



## Vulva cancer in Ghana – Review of a hospital based data



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### 1. Introduction

Vulva cancer is a rare disease representing 3 to 5% of gynecological cancers worldwide and remains an important disease affecting sexuality (De Martel et al., 2012; Hacker et al., 2015). Most published reports include rather small and heterogeneous groups of patients. In an earlier study conducted in Ghana, vulva cancer accounted for 2.1% of all gynecological malignancies (Nkyekyer, 2000). Another study of 5913 gynecological cancers from Nigeria reported 1.2% of Vulva cancers with majority exhibiting squamous cell histology and median age of 49.7 years compared to a median age at presentation above 50 years in the United States (Okolo et al., 2013). Burkina Faso reported that out of 21 patients, 15 presented with stage III or IV, and the median age was 55 years (Zongo et al., 2016).

Over 80% of cases occur in women over 55 years old (Alkatout et al., 2015). Fifteen percent of vulva cancers occur in women <40 years and could be due to the human papilloma virus infection (Siddiqui, 2002; RCOG Publications, 2006). Sixty percent of vulva cancer cases are associated with HPV and HIV infection especially in the developing countries (Smith et al., 2009).

Vulva pruritus is the most common presenting symptom. Other symptoms include bleeding, pain and ulceration or discharge (Hunter, 1975). Over 70% are of squamous cell histology being the most common followed by melanoma (Palmer and Gillespie, 2010). Many women have a long delay in diagnosis due to denial or minimization

of symptoms, presenting with a locally advanced tumor at the time of initial evaluation.

Over the past decade, advances have been made in the management of vulva cancer, with a trend toward more conservative surgery in order to improve psychosexual outcomes (Alkatout et al., 2015). Surgery is the treatment of choice for early stage, and the indications for adjuvant therapy continue to evolve (De Hullu and Van der Zee, 2006). Less mutilating surgery including sentinel node procedures have equal outcomes to extensive and radical surgery (Günther et al., 2014). Chemosensitization of radiation therapy with 5-fluorouracil and cisplatin chemotherapy in the neoadjuvant, adjuvant setting or as definitive or palliative treatment for unresectable disease are available options, however fraught with toxicities requiring frequent and sometimes prolonged treatment breaks (Hacker et al., 2015).

In Ghana, as in other low middle-income countries, majority present with advanced disease (Nkyekyer, 2000). Definitive chemoradiation or palliation is the treatment of choice as options for optimal surgical management is available only in the teaching hospitals and very few patients are surgical candidates. The National Centre for Radiotherapy, Accra is a major referral center including other African countries. This retrospective study will analyze and review all cases of vulva cancer referred to this institution over a fourteen-year period.

### 2. Methodology

This is a retrospective study of histological diagnosed vulva cancers seen in our unit between January 2000 and December 2014. Patients' records were extracted from the institutional database. A data collection index was developed to extract the following information in patients' folder: Age at presentation, symptoms at presentation, initial site of lesion, stage of the disease using revised FIGO 2009 staging system (Pecorelli, 2009), histological type, date of first attendance, date of commencement of treatment, treatment received, duration of treatment interruption and outcome.

Descriptive statistics using excel were generated in the form of rates, ratios and proportions using excel statistical program.

### 3. Result

During the period under study, 3479 cases of gynecological cancers were recorded. Vulva cancers constituted 2% (70). The most common cancer was cervical cancer accounting for 80.4% (2797) whereas the least was vaginal cancer accounting for 1% (22).

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**Table 1**  
Clinical and Histological Characteristics of 52 vulva cancer patients.

	Categories	N (%)	
Age(years)	<45	11(21%)	
	45–54	10(19%)	
	55–64	14(27%)	
	≥65	17(33%)	
Presenting symptom	Swelling	20(38%)	
	Ulceration	18(35%)	
	Pruritus	8(15%)	
	Rash	4(8%)	
	Pain	1(2%)	
	Groin swelling	1(2%)	
	Labia majora	21 (40%)	
	Labia minora	23 (44%)	
Primary site	Fourchette	4 (8%)	
	Mons pubis	2 (4%)	
	Introitus	1 (2%)	
	Clitoris	1 (2%)	
	Squamous cell carcinoma	44 (84%)	
	Adenocarcinoma	1 (2%)	
	Adenoid cystic	2 (4%)	
	Trichilema tumor	1 (2%)	
Histology	Warty carcinoma	1 (2%)	
	Cutaneous T cell lymphoma	1 (2%)	
	Sarcoma	1 (2%)	
	Melanoma	1 (2%)	
	Staging	Stage 1	7 (13%)
		Stage 2	6 (12%)
		Stage 3	8 (15%)
		Stage 4	31 (60%)

3.1. Demography

The mean age for this study was 56.3 years with an age range of 24–79 years. Peak age at presentation was >65 years. 21% (11) of the women were <45 years. Most of the women were of low socioeconomic status.

The commonest presenting symptom was vulva swelling (38%), followed by ulceration (35%). Only 15% reported pruritus (8). (Table 1).

3.2. Histology

Squamous Cell Carcinoma was the commonest histological variant (Table 1).

3.3. Staging

Disease stage was done based on clinical examination, chest x-ray and ultrasound of the abdomen and pelvis, cystoscopy and proctoscopy where indicated and from the latter part of 2008 with CT scans where deemed necessary. Sixty percent presented with stage 4, 15% with stage3, 12% with stage 2 and 13% with stage 1 disease.

3.4. Time lapse

The average time between date of pathological diagnosis and date of first attendance at the Radiotherapy Centre was 52.8 days (1–347). Majority (44%) reported >28 days after histological diagnosis. An average of 38 days elapsed between first attendance and date of commencement of radiotherapy. (Table 2).

3.5. Treatment

Seventy cases of vulva carcinoma were documented at the Radiotherapy Centre. Eighteen did not return after initial registration. Five patients were referred for surgery. Eleven out of 47 scheduled to receive radiotherapy defaulted. Out of the remaining 36, seven patients

**Table 2**  
Characteristics of patients who received radiotherapy.

	Categories	n (%)
Time lapse between date of pathological diagnosis and date of first attendance	<14 days	16 (31%)
	14–28 days	13 (25%)
	>28 days	23 (44%)
	Average	52.3 days
Time lapse between date of first attendance and commencement of radiotherapy treatment	<14 days	5 (14%)
	14–28 days	18 (50%)
	>28 days	13 (36%)
	Average	38 days
Treatment interruptions	None	3 (13%)
	<2 weeks	3 (13%)
	2–4 weeks	8 (35%)
	>2 weeks	9 (39%)
Reasons for interruptions	Average	36 days
	Planned	10 (26%)
	breaks	15 (39%)
	Skin reaction	4 (11%)
	Diarrhea	(22%)1(2%)
	Non compliance	
	Neutropenia	

received palliative radiotherapy and 6 patients who commenced definitive radiotherapy did not complete treatment. Sixteen women had definitive radiotherapy whilst six had concurrent chemo-radiation with IV Cisplatin 50 mg/m<sup>2</sup> day 1 and 5- Fluorouracil 425 mg/m<sup>2</sup> day 1–5 week 1 and 5. One patient treated in 2014 was treated with single agent cisplatin at 40 mg/m<sup>2</sup> weekly for 5 weeks (Fig. 1). Radiotherapy was delivered via a Cobalt 60 teletherapy machine. Anterior and posterior opposing beams with a shrinking field technique to encompass the involved bilateral inguinal and pelvic nodes and primary tumor was used. Electron beam therapy is not available. From the year 2000 to 2008, patients were treated with 2 dimensional techniques. Conformal planning techniques were applied from 2008 to 2014. Palliative radiation doses ranged from 10 to 40 Gy. The average definitive radiotherapy dose was 57Gy (45Gy–65Gy).

The choice of treatment was based on burden of disease, patient preference mainly related to financial constraints, physician preference and availability of evidence to support treatment modality. Notably patients were more likely to be managed with chemo radiation after 2010.

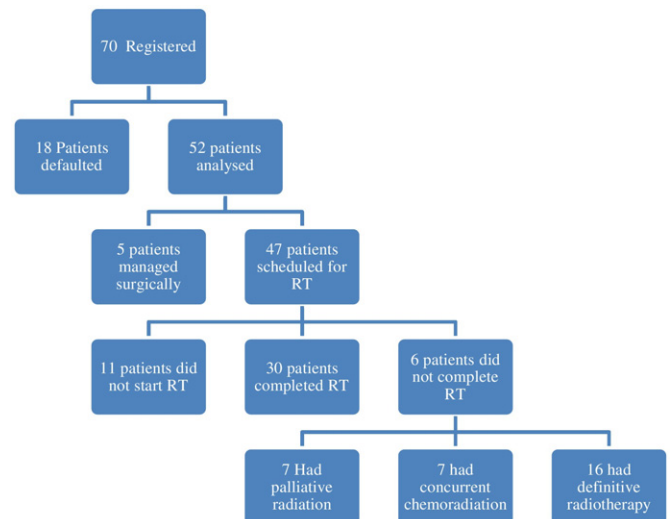


Fig. 1. Treatment characteristics of seventy patients with vulva cancer, Accra Ghana.

### 3.6. Treatment interruptions

Eighty seven percent treated with definitive radiotherapy/chemo radiation had treatment interruptions. The average duration of treatment interruption was 36 days (6–120). Seventy-four percent had interruption of > 14 days. A longer duration of interruption was noted in patients receiving concurrent chemoradiation. Reasons for interruptions included planned breaks (26%), skin complications (39%), diarrhea (11%), neutropenia (2%) and non-compliance (22%) (Table 2).

### 3.7. Outcome

The mean follow up period was 42.4 months (Date of first attendance to date last seen/date of death).

There was an 80% and 74% complete clinical response in the primary lesion and lymph nodes respectively at 12 weeks post radiation for 23 patients who completed definitive treatment.

The 2 and 5 year overall survival for all 30 subjects (70% of which were stage 4) who completed was 56.7% and 36.7% respectively.

## 4. Discussion

Ghana, a low middle-income country in West Africa has an estimated population of 27.4 million (females-51%, males- 49%) and a life expectancy of 62.4 years (World Health Statistics, 2010).

The pattern of gynecological cancers seen over the 14 year period of this study revealed cervical cancer as the most common (80%) and the least being carcinoma of the vagina accounting for 1%. In the USA, cancer of the endometrium was the most common, and carcinoma of the vulva and vagina were the least (4–6% of all gynecological cancers) (Okolo et al., 2013). The disparity in the pattern of gynecological malignancies may be explained by the lack of cervical cancer screening programs in developing countries.

Several reports from African authors reflect the rarity of vulva cancer. Its proportion in relation to other gynecological cancers is highly variable, ranging between 1.3 and 5% (Eke et al., 2010). In our study, cancer of the vulva was the fourth most common diagnosed gynecological cancer. Zaria has prevalence of 2.6%, Lagos 3–5%, Ibadan 1.3% and in the USA 0.6 (Okolo et al., 2013). Developing countries have a relatively high or similar prevalence and incidence when compared to developed nations and may be a reflection of the prevalence of Human Papilloma Virus in sub-Saharan Africa (Smith et al., 2009).

The mean age for vulva carcinoma from this study 56.3 years (Table 1) with a range of 24 to 79 years agreeing with average age ranging between 46 and 61 which has been reported by other African studies (Eke et al., 2010; Tanko et al., 2012). In Western Europe, the average ages are over 70 years (Buttmann-Schweiger et al., 2015). The difference in average ages between Europe and the less developed countries could be explained by the difference in life expectancy at birth. One striking result from our study, was the high number of women below 45 years of age (21%) which present a unique challenge including having to deal with psychosocial and sexuality issues during survival (RCOG Publications, 2006).

In Ghana, women with vulva cancer often present late for treatment. Many women at the initial symptoms of the disease will seek alternate forms of treatment and will only report to a health facility when symptoms do not improve. In instances where women report to health facilities early, there is often inability of primary health care personnel to detect early vulva cancer. Our study shows an average of 52.2 days (Table 2) between date of pathological diagnosis and reporting at the referral center. This may be a result of the complicated referral processes. These reasons may also account for the late stage at presentation (75% presented with Stage III and IV disease) The study revealed an average of 38 days between first attendance and commencement of radiotherapy, with half of the patients commencing treatment between 14 and 28 days (Table 2). These time lapses could be a result of high burden

of patients on the treatment machine, time required for conformal treatment planning and financial constraints.

A significant finding is the high default rate among patients receiving treatment. One third did not start treatment at all or defaulted during radiotherapy). The cost of cancer treatment is not completely covered by national or private health insurance schemes and requires large out of pocket payment coupled with stress of long daily travels for treatment are some of the major factors contributing to this high default rate. The inclusion of cancer treatment to the national health insurance scheme, better patient education and establishment of patient support systems may help reduce the high default rate observed in these patients.

Until recently, radical vulvectomy and inguinal lymphadenectomy was the standard of care for resectable vulva carcinoma, resulting in 90% survival rates but was associated with considerable physical and emotional sequelae (Andersen and Hacker, 1983). Currently, small, favorable lesions,  $\leq 2$  cm in diameter and  $\leq 5$  mm in depth, are managed with wide local excision rather than a radical vulvectomy, with satisfactory outcomes. The local recurrence and disease survival rates are similar with either procedure, ranging from 6% to 7% and 98% to 99%, respectively (Hacker and Van Der Velden, 1993). The use of three separate incisions instead of the en bloc lymph node dissection has contributed to the reduction of long-term effects such as lymph edema and erysipelas (Van der Zee et al., 2008; Sznurkowski, 2016). In spite of our adaptation of current surgical techniques resulting in less mutilating surgery, many patients default surgery as is reflected in all five patients in our study referred for upfront surgery were lost to follow up.

Indications for adjuvant radiotherapy are still evolving and include positive surgical margins < 8 mm, capillary-lymphatic space invasion, and thickness > 5 mm as well as any lymph node macro metastasis  $\geq 5$  mm, two or more lymph node micro metastases (< 5 mm) and any extra capsular spread (Faul et al., 1997; Woelber et al., 2012). Adjuvant radiotherapy was not indicated in any of our treated patients.

In Ghana, as in other low middle-income countries, definitive chemoradiation or palliation is the treatment of choice as options for appropriate surgical management is available only in the teaching hospitals and most of these women present with unresectable disease. Twenty-three patients received definitive radiotherapy with or without chemotherapy (Cisplatin + 5FU). A Cochrane review indicated there was no statistically significant difference in survival between primary chemo radiation and primary surgery in a study that included 63 women with locally advanced disease. (Shylasree et al., 2011) Experience with cervical cancer chemo radiation protocols has led to the preferred use of cisplatin as radio sensitizer for vulva cancer (Gaffney et al., 2009; Moore et al., 2012). Other older chemo sensitizers include 5FU and cisplatin or mitomycin C (Montana et al., 2000; Landoni et al., 1996). We currently recommend single agent cisplatin.

Radiation or chemo- radiation for vulva carcinoma is fraught with severe skin, gastrointestinal and hematological toxicities mandating treatment interruptions. Majority (87%) treated with definitive radiotherapy had treatment interruptions. The average duration of treatment interruption was 36 days (6–120 days) (Table 2). Older protocols mandated treatment breaks after 24–36 Gy as a precautionary measure but has recently been associated with reduced local control and therefore not recommended. (Montana et al., 2000; Landoni et al., 1996). It is however important to note that most institutions in developed countries have capabilities for electron beam therapy and intensity modulated therapies (IMRT) which are known to reduce severe toxicities enabling delivery of full prescribed doses of 64–70 Gy as compared to our situation (Alkatout et al., 2015) Our current protocols does not encourage planned treatment breaks. However, even with conformal treatment planning, it is difficult to treat the primary target to doses beyond 60 Gy without exceeding dose constraints to the femoral heads and bowel in the absence of electron therapy and IMRT.

Radiotherapy plays an important role in supportive care by palliating constipation, bleeding, ulceration, offensive discharge, bone metastasis

and pain in vulva cancer (Mishra, 2011). Seven patients with advanced disease and poor performance status received palliative radiotherapy for pain, bleeding and ulceration with significant relief from their symptoms.

The 2 and 5 year overall survival for all 30 women who completed radiotherapy (70% with stage IVA) was 56.7% and 36.7% respectively. Two and 5 year overall survival according to FIGO for stage 3 and 4 disease ranges from 17 to 54% and 43–14% respectively (Beller et al., 2006). This compares favourably with outcomes from other countries in spite of our limitations (Lai et al., 2014).

Limitations of our study include a small retrospective study and high patient default rate.

## 5. Conclusion

Vulva cancer in Ghanaian patients presents at similar ages as other countries but with a higher proportion presenting with advanced disease. Definitive chemo radiation is associated with modest survival rates even in the absence of sophisticated radiation treatment techniques and is fraught with treatment interruptions as result of severe toxicities. Late presentation and non-compliance among patients present a major challenge in Ghana. Patient and health work force education as well as comprehensive national health insurance schemes may improve the current situation.

## Conflict of interest

All authors declare no conflict of interest.

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