Sociodemographic and clinicopathologic characterization of cervical cancers in northern Nigeria

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Summary

Objective: To evaluate the sociodemographic and clinicopathological characteristics of patients with cervical cancer seen in a tertiary referral center in northern Nigeria. *Materials and Methods:* Between January 2002 and December 2004, 70 consecutive patients with histologically confirmed cervical cancer, with a median age of 48 years (range, 30-75 years), were interviewed on the basis of a structured pro forma. *Results:* Of these patents, 39 (56%) had had no formal education, and 36 (51%) were unemployed housewives. Sixty (86%) had become sexually active before 17 years of age; 44 (63%) were in polygamous families, and 25 (36%) patients were in at least a second marriage. There was an average of 6.8 live births per patient. Vaginal bleeding was seen in all patients, and 55 (79%) had vaginal discharges; 50 (71%) had a bulky cervical mass, and 46 (66%) presented with at least Stage IIIA disease. Squamous cell carcinoma was the commonest histology. The three HIV-seropositive patients were young and had advanced disease. *Conclusion:* Sociodemographic factors, such as low socioeconomic level, early age at first sexual intercourse and multiple sexual partners, place women at high risk of developing cervical cancer in northern Nigeria. Late presentation with advanced disease predominates.

Key words: Cervical cancer; Sociodemographic factors; Epidemiology; Clinical features; Africa.

Introduction

The incidence of cervical cancer in developed countries has been dropping drastically over the past two decades owing to successful screening programs with "Pap smears". On the contrary, the incidence and prevalence of cervical cancer are rising in most African countries [1, 2]. This reflects lack of screening programs and the persistence of sociocultural factors that place the population at risk by increasing the prevalence of human papillomavirus (HPV) infection, the central and necessary cause of cervical cancer [3]. The burden of this cancer in developing countries is alarming, as they have about 80% of all cases worldwide [4].

The true incidence of cervical cancer in Nigeria remains unknown because of lack of a cancer registry, but it remains a major challenge in this environment because of the very low uptake of Pap smear screening and the associated late presentation. The sociocultural practices of the population include marriage at a very young age, polygamy and many divorces and remarriages. It has been observed that cervical cancers are commoner in the northern part of the country, which is predominantly Muslim, than in the southern part, which is predominantly Christian and where breast is the commonest cancer. The aim of this study was to analyse the sociodemographic and clinicopathological characteristics of cervical cancers in a major tertiary institution in northern Nigeria.

Materials and Methods

The study was conducted between January 2002 and December 2004, accruing a total of 70 patients with histologically confirmed cervical cancer. Patients presenting for the first time and those referred to the institution with histologically confirmed carcinoma of the cervix were included. Histologic confirmation was done either by the referring hospital or at presentation if the patient had no histology report. For each patient, data including sociodemographic characteristics, symptoms and signs at presentation, and histology, were collected prospectively on a structured pro forma by a single investigator, by one-to-one interviews with the patients. The data were entered into Epi-Info software and analysed.

The socio-demographic information obtained from the patients included age at time of presentation, age at first marriage, number of marriages, age at first coitus, marital status, religion, parity, menopausal status, history of sexually transmitted diseases, knowledge and practice of Pap smears for screening, number of miscarriages warranting dilatation and curettage, and history of cigarette smoking. Postmenopause was defined as complete cessation of menstruation for at least six months. Bulky cervical mass was defined as a cervical mass greater than 5 cm in at least one dimension by ultrasound measurement.

Written informed consent was obtained from all participants. The first 37 patients in the study were not screened for HIV because this aspect was not included in the initial study protocol cleared by the institutional ethical committee, but subsequent patients were ethically cleared for HIV screening.

Results

Table 1 shows the characteristics of the patients, with the age distribution at the time of presentation. Two-thirds of the patients were in polygamous families, and 25 (36%) were in at least a second monogamous or polyga-

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Characteristics	30-39	Age (ye 40-49	ars) 50-59	60-69	> 70	Total		
	50 57	10 17	50 57	00 07	270	Total		
No. of patients	11	27	14	15	3	70		
Religion								
Christian	3	9	8	6	2	28		
Muslim	8	18	6	9	1	42		
Residence								
Urban	10	25	9	7	1	52		
Rural	1	2	5	8	2	18		
Type of marriage	•							
Monogamous	3	12	6	4	1	26		
Polygamous	8	15	8	11	2	44		
No. of marriages								
First	7	21	8	9	_	45		
Second	3	6	4	2	1	16		
Third or more	1	-	2	4	2	9		
History of divorc	e							
No	8	22	7	9	_	46		
Yes	3	5	7	6	3	24		
No. of deliveries								
0-4	5	4	1	2	_	12		
5-9	6	19	10	11	1	47		
≥ 10	_	4	3	2	2	11		
No. of abortions warranting dilatation and curettage								
0	4	12	8	8	1	33		
1	4	13	2	5	_	24		
2	2	2	2	_	2	8		
≥ 3	1	_	2	2	_	5		
Menopausal status								
Pre-	11	24	3	_	_	38		
Post-	_	3	11	15	3	32		

Table 1. — Characteristics of patients by age.

mous marriage, 24 having divorced their first husband. Sixty (86%) patients had become sexually active before the age of 17, by virtue of early marriage (Figure 1). Twentytwo (31%) had a history of pelvic inflammatory disease or sexually transmitted disease prior to presentation. All the patients' sexual partners had been circumcised. At the time of presentation, 32 (46%) patients were already in postmenopause, and 38 (54%) were in premenopause. Fifty-



Figure 1. — Age distribution at time of first marriage.

Table 2. — Symptoms at presentation in patients with cancer of the cervix.

Symptom	Frequency	%
Post-coital bleeding	32	45.7
Unprovoked vaginal bleeding	38	54.3
Vaginal discharge	55	78.6
Offensive vaginal discharge	30	42.9
Lower abdominal pain	25	35.7
Waist pain	12	17.1
Menstrual irregularities	4	5.7
Lymphedema	1	1.4
Weight loss	3	4.3
Suprapubic swelling	1	1.4
Haematuria	3	4.3
Urinary fistula	2	2.9
Faecal leakage	1	1.4
Painful micturition	3	4.3

Table 3. — Duration of symptoms at time of first hospital presentation.

Duration (months)	Frequency	%
0-3	4	5.7
4-6	19	27.1
7-9	12	17.1
10-12	12	17.1
15-18	4	5.7
24	10	14.3
36	5	7.1
60	3	4.3
72	1	1.4

eight (83%) women had had at least five live births, with an average of 6.8 live births per patient and a range of 1-14. Similarly, 37 patients had had at least one miscarriage warranting dilatation and curettage.

Thirty-nine (56%) patients had no formal education, 16 had completed primary education, 11 had completed secondary education and four patients had a tertiary education. Thirty-six patients were unemployed housewives, seven had white-collar jobs, and the others were farmers, petty traders and artisans. Of the 15 patients with knowledge about Pap smears, only three had had a smear, and only after the onset of symptoms. Fifty-five (79%) of the patients had never smoked cigarettes.

Table 2 shows that vaginal bleeding was a common symptom in all the patients, and 55 (79%) had vaginal discharges, which were malodorous in 30 (43%). Forty-seven patients (67%) presented with symptoms of more than six months' duration (Table 3). The gross findings on digital and speculum examination revealed 49 patients with exophytic, 20 with ulcerative and only one patient with endophytic growth. Fifty (71%) patients had a bulky cervical mass. After adequate staging investigations (without CT scan and MRI), only five (7%) patients were found to have Stage IB, 19 (27%) had Stage II, 30 (43%) had Stage III, 14 (20%) had Stage IVA and two (3%) had Stage IVB disease. The histologic types seen were squamous cell carcinoma, accounting for 90% (63), adenocarcinoma (9%; 6) and adenosquamous carcinoma (1%; 1).

Three of the 33 patients screened for HIV infection were found to be seropositive. Their ages were 30, 32 and 35 years, while the age range of the HIV-negative patients was 32-75 years with a median of 48 years. All three patients with HIV presented with advanced disease: one each with Stage IIIB, IVA and IVB.

Discussion

The results show that most of these patients were married before the age of 17 years and had therefore become sexually active at that time. A large proportion of the patients had high parity and multiple sexual partners, not as a result of sexual promiscuity but because the culture and religion permit divorce, remarriage and polygamy. This directly and indirectly increases the risk of exposure to HPV, the central and necessary cause of cervical cancer [3, 5, 6] and HIV. The educational level of the patients was low, and they presented late to hospital, with symptoms and signs of advanced disease. A significant proportion of the patients were postmenopausal. Cigarette smoking or tobacco consumption was not common. There was poor knowledge and attitudes about screening.

The patients in this study did not represent all the cervical cancers in the region because many patients go to private hospitals, Government peripheral hospitals and traditional or herbal practitioners for treatment, and may never be referred to the teaching hospital for diagnosis and treatment. Other factors that limit patient attendance are the prevailing poverty, the cost of medical services, especially for diagnosis and treatment of cancers, and the bias against women and children, whose health issues are not considered a priority by their immediate families. Not all the relevant investigations necessary for staging and treatment, especially CT scan and MRI, were done for most patients.

None of the patients was tested for HPV infection or checked for the presence of inclusion bodies in histologic specimens, as there are no facilities for these tests. Thus, the role of these infections could not be established. However, in a separate study carried out by the International Agency for Research on Cancer (IARC), the prevalence of HPV types was determined in a random sample of 932 asymptomatic women aged 15 to > 65 years in Ibadan, Nigeria. The overall HPV prevalence was very high (26%), and the most frequent types were HPV 16, 35, 31 and 58. In contrast to populations studied in similar surveys, the HPV prevalence was high not only among young women but also among those in middle and old age [7].

Epidemiological studies conducted over the past three decades have consistently indicated that the risk for cervical cancer is strongly influenced by measures of sexual activity, such as the number of sexual partners, age at first coitus and sexual behavior of the male partner [4], which are correlates of exposure to HPV [3]. We confirmed these observations in our study environment.

The peak age and cluster age for this cancer in our study occurred in the parturient age group of 40-49 years.

In terms of age distribution, parity and menstrual status, cervical cancers in the northern savannah of Nigeria were similar to those reported elsewhere in Africa [8, 9] but significantly different from those in developed countries [10]. The patients not only had had first coitus before the age of 17 years but were sexually active by virtue of their marriage. This also contributes to the high parity, as the religion discourages use of family planning of any kind. A decline in fertility rates in North America over the past four decades has reduced the incidence of and mortality from cervical cancers [11, 12].

Lack of cervical cancer screening, coupled with delay in presentation to hospital, might account for the predominantly advanced stage of disease in developing countries. Cigarette smoking has been incriminated in cervical cancer, as the tobacco components lower local immunity in female genitalia [13]. In our study, however, most of the patients had never smoked cigarettes, and those that did did so very occasionally. In this study, all the male partners were circumcised and therefore did not play a role in spreading HPV [14].

The symptoms at presentation in this environment were that of advanced disease, with unprovoked bleeding, offensive vaginal discharges, lower abdominal pain and waist pain and, in some cases, the presence of fistula. This is the norm in most developing countries but differs significantly from the presentation in developed countries, where patients are seen at an early stage, with post-coital bleeding and occasionally, as a result of screening, with no symptoms [15]. The pattern of histology seen in our study was similar to that in the developed world, adenocarcinoma and adenosquamous carcinoma accounting for about 10% of all cervical cancers [11, 16, 17].

Although only about half of the patients had been screened for HIV, those with HIV antibodies were younger, with more advanced disease and, in terms of histology, had poorly differentiated squamous cell carcinoma. This result, although observed in only a few patients, supports reports in the literature of the pattern of carcinoma of the cervix in HIV-positive patients, suggesting that HIV-infected women with cervical cancer are more likely to have advanced disease at presentation and to have a higher recurrence rate than non-HIV-infected women [18]. Furthermore, cervical intraepithelial neoplasia occurs more frequently in women with HIV infection [18]. Our findings support previous observations on cofactors of HPV [19].

This study lays the foundation for a more comprehensive prospective study of cervical cancer and, on the basis of these findings, in promoting cervical cancer screening and discouraging the population from practicing lifestyles that place the individual at risk. We consider the results to be revealing despite the limitations of the study. Much needs to be done to change these sociocultural factors, and it may take time.

There is also a need for broader, all-encompassing research to address the remaining questions about cervical cancers in African countries, especially in Nigeria, and also to study the impact of the high prevalence of HIV/AIDS on the natural history and therapeutic outcome of cervical cancers. A multidisciplinary protocol for prospective research on cervical cancers is currently being developed to evaluate the outcome of treatment and prognostic factors. HPV vaccines, which have been shown recently to be safe and to be highly effective in preventing precancerous lesions of the cervix and which are being commercialized, offer great hope for the prevention of cervical cancer in Africa and other developing countries where screening programs have been difficult or impossible to establish [20].

Conclusion

In northern Nigeria, the risk factors for cervical cancer include active sex at a young age, multiple sexual partners (due to polygamy, divorce and remarriage) and multiparity. In this environment, because of sociocultural factors including religion, illiteracy and poverty, many women are exposed to these risk factors that increase the chances of acquiring genital HPV infection, the central and necessary cause of cervical cancer. The situation is worsened by poor uptake of screening programs.

References

- Jenkins D., Sherlaw-Johnson C., Gallivan S.: "Can papilloma virus testing be used to improve cervical cancer screening?". *Int.* J. Cancer, 1996, 65, 768.
- [2] Jamal A., Murray T., Samuels A., Ghafoor A., Ward E., Thun M.L.: "Cancer statistics". CA Cancer J. Clin., 2003, 53, 5.
- [3] Muñoz N., Bosch F.X., de Sanjose S., Tafur L., Izarzugaza I., Gili M. *et al.*: "The causal link between human papillomavirus and invasive cervical cancer: a population-based case-control study in Colombia and Spain". *Int. J. Cancer*, 1992, *52*, 743.
- [4] Parkin D.M.: "Cancer in developing countries". Cancer Surv., 1994, 19/20, 519.
- [5] Schiffman M.H., Brinton L.A.: "The epidemiology of cervical carcinogenesis". *Cancer*, 1995, 76, 1888.
- [6] Walboomers J.M., Jacobs M.V., Manos M.M., Bosch F.X., Kummer J.A., Shah K.V. *et al.*: "Human papillomavirus is a necessary cause of invasive cervical cancer worldwide". *J. Pathol.*, 1999, 189, 12.
- [7] Thomas J.O., Herrero R., Omigbodun A.A., Ojemakinde K., Ajayi I.O., Fawole A. *et al.*: "Prevalence of papillomavirus infection in women in Ibadan, Nigeria: a population-based study". *Br. J. Cancer*, 2004, *90*, 638.

- [8] Fonn S., Bloch B., Mabina M., Carpenter S., Cronje H., Maise C. et al.: "Prevalence of pre-cancerous lesions and cervical cancer in South Africa - a multicentre study". S. Afr. Med. J., 2002, 92, 148.
- [9] La Ruche G., Ramon R., Mensah-Ado I., Bergeron C., Diomandé M., Sylla-Koko F. *et al.*: "Squamous intraepithelial lesions of the cervix, invasive cervical carcinoma, and immunosuppression induced by human immunodeficiency virus in Africa". Dyscer-CI Group. *Cancer*, 1998, 15, 2401.
- [10] Ferlay J., Bray F., Pisani P., Parkin D.M.: "GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, version 1.0 Lyon: IARC Press 2001, 5.
- [11] Vizcaino A.P., Moreno V., Bosch F.X., Muñoz N., Barros-Dios X.M., Parkin D.M. *et al.*: "International trends in the incidence of cervical cancer: I. Adenocarcinoma and adenosquamous cell carcinomas". *Int. J. Cancer*, 1998, 75, 536.
- [12] Brinton L.A., Hamman R.F., Huggins G.R., Lehman H.F., Levine R.S., Mallin K. *et al.*: "Sexual and reproductive risk factors for invasive squamous cell cervical cancer". *J. Natl. Cancer Inst.*, 1987, 79, 23.
- [13] Winkelstein W.: "Smoking and cervical cancer: current status-a review". Am. J. Epidemiol., 1990, 131, 945.
- [14] Castellsague X., Bosch F.X., Muñoz N., Meijer C.J.L.M., Shah K.V., de Sanjosé S. *et al.*: "Male circumcision, penile human papillomavirus infection, and cervical cancer in female partners". *N. Engl. J. Med.*, 2002, *346*, 1105.
 [15] Meanwell C.A.: "The epidemiology and etiology of cervical
- [15] Meanwell C.A.: "The epidemiology and etiology of cervical cancer". In: Blackledge G.R.P., Jordan J.A., Shingleton H.M. (eds.). Textbook of Gynecologic Oncology. Philadelphia: WB Saunders, 1991, 250.
- [16] Kostopoulou E., Keating J.T., Crum C.P.: "Pathology". In: Eifel P.J., Levenback C. (eds.). Cancer of the Female Lower Genital Tract. London: BC Decker, Inc., 2001, 9.
- [17] Robert M.E., Fu Y.S.: "Squamous cell carcinoma of the uterine cervix: a review with emphasis on prognostic factors and unusual variants". *Semin. Diagn. Pathol.*, 1990, 7, 173.
- [18] Gates A.E., Kaplan L.D.: "AIDS malignancies in the era of highly active antiretroviral therapy". *Oncology* (Huntingt) 2002, *16*, 441.
 [19] Castellsague X., Muñoz N.: "Cofactors in human papillomavirus"
- [19] Castellsague X., Muñoz N.: "Cofactors in human papillomavirus carcinogenesis-role of parity, oral contraceptives, and tobacco smoking". *Natl. Cancer Inst. Monogr.*, 2003, 31, 20.
- [20] Koutsky L., Harper D.: "Current findings from prophylactic HPV vaccine trials". *Vaccine*, 2006, 24S3, S3/114.

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