

Sexually Transmitted Diseases and Carcinogenesis

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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 papilloma 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 public 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'. Various sexually transmitted pathogens have been implicated in the pathogenesis of cervical cancer", 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.

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 Ayrer'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 leucocytes (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) *Chlamydia trachomatis* - target like inclusions, large distinct inclusion containing vacuoles and (f) Bacterial vaginosis - presence of clue cells. Tests for HIV₁ and HIV₂ 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 X² method. Univariate regression analysis was done to identify potential risk factors and relative risk (RR) was calculated to estimate the risk.

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

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

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Table I : 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 vaginosis	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			
	NoCIN (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)			

$p < 0.01$ $^b P < 0.05$ 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)
SID	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)
Herpes 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)

^aAs 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 χ^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 al³ and 42% reported by Sinha¹. Inflammatory changes in cervical cytology often indicate the presence of STD. One or more sexually acquired infections were present in 22.02% of the patients quite comparable with that reported by others (Sinha¹ 20.4%, Wilson et al⁵ 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 al³ - 10.4%; Sinha¹ - 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 West². 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 al⁵ and Sinha¹ reported the incidence to be 3% and 6.8% respectively, Mishra et al³ 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, 1999⁶. 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 Sinha¹ as 21.2%. However Chhabra et al⁴ 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 vaginosis and bacterial vaginosis were not found to be potential risk factors for CIN in our study in spite 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 P₅₃ and Rb tumour suppressor gene products. The suppression of proto-oncogenes results in cervical neoplasia. However, Koustsky et al⁷ and Murthy et al⁸ 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.

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