

Research Article

Distant Metastases in Uterine Cervical Cancer Patients

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Abstract

Aim and Objectives: This study evaluated the pattern and frequency of distant metastases among cervical cancer patients who presented for treatment in radiotherapy clinic, University College Hospital, Ibadan.

Methodology: Nine hundred and eighty patients with histologically confirmed cancer of the cervix seen in a ten-year period (January 2002 and December 2011) were reviewed for distant metastases at presentation and over a 2 years follow-up period.

Results: 45 (4.6%) patients had distant metastasis at presentation which increased to 119 (12.1%) patients at two years follow-up. One hundred and three (86.6%) of the patients had single organ metastasis while 16 (13.4%) had multiple organs metastases. The sites of distant metastases were lung 31.3%, lymph nodes 22.7%, bones 19.6%, liver 10.4%, cutaneous 9.2%, gastrointestinal 4.9% and brain 1.2%, and others 0.6%. Only 27.8% of the patients with distant metastasis survived beyond 6 months after being diagnosed with metastases. 845 (86.2%) of patients had advanced disease of stage II B and above at presentation.

Conclusion: This study shows that the distribution of metastases in cancer of the cervix has not changed over the years when compared with previous studies but the frequencies of the distribution differs. Late presentation is still a common feature amongst our patients. There is a need to intensify public awareness, could there be a "World Uterine Cervical Cancer Day"?

Keywords

- Uterine cervical cancer
- Distance metastases

INTRODUCTION

Cervical cancer incidence is ranked second to breast cancer in Nigeria [1,2]. It reduces the life expectancy of the affected population, depriving the nation of useful work force with its attendance poverty in countries where the disease is prevalent. Cervical cancer incidence and mortality have declined substantially in Western countries following introduction of screening programs. Screening programs in some African countries are however often rudimentary or non-existent. The screening techniques often used are Papanicolaou (Pap) smear [3], visual inspection of the acetic acid-painted cervix (VIA) [4], and human papillomavirus (HPV) DNA test [5].

In Nigeria the national incidence of cervical cancer is 250/100,000⁶. With the increase in the incidence of HIV/AIDS pandemic in developing countries, the incidence of cancer of the cervix is also on the rise [7]. A study by Babarinsa et al between 1975-1995 reported that cervical cancer constitutes 62.7% of all malignancy seen at the University College Hospital, Ibadan [8]. While another study by Campbell et al reported that nine hundred patients with cancer of the cervix were seen in the Radiotherapy Department of the University College Hospital, Ibadan between the years 1988-1992 [9].

Cervical cancer patients in developing countries such as Nigeria commonly present late either with locally advanced disease or with distant metastasis due to ignorance, poverty and limited access to appropriate treatment. This is well illustrated by the fact that by year 2004 only 3 radiotherapy department were available to treat a population of about 130 million Nigerians [10]. This study describes the pattern of distance metastases among cervical cancer patients attended to in ten years in the Radiotherapy clinic, University College Hospital, Ibadan.

MATERIALS AND METHODS

This is a ten year retrospective review of the pattern of distance metastatic disease in patients with cancer of the uterine cervix. Medical records from nine hundred and eighty patients with histologically confirmed cancer of the cervix seen in the Radiotherapy Department, University College Hospital, Ibadan between January 2002 and December 2011 were obtained for this study.

RESULTS

Nine hundred and eighty patients with histologically confirmed cancer of the cervix were seen. The patients were

between the ages of 32 and 90 years, and the mean age was 54.5 (± 2.02) years. Seven hundred and thirty three (74.8%) patients were married while 198 (20.2%), 33 (3.4%), and 16 (1.6%) were widowed, divorced and single mothers respectively. Four hundred and seven (55.5%) of these patients were married in a monogamous setting while 326 (44.5%) were married in a polygamous setting.

Three hundred and twenty one (32.8%) of the patients were educated up to the primary school levels, 288 (29.4%) had no formal education, 255 (26%) had up to secondary education levels, while 116 (11.8%) had tertiary education. Seven hundred and forty one (75.6%) of the patients were Christians, 230 (23.5%) and 9 (0.9%) were Muslims and traditionalist respectively. Eight hundred and fifteen (83.2%) patients were grand-multiparous; 157 (16%) and 8 (0.8%) were multiparous and nulliparous respectively. Five hundred and ninety three (60.5%) of the patient's age at first coitus was between 16-20 years, while 238 (24.3%), 132 (13.5%) and 17 (1.7%) age at first coitus were between 10-15, 21-25, and 26-30 years respectively. The mean age at first coitus was 18.2 years.

Eight hundred and forty nine (86.6%) patients never used hormonal contraceptives. 131 (13.4%) used hormonal contraceptives, sixty six (50.4%) of these used hormonal contraceptives between 1-5 years duration, while 57 (43.5%) and 8 (6.1%) used hormonal contraceptives for less than 1 year and more than 5 years respectively.

Five hundred and seventy six (58.8%) of the patients denied history of multiple sexual partners while 404 (41.2%) of them had multiple sexual partners. One hundred and thirty one (13.4%) gave positive history of sexually transmitted disease while 849 (86.6%) denied history of sexually transmitted disease.

Four hundred and twenty eight (43.6%) patients were traders while 198 (20.2%), 157 (16.0%), 123 (12.6%), and 74 (7.6%) were self-employed professionals, house-wife/students, farmers and civil servants respectively. In all, over 60% were sedentary workers. Eight hundred and thirty two (84.9%) of the patients neither took alcohol nor smoked cigarette, 116 (11.8%) took alcohol, 17 (1.7%) smoked cigarette while 15 (1.5%) do both. Seven hundred and nine (72.3%) of the patients were postmenopausal while 271 (27.7%) were premenopausal. Squamous cell carcinoma was the most predominant tumor cell type in 861 (87.9%) of the patients while 103 (10.5%) and 16 (1.6%) had adenocarcinoma/adenosquamous and sarcoma respectively. Six hundred and eight (62%) of the histological grade was poorly differentiated while 230 (23.5%) and 142 (14.5%) were moderately and well differentiated respectively.

Average duration of illness before patient presentation was 18.9 (± 10.2) months. 30.2% of the patient population had other comorbid disease like hypertension, diabetes and HIV infection. Three hundred and fifty three (36%) patients presented with stage IIIB, 18.6% stage IIIA, 17.8% stage IIB, 12.2% stage IIA, stage IV A and B accounted for 13.8% while 17 (1.7%) patients had stage IB disease. No patient presented to us with stage IA disease. Only 45 (4.6%) patients had distant metastasis (i.e. stage IVB disease) at time of presentation but over a 2-year follow-up period, there were overall total of 119 (12.1%) patients

with distant metastases. One hundred and three (86.6%) of the patients had single organ metastasis while 16 (13.4%) had multiple organs metastases. The most common site of distant metastases at presentation was the lung, 28 (47.4%) patients. There was no patient with metastasis to the brain at presentation. (Figure 1). The lung was also the commonest site of distant metastasis during follow-up, 23 (22.1%) patients while the brain was the least site, 2 (1.9%) patients (Figure 1). Fifty one (31.3%) of the total number of patients with distant metastases was to the lung, making it the most common site while the brain was the least site with 2 (0.6%) patients (Figure 2). The most predominant histological type among the patients with distant metastasis was squamous cell carcinoma which was seen in 105 (88.2%) of them. Eighty two (69%) of the patients with distant metastasis had poorly differentiated histological grade while 11 (9.2%) had well differentiated histological grade (Figure 3).

DISCUSSION

Carcinoma of the cervix still remains the leading gynecological cancer in Nigerian women, accounting for 62.7% of all gynecological cancers seen in Ibadan, with similar observations in Zaira and Maiduguri (Nigeria) with 65.7% and 72.6% respectively [8,11,12]. The patients' age range in this study was between 32 and 90 years, with mean age of 54.5 years. This finding is similar to the reported peak mean age incidence of cancer of the cervix in

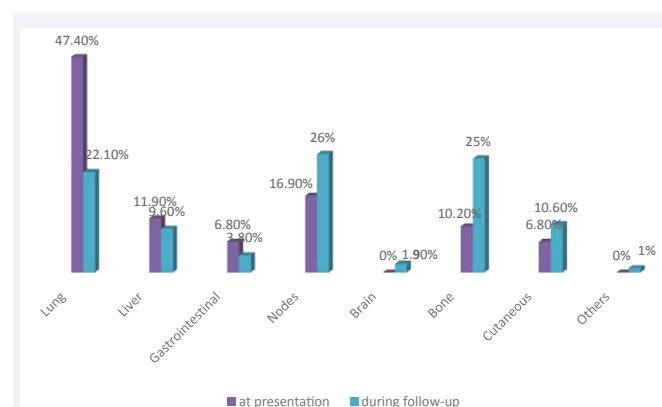


Figure 1 Sites of distant metastases at presentation and during follow-up.

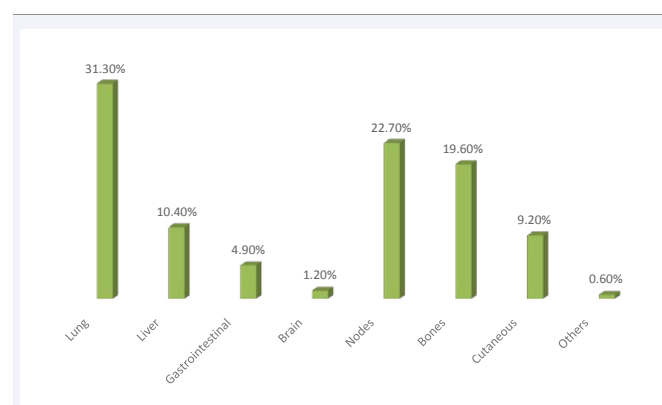
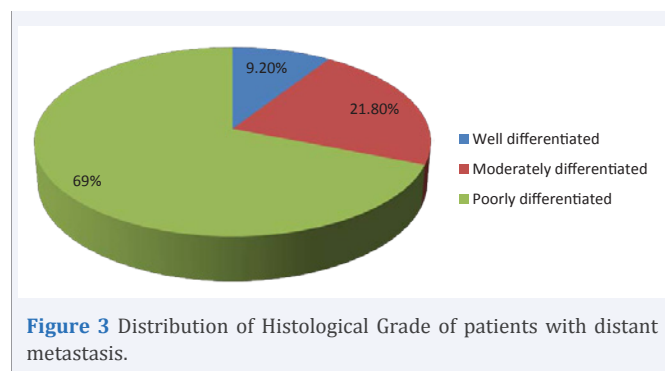


Figure 2 Overall sites of distant metastasis.



Nigeria, which ranges from 43.5-54.6 years [13]. A previous study carried out in the department 19 years earlier however, reported an age range of 21-80 years and a mean age of 46.5 years [9]. The peak age frequency distribution for this study was between the ages of 51-60 years which is similar to a previous study report of 5th-7th decades [14]. The study showed 11.8 % of the patients attained tertiary educational level and over 50% in the low socio-economic class. Similar findings were also reported in a study by Adewuyi et al [15]. The risk of developing cancer of the cervix was highest among grand multiparous women (parity of ≥ 5), which constituted 83.2% of the study population. In fact other studies carried out in Nigeria and Africa in general have demonstrated an association between high number of deliveries and incidence of cervical cancer [16-18]. Squamous cell carcinoma was the commonest histological type encountered, accounting for 87.9% of cases seen; range of 85.7-92% [9,12,18] reported in other previous studies. The predominant histological grade was poorly differentiated, constituting 62%. Minimal attention has been paid to distant metastasis from cancer of developed distant metastasis over a 2 year follow-up. Studies by Carlson et al reported 15.3% over a 5 years follow-up while Humberto et al reported 26.6% over a 3 years follow-up developing metastasis [19,20]. The overall incidence of metastasis in this study increased with stage; 9.2% in IIA, 13.4% in IIB, 16% in IIIA, 19.3% in IIIB, and 42% in stage IVA. Similar findings was also reported in previous studies [19,20].

The sites of overall metastasis reported in this analysis are consistent with those reported by other studies, with the commonest organ being the lungs, accounting for 31.3% [19,20-23]. The nodes were the next most frequent site of metastasis, accounting for 22.7%, which was similar to a report of 22% noted by Humberto et al [19]. Bony involvement occurred in 19.6% of the cases in this study, which is comparable with the incidence range of 15-17% reported in other studies [19,22]. The liver accounted for 10.4%, which is far more than the 4% reported in a similar study [19]. Cutaneous involvement occurred in 9.2%, which was more than the 0.1-3.6% previously reported [22, 24,25]. The findings of 4.9% involving the gastrointestinal tract, was almost similar to 4% previously reported [19]. Brain metastasis from cervical carcinoma is rare, this study is confirmatory of previous reports [19, 26, 27]. The miscellaneous site involved in this study was the peritoneum.

A further review of the specific metastatic sites revealed that 5.9% of the patients with pulmonary metastasis presented with chest x-ray features of lymphangitis carcinomatosa. This is confirmatory of previous reports of the rarity of this pathological

diagnosis in cancer of the cervix [28,29]. This study revealed that the lumbar spine was the most common site of bony involvement accounting for 37.5%, similar findings were also reported in other studies [19-21]. The para-aortic nodes were the most commonly affected nodes, accounting for 45.9% of the nodal involvement, with the supraclavicular node being the next in frequency, accounting for 29.7%. Similar nodal findings were reported in previous studies [19,20]. The umbilical region was the most frequent cutaneous area of involvement in this study, previous studies reported similar findings [24,25]. The large intestine was the most predominant site of metastasis in the gastrointestinal tract and this study was confirmatory [22].

This study showed that the stage at presentation plays a significant role in the outcome of treatment in these patients in relation to the development of distant metastasis over a 2 years follow-up. The number of patients with metastasis increased positively with the stage at presentation. This finding is corroborated by studies which reported the clinical stage and the tumour volume at presentation as important factors in the treatment outcome in carcinoma of the uterine cervix [30,31].

In this study, 27.8% of the patients with distant metastasis survived beyond 6 months after the diagnosis of metastasis. Carlson et al reported 41.3% surviving beyond 6 months after diagnosis of metastasis [20]. In relation to the stage at presentation, it was found out that it plays a very significant role in the overall survival for patients with metastasis. Four (36.4%) of the patients with distant metastasis in stage IIA survived beyond 6 months while 18.8%, 15.8%, 8.7%, and none of the patients with distant metastasis in stages IIB, IIIA, IIIB, and IVA respectively survived beyond 6 months after the diagnosis of metastasis. Various studies reported that the stage at presentation, volume of tumour, and endometrial extension are determinants of survival in these patients [30-34].

Stage at presentation and the histological grade were shown to have a positive association with the development of metastasis in this study. The age at presentation, presence of co-morbidity, and the histological type vis-à-vis the incidence of squamous cell carcinoma and other histological types were shown not to have a strong association. Similar studies reported that the clinical stage at presentation, endometrial extension, and pelvic tumour control enhances the probability of developing metastasis while the age, histological type, and volume of disease were not significant factors [19, 32, 35, 36]. Various studies also reported, the stage at presentation as perhaps the most important prognostic factor correlated with metastasis [20, 32, 37].

This study shows that pattern of distribution of metastasis in uterine cervical cancer have not changed significantly over the years compared with various studies reported, though the frequencies differs [19, 20,21-23,37,38].

CONCLUSION

This study shows that cancer of the cervix occurs commonly in the 5th-7th decades of life among Nigerian women, and over two thirds patients' present with locally advanced disease. The overall incidence of metastasis increases positively with stage of the disease. The commonest site of metastasis was the lung, while the next is the nodes, and the brain having the least

incidence of metastasis. Lymphangitis carcinomatosa was a rare finding in cancer of the cervix and the paraortic node was the most predominant nodal involvement. The lumbar spine and the umbilical region were the most common metastatic sites in the bone and cutaneous anatomical areas respectively. The treatment outcome in relation to the development of distant metastasis over a 2 year follow-up was significantly affected by the stage at presentation. Only 27.8% of the patients with distant metastasis survived beyond 6 months after the diagnosis of metastasis. The stage of presentation and histological grade were identified as the features associated with metastasis in cancer of the cervix in this study while the histological type, patients' age and patient's comorbid ailment were not significant.

The study also shows that no significant change in the distribution of the pattern of metastasis was identified compared with previous similar studies. There is a need for continuous uterine cervical cancer awareness and screening campaign for improved early disease detection in developing world. Perhaps, celebrating a world uterine cervical cancer day could increase public awareness.

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