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Original Research Paper

Gynaecology

ROLE OF CO-INFECTION OF HPV AND HSV IN CERVICAL CANCER

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ABSTRACT

Introduction- Carcinoma cervix (CaCx) is one of the most common malignancy affecting women. Cervical dysplasia is an excellent example of what preventive medicine can accomplish. Thus screening programs for the detection and diagnosis of premalignant and malignant lesions of the cervix have been effective. Human Papilloma Virus (HPV) with their oncogenic strains is virtually primary cause for CaCx. HSV-2 being spread primarily by sexual contact, also has role in CaCx. And if its coinfection, the rate is ??

Methodology- A Cross Sectional Study done among 150 women, having the history suspicious of CaCx. These were subjected to cervical biopsy. The reports of which were followed through histopathology, immunohistochemistry and PCR and were clinically correlated.

Observation – Co-infection of HPV and HSV was found significantly associated with chronic cervicitis (p value =0.011) and squamous cell carcinoma (p value=0.004)

Conclusion – It `can be suggested by these findings that HSV is playing role in the pathogenesis and if the women is secondarily infected with HPV there are increase chances for cervical cancer and therefore the screening levels should go a step ahead in identifying the HSV and coinfection at an early stage.

KEYWORDS : Carcinoma cervix, Co-infection, HSV, HPV.

INTRODUCTION –

Prevention is better than cure is a widely accepted view point. But, like in many diseases where preventive measures are difficult to imply, at least early identification and diagnosis is better than the one made too late. Treatment too is more effective if instituted at early stage that is while primary pathology is still reversible and before any complications have developed.

A very great example has been in relation to cervical malignancies where it is quite indent that initiatives of Cervical Cancer mortality prevention with intensive program of cervical screening have been highly successful in many developed countries (1) with significant drop in its incidence (8,19,9,2).

Early detection of the cervical abnormalities especially dysplastic lesions of the cervix and their adequate treatment will go a long way in reducing the mortality due to Cervical Cancer. The therapy of precancerous lesions plays an important part in cancer prevention. Mass prophylactic examination to detect the precancerous lesion, may, in the long run be cheaper than the treatment of established cancers (7).

Thus regular follow up can decrease cervical cancer incidence. The causative role of high risk types of HPV in the development of CIN II/III and cervical cancer is well established. Other factors postulated to play a role in the development of cervical cancer; include human cytomegalovirus, human herpesvirus6 (4,5) human immuno deficiency virus (18), and HSV-2. HSV-2 is spread primarily by sexual contact, and therefore the risk factors are similar to those of other sexually transmitted diseases. (17).

Of particular interest is the association of HSV with HPV and cervical carcinogenesis. HSV-2 is transmitted sexually (similar to HPV) and can cause recurrent, painful ulcers. Since HSV and HPV are transmitted sexually and infect the same cell type, both viruses have the potential to interact with each other, impacting neoplastic progression.

HSV-2 RNA can be detected in a higher proportion of CIN than of squamous cell carcinoma, supporting the hypothesis that HSV-2 is linked to the initiation of cervical carcinoma (13)

The potential interaction between HPV and HSV is supported with several lines of evidence (14,15,16,10,6,12). First, ulcerative herpetic lesions facilitate HPV access to the basal layer. Second, the inflammatory response induced by herpes may suppress the T helper cell mediated immune response. Third, herpes infection does induce the production of nitric oxide resulting in cellular DNA damage together with direct actions by herpes viruses on host cellular DNA. Fourth, Herpes virus infection accelerates replication of HPV and increases the integration of HPV DNA sequences.

Interaction between HPV and HSV, two important human pathogens in a system where both viruses replicate. HSV-1 and HSV-2 (208) are both able to replicate to high titers in HPV-positive host tissue.

OBJECTIVE-

Thus, this study is conducted to estimate association between cervical cancer and coinfection of HPV and HSV.

MATERIAL AND METHODOLOGY

- Study design- cross sectional.
- Study time period- 1 year.

- **Inclusion Criteria: -**

1.Sexually active women with clinically detected cervical abnormalities.

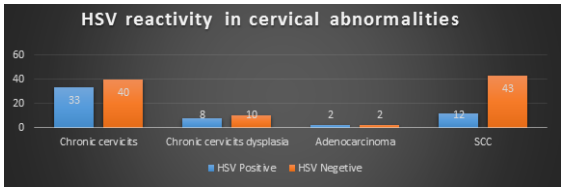
- **Exclusion Criteria: -**

1. Cases exposed to radiotherapy or chemotherapy.
2. Samples showing evidence of clinico-histopathologically infections other than HPV and HSV.
3. Those patients who are not giving consent.

- 150 women were selected randomly by sequential sampling with history suspicious of cervical lesion.. The detailed history was enquired and entered in a predesigned Performa. All these women were clinically examined, visual inspection (VI) was done. And the patients were subjected to cervical biopsy. The biopsy sample were subjected to histopathological and HPV and HSV testing by immunohistochemical examination and PCR, were clinically correlated.

OBSERVATIONS-

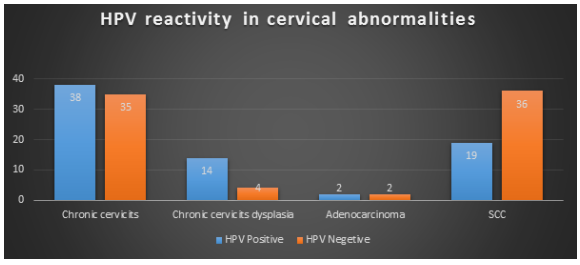
A) Co-relation of HSV reactivity and cervical lesions-



BAR CHART -01

- HSV was significantly assosciated with chronic cervicitis with a p value of 0.035 and also with squamous cell carcinoma with a p value of 0.004 %. (bar chart -01)

B) Co-relation of HPV reactivity and cervical lesions



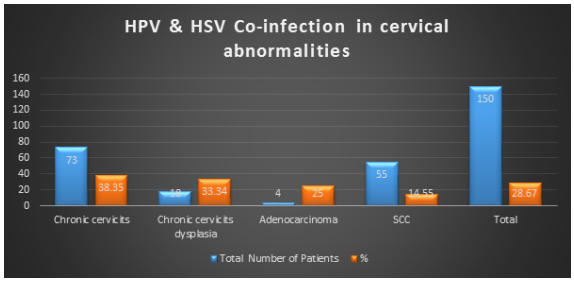
BAR CHART-02

- Chronic cervicitis with dysplasia and HPV has a significant relationship with a p value of 0.008 and with squamous cell carcinoma with a p value of 0.008.(Bar chart -02)

B) Co-relation of HPV & HSV Co-infection and cervical lesions –

TABLE-01

Cervical Biopsy	HPV & HSV Positive	Total Number Of Patients	%	P Value	Association
Chronic Cervicitis	28	73	38.35	0.011	Significant
Chronic Cervicitis Dysplasia	6	18	33.34	0.641	Not Significant
Adenocarcinoma	1	4	25	0.869	Not Significant
Scc	8	55	14.55	0.004	Significant
Total	43	150	28.67		



BAR CHART -03

- The coinfection was significantly associated with chronic cervicitis, with a p value of 0.011 and was also found significantly associated with squamous cell carcinoma, with a p value of 0.004. (Table 03) (Bar chart-03)

DISCUSSION-

These findings were consistent with the study of **jones et al** (3). HSV-2 is transmitted primarily by sexual contact and therefore has been implicated as a risk factor. It is hypothesized that persistent or abortive infections induce permanent genetic alterations that interfere with differentiation of cervical epithelium and subsequently induce abnormal proliferation. Thus, HSV-2 may be a cofactor in some but not all cases of cervical cancer.

Even the coinfection of HPV and HSV increasing the rates cervical cancer were supported by the study conducted by **Zhao Y et al 2012 Dec** (20) stated that HSV 2 coinfection with HPV in cervical intraepithelial neoplasia and squamous cell carcinoma was strongly higher than in healthy women (ORs = 34.2, P < 0.01 for cervical intraepithelial neoplasia; ORs = 61.1, P < 0.01 for squamous cell carcinoma). The obtained results indicated that the presence of HPV is associated closely with cervical cancer, and that HSV 2 infection or co-infection with HPV might be involved in cervical cancer development.

The other study by **baldauf et al** (11) also found in their results that the role of HSV as a cofactor with HPV 16 and HPV 18 in cervical neoplasia.

CONCLUSION-

The coinfection of HPV and HSV was significantly associated with benign lesions of cervix and squamous cell carcinoma so HSV might be setting up the background for HPV to easily infect the preinfected cells of HSV and cause cervical cancer

OR

HSV might be altering the pathogenesis of HPV infection thus increasing the rate of cervical cancer.

And therefore the screening levels should go a step ahead in identifying the HSV, HPV and coinfection at an early stage so that proper treatment can be planned for both HSV and HPV infection and the stages of carcinoma can be reversed.

ABBREVIATIONS

- Cx- cervix
- Ca Cx- Carcinoma cervix
- STDs- Sexually transmitted diseases
- CIN- Cervical intraepithelial neoplasia
- HPV- Human papilloma virus
- HSV- Herpes simplex virus
- Pap- Pap smear
- VI- Visual Inspection
- Eros- Erosion
- CC- Chronic cervicitis
- PCR – Polymerase Chain Reaction

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