ORIGINAL ARTICLE

A STUDY ON CERVICAL PAP SMEAR EXAMINATION IN PATIENT LIVING WITH HIV

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ABSTRACT

Background: Decline in morbidity & mortality due to cervical cancer in developed countries can be mainly attributed to early detection of precancerous & cancerous lesions due to extensive screening programmeof cervical Pap smear examination. HPV infection is a known etiological agent for cervical cancer. HIV infected women are at higher risk of contracting HPV infection due to immune compromised status.
Objective: Present study has been undertaken mainly to detect precancerous & cancerous lesions as well as inflammatory lesions in female patients living with HIV & to emphasize the fact that Pap smear examination should be established as a part of routine protocol for examination in these women.
Methods: The study was carried out on 407 HIV infected females attending Integrated Counseling &Testing Centre of government institute. As controls, 200 females (not falling under high risk category), attending the Obstetrics& Gynecology OPD with various gynecological complaints were taken & results were compared.
Results: Squamous cell abnormalities were found about four times high as compared to control group(*P*value <0.05). High incidences of squamous cell abnormalities were noted in patients with high parity (parity three or more).
Conlcusion: Regular gynecological examination including Pap smear examinations is highly recommended for HIV infected females.Pap smear examination is a simple, cheap, safe & practical diagnostic tool for early detection of cervical cancer in high risk population.

Keywords: HIV, Pap smear, patient living with HIV (PLWH)

INTRODUCTION

Cervical cancer & infection with Human Immuno-deficiency Virus (HIV) are both important public health problems in developing countries. The Human Papilloma Virus (HPV) is the known major etiologic agent for the development of cervical cancer. In immune competent subjects, HPV infections normally clear in 6-24 months in 70% of females. However the studies have shown that the women infected with HIV have a higher prevalence of HPV infection, are more likely to develop persistent HPV infection & are more frequently infected with multiple HPV types & thus are at greater risk (ten times increased risk) of developing cervical intraepithelial neoplasms. Additionally, highly active anti-retroviraltherapydoes not seem to impact this increased rate or persistent HPV infections in this population. Dysplasia has been reported in 15 to 40 % of HIV infected women & these rates are 10-11 times higher than those observed among HIV negative women. Both the Centre for Disease Control & Prevention and the Agency for Healthcare Policy & Research recommend that HIV infected women should have a gynecological evaluation including a Pap smear & pelvic examination as a part of their initial evaluation [1, 2]

Cases & deaths due to cervical cancer have declined markedly in most industrialized countries mainly due to extensive screening programmes. The reason that cytological screening is so effective in preventing cervical cancer is that majority of cancer cases are preceded by a long standing latent period.Pap smear is the standard screening tool to detect the presence of abnormal cells that could become cancerous. Apart from detecting early cervical cancers,Pap smear also initiate the immunological clearance of HPV, therefore reducing the risk of cervical carcinoma.

Present study has been undertaken mainly to detect precancerous & cancerous lesions as well as inflammatory lesions in female patients living with HIV & to emphasize the fact that Pap smear examination

should be established as a part of routine protocol for examination in these women.

MATERIAL & METHODS

In present study, all cases (407 cases) were HIV infected females attending ICTC(Integrated Counseling & Testing Centre)at tertiary level hospitalranging in age from 18 to 71 years with a mean of 35 years& SD of 9 years. As controls, 200 females attending the Obstetrics & Gynecology OPD not falling under high risk category were taken. They were ranging in age from 20 to 71 years with a mean of 38.1 years& SD of 10.5 years. The study has been conducted after getting ethical committee clearance from the same institute.

Their detailed clinical history particularly related with various risk factors, obstetric & menstrual history along with clinical examination findings including per abdominal examination, per speculum examination, per vaginal examination & relevant investigations were recorded.Pap smear of these females (case & control subjects)were collected, fixed, examined & reported as per standard Bethesda system 2001.

Statistical analysis: Forcategorical variables, proportions were compared usingFisher's exact test & chi-square test. A two-tailed *P* valueof< 0.05 was considered significant. The odds & risk based analysis were also done. The statistical analysis was done with the help of EpiInfo™version 7.0.8.3 software, CDC**.**

RESULTS

Out of 407 study cases15 smears & out of 200 controls five smears were reported as unsatisfactory for evaluation (USFE) &were excluded from the study. Cervical Pap smear findings in case vs control group are shown in table 1.

Overall incidence of maximum HIV infected cases were in age group 26-35 years (52.56 %).In control group, maximum subjects were in the age group 36-45 year (36.41 %) followed by 26-35 year (35.38 %).44.56 % of casesubjects had complaints of whitish discharge & 15.85% had abdominal pain.In control subjects 31.80 % had whitishdischarge & 22.06% had abdominal pain.32.65% cases were multiparous with parity three or more. On per speculum examination of case subjects, 58.41 % did not show any abnormality in cervix, 13.52 % had cervical erosion, 13.78 % had discharge per vaginum, 3.32 % had hypertrophied cervix & 2.55 % had uterine descent. In control subjects, 34.35 % subjects did not show any abnormal finding in cervix, 12.83 %were with cervical erosion, hypertrophied cervix in 7.69 %, discharge per vaginum in 14.88 % & uterine descent in 10.76 %.

In cases the most common infection was Bacterial Vaginosis (29.39%) followed by Candida infection (1.78 %). There were 2.01 % females who had infection with more than one organism, 0.5 % had Trichomonasvaginalis infection & 0.24 % had Herpes simplex infection. In control subjects the most common infection was Bacterial Vaginosis (28.72 %) followed by Candida infection (1.54 %).There were 1.03 % females who had infection with more than one organism, 1.03 % had Trichomonasvaginalis infection.
The scenario of CD4count in cases of present study along with Pap smear findingsand statistical comparison of case & control subjectsare shown in table 1.The two tailed *P* value of present study was < 0.05 along with odds ratio of 3.36 & risk ratio of 3.38 for HIV infected women as compare to control subjects. There were about 28 cases of epithelial abnormalities in which women were multiparous with parity two or more, five caseswith parity one & only a single case was of nulliparous woman.

Table 1: Cervical Pap smear findings with clinical history

	Control	Case
Size (n)	200	407
Age (years)	38.1 ± 10.5	35.0 ± 9.0
Use of Contraception	-	376 (92)
Parity	-	2.0 ± 1.2
CD 4 cell count		
>500	-	53 (13)
200 – 500	-	313 (76.9)
< 200	-	41 (10)
Gynecological complaints	200 (100)	107 (26)
Cervical smear cytology		
Unsatisfactory for evaluation	5 (2.5)	15 (3.7)
NILM without inflammatory changes	124 (62)	202 (49.6)
NILM with inflammatory changes	63 (31.5)	132 (32.4)
NILM with atrophic changes	03 (1.5)	24 (5.89)
ASCUS	04 (2)	13 (3.19)
LSIL	00 (0)	11 (2.7)
ASC-H	00 (0)	03 (0.73)
HSIL	01 (0.5)	06 (1.47)
AGUS	00 (0)	01 (0.25)
Squamous cell carcinoma	00 (0)	00 (0)
Adenocarcinoma	00 (0)	00 (0)
Small cell carcinoma	00 (0)	00 (0)
Histocyotology correlation	-	5
Odd Ratio	3.61	
Risk Ratio	3.38	
***P* value**	<0.05	

Values in brackets ( ) reflects %

Out of 33 cases with epithelial abnormalities reported by cytology, follow up for histopathological correlation with cervical biopsy was available only in five cases. A case of ASCUS was reported in histopathology as "Chronic cervicitis"; ASC-H as "moderate to severe dysplasia &LSIL as "In situ squamous cell carcinoma".Out of two cases of HSIL one case was reported as "Moderate to severe dysplasia" & the other was reported as "In situ squamous cell carcinoma" on histopathology.

DISCUSSION

Results were compared with various studies carried out on HIV infected females as well as on general population. In both cases & controls, the most common complaint was whitish discharge per vaginum (46.55 % in cases &33.86 % in controls).In studies on general population the incidence of discharge per vaginum was 42.5 % in Sherwani et al, 27.43 % in Dhaubhadel et al& 28.5 % in Sharma et al. [3-5] The high incidence in case subjects is due to more susceptibility of HIV infected females to infection due to lowered immunity. The second most common complaint was abdominal pain. The other less common complaints encountered during present study were muco-purulant discharge, irregular menstruation, burning micturition, bleeding per vaginum, something coming out per vaginum etc. The findings of present study were quite comparable to other studies.

Table 2: Cervical Pap smear findings in HIV infected females in various studies

	Amphan et al[9]	Leibenson et al[10]	Jennifer et al[11]	Present study
CD4 less than 200/µL (in %)	28.87	39.75	92.67	10.07
No Epithelial cell abnormalities (in %)	84.6	79.76	34.5	87.89
Epithelial cell abnormalities (in %)	15.4	20.24	66.5	8.34
ASCUS	2.8	0	15.3	3.19
LSIL	8.5	19.05	40	2.7
HSIL	3.5	1.19	10.2	1.47
ASC-H	0.6	0	1	0.73
AGUS	0	0	0	0.25

Incidence of infective lesion in general population was 6.05 % in Mulay et al, 9.86 % in Ranabhat et al & 22.02 % in Jain et al.[6-8] It was 33.92 % in case subjects of present study as compared to 32.32% of control subjects in the present study.There were 2.01 % caseswith multiple infections which were almost doubled as compared to 1.03 % in controls subjects. In other studies in general population incidence of multiple infections was0.43 % in Mulay et al &0.47 % in Ranabhat et al. [6, 7]The reason for this difference can be explain by the fact that in present study cases were HIV infected females & had lowered immunity & so more susceptible to multiple infections.

Among various studies on HIV infected women like Amphan et al there were 28.87 % cases with CD4 count less than 200/µL & median CD4 count was 324 /µL.[9] In Leibenson et althere were 39.75 % cases with CD4 count less than 200/µL & median CD4 count was 307 /µL.[10] In Jennifer et al there were 92.67 % cases with CD4 count less than 200/µL & median CD4 count was 125 /µL.[11] In HIV infected femalesof present study there were 10.46 % cases with CD4 count less than 200 /µL & median CD4 count was 328 /µL. The median CD4 count was quite comparable in all of them except in Jennifer et alin which it was very low.

The incidence of epithelial abnormalities in various studies on HIV infected females were 15.4 % in Amphan et al, 20.24 % in Leibenson et al& 66.3 % in Jennifer et al.[9-11] In case subjects of the present study incidence of epithelial cell abnormalities was 8.68 % that was low compared to other studies on HIV infected women.Furthermore the incidence of various epithelial abnormalities in case subjects of present study are shown in details &are compared with other studies in table 2.From the table 2, it appears that incidenceof epithelial abnormalities increases with the more number of cases showing CD4 count less than 200/µL & probably this may be the reason for comparative low incidence of epithelial abnormalities in present study as the number of cases with CD4 count less than 200/ µL was only 10.46 % in present study.

Null hypothesis can be rejected on the basis of statistical analysis of present study. *P* value in present study was< 0.05. It signifies that the difference is statistically significant & signifies that HIV infected women have more risk of having cervical epithelial abnormalities as compared to general population.

In various studies on general population, number of females with parity-3 or more were 50.85 % in Dhaubhadel et al, 47.04 % in Aggarwal et al& 32.65 % in case subjects of present study.There were 32.57 % females with parity-2 in Dhaubhadel et al, 28.18 % in Aggarwal et al & 31.38 % in case subjects of present study.There were 14.87 % females with parity-1 in Dhaubhadel et al, 10.59 % in Aggarwal et al & 26.54 % in case subjects of present study.There were 1.71 % Nulliparous femalesin Dhaubhadel et al,14.19 % in Aggarwal et al & 9.43 % in case subjects of present study.[4, 12]It is very well seen that in all the above studies maximum number of females had parity-3 or more.

CONCLUSION

The incidence of epithelial abnormalities in case subjects was quite high (four to eight times more) as compared to control subject of present study & other studies on general population.The high incidence of dysplasia in HIV infected women supports the recommendation of Centre for Disease Control for regular gynecological examination includingPap smears in all these women even if they do not have any

gynecological symptoms. There is a need to have a regular follow up so that appropriate therapeutic measures can be taken.Health awareness programmes particularly by media &government with their implementation in the form of screening camps would be of great help to these high risk HIV infected women.High incidences of squamous cell abnormalities were noted in patients who had high parity (Parity-3 or more) suggesting that squamous cell abnormalities are directly related to multiparity.

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