Vulvar cancer in Ethiopia
A cohort study on the characteristics and survival of 86 patients

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Abstract

Vulvar cancer (VC) is strongly associated with human papilloma virus (HPV) infections and immunosuppression (e.g., HIV). However, there is limited information on VC patient characteristics and survival in parts of sub-Saharan Africa, including Ethiopia, where chronic HPV and HIV infections are prevalent. The aim of this study is to provide a first view on VC patient characteristics in a sub-Saharan African setting.

We present a retrospective analysis of records of 86 VC patients diagnosed between January 2010 and October 2015 at Addis Ababa University Hospital and other major health facilities in Ethiopia. Follow-up for vital status was obtained by telephone contact with patients or relatives. The primary endpoint was all-cause mortality.

The median age of the patients was 39 (range: 20–85) years, 83% with known HIV status were positive and 81% presented with FIGO stages 2 or 3. The median follow-up time for surviving patients was 17 months (range: 0.1–65.0 months). The 1- and 2-year survival rates were 80% and 51%, respectively. Approximately 37% of patients received surgery, 38% received radiotherapy, and 33% received chemotherapy. Patients who received therapy had better survival than those who did not [adjusted hazard ratios: surgery, 0.44 (95% CI, 0.19–1.03); radiotherapy, 0.36 (95% CI, 0.14–0.90); chemotherapy, 0.42 (95% CI, 0.15–1.12)].

A substantial proportion of VC patients in Ethiopia present at a late stage and receive suboptimal treatment. HIV infections appear to be a common comorbid condition. These conditions result in poor outcomes.

Abbreviations: AA = Addis Ababa, AACCR = Addis Ababa City Cancer Registry, ART = antiretroviral therapy, CI = confidence interval, FIGO = International Federation of Gynecology and Obstetrics, HPV = human papilloma virus, HR = hazard ratio, ICD-O-3 = International Classification of Disease-Oncology-3, SEER = Surveillance, Epidemiology, and End Results Program, VC = vulvar cancer.

Keywords: cumulative survival rate, HIV infections, sub-Saharan Africa, Ethiopia, vulvar neoplasms

1. Introduction

Vulvar cancer (VC) is a rather rare cancer entity, but its incidence has been increasing steadily in recent decades worldwide.[1–5] While in 2007 an estimated 3490 women were diagnosed with and 880 died of VC in the United States, this number rose to 5950 diagnoses and 1110 deaths in 2016.[6,7] Population-based data from the East African countries of Uganda, Zimbabwe, and Malawi show age-standardized incidence rates of 0.6, 1.1, and 1.0 per 100,000 women per year, respectively.[8–10] With an estimated population of 105.0 million people (2017), Ethiopia is the second most populated country in sub-Saharan Africa.[11] Data from Addis Ababa City Cancer Registry (AACCR) show an age-standardized incidence of 1.4 cases of VC per 100,000 women per year in Addis Ababa (AA) (2012 and 2013).[12] Squamous cell carcinoma is the most common histologic type (90%).[13] There are 2 different types: one linked to human papilloma virus (HPV) infection, histologically nonkeratinizing and more common in younger women. Risk factors include impaired immunological status (e.g., HIV coinfection) and smoking. The second is HPV-independent, histologically keratinizing, and not related to HPV infection or smoking. VC is more common in older women with chronic dystrophic diseases (e.g., lichen sclerosis).[14,15] HIV-positive women have a higher risk of VC.[16]

Early-stage VC treatment has high cure rates with low morbidity by radical local excisions with surgical evaluation of lymph nodes. In advanced diseases, surgery and chemoradiation are recommended.[17] The 5-year relative survival rate of VC patients diagnosed from 2006 to 2012 in the United States, based

on the Surveillance, Epidemiology, and End Results Program (SEER) 18 database, is 71.9%.[18] Population-based data from England showed a 1-year survival rate of patients diagnosed between 2007 and 2009 of 85.2%.[3] The outcome varies greatly between early- and late-stage diseases. In a study by Homesley et al,[19] patients with a minimal risk had a 5-year survival rate of 98%; of patients with high risk, only 29% survived 5 years. Between 2009 and 2013, the median age at diagnosis in the SEER population was 68 years.[18] In England, Lai et al[3] reported significantly rising incidence rates in younger women aged 20 to 59 years from 1990 to 2009. This development is attributed to growing numbers of HPV-related cancers.[20]

The objective of our study is to provide the first insights into VC-patients demographics, tumor characteristics, treatment, and resulting overall survival in Ethiopia.

2. Methods

2.1. Patients and methods

This hospital cohort study included 86 Ethiopian women who were diagnosed with VC between January 2010 and October 2015. We included patients from the Radiotherapy Center and the Pathology Department of Tikur Anbessa Specialized University Hospital as well as AACCR. Data were collected between October 5 and November 6, 2015. We found 86 patients admitted for VC. Of these, 81 had a histologically verified primary diagnosis of malignant neoplasm of the vulva [International Classification of Disease-Oncology codes C51.0-9]; 3 were cytologically diagnosed and 2 clinical diagnosis only. In 51 cases, all patient, tumor, therapy, and outcome information was abstracted from patients' files. In 35 cases only limited information was available from the AACCR database including date of diagnosis and last contact, basis of diagnosis, tumor topography, and morphology according to ICD-O-3, age, and planned treatment; no information on HIV status was available. We suspected a potential source of bias in difficulties including patients who died early; however, those patients included from the AACCR were included at first timepoint of diagnosis and therefore included irrespective of early death.

Patients or relatives were contacted via telephone to collect information on survival (n=80) between November 1 and November 13, 2015. For 6 patients without telephone numbers available, the last date of contact was taken from files.

In case of contradicting information between the files and the relatives on dates of death (n=8), the following rules applied: if the date of death given by relatives was before the last date "patient alive" in the file, we assumed that the patient died 3 months after the date in the file. The 3 months were chosen since patients were appointed 3-monthly for follow-up; a missed appointment and known death was thus approximated.

2.2. Staging

Tumors were classified according to the International Federation of Gynecology and Obstetrics (FIGO) staging system.[21] Tumor size (T), lymph node status (N), and metastasis (M) mentioned in the files within the first 3 months after primary diagnosis were used as baseline characteristics (n=48). Because of the lack of detail on lymph node status in 32 cases, we decided to group stages 1 to 3 into one category since lymph node status is the defining factor to distinguish between these stages. Patients without known lymph node status were classified stages 1 to 3 because we assumed that a stage 4 (="fixed or ulcerated inguinofemoral lymph nodes") would have been mentioned in the file.

2.3. Treatment modalities

Information on treatment was abstracted from patient medical files (n=51). If treatment information seemed to be incomplete and for AACCR cases, we used additional information from the follow-up call (n=37) or AACCR database only (n=5).

Patients with VC were referred from all over Ethiopia for chemoradiation, because Tikur Anbessa University Hospital has the only cobalt-60 teletherapy unit in Ethiopia. Surgery was performed if the tumor was considered resectable. Individually, a trial of neoadjuvant chemotherapy or chemoradiation was considered to achieve downstaging for better surgical options. Patients with good performance status received 54 to 60 Gy with concurrent chemotherapy (6 cycles of Cisplatinum 60 mg/m^2 + 5-Fluorouracil 475–500 mg/m^2). Patients who were lymph node positive after surgery received 50 to 60 Gy adjuvant radiotherapy. For palliative treatment, patients received 30 Gy.

2.4. Statistical analysis

The primary endpoint of this study was overall survival. Person time equaled the time from the date of pathologic diagnosis to the date of last contact or death. The survival probabilities were estimated using the Kaplan–Meier method. Multivariate Cox proportional hazard regression analysis was used to estimate adjusted hazard ratios (HR) and corresponding 95% confidence intervals (CI) for prognostic factors. The P values are considered as explorative. The median follow-up time for surviving patients was 17 months (range, 0.1–65.0). Sensitivity analysis was performed on the subgroup of known HIV-positive patients.

Ethical approval was acquired from the AA Medical Faculty and Martin-Luther-University Halle Review Board. Our study was executed without individual informed consent because the data were retrospectively obtained from routine care documentation.

3. Results

3.1. Patient characteristics and therapy

The majority of the 86 patients in this study came from AA (76%). The median age was 39 years (range, 20–85 years). The mean number of children was 3.3 (range, 0–14). None of the patients mentioned ever having smoked. Forty out of 48 patients had FIGO stages 1 to 3 cancer (83%). It is notable that only 1 case would have been classified as stage 1 with a given negative lymph node status. Squamous cell carcinoma was most common (87%). Tumor grading was available in only 11 cases; of those, 73% were well differentiated. Mean tumor size was 7 cm. Information on HPV was not available.

A total of 33 patients (38%) received radiotherapy. In 16 cases, detailed information on radiotherapy was available: 8 patients received 40 Gy in 20 fractions, 6 patients received 30 Gy (n=5 in 10 fractions, n=1 in 15 fractions), 1 patient received 60 Gy (30 fractions), and 1 patient received 20 Gy (10 fractions).

Thirty-two patients (37%) received surgery. Surgical procedures were mentioned in 7 cases; 3 patients received a local excision, 2 were treated by hemi-vulvectomy, and 2 by vulvectomy.

A total of 28 patients (33%) received chemotherapy. Of them, in 16 patients with additional information received Cisplatinum/5-Fluorouracil; of those, 11 completed 6 cycles of treatment. Three patients' files ended after 2 cycles of chemotherapy, 1 patient received only 1 cycle, and in 1 case, no information on the number of cycles was available (Table 1).

Table 1

Clinical and pathological characteristics.

| | Total (n=86) | % | HIV status (n=36) | | | |
			Positive (n=29)	%	Negative (n=6)	%
Place of origin						
Addis Ababa	65	75.6	20	69.0	3	50
Non-Addis Ababa	21	24.4	9	31.0	3	50
Age, y						
<30	10	11.6	1	3.4		
30–39	33	38.4	25	86.2		
40–49	11	12.8	1	3.4	1	16.7
50–59	13	15.1	1	3.4	1	16.7
60–69	10	11.6	1	3.4	3	50.0
≥70	9	10.5			1	16.7
Parity						
0–1	14	31.8	13	50		
2–3	17	38.6	10	38.5	1	16.7
>3	13	29.5	3	11.5	5	84.3
Marital status						
Single	5	19.2	4	21.1		
Married	11	42.3	7	36.8	1	100
Divorced	5	19.2	4	21.1		
Widowed	5	19.2	4	21.1		
Stage (FIGO)						
1–3	40	83.3	22	75.9	6	100
4	8	16.7	5	17.2		
Histology						
Squamous cell carcinoma	75	87.2				
Keratinizing	25	29.1	10	34.5	2	33.3
Nonkeratinizing	12	14.0	5	17.2	1	16.7
NOS	38	44.1	10	34.5	3	50.0
Carcinoma NOS	5	5.8	1	3.4		
Adenocarcinoma	1	1,2				
Verrucous carcinoma NOS	1	1,2				
Unspecified	4	4.7	3	10.3		
Grading						
Well-differentiated	8	9.3	3	75.0		
Moderately differentiated	1	1.2				
Poorly differentiated	1	1.2	1	25.0		
Undifferentiated	1	1.2				
Unknown	75	87.2				
Tumor size (mean, SD)	7.00±4.15 cm		7.64±4.36 cm		8.00±4.69 cm	
Surgery						
Yes	32	37.2	6	20.7	1	16.7
No	54	62.8	23	79.3	5	83.3
Radiotherapy						
Yes	33	38.4	13	44.8	4	66.7
No	53	61.6	16	55.2	2	33.3
Chemotherapy						
Yes	28	32.6	8	27.6	2	33.3
No	58	67.4	21	72.4	4	66.7

FIGO = International Federation of Gynecology and Obstetrics, NOS = not otherwise specified, SD = standard deviation.

3.2. HIV characteristics

Of 51 patients with a file available, information about HIV status was reported for 35 patients (found in 69% of files, n=16 unknown) and 83% (n=29) of these were HIV positive. Ninety percent of the HIV-positive patients were younger than 40 years (n=26); only 3 were above 40 years old (10%). None of the known HIV-negative patients was younger than 40 years. Most patients were on antiretroviral therapy (ART) treatment at the time of diagnosis (86%; n=25) and the mean time from the start of ART to VC diagnosis was 40.7 months (range, 29.8–84.1 months). Among the 10 patients with known WHO-HIV stage,

90% were stage 4. Patients with known HIV-positive status were more likely to receive radiotherapy (HIV-positive, 45%; HIV-negative, 57%) compared with the total cohort (38%) but less likely to receive surgery (HIV-positive, 21%; HIV-negative, 17%; total cohort, 37%). The proportion of patients receiving chemotherapy was generally similar among the 3 groups of patients (approximately 30%) (Table 2).

3.3. Survival

Of the 51 patients with files available, 29 returned for regular follow-up visits (57%) with a median of 19 months (range, 8–58).

Table 2

Characteristics of HIV-positive patients (n=29).

	All patients known HIV positive (n=29)
ART at point of diagnosis? yes/no	25 (86%)/4 (14%)
WHO Stage at point of diagnosis Stage 3/4	1 (10%)/9 (90%)
CD4 cell count (done ±4 mo from diagnosis) (n=10)	
Mean cells/mm^3 [SD]	415 [230–600]
Minimum/maximum	200/750
Time from start of ART to diagnosis (mo) (n=23)	
Mean [range]	40.7 [−29.8–84.1]

ART = antiretroviral therapy, SD = standard deviation.

Twenty-two women (43%) did not have regular follow-up visits (maximum follow-up time: 8 months after primary diagnosis).

Of all women 34 died during follow up. The cumulative overall survival rate after 1 and 2 years was 80% and 51%, respectively, with a median survival of 33 months (95% CI: 10–55) (Fig. 1).

The survival of patients receiving surgery (adjusted HR, 0.44; 95% CI, 0.19–1.03), radiotherapy (HR 0.36; 95% CI 0.14–0.90), or chemotherapy (HR, 0.42; 95% CI, 0.15–1.12) tended to be prolonged compared to those without these therapies (Fig. 2). FIGO stage 4 patients had unfavorable outcomes (adjusted HR = 2.06; 95% CI, 0.75–5.62) compared to patients stage 1 to 3 (Table 3).

4. Discussion

Our study is the first to provide patient characteristics and survival for VC patients in a sub-Saharan African setting. The median age was 39 years; a high rate of patients with information available were HIV positive (n=29, 83%). Ninety percent of the HIV-positive patients were younger than 40 years (n=26). The 1- and 2-year survival rates for all VC patients were 80% and 51%, respectively. Surgery and radiotherapy were received by 37% and 38% of the patients, respectively; 33% received chemotherapy.
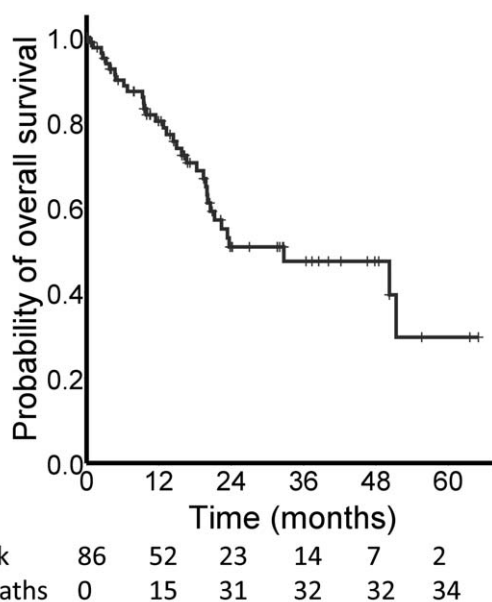

Figure 1. Cumulative overall survival probability of the total cohort of VC patients. No. = number, VC = vulvar cancer.
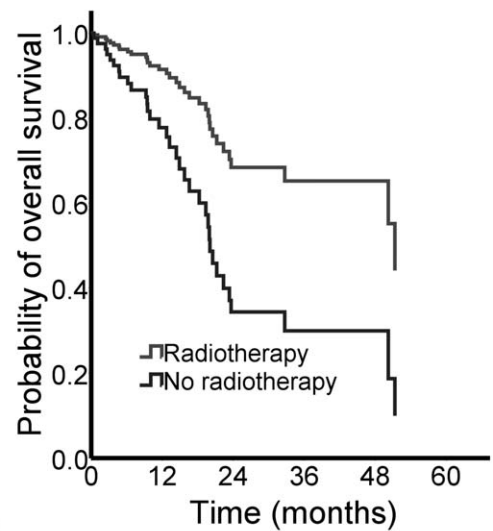

Figure 2. Probability of overall survival for VC patients stratified by radiotherapy received or not received. Adjusted for age (binary), FIGO stage, surgery, and chemotherapy. No. = number, VC = vulvar cancer.

4.1. Age

With a median age of 38 years, the cohort was considerably younger than patients in, for example, the United States (SEER, 68 years).[18] A study from Germany shows a change in the mean age of diagnosis from 65.6 years in the 1980s to 57.0 years around the year 2000. In the first period, 11% of patients diagnosed were under 50 years of age, whereas in the second, this share rose to 41%, probably due to growing numbers of HPV-related cancers.[20] In our hospital-based cohort, the low median age is attributable to the young population structure in Ethiopia.[22] We noted that gynecologists in low-resource settings have to treat young patients with VC and treatment plans (especially surgery) must consider sexually active premenopausal women.

4.2. HIV

The proportion of HIV-positive patients is high, especially in the age group below 40 years. We assumed that most of the patients of unknown HIV status were negative, because VC appears

Table 3

Unadjusted and adjusted HRs for death.

Characteristic	Unadjusted HR (95% CI)	P	Adjusted HR (95% CI)	P
Age (per additional year)	1.01 (0.98–1.03)	.53	1.01 (0.98–1.03)	.65
FIGO (Stage 1–3*)				
Stage 4	2.05 (0.80–5.24)	.14	2.06 (0.75–5.62)	.16
Unknown	0.70 (0.34–1.63)	.46	0.55 (0.23–1.30)	.17
Surgery (yes vs no*)	0.47 (0.21–1.03)	.06	0.44 (0.19–1.03)	.06
Radiotherapy (yes vs no*)	0.40 (0.19–0.82)	.01	0.36 (0.14–0.90)	.03
Chemotherapy (yes vs no*)	0.31 (0.14–0.70)	.01	0.42 (0.15–1.12)	.08

CI = confidence interval, FIGO stage = International Federation of Gynecology and Obstetrics stage, HR = hazard ratio.
Adjusted for surgery, chemotherapy, age (binary), and FIGO stage (* reference category).

primarily in HIV-positive patients with low CD4 T-cell counts[23]; such HIV-positive patients would have been clinically suspicious and received a test. Altogether, this would result in an estimated proportion of 57% HIV-positive cases among the subgroup in our cohort with files available. This estimate is consistent with data from Cape Town, South Africa; 50% (in 2014) and 41% (in 2015) of VC patients were HIV-positive.[15] It is notable that the HIV prevalence in South Africa was 19.2% in 2015, while the HIV prevalence in Ethiopia was merely 2.3% in 2012 (4.4% in AA).[24,25] Despite the lower prevalence of HIV in Ethiopia, there is a similarly high rate of HIV positivity in our cohort. We propose that every VC patient should be tested for HIV.

We do not think that morbidity due to HIV had a large effect on our VC patients' overall survival time. Most patients had long been on ART at the point of diagnosis for a mean time of more than 3 years. Studies from Ethiopia and Uganda showed that HIV morbidity is very low 2 years after ART initiation.[26,27] Of 10 patients with known WHO-HIV stage, all but one were stage 4. This probably led to lower proportions of HIV-positive patients receiving surgery, radiotherapy, or chemotherapy. Patients with known HIV-positive status should easily be checked for VC in addition to cervical cancer screening in the same procedure by simple inspection.

Because HIV is a risk factor for the HPV-related VC type, information on HPV status would be very interesting.[15] Unfortunately, no patient was tested for HPV. A population-based cohort with complete information would be needed to assess the impact of HIV and HPV on the incidence of VC in Ethiopia.

4.3. Survival

The 1-year survival rate was almost as high as the survival rate of VC patients from England (2003–2005; 83.1%). Whereas the 5-year survival rate of the English cohort was still 69.9% (SEER database 71.9%),[18] the 2-year survival of the Ethiopian cohort already decreased to 51%.[3] This is probably due to advanced stage—only one patient in our cohort met the criteria for FIGO stage 1, whereas 43% of patients in the English study with FIGO stage available were stage 1.[3] More awareness among health care workers and the community could possibly achieve downstaging.

Another contributing factor for lower survival in Ethiopia is the lack of standard treatment. There are long waiting times until the start of radiotherapy because there is only one radiotherapy machine for the country. A study on cervical cancer patients in Ethiopia found that the FIGO stage increased considerably between the point of diagnosis and the start of treatment (waiting time 3.8 months).[28] In our study, waiting times were even longer (median of 7.3 months). This highlights the urgent need to increase radiotherapy capacity in the country.

In cases where patients received radiotherapy, they tended to have longer survival (HR 0.36; 95% CI, 0.14–0.90). Surgery and chemotherapy, also tended to be associated with prolonged survival (HRs 0.44, 95% CI, 0.19–1.03 and 0.42; 95% CI, 0.15–1.12, respectively). These finding are in line with current treatment concepts that include surgery, radiotherapy, and chemotherapy.[17]

4.4. Limitations

There are limitations to our retrospective study: Nodal status was available in only 16 cases, limiting precise information on FIGO stage. Therefore, we decided to group stages 1 to 3, because nodal status is the defining factor for stage 3. For the 35 cases for whom there were no patient files, little information on patient characteristics was available. HIV status was absent in 51 cases. We assume that, even without complete information on all patients, our findings contain valuable insight into VC patients in a sub-Saharan setting. Second, we were unable to include cases from the surgical departments of TAH. This presumably led to a reduced number of patients with early-stage cancers who were treated by surgery only. According to the information provided by gynecologists, we assume that those were few cases. Third, because recently VCs are grouped into HPV-associated and non-HPV associated cancers, information on HPV would have been of high interest. To date, there is no option for HPV testing in Ethiopia. Fourth, the date of death obtained from family members during the follow-up call was sometimes vague, leading to a lack of precision in survival time. We assume that the error was in both directions and thus did not affect the results.

Despite these limitations, our study adds new information on a previously underexplored type of cancer to the literature, because it is the first to describe the characteristics and outcome of more than 50 VC patients in a sub-Saharan African setting.

5. Conclusion

This is the first study to describe the characteristics and outcome of VC patients on the basis of 86 patients diagnosed between 2010 and 2015 in AA. Even patients with late stage presentation, due to the nature of slow-growing tumors, usually survive the first year. Our 2-year survival rapidly declined due to the limited treatment options and urgently highlights the need for palliative care. The very low median age of 39 years probably results from the young population structure in Ethiopia. The surprisingly high share of 57% HIV-positive patients does not reflect the HIV prevalence in Ethiopia of 3.2%. Due to the high HIV positivity rate, we suggest that all VC patients should be tested and HIV patients should have an inspection of the vulva during cervical cancer screening. FIGO stage 4 was related to worse outcome. Treatment had a positive effect on patient survival, despite long waiting times until the start of radiotherapy and resulting urgent need for more than one radiotherapy facility in Ethiopia. Ginsburg et al[29] recently described the vast discrepancies between breast and cervical cancer patients in low- and high-come countries. Similar disparities can be seen in VC, highlighting the crucial necessity of an increasing awareness of women's cancers and their priority in women's health policies, including preventive measures, treatment options, and patient education to reduce the high frequency of patients with FIGO stage 4 who do not receive treatment and the resulting poor prognosis.

References

[1] Akhtar-Danesh N, Elit L, Lytwyn A. Trends in incidence and survival of women with invasive vulvar cancer in the United States and Canada: a population-based study. Gynecol Oncol 2014;134:314–8.

[2] Schuurman MS, van den Einden LCG, Massuger LF, et al. Trends in incidence and survival of Dutch women with vulvar squamous cell carcinoma. Eur J Cancer 2013;49:3872–80.

[3] Lai J, Elleray R, Nordin A, et al. Vulval cancer incidence, mortality and survival in England: age-related trends. BJOG 2014;121:728–38.

[4] Buttmann-Schweiger N, Klug SJ, Luyten A, et al. Incidence patterns and temporal trends of invasive nonmelanotic vulvar tumors in Germany 1999–2011. A population-based cancer registry analysis. PLoS ONE 2015;10:e0128073.

[5] Caspritz SCM, Ernst A, Folkerts J. Krebs in Deutschland 2011/2012. [GEKID Website]. Robert Koch-Institut und die Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V. (Hrsg). Berlin, 2015. Available at: http://gekid.de/Doc/krebs_in_deutschland_2015.pdf. Accessed November 10, 2016.

[6] Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2007. CA Cancer J Clin 2007;57:43–66.

[7] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016;66:7–30.

[8] Wabinga HR, Parkin DM, Nambooze S, et al. 2013. Cancer Incidence in Uganda, Kyadondo County (2003–2007). In: Forman D, Bray F, Brewster DH, et al., editors. Cancer Incidence in Five Continents, Vol. X (electronic version). Lyon: International Agency for Research on Cancer. Available at: http://ci5.iarc.fr. Accessed November 10, 2016.

[9] Chokunonga E, Borok MZ, Mauchaza BG, et al. 2013. Cancer Incidence in Zimbabwe, Harare (2003–2007). In: Forman D, Bray F, Brewster DH, et al., editors. Cancer Incidence in Five Continents, Vol. X (electronic version). Lyon: International Agency for Research on Cancer. Available at: http://ci5.iarc.fr. Accessed November 10, 2016.

[10] Dzamalala C, Huwa-Kandoje D, Chirwa M, et al. 2013. Cancer Incidence in Malawi, Blantyre (2003–2007). In: Forman D, Bray F, Brewster DH, et al., editors. Cancer Incidence in Five Continents, Vol. X (electronic version). Lyon: International Agency for Research on Cancer. Available at: http://ci5.iarc.fr. Accessed November 10, 2016.

[11] United Nations, Department of Economic and Social Affairs, Population Division. World Population Prospects: The 2017 Revision, Key Findings and Advance Tables. *Working Paper No. ESA/P/WP/248.* 2017.

[12] Timotewos G, Solomon A, Mathewos A, et al. First data from a population based cancer registry in Ethiopia. Cancer Epidemiol 2018;53:93–8.

[13] Hacker NF, Gambone JC, Hobel CJ. Hacker & Moore's Essentials of Obstetrics and Gynecology. Elsevier Health Sciences, Philadelphia, PA:2015.

[14] Ueda Y, Enomoto T, Kimura T, et al. Two distinct pathways to development of squamous cell carcinoma of the vulva. J Skin Cancer 2011;2011:Article ID 951250.

[15] Saidu R. Vulvar cancer, HPV infection, and HIV status. Curr Obstet Gynecol Rep 2016;5:196–202.

[16] Sitas F, Pacella-Norman R, Carrara H, et al. The spectrum of HIV-1 related cancers in South Africa. Int J Cancer 2000;88:489–92.

[17] Zweizig S, Korets S, Cain JM. Key concepts in management of vulvar cancer. Best Pract Res Clin Obstet Gynaecol 2014;28:959–66.

[18] Howlader N, Am Noone , Krapcho M, et al. SEER Cancer Statistics Review, 1975–2010. National Cancer Institute, Bethesda, MD:2013.

[19] Homesley HD, Bundy BN, Sedlis A, et al. Assessment of current International Federation of Gynecology and Obstetrics staging of vulvar carcinoma relative to prognostic factors for survival (a Gynecologic Oncology Group study). Am J Obstet Gynecol 1991; 164:997–1004.

[20] Hampl M, Deckers-Figiel S, Hampl JA, et al. New aspects of vulvar cancer: changes in localization and age of onset. Gynecol Oncol 2008;109:340–5.

[21] Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynecol Obstet 2009;105:103–4.

[22] World Health Organization. Global Health Observatory data repository [WHO Website]. June 6, 2016. Available at: http://apps.who.int/gho/data/node.main.688?lang=en. Accessed November 10, 2016.

[23] Chaturvedi AK, Madeleine MM, Biggar RJ, et al. Risk of human papillomavirus-associated cancers among persons with AIDS. J Natl Cancer Inst 2009;101:1120–30.

[24] UNAIDS. AIDSinfo. [UNAIDS Website]. Available at: http://aidsinfo.unaids.org. Accessed November 11, 2016.

[25] World Health Organization. ETHIOPIA Update sheet on HIV/AIDS programme 2014. [WHO Regional Office for Africa Website]. Available at: http://www.afro.who.int/en/ethiopia/ethiopia-publications.html. Accessed November 11, 2016.

[26] Ayele W, Mulugeta A, Desta A, et al. Treatment outcomes and their determinants in HIV patients on Anti-retroviral Treatment Program in selected health facilities of Kembata and Hadiya zones, Southern Nations, Nationalities and Peoples Region, Ethiopia. BMC Public Health 2015;15:826.

[27] Mills EJ, Bakanda C, Birungi J, et al. Life expectancy of persons receiving combination antiretroviral therapy in low-income countries: a cohort analysis from Uganda. Ann Intern Med 2011;155:209–16.

[28] Kantelhardt EJ, Moelle U, Begoihn M, et al. Cervical cancer in Ethiopia: survival of 1,059 patients who received oncologic therapy. Oncologist 2014;19:727–34.

[29] Ginsburg O, Bray F, Coleman MP, et al. The global burden of women's cancers: a grand challenge in global health. Lancet 2016;389:847–60.