TREATMENT OUTCOME OF CERVICAL CANCER PATIENTS AT OCEAN ROAD CANCER INSTITUTE, DAR ES SALAAM.

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M. Med (Obstetrics and Gynecology) Dissertation

Muhimbili University of Health and Allied Sciences

November 2011
TREATMENT OUTCOME OF CERVICAL CANCER PATIENTS AT OCEAN ROAD CANCER INSTITUTE, DAR ES SALAAM.

By

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine in Obstetrics and Gynecology of the Muhimbili University of Health and Allied Sciences

Muhimbili University of Health and Allied Sciences

November 2011
CERTIFICATION

The undersigned certify that he has read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences in Dar es Salaam, a dissertation entitled: TREATMENT OUTCOME OF CERVICAL CANCER PATIENTS AT OCEAN ROAD CANCER INSTITUTE, DAR ES SALAAM, in fulfillment of the requirements for the degree of Master of Obstetrics and Gynaecology of the School of Medicine.

...........................................................

Dr Projestine MUGANYIZI

(SUPERVISOR)

Date..............................................
DECLARATION AND COPYRIGHT

I, Dr Peter Mapigano Charles Majinge declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature……………………………

Date ………………………………..

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DEDICATION

This book is dedicated to my lovely wife Abera and my sons Charles and Ethan.
ACKNOWLEDGEMENTS

I wish to express my sincere gratitude and appreciation to Dr Projestine Muganyizi for his supervision, constructive criticisms and encouragement during the preparation of the study proposed and this dissertation.

I am also grateful and indebted to all consultants and specialists in the department who gave their assistance and guidance.

I would like to extend my deepest thanks to my family for their encouragement, understanding, sacrifices and acceptance of my absence during the period of preparation of this dissertation.
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ABBREVIATIONS

CIN  Cervical Interepithelial Neoplasia

DNA  Deoxyrebose Nucleic Acid

EBR  External beam radiation(Teletherapy)

FIGO  International Federation of Obstetrician and Gynecologists

HPV  Human Papilloma Virus

ICT  Intracavitary Radiation (Brachytherapy)

LVI  Lymphovascular Space Invasion

MUHAS  Muhimbili University of Health and Allied Sciences

ORCI  Ocean Road Cancer Institute

PALN  Para-Aortic Lymph Nodes

SCLN  Squamous Cell Lympnodes

RT  Radiotherapy
ABSTRACT

Background: Cervical cancer is the second commonest malignancy in females globally. Cancer of the cervix has a devastating impact on women’s health in developing countries especially Africa since more than 75% of the worldwide burden of the disease occurs in these countries. It is the leading malignancy among women in Tanzania. Patients’ late presentation to hospitals and poverty lead to very poor treatment outcome of the disease. Many of these countries put much resources and efforts on the treatment aspect of the disease, and hence the need to investigate the treatment outcome among patients with cervical cancer.

Objectives: To describe the treatment outcome among patients diagnosed to have cervical cancer and treated at the Ocean Road Cancer Institute (ORCI).

Methodology: The study was a retrospective review of case files of women with histologically proven cancer of cervix who were treated at ORCI from 1st January to 31st December 2007. Each individual had had a three year follow up as of 31st December 2010. Patients file number, residence and phone numbers were obtained from a registration book, files were then collected and the required information extracted using a designed checklist.

Results: A total of 630 patients were included in the study with median age of 51 years (± 12.7 SD), range of 24 - 90 years. At the end of a three-year follow-up of these patients, 135 (21.4%) were alive and 114 (18.1%) had died while 381 (60.5%) were lost to follow-up; number of lost in follow up was increasing in subsequent years. More than three quarters of patients presented with advanced stage of the disease (beyond stage IIb, and squamous cell carcinoma was the most common (> 90%) whereas a few
had adenocarcinoma and adenosquamous. Majority of patients (83.7%) were treated with teletherapy (external beam radiation) only while a very few patients had an addition of brachytherapy

**Conclusion:**

Most patients presented with advanced stage of the disease.

External beam radiation was seen to be the mode of treatment which was given to most of the patients, dose of radiation given as well as the stage of cervical cancer play a big role in the treatment outcome. Adherence to the follow up clinics seems to be a problem to most of patients, hence the outcome of treatment to most of patients was difficult to assess though the outcome seems to be poor

**Recommendation:** More centers for cancer detection and treatment are needed nationwide, installation of national cancer registry and cancer treatment protocols is very important.
INTRODUCTION

Cervical cancer arises most commonly at the squamo-collumnar junction of the cervical canal of the uterine cervix. It commonly affects postmenopausal women, and is characterized by abnormal contact bleeding and abnormal vaginal discharge.

Cancer of the cervix has a devastating impact on women’s health around the world, especially in developing countries, where it is the most common cancer and the leading cause of death of cancer in women. Cervical cancer is the second most common cancer in women following breast cancer. It is estimated that 500,000 new cases occur every year worldwide, the majority (80%) being in the developing world (1), and therefore making cervical cancer one of the big threats to women lives (1).

Although cervical cancer is a preventable disease, it still remains a major burden on public health resources in sub-Saharan Africa. Countries in this region have some of the world’s highest age-standardized death rates from invasive cervical cancer, for example 67 per 100 000 people in Harare, Zimbabwe and 40.8 per 100 000 in Kampala, Uganda in 1997. Data from hospital-based registers in Nairobi Kenya have indicated that cancer of the cervix accounted for 70–80% of all cancers of the genital tract and 8–20% of all cancer cases for the period 1981–90. It has been reported that there are 10–15 new cases of cervical cancer in Nairobi Kenya each week (1).

In East Africa cervical cancer comprises about 13.7%, leading among all malignancies in the general population, resulting to 13.9% of all cancer-related deaths just the second after Kaposi’s sarcoma (2).
There are two types of cervical cancer and the treatment may differ from one type to another, though generally the clinical appearance of invasive cervical lesion is mainly of two types: exophytic (proliferative) and endophytic (ulcerating) lesion. (1)

The use of widespread screening programs and modifying of the risk factors can be used as a tool to prevent cervical cancer. (3) Additionally, a recent availability of vaccines against Human papilloma virus (HPV) can play a role in controlling cervical cancer.

The treatment protocol for optimum outcome is the combination treatment including teletherapy, brachytherapy as well as chemotherapy, though at ORCI patients gets largely teletherapy and only few get combination therapy and hence poor outcome.

In Tanzania the prevalence of cervical cancer is still not known but it is reported to be the leading malignancy among women (4). The disease is usually seen in an advanced stage; hence the main treatment options are palliative radiotherapy and chemotherapy (5), but there is generally scanty data on treatment outcome of the invasive cervical cancer.

Tanzania has one cancer only, the Ocean Road Cancer Institute (ORCI), which provides radiotherapy and serves as the national referral facility for all regions; and therefore often congested with many patients.
LITERATURE REVIEW

The association between sexual activity and cervical cancer has been known for over a century. Cervical cancer is largely a sexually transmitted disease caused by HPV. Other risk factors include early age at first coitus, multiple sexual partners, low socio-economic status, a high risk sexual partner, excessive vaginal acidity and sexually transmitted infections (6, 7).

Histologically cervical cancer can either be squamous or adenocarcinoma, with the squamous cell carcinoma accounting for 85-95% of all cancers and adenocarcinoma comprising 5-15% (7, 8). Furthermore, the squamous cell carcinoma is divided into three subtypes: large cell keratinized, large cell non-keratinized and small cell (9). The small cell squamous cell carcinoma includes poorly differentiated squamous cell carcinoma and small cell anaplastic carcinoma. The latter infiltrates aggressively and diffusely with a poorer prognosis than the former (9). Patient with large cell type of carcinoma with or without keratinization has a better prognosis as compared with small cell type (9). The cervical cancer normally spread by direct local invasion and via lymphatic system whereby the local spread involves paracervical tissues, vagina or endometrium. Continuing local spread involves the pelvic side walls laterally, the bladder anteriorly and the rectum posteriorly. Normally metastases occur by means of lymphatics though hematogenous spread also occurs in less than 5%. Distant organ metastases are to the lungs and liver (10).

The major prognostic factors affecting survival are disease stage, nodal status, tumor volume, depth of cervical stromal invasion, lymphovascular space invasion (LVI), and histologic type and grade. According to the International Federation of Obstetric and Gynecologists (FIGO) the
survival rate was seen to be good in stage IA of the disease with a survival rate of 99.8%, 99.5%, 98.7% in 1, 2 and 5 years respectively where as the prognosis decreased with the stage of the disease to 45.8%, 23.9% and 15% in 1, 2 and 5 years (FIGO).

Disease stage is the most important prognostic factor, followed by lymph node status. After radical hysterectomy and lymphadenectomy, women with stage IB or IIA disease who have negative pelvic lymph nodes have a five-year survival of 88–96% compared to 64–74% for those with similar stage disease and pelvic nodal metastasis. The five-year survival outcomes are far worse for women with involvement of paraaortic nodes(11). The presence of persistent human papillomavirus (HPV) and specific HPV subtypes may also impact on prognosis after surgery or radiation therapy (12).

One study estimated that 35-50% of cervical cancer patients had either persistence or recurrent disease, with 75% of the recurrences and/or mortality occurring in the first 2 years after treatment (13). Symptoms of recurrence are varied and insidious with most patients enjoying a period relative good health between completion of primary treatment and recurrence.

Most of the recurrent disease are treated by chemotherapy, surgery and/or combination and most of these are only palliative radiotherapy has a limitation here as mostly the maximum dose is attained during primary treatment. Most end up getting chemotherapy and preferably cisplatin as their last resort.

After radiotherapy the 5-year survival rate was 79% in stage I disease, 61% in stage II, 31% in stage III and 17% in stage IV after controlling for the patients’ age, tumor bulk, nodal status, anemia, renal failure and overall treatment time (14).
A study done in Australia revealed that patients with cervical cancer may develop recurrence, distant metastases or a combination of both. A recurrence rate of 20% has been reported following primary surgery or radiotherapy in women with IB-IIA while about 70% of patients with advanced cervical tumor have relapses (15). As the pelvic tumor bulkiness increases the proportion of patients with disease recurrence in the pelvis as the only site of treatment failure increases than the proportion of developing distant metastases. Perez et al reported s total pelvic failure in stage IB (10%), stage IIA (17%), stage IIB (23%), stage IIIB (42%), stage III (42%), and stage IVA (74%) after radiotherapy alone (16).

There are limitations in studies conducted in African countries aiming at assessing the outcome of treatment of cervical cancer. But generally most of patients present with advanced disease, which result into poor treatment outcomes. On the other hand, Africa has a considerable shortfall of radiotherapy services for cost-effective management of cancer. The outcome of treatment of cervical cancer in most of developing countries depends also on availability of treatment facilities; lack of these facilities leading to very poor outcomes while globally the poor outcome is mainly associated to poor oxygenation of the tumor (17) this is due to bulky tumor and anemia of malignancy. For instance, when comparing Africa and Europe, the European standard of 250,000 population served by a single teletherapy machine is not matched in any country in Africa(18).

A three-year follow up of the patients treated for cervical cancer in 1995-1997 in Kampala Uganda, where there is a well established cancer registry and a good follow up of patients after treatment, showed that 31.4% of patients were dead and 40.2% were alive at the end of that period; the remaining 74 cases (28.4%) were lost during the follow-up period. Overall observed
and relative survival at 3 years was 52.4 and 59.9%, respectively. Of these cases, one-quarter had been treated with the radiotherapy, and they had a better survival (82.6%) than non-treated patients (78.5%) after 1 year of follow-up, but without difference at 3 years. While HIV status was not significantly related to prognosis, the cancer stage was an important determinant of survival since cases with distant metastasis had a three-fold increased risk of death over that of patients with localized disease (19).

A hospital-based study done at Kenyatta National hospital in Kenya assessing the outcome of treatment of cervical cancer showed that 76.9% of patients were treated by EBR alone, intracavitary was added in 8.3% and concomitant chemotherapy in 4.2% while 7.2% had prior surgery. Tumor recurrence occurred in 17.7% with 9.4% presented with local involvement, 6.1% distant metastases and 2.2% combined metastases. About 45.7% had no disease symptoms at all. Stage II was found to have high recurrence rate (81.1%) as compared to the other stages (20).
PROBLEM STATEMENT

Worldwide, cervical cancer is the leading cause of death among women and is the most common cause of cancer-related morbidity and mortality among women (6, 7). In Tanzania the invasive cervical malignancy is the most common gynecological malignancy (5). The actual prevalence of cancer of the cervix is not known and many patients usually present very late to the health facilities (5) so that radiotherapy remain the main stay for their treatment in Tanzania.

Many developed countries have reduced the incidence of the cancer and hence treatment burden through screening programmes. Unfortunately Tanzania does not have a routine screening scheme like many other resourced-poor countries and consequently patients present at late stage which results into significantly high morbidity and mortality related to cervical cancer. The late presentation mostly requires costly and advanced treatment methods presenting a challenge to the government inadequate health resources. There are however no concrete data on the exact burden of the disease in the country, and the treatment outcome of cervical cancer patients who are managed at the ORCI.

STUDY RATIONALE

In Tanzania, cervical cancer is the most common gynaecological malignancy and patients usually present advanced stage to the health facilities. The late presentation not only leads to high morbidity and mortality, but also makes it difficult to achieve the best cure rates among these patients. Tanzania being a developing country has a single cancer treatment centre for the whole population the Ocean Road Cancer institute (ORCI).
Therefore, this study aims to determine the treatment outcome of cervical patients who are treated at the ORCI.

Hopefully the outcome of treatment seen may help to shift the focus towards more prevention aspect like screening, vaccine and thus early treatment of precancerous lesions and possibly surgery among early cases and hence to reduce the burden to the radiation department but also this study will help on guiding health providers especially on the aspect of counseling.

These measures will ultimately decrease the number of patients requiring radiation and hence increase the quality of services offered.
OBJECTIVES

Broad Objective:

To describe the treatment outcome among patients diagnosed with cervical cancer at the Ocean Road Cancer Institute.

Specific Objectives

1. To describe the treatment modalities offered to the patients with cervical cancer at ORCI
2. To determine treatment outcome in terms of recurrence and survival among patients with cervical cancer at ORCI
3. To assess the proportion of women treated for cervical cancer that completed one, two or three years follow-up after full course of treatment.
METHODOLOGY

Study design

A retrospective review of patients with histological proven cervical cancer who were treated at ORCI from 1st January to 31st December 2007 and followed up to December 2010.

Study Period

The study period was from 1st September to 31st December 2010

Study Population

The study population was women with histological-proven cervical cancer treated at ORCI from 1st January 2007 to 31st December 2007 and each individual patient was followed up to complete three years follow up.

Study setting

The study was done at Ocean Road hospital in Dar es Salaam, which is the only cancer treatment centre in the country, providing radiotherapy and chemotherapy as well as the palliative care. It has a total of 120 beds but it normally accommodates up to 220 in-patients at a given time some of whom have to occupy the floor. It also runs outpatient clinics, nuclear medicine services, diagnostic imaging as well as screening for various types of cancers. ORCI consists of four separate clinics: a new-patient clinic, follow-up clinic, radiation treatment clinic and chemotherapy treatment clinic.
The new-patient clinic sees patients with all types of cancer that have confirmed biopsies and have been referred to ORCI for treatment. This is the patient's first appointment with a physician to discuss diagnosis and treatment options.

The follow-up clinic is for patients that have completed their treatment regimen and are consulting with oncologists for follow-up of treatment protocols, side effects, or recurrence. The radiation and chemotherapy treatment clinics are for the administration of treatment only on outpatient basis.

The in-patient wards are for patients undergoing treatment that are either too sick to commute to the hospital or for patients who receive outpatient services but who reside outside of Dar es Salaam.

Observation have shown that, most of patients present late at ORCI and hence rule out the surgical option but also the surgical approach to the treatment of cancer of cervix has not been well developed in the country so even few patients who will come early cannot benefit. Three teletherapy Cobalt-60 machine and only two low-dose brachytherapy machine are available at the institute. Out of more than 1200 cervical cancer patient treated in 2007/2008, only 136 were able to get intracavitary sessions (ORCI annual report 2008).

The treatment protocols are still under development but generally patients with up to stage three are given a combination of external beam, cisplatin-based chemotherapy and intracavitary. After completion of treatment a three-monthly follow up for the first year, a six-monthly follow up for the next one year and a twelve-monthly follow up to complete ten years. During follow up, history is taken and the patient is examined including the speculum examination, abdominal-pelvic ultrasound and chest X-ray.
A screening clinic, separate from the main cancer hospital and the above-mentioned clinics, was established in 2003. Although the aim of the clinic was screening and education, 62% of the women present with some kind of medical complaint.

Exclusion criteria

Patients who were diagnosed with other cancer alongside cervical malignancy

DATA SOURCE

The study instruments consisted of files and a survey form which is divided into the following sections:

a) Socio-demographic characteristics
b) Reproductive data
c) Stage, treatment and follow up.

Method of Data collection:

Medical records at Ocean Road Cancer Institute stores files of all patients attended at the institute. Patients name, file number, residence and phone numbers of the next of kin are registered in the register book. Two trained research assistants were recruited to assist the principal investigator in the study. Research assistants were responsible for collecting and sorting out the files after having the file numbers
from the registration book. Extraction of information from the files and filling up of the check lists was done by the Principal Investigator. The Principal Investigator cross-checked the lists of files with the selected files for the study to ensure quality control during data collection.

The files of women with confirmed diagnosis of invasive cervical cancer undergoing treatment at ORCI from January to December 2007 were collected from medical records.

Then, all needed relevant information was transferred from the files to the check list.

The phone numbers of next of kin of patients which is recorded in the patient file were noted, and for those who were not seen in the follow up, and their phone numbers found to be working were contacted directly to know their status.

The operational definitions:

1. Live: patients who were alive at the end of treatment and at the end of a three-year follow up.

2. Dead: patients who were treated for cervical cancer and were dead at the end of treatment and at the end of a three-year follow up.

3. Recurrence: This is defined as the occurrence of the disease symptoms and clinical signs six months after optimal treatment. Any occurrence before six months is regarded as persistence of the disease.
Data analysis:

Data entry was done using Statistical Package for the Social Sciences (SPSS) version 16.0 for statistical analysis. Descriptive data were summarized as percents or means.

Ethical considerations:

The study was approved by the Research and Publication Committee of the Muhimbili University of Health and Allied Sciences. The permission was sought from the director of Ocean Road Cancer Institute.

To ensure confidentiality and anonymity, names of patients were not included on the check lists since a distinct study identification code was assigned to each check list. The obtained information was used for the approved research purposes only.
RESULTS

A total of 826 patients were treated for cervical cancer at Ocean Road Cancer Institute in 2007 but only 630 (76.3%) met the inclusion criteria. Cervical cancer contributed to 32% of all malignancies admitted at ORCI in that year and contributed 45% of all female malignancies.

Table 1: Socio-demographic characteristics of study subjects (N=630)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Groups</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-35</td>
<td>50</td>
<td>7.9</td>
</tr>
<tr>
<td>36-50</td>
<td>257</td>
<td>40.8</td>
</tr>
<tr>
<td>51-65</td>
<td>223</td>
<td>35.4</td>
</tr>
<tr>
<td>≥ 66</td>
<td>100</td>
<td>15.9</td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>411</td>
<td>65.2</td>
</tr>
<tr>
<td>Single</td>
<td>17</td>
<td>2.7</td>
</tr>
<tr>
<td>Divorced/Separated</td>
<td>51</td>
<td>8.1</td>
</tr>
<tr>
<td>Widowed</td>
<td>147</td>
<td>23.3</td>
</tr>
<tr>
<td>Unknown**</td>
<td>4</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Occupation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peasant</td>
<td>438</td>
<td>69.5</td>
</tr>
<tr>
<td>Business</td>
<td>32</td>
<td>5.1</td>
</tr>
<tr>
<td>Employed</td>
<td>16</td>
<td>2.6</td>
</tr>
<tr>
<td>Student</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>House Wife</td>
<td>128</td>
<td>20.3</td>
</tr>
<tr>
<td>Unknown**</td>
<td>15</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>Level of Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal Education</td>
<td>386</td>
<td>61.3</td>
</tr>
<tr>
<td>Primary school</td>
<td>212</td>
<td>33.7</td>
</tr>
<tr>
<td>Secondary education</td>
<td>13</td>
<td>2.1</td>
</tr>
<tr>
<td>University</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Unknown**</td>
<td>18</td>
<td>2.9</td>
</tr>
<tr>
<td><strong>Religion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christian</td>
<td>342</td>
<td>54.3</td>
</tr>
<tr>
<td>Moslem</td>
<td>287</td>
<td>45.6</td>
</tr>
<tr>
<td>Unknown**</td>
<td>1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

** Unknown: not documented
The age of the study population ranged from 24 to 90 years, with a median age of 51 years (± 12.7 SD); majority of the study subjects (40.8%) were in the age group 36-50 years (table 1). Majority of the patients (65.2%) were married, and the widowed comprised 23.3% of all women. Most of the patients (69.5%) were peasant while majority (61.3%) had no formal education and 33.7% had at least a primary school education (table 1).

Figure 1: Distribution of patients by the zones of residence

Forty percent were from the Eastern zone which includes Dar es Salaam, Morogoro, and Coast. Fifteen percent of all patients were from the regions surrounding Lake Victoria including Kagera, Mwanza, Mara and Shinyanga. About 1% patients came from neighbouring countries like Kenya, Malawi, Mozambique and Comoros (figure 1).
Table 2: Clinical characteristics of patients (N=630)

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage of the disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>49</td>
<td>7.8</td>
</tr>
<tr>
<td>II</td>
<td>280</td>
<td>44.4</td>
</tr>
<tr>
<td>III</td>
<td>253</td>
<td>40.2</td>
</tr>
<tr>
<td>IV</td>
<td>48</td>
<td>7.6</td>
</tr>
<tr>
<td><strong>Histological type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>577</td>
<td>91.6</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>48</td>
<td>7.6</td>
</tr>
<tr>
<td>Adenosquamous carcinoma</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Mode of treatment given</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiotherapy (EBR)</td>
<td>527</td>
<td>83.7</td>
</tr>
<tr>
<td>EBR &amp; Intracavitary</td>
<td>55</td>
<td>8.7</td>
</tr>
<tr>
<td>EBR &amp; Chemotherapy</td>
<td>29</td>
<td>4.6</td>
</tr>
<tr>
<td>EBR, Intracavitary &amp; Chemotherapy</td>
<td>4</td>
<td>0.6</td>
</tr>
<tr>
<td>Surgery &amp; EBR</td>
<td>9</td>
<td>1.4</td>
</tr>
<tr>
<td>surgery,EBR &amp; Chemotherapy</td>
<td>5</td>
<td>0.8</td>
</tr>
<tr>
<td>Intracavitary</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Recurrence of symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence of symptoms</td>
<td>76</td>
<td>12.1</td>
</tr>
<tr>
<td>No recurrence</td>
<td>318</td>
<td>50.5</td>
</tr>
<tr>
<td>Persistence of symptoms</td>
<td>95</td>
<td>15.1</td>
</tr>
<tr>
<td>Unknown**</td>
<td>141</td>
<td>22.4</td>
</tr>
</tbody>
</table>

** Unknown: not documented

The study findings show that most of patients were diagnosed to have cervical cancer stage II (44.4%) and stage III (40.2%) while a very few (7.8%) had stage I of the disease (table 2). Squamous cell carcinoma (91.6%) was the leading histological type, whereas adenocarcinoma contributed (7.6%) and others were adenosquamous and sarcoma (table 2). Most patients (83.7%) were treated by external beam radiation only, and few (8.7%) had an additional of intracavitary radiation while only 4.6% had both external beam and chemotherapy. Recurrence of symptoms was observed in 12.1% (table 2).
Table 3: Showing the status of the patient after treatment (N=630)

<table>
<thead>
<tr>
<th>Status of the Patient</th>
<th>Just after treatment</th>
<th>After 3 years follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Dead</td>
<td>15(2.4)</td>
<td>114(18.1)</td>
</tr>
<tr>
<td>Alive</td>
<td>609(96.6)</td>
<td>135(21.4)</td>
</tr>
<tr>
<td>Unknown**</td>
<td>6(1.0)</td>
<td>381(60.5)</td>
</tr>
<tr>
<td>Total</td>
<td>630(100)</td>
<td>630(100)</td>
</tr>
</tbody>
</table>

** Unknown: not documented

At the end of treatment only 15 (2.4%) of patients were dead but after a three years follow-up 114 (18.1%) were dead, and this is almost 46% of those with a known outcome at the end of the three years follow-up (249 patients). Table 3

Table 3: Proportion of women followed up for three years (N=630).

<table>
<thead>
<tr>
<th>Number of visits</th>
<th>First Year</th>
<th>Second Year</th>
<th>Third Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>None</td>
<td>293 (33.8)</td>
<td>389 (61.7)</td>
<td>492 (78.1)</td>
</tr>
<tr>
<td>1</td>
<td>217 (34.4)</td>
<td>144 (22.9)</td>
<td>106 (16.8)</td>
</tr>
<tr>
<td>2</td>
<td>136 (21.6)</td>
<td>70 (11.1)</td>
<td>23 (3.7)</td>
</tr>
<tr>
<td>3</td>
<td>33 (5.2)</td>
<td>16 (2.5)</td>
<td>4 (0.6)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>31 (4.9)</td>
<td>11 (1.7)</td>
<td>5 (0.8)</td>
</tr>
<tr>
<td>Total</td>
<td>630 (100)</td>
<td>630 (100)</td>
<td>630 (100)</td>
</tr>
</tbody>
</table>

Table 5 shows that the proportion of patients were decreasing in all follow-up visits
DISCUSSION

In the year 2007, a total of 826 patients were treated for cervical cancer at ocean road cancer institute of which 630 were proven histologically and their records were available to be included in the study. Cervical cancer contributed 32% of all malignancies treated at ORCI in the year 2007 and 45% of all female malignancies.

Ocean road cancer institute being the only centre in the country providing radiotherapy treatment to all types of cancer, many patients go there from all over the country. It was found in this study that many patients were from the Eastern zone which included Dar es Salaam, this can be explained by the fact that people in Dar es salaam and nearby regions have easy access to Muhimbili National hospital for diagnosis and then sent to ORCI for treatment. Next to Eastern zone was the Lake zone (15%) comprising Mwanza, Mara, Kagera and Shinyanga regions; where the diagnosis can be made at Bugando Medical Centre and patients are sent directly to ORCI with their results to start treatment. The study population had a median age of 51 years (range 24–90 year). Two peak age groups were observed 30–50 (40.8%) and 51 – 65 (35.4%), this is almost similar to what was observed in a Kenyan study (20). This is in support of what has been reported earlier (10) in both studies as it can be seen, the population at risk is the countries’ work force and hence crucial efforts has to be put forward and protect this population for the benefits of the country.

This study reveals that more than three quarters of patient presented to the hospital with disease at stage IIb and above. This late presentation was also observed by Kilewo et al among patients with cervical malignancy at Muhimbili (21).This could be due to low knowledge of the basic symptoms of cervical malignancy and hence the major contributory factor for the late appearance to the hospitals. This was supported by the finding in this study that many patients had no formal education and hence less knowledgeable. Another study done by Msaki et al at ocean Road cancer institute also demonstrated a similar picture of late presentation and hence advanced stage of the disease(22).
Squamous cell carcinoma was the leading type of histology more than 90% and only few patients had adenocarcinoma and adenosquamous; which is similar to what is elaborated in the guidelines of the International Federation of Obstetrics and Gynaecologists (FIGO) that squamous cell carcinoma contributes to 85-95% and adenocarcinoma contributes to 5-15% (7, 8). And this shows that the pattern of histological distribution has not been changed for decades despite of HIV and other viral diseases. This is a good prognostic indicator as the Squamous cell carcinoma respond well with radiotherapy compared to the adenocarcinoma.

Teletherapy (external beam radiation) only was the major mode of treatment (83.7%) while a very few patient got an addition of brachytherapy (8.7%). Also this study showed that very few patients had a combination of radiotherapy and chemotherapy (radiochemo). This small number of patient receiving intracavitary treatment can be explained by the machine failure and long queue of patients who are waiting for the treatment as the machine was using low dose radiotherapy which takes long time to treat just a single patient this was observed even during the study period. Furthermore, having only one machine it makes so difficult for many patients to have the opportunity of getting intracavitary therapy (ICT) hence the combination of external beam and intracavitary was difficult to achieve to most of the patients. The recommended chemotherapy being a weekly dose of cisplatin for not less than five weeks. And as it has been shown many patients did not get an addition of chemotherapy, this might be due to availability of chemo but also the priority is given to other chemosensitive types of tumours, this is different to what is done in other centres whereby they are going even for combination chemotherapy in advanced stages of cervical cancer (23). This lack of sticky to the protocols observed can lead to the poor outcome of the disease observed. This is more or less the same to a study which was done in Kenya (20). Studies has shown good results when combining EBR and ICT as well as the combination of chemotherapy (24), also when the combination of external beam and intracavitary therapy is given, it has good survival rate depending to the stage of the disease at presentation (14).
In our study it has been shown that very few patients (5.2%) were treated with the combination of radiotherapy with chemotherapy (radiochemo); In the current study, 60% of the study group had unknown treatment outcome as only 18.1% were alive and 21.4% were dead at the end of a three-year follow up. Msaki and colleagues (22) studied cervical cancer survival rate and found that 45.6% of patient were dead, 13.9% were alive and 40.5% had status unknown after ten years follow up. Basing on these findings an assumption can be made that most patients whose status is not known may be dead and due to unavailability of the national cancer registry their deaths are not reported and/or documented; and thus can not be retrieved. In places were a cancer registry is well developed like Uganda 31.4% of patients were found to be dead and 40.2% were alive with only 28.4% lost during follow up(19). In Kenya at Kenyatta Hospital the five-year mortality rate was calculated to be 28% but this was a hospital based survey (20). Generally the cancer registry is a very important tool which significantly helps in planning and implementing policies on prevention and treatment of cervical cancer and other types of cancers.

This study shows that more than 60% of patients had at least one follow up visit in the first year after completion of treatment and the number keeps on decreasing in the subsequent years, whereby at the end of a three-year follow up only 22% had at least one follow up visit. A study done in Iran found that only 50% came for visit in first few months and the number kept on decreasing in subsequent years (25). In our setting due to late presentation of patients to the hospital, it is plausible to assume that these patient died of the disease as Msaki et al assumed (22) but it may also be due to poverty given that many patients can not travel from up country to Dar es Salaam for follow up. Moreover, a study in Iran suggested that knowledge and awareness of patients toward follow up is low, and therefore hinders patients from completing their follow up schedules.
Limitation to the Study:

Lost of follow up as observed in the study was the major limitation of the study, this made difficult to draw a clear conclusion as what happened to those who did not complete their follow up schedule.

Although the phone numbers were used to trace some of those who were lost to follow up, still most of these numbers were not working. This led to difficult in drawing a clear conclusion about the outcome of cervical malignancy.

CONCLUSION

Most patient present late for treatment with advanced stage of the disease. Although there are lots of lost of follow up, for those with a known outcome a big number of patients who were treated for cervical cancer was found to be dead at the end of three years follow up and hence poor outcome of the disease.

External beam radiation alone was seen to be the mode of treatment which was given to most of the patients, combination therapy of radiation and chemotherapy was only given to a small proportion of the patients treated at ORCI. Lack of optimized cancer treatment regimens in Tanzania and especially at ORCI appears to be playing an important role on outcome of cervical malignancy at ORCI, as well as late detection and treatment of cervical cancer. Adherence to the follow up clinics seems to be a problem to most of patients, hence the outcome of treatment to most of patients was difficult to assess though the outcome seems to be generally bad.
RECOMENDATION

Surgical approach to early cases of cancer of cervix has to be emphasised.

Health education and sensitization on preventive approach through screening to prevent the late stage presentation at health facilities. The use of available HPV vaccine has to be emphasised and if possible has to be integrated in national extended programme of immunization. Also education on the necessity of the follow up after optimal treatment.

There is a need of implementing a National cancer registry, which can help to make follow up of patients who lost in follow up.

Cancer treatment facilities at Ocean Road Cancer Institute, especially the brachytherapy machines, need to be improved and functioning at all times and development of treatment policy for cervical cancer which has to be adhered.
REFERENCES


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20. Ogweno GM. Treatment (Teletherapy) Outcome and mortality of cancer of the cervix at Kenyatta National Hospital: 5 years Review. University of Nairobi, Department of Obstetrics and Gynecology (unpublished).


APPENDIX

TREATMENT OUTCOME OF CERVICAL CANCER PATIENTS AT OCEAN ROAD CANCER INSTITUTE: DAR ES SALAAM

Study ID # _____ _____ ____
Enrolment date _____ _____ ____

STUDY CHECKLIST

A: Sociodemographic Data:

1. Age (years) ______
2. Marital status :
   a) Married (     )
   b) Single (     )
   c) Divorced / separated (     )
   d) Widowed (     )
3. Ethnicity (tribe)
4. Current residence
5. Home residence and phone number
6. Religion:
a) Catholic ( )
b) Christian ( )
c) Moslem ( )
d) Other specify ____________

7. Occupation:
   a) Peasant
   b) Business
   c) Employed
   d) Student

8. Level of Education
   a) No formal Education ( )
   b) Primary school ( )
   c) Secondary education ( )
   d) College ( )
   e) University ( )
   f) Other specify ____________

REPRODUCTIVE DATA:

9. Menarche (Years) ___ ___

10. Parity ___ ___

11. First delivery (Year) ___/___/___

12. History of contraceptives
   a) Yes
b) No

13. If yes, Which method:
   a) Condoms
   b) Oral pills
   c) Injectables
   d) IUD
   e) Norplants
   f) Tubal ligation
   g) Others specify

14. HIV status:
   a) Positive
   b) Negative
   c) Unknown

TREATMENT, FOLLOW UP AND COMPLICATIONS:

15. Histological cell type
   a) Squamous cell carcinoma
   b) Adenocarcinoma
   c) Adenosquamous
   d) Others specify ________________________

16. Histological differentiation of tumor cell
   a) Well differentiated
   b) Moderately differentiated
c) Poorly differentiated
d) Unknown

17. Clinical stage (FIGO) at diagnosis  __________

18. Pelvic node status:
   a) Positive
   b) Negative
c) Not assessed
d) Unknown

19. Date of commencement of treatment  _____/_____/_____  

20. Duration of treatment  __________

21. Mode of treatment given:
   a) Radiotherapy (EBR)
b) Intracavitary
c) Chemotherarapy
d) EBR & Intracavitary
e) EBR & Chemotherapy
f) EBR, Intracavitary&chemotherapy
g) Surgery & EBR

22. If Radiotherapy  total dosage of irradiation  __________

23. Number of fraction  ______________

24. If intra cavitary dosage

25. If surgery was done the type :
a) TAH
b) STAH
c) Werthiems hysterectomy
d) Others specify ________________

26. Radiation complications during radiotherapy:
   a) Hematological
   b) Gastrointestinal
   c) Cutaneous
   d) Neurological
   e) Others Specify_______________

27. Recurrence of symptoms
   a) Yes
   b) No

28. After how long did the symptoms reappear? ____________

29. Clinical or Radiological examination of the cervix
   a) Presence of the tumor
   b) No tumor seen

30. How many follow up visits within the first year
   a) Not at all
   b) One
   c) Two
   d) Three
   e) More than three
31. How many visits in the second year post treatment
   a) Not at all
   b) Once
   c) Twice
   d) Thrice
   e) More than thrice

32. How many visits made in the third year post treatment
   a) Not at all
   b) Once
   c) Twice
   d) Thrice
   e) More than thrice

33. Status of the patient?
   a) Dead
   b) Alive
   c) Unknown

34. If dead when?
   a) During treatment
   b) Just after treatment
   c) Less than one year
   d) 2-3 years

35. What was the cause of death ________________