
RESEARCH COMMUNICATION

Cervical Carcinoma in a Muslim Community

Farhana Badar*, Natasha Anwar, Fouzia Meerza, Faisal Sultan

Abstract

Objectives: The aim of the research was to review the distributions of age, stage at presentation, and morphology of patients presenting with carcinoma of the cervix in a predominantly Muslim population. **Study design:** This retrospective study was conducted at a comprehensive cancer diagnostic and treatment facility situated in Lahore, Pakistan, reviewing the medical records of the patients. **Patients and methods:** Four-hundred and nineteen cervical cancer patients were registered at the hospital during a nine-and a half year time period extending from December 1994 to June 2004. Histology was confirmed by exfoliative cervical cytology typically by means of Papanicolaou smear. The International Federation of Gynecology and Obstetrics classification was used to stage the disease. Univariate analysis on factors as age, stage at presentation, and morphology was conducted. **Results:** 1) The age distribution of the 419 patient cohort was recorded to be as follows: mean 49.2 years (SD 11.7, range 11-85 years) and mode 50 years (37 patients). Only one patient was less than 18 years. 2) Of these 419 patients, 73.5% (308/419) had squamous cell carcinoma (SCC), 7.9% (33/419) had adenocarcinoma, and 0.7% (3/419) had adenosquamous carcinoma; of the remainder, 1.4% (6/419) had rare types (3 each of sarcoma and small cell carcinoma) and 16.5% (69/419) had unspecified carcinoma. 3) Only two patients (0.5%) were identified as being in stage 0, 49/419 (11.7%) in stage I, 140/419 (33.4%) in stage II, 90/419 (21.5%) in stage III, 52/419 (12.4%) in stage IV, and 86/419 (20.5%) as not being evaluable. **Conclusions:** A large proportion of patients (67%) presented in stages II to IV and only 12% presented early at stages 0 or I. This emphasizes the need for early detection of this tumor in our population. Accordingly, the importance of detection of the pre-clinical stage of the disease by considering the possibility of initiating a cost-effective screening measures needs to be emphasized in our setting.

Key Words: Cervical cancer - cost-effective measures - early detection

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Introduction

In a developing country like Pakistan, the availability of limited information on disease prevalence is an impediment to program planning and evaluation that are required for prevention and control of disease. The country is marred by problems as poverty, malnourishment, and infectious diseases, which are major causes of morbidity and mortality in the region. Resources for chronic diseases are scarce and the vast majority of cancer patients are diagnosed in advanced stage in the course of the disease. Also, infrastructure for cancer control and prevention is close to being non-existent (Brundtland, 2002).

In low-resource settings, in order to enable cancer detection at an early stage in the natural history of the disease, the World Health Organization (WHO) recommends the use of a low-cost and cost-effective community approach in a pilot area with a relatively good access to diagnosis and treatment (Brundtland, 2002). In the city of Lahore in Pakistan, a complete cancer care facility has been identified that treats the vast majority of patients free of cost. An attempt was made to study the

age, stage, and morphology of carcinoma of the cervix uteri with a public health perspective. The objective of carrying out this pilot study was not to draw any inferences about cause and effect from the results, but to have a preview of the disease in a low-income country with a predominantly Muslim population, where scarcity of data has caused hindrance in designing projects for prevention and early detection of disease.

Cervical cancer is the second commonest malignancy in women all over the world with over 470,000 new cases recorded every year (Stewart, Kleihues, 2002). Globally, it accounts for 230,000 deaths annually, of which more than 80% occur in developing countries of the world (Stewart, Kleihues, 2002). At the Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH & RC) located in Lahore, Pakistan, cancer of the cervix accounted for the fourth commonest malignancy, following cancers of the breast, ovary, and oral cavity, amongst female patients registering at the hospital (1994 – 2005) (<http://www.shaukatkhanum.org.pk>). Even though cancer of the cervix uteri was the fourth most common cancer seen in our hospital population, 5-year

*For Correspondence: Cancer Registry and Clinical Data Management, Shaukat Khanum Memorial Cancer Hospital and Research Center, 7/A, Block R-3, MA Johar Town, P O Box 13014, Postal Code 54770, Lahore, Pakistan. Email farhana@skm.org.pk; farhana_badar@yahoo.com

data from the a population-based registry in Karachi South (Bhurgr, 2001) suggest a lower ASIR (7.4/100,000) compared with India (ASIR 20-35/100,000) and high prevalence countries like Peru (ASIR 35-93/100,000) (Stewart and Kleihues, 2002).

Epidemiological studies conducted during the past 30 years have consistently indicated that cervical cancer risk is strongly influenced by measures of sexual activity: number of sexual partners, age at first sexual intercourse, and sexual behaviour of the women's male partners. Genital infection with certain types of human papillomavirus (HPV) is the most important risk factor for cervical cancer. The male sexual partner is supposed to be the vector of the infection. A study in Denmark demonstrated lower HPV DNA detection rate in circumcised men consistent with the suggested lower risk of cervical cancer in female partners of circumcised men (Svare et al., 2002). Other studies have shown that circumcised men are more likely than uncircumcised men to have genital warts, but when present, warts are more often located on the distal portion of the penis amongst uncircumcised men. This could be explained by either non-specific resistance to proximal penile warts conferred by the foreskin, or heightened susceptibility to various HPV types in uncircumcised men, some of which may confer subsequent immunity to genital warts (Jensen et al., 1993). Identification of the subtype of HPV present is important as genital warts are caused by the non-oncogenic types HPV 6 and 11, whereas other subtypes, notably types 16 and 18, 31 and 33, have been confirmed as agents which cause cervical cancer. 'High risk' HPV types have been found to be present in close to 100% of all cervical cancers. Research has indicated that women with a mild or borderline smear result who have no evidence of high risk HPV infection are very unlikely to develop cervical cancer. HPV testing has therefore been proposed as a means of distinguishing women in this group who have a higher risk of developing cervical cancer from those who have very low risk.

Patients and Methods

The authors reviewed the records of cervical cancer patients who were registered at SKMCH & RC during a nine and a half year time period extending from December 1994 to June 2004. Histology was confirmed by exfoliative cervical cytology typically by means of Papanicolaou smear. Disease stage was determined using the clinical staging system adopted by the International Federation of Gynecology and Obstetrics. Descriptive statistics were obtained for variables under study. These included age at presentation, histology, and stage at diagnosis. Analysis was conducted using the Statistical Package for Social Sciences (SPSS), version 10.0. Results were considered significant at a p-value of 0.05.

Results

The age distribution of the 419 patient cohort was recorded to be as follows: mean 49.2 years (range 11-85, SD 11.7) and mode 50 years (37 patients). Only one patient

was less than 18 years. The 25th percentile was 41 years, 50th percentile, 50 years and, 75th percentile, 56 years. Of these 419 patients, 73.5% (308/419) had SCC, 7.9% (33/419) had adenocarcinoma, and 0.7% (3/419) had adenosquamous carcinoma; of the rest, 1.4% (6/419) had the rare types (3-small cell carcinoma, 2-rhabdomyosarcoma, and 1-leiomyosarcoma) and 16.5% (69/419) had unspecified carcinoma. Statistics on age of the 308 cases of squamous cell carcinoma patients was nearly the same as that of the original cohort of 419 except for the age range, which was 25-82 years. Table 1 summarizes the stage and age distribution, after removing 86 whose stage was not evaluable. The average age increased from stage I to IV ($p > 0.05$). The mean age of those in stage I was 45.9 years versus 50 years for those in stage IV.

Discussion

Our hospital data show that the average age at presentation of the cervical cancer patients increased from 45 to 50 years with an advancement in disease stage. However, the means were not substantially different from one another. The distribution of cervical carcinoma cases was highest in stage II (140/333; 42.04%). This is despite the fact that the majority of cases had SCC, which has a pre-invasive stage and there is a long latent period of intraepithelial neoplasia.

Only two patients in the 419 patient cohort were identified in stage 0, the pre-invasive stage. The question that arises is, if this scenario also reflects a lack of awareness amongst females about the importance of screening for latent disease. To expand this debate a little further, it has been reported in a 72,613 patient study carried out in England that a very high proportion of South-Asian women (nearly a third of those born overseas) were recorded as "never screened" (Webb et al., 2004). Also it has been documented in a study conducted in the United States, that despite the high socio-economic status of women of South-Asian ethnicity, the rates of Pap smear receipt were lower than the national recommendations (Chaudhry, 2003). In essence, this may show a deficiency of knowledge amongst Asian women about the significance of screening for cervical cancer.

In context of a Muslim population, low frequency of dysplastic smears in a hospital population has recently been reported by Wasti and colleagues but, as the authors note, the population studied may not be representative of the overall population (Wasti et al., 2004). The average age at presentation in this study was 49 years which is four to nine years after the peak age with dysplasia seen by Wasti. This would be consistent with the natural history of

Table 1. Ages of the Patients Stratified by Stage of the Disease (N=333)

Stage	N	Mean (years)	Min. age	Max. age
0	2	37.5	30	45
I	49	45.9	18	81
II	140	49.5	18	76
III	90	50.3	25	85
IV	52	49.5	32	81

disease. The detection of 50% abnormal smears, as reported by Wasti, was also seen in another study conducted in Pakistan (Rasul et al., 1991). However, in this case, the highest rate of abnormal smears was found in the 45-54 year age group (Rasul et al., 1991).

The crux of the matter is that a proper screening program makes it possible to detect the precursor lesions and prevent the debility associated with advanced disease. The reason for this is that the treatment given at the stage of intraepithelial neoplasia is very effective. It has been documented that 2-5 times as many women may have potential precursor lesions of cervical cancer as have invasive cancer (Herdman, 2000). It has also been proven that there are striking benefits associated with conducting an organized screening through Papanicolaou-stained cervical smear once in every woman's life-time and that, these go up exponentially with regular screening (Herdman, 2000). Moreover, the value of cervical cancer screening with the Pap test or, potentially, with HPV testing, is that pre-cancers and early cancers found by these tests are completely curable. Some studies suggest human papillomavirus testing is as sensitive as the Pap test for detecting cervical cancer and high-grade precancerous changes (Wright et al., 2000; Schiffman et al., 2000). Experts say HPV testing has potential value in countries that lack adequate Pap screening services. The value of HPV testing is strongly influenced by a woman's age. HPV infection is quite common amongst young women but most of these infections eventually resolve themselves without treatment and never lead to a cancer or even a high-grade pre-cancer. Amongst women over 40, however, HPV infection carries a greater risk of eventually leading to cancer.

Since the cytology-based screening is cost-prohibitive as a community program in low-resource settings including ours, the role of alternative, low-technology approaches has to be considered here. One of the recommended techniques is "Visual Inspection with Acetic acid" (VIA) (Herdman and Sherris, 2000; Sankaranarayanan et al., 1998); another "Visual Inspection with Lugol's Iodine" (VILI) is being evaluated as an independent primary screening test. In the visual inspection test following the application of 5% acetic acid to the cervix, detection of a white area along the squamocolumnar junction constitutes a positive test. The application of VIA does not require a laboratory infrastructure and the results are available immediately, permitting further investigation and treatment on the same day. It can be used as a community-based approach by designing a screening program for married women who are 35 years or older (Brundtland, 2002; Rasul et al., 1991).

This approach is based on the premise that providing a limited number of screenings (once in every woman's lifetime) in the target group (35-50 years) will provide maximum population coverage in the community. This may be feasible in the Pakistani city of Lahore where the existence of a cancer care facility with appropriate services for diagnosis and treatment can be utilized. This may also be a fruitful area for future research work on the epidemiology of cervical cancer in a predominantly Muslim population. Further, since the acquisition of

human papillomavirus type 16 (HPV-16) may cause the formation of genital cancer in a proportion of patients, there have been endeavors to prevent this infection. A large controlled trial of a vaccine against HPV-16 showed reduced incidence of HPV-16 infection as well as related cervical intraepithelial neoplasia (Koutsky et al., 2002). A vaccine against HPV is now approved by the US Food and Drug Administration (2006), and there is hope, that this will form an important component in strategies to prevent cervical cancer.

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