Clinical Medicine Insights: Oncology

ORIGINAL RESEARCH

A Six-Year Study of the Clinical Presentation of Cervical Cancer and the Management Challenges Encountered at a State Teaching Hospital in Southeast Nigeria

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Abstract: Cervical cancer is still a major contributor to cancer-related mortality amongst women living in poor, rural communities of developing countries. The objective of this study is to establish the clinical presentation of cervical cancer and the management challenges encountered in Abakaliki, southeast Nigeria, with a view to finding intervention strategies. This study is a retrospective descriptive assessment of cases of clinically diagnosed cervical cancer managed at a state teaching hospital over six years. Of 76 cases managed, 61 (80.3%) cases notes were available for study. The mean age and parity of patients were 53.8 years and 6.8 years, respectively. The majority (75.4%) were illiterate. All had been married, but 42.6% were widowed. The main occupations were farming or petty trading. One patient (1.6%) had had a single Pap smear in her life. The major presenting complaints were abnormal vaginal bleeding (86.9%), offensive vaginal discharge (41.0%), and weight loss. Twenty patients (32.8%) were lost to follow-up prior to staging. Of the remaining 41 patients, 16 (39.0%) had stage III disease and 17.1% stage IV. Fifteen patients (24.6%) with late stage disease accepted referral, and were referred for radiotherapy. Those who declined were discharged home on request, though 4 (9.8%) died in the hospital. There was no feedback from referred patients confirming that they went and benefitted from the referral. The presentation followed known trends. Illiteracy, poverty, early marriages, high parity, widowhood, non-use of screening methods, late presentation, non-acceptance of referral, and lack of communication after referral were some of the major challenges encountered. These underscore the needs for health education and awareness creation, women educational and economic empowerment, legislation against early marriages and in protection of widows, and creation of a well-staffed and well-equipped dedicated gynecologic oncology unit to forestall further referral.

Keywords: cervical cancer, late presentation, cancer-related deaths, management challenges, referral

Introduction

Globally, cervical cancer constitutes about 12% of all cancers in women,[1] and reflects striking health inequity more than any other cancer.[2] It is the second most common cancer in women worldwide, but is the most common among women in developing countries.[1–3] More than 85% of approximately 529,800 cases diagnosed annually occur in developing countries, a proportion that is expected to increase to 90% by 2020.[2,4] In addition, cervical cancer is the leading cause of cancer deaths among women in low-resource settings.[1,2] For instance, every two minutes a woman dies from the disease, equating to more than 275,000 cancer deaths annually, of which more than 87% occur in developing countries.[4] It also affects relatively young women and is the largest single cause of years of life lost to cancer in the developing world.[2] The deaths of these women who are in their most productive years have devastating effects on the well-being of their families, and results, for example, in decreases in school attendance and nutritional status among their children.[2,5] Cancer of the cervix affects women at a time of life when they are critical to social and economic stability.[6]

Although mortality from cancer of the cervix has declined in many developed countries,[7–9] such as the United Kingdom and Sweden, the story is different with the sub-Saharan African region. The sub-Saharan African region posts the highest incidence rates for cervical cancer in the world.[4,6] Here, cervical cancer is not only the most frequently occurring cancer among middle-aged women, but also a leading cause of death.[10] The disproportionately high burden of cervical cancer in this region and elsewhere in medically underserved populations is largely due to a lack of screening that allows detection of precancerous and early stage cervical cancer.[6,10] So, while about 75% of cases present early in developed countries thereby making expectation of cure realistic, in developing countries, the majority of cases present with advanced disease.[6] For instance, Ibrahim et al[10] found that about 72% of the cervical cancer cases in a Sudanese study conducted in 2007 were diagnosed at an advanced stage.

In Nigeria, cancer management is domiciled in teaching hospitals located in urban cities, and reported incidence rates for cervical cancer are institution-based. Cervical cancer is the second most common cancer in females and the most common female genital tract cancer, constituting about 62.3%–70.5% of all gynecological cancers.[11–14] Literature reveals a peak mean age incidence range of 43.5–59.7 years,[12–19] endorsing the assertion that women are afflicted at an age in life when they are critical to social and economic stability.[6] Other risk factors reported in the patients include poverty and low socio-economic status, grand multi-parity, limited educational attainment, early age at onset of sexual intercourse, polygamous marriages, and history of multiple sex partners.[10–13,20] The documented clinical features[7,12–15] include abnormal vaginal bleeding (inter-menstrual, post-coital, post-menopausal bleeding) in about 51.9%–100% of cases, offensive vaginal discharge in some 25%–79% of cases, and pain from nerve involvement on pelvic side wall. Majority of the cases (75%–86%) tended to present very late, with advanced disease,[13,14,19] and these later patients were apt to have weight loss, backache, leg pain, edema, and haematuria.[12,13,16,17] This assemblage of problems may increase the challenges care givers faced in the management of cervical cancer in Nigeria.

This study aimed to establish the clinical presentation of cervical cancer at a tertiary hospital in Abakaliki, southeast Nigeria, and to identify the challenges care givers faced in its management with a view to finding strategies for intervention.

Methodology

The Ebonyi State University Teaching Hospital (EBSUTH) was a state-owned teaching hospital and one of the two tertiary hospitals in Abakaliki, the Ebonyi State capital. EBSUTH offered tertiary health-care services. The major beneficiaries of the services were Ebonyi State indigenes. Patients also came from the other neighboring states of Abia, Akwa Ibom, Benue, Cross River, Enugu, and Imo. The main occupations of the major beneficiaries included farming, fishing, and petty trading. Illiteracy was rife amongst them and their health seeking behavior poor.

EBSUTH had a well-developed Department of Obstetrics and Gynecology (O&G), but did not have a dedicated oncology unit. It also lacked facilities for radiotherapy. And although the department had a designated Oncology Team, cases of gynecological oncology were not usually referred to this team. Rather, they were managed by other teams as they

deemed best, based on their experience and the facilities at their disposal.

This was a six-year (January 2005 to December 2010 inclusive) retrospective descriptive study of all the cases of cervical cancer clinically diagnosed and managed at EBSUTH, Abakaliki. Data on patient's age, parity, education, marital status, presenting complaints, management and outcome, and referral were collected from patients' case notes, theatre records, and pathological records. Analysis was done using simple percentages and inferential statistics.

The research was approved by the Hospital's Research Ethics Committee.

Results

Of the 76 cases clinically diagnosed as cervical cancer, 61 case notes (80.3%) were able to be retrieved and studied. Table 1 shows their demographic characteristics. Their ages ranged from 32 to 78 years, the modal age range was 60–69 years, and the mean age (±SD) was 54.0 (±12.7) years. Also, their parity ranged from 0 to 16 with a mean of 7.0 (±3.2); 47 of them (77.0%) were grand multiparous. Illiteracy was high as 22 (36.1%) had no formal education and 39.3% had only primary education. All the women had been previously married, but 26 (42.6%) were widows at presentation. Also, 15 (24.6%) married early (before menarche), 16.4% were in polygamous marriages, and 6.6% remarried. Their occupations were basically petty and some had more than one occupation: 37 (60.7%) were farmers, and 37.7% traders, while the rest were dependent either on their children and/or other relations, or were retirees. The sexual histories also showed that 45.9% had single sexual partners, 26.2% had multiple sex partners, and in 27.9% the number of sex partners was not documented. Only one of the patients (1.6%) had done Pap smear once in the past and the result was negative.

Table 2 depicts the patients' presenting complaints, the initial medical care offered to them, and their acceptance and rejection of further care. The most common presenting complaint, abnormal vaginal bleeding, was documented in 88.5% of the patients. Other common complaints were offensive vaginal discharge (42.6%), weight loss (39.3%), and pain (Table 2). Twenty-nine (46.8%) of the patients were admitted in the first instance and transfused with between 2 to 6 units of blood to correct anemia

Table 1. Demographic characteristics of patients who were clinically diagnosed with cervical cancer (N = 61).

Item	Frequency (%)	Range	Mean (±standard deviation)
Age (years)		32–78	54.0 (±12.7)
≤39	8 (13.1)		
40–49	16 (26.2)		
50–59	12 (19.7)		
60–69	17 (27.9)		
≥70	8 (13.1)		
Parity		0–16	7.0 (±3.2)
0	1 (1.6)		
1–4	13 (21.4)		
≥5	47 (77.0)		
Educational status			
No formal education	22 (36.1)		
Primary school	24 (39.3)		
Secondary school	14 (23.0)		
Tertiary	1 (1.6)		
Marital status and marriage characteristics			
Married	35 (57.4)		
Widowed	26 (42.6)		
Early marriage	15 (24.6)		
Polygamous marriage	10 (16.4)		
Remarried	4 (6.6)		
Occupation			
Farming	37 (60.7)		
Trading	23 (37.7)		
Dependent	22 (36.1)		
Retired	4 (6.6)		
Sexual partners			
Multiple partners	16 (26.2)		
Single partner	28 (45.9)		
Undocumented	17 (27.9)		

Table 2. Presenting complaints and medical care offered to patients clinically diagnosed with cervical cancer (N = 61).

Item	Frequency (%)
Presenting complaints	
Abnormal vaginal bleeding	54 (88.5)
Offensive vaginal discharge	26 (42.6)
Weight loss	24 (39.3)
Pain	14 (23.0)
Constipation	5 (8.2)
Haematuria	3 (4.9)
Leg swelling	2 (3.3)
Haemoptysis	1 (1.6)
Blood transfusion/acceptance of further medical care	
Transfusion	29 (46.8)
Rejected further care	20 (32.8)
Accepted	41 (67.2)

and stabilize their clinical state prior to further management. Following counseling for examination under anesthesia (EUA), staging, and definitive care, 20 patients (32.8%) rejected further medical care. Of those who rejected further care, 15 (75%) benefited from blood transfusion and then signed against medical advice, while five (25%) ceased coming to the clinic before staging could be done. One of the patients who rejected further care died in the hospital while waiting to go home.

Table 3 shows the stages of the disease amongst the cases and the further medical care offered to the 41 patients who consented to post-counseling. The majority, 23 cases (56.1%), had advanced stage disease (39.0% stage III and 17.1% stage IV), while stage I comprised only 9.8% (Fig. 1). Two of the patients with late stage disease had had previous hysterectomies in peripheral hospitals for unstated gynecological indications, but the specimens did not undergo histopathological analysis. Eventually, 40 patients (97.6%) underwent EUA and staging and afterwards, 26.8% had a hysterectomy while 48.8% were referred for radiotherapy. One of the patients considered to have stage IV disease was referred for radiotherapy without undergoing EUA. None of the patients were tested for human papilloma virus (HPV) as the HPV test was not readily available in the hospital. Table 4 shows disease stage-specific interventions and outcomes. Twenty-one of the patients (51.2%), 14 of whom belonged to stages III and IV, had biopsy during EUA, while 11 had hysterectomy (all the patients with stage I and 50% of the patients with stage II). Twenty (48.8%) of the patients, of which 31.7% had late stage disease, were referred for radiotherapy.

Table 3. Stage of disease amongst and further management of patients with cervical cancer who accepted care (N = 41).

Item	Frequency (%)
Stage	
Stage I	4 (9.8)
Stage II	14 (34.1)
Stage III	15 (36.6)
Stage IV	8 (19.5)
Further management	
EUA/staging	40 (97.6)
Hysterectomy	11 (26.8)
Referred	20 (48.8)

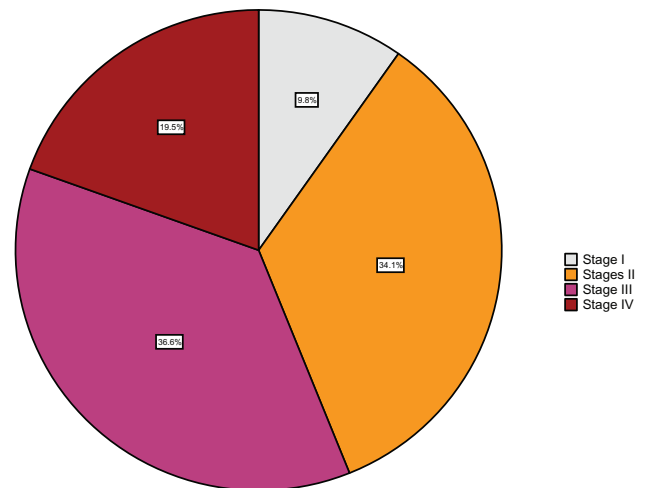**Abbreviation:** EUA, Examination under anesthesia.

Figure 1. Stage of disease at presentation amongst patients clinically diagnosed with and managed for cervical cancer (N = 41).

No back referral was recorded for any of the referred cases. Eleven patients, 26.8%, signed against medical advice during the course of management, 14.6% became lost to follow-up, while 9.8% died in care.

Discussion

Cervical cancer has continued to have a devastating impact on women's health globally, and particularly in developing countries like Nigeria where it has remained the most common cancer of the female genital tract.[12,14,15,17–19]

The demographic characteristics of the patients in this study share similarities with results from several other centers Nigeria. For instance, the mean age of patients in this study falls within the peak mean age range of about 43.5–54.5 years,[11–16,21] and the high mean parity agrees with the results from other studies.[11,16,20,21] These findings further affirm that cervical cancer afflicts women at a time when they are vital to social and economic stability[6] and that grand multiparity is an important causal risk factor.

One of the major challenges and risk factors found in the study is high rate of illiteracy or low educational attainment.[12–14] A low education level increases the risk of invasive cervical cancers and illiteracy has been shown to greatly increase this risk.[22] Other risk factors identified were significant levels of early marriages, polygamous marriages, repeat marriages, and multiple sexual partners.[12–14] And, although most cervical cancers (94%–100%) are associated with sexually transmitted genital infection by HPV,[23] testing for

Table 4. Stage of disease, stage-specific management offered and outcome (N = 41).

Item	Stage I	Stage II	Stage III	Stage IV	Overall (%)
EUA/staging	4	14	15	7	40 (97.6)
Biopsy	–	7	10	4	21 (51.2)
Hysterectomy	4	7	–	–	11 (26.8)
Referred	2	5	7	6	20 (48.8)
Back referral	–	–	–	–	– (0.0)
Signed against	–	2	4	5	11 (26.8)
Lost to follow up	–	2	4	–	6 (14.6)
Died	–	–	2	2	4 (9.8)

Abbreviation: EUA, Examination under anesthesia.

HPV could not be performed on the patients in this series as the service was not available in the hospital. This is not surprising as the HPV testing for a study conducted at Ibadan, Nigeria, by Okolo et al was done in The Netherlands.[24] The study confirmed that HPV16 and 18 are the two most frequently detected types among invasive cervical cancer in Nigeria, and that they account for 78% of HPV positive invasive cervical cancer.[24] Fundamentally, unprotected coitus encourages HPV infection. So, early marriages, polygamy, remarriages, and multiple sexual partners are high risk factors[25,26] as they increase the duration of exposure to and the probability of contracting HPV infection. Basically, these findings support the causal association between sexual activity and cervical cancer.[25]

More than 40% of the patients in this study were widows. Widows are vulnerable in the society because they are likely to be sexually exploited.[26] Widowhood has been found to be at increased risk of HPV infection and cervical cancer than married women. Poverty, as shown by the petty occupations documented in this study, and widowhood could catalyze the likelihood of women succumbing to sexual advances by multiple sexual partners, thereby increasing the chances of HPV transmission. Poverty makes women unduly dependent on their husbands and partners for financial support and sustenance, and can lead to sexual promiscuity with its attendant short- and long-term cervical cancer-related risks.[27] Poverty and/or widowhood also contribute to late presentation for obvious reasons. Poverty, early marriage, polygamy, grand multiparity, and illiteracy have all been found to be significantly associated with increased risk of occurrence of cervical cancer and could contribute to the high incidence of late presentation.[17]

Although cervical screening services are poorly developed in Nigeria,[27] the available ones are also poorly utilized: only 1.6% of the patients in this case series was screened. Unfortunately, this finding compares favorably with the 0.6% documented amongst gynecological clinic attendees is southeast Nigeria,[27] and confirms that cervical cancer screening uptake is very low in Nigeria, especially amongst the poor and illiterate women. Non-use of screening methods implies that cases are more likely to present or be discovered late, at a time when they are less probable to benefit from the commonly available management options.

The presenting complaints were essentially similar to the reports in the literatures reviewed. The incidence of abnormal vaginal bleeding was marginally higher than the 55.9%–84.0%[11,13–15,18,19] reported in literature, thus affirming that abnormal vaginal bleeding is an important sign in cervical cancer. Abnormal vaginal bleeding normally occurs as post-coital, inter-menstrual, or postmenopausal bleeding. Should every case of abnormal vaginal bleeding be promptly investigated, cervical cancers would be diagnosed in early stages, at a time when there could be hopes of cure. However, due to the amalgamation of illiteracy, poverty, ignorance, non-utilization of screening services, and a host of others factors particular to the underserved in the poor rural communities of southeast Nigeria, the majority of the women present in late stage disease.[11,13,15,16,19] Offensive vaginal discharge and weight loss were two other presenting complaints that occurred in about 40.0% of the cases in this study. Both of these complaints have been report with varying frequencies in association with cervical cancer.[11,13–16,19]

One of the major management challenges encountered was late presentation, as more than 56.0% of

the cases presented in stages III and IV. Though less than 75.0% reported from Ilorin,[13] 85.5% from Zaria, 86.0% from Abuja,[16] 78.6% from Sagamu,[15] and 89.3% from Nnewi,[11] the results generally affirm that cervical cancer patients present very late to tertiary hospitals in Nigeria. Patients' delay in seeking health-care and care providers' delay in referring patients to a tertiary hospital have been shown to contribute immensely to the late presentation.[19] Patients that pre-sented late tended to have multiple complaints and complications (Table 2). They were often anemic and needed blood transfusion and other forms of resusci-tation prior to definitive investigations and treatment. This was a huge challenge in our centre as more than 46% needed transfusion, and blood for transfusion is not readily available, such that the blood bank opera-tors had to often recourse to the poor relatives of the poor patients for blood, without success.[28]

Another frustrating challenge was that after the initial resuscitation, some 33% of the patients rejected further medical care, and an additional 14.6% of the patients that accepted further medical care became lost to follow-up later on. Their reasons were not known, but may not be unconnected with illiteracy, poverty, ignorance, and societal myths and beliefs. There is need for further research on this. Umezulike et al[16] working in Abuja, Nigeria, reported a 44.4% lost to follow-up rate.

Approximately 98% of the patients that consented to further medical care had EUA and staging, and around 27% finally had a hysterectomy as they were adjudged to have early stage diseases. The rest, con-sidered to have late stage diseases, were counseled and subsequently referred for radiotherapy. Regrettably, not every patient that was counseled and referred finally acceded to the referral. Moreover, amongst the patients that left promptly following their referral, there were no means of ascertaining if they actually heeded the referral, and there were no back referrals to confirm that patients complied with the referrals. So, although the patients were referred for optimal care, one cannot categorically state that they bene-fited from such referrals.

A cancer-related mortality rate of approximately 10% was recorded in this study amongst the patients who accepted further medical care and remained in the hospital long enough for the mortality to occur. There were no records of the outcomes of the patients that refused further medical care after the initial resuscita-tion and those who refused medical advice. Indeed, taken holistically, the cancer-related death rate could be much higher as most of the patients signed against further medical care and the majority of those referred were expected to succumb to the disease sooner if they did not receive further treatment. Unfortunately, there were no ways of tracking the patients.

By and large, cervical cancer still remains a major cause of cancer-related deaths in women from developing countries[1,2,4] including Nigeria, with illiteracy, poverty, early marriages, polygamy, remarriages, grand multiparity, and late presentation as facilitators.[29] In India, Thulaseedharan et al[30] also found that illiterate women of increasing age and hav-ing many pregnancies were at significantly increased risk of cervical cancer.

Conclusion

Cervical cancer most often afflicts women in develop-ing countries, like Nigeria. It reflects gross imbalance that results from inequalities in social and economic development, and in the infrastructural and human resources required for care.[31] The risk factors for cer-vical cancer and management challenges identified in this study include high incidences of high parity, early marriages, polygamy, remarriages and widow-hood, multiple sexual partners, poverty, illiteracy, and low educational attainment. Others factors include low cervical screening uptake, late presentation, lack of a dedicated gynecological oncology unit, poorly functioning blood bank, rejection of medical care, loss to follow-up, inability to perform HPV testing on cervical specimens collected from patients with cervical cancer, no-tracking of referrals, and absence of back referrals. To stem the incidence of cervical cancer in women, there is a need to curb these factors and challenges.

Sustained health education and awareness creation could mitigate high parity, early marriages, polyg-amy, multiple sexual partners, illiteracy, and late pre-sentation, and improve uptake of cervical screening. Education and economic empowerment of women and girls would palliate illiteracy, early marriages, polygamy, high parity, multiple sexual partners, and late presentation, as well as improve cervical screen-ing uptake. There is need for legislation in favor of widows and against early marriages. Tertiary hospitals

should be encouraged to create dedicated gynecologic oncology units with appropriate services in place such as HPV testing of cervical specimens. Experiences pooled from such units could improve patient care and record keeping. They should also have functional blood banks to cushion the blood transfusion requirements of late presenters. Additionally, there is need for a patient tracking system to help recognize the whereabouts and outcomes of patients presenting with cervical cancer as a means of forestalling the dilemma of loss to follow-up.

In the interim, treatment for cervical cancer needs to be free or highly subsidized to make the care and benefit received by the patients independent of their financial abilities. Truly, reductions in cervical cancer rates can be achieved by reducing inequalities in socioeconomic conditions, availability of preventive health services, and improving women's social status.[31] To achieve these, there is a need for team work between the hospitals, government, non-governmental organizations, philanthropists, and the people. The Federal Government of Nigeria has commenced vaccination of young girls aged 9–15 years with HPV vaccines as part of the long-term preventive measures for cervical cancers in Nigeria. However, this vaccination may remain inaccessible to many without international assistance with funds,[32] therefore amplifying the need for team work.

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Author Contributions

Conceived and designed the experiments: JNE. Analyzed the data: JNE, ENE-I. Wrote the first draft of the manuscript: JNE. Contributed to the writing of the manuscript: JNE, ENE-I. Agree with manuscript results and conclusions: JNE, ENE-I, FOE. Jointly developed the structure and arguments for the paper: JNE, ENE-I. Made critical revisions and approved final version: JNE, ENE-I, FOE. All authors reviewed and approved of the final manuscript.

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Disclosures and Ethics

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