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Characteristics and geographic distribution of HIV-positive women diagnosed with cervical cancer in Dar es Salaam, Tanzania

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Summary

Background—Cervical cancer is the leading incident cancer and the main cause of cancer-related mortality among women in sub-Saharan Africa. Furthermore, HIV-infected women are at a higher risk of developing cervical cancer than are HIV-negative women. The purpose of this study was to distinguish differences in characteristics of HIV-positive and HIV-negative patients with cervical cancer in Dar es Salaam, Tanzania.

Methods—The HIV status of cervical cancer patients diagnosed and/or treated at Ocean Road Cancer Institute in Dar es Salaam, Tanzania, during the period 2007–2011 was abstracted from the medical records. Additional abstracted information included patient's name, age, place of residence, occupation, education, marital status, age at marriage, gravidity, and screening clinic visit results. Ocean Road Cancer Institute patients came from two sources, the screening clinic followed by treatment clinic or the treatment clinic without prior screening. HIV-positive and HIV-negative patients were compared regarding the above-listed clinical and epidemiologic factors. Multivariable analysis was also performed to assess the risk factors associated with cervical cancer treatment without prior screening at Ocean Road Cancer Institute.

Results—HIV-positive cervical cancer patients tended to be younger, with higher education, and lower parity. Patients screened for cervical cancer prior to treatment were more likely to be HIV-positive (OR: 2.09, 95% CI: 1.36, 3.21), less likely to have higher disease stages (OR: 0.64, 95% CI: 0.43, 0.94), and less likely to reside outside of Dar es Salaam (OR: 0.44, 95% CI: 0.30, 0.65).

Conclusions—Screening for cervical cancer at Ocean Road Cancer Institute is utilised by more HIV-positive patients from Dar es Salaam. Future studies should focus on identifying the reasons

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Conflict of interests

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for lower utilisation of screening by HIV-negative patients and patients from other distant rural regions in Tanzania.

Keywords

Tanzania; cervical cancer; HIV; screening

Background

Cervical cancer is a rare disease in most developed countries. It is preventable with screening and human papillomavirus (HPV) vaccination and curable if caught early enough.^{1,2} However, cervical cancer is the leading incident cancer and the main cause of cancer-related mortality among women in sub-Saharan Africa.^{3–5} Tanzania in particular has an estimated cervical cancer incidence rate of 54 per 100,000 women per year, a rate almost five times higher than the incidence rate of breast cancer, the next most common cancer.⁶

HIV infection is also endemic in Tanzania, which has the thirteenth highest adult HIV infection prevalence in the world with 5.1% of the population and 6.2% of women aged 15–49 being HIV-positive.⁷ Our previous study done in Dar es Salaam, Tanzania, found that women with cervical cancer were 2.9 times more likely to be HIV positive than women without cervical cancer.⁸ According to another study done in northern Tanzania, women who were HIV positive were 13.3 times more likely to develop cervical squamous intraepithelial lesions (SIL). In addition, low CD4+ T lymphocyte cell count was associated with higher prevalence of SIL, suggesting that the risk of cervical SIL increases as HIV infection progresses and the immune system is more and more suppressed.⁹

Increased immunosuppression of HIV-positive women also increases the likelihood of opportunistic infections, such as HPV, which is a necessary cause of cervical cancer.^{10,11} Studies in South Africa found HIV-infected women were more likely to have a high-risk HPV infection and to have multiple concurrent HPV infections.¹² In addition, a study conducted in Nigeria found that, HIV-positive women were 4.71 times more likely to have any instance of single high-risk HPV infection than were HIV-negative women. HIV-positive women were also 8.68 times more likely to have any instance of multiple high-risk HPV infections.¹³

Because HIV-positive women are at an increased risk of cervical cancer, it is important they are screened early and often. Cervical cancer screening in Tanzania is done by visual inspection with acetic acid, in which an acetic acid solution is swabbed on the surface of cervix. Precancerous lesions will turn white in colour after contact with the acetic acid and are then frozen off using cryotherapy. This type of screening is ideal for developing countries because it does not require special training of staff or the use of a laboratory, it is cost-effective, and has been shown to produce accurate results.^{14–16}

Our previous study found that 84.6% of women referred for treatment from the cervical cancer screening unit at Ocean Road Cancer Institute (ORCI) in Dar es Salaam, Tanzania, followed up with their treatment. This study also found that screened women tended to have lower disease stage than unscreened women.¹⁷ However, differences between HIV-positive

and HIV-negative patients were not distinguished. So we conducted this study to determine the characteristics of HIV-positive women seeking treatment for cervical cancer at ORCI.

Methods

Since the program was initiated in November 2002, women visiting the cancer screening unit at ORCI are routinely entered into an EpiInfo database by ORCI staff. Variables available in this database consist of patient name, age, place of residence, occupation, education, marital status, age at marriage, gravidity, and screening clinic visit results. Our previous study used this database to create a dataset of women referred for treatment of invasive cervical cancer between November 2002 and June 2011. Women were considered referred if they had a histopathology result of invasive cancer, a listed final diagnosis of invasive cancer, or a stage of invasive cancer listed in the screening clinic database.¹⁷ This dataset was used for the population of women screened and diagnosed with cervical cancer in this study. Our previous study also used a dataset of all women attending ORCI for cervical cancer treatment. This database was used to create a set of women who came in for treatment of cervical cancer without attending the screening unit at ORCI. Women who were referred from the screening unit at ORCI were removed from this dataset and we were left with a set of women who only attended ORCI for treatment. Variables listed in patient log books included name, age, disease stage, and place of residence.¹⁷

Patient files and HIV logbooks from the records department at ORCI were used to collect the HIV status for these sets of patients. HIV testing at ORCI is done using a rapid immunoassay SD Bioline HIV-1/2 3.0 test. A Determine HIV-1/2 test is then done if the woman is positive for HIV antibodies to control for false-positive results.¹⁶ These results are either reported in a HIV logbook or the patient's files. HIV status was also obtained from doctor's notes within the patient files. Most patient files from 2002 to 2006 were not available, therefore only patients from 2007 to 2011 were included in this study. All patient files from the screened population from 2007 to 2011 (n=550) were analysed. There were 4344 patients that came in for cervical cancer treatment without visiting the screening unit from 2007 to 2011. For this population, every third patient file was analysed. Of 550 women screened through the cervical cancer screening unit at ORCI, 55 were HIV positive, 88 were HIV negative, and 407 had unknown HIV status. Of about 1500 records abstracted for patients who only attended the treatment clinic, 165 with HIV positive and 586 were HIV negative.

To assess regional variations in the population, patients were divided into seven regions based on their place of residence. Those residing in the administrative regions of Arusha, Kilimanjaro, Tanga, Manyara, Mara, and Simiyu were grouped in the Northeast region of Tanzania. Those residing in the administrative regions of Mwanza, Shinyanga, Geita, Kagera, and Kigoma were grouped in the Northwest region. Those residing in Morogoro, Iringa, Dodoma, Singida, and Tabora were grouped in the Central region. Those residing in Katavi, Rukwa, Mbeya, and Njombe were grouped in Southwest region and those residing in Pwani, Lindi, Mtwara, and Ruvuma were grouped in the Southeast region. Other countries outside of Tanzania were included with Zanzibar and those from Dar es Salaam were categorised as such.¹⁸

SAS 9.3 was used for statistical analysis. We first used Chi square and Fischer's exact tests to compare categorical patient characteristics (age, disease stage, occupation, etc...) between the HIV-positive vs. HIV-negative groups as well as between the screening clinic vs. the treatment clinic groups. We also used these same tests to compare characteristics of HIV-positive women in the screened and treated populations and also to compare characteristics of HIV-negative women in the screened and unscreened populations. In addition, the percentage of women residing in each region of Tanzania for each group (HIV+/Screening Clinic, HIV-/Screening Clinic, HIV+/Treatment Clinic and HIV-/Treatment Clinic) was calculated. We then performed multivariable analysis with logistic regression to assess age, disease stage, place of residence, and HIV status as predictors of being screened for cervical cancer.

This study was approved by the University of Nebraska Medical Center IRB and by the ORCI Academic, Research, Publications and Ethics Committee.

Results

Descriptive analysis shows that HIV-positive women tended to be diagnosed with cervical cancer at a younger age than were HIV-negative women. These results are statistically significant with a p value of 0.0001 (Table 1). In all, 69% of HIV-positive women who attended the screening clinic were diagnosed with cervical cancer at age 45 or when younger, whereas only 39% of screened HIV-negative women were diagnosed with cervical cancer at age 45 or when younger (Table 1). Treated women showed similar results. From this group, 66% of HIV-positive women (Table 2) and 34% of HIV-negative women (Table 2) were diagnosed with cervical cancer at age 45 or when younger. However, there was no difference in age between the screened and the treated groups all together (OR=0.99, 95% CI: 0.98, 1.01; Table 3).

HIV-positive women were also significantly more educated than HIV-negative women ($p=0.005$). A total of 82% of HIV-positive women had at least a primary school education, whereas only 57% of HIV-negative women had at least a primary school education. This is also in line with our results with regard to patient's occupation. Though these results are not statistically significant, HIV-positive patients tended to have more professional careers compared to HIV-negative women; 38% of HIV-positive women had careers other than housewife; however, only 25% of HIV-negative women had careers other than housewife ($p=0.23$; Table 1).

In regard to stage of cancer at time of diagnosis there was not much difference between HIV-positive and HIV-negative women; 62% of HIV-positive women and 64% of HIV-negative women from the screening clinic were diagnosed with stage 1 or 2 cervical cancer (Table 1). However, slightly less women were diagnosed with low-stage cervical disease among the population of women only treated for cervical cancer. In all, 47% of HIV-positive women and 55% of HIV-negative women who were just treated were diagnosed with stage 1 or 2 cervical cancer (Table 2). Results from our logistic regression suggest that cervical cancer screening is protective against late-stage disease diagnosis. Screened women had 0.64 lower

odds of being diagnosed with late-stage disease than women who were just treated for cervical cancer at ORCI (95% CI: 0.43, 0.94; Table 3).

Additionally, there was little difference in the marital statuses of cervical cancer patients. 65% of HIV-positive women and 68% of HIV-negative women reported being married at the time of diagnosis. There was also little difference in the age at marriage between HIV-positive and HIV-negative women. However, HIV-positive women did have significantly less pregnancies than HIV-negative women. In all, 44% of HIV-negative women had seven or more pregnancies, whereas only 19% of the HIV-positive women had seven or more pregnancies ($p=0.004$; Table 1). The lower number of pregnancies among the HIV-positive population is most likely due to their younger age at cervical cancer diagnosis.

HIV-positive women were also significantly more likely to attend cervical cancer screening than HIV-negative women; 38% of women who were diagnosed with cervical cancer from the ORCI screening clinic were HIV positive, whereas only 22% of women who came in for cervical cancer treatment without first visiting the screening clinic were HIV positive ($p<.0001$; Table 3). Results from our logistic regression further support this by showing that screened women have 2.09 times greater odds of being HIV positive than do treated women (95% CI: 1.36, 3.21; Table 3). In addition, 49% of HIV-positive women diagnosed with cervical cancer through the screening clinic knew they were seropositive for HIV upon their arrival to the clinic. However, only 24% of treated, HIV-positive women knew they were seropositive for HIV upon their arrival at ORCI ($p=0.0005$; Table 2).

Results show that HIV-positive women who were screened for cervical cancer are most likely to reside in Dar es Salaam. A total of 65% of screened HIV-positive women reported their place of residence as Dar es Salaam, whereas only 44% of treated HIV-positive women resided in Dar es Salaam (Table 2). In addition, 37.5% of screened HIV-negative women and 22% of treated HIV-negative women established residences in Dar es Salaam (Table 2). Furthermore, results from our logistic regression analysis show that screened women had 0.44 lower of odds of residing outside of Dar es Salaam than women who were just treated for cervical cancer at ORCI (95% CI: 0.30, 0.65; Table 3). Geographic discrepancies among the HIV-negative population were also found. In all, 14% of HIV-negative patients from the treatment clinic resided in northwest Tanzania, whereas only 2% of the HIV-negative patients from the screening clinic resided in northwest Tanzania; 28% of HIV-negative patients from the treatment clinic resided in central Tanzania, whereas only 17% of HIV-negative patients from the screening clinic resided in central Tanzania. However, more HIV-negative patients from the screening clinic resided in southeast Tanzania than HIV-negative patients from the treatment clinics with 24% and 13% residing in southeast Tanzania, respectively (Table 4).

Discussion

This study revealed the following interesting observations. First, HIV-positive patients from the cervical cancer screening clinic at ORCI tended to be younger, more educated, and with lower parity than the HIV-negative patients from the cervical cancer screening clinic. Second, HIV-negative patients from both the cervical cancer screening clinic and treatment

clinic tended to reside outside of Dar es Salaam. Third, patients from the cervical cancer screening clinic tended to have lower-stage disease than patients from the treatment clinic, regardless of HIV status. Fourth, HIV-positive patients from the screening clinic were more likely to know their HIV status than HIV-positive patients from the treatment clinic. Fifth, patients from the cervical cancer screening clinic were more likely to be HIV-positive than patients from the treatment clinic.

Our finding that HIV-positive patients tended to be diagnosed with cervical cancer at a younger age than HIV-negative women is consistent with other studies, which have shown an early age at diagnosis of invasive cervical cancer and a shorter pre-invasive stage among HIV-infected women.^{19,20} In addition, both incidence and progression of cervical lesions increases with lower CD4 T-cell counts.²¹ This could be due to the immunocompromised state of HIV-positive women, which makes them more susceptible to persistent HPV infections. Another study has also cited an increased potential for unregulated cell growth in HIV-positive women, suggesting a decrease in p53 expression in HPV-infected lesions and alterations in oncogenic and immunogenic protein expression.²² Regarding our finding that HIV-positive patients tended to have lower parity than HIV-negative patients, this is most likely due to the younger age at cancer diagnosis in HIV-positive patients.

Our finding that HIV-positive patients tended to have higher level of education is supported by research performed by the London School of Hygiene and Tropical Medicine, that found that increased education attainment was associated with an increased risk of HIV infection in both men and women in Africa and Asia.^{23,24} However, another study done in South Africa found that higher educational attainment was not a protective factor against HIV infection.²⁵ Increased socio-economic status and lifestyle changes that come with increased educational attainment and the associated behaviours linked to increased risk of HIV infection. In addition, more educated women may also be more likely to attend HIV screening, which would in turn increase the prevalence of HIV infection among the more educated population.²⁵ However, another study has also supported the idea that educational attainment decreases the risk for HIV infection. Increased years of education increase women's access to health information and also increase their income and independence, which in turn increase health literacy and decrease risk for HIV.²⁶

Another major finding in our study was that the majority of HIV-positive women who attended the cervical cancer screening clinic at ORCI resided in Dar es Salaam, the largest city in Tanzania. This percentage was smaller among the unscreened HIV-positive women and even smaller among the unscreened HIV-negative women seen at the treatment clinic. HIV-positive women primarily came from Dar es Salaam, whereas HIV-negative women came from different parts of Tanzania. The greater distribution of patients among the unscreened and HIV-negative populations suggests that these patients are only coming to ORCI because they are already experiencing severe and extensive symptoms as a result of advanced-stage cervical cancers.

Regarding our finding that cervical cancer patients from the screening clinic tended to have lower-stage disease than patients from the treatment clinic, regardless of HIV status, other studies have reported similar findings. Studies from Kenya found that the majority of HIV-

positive women, who underwent cervical cancer screening, had stage 1 disease at the time of diagnosis of invasive cervical cancer and this was attributed to the availability of screening.²⁷ This aspect is consistent with our study, which found the biggest factor associated with cervical cancer disease stage is whether the women were screened or not. However, there was not much difference in cervical cancer disease stage based on the HIV status.

Our previous study performed at ORCI found that among cervical cancer patients from 2002–2008, screened women were 1.6 times more likely to be HIV positive than treated women.²⁸ Our current study found that HIV-positive women diagnosed with invasive cervical cancer from 2007 to 2011 were 2.1 times more likely to be screened for cervical cancer than HIV-negative women, showing that the referral between the HIV Care and Treatment (CTC) clinics and the cervical cancer screening program in Dar es Salaam has grown stronger with time. Linkage between HIV screening and cervical cancer screening has proven to be cost-effective approach to detecting cervical cancer in HIV-positive women, because this allows women at increased risk of disease to be diagnosed at an earlier, more treatable disease stage.²⁹ Another study done in South Africa also provided evidence that women attending HIV clinics tended to be more knowledgeable about cervical cancer and screening than those of unknown HIV status, lending further support that attendance at an HIV clinic is positively associated with attendance for cervical cancer screening.³⁰ Because of their increased risk of disease, women from HIV CTC clinics in Dar es Salaam are encouraged to attend cervical cancer screening, which offers an explanation as to why women who are HIV positive and knowledgeable of their HIV status are more likely to attend cervical cancer screening.

To our knowledge, this is the only study to compare HIV-positive and HIV-negative women with cervical cancer in this area and the only study to look at the geographic distribution of women with cervical cancer by their HIV status in this area. However, there are some limitations to our study. The HIV status could not be found for a number of patients from this cohort, therefore the study population is relatively small. Strengths of this study include the large number of years included, the continuation from our previous studies, and the conduction of this study at ORCI, which receives referrals from all regions of Tanzania and has the largest screening centre in Tanzania. However, the study has a limitation. This sample of patients included in the study might not be representative of all women in Tanzania. Unfortunately, unknown HIV status is a limitation that has been reported in previous studies and the results of this study should be taken with caution.^{31,32} However, it is still important to report the results for this hospital-based study in order to further understand the HIV-positive cancer patients in this population and other similar underserved populations in developing countries.

Findings from this study can be used to facilitate improvements to the Cervical Cancer Screening Unit at ORCI and the HIV CTC clinics, and support the association of these two programs. Future studies should focus on identifying the reasons for lower utilisation of screening by HIV-negative patients and patients from other distant rural regions in Tanzania.

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Ocean Road Cancer Institute (ORCI) Cervical Cancer Screening Unit patient characteristics by HIV status (2007–2011).

Table 1

	HIV positive (n =55)		HIV negative (n =88)		p Value
	No.	%	No.	%	
Age (n = 143)					
26–35 years	14	25%	5	6%	<0.0001 ^a
36–45 years	24	44%	29	33%	
46–55 years	14	25%	26	29%	
56 and older	3	6%	28	32%	
Disease Stage (n =139)					
Early Stage	33	62%	55	64%	0.84 ^b
Late Stage	20	38%	31	36%	
Occupation (n =142)					
Housewife	34	62%	65	75%	0.23 ^b
Technical/Manual career	7	13%	9	10%	
Professional/Office-going career	14	25%	13	15%	
Education (n =139)					
None	10	18%	37	43%	0.005 ^b
Primary	36	67%	43	51%	
Middle or more	8	15%	5	6%	
Marital status (n =142)					
Married	36	65%	59	68%	0.88 ^b
Widowed	12	22%	16	18%	
Separated	7	13%	12	14%	
Age at marriage (n =123)					
17 years or younger	7	15%	23	30%	0.12 ^b
18–20 years	23	49%	38	50%	
21–23 years	7	15%	6	8%	
24 years or older	10	21%	9	12%	
Total pregnancies (n =139)					

	HIV positive (n =55)		HIV negative (n =88)		p Value
	No.	%	No.	%	
2 or less	15	26%	8	9%	0.002 ^b
3–6	29	55%	40	47%	
7 or more	10	19%	38	44%	
Cancer treatment completion (n =137)					
Finished prescribed radiation	43	86%	74	85%	0.88 ^b
Did not finish presc. radiation	7	14%	13	15%	
Seen at another health facility prior to visit at ORCI (n =137)					
Seen at another facility	6	12%	16	18%	0.33 ^b
First visit at health facility	44	88%	71	82%	

^aFischer's Exact test.

^bChi square test.

Table 2
Cervical cancer patient characteristics for HIV-negative and HIV-positive women by referral clinic (2007–2011).

	HIV negative (n = 668)				HIV positive (n = 220)				p Value
	Screening Clinic (n = 88)		Treatment Clinic (n = 580)		Screening Clinic (n = 55)		Treatment Clinic (n = 165)		
	No	%	No	%	No.	%	No.	%	
Age (n = 664) (n = 220)									
26–35 years	5	6%	49	8%	14	25%	31	19%	0.12 ^b
36–45 years	29	33%	151	26%	24	44%	78	47%	
46–55 years	26	29%	177	31%	14	25%	29	18%	
56 and older	28	32%	199	35%	3	6%	27	16%	
Disease Stage (n = 595) (n = 175)									
Early Stage	55	64%	279	55%	33	62%	57	47%	0.06 ^a
Late Stage	31	36%	230	45%	20	38%	65	53%	
Place of residence (n = 668) (n = 220)									
Dares Salaam	33	37.5%	128	22%	36	65%	73	44%	0.00 ^a
Other	55	62.5%	452	78%	19	35%	92	56%	
Knowledge of HIV status (n = 668) (n = 220)									
HIV test from ORCI	86	98%	579	99%	28	51%	125	76%	0.0005 ^a
HIV status self-reported	2	2%	1	1%	27	49%	40	24%	

ORCI: Ocean Road Cancer Institute.

^a Chi square test.

^b Fischer's exact test.

Predicting the probability of coming from the cervical cancer screening clinic at ORCI (2007–2011).

Table 3

	Screening Clinic (n =143)		Treatment Clinic (n =745)		p Value	OR	95% CI
	No/mean	%/SD	No/mean	%/SD			
HIV Status (n =888)							
Negative (n =668)	88	62%	580	78%	<.0001 ^a	1	1
Positive (n =220)	55	38%	165	22%		2.09	(1.36, 3.21)
Disease Stage (n =770)							
Early Stage (n =424)	88	63%	336	53%	0.03 ^a	1	1
Late Stage (n =346)	51	37%	295	47%		0.64	(0.43, 0.94)
Place of residence (n =888)							
Dar es Salaam (n =270)	69	48%	201	27%	<.0001 ^a	1	1
Other (n =618)	74	52%	544	73%		0.44	(0.30, 0.65)
Age (n =887)							
Continuous	47.7	11.9	49.5	12.3	0.10 ^b	0.99	(0.98, 1.01)

ORCI: Ocean Road Cancer Institute.

^aChi square test.

^bt-test with equal variance.

Cervical cancer patient percentages for each region by referral clinic and HIV status (n=888) (2007–2011).

Table 4

	Screening Clinic (n =143)			Treatment Clinic (n =745)			
	HIV positive (n =55)		HIV negative (n =88)	HIV positive (n =165)		HIV negative (n =580)	
	No	%	No	No	%	No	%
Dar es Salaam	36	65%	33	73	44%	128	22%
Northeast	2	4%	14	15	9%	80	14%
Northwest	2	4%	2	16	10%	82	14%
Central	7	12%	15	30	18%	160	28%
Southwest	2	4%	1	14	9%	37	6%
Southeast	6	11%	21	15	9%	74	13%
Zanzibar/other	0	0%	2	2	1%	19	3%
Total	55	100%	88	165	100%	580	100%