J Obstet Gynecol Ind Vol. 54, No. 1 : January/February 2004 Pg 73-76

# Sexually Transmitted Diseases and Carcinogenesis

Jain *Madhu*, Gupta *Charu*, Kumar *Mohan*

*Department of Obstetrics and Gynecology, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221 005.*

**OBJECTIVE** – To find out the prevalence of various sexually transmitted diseases (STD) and cervical intraepithelial neoplasia (CIN) in our community and the correlation between them and to study the other risk factors associated with CIN. **METHODS** – In this cross sectional study, 1308 sexually active women attending gynecological OPD were screened cytologically for cervical dysplasia CIN and STDs. **RESULTS** – STDs were detected in 22.02% and CIN in 21.3% of our patients. Presence of STD was strongly associated with CIN (RR-2.42; 95% CI 1.68-3.45). The most prevalent genital infection detected on cytological examination was trichomonal vaginalis in 7.04% followed by human papillama virus (HPV) and herpes simplex virus (HSV) each in 4.89% of women. Individually HPV infection showed strongest association with CIN (RR-5.21; 95% CI 4.10-6.59). **CONCLUSION** – There is a definite need for routine cytological screening for early detection of CIN in all patients with STDs.

Key words : cervical intraepithelial neoplasia, carcinogenesis, sexually transmitted diseases

## Introduction

Sexually transmitted diseases (STDs) are a major pubic health problem. An estimated 685,000 people are infected worldwide everyday with a sexually transmitted disease (STD). STDs are highly prevalent in India too, being placed 3rd among diseases by WHO, next only to malaria and pulmonary tuberculosis[1]. Various sexually transmitted pathogens have been implicated in the pathogenesis of cervical cancer[2]. In India, more than 90,000 women report with cervical cancer annually and 75% of them are diagnosed in the advanced stage. (R. Ananth, Personal Communication, December 1995). This work was undertaken with following objectives: (a) to find out the prevalence of various STDs and cervical intraepithelial neoplasia (CIN) in our community (b) to find out correlation between STDs and CIN, which will confirm the need for routine cytological screening in STD patients and (c) to study the other risk factors associated with CIN.

## Methods

The study was carried out on 1308 sexually active women attending the gynecological outpatient department. They were randomly selected, using a table of random numbers. The patients who had received antibiotics in the month before enrollment or those with bleeding per vaginum were excluded. A proper history to assess the risk factors for cervical intraepithelial neoplasia in the form of age at consummation of marriage, number of children, number of sexual partners, smoking and use of contraception was recorded. However, it was difficult to establish the number of sexual partners. After clinical examination, the endocervical canal was sampled. The pointed end of the Arye's spatula was used to obtain the sample, the spatula being rotated through 360° lightly, scraping the cervix to obtain a surface biopsy. It was smeared on a slide and fixed. Cytological evaluation was done following Bethesda System, 1991. Various organisms were detected on cytology by following features (a) Candida albicans – presence of hyphae and spores in smears (b) Trichomonas vaginalis – presence of trichomonads, presence of five or more lymphocytes and more than three polymorphonuclear leucocyles (c) Herpes Simplex – ground glassing of nuclei, binucleation with nuclear moulding, enlargement of nuclei, peripheral thickening of nuclear chromatin (d) Human papillomavirus – koilocytes, peripheral thickening of cytoplasm, perinuclear cytoplasmic clearing (halo), dyskaryosis (e) Chalamydia trachomatis – target like inclusions, large distinct inclusion containg vacuoles and (f) Bacterial vaginosis – presence of clue cells. Tests for $HIV_1$ and $HIV_2$ were carried out using UBI HIV ½ EIA kit. RPR Test was done for serological diagnosis of syphilis specifically. The data were analysed using statistical analysis system (SAS). Tests of significance were performed using $X^2$ method. Univariate regression analysis was done to identify potential risk factors and relative risk (RR) was calculated to estimate the risk.

## Results

The patients' age varied from 12 to 55 years with STD present in one form or the other in 288 (22.02%) patients. At the top of the list was trichomonas in 7.04%, followed by HPV and HSV each in 4.89% of the women. Surprisingly syphilis was detected in

*Paper received on 27/06/03 ; accepted on 20/11/03*

Correspondence :
Dr. Jain Madhu
2-B, Brij Enclave, Sunderpur, Varanasi - 221 005.
Tel : 0542-2316146, 231703 email:drpmjain@rediffmail.com

**Table 1 : Prevalence of Various Sexually Transmitted Infection**

| Organism / Infection | Number (n=1308) | Percentage (%) |
|---|---|---|
| Human papilloma virus | 64 | 4.89 |
| Herpes simplex virus | 64 | 4.89 |
| Trichomonas vaginalis | 92 | 7.04 |
| Candida | 08 | 0.61 |
| Bacterial vaginalis | 40 | 3.06 |
| Chlamydia | 12 | 0.92 |
| Syphilis | 08 | 0.61 |
| Total | 288 | 22.02 |

**Table II : Prevalence of HIV Seropositivity Among Women Studied.**

| Elisa for HIV | Number (n=400) | Percentage (%) |
|---|---|---|
| Positive | 02 | 0.5 |
| Negative | 398 | 99.5 |

**Table III : Cytological Results Among Women with STDs**

| Organism/infection | Number (%) of women with | | | |
|---|---|---|---|---|
| | No CIN (n=1024) | CIN (n=284 | Low Grade CIN (n=204) | High Grade CIN (n=80) |
| Human papilloma Virus | 04 (0.4) | 60 (21.1)[a] | 56 (27.45) | 04 (5.00) |
| Herpes simplex virus | 36 (3.50) | 28 (9.90)[b] | 20 (9.80) | 08 (10.00) |
| Trichomonas | 80 (7.80) | 12 (4.20) | 12 (5.90) | - - |
| Candida | 08 (0.08) | - - | - - | - - |
| Bacterial Vaginosis | 36 (3.50) | 04 (1.40) | 04 (1.96) | - |
| Chlamydia | 04 (0.40) | 08 (2.80) | - - | 08 (10.00) |
| Syphilis | 08 (0.80) | - - | - - | - - |

[a] $p < 0.01$ [b] $p < 0.05$ Figures in brackets represent percentages.

**Table IV : Risk Factors for CIN (Univariate Logistic Regression Analysis)**

| Variables Risk factors | CIN (Present) (n=284) | CIN (Absent) (n=1024) | RR (95% CI) |
|---|---|---|---|
| STD | 100 (35.21) | 188 (18.35) | 2.42 (1.68-3.45) |
| Smoking | 24 (8.45) | 48 (4.68) | 1.59 (1.01 – 2.47) |
| Parity ≥ 3 | 36 (12.67) | 212 (20.70) | 0.62 (0.29-1.26) |
| Age at Consummation of marriage < 18 yrs | 204 (71.83) | 588 (57.42) | 1.66 (1.07-2.55) |
| Human papilloma virus | 60 (21.12) | 4 (0.39) | 5.21 (4.10-6.59) |
| Herpas simplex virus | 28 (9.85) | 36 (3.51) | 2.13 (1.44-3.11) |
| Trichomonal vaginals | 12 (4.22) | 80 (7.81) | 0.58 (0.26-1.21) |
| Bacterial vaginosis | 4 (1.40) | 36 (3.51) | 0.45 (0.18-1.04) |
| Contraception used | 5 (1.76) | 203 (19.82) | 0.10 (0.01-0.53) |
| Illiterate women | 193 (67.95) | 682 (66.60) | 1.21 (0.71-2.01) |
| Lower socioeconomic status[a] | 193 (67.95) | 416 (40.62) | 2.40 (1.67-3.42) |

[a] As per modified Kuppaswamy socioeconomic status Figures in brackets represent percentages.

only eight women (0.61%). Bacterial vaginosis was present in 3.06% (Table I). Out of 400 women screened for HIV, antibodies could be detected only in two i.e. in 0.5% (Table II). The cervical cytological findings were consistent with cervical intraepithelial neoplasia in 284 patients (21.3%). HPV was seen in 21.1% of CIN cases and this association was significant ($p<0.01$). HSV also showed significant association with CIN ($p<0.05$). Other organisms failed to show any significant association with CIN by simple $X^2$ test and p-value (Table III).

Univariate logistic regression revealed that all those women who married below the age of 18 years, smokers (>12 biri/day), suffering from STDS, belonging to lower socioeconomic status and illiterate ones had increased chances of CIN (Table IV). All those women who showed STDs, either one or two, had a significant increase in CIN (RR 2.42, 95% CI 1.68-3.45) compared to those without STDs. Amongst the STDs, the HPV infection revealed maximum chances of CIN (RR, 5.21) followed by HSV (RR 2.13). Similarly women with <18 years age at consummation of marriage had 1.66 fold higher risk of development of CIN as compared to those over 18 years at consummation. However, those with three or more pregnancies did not carry a higher risk for CIN in our study.

**Discussion**

Women with STDs commonly share two major risk factors for cervical carcinoma: early onset of coitus and multiple sex partners. A random sample of sexually active women revealed inflammatory changes in cervical smears in 34.4% in our study which is close to 41% reported by Mishra et al[3] and 42% reported by Sinha[4]. Inflammatory changes in cervical cytology often indicate the presence of STD. One or more sexually acquired infection were present in 22.02% of the patients quite comparable with that reported by others (Sinha[4] 20.4%, Wilson et al[5] 21.6%).

Since inflammatory conditions predispose to precancerous manifestations in cervical epithelium, it is imperative to determine their cause and likely association with coexisting pathogens in the genital tract. The most prevalent infection in our study was Trichomonas vaginalis (7.04%). Other Indian studies have also found it to be most common (Mishra et al[3] - 10.4%; Sinha[4] - 8%). It may be attributed to poor hygiene. What came as a surprise was very low detection rate of Chlamydia trachomatis (0.92%). On the contrary, it has been reported to be the most common STD in the West[5]. Since genital infection with Chlamydia trachomatis in young women is often asymptomatic, it could be the reason for low detection rate in our patients. It is also important to remember that Chlamydia trachomatis has no specific cytological feature other than inflammatory changes and may coexist with other infections as well.

Herpes simplex virus (HSV) and human papilloma virus (HPV) each were present in 4.89%. While Wilson et al[5] and Sinha[4] reported the incidence to be 3% and 6.8% respectively, Mishra et al[3] reported it to be quite low (HPV 0.6%; HSV 0.1%).

Seropositivity for AIDS in India has been reported to be as 24.22 per thousand by National AIDS Control Organization (NACO) in March, 1999[6]. Sexually transmitted diseases enhance HIV transmission as they increase the number of white blood cells which are both targets as well as source of HIV in the genital tract. Genital inflammation may also cause microscopic cuts that can allow HIV to enter the body. Finding of CIN in 21.3% of cytologic smears in our study is similar to that reported by Sinha[4] as 21.2%. However Chhabra et al[7] could find dysplastic smears in 3.8% of patients only. This was perhaps because of the latter being community based study in contrast to our institution based study.

Various sexually transmitted diseases have been implicated in the etiology of CIN. Our study also revealed significantly higher chances of occurrence of CIN in women with STDs as compared to women without STD (RR 2.82, 95% CI 1.68-3.85). This is consistent with the view that carcinoma of cervix is a STD.

Women suffering from either HPV or HSV stand significantly higher risk of developing CIN as compared to those without these infections (HPV RR 5.21; 95% CI 4.10-6.59 and HSV RR 2.13; 95% CI 1.44-3.11). However, trichomonal vaginalis and bacterial vaginosis were not found to be potential risk factors for CIN in our study inspite of their high prevalence. High risk of HPV infections for development of CIN might be due to E6 and E7 oncoproteins which are produced as transcriptional products after integration of HPV DNA into host genome and cause the degradation of $P_{53}$ and Rb tumour suppressor gene products. The suppression of proto-oncogenes results in cervical neoplasia. However, Koustsky et al[8] and Murthy et al[9] have reported a higher risk for development of CIN due to HPV infection (RR 11 and 5.9 respectively) in comparison to those women who are not associated with this infection.

Early detection and treatment of various STDs may thus considerably reduce the mortality from cervical carcinoma. The communities should be educated on safe sex practices, avoiding multiple partners and casual sex

and encouraged to use barrier contraceptives to decrease the occurrence of STD and hence cervical carcinogenesis.

**References**


1. Kapur TR. Pattern of STDs in India. *Ind J Dermatol Venerol Lepr 1982; 48: 23-34.*
2. Population Reports Series L, Number 9: *Issues in World Health, June, 1993.*
3. Mishra JS, Das K, Tandon PJ et al. Sexually transmitted pathogens and cervical carcinogenesis. *J Obstet Gynecol Ind 1992; 43: 380-3.*
4. Sinha G. The prevalence of wart virus infection and its association with premalignant lesions of the cervix. *J Obstet Gynecol Ind 1994; 44: 931-5.*
5. Wilson JD, Robinson AJ, Kinghorn SA et al. Implications of inflammatory changes on cervical cytology. *Br Med J 1990; 300 : 638-40.*
6. National AIDS Control Organisation: Ministry of Health and Family Welfare, Govt. of India. Surveillance for HIV infection in India, *Period of Report - March 1999.*
7. Chhabra MS, Swarup G, Swarup K et al. Correlation of cervical abnormalities with abnormal smears in mass screening programme of cervical cytology. *J Obstet Gynecol Ind 1991; 41: 681-3.*
8. Koutsky LA, Holmes KK, Critchlow NS et al. A cohort study of the risk of cervical intraepithelial neoplasia grade 2 or 3 in relation to papilloma virus infection. *N Engl J Med 1992; 327 : 1272-8.*
9. Murty NS, Sehgal A, Satyanarayana L et al. Risk factors related to biological behaviour of precancerous lesions of uterine cervix. *Br J Cancer 1990; 61: 732-6.*