Original Research Article

Prevalence of cervical abnormalities amongst HIV-positive women

Amisha Gheewala[1],*, Suchita Patel[2], Ragini Verma[3]

[1]Dept. of Obstetrics and Gynecology, Shalby Hospital, Surat, Gujarat, India
[2]Dept. of Obstetrics and Gynecology, First Cure Hospital, Surat, Gujarat, India
[3]Dept. of Obstetrics and Gynecology, Government Medical College, Surat, Gujarat, India

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ABSTRACT

Objective: To study the prevalence and variety of cervical squamous intra-epithelial lesions (SIL) by Pap smear screening as an indicator of suspected HPV infection among HIV-infected women in Surat, Gujarat, India.

Materials and Methods: All consecutive asymptomatic HIV seropositive women 18 years and older and attending the Anti-Retroviral Therapy Centre at New Civil Hospital, Surat, India between October 2009 to September 2011 were eligible for inclusion in the study. Participants constituted 439 asymptomatic HIV seropositive women receiving care at the ART centre underwent detailed history taking, physical examination and Pap smear screening.

Results: The incidence of SIL was 8.7% (38/439) in the participants. Further, statistical significance (p value > 0.05) was observed in parity more than two, lost their husband, duration of marriage more than 10 years and CD4 count greater than 250.

Conclusion: An association between HIV infection with pre-invasive changes in the cervical epithelium is noted. Early detection and prompt treatment of these changes after a thorough understanding of the natural history of disease in these women would go a long way in improving the survival as well as the quality of life in this increasing seropositive younger population.

1. Introduction

Carcinoma cervix is the most common gynaecological malignancy in the developing countries and the third most frequently diagnosed cancer in the Indian women.

While evidence of effective screening programs can be seen throughout the developed world, the burden and impact of the disease remains high in developing countries, where 85% of disease related deaths occur. India, which accounts for one sixth of the world's population also bears one fifth of the world's burden of Cervical cancer.[1,2] India's Cervical cancer age-standardized incidence rate (30.7 per 100,000) and age-standardized mortality rate (17.4 per 100,000) are highest in South Central Asia.[1,3]

Data from Mumbai suggest that there may have been a slight decline in cervical cancer incidence in recent years. However, the absolute incidence is still very high, especially in rural areas, and the number of cases grows due to high population growth.[1,2]

India has the highest incidence of invasive cervical cancer (ICC) globally, with 96,922 cases and 60,078 deaths annually[4]— more than three times the combined number of cervical cancer deaths in the western world.[5] India accounts for 10% of the global HIV burden and 85% of the HIV transmission is heterosexual.[5] HIV-infected women have a 3-6 times increased risk for ICC.[6,7]

The Indian National AIDS Control Organization estimates that the number of people living with HIV is approximately 2.14 million (42% of whom are women).[1] This suggests cause for concern given the strong association

* *Corresponding author.*
E-mail address: dramishagheewala@gmail.com (A. Gheewala).

between HIV and HPV infections and evidence of more rapid progression of HPV infections to Cervical neoplasia in HIV infected women. [1,8]

HPV infections, SIL (Squamous Intra-Epithelial Lesions) and Invasive cervical carcinomas occur more commonly in HIV infected women. Cervical dysplasia and Invasive Cervical cancer are more prevalent in HIV-positive women. The latter have a higher rate of HPV infections which is strongly associated with high-grade SIL and invasive cervical cancer. Immune suppression is the factor predisposing HIV positive women to HPV infections. CIN is commoner in HIV infected women with a lower CD4 count or AIDS.

Currently, cervical cytology screening and HPV immunisation are the two methods for ICC prevention. With access to HAART, HIV-infected women are expected to live longer in an immuno-compromised state, thus likely increasing their risk of cervical intra-epithelial lesions and malignancy.

This study assesses the prevalence and variety of cervical squamous intra-epithelial lesions (SIL) by Pap smear screening as an indicator of suspected HPV infection among HIV-infected women.

2. Objectives

Following objectives are considered in this study:

1. To study the varieties of Pap smear abnormalities in HIV positive women with or without other STDs in relation to control group.
2. To offer appropriate treatment for the observed abnormalities.
3. To encourage regular follow up of HIV positive women in ART center, Surat.

3. Materials and Methods

It is a cross-sectional study which was carried out from August 2009 till November 2011. This study recruited 439 PLWHA women registered in the ART center of New Civil Hospital Surat. The study participants were consenting adult (>18 years) PLWHA women registered in the ART center of New Civil Hospital Surat.

3.1. Inclusion criteria

1. All seropositive symptomatic and asymptomatic women attending ART center.
2. Known seropositive women attending gynecology OPD with STIs.

3.2. Exclusion criteria

1. Known case of Invasive Squamous Cell Carcinoma of cervix

2. Seropositive women who had already undergone hysterectomy

Following is the comparison of different terminologies used in the study:

Table 1:

Papanicolaou Class system	World Health Organization	CIN	Bethesda System
Class I	-	-	Within normal limits
Class II	Mild dysplasia	CIN -I	Benign cellular changes ASCUS Low-grade SIL (LSIL)
Class III	Moderate dysplasia	CIN -II	High-grade SIL (HSIL)
	Severe dysplasia	CIN - III	
Class IV	Carcinoma in situ	CIN- III	-
Class V	Micro invasive carcinoma Invasive carcinoma	Invasive Carcinoma	Invasive carcinoma

We have used the Bethesda System of classification by liquid cytology in the study.

4. Results

The Table 2 shows the different Pap smear findings having cervical changes in PLWH

4.1. Locality

The distribution of ASCUS, LSIL and HSIL was almost similar in the rural and urban sub groups.

4.2. Age group

Majority (29/38 – 76.3%) of SIL were noted in less than 40 years age group though the overall frequency of SIL in this age group was 29/360 i.e. 8.1%. Though only 9 out of 38 (23.7%) participants with SIL were above 40 years of age, the overall frequency of SIL in this age group was 9/79 i.e. 11.4%. We apparently noted a higher frequency (11.4%) of SIL in the above 40 years of age group versus 8.1% in the below 40 years of age group – but this difference was not statistically significant (p-value-0.33 with OR-0.68). The split up of SIL in relation to age of the participants is present in Figure 1.

17 of the 38 SIL (44.7%) were noted in the 31-40 years age group which is an important age group for persistence of HPV infection resulting in cervical carcinogenesis.

Table 2:

| Cytological Abnormality→	Pap Smear Finding				P value (Crude
Variables ↓	ASCUS	LSIL	HSIL	Total SIL (n = 38)	OR)
Locality					
Rural (n=312)	6 (4.7)	4(3.1)	2(1.6)	12(9.4)	0.7(1.15)
Urban (n=127)	15 (4.8)	7(2.2)	4(1.3)	26(8.3)	
Age group					
≤ 40 yrs (n=360)	16 (4.4)	9(2.5)	4(1.1)	29(8.1)	0.33(0.68)
> 40 (n=79)	5(6.3)	2(2.5)	2(2.5)	9(11.4)	
Education					
Illiterate (n=153)	5 (3.3)	5(3.3)	2(1.3)	12(7.8)	0.06 (0.85)
Literate (n=286)	16(5.6)	6(2.1)	4(1.4)	26(9.1)	
Age at marriage					
≤ 20 (n=291)	13 (4.5)	7(2.4)	5(1.7)	25(8.6)	0.94 (0.98)
> 20 (n=148)	8(5.4)	4(2.7)	1(0.7)	13(8.8)	
Parity					
≤ 2 (n=307)	11 (3.6)	5(1.6)	4(1.3)	20(6.5)	0.01(0.44)
> 2 (n=132)	10(7.6)	6(4.5)	2(1.5)	18(13.6)	
Alive status of husband					
Live (n=380)	16 (4.2)	7 (1.8)	3 (0.8)	26 (6.8)	0.0006(0.29)
Dead (n=59)	5 (8.4)	4 (6.7)	3 (5.1)	12 (20.3)	
Duration of Marriage					
≤ 10 (n=228)	7 (3.1)	1(0.4)	0	8(3.5)	0.000058 (0.21)
> 10 (n=211)	14(6.6)	10(4.7)	6(2.8)	30(14.2)	
Number of lifetime sexual partners					
One (n=417)	20(4.8)	11(2.6)	6(1.4)	37(8.9)	1.0 (0.94)
More than one(n=22)	1 (4.5)	0	0	1 (4.5)	
Presence of Symptoms					
Symptomatic (n=66)	4 (6.1)	1(1.5)	2(3.0)	7(10.6)	0.54 (1.31)
Asymptomatic(n=373)	17(4.6)	10(2.7)	4(1.1)	31(8.3)	
CD$_4$ count at the time of pap smear					
≤ 250 (n=342)	6 (1.8)	3(0.9)	1(0.3)	10(2.9)	0.0000 (0.27)
> 250 (n=97)	15(15.5)	8(8.2)	5(5.2)	28(28.9)	
ART status					
On ART (n=332)	16 (4.8)	10(3.0)	5(1.5)	31(9.3)	0.38 (1.47)
Not on ART (n=107)	5(4.7)	1(0.9)	1(0.9)	7(6.5)	
Baseline CD$_4$ count					
≤ 250 (n=188)	8 (4.3)	5(2.7)	2(1.1)	15(8.0)	0.33 (0.69)
> 250 (n=144)	8(5.6)	5(3.5)	3(2.1)	16(11.1)	
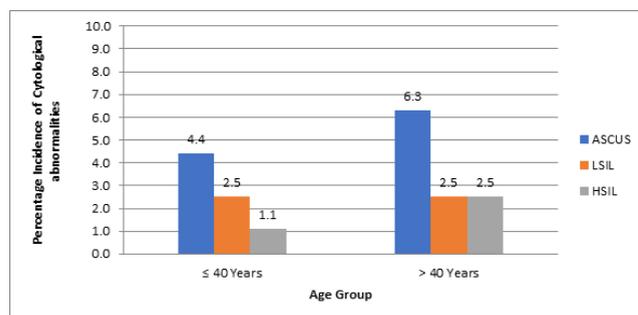
Fig. 1: Comparison of age with Pap smear results

4.3. Education

The incidence of ASCUS, LSIL, HSIL were almost similar in both the educated as well as the illiterate.

4.4. Age at marriage

The participants were divided into two groups with 20 years as cut off for the age at marriage. The incidence of all subgroups of SIL was similar in the two groups.

4.5. Parity

SIL in participants with parity less than two was 6.5% (20/ 307) and in parity more than two was almost double i.e. 13.6% (18/132). On applying the tests of significance the difference was statistically significant (p- value- 0.01, OR- 0.44) i.e. as the parity increased the incidence of SIL increased.

The likelihood of having SIL in parity less than two was 0.44 times that of parity more than two. The frequency of ASCUS and LSIL was almost doubled in the parity more

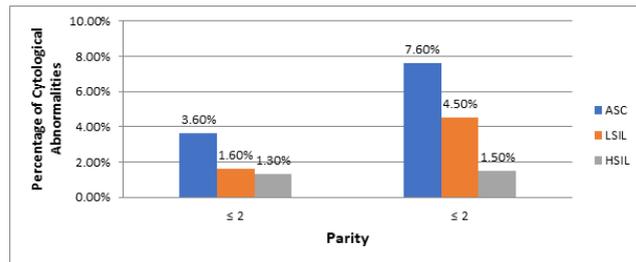than two groups while that of HSIL was almost similar (1.3% and 1.5%).

Fig. 2: Parity and SIL on Pap Smear

4.6. Status of husband

SIL was noted in 26/380 (6.8%) participants whose husbands were alive, while the corresponding figure for those who had lost their husbands was almost three times i.e. 12/59 (20.3%). The difference in SIL between the two subgroups (husband –alive or dead) was statistically significant (p- value- 0.0006, OR-0.29). This suggests that participants whose husbands were alive had less chances of having SIL compared to those who had lost their husbands. The likelihood of having SIL with living husbands was 0.29 times that with expired husbands. Considering that most participants had acquired the infection from their partners (since most participants were monogamous, concordant for the disease, did not have other risk factors for acquiring the infection), those whose husbands were alive probably had higher immunity and thus less chances of having SIL.

4.7. Duration of marriage

SIL was noted in 8/228 (3.5%) of those who had been married for less than ten years versus in 30/211(14.2%) of those who had been married for more than ten years. This difference (almost four times) was statistically significant (p- value – 0.000058,OR – 0.21).ASCUS, LSIL, HSIL were also individually higher in those participants who had been married for more than ten years. (6.6%, 4.7%, 2.8% versus 3.1%, 0.4%, 0%). This is accordance with the view that the changes of cervical intraepithelial neoplasia increase as time from the onset of sexual activity increases.

4.8. Number of lifetime sexual partners

Of the 38 participants noted to have SIL –majority i.e. 97.02% (37/38) had a single lifetime partner. SIL was noted in 37/417 (8.9%) of participants with single lifetime partner versus 1/22 (4.5%) of those with multiple lifetime partners. This apparent difference (almost double) was not statistically significant (p- value>0.05) in this study.

4.9. Presence of symptoms

Majority - 81.6% (31/38) of the participants with SIL were asymptomatic as against 18.4% (7/38) who were symptomatic (vaginal discharge). SIL was noted in 7/66 (10.6%) of participants with symptoms versus 31/373 (8.3%) of those without symptoms. This apparent difference was not statistically significant (p- value- 0.54).

4.10. CD_4 count at the time of Pap smear

SIL was noted in 28.9% (28/97) participants with CD_4 count greater than 250 at the time of Pap smear versus 2.9% (10/342) of those participants with CD_4 count less than 250 at the time of Pap smear. This difference in SIL with respect to the CD_4 count at the time of Pap smear was highly statistically significant (p- value- 0.00008, OR- 0.27) and is represented in Figure 3.
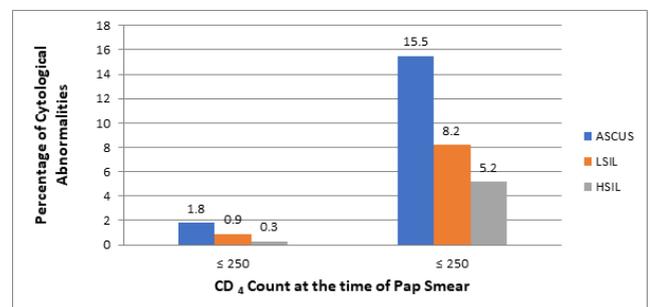

Fig. 3:

This result reiterates the importance of cervical screening in patients with CD_4 count more than 250 especially to improve the quality of life in the remaining longer years of survival as compared to the less than 250 CD_4 count group.

4.11. ART status

SIL was noted in 31/183 (9.3%) of participants on ART versus 7/144 (6.5%) of those not on ART. This apparent difference (almost double) was not statistically significant (p- value – 0.37).

4.12. Baseline CD_4 count

SIL was noted in 15/188 (8%) of participants with baseline CD_4 count less than 250 versus 16/144 (11.1%) of those with baseline CD_4 count more than 250. Not on ART. This apparent difference was not statistically significant (p- value – 0.33) i.e. SIL was equally distributed in both the groups.

4.13. Duration of ART

SIL was noted in 14/183 (7.7%) participants on ART for less than three years versus 17/149 (11.4%) of those on ART for more than three years. This apparent difference also was not statistically significant (p- value – 0.24).

5. Management

Amongst the 38 participants with SIL – seven were found to be in the high-risk category (ASCUS-H -1 and HSIL -6) and were advised cervical biopsy in the absence of Colposcope. The remaining thirty –one participants were counselled for repeat Pap smear at six months interval. Amongst the high-risk group – two were lost to follow up and the results of cervical biopsy of the remaining five are, CIN –III in three and CIN – II in two participants. The three subjects with CIN –III underwent hysterectomy, while those with CIN-II have been kept under regular follow-up.

6. Discussion

In our study SIL prevalence of 9% among HIV infected women was lower than 19% among HIV-infected women—mainly commercial sex workers—in Pune and higher than 6.3% among women from an urban and suburban population in Pune 7 as reported by Joshi et al.

Our SIL prevalence was also different from 16.4% prevalence of ≥CIN-2 lesions reported by Sahasrebuddhe et al., possibly because all participants in the latter study underwent colposcopy for detection of abnormalities. Additionally, their sample of women was different from ours with 13% reporting multiple partners and 62% widowed compared with 5% reporting two or more partners and 13.4% widowed in our study.

7. Conclusion

HIV infected asymptomatic women from Surat have a high prevalence of cervical squamous intra-epithelial lesions predisposing them to invasive cervical cancer.

It is essential to screen HIV infected women regularly to detect cervical squamous intra-epithelial lesions (SIL) early and prevent advancement to ICC with early appropriate treatment.

HPV screening as an alternative method to Pap screening must be considered and future studies are needed to assess the most cost-effective screening strategy for this high-risk population in a resource-limited setting.

8. Source of Funding

None.

9. Conflict of Interest

None.

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Author biography

Amisha Gheewala, HOD

Suchita Patel, HOD

Ragini Verma, HOD