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**OUTCOME OF MANAGEMENT OF CERVICAL CANCER PATIENTS IN A TERTIARY HOSPITAL IN SOUTH WESTERN, NIGERIA**

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**ABSTRACT**

**Introduction:** Cervical cancer is the second most common cancer among women in Nigeria and is rated as the fourth most prevalent worldwide. While improved survival rates have occurred in high-income countries, consequent to wide screening and adequate treatment, survival remains poor in low-income countries, including Nigeria.

**Objective:** This study aimed to determine the survival rates of cervical cancer patients, their socio-demographic and clinic-pathologic characteristics and factors that influence their outcomes.

**Methods:** This was a retrospective cross-sectional study. Socio-demographic characteristics and treatment details were obtained from the case notes and treatment cards of patients who presented to the Radiation Oncology Department of University College Hospital, Ibadan, Oyo state, Nigeria from 2006 to 2015. Survival analyses were done using the Kaplan-Meier method and Cox regression.

**Results:** A total of 544 patients were included. The age of patients ranged from 25 to 90 years, with a mean age of 55.49 years  $\pm$ 11.69. Majority of the patients, 88.6%, had squamous cell carcinoma, while 72.9% presented with stage IIB or more advanced diseases. The 2-year and 5-year survival rates were 69.6% [SE  $\pm$ 0.026] and 45.8% [SE  $\pm$ 0.034], respectively. Poorer survival was associated with anemia, leukocytosis, high urea and creatinine levels at presentation, the presence of hydronephrosis at presentation, elderly patients, non-squamous cell carcinoma histology, late stage at presentation, and positive HIV status.

**Conclusion:** In Nigeria, cervical cancer is characterized by a dismal survival rate. Therefore, the institution of widespread cervical cancer screening, HPV vaccination and provision of affordable treatment options will help improve the survival of patients with the disease.

**KEY WORDS:** Cervical cancer, overall survival, outcome, Nigeria

## INTRODUCTION

Cervical cancer is the fourth most common malignancy among women worldwide and remains a leading cause of cancer-related mortality in developing countries.<sup>1,2</sup> According to data from the GLOBOCAN database, in 2018,<sup>2</sup> Nigeria recorded 14,943 new cases of cervical cancer but the current database shows a decline in the numbers with 12,075 new cases diagnosed in 2023 and 7968 deaths.<sup>3</sup> This malignancy is the second most frequent cancer in women in Nigeria and represents 12.8% and 31.2% of cancers among women under 45 years and above 45 years of age, respectively, according to the Ibadan cancer registry. Cervical cancer constituted 8 and 24.1% of cancers among women under 45 and above 45 years, respectively, as recorded by the Abuja cancer registry.<sup>4</sup> Cervical cancer forms 58.5% to 81.7% of the gynecological malignancies in Nigeria and 9.2% to 13.4% of all admissions in gynecological clinics.<sup>5-7</sup> It is estimated that there are approximately 50.33 million women aged 15 years and above who are at risk in Nigeria,<sup>8</sup> thus indicating a very high disease burden from the public health standpoint. Of even greater concern is the estimated prevalence of 3.5% of women in the general population who, at any given time, are believed to be harboring cervical HPV-16/18 infection, and that 66.9% of invasive cervical cancers were attributed to these high-risk HPV types. Cervical cancer accounts for 12.7% of cancers in South Western Nigeria,<sup>9</sup> and in the North, it represents the most common malignancy among females,<sup>5</sup> constituting 77% of all female genital tract cancers<sup>10</sup> and 15.5% of all cancers treated at Ahmadu Bello University Teaching Hospital in Zaria.<sup>6</sup>

While the overall incidence of cervical cancer remains high in many developing countries it has been falling during the last few decades in high-income countries such as the United

States. A large portion of this decline can be attributed to the introduction of mass screening programs-most especially the Pap test, which has facilitated the early detection and treatment of pre-invasive lesions. The recognition that Human Papillomavirus (HPV) is one of the major etiological factors in cervical cancer has led to the inclusion of HPV testing in the screening protocols of women aged 30 to 65 years, enhancing its early detection. Secondly, the introduction of the HPV vaccine among girls aged between 9 and 13 years has significantly reduced infections with human Papillomavirus, which is strongly linked to cervical cancer. This, in turn, has reduced the incidence rates of invasive cervical cancer in countries where vaccination was implemented. It is, however, still a leading health burden in Nigeria due to late presentation and inadequate care for the disease.

There is a paucity of data on survival statistics of cervical cancer patients in Nigeria in scientific literature. Knowing the survival statistics of these patients is highly relevant for clinicians, researchers and policy makers in helping to reduce the impact of the disease. Survival statistics would help them assess the disease burden, by evaluating public health strategies which is quite important in Nigeria where late presentation and limited resources impact the outcomes of these patients. It would also help provide insights into the effectiveness of current treatments, enabling healthcare providers to identify gaps in literature and improve care protocols. By being able to compare survival statistics across regions or countries, policy makers will be able to benchmark progress and prioritize resource allocation. Other benefits of survival statistics of cervical cancer patients in Nigeria include advancing research through identification of certain factors that influence prognosis, provision of realistic prognostic information to

patients and their relatives by clinicians, advocacy for better healthcare funding and measurement the impact of interventions.

Therefore, this study aims at assessing the survival statistics of cervical cancer patients presenting at the Radiation Oncology Clinic of University College Hospital, Ibadan, South-West Nigeria, besides highlighting variables that could potentially affect such survival. The primary objective was to determine the overall survival of cervical patients who presented at the department. Secondary objectives were to determine the sociodemographic and clinicopathologic characteristics of cervical cancer patients who presented in the Department and thirdly to determine factors associated with poorer survival in these patients.

## **MATERIALS AND METHODS**

It was a retrospective cross-sectional study in which the clinical records of cervical cancer patients who presented to the Radiation Oncology Clinic of University College Hospital, Ibadan, Oyo state, Nigeria between January 2006 and December 2015 were reviewed and analyzed.

### **Study Area**

The study setting was University College Hospital, Ibadan, Oyo state, Nigeria, which is the first Teaching Hospital in Nigeria, established in August 1952. It has a total of 65 departments presently; one of which is the Radiation Oncology Department. It is the second oldest Radiation therapy Department in Nigeria. The department has two brachytherapy machines and one telecobalt machine. Patients attended to were from all the six geopolitical zones of the country.

### **Study Population**

The target population consisted of all patients diagnosed with cervical cancer who presented in the Radiation Oncology Department from January 2006 to December 2015.

### **Inclusion Criteria**

Patients with histologically diagnosed cervical cancer.

### **Exclusion Criteria**

- Any patient without histological confirmation of cervical cancer.
- Those patients whose medical records were missing or with scanty treatment records.

### **Ethical Considerations**

Ethical clearance was obtained from the Joint Ethical Committee of University of Ibadan/ University College Hospital.

### **Survival Information**

Data on survival were extracted from case notes of the patients. For patients who defaulted follow-up or were transferred for management in other centers, patients or their relatives were contacted by phone calls to ascertain the patient's survival status. Those patients who could not be contacted were censored as alive at last known follow-up.

### **Statistical Analysis**

Sociodemographic, disease and treatment data were entered into the Epidata Manager and Entry Client (v4.6.0.6) and analyzed using SPSS version 26.0. The categorical variables were summarized as frequencies and percentages while continuous variables as mean ( $\pm$  standard deviation), if normally distributed or median (interquartile range) if not normally distributed. The assumption of

normality for continuous variables was checked using both the skewness-kurtosis test and by looking at histograms.

Overall survival was defined as the time from diagnosis to death of any cause or last follow up visit alive. Survival estimates were computed using Kaplan-Meier survival curves and differences determined by the Mantel-Cox log-rank test. Factors associated with survival were determined using Cox regression analysis. Variables with p value >0.10 on bivariate analysis were excluded stepwise in multivariate analysis. In the final step any factor with a p-value <0.05 was included into the multivariate model. Missing data was

categorized as unknown, not documented or missing.

## RESULTS

### Patient and Tumor Characteristics

A total of 544 patient case records met the selection criteria. Ages of the patients ranged from 25 to 90 years, with an average age of 55.49± 11.65 years. Patients were grouped into two categories according to their age, including below 60 years (61%, n = 332) and 60 years and above (39%, n = 212). Of the respondents, 68.2% (n=371) were married. The predominant ethnic group was Yoruba and the most common religion, Christianity. Most of the patients were unskilled workers, 72.6% (n=395). This is depicted in Table 1.

Table 1: Sociodemographic Features of Cervical cancer Patients

Variable	Frequency	Percentage
Age		
<b>Less Than 60 years</b>	332	61.0
<b>60 years and above</b>	212	39.0
Marital Status		
<b>Single</b>	13	2.4
<b>Married</b>	371	68.2
<b>Widowed</b>	145	26.7
<b>Divorced/ separated</b>	18	3.3
Occupation		
<b>Professional</b>	2	0.4
<b>Skilled</b>	53	9.7
<b>Semi-skilled</b>	2	0.4
<b>Unskilled</b>	395	72.6
<b>Unemployed</b>	56	10.6
<b>Unspecified civil servants</b>	22	4.0
<b>Missing</b>	14	
Tribe		
<b>Yoruba</b>	276	50.7
<b>Ibo</b>	148	27.2
<b>Other tribes</b>	120	22.1
Religion		
<b>Christianity</b>	430	79.3
<b>Islam</b>	108	19.9
<b>Jehovah's witness</b>	3	0.6
<b>Traditionalist</b>	1	0.2

### Symptom Duration and Stage of Disease

The duration of symptoms before presentation ranged from 1-121 months, with a median of 8

months (interquartile range (interquartile range (IQR): 4.75–12.00 months)). Majority presented with late-stage disease, that is, stages IIB to IVB, (77.9%, n=424), with locally advanced disease (stages IIB-IVA) comprising 63.2% (n=344). Metastases was seen in 52 patients at presentation. The commonest sites of metastases were the lungs (20, 38.5%), liver (11, 21.2%), inguinal nodes (12, 23.1%), intra-abdominal masses (8, 15.4%), sister Mary

Joseph nodes (6, 11.5%), supraclavicular nodes (4, 7.7%) and the spine in 3 patients (5.8%). Other less common sites with 1 frequency include the brain, para-aortic nodes, vulva, cervical nodes and the spleen. Majority (73.1%) of the patients presented with 1 site of metastases, while 13 (25.0%) presented with 2 sites and 1 patient each presented with 3 and 4 sites of metastases.

Table 2: Clinical features of patients with cervical cancer

Variables	Frequency	Percentage
Serum urea/creatinine at presentation		
Normal serum urea/creatinine	385	71.5
Raised urea/creatinine	46	8.5
Missing	109	
Presence of hydronephrosis on ultrasound at presentation		
Unilateral hydronephrosis	74	17.1
Bilateral hydronephrosis	56	13.0
No hydronephrosis	302	69.9
Missing	112	
Presence of fistulae (VVF/RVF) at presentation		
Present	50	9.8
Not present	458	90.2
Missing	36	
Retroviral status		
Positive	14	3.1
Negative	432	96.9
Missing	98	
Menopausal status		
Premenopausal	137	25.8
Menopausal	394	74.2
Missing	13	
Hormonal contraceptive use		
Didn't use hormonal contraceptive	81	19.0
Used hormonal contraceptives	345	81.0
Missing	55	
Parity		
Nulliparous (no parous experience)	12	2.3
Primiparous (1 parous experience)	16	3.1

Multiparous (2-4 parous experiences)	96	18.6
Grand multiparous ( $\geq 5$ parous experiences)	392	76.0
Missing	28	
History of multiple sexual partners		
Positive	155	39.7
Negative	235	60.3
Missing	154	
History of hormonal contraceptive use		
Positive	81	19.0
Negative	345	81.0
Missing	118	
History of alcohol intake		
Yes	76	16.3
No	465	83.7
Missing	79	
History of tobacco use		
Yes	11	2.5
No	426	97.5
Missing	107	
Presence of comorbidities		
No comorbidities	337	32.3
Comorbidities	161	67.7
Missing	46	
Presence of anaemia during treatment		
No anaemia (PCV $\geq$ 30%)	139	38.5
Anaemia during treatment (PCV<30%)	87	61.5
Missing	318	
Treatment Received		
Chemotherapy+ EBRT+Brachytherapy	115	21.1
Chemotherapy+ EBRT	157	28.9
Chemotherapy+ Brachytherapy	19	3.5
Chemotherapy alone	18	3.3
EBRT+Brachytherapy	23	4.2
EBRT alone	103	18.9
Brachytherapy alone	7	1.3
No treatment	102	18.8
Treatment in 2 groups		
Treatment	442	81.2
No treatment	102	18.8

EBRT-External Beam Radiation Therapy, PCV- Packed cell volume, VVF- vesicovaginal fistulae, RVF- rectovaginal fistulae

### Histological Subtypes

Histologically, the majority were squamous cell carcinoma, 83.3% [n = 453]. This is depicted in Table 2. Rarer histologies found in 14 patients included clear cell carcinoma (n=4), adenoid cystic carcinoma (n=3), Papillary carcinoma (n=3), small cell neuroendocrine carcinoma (n=1), pleomorphic rhabdomyosarcoma (n=1), carcinosarcoma (n=1) and undifferentiated carcinoma (n=1). Of the patients with squamous cell carcinoma, 44.5% [n = 171] were of large cell non-keratinizing subtype, 35.4% [n = 136], large cell keratinizing subtype, and 20.1% [n = 77] presented with small cell non-keratinizing squamous cell carcinoma.

### Clinical Features at Presentation and Complications of the disease

Majority (98.1%) of patients presented with abnormal vaginal bleeding, 74.9% had abnormal vaginal discharge. Pain was present in 54.5% of patients. Other less common symptoms at presentation include, weight loss (107, 19.7%), dysuria (39, 7.2%), anorexia (27, 5.0%), constipation (22, 4%), vesicovaginal fistulae (VVF) (16, 2.9%), nausea and vomiting (16, 2.9%), abdominal swelling (11, 2.0%), bladder outlet obstruction (10, 1.8%), leg swelling (6, 1.1%), rectovaginal fistulae (RVF) (4, 0.7%) and feeling of a vulval/vaginal mass in 4 patients (0.7%). There were no patients who presented because of abnormal Pap smear results which revealed carcinoma after further investigations.

At presentation, 71.5% (n=385) had normal serum urea and creatinine levels. Hydronephrosis was seen in 17.1% (n=74). Fistulae, either vesicovaginal, or rectovaginal were present in 9.8% (n=50) of patients. The

retroviral status was available for 446 patients and 3.1% (n = 14) tested positive.

### Risk factors associated with cervical cancer

Age at menarche was documented in 367 patients and it ranged from 10 to 24 years. The mean age at menarche was 15 (SD±2.18) years. Age at coitarche was documented in 306 patients and it ranged from 10 to 42 years. The median age at coitarche was 18 (IQR: 16, 20) years. The parity of patients ranged from 0 to 15 parous experiences. The median parity of patients was 6. Parity was stratified into nulliparous (no parous experience), primiparous (1 parous experience), multiparous (2-4 parous experiences) and grand multiparous (≥5 parous experiences). Majority of patients (n=392, 76%) were grandmultiparous (see table 2). History of multiple sexual partners was noted among 39.7% (n = 155) patients, while the use of hormonal contraceptives was noted among 19% (n = 81). Majority (74.2%, n = 394) were postmenopausal at presentation with a mean menopausal age of 48.81±5.21 years.

### Treatment Modalities

Treatment data revealed that 81.2% (n=442) of patients received some form of therapy, with the most common modality of therapy received being EBRT alone or in combination at 69% (n=376). However, 18.8% (n=102) of patients had no treatment. Modal dose of EBRT administered was 45Gy while 184 patients received intracavitary brachytherapy at a modal dose of 15Gy.

### Overall Survival Outcomes

By the end of the study in December 2020, 68% of the patients, (n=370), were either alive or censored alive at various times from

diagnosis (see table 3) with an overall survival rate of 69.6% at 2 years and 45.8% at 5 years (see table 4). The estimated median survival time was 51 months, 95% CI: 36.8–65.2 months. This is shown in Figure 1. Survival rates for 5 years varied significantly with age, histological subtype, and the stage of the

disease. For women less than 60-years of age, 5-year survival rate was 52.3%, while it was 36.1% for patients aged 60 years or above. For patients who presented with early-stage disease, the 5-year survival rate was 54.9% in contrast to metastatic disease, which was only 18.7% as seen in Table 5.

Table 3: Patients outcome

Variable	N (%) or median (95% CI)
Survival status, n (%)	
Alive/ censored alive	370
Dead	174
Time from diagnosis to death (months), median (95% CI)	51 ±7.3 (95% CI: 36.8- 65).
Range (Min, - Max.)	0- 160

Table 4: Survival times at specific time points

Time (years)	0.5	1.0	1.5	2.0	5.0
Beginning total	349	277	208	163	69
Deaths	40	66	88	105	151
Survival rate (%)	91.0 ± 1.4	83.6 ± 1.9	76.8 ± 2.3	69.6 ± 2.6	45.8 ± 3.4

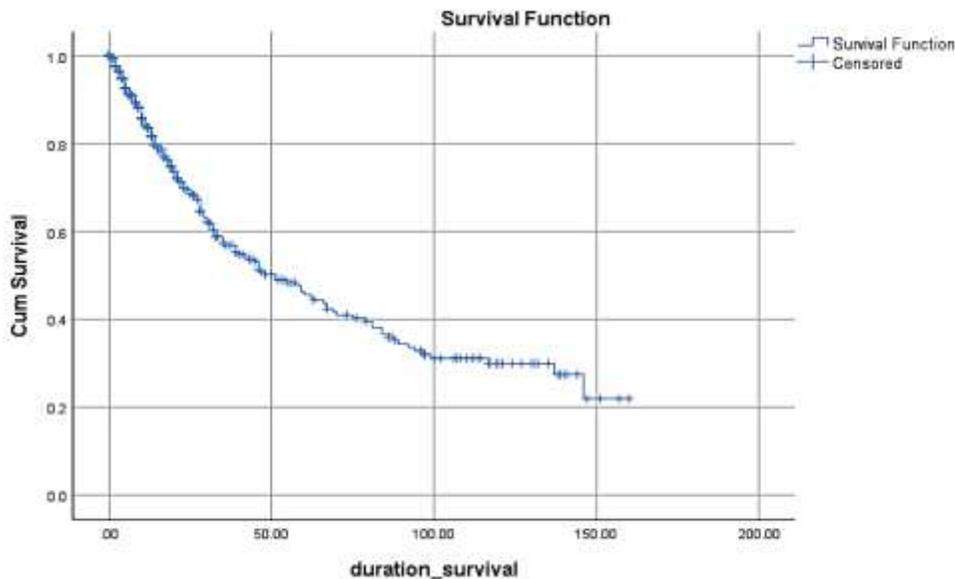


Figure 1: Kaplan-Meier curve showing the median survival of cervical cancer patients

Table 5: Two- and Five-Year Survival Rates of Selected Variables in cervical cancer patients

Variable	2-year Survival Rate (%)	5 Year Survival Rate (%)
Age		
Younger than 60 years	71.7±3.3	52.3±4.4
60 years and above	64.5±4.3	36.1±5.0
Histology		
Squamous cell carcinoma	73.1±2.7	48.4±3.7
Adenocarcinoma	38.7±12.8	15.5±12.6
Adenosquamous carcinoma	50.0±35.4	Not reached
Others	35.4±15.3	35.4±15.3
Stage in 3 groups		
Early	83.1±3.9	54.9±6.8
Locally advanced	64.1±3.5	41.3±4.2
Metastatic	49.8±10.1	18.7±14.7

### Predictors of Survival

Kaplan-Meier analysis demonstrated significant survival differences based on clinical variables as seen in table 6. Patients with early-stage disease had a significantly longer median survival time (70 months) compared to those with late-stage disease (39 months,  $p = 0.001$ ) (Figure 2). Survival was also significantly higher in patients with

squamous cell carcinoma histology ( $p=0.008$ ) see figure 3, normal serum urea and creatinine levels ( $p = 0.0001$ ) see figure 4, no fistulae ( $p = 0.0001$ ) see figure 6, negative retroviral status ( $p=0.042$ ), see figure 7, absence of anemia during treatment ( $p = 0.007$ ), see figure 8, and those who received treatment ( $p = 0.0001$ ), see figure 9.

Table 6: Comparative Median Survival Times of Patients by Stage for all patients with Cervical Cancer

Variable	Frequency	Median Survival time in months	Log-rank test	p-value
Stage			11.277	.001 <sup>^</sup>
Early	112	70		
Late	396	39		
Age			4.805	0.028 <sup>^</sup>
Less than 60 years	332	67		
60 years and above	212	42		
Histology			7.103	0.008 <sup>^</sup>
Squamous cell carcinoma	453	58		
Non squamous histologies	58	22		
Treatment			63.996	0.0001 <sup>^</sup>

No treatment	102	11		
Treatment	442	60		
Raised urea and creatinine at presentation			28.214	0.0001 <sup>^</sup>
Present	46	15		
Absent	389	55		
Presence of VVF/RVF at presentation			12.998	0.0001 <sup>^</sup>
Present	50	21		
Absent	458	51		
Anemia during treatment			7.235	0.007 <sup>^</sup>
No anemia	139	63		
Anemia present	87	33		
Alcohol intake			0.596	0.440
Positive	76	67		
Negative	389	51		
Tobacco intake			1.387	.239
Positive	11	47		
Negative	426	59		
Menopausal status			.315	.575
Premenopausal	137	89		
Menopausal	394	48		
Parity			5.04	.169
Nulliparous	12	Not reached		
Oligoparous	16	27		
Multiparous	96	55		
Grand multiparous	392	51		
Hormonal contraceptive use			0.030	.864
Didn't use hormonal contraceptive	345	51		
Used hormonal contraceptives	81	66		
Retroviral status			4.123	.042 <sup>^</sup>
Positive	14	35		
Negative	432	51		
Presence of comorbidities			.176	.675
No comorbidities	337	51		
Comorbidities	161	55		

<sup>^</sup> statistically significant at  $p < 0.05$

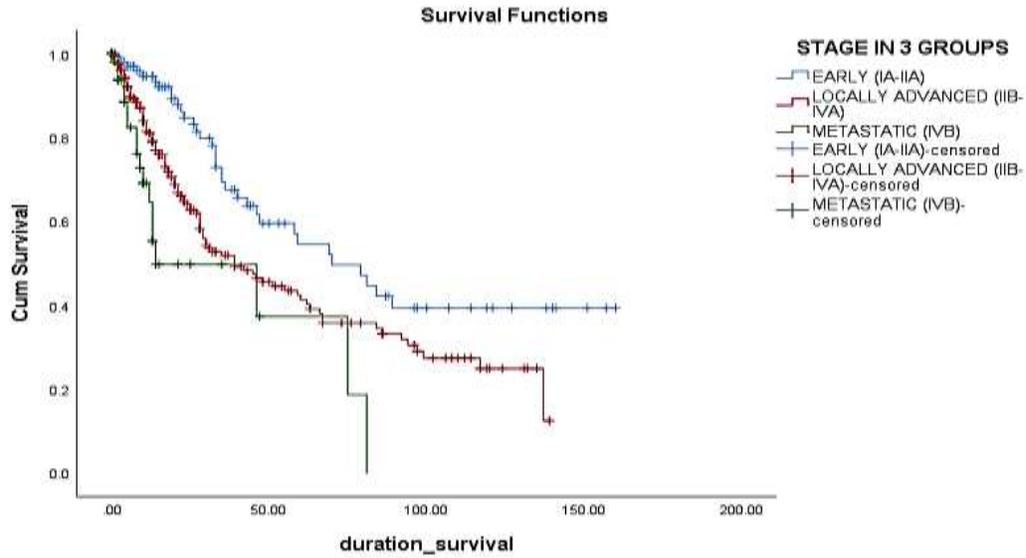


Figure 2: Kaplan-Meier curve for stage at presentation in cervical cancer patients

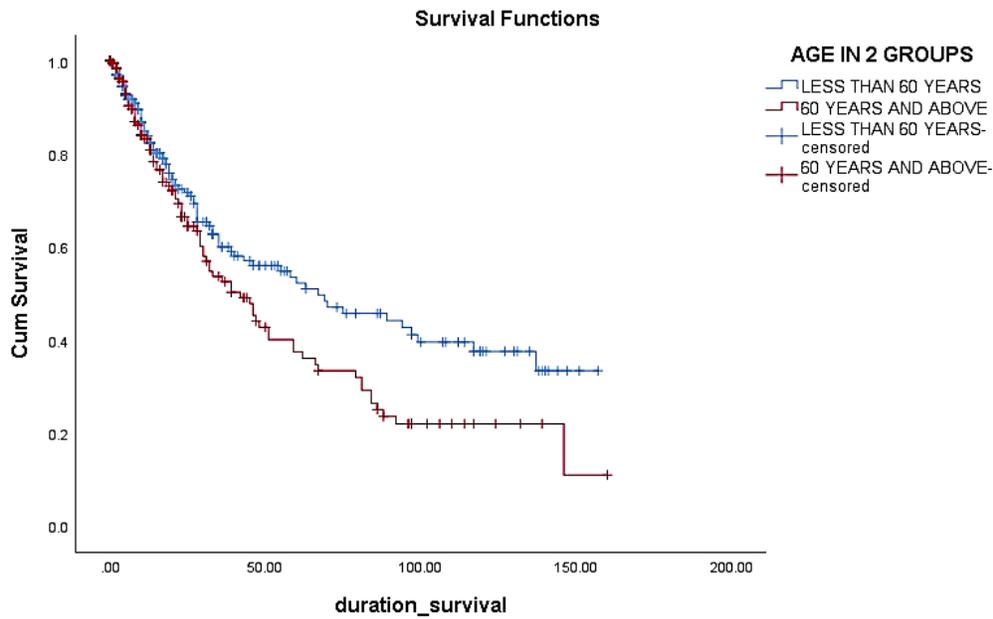


Figure 3: Kaplan-Meier curve for age at presentation in cervical cancer patients

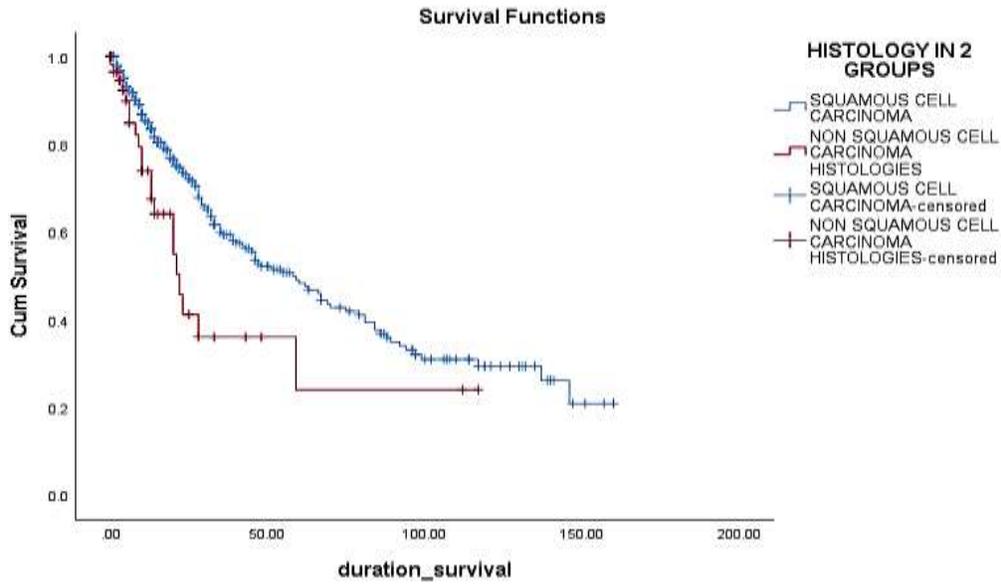


Figure 4: Kaplan-Meier curve for different histologies in cervical cancer patients

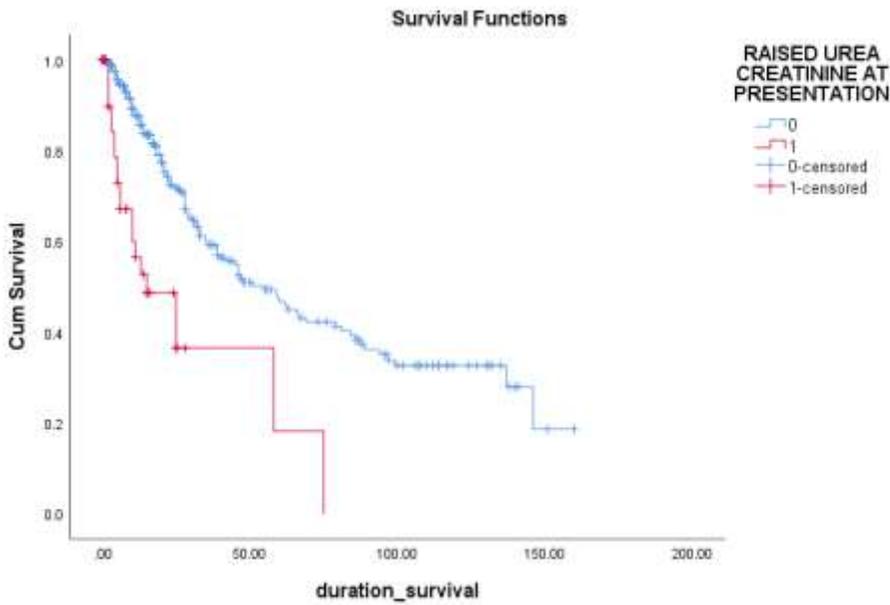


Figure 5: Kaplan-Meier curve for the presence of raised urea and creatinine at presentation in cervical cancer patients

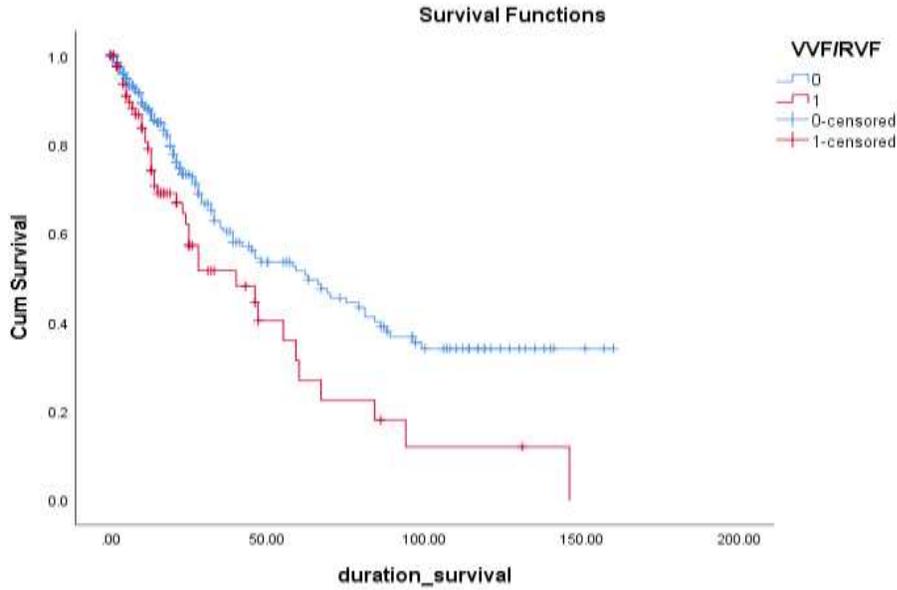


Figure 6: Kaplan-Meier curve for the presence of fistulae at presentation in cervical cancer patients

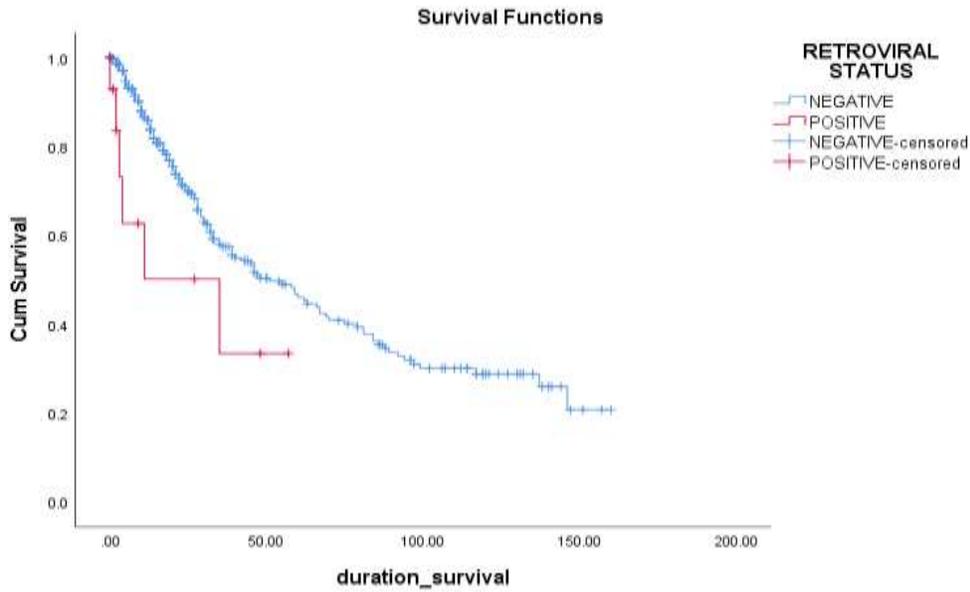


Figure 7: Kaplan-Meier curve for the retroviral status in cervical cancer patients

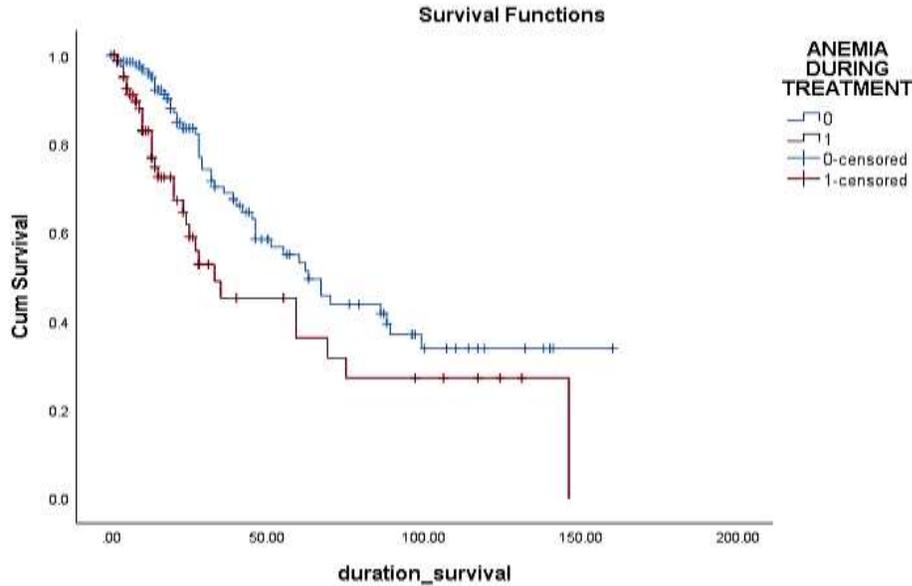


Figure 8: Kaplan-Meier curve for the presence of anemia during treatment in cervical cancer patients

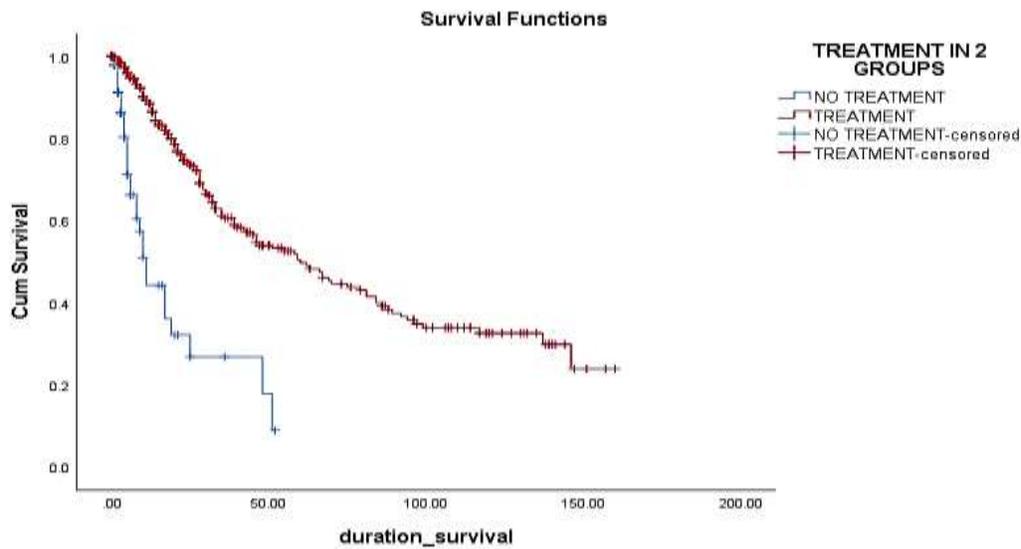


Figure 9: Kaplan-Meier curve for treatment in cervical cancer patients

By Cox regression analysis, histological type and stage of disease were identified as independent prognostic factors of survival. In the non-squamous histologies, after adjustment for confounders, the prognosis was significantly worse: HR = 0.024, 95% CI: 0.003–0.208, p = 0.001 (Table 7).

Table 7: Unadjusted and adjusted hazard ratios of variables using Cox regression analysis in cervical cancer patients

Variable	Unadjusted	Adjusted
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	Hazard ratio	95% CI	Sig	Hazard ratio	95% CI	Sig
Age < 60 years 60 years and older	.583 1	.332-1.024	.060	.579 1	.146-2.292	.436
Histological type Squamous cell carcinoma Non-squamous histology	.288 1	.122-.684	.005 <sup>^</sup>	.024 1	.003-.208	.001 <sup>^</sup>
Stage in groups Early Late	.357	.150-.846	.019 <sup>^</sup>	.703 1	.17-2.92	.628

<sup>^</sup> Statistically significant at .05

## DISCUSSION

In this study the 2-year and 5-year survival rates were 69.6% [SE  $\pm$ 0.026] and 45.8% [SE  $\pm$ 0.034], respectively. Poorer survival was associated with the presence of anemia during treatment, high urea and creatinine levels at presentation, the presence of hydronephrosis at presentation, elderly patients, non-squamous cell carcinoma histology, late stage at presentation, and positive HIV status. Independent prognostic factors were stage at presentation and the histological subtype.

The 5-year survival rate of 45.8% observed in this study further reflects the grim prognosis of cervical cancer patients in the country, similar to other developing countries.<sup>8,11,12</sup> This is in contrast to findings from developed countries like the United States of America where the 5 year survival rate is 67.4% were there is organized screenings, HPV vaccinations, adequate health insurance coverage and treatment infrastructure.<sup>13</sup> Contributing factors to this low survival rate in Nigeria include socio-economic challenges faced by women at risk, inadequate health infrastructure, and a lack of organized screening programs as well as inadequate treatment facilities. The fact that majority of cancer patients pay out of pocket in

this environment reduces the ability of patients to pay for adequate treatment and even treatment at all. In this study, 32.0% of the patients died, lower than the 68.1% reported by Musa et al.<sup>11</sup> The difference may relate to the accessibility of treatment, especially radiotherapy facilities available in University College Hospital, Ibadan, the study Centre which was not available in Jos University Teaching Hospital where the study by Musa et al was conducted.

Generally, in Nigeria, the modal age group for cervical cancer lies between 41 and 69 years,<sup>6, 7, 14-22</sup> with mean ages of incidence ranging from 40 to 55.08 years across the country.<sup>6, 14-16, 18, 23-27</sup> this is similar to findings in this study as the mean age was 55.49 $\pm$  11.65 years. This age trend in Nigeria is in variance to what obtains in other developing countries where 80% of patients with cervical cancer are aged 60 years and above. This may be because of the dominance of younger women in Nigeria due to low life expectancy, high rates of illiteracy, and poverty, in addition to problems with birth registration.

Research by Osakwe and Osakwe at Nnamdi Azikiwe University Teaching Hospital

revealed that cervical cancer formed 9.2% of total gynecological admissions, with the highest prevalence in the 50-59 age group (31.2%).<sup>7</sup> Majority (77.8%) of the 62 histologically diagnosed cervical cancer patients presented with advanced disease (stage IIB and above). Most patients had squamous cell carcinomas, which constituted 88.9%, while adenocarcinomas accounted for 6.7% and adenosquamous carcinomas accounted for 4.4% of cases. This is similar to findings in this study. Adewuyi et al. presented a review of gynaecological malignancies seen at a radiotherapy facility in Northern Nigeria and confirmed that cervical malignancy was the most common gynecological malignancy diagnosed, accounting for 81.7%.<sup>14</sup> The majority of the patients presented to the facility with locally advanced disease, 85.4%, whereas only 5.4% of the patients presented with early stage disease.

Certain factors can explain this trend in cervical cancer rates, and they include early age of first sexual intercourse, high divorce and remarriage rates, poverty, poor health seeking behaviors, apathy for orthodox medicine, cultural practices in which women are often neglected by their husbands and parents and a pattern of multiple sexual partners.<sup>14,27,28</sup> Others are the roles played by spiritualists and herbalists as most patients have admitted to seeking non-orthodox assistance before presenting to the hospital. This is similar to findings in other developing countries.<sup>26,27,29</sup>

Relatively, the high incidence of cervical cancer in Nigeria is in contrast with studies from stricter religious societies where pre-marital sexual activities are at low levels, such as some Middle Eastern countries,<sup>1</sup> but follows

the trends in other under-developed and developing nations.<sup>14</sup>

One of the worrying features of the disease in Nigeria includes a high grand multiparity rate, as observed in 68.3% to 83.2% of patients,<sup>16,18,19,21,26</sup> with a median of 6 parous experiences, documented in previous studies. Patients were more frequently married with about 16.4 to 57.1% in polygamous marriages,<sup>16, 19, 26</sup> with higher rates of polygamous marriages seen in northern Nigeria and South western Nigeria. These findings are similar to what was seen in this study. Previous studies have shown that low literacy levels was high among cervical cancer patients with 62.2% to 75.7% of patients having a low educational level less than secondary school education.<sup>18,25,26</sup>

Previous studies have shown that most patients deny having multiple sexual partners with only 26.2 to 41.2% saying they have had multiple sexual partners.<sup>18</sup> This is similar to findings from this study where the history of multiple sexual partners could not be gotten from about a third of the patients. This could be due to fear of stigmatization and the fact that Nigeria is a somewhat religious country. The role of contraceptive pills and smoking in cervical cancer was not significant previous studies in Nigeria as it was documented in 12.7 to 13.4%<sup>19,26</sup> and 1.7% of patients<sup>26</sup> respectively. This is similar to findings in this study. Previous studies have shown HIV seropositivity in 2.7% to 11.8% of patients in Nigeria.<sup>14, 19, 28</sup> this is similar to findings in this study. Cervical cancer is the most common cancer in HIV positive people in Nigeria.<sup>24</sup>

In Nigeria, patients rarely present with asymptomatic disease detected by abnormal Pap smear results due to lack of organized

widespread screening in the country. Previous studies have shown that majority (76.7 to 88.5%) of patients present with abnormal vaginal bleeding, although postcoital bleeding was seen in only 20.9%. Postcoital bleeding is a rare presenting complaint as many may not understand its clinical significance. Previous studies in Nigeria also showed that abnormal vaginal discharge occurred in 42% to 72%,<sup>16,18,19,21</sup> pain in 23%,<sup>18</sup> and weight loss was reported in 39.3% of patients.<sup>18</sup> This is similar to findings in this study. Previous studies showed that a significant number of patients presented due to complications, which included severe anemia requiring blood transfusions (as much as 7 units of blood),<sup>16,18,19</sup> urological and surgical complications such as rectovaginal and vesicovaginal fistulae<sup>18,19,26</sup> as well as uremia due to obstructive uropathy needing dialysis.<sup>16,19</sup> This is similar to findings from this study where a significant portion of patients presented with anemia, raised serum urea and creatinine and fistulae.

Most studies in Nigeria have shown that majority (77.8% to 94.8%) of the patients present with advanced disease, i.e. from stage IIB and above,<sup>7,14,16-18,21,26</sup> while few (4.6% to 17.4%) presented with metastatic disease.<sup>14,18,26</sup> This is similar to findings from this study. Overall, the high proportion (72.8%) of patients presenting with late-stage disease (stage IIB-IVB) in this study reflects trends observed in other Nigerian studies,<sup>7,14,16-19,21</sup> other developing countries<sup>30-32</sup> and contrasts sharply with patterns seen in developed countries,<sup>13,33-35</sup> where early-stage disease is more common (42%).<sup>13</sup> The staging of malignant diseases is crucial for prognosis, as evidenced by the median overall survival of 70 months for early-stage cases versus 39

months for late-stage cases. This highlights the urgent need for improved screening, early detection strategies and adequate treatment facilities in the country.

In this study, 3.49% of patients were retroviral positive at presentation, aligning somewhat with prior studies in our environment, where HIV prevalence among cervical cancer patients ranged from 2.7% to 11.8%.<sup>14, 19, 23, 24, 36-41</sup> This contrasts sharply with findings from a study in Botswana, where HIV-positive patients constituted 66.4% of cases.<sup>42</sup> HIV positivity is known to increase the risk of developing precancerous lesions due to impaired clearance of high-risk HPV infection. The shortened median survival times observed among HIV-positive patients in this study are consistent with other studies,<sup>31, 42, 43</sup> potentially resulting from reduced treatment access, an increased likelihood of incomplete treatment, or limitations on receiving comprehensive care due to lower CD4 counts.<sup>42, 44</sup> However, Cox regression analysis in this study did not identify HIV positivity as an independent predictor of mortality risk in cervical cancer patients.

In this study 21.1% of patients had combination treatment with chemotherapy, external beam radiotherapy and brachytherapy. However, the proportion of patients who had no treatment was quite high consisting of 18.8% of patients. This is higher than that recorded in other studies where patients with no treatment at all constituted 7.04 -9.2% of the patients.<sup>45,46</sup> The major reason for this in our environment is probably due to poverty as patients can't pay for cancer treatment. In a country where most people pay out of pocket for their health care the number of people who can't afford treatment would be high. A study in USA showed patients who paid for their

cervical cancer treatment themselves or who were uninsured accounted for 3.2 – 25.8% of patients across different age groups.<sup>47</sup> This is quite low compared to Nigeria where the NHIS coverage is quite low and does not cover adequately the patients who are at high risk of being unable to afford treatment (elderly patients, widows and petty traders). Many patients opt for no treatment or go to traditional healers or religious homes seeking somewhat cheaper treatment.

In this study patients who had treatment whether it included external beam radiotherapy or not had statistically significant longer survival than those who had no treatment. Studies have shown that even offering patients less aggressive treatments like brachytherapy alone improves their survival significantly.<sup>46</sup>

A higher proportion of patients in this study who were treated did not have brachytherapy as part of their treatment. Patients may not have had brachytherapy as a result of machine breakdown between January 2006 to June 2008 and September 2013 to December 2015 which fell within the study period. Patients would have been referred to complete treatment at the sister Centre, Ahmadu Bello University Teaching Hospital, Zaria but a sizeable number of them may not have gone as a result of distance and cost. This is similar to the findings of Adewuyi, which showed that the some of the barriers to assessing oncology care were cost and distance.<sup>48</sup>

### **Implications and Limitations**

This study provides a valuable basis for public health initiatives and policies aimed at improving cervical cancer outcomes in Nigeria. However, as a retrospective study, it is limited by missing data and potential recall bias in follow-up data. Limited available funds made the possibility of visiting patients

difficult so as to get the survival details of the patients lost to follow up. Lastly, this was a single institutional experience and hence the ability to translate these findings to other settings maybe limited compared with prospective, multi-institutional trials. Further prospective studies are recommended to strengthen the understanding of cervical cancer survival trends in Nigeria.

### **Recommendations**

Social and economic barriers should be surmounted through proper awareness about the disease, while comprehensive screening should be pursued aggressively to improve outcomes among women in Nigeria. Additionally, HPV vaccination for preschool-aged girls should be strongly promoted as a preventive measure to help reduce the incidence of cervical cancer. Also, there should be Comprehensive Cancer Centres in each geopolitical zones, if not each State, fully equipped with all the treatment facilities needed for the management of this disease.

### **CONCLUSION**

This means that as much as the 5-year survival rate in this study is 45.8%, the challenges are huge, yet the need to enhance access to timely and appropriate treatment modalities cannot be overemphasized. Therefore, the institution of widespread cervical cancer screening, HPV vaccination and provision of affordable treatment options will help improve the survival of patients with this disease.

### **Conflict of Interest**

There is no conflict of interest.

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