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# Human Immunodeficiency Virus and Carcinoma Cervix

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**Abstract: Problem statement:** Carcinoma of the cervix is the second leading cause of death in women in the world. Human Papilloma Virus (HPV) which plays a major role in the etiology of cervical cancer is said to have the same mode of transmission as the Human Immunodeficiency Virus (HIV). Hence the curiosity to learn the prevalence, incidence and association of cervical cancer in HIV positive patients paves the way for the present study. **Approach:** Forty patients who were positive for HIV were scrutinized for other diseases at our hospital. The patients underwent gynaecological examination at the department of obstetrics and gynaecology. The blood samples of the patients were tested by both the Enzyme Linked Immunosorbent Assay (ELISA) and confirmed by Western Blot in the Serology Department. The cervical biopsies were examined microscopically in the Department of Pathology. **Results:** Two of the patients had invasive cervical carcinoma and were undergoing radiotherapy for the same. One patient was detected HIV positive when his spouse was diagnosed with cervical invasive carcinoma. A total of three out of forty patients had cervical cancer. Therefore the prevalence of invasive cervical cancer in HIV infected patients is 7.5%. **Conclusion:** A percentage of 7.5 is nearly close to the prevalence of 6 and 5% reported by other studies. This study therefore emphasized the association of cervical cancer and possibly the human papilloma virus with HIV infection. Further studies using HPV DNA probes in concurrence with HIV testing in patients with carcinoma cervix and intraepithelial lesions would contribute much and confirm the association of HPV and HIV co-infection.

**Key words:** Invasive cervical cancer, human immunodeficiency virus, human papilloma virus, co-infection

## INTRODUCTION

Cervical cancer is the most common cancer among women in India and its incidence in India alone is estimated as 100,000. The incidence of HIV infection in India is increasing at an alarming rate. The relation between HIV infection and cervical neoplasia was recognized in the 1980s and, in 1993, the CDC criteria for defining AIDS were modified to include invasive squamous cancer of the cervix as an AIDS defining condition in a HIV positive woman. Since both HIV and HPV are sexually transmitted these two infections commonly coexist. HIV infection may increase risk for persistent HPV (Schiffman *et al*., 2005) infection and promote reactivation of latent HPV infection increasing the risk for cervical and anal cancers. The aim of the present study is to identify the prevalence of invasive cervical cancers (Ylitalo *et al*., 2000) in HIV infected individuals. Cervical cancer is probably one of the best known examples of how infection with a virus can lead to cancer. In humans and animals, cell division is regulated largely by two proteins-one called Rb and the other p53. Recently it has been found that two genes in HPV, the so-called E6 and E7 genes, produce proteins that can attach themselves to Rb and p53 and block their effect on regulating cell division (Massimi and Banks, 1997). When this happens, the infected cells reproduce without any control. While the virus serves only as the initiating event, over time some of the wildly growing cells develop permanent changes in their genetic structure that cannot be repaired. Once this happens, some may eventually turn into cancer cells.

## MATERIALS AND METHODS

Forty patients who were HIV positive by the Elisa were confirmed by the Western Blot in the Serology department of our Hospital Laboratory. They were

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chosen at random among the HIV positive patients. The age range was between 25-60 and they were females. They were screened in the department of Obstetrics and Gynaecology for genital lesions. Cervicovaginal smears and cervical biopsies were done using colposcopic guidance (De Vuyst *et al*., 2005). The smears and biopsies were processed, sectioned and stained in the department of Pathology. The Papaniculaou method and Hematoxylin and Eosin stains were used for the staining procedure. Microscopic evaluation of the smears and cervical biopsies revealed the lesions. Forty patients in the same age range whose serology was HIV negative were studied as the control group. Their cervicovaginal smears and cervical biopsies were taken on the basis of routine screening (Syrjänen *et al*., 2005). Similar microscopic evaluation was done and the results were compared.

## RESULTS

It was observed that 3 out of the 40 patients had frank invasive carcinoma of the cervix on histopathological examination. They were Squamous cell carcinoma, one was grade 2 and two were grade 1. Three of the patients had Cervical Intraepithelial Neoplasia (CIN). One had low grade CIN and two were high grade lesions. Two of the patients had Atypical Squamous Cells of Undetermined Significance (ASCUS). The forty subjects in the control group had no evidence of cervical carcinoma. Only one patient had cervical intraepithelial lesion, low grade CIN and one ASCUS was reported.

## DISCUSSION

The observation in this study highlights the fact that there is a higher prevalence rate of cervical carcinoma in HIV positive individuals as compared to the HIV negative group. Further, the cervical intraepithelial lesions which could possibly be the precursors of invasive carcinoma are more prevalent with HIV positive subjects. These findings imply an indirect evidence to the association of Human papilloma virus infection along with human immunodeficiency virus (Yu *et al*., 2005). But further studies using DNA probes for the HPV could serve as a direct evidence for its association with HIV. Moreover, mere association of HPV with HIV cannot justify that HIV is the cause for HPV infection and therefore for carcinoma cervix. The patient could have had an intraepithelial lesion or carcinoma cervix prior to contracting a HIV infection or HIV serology testing could have been done at a later stage when CIN has progressed to carcinoma. These analytical flaws could be well addressed if the study starts at a much earlier stage before the woman becomes sexually active and follow up studies should continue to the ultimate point of progression to carcinoma cervix. This mandates a really long term study indeed added with the HPV antigen assay or HPV DNA detection in cervical smears and biopsies to certify its presence.

Patients affected by Human Immunodeficiency Virus (HIV) infection present an elevated risk of developing cancer. In the last 10 years, the relationship between Human Papilloma Virus (HPV) infection and female Cervical Intra-epithelial Neoplasia (CIN) has been established. Several studies have described an increased prevalence of both cervical HPV infection and CIN among HIV-positive women compared to HIV-negative ones. A high recurrence rate of CIN after standard treatment has been noted in HIV-infected women (Strickler *et al*., 2005) and the severity of these lesions seems to be inversely correlated to immune function. Taking into account these data, the Centers for Disease Control (CDC) since 1993 have included invasive cervical carcinoma among the AIDS-defining conditions. Once cervical cancer develops in HIV-positive women, the disease may be aggressive and less responsive to treatment. A primary means by which HIV infection may influence the pathogenesis of HPV-associated cervical pathology (Tjalma *et al*., 2005) is by molecular interaction between HIV and HPV genes. Although these have not been well defined, an upregulation of HPV E6 and E7 genes (Nicol *et al*., 2008) expression by HIV proteins (such as tat) has been postulated by some authors. Cervical cytology appears to be adequate as a screening tool for the cervical intra-epithelial neoplasia in HIV-positive women, but the high recurrence rate and multifocality of this disease reinforces the need for careful evaluation and follow-up of the entire anogenital tract in these women. Probably in the next few years, cervical tumors will represent one of the most frequent complications of HIV infection, a part of progression through AIDS. This points to a need for greater interdisciplinary co-operation for a best disease definition and for the development of effective prevention measures.

## CONCLUSION

A percentage of 7.5 is nearly close to the prevalence of 6 and 5% reported by other studies. This study therefore emphasized the association of cervical cancer and possibly the human papilloma virus with HIV

infection. Further studies using HPV DNA probes in concurrence with HIV testing in patients with carcinoma cervix and intraepithelial lesions would contribute much and confirm the association of HPV and HIV co-infection.

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