A retrospective study of clincal profile and treatment outcome of vulvar cancer patients attended at ORCI from January 2006 to December 2017

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A RETROSPECTIVE STUDY OF CLINCAL PROFILE AND TREATMENT OUTCOME OF VULVAR CANCER PATIENTS ATTENDED AT ORCI FROM JANUARY 2006 TO DECEMBER 2017

By

Irene Jeremiah Nguma

A Dissertation Submitted in (Partial) Fulfilment of the Requirements for the Degree of Masters of Medicine (Clinical Oncology) of the

Muhimbili University of Health and Allied Sciences
October, 2019

CERTIFICATION

The undersigned certify that she have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: **"A retrospective study of clinical profile and treatment outcome of vulvar cancer patients attended at ORCI over 11 years",** in (partial) fulfilment of the requirements for the degree of Master of Medicine (Clinical Oncology) of the Muhimbili University of Health and Allied Sciences.

_____

Mamsau Ngoma, MD, MMed

(Supervisor)

_____

Date

DECLARATION AND COPYRIGHT

I, **Irene Jeremiah Nguma,** declare that this **dissertation** is my own original work and that it has not been presented and it will not be presented to any other University for the similar or any other degree award.

Signature: ..... **Date: .....**

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DEDICATION

I dedicate this dissertation to My beloved husband George Vedasto for his endless support, encouragement and patience, my father and mother for their continuous encouragement and to my children for their patience and love through our my MMED studies

ABSTRACT

Background

Vulva includes labia majora, mons pubis, labia minora, clitoris, vestibule of the vagina, bulb of the vestibule, greater and lesser vestibular glands, and vaginal orifice. Vulvar cancer is type of cancer that affects external genital organs that protect a woman's reproductive system. It commonly appears at labia majora. less frequently involve the labia minora, perineum, clitoris, and Mons. In 10% of cases, the lesion is too extensive to determine the actual site of origin. About 5% of cases have multifocal lesions i.e. all vulvar and perianal skin surfaces, as well as the cervix and vagina, should be evaluated. A synchronous second malignancy, most commonly cervical neoplasia, is found in up to 22% of patients with a vulvar malignancy.

An increase in incidence of vulva cancer has been seen worldwide for two decades now. Less than 20% of cases are women younger than 50 years, and more than 50% occur in women over the age of 70 years. The average age of diagnosis of invasive VC is 70 years where as non-invasive VC average age is about 20 years younger.

In our region i.e., East Africa and Tanzania per se there is paucity of vulva cancer studies and currently the vulva cancer incidence is increasing where by more studies are needed to give out clear picture of the disease.

Objectives

This study aimed to describe vulva cancer social demographic characteristics like age, clinical characteristics of the disease, stage of the disease at the time of diagnosis, histological type and grade, clinical signs and symptoms, associated factors for VC such as HIV status and pre-existing genital warts, treatment intent and modality and treatment outcome in terms of symptoms relief and disappearance and one year overall survival for all patients attended at ORCI from January 2006 to December 2017.

Methods

Retrospective cohort study conducted at ORCI for all those patients with histological confirmed primary vulva cancer who fits inclusion criteria attended between January 2006 to December 2017. Data were collected by using Data extracting form extracting information from the patient's files then processed by using SPSS version 24. Also measures of Descriptive statistics were used in analysing some of the clinical and demographic data like age, stage of the disease and grade. Survival rate was estimated by using the date of diagnosis and date of death or date of last visit. Cox proportional hazard model was used to examine various factors with time to death hazard ratios (HRs) and 95% confidence interval is presented. Two sided P-value < 0.05 is considered as statistically significant.

Results

Total number of 61 cases attended during study period of 12 years were analysed.9 cases were = or > 60 years (14.80%) and 52 cases were < 60 years (85. 2%), 37 were HIV positive (60.70%),19 were HIV negative (31.10%).

Main reasons for consultation was lesion at the vulva (100%).Other symptoms include pain (83.60%) pruritis (36.10%) watery discharge and foul smelling vagina discharge (26.20%). Common histology types were squamous cell carcinoma 90.20%, others were adeno carcinoma, basal cell carcinoma and verrucous carcinoma were 3.3%, 3.3% and 3.3% respectively. Grade I tumours were 47.5% followed by grade II 21.3%. Grade III and IV were 13.1%.18% of the cases tumor grades not known. Only 4 cases were staged (6.5%), all were stage III and IV.

Only 2 cases (3.3%) received curative treatment, remaining 59 cases (96.7%) were given palliative treatment. The most common treatment modality used was CCRT (44.3%), others were RT alone 34.4%, medical palliation 16.4%, surgery and radiotherapy 1.6%, surgery alone 1.6% and chemotherapy alone was 1.6%.

Symptoms relief was found in 68.9% of the cases, it was associated with treatment modality, RT technique, RT Dose and RT Field used.

It was also observed that HIV negative cases survived more than HIV positive cases, the median 1-year overall survival for HIV negative patients was higher (4 months) than that of HIV positive cases (3 months).

Conclusion

VC common occurs at younger below 60 years (85.2%). Was associated with HIV infection. Few cases which were staged had advanced disease. Majority were given palliative treatment with poor outcome in terms of symptom relief.1year Overall survival is still very poor. HIV infection and treatment modalities are the factors which affects survival. There was no relationship between age and survival status

Recommendation

Since it occurs more common to younger age, awareness to the community should be increased so that people to avoid the risk factors which predispose them to the disease, also it will make them to do early consultation to the health facilities once they start to experience signs and symptoms of disease. Health care provider also will know early clinical signs and symptoms for early diagnosis or early referral for those facilities which they can’t diagnose, which might lead to early initiation of treatment with good outcome and increased survival.

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LIST OF ABBREVIATIONS

AI	Allelic imbalance
AJCC	American Joint Committee on Cancer.
CIN	Cervical Intraepithelial Neoplasia
CT	Chemotherapy
DFS	Disease free survival
EBRT	External beam radiotherapy
FIGO	Federation International of gynaecology and Obstetric
GIT	Gastro intestinal tract
GUT	Genital Urinary system
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
LPFS	Local progression free survival
LS	Lichen sclerosis
MSI	Microsatellite instability
ORCI	Ocean Road Cancer Institute
OS	Overall survival
PORT	Post-Operative Radiotherapy
RT	Radiotherapy
SCC	Squamous cell carcinoma
SCH	Squamous cell hyperplasia
STIs	Sexually transmitted infections
VC	Vulva cancer
VIL	Vulvar intraepithelial lesions
VIN	Vulva Intraepithelial Neoplasia
VSCC	Vulva squamous cell carcinoma

DEFINITION OF KEY TERMS

Overall survival - Is the time from when the patient diagnosed with VC and still alive.

Complete response - Complete disappearance of symptoms after treatment.

Partial response - Minimal improvement of symptoms after treatment.

Worsening - Progression of the symptoms despite of patient being on treatment

Concurrent chemo radiotherapy - Chemotherapy being delivered concurrently with radiotherapy

CHAPTER ONE

1.1. INTRODUCTION

1.2. Background

Although vulva cancer is a relatively uncommon gynaecological malignancy, the increase in its incidence is striking over the last several decades. It accounts about 3-5% of gynaecological malignancies worldwide. About 80% occurs at the labia, mainly the labia majora (~50%). About 10% involve the clitoris, and another 10% involve the perineum. In about 5% of cases, it can occur at more than one site(1)

In developed countries, patients diagnosed with FIGO stage I increased from 31% to 52%, whereas metastatic stage IV decreased from 21% in 1993 to 10% in 2013, respectively(2).Also mortality rates decreased by 25% from 1992 to 2010. Since then survival has improved to 70% in 2005 for five-year survival. This is due to the advancement and paradigm shift in recognition of aetiology and natural history (3).
In Sub-Saharan Africa most of the patients presented at Stage III (53.8%), followed by stage II (28.2%), Stage I (17.9%) and (0.1%) stage IV at diagnosis. About 25% of the patients had a palpable lymph node (4).

Common risk factors are age**,** HPV Infections with High-risk subtypes (HPV 16 and HPV 18),Vulvar Intraepithelial Neoplasia (VIN)(5),Lichen Sclerosis causes the vulvar skin to become very thin and itchy (6). Smoking(7) and HIV infection due to damages of the immune system that plays a role in destroying cancer cells (8).

Its pathogenesis has got two pathways HPV related pathway which develops through VIN triggered by infection with high-risk type HPVs, predominantly HPV 16 and 18. The viral gene produces E6 and E7 which interact with host cell p53 and Rb proteins, resulting in p53 dysfunction and inactivation of Rb, respectively. Degradation and inactivation of the tumour suppressor genes p53 and Rb leads to absence of cell-cycle arrest and hyper proliferation of tumour cells (9).HPV Independent pathway; occur in elderly patients through differentiated VIN associated with LS (10). Mechanism has not yet been fully elucidated. Studies showed that LS lesions exhibited monoclonality, implying that certain molecular alterations might occur in some LS lesions before histologically apparent

malignant transformation occurs. A recent study demonstrate hyper methylation of RASSF2A, MGMT, and TSP-1 genes in SCC associated with LS, suggesting a possible role of these genes in HPV-independent carcinogenesis(11).

Many patients are asymptomatic at the time of diagnosis, but few may present with symptoms like vulvar pruritus or bleeding (12).Vulvar lesion is a common presented feature on the labia majora; less frequently it can involve the labia minora, perineum, clitoris, and Mons. A synchronous second malignancy, cervical neoplasia, is found in up to 22% of patients. Other symptoms are pruritus, bleeding or pain. Dysuria, dyschezia, rectal bleeding, an enlarged lymph node in the groin, or lower-extremity oedema are less frequently encountered symptoms, and are suggestive of advanced disease

Common histological types are Squamous cell carcinoma comprising at least 75% or more of cases (13).Verrucous carcinoma which is type of SCC that has features of slow growth and rarely metastasizes to lymph nodes, but it is locally destructive. It is differentiated from SCC with a verrucous configuration by biopsy (14).Basal cell carcinoma which is about 2%(15). It may be locally invasive, and usually non-metastasizing.(16).Melanoma is the second most common histology, accounting for about 10% of primary vulvar neoplasms(17).Sarcoma include leiomyosarcomas, rhabdomyosarcomas, lip sarcomas, angiosarcomas, neurofibrosarcomas, epithelioid sarcomas, and undifferentiated/unclassified soft tissue sarcomas) contribute 1 to 2% of vulvar malignancies. The prognosis is poor. (18)(5).Paget disease which accounts for less than 1% of all vulvar malignancies (19).The lesion has an eczematoid appearance. Bartholin gland carcinoma that comprises approximately 0.1 to 5% of all vulvar cancer(20).Metastatic disease is common because of the rich vascular and lymphatic network in this area. (21).
Diagnosis is made by biopsy(22) taken during colposcopy .Other investigation is done to determine general health, size, and whether the cancer has spread. These tests may include: Blood test like FBP,RFT and LFT ,cystoscopy(23).Imaging may have a role in evaluation of the local extent of disease in advanced cases, (US, CT, MRI,CHEST X-RAY) and distant metastatic disease (CT and PET-CT) (24).

It can be staged by either AJCC or FIGO staging system. Both are hybrid clinical and surgical/pathologic system. They are similar; both classify VC on the basis of three factors: The size of the tumour (T), spread to lymph nodes (N), and spread to distant sites (M)

Most common classification used is FIGO staging system as follows

Stage I: The tumour is only in the vulva or the vulva and perineum. It has not spread.

IA: The tumour is only in the vulva or the vulva and perineum, is 2 cm or smaller, has not spread, and is no deeper than 1 mm.

IB: The tumour is larger than 2 cm or is deeper than 1 mm, but is only in the vulva or the vulva and perineum.

Stage II: The tumour is of any size and has spread to nearby structures, including the lower part of the urethra, vagina, or anus. It has not spread to lymph nodes or other parts of the body.

Stage III: The cancer has spread to nearby tissue, such as the vagina, anus, or urethra, and to the groin lymph nodes. There are no distant metastases.

IIIA: The cancer has spread to nearby tissue (the vagina, anus, or urethra). There are 1 or 2 metastases to lymph nodes, but they are smaller than 5 mm, or there is 1 metastasis that is 5 mm. There are no distant metastases.

IIIB: The cancer has spread to nearby tissue (the vagina, anus, or urethra). There are 3 or more metastases to lymph nodes, but they are smaller than 5 mm, or there are 2 or more metastases that are 5 mm. There are no distant metastases.

IIIC: The cancer has spread to nearby tissue (the vagina, anus, or urethra) and to 1 or more lymph nodes and their surrounding lymph node capsule, or covering. There are no distant metastases.

Stage IV: The cancer has spread to the upper part of the vagina or upper part of the urethra, or it has spread to a distant part of the body.

IVA: The tumour has spread to the upper part of the urethra, vagina, or anus; the cancer has spread to regional lymph nodes and caused ulceration; or it has attached the lymph node to the tissue beneath it. There are no distant metastases.

IVB: Cancer has spread to a distant part of the body.(25)

In Tanzania current there is scarcity of data about vulva cancer so this study is going to fill up the gap by describing the disease in terms of social demographic data, risks factors, clinical presentation, histological types, grade and stage, treatment modalities, intent and outcome for patients attending at ORCI.

CHAPTER TWO

2.0 LITERATURE REVIEW

Vulvar cancer is rare disease, accounting for about 3-5% female genital tract malignancies. It is commonly seen in elderly women with a median age of 65–70.Common histology is squamous cell carcinoma as it has been seen in a study done in German (26).

In developing countries, it has been observed that mean age is lower than in developed countries. A study done in Nigeria reported 1.2% of Vulva cancers median age is 50 years and over 70% of cases being squamous cell followed by melanoma (27).Both countries the common histology is Squamous cell carcinoma.

Risk factors for the developing vulvar cancer include age, smoking, immunosuppressive disease, venereal diseases and chronic skin diseases of the vulva such as lichen sclerosis, these trends can most likely be attributed to an increasing number of human papillomavirus (HPV) infections. This was shown by study done by Madsen in Denmark where by it identifies risk factors to be advanced age more than 65 years, cigarrete smoking, immune suppression venereal diseases like genital warts, pre invasive or invasive cervical cancers and chronic skin diseases like lichen sclerosis. (27).

In developing countries most of cases is associated with HPV and HIV infections which is about 60% as shown in a study done by Smith (28) .

Vulva pruritus is the most common presenting symptom. Other symptoms include bleeding, pain and ulceration or discharge. A study done by Alkaout showed that Pruritus is the most common and long-lasting reported symptom of vulvar cancer, followed by vulvar bleeding, discharge, dysuria, and pain(24).

It has been observed that in developing countries many women have a long delay in diagnosis due to denial or minimization of symptoms, so presenting at the hospital with a locally advanced tumour at the time of initial evaluation A study done in Ghana by Dadzie with total number of 70 cases of vulva cancer, 60% presented with stage 4, 15% with stage 3, 12% with stage 2 and 13% with stage 1 disease.While in developed countries about 90%

of cases diagnosed with in situ or early stage invasive disease. Kang Y did a study which showed majority of the patients diagnosed at an early stages except for the older patients where by majority presented at advanced stages (29)

Treatment approach depends on the results of surgical staging. Early stage disease standard treatment is surgical excision with adjuvant treatment based on the findings at the time of surgery. A tumour-free margin >1 cm is required since a smaller margin is associated with an increased local recurrence risk. This was shown in a retrospective cohort study in Italy with 135 patients whereby there was lower rate of local recurrence in cases with a normal tissue margin of >1 cm compared to those cases with normal tissue margins of 0.8 cm (30).

Lymphadenectomy is also indicated depends on the stromal invasion especially if the infiltration is equal or more than 1mm. A Study which was done by Iacopon showed that Infiltration of 1 mm should be treated using at least an ipsilateral inguinofemoral lymphadenectomy or a sentinel lymph node biopsy in the case of inconspicuous groins. He also recommends that bilateral groin node dissection should be performed for midline tumours and for those involving the anterior labia minora. Large lateral tumours should probably also have bilateral dissection, and definitely if the ipsilateral nodes are positive (31).

Locally advanced stage surgery is preferred whenever feasible. Patients who are not surgical candidates should receive primary chemo radiation. Cisplatin mono, 5-FU, or also mitomycin C in combination with radiation therapy. In some cases, surgery is possible after chemotherapy and radiation because of reduced tumour mass. This was showed in retrospective KROG 1203 study where by patients given concurrent chemo radiotherapy about 47.9% to 63.8% of patients tumour reduced in size and able to undergo surgery (32).

Distant metastases primary chemotherapy is recommended, provided patients are candidates for systemic treatment. If not, palliative care is appropriate. Most frequently used chemotherapy regimens are platinum based, meaning they consist of cisplatin, given alone or in combination with another agent, such as 5-Fluouracil, paclitaxel, vinorelbine, or mitomycin C. As it has seen in a study done by Alkatout which recommend platinum-

based chemotherapy, meaning they consist of cisplatin, given alone or in combination with another agent, such as 5-Fluouracil, paclitaxel, vinorelbine, or mitomycin C. Because of the small number of cases becoming necessary for a chemotherapy, there is no standard treatment yet. The actual response rate to these chemotherapies is low (24).

Prognosis of patients with vulvar cancer is quite good when convenient treatment is provided in a timely manner. Also, Inguinal and/or femoral node involvement is the most significant prognostic factor for survival in patients with vulvar cancer. The overall 5-year survival rate ranges from 70% to 93% for patients with negative nodes and from 25% to 41% for those with positive nodes as it was reported on 26th annual report on results of treatment in gynaecological cancer volume 25, Issue S1 published in December 2006.

Recurrent lesions in the lymph nodes, as well as in distant sites, are not amenable to surgery or radiotherapy. They are difficult to treat, and the 5-year survival rate is generally less than 5%. This is also reported on the Study done by Saito T in Japan showed that prognosis for patients with groin lymph nodes recurrence of VC is very poor with 5-year survival rates of only 0% to 10% (33).

2.1 Problem statement

An increase in vulva cancer incidence, particularly in younger women, has been reported. This increase has been associated with the presence of oncogenic human papillomavirus (34). Africa had the highest prevalence of HPV (22.1%) in a large meta-analysis of women with normal cytology (35).

The rate of HPV infection among women in Tanzania is also high. About 3.3% of women in general population are estimated to harbour HPV-16/18 infection at a given time, and 68.0% of invasive cervical cancers is attributed to HPVs 16 or 18 (34). Cervical cancer incidence rates mirror HPV prevalence, and as vulvar cancer has been linked to HPV infection, it follows that the prevalence of vulvar cancer in young women may also be increased in the Tanzania population.

Majority of the patients in Tanzania are referred at ORCI for treatment. No study has been done to verify the profile for these patients with this cancer and their treatment outcome.

2.2 Rationale

Vulva cancer for many years has been considered as a rare cancer and therefore there hasn't been enough effort to research this cancer. Unfortunately, in Sub-Saharan Africa incidence of HIV and HPV is high and hence there has been a noticeable increase in the incidence of vulva cancer.

Majority of patients came to hospital with advanced stage. So, it is important to clearly understand the risk factors associated with this disease clinical signs and symptoms in our settings. This information will in turn help increase the society's awareness, will promote early diagnosis and treatment hence improving the prognosis.

2.3 Research questions

i. What is the clinical profile of VC for patients treated at ORCI?
ii. What are the associated factors for vulva cancer?
iii. What are clinical pathological features of vulva Cancer?
iv. How is VC treated at ORCI?
v. What is treatment outcome?
vi. What is the overall 1- year survival for patient's VC?

vii. What are the factors that influence the survival for VC patients at ORCI?

2.4 Objectives

2.4.1 Broad objective

1. To describe social demographic, clinical pathological characteristics, treatment intent and modalities and treatment outcome and one-year overall survival of patients with VC attended at ORCI from January 2006- December 2017.

2.4.2 Specific objectives

1. To describe pattern of VC in terms of histologic subtype, stage at presentation, and tumour grade.
2. To identify common age of occurrence, HIV status and pre-existing genital warts for patients who will be requited in the study.
3. To describe type of treatment given in terms of intent and modality.
4. To describe outcome of the treatment including symptoms relief or disappearance.
5. To determine 1-year overall survival among patients with VC.
6. To identify the factors that influence survival of VC patients.

CHAPTER THREE

2.0 METHODOLOGY

2.1 Study design

This was a retrospective cohort hospital-based study design. It includes all patients who meet inclusion criteria who were treated between January 2006 to December 2017 at ORCI.

2.2 Study setting

It was conducted at Ocean road cancer institute (ORCI) which is in Ilala district in Dar-es Salaam, Tanzania. It is a cancer National hospital which receives patients from all other parts of Tanzania and also neighbours' countries like Mozambique, Malawi and Burundi. It offers RT and CT for either curative or palliative intent depending on the stage of the cancer. It receives approximate 4000 to 5000 cancer patients per year 0.14% being vulva cancer patients.

2.2.1 Study participants

Target population; All patients with vulva cancer referred from District, Regional or Zonal hospitals in Tanzania and all those came from neighbour countries like Mozambique, Malawi and Burundi treated at ORCI from January 2006 to December 2017.

Accessible population; All patients with vulva cancer referred from District, Regional or Zonal hospitals in Tanzania and all those came from neighbour countries like Mozambique, Malawi and Burundi treated at ORCI from January 2006 to December 2017.

Study population; All patients with histological conformation of Vulva cancer and fulfil eligibility criteria.

Sample size estimation;

Sample size was calculated by using a single proportion formula

$n=z2\ p\ (100-p)/\ e2$

Where

n= minimum sample size designed.

Z= the point on standard normal deviation corresponding to 95% Confidence interval which is 1.96

P= the proportion of 1-year overall survival VC patients from previous studies in Sub Saharan countries is 80% (0.8) (15)

e= Marginal error 104% (0.104).

n=1.962 x 0.8(1-0.8)/ (0.104)2

n= 62

From the formula the minimum number of patients with VC requited in the study was 62 patients.

2.3 Eligibility Criteria

2.3.1 Inclusion criteria

- All patients with histological confirmed primary VC treated at ORCI from January 2006 to December 2017.
- All patients with baseline investigation determined before initiation of the therapy.

2.3.2 Exclusion criteria

- All patients with no histological confirmed diagnosis.
- All patients with secondary vulva cancer.
- All patients with incomplete medical records.

2.4 Variables

2.4.1 Independent variables

- Social demographic characteristics specifically age
- Risk factors i.e. history of cervical cancer, pre-existing genital warts.
- HIV status positive, negative or unknown.

2.4.2 Dependent variables

- Clinical presentation i.e. pain, pruritus, vulva lesion and bleeding.
- Stage of the disease either FIGO stage I, stage II, Stage III or Stage IV.
- Histological type of the disease e.g.; - SCC, melanoma, verrucous carcinoma, basal cell carcinoma, Sarcoma, Paget disease and Bartholin gland Carcinoma.

- Treatment modalities like surgery, radiotherapy alone, radiotherapy and chemotherapy and chemotherapy alone.
- Treatment outcome in terms of relief or disappearance of symptoms.
- Treatment related toxicity on Skin, GIT and GUT.
- 1year Overall survival either still alive or dead.

2.5 Data Collection

All patients who attended ORCI between 1st January 2006 to 31st December 2017 with a diagnosis of VC were identified from the respective central hospital register. Hospital case notes were retrieved for each patient. Research assistants under supervision of principal investigator use data extraction forms to retrieve data from patients' records stored in manual files and or files on the computer.

Data collection was done by using patient's files from medical record department so case clinical notes were retrieved for each patient. All required information was recorded on study design data extraction forms. Data extraction forms captured socio-demographic characteristics such as age, date of diagnosis, HIV status, possible associated factors, treatment modalities and outcome of the treatment, survival status weather patient was alive or died,1-year overall survival and other variables of interest.

2.6 Data analysis

Data extraction forms were carefully reviewed for completeness and consistency while patient confidentiality was insured in records and identity.

The data obtained were given identification numbers, codes, editing and cleaned up before statistical analysis was done. Analysis was done by using SSPS version 24.

Continuous variables were summarized by median, mean, standard deviation and range. Histograms used for pictorial display.

Categorical variables summarized by percentages, frequencies, bar graphs, and pie charts for general description. Kaplan- Meier curves was used to identify and compare overall survival over the stipulated period.

The survival rate was estimated using the date of diagnosis and date of death or date of last visit. Cox proportional hazard model was used to examine various factors with time to

death hazard ratios (HRs) and 95% confidence interval presented. Two sided P-value < 0.05 is considered as statistically significant.

2.7 Ethical consideration

2.7.1 Ethical clearance

Ethical clearance to conduct this study was obtained from higher degree research and Publication committee of MUHAS after requesting a waiver to obtain an informed consent to use patient information from files.

Permission to access patient's files from medical records obtained from ORCI management.

Confidentiality of patient information was insured by using initials and unique numbers assigned to patient files instead of full names.

2.7.2 Consent process

Informed consent was requested from MUHAS Research Ethics Committee since it was Retrospective study hospital based where by information was gathered from patient's files and hospital registers and some of the patients have died by the time of data collection so it was difficult to obtain consent from individual participants.

CHAPTER FIVE

5.0 RESULTS

It is a hospital based retrospective study with total number of 61 cases attended at ORCI between January 2006 to December 2017.
85.2% were below 60 years, 14.8% were equal or more than 60 years. Mean age was 46.5 year (Standard deviation = 13.6 years). 60.7% cases were HIV positive, 31.1% were HIV negative.Patients that were less than 60 years were 10 times more to be HIV positive than those who were equal or more than 60 years. 22.2% who were equal or more than 60 years were HIV positive.

The main reasons for consultation were lesion at the vulva which constitutes about 100%, followed by pain 83.6% and pruritis 36.1%. Other presentations were watery discharge and foul smelling vaginal discharge about 26.2%.

Common histology were squamous cell carcinoma about 90.2% , followed by adeno carcinoma 3.3%, basal cell carcinoma 3.3% and verrucous carcinoma were 3.2%.
Grade I tumors were 47.5% and grade II 21.3%. Grade III and IV were 13.2% and about 18% cases grade was not known. Out of 61 cases only 4 cases were staged, 1 case was stage III and 3 cases were stage IV, 57 cases were not staged.

Table 1: Demographic and pathological characteristics of study cases (n=61)

Characteristics	Number	%
Age in years		
<60	52	85.2
=>60	9	14.8
Mean age +/-SD)		46.5±13.6
HIV status		
Positive	37	60.7
Negative	19	31.1
Unknown	5	8.2
Pre-existing genital warts		
Yes	5	8.2
No	56	91.8
Histology		
Squamous cell carcinoma	55	90.2
Adeno carcinoma	2	3.3
Basal Cell Carcinoma	2	3.3
Verrucecous carcinoma	2	3.2
Tumor grade		
Grade I	29	47.5
Grade II	13	21.3
Grade III	6	9.8
Grade IV	2	3.3
Unknown	11	18
Total	61	100
Tumor stage		
Stage I	0	0
Stage II	0	0
Stage III	1	1.6
Stage IV	3	4.9
Unknown	57	93.4
	61	100

5.1 Reasons for consultation

100% of cases presented with lesion at vulva, 36.1% with Pruritis, 34.4% *bleeding* , 83.6% *pain* and 26.1% with *other* symptoms.

Table 2: Reasons for consultation (N=61)

Reasons for consultation	**N**	**Percent of Cases**
Lesions at vulva	61	100.0%
Pruritis	22	36.1%
Bleeding	21	34.4%
Pain	51	83.6%
Others	16	26.2%
Total	171	280.3%

Note: Others means symptoms; abnormal watery or foul smelling **vaginal discharge**

5.2 Treatment modalities used.

Treatment modalities used in this study were CCRT 44.3%, followed by RT alone 34.4%, medical palliation 16.4%, surgery and radiotherapy 1.6%, surgery alone 1.6% and chemotherapy alone was 1.6%.

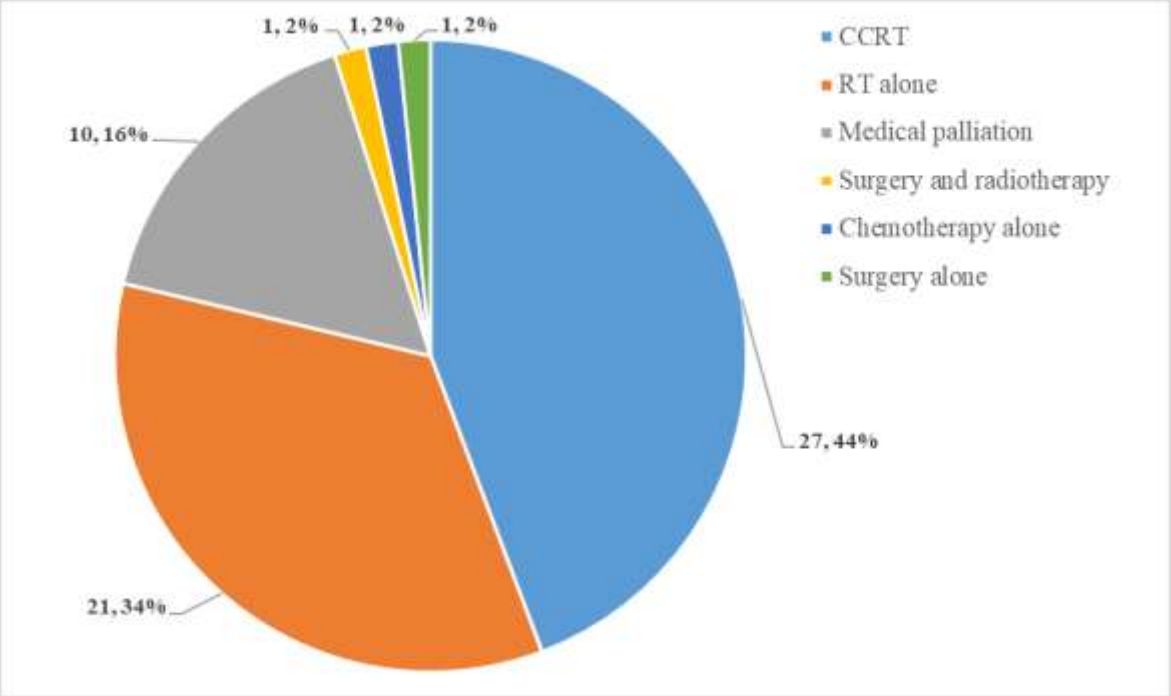


Figure 1: Treatment modalities used

5.3 Treatment intension

3.3% of cases received curative treatment, 96.7% cases received palliative treatment.

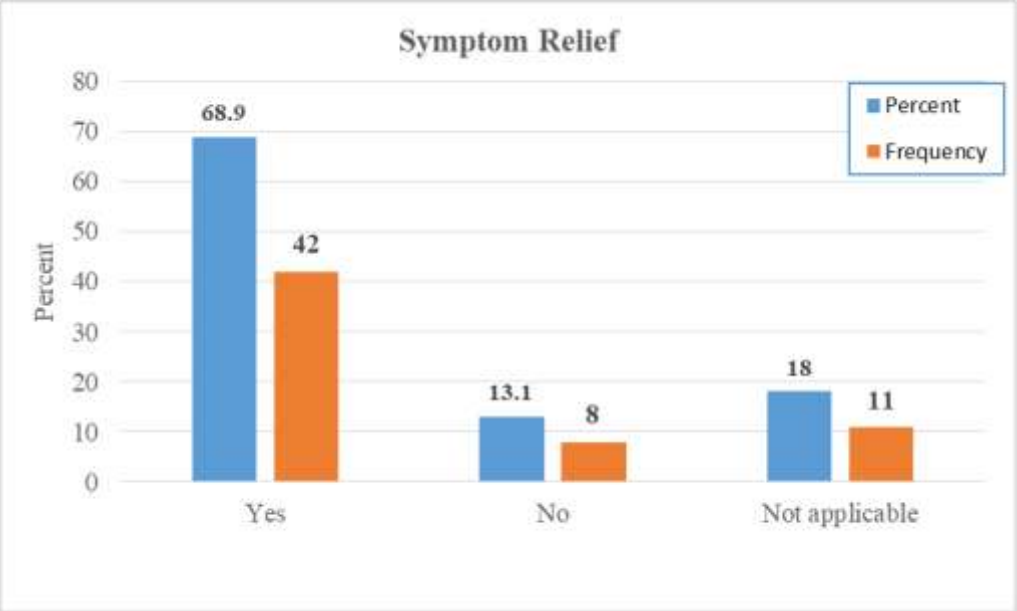
Table 3: Prevalence of Treatment intention

Treatment intent	Frequency	Per cent
curative	2	3.3
palliative	59	96.7
Total	61	100

5.4 Treatment outcome

68.9% of cases get symptoms relief, 13.1% didn't get a relief.

Treatment modalities, RT Dose and RT Field had shown a relationship with symptoms relief. 68.9% of cases treated by EBRT, CCRT, Surgery alone, surgery and RT and chemotherapy alone get symptoms relief while 18% didn't get relief. Results were statistically significant ($\chi 2$ (1, N=61) =12.05, p=.001).96.2% of cases who received 50Gys get relief compared to 80% who received 30Gys and 25% who were not given RT didn't get relief. This finding was statistically significant ($\chi 2$ (1, N=61) =10.98, p=.004).



Note; Not applicable means not given VC treatment

Figure 2: Distribution of symptoms relief

5.5 Survival

Median survival period for cases in this study was 4 months.

Table 4: Median survival time for VC cases

	Estimate	Std. Error	95% Confidence Interval
Median	4 Months	27.897	65.894, 175.249

5.5.1 Factors which influence survival

Table 5: Factors affects survival

Factors	Survival status					OR	95% CI		χ^2 (p-value)
	alive		dead				Lower	Upper	
	n	%	n	%					
HIV status									
positive	5	17.2	24	82.8	29	0.417	0.098	1.763	1.458 (0.227)
negative	5	33.3	10	66.7	15				
Age group									
<60	9	22.0	32	78.0	41	0.844	0.145	4.919	0.036 (0.850)
=>60	2	25.0	6	75.0	8				

HIV Status

HIV negative cases survive more than HIV positive cases .Median survival period for HIV negative patients were 4 months compared to 3 months for HIV positive cases. However, these results were not statistical significant (OR for HIV infected and VC patients was 0.417, 95% CI (0.098 - 1.763), p >.05).

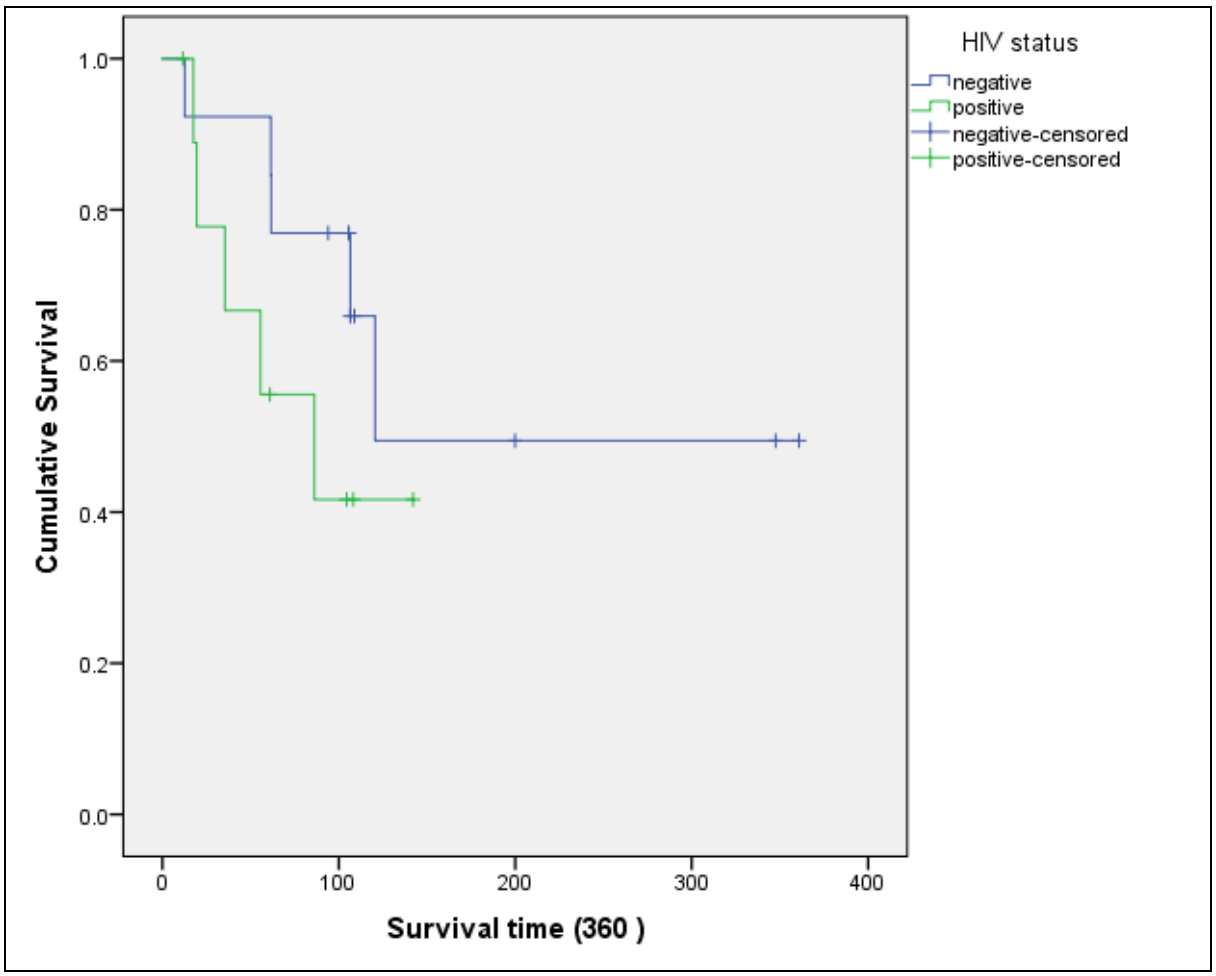


Figure 3: Survival probability by HIV status.

Age group

There was no relationship between age and survival for VC cases. Results were non-significant. OR=0.844, 95% CI (0.145- 4.919), p >.05.

Table 6: Age as factor affecting survival

Factors	Survival status					OR	95% CI		χ^2 (p-value)
	alive		dead						
	n	%	n	%			Lower	Upper	
Age group									
<60	9	22.0	32	78.0	41	0.844	0.145	4.919	0.036 (0.850)
=>60	2	25.0	6	75.0	8				

Treatment modalities

There was a significant relationship between treatment modalities and survival (χ^2 (5) =16.04, and a p-value of p = .007. Cases treated with CCRT had remarkable improvement on the survival i.e 72.7% survived while 31.6% of all death was treated by the same modality. Radiotherapy alone, chemotherapy alone and surgery alone have equally impact on survival with patient survival of 9.1%. Cases received medical palliation and surgery followed by radiotherapy none of them survived (0.0%).

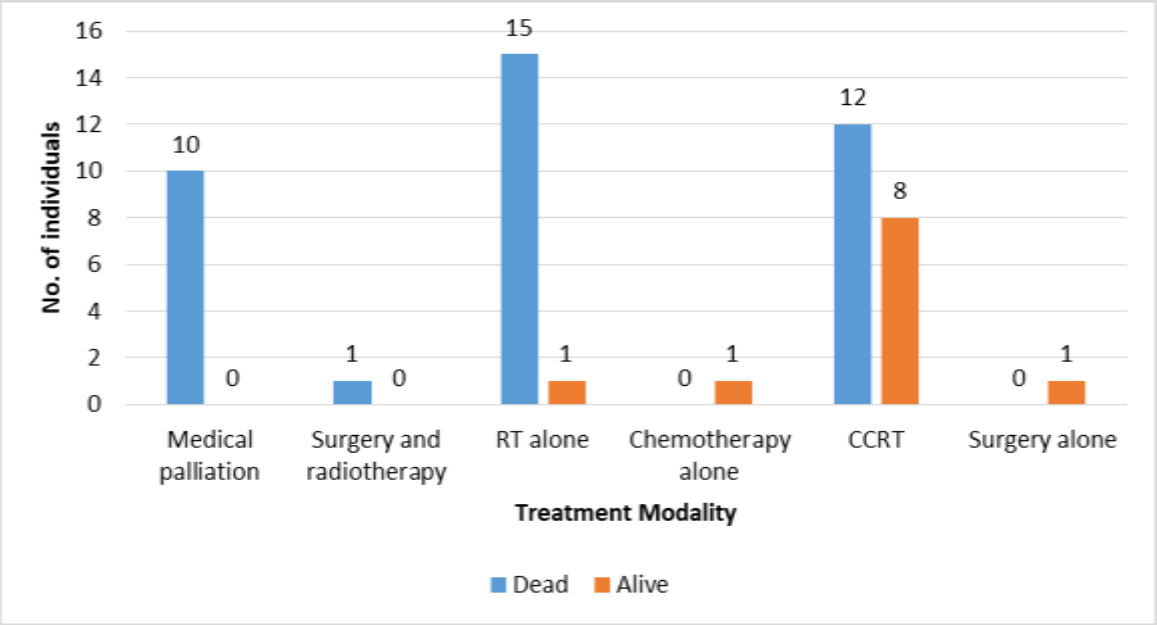


Figure 4: Association between treatment modalities and survival.

CHAPTER SIX

6.0 DISSCUSION

Although vulva cancer is a relatively uncommon gynaecological malignancy, there has been an increase in its incidence over the last several decades. It mainly affects menopausal and oestrogen-deficient women. The average age of its occurrence is 60 years. In this study 85.2% of cases were < 60 years, 14.8% were = or > 60 years. The mean age was 46.5 years. These results go hand in hand with other studies done in Africa, were it has been observed that the mean age is normally below 60 years like the study done in Burkina Faso, median age was 57 years (36).This is different in developed countries as its seen in a study which was done in USA where by 80.7% were older, with mean age of 73 years (range, 50-102 years)(37)

Women with HIV infection are at an increased risk of vulvar cancer. A study done in Ethiopia for 51 patients,83% were HIV positive. 90% of the HIV-positive patients were younger than 40 years (38).

In this study 60.7% of the cases were HIV positive. High incidence of HIV in developing countries has been thought to be among the reasons for having lower age VC cases.

The most common type of histology is squamous cell carcinoma (SCC), this was also observed in this study, it constituted about 90.2% of the cases followed by adeno carcinoma 3.3%, basal cell carcinoma 3.3% and verrucous carcinoma were 3.2%.This has been observed in studies done in developed and developing countries.

The common symptom is vulva lesion on the labia majora; but it can less commonly involve the labia minora, perineum, clitoris, and Mons pubis. Other symptoms include dysuria, dyschezia, rectal bleeding, an enlarged lymph node in the groin, or lower-extremity edema but they are less frequently encountered symptoms, and are suggestive of advanced disease .In this study main reason for consultation was vulva lesion 100%,pain 83.6%, pruritis 36.1% and bleeding 34.4%.

A study describing trends in rate, treatment, and survival of late-stage vulvar carcinomas (LSVCs) over a 20-year period in the United States between 1988 and 2007 showed that the rate of LSVC at diagnosis was 32.4% compared with early-stage disease (67.6%) did not change significantly from 1988 to 2007 (P = 0.59). In a more recent study, during the period of 2004 to 2011, Noori Akhtar-Danesh et al. found nearly the same rates with 35.7% patients diagnosed at LSVCs (39).This is contrary to what has been observed in developing countries . The same rates were reported In India where 80% of patients were staged as FIGO II–III (39).In this study majority of the cases were not staged. Only 4 cases were staged out of 61,3 were stage IV,1 was stage III. Most of the patients were stated as advanced disease, though physical examination and imaging modalities was done to each patient but there was no proper documentation on stage of the disease.

Different treatment modalities can be used depending on stage of the disease, functional status of the patient and intension whether it's curative or palliative.

In this study treatment modalities used were medical palliation (16.4%), surgery and radiotherapy (1.6%), radiotherapy alone (34.4%), chemo therapy alone (1.6%), CCRT (44.3%) and surgery alone (1.6%).3.3% cases received curative treatment while 96.7% received palliative treatment. Cases treated curatively were those who underwent surgery alone and those who underwent both surgery and radiotherapy both constitute about 3.3%. Cases which got CCRT, Chemotherapy alone, RT alone and medical palliation intension was palliative constitute 96.7% of total cases. Decision to treat curatively or palliative were made depending on functional status of the patients where by those with ECOG of 3 and above were given palliate treatment and those with ECOG of 0-2 were treated curatively, also from physical examination and results of laboratory and imaging investigations though there was no proper documentation of staging. Doses of RT which was used in curative treatment together with chemotherapy was 50Gys in 25 fractions concurrent with chemotherapy either Cisplatin (50mg per metre square) on day 1 and 5-FU infusion 1000mg per metre square on day 1-4 on 1st day and 28th day of EBRT. Very few who were HIV negative were treated with Cisplatin and Mitomycin C(15mg per metre square on day 1 and 28 concurrent with RT).Those who received palliative RT dose were 30Gys in 10# without chemotherapy, as per NCCN Clinical practice guidelines in oncology, Vulvar

cancer version1 2017 (40)

Treatment outcome depends on stage of the disease and treatment modalities used. Results from this study has shown that there is an association between treatment modalities **,**RT doses and symptoms relief.91.1% of cases treated by RT got symptom relief than those who did not received RT (20%), and these results are statistically significant ($\chi 2$ (1, N=61) =12.05, p=.001). Likewise, dosage given showed association to symptom relief. 96.2% of cases that received 50Gys got symptom relief while 80% of those who received palliative dose of 30Gys and 25% of those who didn't receive radiotherapy didn't get symptom relief. This finding was statistically significant ($\chi 2$ (1, N=61) =10.98, p=.004).

Overall survival depends on age, histological types, stage of the disease, HIV infection HPV infection, general status of the patient and treatment given.

In this study one-year overall survival rate is 3.3% with median survival of 4 months.
Factors which were assessed to affect survival were HIV status, age and treatment modalities. Results showed few HIV positive cases survived (17.2%) and majority died (82. 8%).OR=0.417, 95% CI (0.098 - 1.763), *p* >.05. However, these results were not statistically significant (p>.05). Also relationship between age group and survival is non-significant OR=0.844, 95% CI (0.145- 4.919), *p* >.05.
For treatment modalities there was significant relationship (variables χ^2 (5) =16.04, and a p-value of p = .007) with survival. Cases treated with CCRT 1-year survival was good i.e. 72.7% cases survived compared to 31.6% who died. Radiotherapy alone, chemotherapy alone and surgery had equally impact on survival with 9.1%. Also patients who received medical palliation and those who underwent surgery followed by radiotherapy none of them survived (0.0%).

A Study done in South Africa overall survival rate after 1 year was 80%, with a median survival of 33 months.The survival of patients receiving surgery, radiotherapy, or chemotherapy was prolonged compared to those without these therapies. FIGO stage 4 patients had unfavourable outcomes compared to patients' stage 1 to 3

CHAPTER SEVEN

7.0 CONCLUSION

This study revealed that VC occurs mostly at younger age, majority of the cases were HIV positive. Very few cases were staged and all of them had advance staged, hence given palliative treatment. There was minimal symptom improvement and one year overall survival rate was very low. Treatment modalities is a key factor that affects survival.

7.1 Recommendations

Clinicians should be reminded to document all the necessary information clearly and precisely as majority of the patients were not staged.

Public awareness about disease should be increased for people to be diagnosed at earlier stages. It can be done through different media like local radio, TV and Newspaper, also through social networks and by organizing an event which will bring people together.

7.2 Study Limitations

Since it is a retrospective study there is missing of important information's like size of the tumour, location, staging to majority of the patients and status of the pelvic lymph nodes which will affect important assessment on the full picture of the disease.

It was difficult to assess some of the factors which might affect survival like stage of the disease since majority of the cases were not staged.

It is a single institutional study therefore it does not represent the total number of vulva cancer cases in Tanzania since some cases are treated with surgery alone at other hospitals like Muhimbili National Hospital.

A number of patients were lost to follow up and this makes a challenge on the overall survival estimation since it is difficult to know whether patient was alive or dead.

REFFERENCES

1. El-Naby NEH, Hassan Mohamed H, Mohamed Goda A, El Sayed Mohamed A. Epstein-Barr virus infection and breast invasive ductal carcinoma in Egyptian women: A single center experience. J Egypt Natl Canc Inst. 2017;29(2):77–82.

2. Holleczek B, Sehouli J, Barinoff J. Vulvar cancer in Germany : increase in incidence and change in tumour biological characteristics from 1974 to 2013. Acta Oncol (Madr). 2018;0(0):324–30.

3. Trends O. Vulval Cancer – Trends and Variations by Age. 2014;(May).

4. Kehila M, Harabi S, Mhiri R, Touhami O. Journal of the Egyptian National Cancer Institute Vulvar cancer in Tunisia : Epidemiological and clinicopathological features multicentric study Mohamed Badis Chanoufi PhD a. J Egypt Natl Canc Inst [Internet]. 2017;29(2):95–8. Available from: http://dx.doi.org/10.1016/j.jnci.2017.02.001

5. Van De Nieuwenhof HP, Bulten J, Hollema H, Dommerholt RG, Massuger LFAG, Van Der Zee AGJ, et al. Differentiated vulvar intraepithelial neoplasia is often found in lesions, previously diagnosed as lichen sclerosus, which have progressed to vulvar squamous cell carcinoma. Mod Pathol. 2011;24(2):297–305.

6. Bleeker MCG, Visser PJ, Overbeek LIH, van Beurden M, Berkhof J. Lichen Sclerosus: Incidence and Risk of Vulvar Squamous Cell Carcinoma. Cancer Epidemiol Biomarkers Prev. 2016;25(8):1224–30.

7. Petoud S, Muller G, Moore EG, Xu J, Sokolnicki J, James P, et al. NIH Public Access. 2009;129(1):77–83.

8. Simbiri KO, Jha HC, Kayembe MK, Kovarik C, Robertson ES. Oncogenic viruses associated with vulva cancer in HIV-1 patients in Botswana. Infect Agent Cancer. 2014;9(1):1–9.

9. Ueda Y, Enomoto T, Kimura T, Yoshino K, Fujita M, Kimura T. Two Distinct Pathways to Development of Squamous Cell Carcinoma of the Vulva. J Skin Cancer [Internet]. 2011;2011:1–7.

10. Nieuwenhof HP Van De, Avoort IAM Van Der, Hullu JA De. Review of squamous premalignant vulvar lesions. 2008;68(February):131–56.

11. Esteller M, Barba-ramos E, Garcia-bragado F, Puras A. Differential hypermethylation of genes in vulvar cancer and lichen sclerosus coexisting or not with vulvar cancer. 2011;

12. Vapiwala N, Shinohara ET, Vachani C. All About Vulvar Cancer | OncoLink. 2016; Available from: https://www.oncolink.org/cancers/gynecologic/vulvar-cancer/all-about-vulvar-cancer

13. Schuurman MS, Van Den Einden LCG, Massuger LFAG, Kiemeney LA, Van Der Aa MA, De Hullu JA. Trends in incidence and survival of Dutch women with vulvar squamous cell carcinoma. Eur J Cancer [Internet]. 2013;49(18):3872–80. Available from: http://dx.doi.org/10.1016/j.ejca.2013.08.003

14. R C, Campaner AB, Fernandes GL. Verrucous carcinoma of the vulva : diagnosis and treatment *. 2017;92(2):243–5.

15. Giorgi V De, Salvini C, Massi D, Rosaria M, Carli P. Vulvar basal cell carcinoma : retrospective study and review of literature. 2005;97:192–4.

16. Eke AC, Alabi-Isama LI, Akabuike JC. Management options for vulvar carcinoma in a low resource setting. World J Surg Oncol. 2010;8:5–10.

17. Stang A, Streller B, Eisinger B, J KH. Population-based incidence rates of malignant melanoma of the vulva in Germany. 2005;96:216–21.

18. Hee C, Li X, Khanna N. Gynecologic Oncology Reports Epithelioid sarcoma of the vulva and its clinical implication : A case report and review of the literature. GORE. 2016;15:31–3.

19. Parker LP, Parker JR, Bodurka-bevers D, Deavers M, Bevers MW, Shen-gunther J, et al. Paget ' s Disease of the Vulva : Pathology , Pattern of Involvement , and Prognosis. 2000;189:183–9.

20. Report C. CASE REPORT Adenoid Cystic Carcinoma of Bartholin ' s Gland : A Review of the Literature and Report of a Patient. 1996;125(61):122–5.

21. Cardosi RJ, Speights A, Fiorica J V, Grendys EC, Hakam MDA, Hoffman MS. Bartholin ' s Gland Carcinoma : A 15-Year Experience. 2001;251:247–51.

22. Health B, Trust NHS. Standards and datasets for reporting cancers Dataset for histopathological reporting of vulval carcinomas January 2018. 2018;(January):1–37.

23. Reusser NM, Downing C, Guidry J, Tyring SK. HPV Carcinomas in Immunocompromised Patients. 2015;260–81.

24. Alkatout I, Schubert M, Mundhenke C, Günther V. Vulvar cancer : epidemiology , clinical presentation , and management options. 2015;305–13.

25. Rogers LJ, Cuello MA. Cancer of the vulva. 2018;143:4–13.

26. Mundhenke CDAKC, Fischer MTD. Epidemiology of vulvar and vaginal cancer in Germany. 2011;169–74.

27. Madsen BS, Jensen HL, Brule AJC Van Den, Wohlfahrt J, Frisch M. Risk factors for invasive squamous cell carcinoma of the vulva and vagina — Population-based case – control study in Denmark. 2008;2834(March):2827–34.

28. Smith JS, Backes DM, Hoots BE. Human Papillomavirus Type-Distribution in Vulvar and Vaginal Cancers and Their Associated Precursors. 2009;113(4):917–24.

29. Kang Y, Smith M. Vulvar cancer in high-income countries : Increasing burden of disease. 2017;2186(June):2174–86.

30. Micheletti L, Preti M, Cintolesi V, Corvetto E, Privitera S, Palmese E, et al. Prognostic impact of reduced tumor-free margin distance on long-term survival in FIGO stage IB / II vulvar squamous cell carcinoma. 2018;29(5):1–11.

31. Iacoponi S, Zapardiel I, Diestro MD, Hernandez A, Santiago J De. Prognostic factors associated with local recurrence in squamous cell carcinoma of the vulva. 2013;24(3):242–8.

32. Kim Y, Kim JY, Kim JY, Lee NK, Kim JH, Kim YB, et al. Treatment outcomes of curative radiotherapy in patients with vulvar cancer: Results of the retrospective KROG 1203 study. Radiat Oncol J. 2015;33(3):198–206.

33. Saito T, Tabata T, Ikushima H, Yanai H, Tashiro H, Niikura H. Japan Society of Gynecologic Oncology guidelines 2015 for the treatment of vulvar cancer and vaginal cancer. Vol. 23, International Journal of Clinical Oncology. Springer Japan; 201-234 p.

34. De Vuyst H, Clifford GM, Nascimento MC, Madeleine MM, Franceschi S. Prevalence and type distribution of human papillomavirus in carcinoma and intraepithelial neoplasia of the vulva, vagina and anus: A meta-analysis. Int J Cancer. 2009;124(7):1626–36.

35. Lowy DR, Schiller JT. NIH Public Access. 2013;5(1):18–23.

36. Zongo N, Korsaga-somé N, Gang-ny AB, Ouangré E, Zida M, Ouédraogo AS, et al. Cancer of the vulva in Burkina Faso : a hospital-based case series. Infect Agent Cancer [Internet]. 2016;1–6. Available from: http://dx.doi.org/10.1186/s13027-016-0080-y

37. Kumar S, Shah JP, Bryant CS, Imudia AN, Morris RT, Malone JM. Residents ' Papers A comparison of younger vs older women with vulvar cancer in the United States. YMOB [Internet]. 2009;200(5):e52–5. Available from: http://dx.doi.org/10.1016/j.ajog.2008.09.869

38. Kroeber ES, Mathewos A, Wondemagegnehu T, Aynalem A, Gemechu T, Piszczan S, et al. Vulvar cancer in Ethiopia. 2012;

39. Akhtar-danesh N, Elit ÞL, Frcs C, Lytwyn A, Frcpc Þ. Further Insights Into Long-Term Trends in Relative Survival of Vulvar Cancer Patients A Population-Based Study. 2015;25(1):125–30.

40. Chon HS, Chu C, Cohn D, Crispens MA, Dizon DS, Dorigo O, et al. Vulvar Cancer , Clinical Practice Guidelines in Oncology. 2017;15(1):92–120.

APPENDICES

Appendix I: Data Collection - English Version

Vulva cancer data collection tool

SOCIAL DEMOGRAPHIC CHARACTERISTICS

Parameter	**Response**
1. Age (years)	……
2. Residence	……
3. Occupation	……
4. Reason for consultation	
• Lesions at vulva	……
• Pruritus	……
• Bleeding	……
• Pain	……
• Others	……
5. Date of diagnosis	……
6. Histological types	
• Squamous cell carcinoma	……
• Adenocarcinoma	……
• Others	……
7. Tumour grade	
Grade I	……
Grade II	……
Grade III	……
Grade IV	……
8. FIGO Stage	
• I	……
• II	……

- III ……
- IV ……

RISK FACTORS

9. HIV status
    - Positive ……
    - Negative ……
    - Unknown ……

10. Pre-existing genital warts
    - Yes ……
    - No ……
    - Unknown ……

TREATMENT RELATED CHARACTERISTICS

11. Modality
    - Not yet started any treatment ……
    - Medical palliation ……
    - Surgery and radiotherapy ……
    - RT alone ……
    - Chemotherapy alone ……
    - CCRT ……

12. RT Field
    - Vulva only ……
    - Vulva + Inguinal ……
    - Vulva + Inguinal + whole pelvis ……

13. RT Dose to the vulva
    - Less than 60Gys ……

- Equal or more than 60Gys ……
- Dose of 60Gys ……
- Palliative dose of 30Gys ……

14. RT technique
    - 2D RT ……

15. Was prescribed dose given
    - YES ……
    - No ……
    - Why ……

TREATMENT OUTCOME

16. Symptoms relief……
    disappearance…….
17. Survival status; Alive……
    Dead……Date of Death…….
    Not known…….
18. If alive not known, the date of the last follow up visit……..
19. Treatment related toxicity
    - Skin toxicity ……
      Yes ……
      No ……
    - GI toxicity ……
      Yes ……
      No ……
    - GU Toxicity ……
      Yes ……
      No ……

Appendix II: Data Collection - Kiswahili version

DODOSO LA KUPATA TAARIFA KUHUSU SARATANI YAKWENYE SEHEMU ZA SIRI ZA MWANAMKE (KUMA)

SIFA BINAFSI ZA KIJAMII ZA WAGONJWA

Vigezo	**Majibu**
20. Umri (miaka)	……
21. Makazi	……
Kazi	……
22. Sababu za kumuona Daktari	
• Uvimbe sehemu za siri (kuma)	……
• Kuwashwa sehemu za siri	……
• Kuvuja damu sehemu za siri (kuma)	……
• Maumivu	……
• Mengineyo	……
23. Tarehe ya kugundulika na saratani	……
24. Aina ya kiini cha saratani	
• Squamous cell carcinoma	……
• Adenocarcinoma	……
• Aina nyingine	……
25. Hatua ya saratani kwa mfumo wa FIGO	
• I	……
• II	……
• III	……
• IV	……

SABABU HATARISHI ZINAZOWEZA KUSABABISHA SARATANI YA SEHEMU ZA SIRI KWA MWANAMKE (KUMA)

26. Hali ya maambukizi ya virus vya ukimwi

- Chanya ……
- Hasi ……
- Haijulikani ……

27. Historia ya maambukizi katika via vya uzazi

- Ndiyo ……
- Hapana ……
- Haijulikani ……

AINA YA MATIBABU YALIYOTOLEWA

28. Mfumo

- Hajaanza matibabu ……...
- Huduma za kupunguza maumivu ……..
- Upasuaji na mionzi ……
- Mionzi peke yake ……
- Dawa za saratani na mionzi ……..
- Dawa za saratani peke yake ……..

29. Field za mionzi zilizotumika

- Kuma peke yake ……
- Kuma + Inguino ……
- Kuma+ Inguino + sehemu za siri kwa ujumla …….

30. Dose ya mionzi iliyotolewa

- Chini ya 60Gys ……
- Sawa au zaidi ya 60Gys ……
- Sawa ya 50Gys ……
- Sawa ya 30Gys ……

31. Mbinu ya mionzi iliyotimika

- 2D RT ……

32. Idadi ya mionzi yote aliyoandikiwa alipata

Ndio ……

Hapana ……

Kwanini ……

MATOKEO YA MATIBABU

33. Kupata unafuu wa maumivu …….

Uvimbe kuisha kabisa ……..

34. Tarehe ya kugundulika kwa saratani …….

35. Hali ya kuishi ya mgonjwa; Yupo hai ……....

Amekufa ……Tarahe ya kifo…….....

Haijulikani ……

36. Kama yupo hai au haijulikani tarehe ya mwisho kuja clinic …….

37. Madhara yanayotokana na Matibabu

- Madhara kwene Ngozi ……

  Ndiyo ……

  Hapana ……

- Madhara kwene mfumo wa chakula ……

  Ndiyo ……

  Hapana ……

- Madhara kwene mfumo wa mkojo ……

  Ndiyo ……

  Hapana ……