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Cervical cancer management in a low resource setting: A 10-year review in a tertiary care hospital in Kenya

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ABSTRACT

Background: Cervical cancer is one of the leading causes of cancer mortality among women in Kenya due to late presentations, poor access to health care, and limited resources. Across many low- and middle-income countries infrastructure and human resources for cervical cancer management are currently insufficient to meet the high population needs therefore patients are not able to get appropriate treatment.
Objective: This study aimed to describe the clinicopathological characteristics and the treatment profiles of cervical cancer cases seen at Moi Teaching and Referral Hospital (MTRH)
Methods: This was a retrospective cross-sectional study conducted at MTRH involving the review of the electronic database and medical charts of 1541 patients with a histologically confirmed diagnosis of cervical cancer between January 2012 and December 2021.
Results: Of the 1541 cases analyzed, 91% were squamous cell carcinomas, 8% were adenocarcinomas, and 1% were other histological types. Thirty-eight percent of the patients were HIV infected and less than 30% of the women had health insurance. A majority (75%) of the patients presented with advanced-stage disease (stage IIB-IV). Only 13.9% received chemoradiotherapy with curative intent; of which 33.8% received suboptimal treatment. Of the 13% who received surgical treatment, 45.3% required adjuvant therapy, of which only 27.5% received treatment. Over 40% of the women were lost to follow-up.
Conclusion: Most of the patients with cervical cancer in Kenya present at advanced stages with only a third receiving the necessary treatment while the majority receive only palliative treatment or supportive care.

1. Background

Cervical cancer is the leading cause of cancer mortality in women, every 2 min a woman dies of cervical cancer, with over 90 % of these deaths occurring in low and middle-income countries (LMICs) (Gaffney et al., 2018; Sung et al., 2021). Incidence and mortality are two to four-fold higher in LMICs as compared to high income countries (Arbyn et al., 2020). In particular, the highest rates of cervical cancer mortality are observed in Eastern, Southern, and Central Africa (Sung et al., 2021). In Kenya cervical cancer is the number one cause of cancer deaths in females. In the year 2020, an estimated 5236 cases of cervical cancer were diagnosed and the total deaths due to cervical cancer were 3211 (Sung et al., 2021). Low- and middle-income countries continue to bear a disproportionate burden of cervical cancer due to lack of resources for prevention, early detection and access to quality care including surgery and radiotherapy (Ginsburg et al., 2017; Runge et al., 2019; Makau-Barasa et al., 2018).

Locally advanced and metastatic cancer of the cervix occurs predominantly in LMICs, with the cases expected to rise to twice their numbers by the year 2040 (Sharma et al., 2022). Across many countries in sub-Saharan Africa (SSA), infrastructure and human resources for cervical cancer diagnosis and treatment are currently insufficient to meet the high population needs with only 30 % available public cancer treatment and palliative care services (Tapela et al., 2016; World Health

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Organization, 2020). Moreover, the cost of treatment, long distances to access diagnostic and treatment services, and inadequate implementation of cancer policy have hindered access to and abandonment of cancer treatment in Kenya. There is anecdotal evidence that only a third of the cervical cancer patients in Kenya receive treatment, which could largely be attributed to these limitations.

Moi Teaching and Referral Hospital (MTRH), being the main referral hospital in Western Kenya receives a huge number of cervical cancer patients. Prior to 2009 women with cervical cancer who presented to MTRH with symptoms like bleeding, foul smelling discharge or pain, received only the basic care such as blood transfusions when necessary. No additional treatment was offered as none was available, they were referred to Kenyatta National Hospital (KNH) in the country's capital, for radiotherapy/surgery. Many patients were not able to access this treatment due to the challenges associated with travel and the costs involved (Rosen et al., 2017). To counter this Moi university/MTRH in collaboration with Academic Model Providing Access to Healthcare (AMPATH) organization, a consortium of North American universities and medical schools led by Indiana University started a screening program in 2009 followed by a fellowship in 2013 (Rosen et al., 2017). As a result of this, there was a surge in screening efforts and the training of specialists capable of performing complex cervical cancer surgeries. This also led to a dramatic increase in the number of cervical cancer patients seen and managed over the past 10 years. Adaptions of treatment guidelines were made due to limited access to radiotherapy to ensure that cervical cancer patients received the best care possible within the constraints of the local healthcare system and available resources. These adaptations focused on cost-effective, feasible, and sustainable strategies to improve patient outcomes.

The objective of this retrospective institutional study is to provide a comprehensive description of the clinicopathological characteristics and treatment profiles of cervical cancer cases reviewed at MTRH, contributing to an improved understanding of the treatment landscape that has evolved over the past decade. This will help identify the existing gaps in care in a low-resource setting over the last decade and their global implications. Moreover, it will also provide a comprehensive and accurate records on patients receiving treatment. The ultimate goal is to provide insights into areas where improvements are urgently needed for enhancing healthcare delivery in regions with limited resources and ultimately leading to better outcomes.

2. Methods

2.1. Study setting

The study was carried out at Chandaria Cancer and Chronic Diseases Centre (CCCDC) in MTRH in Eldoret. It is the country's second-largest referral hospital located about 330 km west of the country's capital Nairobi. Being the main referral hospital in Western Kenya, it has a catchment population of 20 to 25 million people, which comprises approximately 40 percent of the Kenyan population, and also serves patients from neighboring countries. The hospital has 2 gynecologic oncologists with the additional support of 2 more from North America under the Ampath program and 3 to 5 fellows. Every week 50 to 60 patients with gynecologic cancers are attended, 80 % of which have cervical cancer, of which 90 % have locally advanced and metastatic disease. The patients are reviewed by the gynecologic oncologists and fellows and appropriate work-up and staging are done. The surgical cases are then booked for surgery, those who require radiotherapy are referred to the radiation oncology clinic for further management, and cases with metastatic disease are offered palliative treatment with radiotherapy, chemotherapy, or only palliative care. The hospital has one fully functional radiotherapy machine, acquired in 2021 and approximately 20 new patients with cervical cancer receive curative intent radiotherapy in a month. Patients have a long waiting period before receiving treatment, sometimes as much as 4 to 6 months.

2.2. Study design

This was a retrospective cross-sectional study that reviewed the database for cervical cancer patients seen at MTRH from January 1st, 2012 to December 31st, 2021.

2.3. Data collection

Data was collected from two sources; abstraction from medical charts and review of the prospectively kept electronic database. The maximum number of records retrieved were reviewed. The list of all cervical cancer cases was taken from the cancer registry, then files were retrieved physically from the records department and data was supplemented from an electronically kept database. Staging was done clinically per the 2018 FIGO clinical staging (as detailed in the Supplementary file). For cases diagnosed prior to 2018, their staging was retrospectively reassessed based on the clinical findings documented in the available records. Imaging and pathologic analysis, where available, were used to supplement clinical findings for all stages. Patients who underwent surgical treatment, were considered at a high risk of disease recurrence based on the Peters criteria, if any of the following were present on final histology review; positive surgical margins or microscopic involvement of the parametrium or pathologically confirmed involvement of the pelvic lymph nodes (Peters et al., 2000). While those at an intermediate risk of disease recurrence based on Sedlis criteria included; a combination of depth of stromal invasion, lymphovascular space invasion and tumor size (Sedlis et al., 1999).

2.4. Study population

Records of all patients with a histologically confirmed diagnosis of cervical cancer at the MTRH between January 1st, 2012, and December 31st, 2021 were reviewed.

Inclusion Criteria: Histologically proven cervical cancer of any stage.

Exclusion Criteria: Metastatic cancers to the cervix where the cervix is not the primary, and files with incomplete data.

2.5. Data analysis

IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp computer program was used for analysis. Descriptive statistics such as median and interquartile range were used to summarize the age. Frequencies and the corresponding percentages were used to summarize categorical variables such as parity, smoking status, HIV status, health insurance status, symptoms at presentations, stage of the cancer, tumor grade, histological types and treatment profile.

Ethical consideration: Ethical approval was obtained from the Institutional Research and Ethical Committee of Moi University/MTRH, the approval number is FAN:0004092. All electronic databases used in this study were protected by procedures consistent with applicable laws, directives, policies, regulations, and standard in Kenya. Each entry was assigned a unique identification number and all data collected as part of the study was identified with this number. Data in tablets and computers was encrypted and password protected, and could only be accessed by a user with a login and password. Participant files were accessible only to study investigators and stored in a locked cabinet in a locked office. No data collected or abstracted from the database contained personally identifiable information.

3. Results

A total of 1642 files were retrieved; 101 files had missing data and were excluded. A total of 1541 files were evaluated in this study.

Table 1 shows that 38 % of the women were HIV infected and less than 30 % of the women had health insurance.

Table 1
Demographic characteristics of patients with cervical cancer, N = 1541.

Variable	n (%)
Age (years)	
Less than 30	61 (4)
30 –65	1260 (81.7)
More than 65	220 (14.3)
Median age	50
IQ range	25–75
Parity	
Nulliparous	181 11.7)
1 – 5	712 (46.2)
More than 5	648 (42.1)
Smoking status	
Yes	76 (4.9)
No	1465 (95.1)
HIV Status	
Positive	592 (38.4)
Negative	761 (49.4)
Unknown	188 (12.2)
Health insurance	
Yes	445 (28.9)
No	1096 (71.1)

Table 2 shows that the most common presenting symptom was vaginal bleeding. Less than 10 % of the patients presented in early stages (IA-IB2).

Table 2
Clinicopathological characteristics of patients with cervical cancer, N = 1541.

Variable	n (%)
Symptoms at presentation	
Vaginal bleeding	1218 (79)
Foul-smelling vaginal discharge	835 (54.2)
Pelvic pain	767 (49.8)
Leakage of urine	51 (3.3)
Weight loss	137 (8.9)
Fatigue	70 (4.4)
Stage	
IA1	5 (0.3)
IA2	12 (0.8)
IB1	23 (1.5)
IB2	104 (6.7)
IB3	137 (8.9)
IIA	108 (7.0)
IIB	298 (19.3)
IIIA	93 (6.0)
IIIB	371 (24.1)
IIIC1	154 (10.0)
IIIC2	70 (4.5)
IVA	72 (4.7)
IVB	94 (6.1)
Tumor Grade	
Well-differentiated	148 (9.6)
Moderately differentiated	745 (48.3)
Poorly differentiated	365 (23.7)
Not indicated	283 (18.4)
Histopathological type	
Squamous cell carcinoma	1400 (90.9)
Adenocarcinoma	124 (8.0)
Adenosquamous carcinoma	11 (0.7)
Others (4 small cell and 2 carcinosarcoma)	6 (0.4)

Table 3 shows that 13 % of patients had surgical treatment. Of the 83 patients who received NACT, 24 had a partial or no response and received no further treatment due to financial constraints. A total of 13.9 % patients received radiotherapy, and over 14 % received no treatment.

Table 4 shows of the 91 patients referred for adjuvant radiotherapy only 25 received adjuvant treatment.

Table 5 shows 1222 patients required curative intent radiotherapy based on their stage (locally advanced), of which only 213 patients got radiotherapy with 33.8 % getting partial treatment.

4. Discussion

Cervical cancer imposes a huge global burden and is the most common cause of cancer death among women in Kenya (Sung et al., 2021). The most common histological type being SCC with incidence rates ranging from 70 to 75 % followed by AC with rates ranging from 20 to 25 % (Watson et al., 2008). The low incidence of AC which was less than 10 % as observed in this review can be attributed to several factors. These factors may include increased prevalence of HPV type 16 in Kenya (De Vuyst et al., 2010) or potential variations in interpretation by less experienced pathologists who may find the diverse characteristics of AC more challenging to identify compared to SCC. Additionally, the absence of gynecologic oncology pathologists in Western Kenya might contribute to these differences. The notably high rate of human immunodeficiency virus (HIV) infection seen among the women in this institutional review can be attributed to the fact that our center serves as the primary referral hospital in Western Kenya, an area known to have the highest prevalence of HIV in the entire country (Kimanga et al., 2014). Women with HIV infection are six times more likely to develop cervical cancer than women without HIV infection (Stelzle et al., 2021).

Late presentations of women with cervical cancer is a significant public health concern in LMICs, which puts the women at a higher risk of death (Maranga et al., 2013). Consistent with the results of our study, over 70 % of the patients in LMICs tend to present with advanced stage disease leading to poor prognosis and treatment outcomes (Mlange et al., 2016; Zeleke et al., 2019). Several factors contribute to this trend, and one key factor is that women in Kenya frequently lack the autonomy to seek healthcare on their own. The majority of women typically need finances or permission from their husbands or elders to seek care (Isaacson et al., 2023; Were and Buziba, 2001). Many of these women would need to travel, often hundreds of kilometers, to the nearest cancer hospital. The situation is worsened by widespread myths and stigma that surround reproductive system cancers, which is often associated to promiscuity, HIV or perceived failure to fulfil one's role as a caregiver (Isaacson et al., 2023). Furthermore, women are apprehensive about

Table 3
Documented Treatment profile of all the patients, N = 1541.

Variable	n (%)
Conization	2 (0.1)
Radical hysterectomy + PLND	140 (9.1)
NACT + radical hysterectomy + PLND	59 (3.8)
EBRT alone	20 (1.3)
EBRT + cisplatin	52 (3.4)
EBRT + ICBT	4 (0.3)
EBRT + ICBT + cisplatin	137 (8.9)
Palliative chemotherapy	145 (9.4)
Palliative radiotherapy	10 (0.6)
Palliative radiotherapy + Chemo	4 (0.3)
NACT alone (surgery abandoned)	24 (1.6)
Supportive care	222 (14.4)
Awaiting NHIF activation	23 (1.5)
Awaiting to start radiotherapy at MTRH	40 (2.6)
Loss to follow-up after referral for radiotherapy	659 (42.8)

PLND – pelvic lymph node dissection, NACT – neoadjuvant chemotherapy, EBRT – external beam radiotherapy, ICBT – intracavitary brachytherapy.

Table 4
Treatment profile of patients who received surgical treatment, N = 201.

Variable	n (%)
Types of surgical treatment	
Conization	2 (0.9)
Radical hysterectomy + PLND	140 (69.7)
NACT + radical hysterectomy + PLND	59 (29.4)
Risk of recurrence	
High-risk (one factor)	82 (40.8)
Intermediate-risk (at least two factors)	9 (4.5)
None	47 (23.4)
Unknown (incomplete histology report)	63 (31.3)
Referred for adjuvant treatment	
Yes	91 (45.3)
No	110 (54.7)
Received adjuvant treatment*	
Yes	25 (27.5)
No	66 (72.5)

N* = 91, number of patients who were referred for adjuvant treatment based on the risk factors for recurrence.
NACT – neoadjuvant chemotherapy, PLND – pelvic lymph node dissection

Table 5
Treatment profile of all patients who received radiotherapy, N = 213.

Variable	n (%)
Those who required curative intent radiotherapy#	
Yes	1222 (79.3)
No	319 (20.7)
Those who received radiotherapy *	
Yes	213 (17.4)
No	1009 (82.6)
Types of radiotherapy received	
EBRT alone	20 (9.4)
EBRT + Cisplatin	52 (24.4)
EBRT + ICBT	4 (1.9)
EBRT + ICBT + Cisplatin	137 (64.3)
Duration of radiotherapy	
≤56 days	144 (67.6)
More than 56 days	69 (32.4)

N# = 1541, total number of patients.
N* =1222, number of patients who required curative intent radiotherapy (locally advanced i.e., 1B3-IVA).
EBRT – external beam radiotherapy, ICBT – intracavitary brachytherapy.

their diagnosis becoming public knowledge as there is a fear of rejection and are often abandoned by their partners or families after receiving a diagnosis of cervical cancer (Ginjupalli et al., 2022). Moreover, many women often do not realize they are sick, and may try many herbal remedies first before seeking help. Another major contributor to late presentation in Kenya is the interplay between the healthcare workers knowledge and attitude about the disease, its treatment and timely referrals (Kivuti-Bitok et al., 2013).

At our center women with locally advanced tumors (IB3- II) who were either unable to access radiotherapy or lacked finances received single agent cisplatin 50 mg/m^2 biweekly then underwent radical hysterectomy with pelvic lymphadenectomy. In low resource settings like ours, the scarcity of resources and high cost of radiotherapy coupled with almost non-existent health insurance coverage, makes NACT followed by surgery a viable option for even more locally advanced tumors (Chuang et al., 2016). In many situations the default is to do nothing, which means certain death, therefore healthcare providers and policymakers often direct their efforts towards finding an effective approach on how best to utilize the existing resources to achieve improved outcomes. Neoadjuvant chemotherapy is effective in reducing the tumor size, increasing the operability with minimal side effects (Benedetti Panici et al., 2015). It is important to note that not all women may respond sufficiently to become eligible for a hysterectomy. However, with regards to survival rates, radiotherapy has been noted to have better outcomes (Gadducci et al., 2013; Benedetti Panici et al., 2015).

Consistent with our findings Tonui et al in another study done at MTRH reported that of those who required adjuvant radiotherapy following surgery, only one third of women received it (Tonui et al., 2020). Apart from the cost and access factors, this situation may also be amplified by the common belief among patients in Kenya that surgery is a sufficient treatment, and additional treatment is not necessary. Studies have reported increased relapses and poorer survival outcomes in such patients (Peters et al., 2000; Sedlis et al., 1999).

Histopathology represents a key component and should be comprehensive of all features which allow risk stratification of the patients and guidance on adjuvant treatment. The lack of trained pathologists with expertise in gynecologic oncology at our center significantly impacts histology reporting. Individual pathologists may omit parameters that they deem not important, which ultimately affects outcomes. Additionally, the limited number of pathologists at our center contributes to significant delays in reporting and reduced accuracy of histology reports. There is limited data regarding the adequacy of pathology reports in cervical cancer, however, studies evaluating the adequacy of histopathology reports of endometrial and breast malignancies in LMICs have reported similar or higher rates of incomplete reports impacting adjuvant treatment decisions (Yesufe et al., 2018; Bansal et al., 2022). This highlights the need for continuous training for all pathologists to ensure that reporting reflects the current knowledge and training of gynecologic oncology pathologists. It also highlights the importance of audits, standardized reporting format, and proper communication between clinicians and pathologists.

Radiation therapy had been the biggest limitation in our facility until July 2021. The only radiotherapy machine in the public hospital was located in the country's capital, 300 km away. In 2017, a private hospital in Western Kenya acquired a radiotherapy unit, but the cost of treatment there were beyond the means of many patients. Most cervical cancer patients in Western Kenya have been reported to be of low-income status and do not have adequate medical cover or funds to relieve their financial burden (Owenga and Nyambedha, 2018). Patients often lack health insurance, even a modest amount like $5 for health insurance can account for a substantial 20–25 % of a family's monthly income. For those who have insurance only 70–80 % of the treatment cost is covered and patients often have to top-up to complete the treatment. This combination of the distant location of radiotherapy services and high cost of treatment results in significant financial hardship for the patient and their families, where some families end up selling their livestock or farms/land to raise the money, in order to complete the treatment. This results in significant interruptions, incomplete or abandonment of treatment in our setting making it less effective. Maranga et al reported that only 6.7 % of patients at KNH received complete recommended treatment, while majority only received partial treatment with EBRT alone (Maranga et al., 2013). A retrospective analysis showed treatment with EBRT alone produced the lowest 5-year disease-free survival, while the inclusion of ICBT significantly improved disease-free survival (Shanta et al., 2010). For optimal outcomes, treatment should be completed within 56 days, delays result in treatment failures or suboptimal treatment and a 1 % reduction in survival per day for more than 56 days (Petereit et al., 1995; Perez et al., 1995). A study done in Taiwan noted higher rates of delays in public hospitals and those who had treatment delays had a twofold increased mortality as compared to those who had timely treatment (Shen et al., 2016). Radiation therapy is the most common limitation in many African Countries (Chuang et al., 2021; Beltrán Ponce et al., 2023).

At our center we adapted the use of Cisplatin 50 mg/m2 with a 3–4-week interval as an alternative for women with locally advanced cervical cancer who were not able to afford radiotherapy and were not surgical candidates (Orang'o et al., 2016). Previously these women were only afforded certain measures such as blood transfusions for low hemoglobin and send home to die. This approach improved distressing and debilitating symptoms like bleeding, intense pain, and foul-smelling discharge. Several women at our center were only provided with supportive care because they were either too ill, unfit due to renal derangement, or chose not to undergo treatment for reasons such as the long distance required to access chemotherapy or a belief that the treatment would be ineffective.

Due to poor tracking of patients in our center, we do not know whether patients who were LTFU received treatment elsewhere. These proportions are consistent with those reported in another study from Kenya (Maranga et al., 2013), while other LMICs reported even lower rates of LTFU of 20–30 % (Habinshuti et al., 2020; Paul et al., 2010). A study performed in India reported that patients with advanced stages had higher rates of LTFU than those with early stages which was attributed to the high financial implications and poor outcomes of treatment as perceived by the patients (Paul et al., 2010). In low-resource countries LTFU is a well-documented challenge that could be attributed to various factors such as patients seeking care elsewhere for example herbal treatment, patients with advanced may not want any further treatment due to cost implications or financial burden on the family, distance and travel burden and unclear benefits from a patients perspective (DeBoer et al., 2022).

This study's main limitation was its retrospective nature. Missing data such as missing histology reports and treatment details. Some patients' medical charts could not be traced. Data were scanty on management outcomes and records of deaths from cervical cancer. Finally, the limitations of clinical staging are well appreciated. Parametrial and sidewall invasion, as well as metastases to lymph nodes, can be difficult to assess accurately using physical examination alone and can lead to under-staging of some patients.

5. Conclusion

Most of the patients with cervical cancer in Kenya present at advanced stages with only a third receiving the necessary treatment while the majority receive only palliative treatment or supportive care.

Recommendations

There is a need to invest in primary health facilities to promote early diagnosis and referrals to appropriate facilities and to subsidize the cost of diagnosis and treatment of cervical cancer.

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Author contribution

AFS and EBO conceptualized and designed the study. AFS supervised the data collection, analysis and drafted the initial manuscript. PMI, PKT, AWM, AR, BPR, and ALC critically reviewed and edited the manuscript and all authors approved the final manuscript as submitted.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2024.101331.

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