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Original Research Paper

Gynaecology

A STUDY ON PAP SMEAR IN HIV POSITIVE WOMEN IN TERTIARY CARE HOSPITAL

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ABSTRACT HIV positive women have a higher risk of HPV infection and its persistence as well as infection by multiple HPV genotypes due to their immunocompromised state. With the advent of antiretroviral therapy, life expectancy has been considerably increased in HIV positive individuals. This benefit gives an ample time and opportunity to detect precancerous lesions at an early stage thus preventing their progression with adequate treatment. Early detection by pap smear has been recognized as an effective screening tool in this population. **MATERIALS AND METHODS** It is a hospital based cross-sectional analytical study carried out in Gauhati Medical College and Hospital from March 2019 to June 2020. Pap smears from 100 HIV positive women between 18 years to 60 years were taken randomly. CD4 counts were obtained. Association between risk factors and pap smear abnormality was determined by calculating chi square and p value. Attributable risk and relative risk of the study population in relation to risk factors were determined. **RESULTS AND DISCUSSION** Out of the 100 cases, most cases had NILM (79%). 19% cases had intraepithelial lesions (14 ASCUS, 3 LSIL, 2 HSIL) and none had invasive cancer. CD4 count below 200cells/cu mm, unhealthy cervix, early age at coitarche (<18 years), multiple partners of spouse and postmenopausal state are significant risk factors for developing pap smear abnormality (P <0.05). Even though association of multiple sexual partners was not found to be significant, but such women were found to have a higher relative risk of developing Pap smear abnormality. Parity, complaints of vaginal discharge, bleeding per vaginum, post coital bleed, age, pregnancy, multiple partners are not significant risk factors for pap smear abnormality (P> 0.05). **Conclusion:** In our study we found that HIV positive women were at a risk of developing pap smear abnormality. Various risk factors were found to have significant association with development of pap smear abnormality in these women. As HIV positive patients are in touch with health care professionals for their primary disease, this opportunity should be utilised and screening for cervical cancer should be implemented and awareness about riskfactors and the disease should be raised.

KEYWORDS : Pap smear, HIV positive, risk factor, cervical cancer

1. Introduction

Cervical cancer is the most common gynaecological cancer in women worldwide. It ranks fourth among all malignancies in women. It causes 7.5% cancer deaths in women which accounts for around 275,000 deaths annually. As compared to other malignancies, cancer cervix is preceded by a long latent periodand are asymptomatic. Most new cases are diagnosed following histological evaluation of cervical smears collected during routine screening or biopsies taken from grossly abnormal cervix. Women have a 1 in 132 lifetime risk of developing this cancer[11]. In 2015, the American Cancer Society estimated 12,900 new cases and 4100 deaths due to cancer cervix. Various risk factors for developing cervical cancer have been identified out of which first intercourse below 16 years, multiple sexual partners, high parity, low socioeconomic status, chronic immune suppression and race plays an important role. Most of these risk factors are related to promiscuous sexual activity and exposure to sexually transmitted infections. In third world countries like India, the proportion of secondarilyinfected women with HIV are much higher where predominantly heterosexual route is the most common mode of transmission. Persistent infection with oncogenic HPV is postulated to be the major pathogenic factor. Pathogenesis by HPV starts with the entry of the virus into the basal epithelium of the host via micro trauma or micro abrasions. Majority of the population clears HPV infection in 12 to 18 months. Only a small section of women (10%) fail to clear HPV infection resulting in persistent HPV infection which later leads to abnormal cervical cytological changes. The early recognition of the frequency of cervical cancer in patients with advanced HIV disease led to its definition as an AIDS- defining condition6. On 1st January 1993, Centre for Disease Control and Prevention expanded the surveillance case definition of AIDS which included HIV positive women with invasive cervical cancer even in absence of an opportunistic infection. US AIDS and Cancer Registry have observed that cervical cancer cases in HIV infected women were up to 9 folds higher than the expected number of cases. Prevention of cervical cancer by early detection and treatment of cervical cancer precursors is key, since treatment resources for invasive disease are very scarce.[10] With the advent of antiretroviral therapy, life expectancy has been considerably increased in HIV positive individuals. This benefit gives us an ample time and opportunity to detect precancerous lesions at an early stage thus preventing their progression with adequate treatment. Cervical Cancer could potentially be a major cause of mortality in women on ART if they are never screened. Several studies have noted that if a woman is screened for even once in her lifetime between 30-40 years, her risk of cancer reduces by 25-36% (Goldie et al, 2005, cervical cancer action, 2007).[5,6]

2. MATERIALS AND METHODS

This hospital based cross-sectional analytical study was carried out in the department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital during the period of March 2019 to June 2020. Pap smears from one hundred HIV positive women between age group 18 years to 60 years attending antenatal OPD, Gynaecology OPD and ART centre were taken randomly who fulfilled the inclusion criteria after taking written and informed consent. Strict confidentiality of the patients' identity was maintained throughout the study.

INCLUSION CRITERIA

All HIV positive women attending Antenatal OPD, Gynaecology OPD, ART centre, GMCH from March 2019 to June 2020

EXCLUSION CRITERIA

1. HIV positive females less than 18 years and more than 65 years
2. HIV positive women who have undergone total hysterectomy
3. HIV positive women diagnosed with carcinoma cervix

STEPS

Written and informed consent was taken in a specified consent form. The proforma was filled after a thorough history and general as well as pelvic examination. Speculum examination of cervix and vagina was done followed by pap smear collection. The slides were then stained and analysed according to Bethesda 2001 reporting guidelines. The findings were recorded and the slides were sent to Pathology department, Gauhati Medical college and Hospital for reporting. CD4 count of all the patients were obtained. Association between risk factors and pap smear abnormality was determined by calculating chi square value and p value.Attributable risk and relative risk of the study population in relation to risk factors were also determined.

4. RESULTS AND DISCUSSION

The mean age of the study population was found to be 35.69 years with a standard deviation of 9.74 years (standard error of mean: 0.97).

Mean age of coitarche was 19.84 +/- 3.25 years (standard error of mean: 0.32).

88% of women were in the reproductive age group (menstruating).

14% of the studied subjects were pregnant.

The mean parity was found to be 2.23 with a standard deviation of 0.6.

Table 1: complaints of the subjects

Complaints	no
No complaints	68
Pain abdomen	9
Irregular bleeding per vaginum	4
Discharge per vaginum	16
Post coital bleed	2
Pruritus vulva (leukoplakia)	1

Table 2: per speculum findings

SPECULUM FINDINGS	CASES
Normal cervix	74
Erosion of cervix	21
Cervix bleeds on touch	05
Growth in cervix	0

Table 3: pap smear results

Sl No	RESULTS	NO OF CASES	%
1	NILM (negative for intraepithelial lesion or malignancy) (a) No inflammation (b) Inflammation (c) Organisms (d) Inflammation +Organism	79 28 45 2 4	79% 28% 45% 2% 4%
2	ASCUS	14	14%
3	LSIL	3	3%
4	HSIL	2	2%
5	Invasive cervical cancer	0	0%
6	Inadequate smear	2	2%

Out of the 100 women, 89% had never undergone any previous pap smear tests. 5% were not aware of pap smear tests at all and of the 6% women only half of them knew about their pap smear results. Various established risk factors for cervical carcinoma were studied and their association with development of pap smear abnormality in the study group was estimated.

Table 4: P values of the risk factors studied

RISK FACTOR	P value
Parity (>/=4)	0.23
Age at coitarche	0.0013
HAART duration	<0.001
Multiple partners	0.08
Multiple partners of spouse	0.032
Pregnancy	0.29
CD4 count	<0.0001
Menopause	<0.0001
Age	0.084
Unhealthy cervix	<0.0001
Gynaecological complaints	0.09

Calculated value of chi square is 3.18 and tabulated value is 12.592 at 6 degrees of freedom (d.f) and 5% probability level and hence it is not significant. p value for early age of coitarche (<18 years) is 0.0013. The relative risk of women with coitarche before 18 years for development of pap smear abnormality is 3.80 (95% CI 1.7 to 8.2) and attributable risk 0.32 (95% CI 0.10 to 0.52). The Calculated value of x^2 is 24.51 and tabulated value is 21.026 at 12 d.f in 5% probability level, thus implying lower age of coitarche to be significantly associated with pap smear abnormality. The association between multiple sexual partners and pap smear abnormality is not statistically significant. P value 0.08. Calculated value of chi square is 10.45 and tabulated value is 12.592 at 6 d.f in 5% probability level. However, owing to sociocultural restrictions, promiscuity may not be confided by the subjects which may result in a false interpretation.

The relative risk for developing cervical cytological abnormalities for a woman with multiple partners is 2.85 (95% confidence interval 0.99-5.94). Attributable risk is calculated to be 0.32 (95% CI -0.04 to 0.69). There is significant association between multiple partners of spouse with that of cervical cytological abnormality with a p value of 0.032 (Chi square test). The relative risk was calculated as 1.81 with 95% CI 0.81-3.89 and attributable risk of 0.12 with 95% CI -0.05 to 0.34.

Women who were on HAART for more than 5 years did not show statistically significant risk of developing pap smear abnormality (p value 0.38). A woman who has been on HAART for more than 5 years has a relative risk of 0.54 (95% CI 0.17 to 4.78) and attributable risk of 0.1 (95% CI -0.04 to 0.31) thus implying the effect of risk reduction by HAART usage over 5 years. Calculated value of chi square for duration of HAART is 374.64 and tabulated value is43.773 at 30 d.f in 5% probability level. Thus duration of HAART is a highly significant protective factor.

Women with CD4 count <200cells/cu mm are found to be significantly at risk of developing pap smear abnormality with a p value <0.0001 (Fisher's exact test). The relative risk is 7.43 with 95% CI of 41.3 to 13. and attributable risk of 0.74 (95% CI 0.5 to 0.86). the calculated value of x2 is 51.28 and tabulated value is 21.026 at 12 d.f in 5% probability level thus implying high significance.

Unhealthy cervices on visual inspection by perspeculum examination was found to be significantly associated with

abnormal pap smear results, p value <0.0001 by Fisher's exact test. Calculated value of x2 is 121.18 and tabulated valueis 28.869 at 18 df in 5% probability level thus implying high significance. A woman with an unhealthy cervix has a relative risk of 6.32 with 95% CI 2.76 to 14.60 and an attributable risk of 0.43 with 95% CI 0.2-0.6 for developing cervical epithelial abnormalities.

postmenopausal women are at increased risk of developing cervical epithelial abnormalities. The p value by Chi square test was <0.0001 which is statistically significantwith a relative risk of 5.33 (95% CI 2.56 to 10.22) and attributable risk of 0.54 (95% CI 0.21 to 0.76) .The calculated value of chi square was found to be 32.30 and tabulated value is 14.067 at 7 d.f in 5% probability level.

Higher parity >/=4 doesn't have significant association with cervical epithelial abnormality (p value 0.23). A woman with >/=4 pregnancies has a relative risk of 0.406 with 95% CI 0.107-1.36 and attributable risk of 0.13(95% CI -0.002 to 0.36) for developing cervical epithelial abnormality.

5. CONCLUSION

From the results obtained from this study it is evident that HIV positive women has various risk factors which have significant association with developing cervical epithelial abnormalities which if not treated and followed up will lead to invasive lesions in the cervix. Low CD4 count, age at coitarche, duration of HAART intake and unhealthy cervix have a very strong association with development of pap smear abnormality. Postmenopausal status and multiple partners of spouse are also significant risk factors. However in our study, multiple partners, age and high parity were not found to be significant risk factors for development of pap smear abnormality. This may be attributed to incorrect history given by the subjects and the small sample size.Women with multiple partners have a high relative risk of pap smear abnormality which points towards its positive correlation.It was also noted that the technique of collecting pap smear allows a complete visual inspection of the vulva, vagina and ecto-cervix and this helps in downstaging the disease and prompt referral to a higher centre can be achieved if any suspicious lesion is noted in the genital tract. As HIV positive patients are in touch with health care professionals for their primary disease, this opportunity should be utilised and screening for cervical cancer should be implemented and awareness about risk factors and the disease should be raised.

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