

CYTOLOGICAL STUDY OF VIRAL INFECTIONS IN CARCINOMA CERVIX

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SUMMARY

Cervical cytological studies have been carried out in 5278 women attending Gynaec OPD of Queen Mary's Hospital, Lucknow (March 1989 - December 1994) for early detection of cervical cancer, to identify any evidence of viral STDs (Herpes and Condyloma) and to find out if these pathogens have any etiological role in causation of the dreaded disease. Cytomorphological manifestations of herpes simplex was seen in 9 cases (0.1%) while Koilocytosis suggestive of condylomatous lesions in cervix was detected in 35 cases (0.6%). Thus condyloma was six times more frequent than herpes.

A total of 429 cervical dysplasias and 49 malignant smears were encountered in the study. Herpes was associated with cervical dysplasia in 66.6% while condyloma with 45.7% of cases. Malignancy was noticed in 3 herpes cases (33.3%) but in none of the condyloma cases. There is thus some relation between onset of premalignancy with presence of these two viral organisms.

INTRODUCTION

Implication of sexually transmitted viral pathogens in causation of cervical neoplasia have been a focus of great attention in recent years. The two viruses - herpes simplex (HSV) and human papilloma (HPV) have been found frequently infesting human

female genital tract and it is found that both these viral pathogens induce malignant changes in the cervical epithelium, initially being incorporated at molecular level (DNA) and subsequently producing profound characteristic cytopathological changes in epithelial squames.

The herpes simplex virus produces herpes genitalis which is very common in low

socio-economic class. The cervical and vaginal lesions generally do not produce any sign or symptom and hence are unable to get identified on clinical examination. Since herpes infection can easily be detected in routine cervical smears by their characteristic ground glass appearance of nuclei and intra-nuclear inclusions, clinically silent form of the disease can thus be easily diagnosed and treated.

Human papilloma virus manifests clinically in the form of warts with papillary projections in the lower genital tract of female. These condylomatous lesions are easily identifiable due to their typical koilocytotic pattern in epithelial cells.

Cytological screening of women attending Gynae OPD of Queen Mary's Hospital, Lucknow was carried out from March 1989 for cytological diagnosis of different sexually transmitted diseases and cervical smears in 5278 patients have been cytologically examined till December 1994. The present paper deals with cytological findings of these two viruses in routine cervical smears in the perspective of their probable association with dysplasia of uterine cervix and cervical carcinoma.

MATERIALS AND METHODS

The present study comprised of 5278 women attending Gynae OPD of Queen Mary's Hospital, Lucknow from March 1989 to December 1994. The age of patients ranged from 18 to 60 years and parities from 0 to 8. Since these women presented themselves at the clinic because of some complaints, majority were either symptomatic or revealed pathological lesions on the cervix on clinical examination. In each case, after careful gynaec checkup, a scrape

smear was collected from the squamocolumnar junction of the cervix. Endocervical smears were also made whenever needed. The smears were immediately fixed in absolute alcohol and later stained according to the Papanicolaou's technique. Cytopathological grading of cervical smears was carried out in accordance with WHO classification of 1973. Presence of herpes simplex and condyloma were reported whenever their characteristic cytomorphological changes were seen in the squamous cells. Serological tests, however, could not be performed in any of the cytologically detected herpes and condyloma cases due to lack of facility.

RESULTS

Incidence of Herpes simplex and condyloma in cervical smears of 5278 women was found to be as follows :-

Herpes simplex - 0.1% (9 cases)
Condyloma - 0.6% (35 cases)

The frequency of the condylomatous lesions was thus six times higher in routine cervical smears than that of herpes.

Cervical dysplasia was seen in 429 smears of total 5278 women examined (8.1%) while malignant smears were encountered in 49 cases (0.9%). Herpes and condyloma was found associated with following number of dysplastic and malignant smears :-

Type of infection	NO. of cases	Dysplasia	Carcinoma cervix
Herpes	9	6 (66.6%)	3 (33.3%)
Condyloma	35	16 (45.7%)	-

Herpes was associated with dysplastic changes in cervical epithelium in 66.6% of cases (6 out of 9) while this was

seen in 45.7% of condyloma cases (16 out of 35). As regards malignancy, 3 malignant smears showed presence of herpes infection while none of condyloma cases displayed evidence of malignancy. Herpes had thus more affinity with cervical carcinoma while in condyloma cases, the smears were predominately dysplastic only.

Incidence of both viral infections and cytopathological changes in the cervix were also investigated in relation to different predisposing factors such as pathological lesions of cervix, gynaecological symptoms, age and parity. The purpose of the analysis was to identify high risk group from these factors and also to find out any correlation between viral infections and cytopathological changes in the cervix among these parameters.

Different types of clinical lesions detected in 5278 women of the study group are shown in Table I along with distribution of viral infections and cervical neoplasia.

Prevalence of both herpes and condyloma was maximum in women with cervixes which bled on touch. Incidentally, the dysplasia rate was also maximum in this group. Malignant smear was also detected in 1 case of this group. Hence cervixes bleeding on touch appear prone to viral infections and cytopathological changes and need mandatory cytological check up. Condyloma was also frequent in eroded or hypertrophied cervixes while herpes was next common in clinically diagnosed cases of cervical carcinoma.

Number of viral infections and cervical dysplasia and malignancy detected with different types of gynaecological symptoms have been depicted in Table II. Maximum number of herpes cases were seen in contact bleeding cases (6.9%) while incidence of condyloma was highest in women complaining of pain in lower abdomen (5.1%). Cervical dysplasia was maximum in women complaining of

Table I
Incidence of viral infections, Cervical dysplasia and carcinoma
in different types of cervical lesions.

Cervical Lesions	No. of cases (5278)	Herpes simplex (9 cases)	Condyloma (35 cases)	Dysplasia (429 cases)	Carcinoma Cervix (49 cases)
Erosion cervix	653	1 (0.1%)	8 (1.2%)	26 (3.9%)	1 (0.07%)
Hypertrophied cervix	1452	1 (0.06%)	16 (1.1%)	196 (13.5%)	1 (0.05%)
Cervixes bleeding on touch	103	2 (1.9%)	4 (3.8%)	28 (27.4%)	1 (0.1%)
Endocervicitis	69	-	-	14 (20.2%)	-
Cancer cervix	282	3 (1.1%)	-	25 (8.9%)	46 (16.3%)
Healthy cervixes	2719	2 (0.07%)	7 (0.2%)	140 (5.1%)	-

Table II

Association of viral infections, cervical dysplasia and carcinoma with
Gynaecological symptoms

Symptoms	No. of cases (5278)	Herpes simplex (9 cases)	Condyloma (35 cases)	Dysplasia (429 cases)	Carcinoma Cervix (49 cases)
Contact bleeding	29	2 (6.9%)	3 (3.4%)	5 (17.2%)	-
Menorrhagia	114	-	2 (1.5%)	16 (14.1%)	6 (5.2%)
Leucorrhoea	255	3 (1.2%)	4 (1.6%)	55 (22.1%)	10 (4.1%)
Postmenopausal bleeding	47	-	-	4 (9.3%)	1 (1.7%)
Pain in lower abdomen	58	-	3 (5.1%)	4 (6.8%)	-
Asymptomatic	4775	4 (0.09%)	25 (0.05%)	345 (7.1%)	32 (0.7%)

Table III

Relation between age and incidence of viral S.T.Ds
and cervical cytopathology

Age Group	No. of cases (5278)	Herpes simplex (9 cases)	Condyloma (35 cases)	Dysplasia (429 cases)	Carcinoma Cervix (49 cases)
Upto 20 yrs	59	-	-	11 (20.3%)	-
21 - 30 yrs	848	-	5 (0.5%)	103 (12.1%)	4 (0.5%)
31 - 40 yrs	976	2 (0.2%)	13 (1.3%)	181 (19.2%)	5 (0.5%)
above 40 years	3395	7 (0.2%)	8 (0.2%)	174 (5.1%)	19 (0.5%)

leucorrhoea (22.1%) followed by contact bleeding (17.2%). Malignant smears were, however, more frequent in menorrhagia cases (5.2%) followed by vaginal discharge (4.1%). Thus symptomatic women especially complaining of contact bleeding and leucorrhoea warrant cytological check up to rule out any occurrence of viral STDs

and precancerous manifestations in the cervical epithelium.

Age distribution of 5278 women of the study has been shown in Table III. Herpes was not found earlier than 30 years of age while condyloma was also detected in age group of 21-30 years. The dysplasia rate did not show any progression with

Table IV
Relation between parity and viral infections and cervical cytopathology

Parity	Herpes cases (5278)	simplex (9 cases)	Condyloma (35 cases)	Dysplasia (429 cases)	Carcinoma Cervix (49 cases)
Nulliparous	34	-	-	8 (23.5%)	-
Para 1	137	-	-	17 (12.1%)	-
Para 2	355	1 (0.3%)	3 (0.8%)	93 (26.4%)	2 (0.5%)
Para 3	1483	2 (0.1%)	15 (1.1%)	156 (10.7%)	8 (0.5%)
Para 4 and above	3169	6 (0.1%)	17 (0.5%)	197 (6.1%)	39 (1.2%)

increasing age. On the contrary, the incidence of dysplasia was maximum in younger women upto 20 years of age (20.3%) in contrast to 5.1% observed in older women beyond 40 years. This raises need for including younger women in cytological screening programme. The malignant smears were not detected earlier than 28 years.

Partitywise distribution of 5278 women has been shown in Table IV along with incidence of viral STDs and cervical dysplasia and malignancy. Both herpes and condyloma were seen in women with 2 children or more and incidence of both these viral STDs did not show any rise with increasing parity. The dysplasia rate was interestingly enough maximum in nulliparous women (23.5%) as against 6.1% in para 4 or more. Malignant smears were encountered in women with para 2 and above and there was a definite rise in incidence with high parity.

COMMENTS

Cytological investigation of two viral infestations (herpes and condyloma) revealed their low incidence in 5278 women

screened. Condyloma was, however, six time more frequent than herpes (0.6% as against 0.1%). Prevalence rate of condyloma has been reported very high (20.6 per thousand) in Western countries (Morin & Miesels 1981). Since condylomatous lesions have been found sexually transmitted due to human papilloma virus harboured by them, sexual promiscuity which is very high in West (Waugh 1971) and rare in Indian women, may be the reason for such a remarkable difference in incidence between two continents.

The present study revealed association of Herpes infection with cervical dysplasia in 66.6% of cases (6 out of 9) while this figure was 45.7% in condyloma cases (16 out of 35). Herpes was also seen in 3 malignant smears (33.3%) while none of the condyloma cases showed evidence of malignancy. Miesels & Fortin (1978) have also reported association of condyloma in 42.6% of dysplastic lesions of cervix and have noticed progression of condylomatous lesions to dysplasia and carcinoma-in-situ in 4.9% of cases. It is thus very likely that these genital viruses induce precancerous

manifestations in the cervical epithelium and picking up of viral infections by cytology smears and subsequent treatment may help in checking progression of the lesion to carcinoma.

All of the herpes cases were seen beyond 30 years of age while condyloma was also seen in 21-20 years age group. Miesels & Fortin (1978) have also reported peak incidence of condyloma in younger women of 21-25 years in Canada. Parity, however, was found not to have any bearing on the

prevalence rate of viral STDs.

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REFERENCES

1. W.H.O. *Monograph Series 3* : 1973.
2. Morin C. and Miesels A., *Gynaec Oncol.* 12: 111, 1981.
3. Waugh M. *Brit. Med.* 2 : 527, 1971.
4. Miesels A. and Fortin R. *Acta Cytol.* 20 : 505, 1978.