the patient population align with the demographic profile of the study area where the Yoruba ethnic group is predominant. The significant representation of married women (66%) indicates that a considerable number of patients may have experienced prolonged exposure to HPV, the primary causative agent of cervical cancer, which is transmitted through sexual contact. Furthermore, the substantial proportion of Christian patients (82.7%) likely reflects the large proportion of patients from the South East and South South of Nigeria, who are by a large margin predominantly Christian in the study population, rather than being directly associated with an increased risk of cervical cancer

Furthermore, the predominant histological variant identified in both HIV-positive and HIV-negative cervical cancer cases was squamous cell carcinoma, consistent with our findings and those reported by Musa *et al.*¹¹ This is also akin to a study by Awolude *et al.* However, reported Adenocarcinoma being slightly higher variant seen amongst HIV-positive.⁹

In this retrospective study, we found that most of the patients with diagnosis of cervical cancer were seronegative. This study revealed that 6.4% of our cervical cancer patients were positive. This showed a small increase from our previous study in which 2.71% of our cervical cancer patients were seropositive.¹² However, the findings still showed low prevalence of HIV seropositivity which is consistent with the findings of Awolude *et al.* in the same institution which found a prevalence of 6.8% among cervical cancer patients presenting to the Department of Obstetrics and Gynaecology between 2009 and 2011 indicating stabilization of cervical cancer prevalence which could suggest effective public health interventions.⁹ This is in tandem with another study in ABUTH, Zaria by

Abdullah *et al.* who, in a retrospective analysis among cervical cancer patients seen between 2014 and 2016 reported 4% HIV positivity.¹³ Similarly, a study in Nairobi among 200 cervical cancer patients by Rogo *et al.* found HIV prevalence of 1.5%.¹⁴ In a one year study between January 1997 to June 1998, Lomalisa *et al.* found HIV prevalence of 7.2% among women with cervical cancer in South Africa.¹⁵ This is in sharp contrast to another South African study between 2010 and 2013 by Mohosho *et al.* to assess the prevalence of HIV in cervical cancer where they found HIV prevalence of 52.4%.¹⁶ Similarly, in a two centre study in JOS and LUTH, Musa *et al.* found seropositivity of 19.7%.¹¹ Differences in HIV prevalence rates across various populations may account for these discrepancies.

Our study found that women with HIV were approximately a decade younger than HIV negative women. A larger cohort of cervical cancer patients in Zambia revealed that women with HIV were diagnosed approximately ten years earlier than their HIV-negative counterparts, exhibiting a poorer prognosis.¹⁷ This observation aligns with findings from a related study conducted in Botswana, which similarly indicated that women with HIV were diagnosed with cervical cancer at a significantly younger age, with a notably higher risk of early mortality.¹⁸ The consistent evidence suggesting that women living with HIV are diagnosed with cervical cancer at a younger age implies that the progression from cervical precancerous lesions to invasive cancer may be expedited by the presence of HIV viremia.

In our study, we observed that HIV-negative women presented with more advanced stages of cervical cancer, which contrasts with earlier reports indicating that women living with HIV were more likely to be diagnosed at advanced stages.¹⁹ This discrepancy may be attributed to the lower prevalence of HIV in our cohort and poor screening behaviour as compared to HIV positive women with good screening behaviour as reported in some studies.²⁰

CONCLUSION

As a follow up to our previous study on HIV seroprevalence in patients with carcinoma of the cervix, it appears that not much has changed from our previous findings, as the prevalence of HIV in cervical cancer remains relatively low.

This research highlights the significant impact of cervical cancer within the examined population and emphasizes the role of HIV in the manifestation of the disease. The earlier age of diagnosis observed in HIV-positive individuals suggests evolving

epidemiological pattern that warrants public health attention.

To control the burden of HIV among young women, particularly in settings with limited resources. We recommend strengthening comprehensive sexual health education, access to HIV testing, cervical cancer screening and vaccination. A multi-sectoral approach involving healthcare practitioners, health educators, policymakers is essential to protect women from the dual burden of HIV and cervical cancer.

LIMITATIONS

The retrospective study design limits the availability and consistency of data such as CD4 counts, Anti-retroviral use which could have helped in providing more clinical context to the study.

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