PSYCHOSOCIAL BURDEN OF ABNORMAL PAP SMEARS AMONG HIV-INFECTED WOMEN AT CHON BURI HOSPITAL, THAILAND

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Abstract. This retrospective case-control study assessed the psychological burden of abnormal Pap smears, and their prevalence and characteristics among HIV-infected women attending an HIV clinic. Women with positive (n = 73) and negative Pap-smear results (n = 317) were assessed for psychosocial burden using 4 questionnaires: Psycho-Social Impact of Abnormal Pap Smears (PEAPS-Q), Hospital Anxiety and Depression Scale (HADS), Work Productivity and Impairment (WPAI) and the EURO-Qol Thermometer. The prevalence of pre-cervical cancer lesions in HIV infected woman was 17.5% (ASCUS 2.9%, LSIL 3.8%, HSIL 7.4%, SCC 1.7%, and atypical glandular cells including adenocarcinoma 1.7%). HIV infected women with abnormal Pap smears showed higher anxiety levels on the HADS questionnaire (p = 0.015); this had a significant effect on regular daily activities (p = 0.009) per the WPAI questionnaire compared to HIV positive women with normal Pap smear. Ever married HIV infected woman with an abnormal Pap smear had a significantly lower psychosocial burden using the PEAPS-Q questionnaire (p<0.001). After adjusting for age and duration since last Pap smear, the education level of the patient was a strong predictor for anxiety. Patients, with a college education had significantly lower anxiety (p = 0.001, 95% CI -5.74 to -1.37) than those with lower or higher education. Women with HSIL were more anxious (p = 0.014, 95% CI 0.491- 4.39) than those with low grade or normal lesions.

Key words: Pap smears, psychosocial burden, HIV-infected, human papillomavirus, HPV, cervical cancer, Thailand

INTRODUCTION

Women infected with HIV have a higher prevalence of infection with Human Papilloma Virus (HPV), and are more likely to develop persistent infection with multiple HPV types (Palefsky *et al*, 1999). This results in a higher incidence and prevalence of Cervical Intraepithelial Neoplasia (CIN) lesions with a greater likeliness to progress to invasive cervical cancer, possibly due to HIV-induced cell-mediated immune-suppression with the consequence of inadequate clearance of HPV infections and rare spontaneous regression of low-grade lesions (Ellerbrock

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et al, 2000; Hawes *et al*, 2003; Schuman *et al*, 2003). According to US Centers for Disease Control (CDC) data, cervical cancer was the most common (1.3%) type of cancer diagnosed among 16,784 women with AIDS (CDC, 1993). As a result, the CDC added invasive cervical cancer to its list of AIDS-defining illnesses, a position supported by other studies (Maiman *et al*, 1997). Pap smear is the most appropriate means for cervical cancer screening at present (Kritpetcharat, 2003). It helps reduce the mortality and morbidity of cervical cancer by increasing detection of cytological abnormalities, thus allowing prompt initiation of treatment and follow-up management. However, this indirectly results in significant psychosocial consequences to patients. The psychological costs of Pap smear screening and follow-up might outweigh the benefits. Moreover, there is concern these psychological sequelae may interfere with compliance with subsequent treatment (Bennetts *et al*, 1995). A higher psychosocial burden may be expected among HIV infected patients with abnormal Pap smear results, which could increase psychosocial stressors making their lives more miserable. The objective of this study was to use a self-administered questionnaire to describe and compare the psychosocial burden on HIV infected women who receive abnormal Pap results compared with HIV infected women who received normal Pap smear results, after screening.

MATERIALS AND METHODS

The study was conducted at Chon Buri Hospital, Chon Buri, Thailand from April to November 2008. All medical records of HIV-infected women, who had undergone a Pap smear since 2006 were reviewed for Pap smear data. Those who had their last Pap smear during the previous year, were ≥18 years old and were aware of the results of their last Pap smear, were selected for the study. Subjects with chronic severe medical problems or who were diagnosed with psychiatric problems were excluded from the study. Categorization into 2 groups was done according to the cytological findings on Pap smear.

The normal Pap smear group included all negative Pap smears, those with atrophic changes, inflammatory changes and infections of the cervix. Abnormal Pap smear group consisted of all those with cytological abnormalities of Atypical Squamous Cells of Undetermined Significance (ASCUS) and above lesions of squamous cells and all glandular cell abnormalities, according to the Bethesda 2001 classification. All women gave written informed consent and completed a self-administered questionnaire. Ethical approval was received from the Ethics Committees of the Faculty of Tropical Medicine, Mahidol University and Chon Buri Hospital, before beginning the study.

Instruments used to assess psychosocial burden

Four validated questionnaires used to assess psychosocial burden were delivered to the clinic. Study staff explained the questionnaires and instructions were given on how to complete them. The subjects were provided with a quiet, private location and given adequate time to complete the questionnaire with a Thai speaking research assistant available at the site to answer any questions. All questionnaires used had been validated and the details are as follows.

Psychosocial Effects of Abnormal Pap Smears Questionnaire(PEAPS-Q)

The primary study measurement was the set of scores derived from the PEAPS-

Q. The self-administered questionnaire contained 14 items scored individually, combined into a total burden score. It examined four main aspects of psychosocial burden: procedural distress, patient's feelings about beliefs and changes in perception of self, worry about infectivity and effect of disease on sexual relationships. With the scoring system in PEAPS-Q, the higher the score the better the outcome, favoring less psychosocial burden (Bennetts *et al*, 1995).

Hospital Anxiety and Depression Scale (HADS)

The HADS measured depression and anxiety. The two subscales, anxiety and depression, were independent measures and were divided scored into four ranges: normal, mild, moderate and severe, according to the score in each subscale. Scores up to 8 were designated as normal cases, 8-10 as mild cases, 11-13 as moderate cases and >14 as severe cases. The scale refered to the mood during the past week to avoid the influence of other factors, such as stress due to attending the clinic (Mcdowell, 2006).

Work Productivity and Activity Impairment Questionnaire (WPAI)

This questionnaire assessed the quantitative impact of health conditions on loss of time and impaired productivity for functional activities, such as work-for-pay, schoolwork, and work around the house. It specifically assessed the quantitative impact of work loss in terms of hours per week (Mcdowell, 2006).

EuroQol Thermometer (EQT-VAS)

EQT-VAS measured general health through a self-administered visual analog scale (VAS). The VAS resembles a thermometer on which subjects are asked to select their current health status on a scale from zero to 100, where 100 represents perfect health and zero represents death (Mcdowell, 2006).

Statistical methods

Demographic and clinical characteristics of the two groups were analyzed using chi-square test and the study hypothesis was tested using as Student's *t*-test and chi-square test. Multiple linear regression was used to ascertain the best predictors of psychosocial burden, and associated risk factors for pre-cervical lesions were analyzed using logistic regression methods. SPSS V.15 and STATA V.9 were the statistical software packages used for analysis throughout this project.

RESULTS

The self-reported demographic and gynecological data for the 390 subjects recruited for this study are shown in Table 1. Most of HIV infected women in the normal Pap smear group (51.4%) were 35 to 44 years old. The largest group with abnormal Pap smears was the 25-34 year old age group (43.4%). However, the mean ages were not significantly different between the two groups. The majority of participants in both groups (51.1 and 41.1%, respectively) were married and were living with their husbands. In the normal Pap smear group, housewives represented the majority (43.6%), whereas the abnormal group consisted mainly of factory workers (35.6%), which should be a matter of concern. Low education level was a prominent feature in this study sample where, 48.9 and 46.5% of the two groups, respectively, had an education only up to primary school or lower. Greater than 50% of participants had an income THB <5,000 per month. With regard to the sexual behavior, 1/3 of participants had their first sexual encounter below the age of 18 years and nearly half

Table 1
Demographic characteristics of women participated in psychosocial study (*n*= 390) (missing values are indicated in brackets).

Characteristic	Normal group (*N*=317)	Abnormal group (*N*=73)	*p*-value
Mean age (years)	37.94	36.42	0.128
Education level			
Primary school/or lower	153 (48.9)	33 (46.5)	
Secondary school	96 (30.7)	25 (35.2)	0.872
College	38 (12.1)	7 (9.9)	
University/diploma/postgraduate	26 (8.3)	6 (8.5)	
Marital status			
Unmarried	51 (16.2)	15 (20.5)	
Married	161 (51.1)	30 (41.1)	0.488
Widow/Separated	103 (32.7)	28 (38.4)	
Occupation			
Laborer	44 (14)	11 (15.1)	
Housewife	137 (43.6)	23 (31.5)	0.337
Factory worker	74 (23.6)	26 (35.6)	
Other	59 (18.8)	13 (17.8)	
Income Baht/month			
<5,000	198 (63.2)	37 (50.7)	
5,000-10,000	86 (27.5)	26 (35.6)	0.223
> 10,000	29 (9.2)	10 (13.7)	
Number of children			
None	80 (25.3)	16 (22.2)	
1 or more	236 (74.7)	56 (77.8)	0.583
Age at first sex			
<18 years	95 (30)	27 (37)	
18-24years	158 (49.8)	37 (50.7)	0.234
>24years	64 (20.2)	9 (12.3)	
Number of sexual partners			
1	258 (86.6)	55 (80.9)	0.229
2 or more	40 (13.4)	13 (19.1)	
Period of HIV infection(years)	6.52	7.21	0.346

(49.8%) had their first experience between 18 and 24 years old. The majority of the women had one sexual partner during their lifetime (>83%). No significant differences in demographic data were detected between groups with respect to age, education level, income, occupation, marital status or number of children. The two groups were similar in the number of sexual partners and type of contraceptives used.

Out of 476 study subjects, 46% had normal Pap smear results; 24.4% had inflammatory changes on Pap smear and 9.5% had ongoing infection (mostly mixed infections) of their cervices (Table 2). Seven point four percent had High grade Squamous Intraepithelial Lesions (HSIL). The

Table 2
Prevalence and characteristics of Pap smear results of HIV infected women at Chon Buri Hospital (from 15 July 2006).

Last Pap smear result	Total number	Percentage	Number in selected group	Percentage
Negative for cytological abnormalities	219	46	170	43.6
Inflammation	116	24.4	103	26.4
Infection	45	9.5	33	8.5
Atropy	13	2.7	11	2.8
ASC-US	14	2.9	12	3.1
LSIL, including HPV changes	18	3.8	14	3.6
HSIL, including CIS	35	7.4	31	7.9
Squamous cell carcinoma	8	1.7	7	1.8
AGC (Atypical Glandular Cells, AIS and Adenocarcinoma)	8	1.7	9	2.3
Total	476	100	390	100.0

second most prevalent abnormality was Low grade Squamous Intraepithelial Lesions (LSIL) (3.8%) followed by ASCUS (2.9%).

Opportunistic infections were more common in those with abnormal Pap smears (54.8%) than in those with normal Pap smears (36%) (p=0.003). Both groups were similar in co-morbid conditions, type of antiretroviral regimen, number of immune reconstitution syndrome events and drug resistance levels. Twenty-six percent of participants with abnormal Pap smears had undergone colposcopy and biopsy and 13.7% had both diagnostic and treatment procedures as part of their management by the time of enrollment in the study.

The mean durations from last Pap smear result to date of enrollment for the two groups (normal and abnormal Pap smears) were 5.49 and 4.96 months, respectively, which are not significantly different (p=0.346). A summary of the results of the four instruments is found in Table 3.

Analysis of psychosocial burden

Analysis of the psychosocial burden with the 4 components of the PEAPS-Q questionnaire revealed women with normal Pap smears scored higher in all four components, though the difference was not significant. However, a significantly higher anxiety level was detected in the abnormal Pap smear group, as measured by the HADS questionnaire (p=0.015). However, there were no significant differences in terms of depression (p=0.102) despite slightly high scores in the abnormal group than the normal group. Greater than 64% of women in both groups were employed and their mean working hours per week were similar. An abnormal Pap smear had a significant effect on regular daily activities (p=0.009) as measured by the WPAI questionnaire, whereas scores on the Euro-Qol thermometer questionnaire were similar between the 2 groups (Table 3).

The ranges of total scores with the PEAPS-Q and HADS are shown in Fig 1.

Table 3
Psychosocial burden of Pap smear results in normal and abnormal Pap smear groups (*n*=390, normal 317 and abnormal 73).

Measurement	Normal Pap smear group (*N*=317)	Abnormal Pap smear group (*N*=73)	*p*-value
PEAPS-Q Questionnaire (*n*=389)			
Experience of medical procedure	22.10 ± 3.06	21.71 ± 3.04	0.324
Beliefs/feelings and changes in perception of self	15.18 ± 3.7	14.64 ± 3.6	0.269
Worry about infectivity	7.60 ± 2.5	7.23 ± 2.7	0.265
Effect on sexual relationships	11.37 ± 3.2	10.96 ± 3.6	0.344
Total score	56.10 ± 9.3	54.55 ± 9.7	0.207
HADS (*n*=390)			
Anxiety measurement	6.95 ± 3.8	8.16 ± 3.8	0.015
Depression measurement	5.07 ± 3.4	5.81 ± 3.4	0.102
Total score	12.03 ± 6.5	13.97 ± 6.6	0.022
WPAI Questionnaire (*n*=388)			
Work for pay	225 (72%)	53 (64%)	0.841
Working hours/week	35.66 ± 27.26	35.67 ± 27.43	0.998
Loss of work	0.96 ± 3.32	1.36 ± 3.8	0.386
Effect on productivity	1.24 ± 2.0	1.74 ± 2.5	0.076
Effect on regular daily activities	1.19 ± 2.0	1.92 ± 2.5	0.009
EURO-Q Thermometer (*n*=388)			
How do you feel your health status is today?	75.05 ± 17.0	73.42 ± 18.2	0.470

The normal Pap smear group had a higher mean score indicating less psychosocial burden compared to the abnormal Pap smear group (Fig 1a). Fig 1b shows a higher psychological burden (anxiety and depression) in the abnormal Pap smear group with higher scores representing a greater burden with the HADS.

Using the PEAPS-Q questionnaire and adjusting for age, period of HIV infection, income and education, patients who received Pap smear results 3-6 months before the date of enrollment had a greater psychological burden (p=0.028, 95% CI -6.28 to -0.36) than those who received their results within the previous 3 months or longer than 6 months. Ever married (married, widowed or separated) women scored significantly higher on the PEAPS-Q questionnaire (indicating less psychosocial burden) than never married women (p<0.001, 95% CI 2.34-7.51).

HADS

After adjusting for age and time duration since last Pap smear, education level of the patient was a strong predictor for anxiety. Patients with a college education had significantly less anxiety (p=0.001, 95% CI -5.74 to -1.37) than those who had lower or higher levels of education. The effect of high-grade lesions on psychological burden was prominent on the HADS. (p=0.014, 95% CI 0.491-4.39). Previous CD4 counts of 200-400 cells/μl (n=200) and >400 (n=138) were also significantly associated with anxiety and depression on the HADS, (p=0.008 and 0.028, respectively).

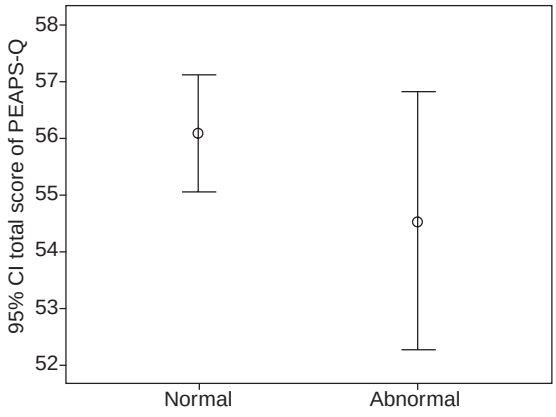

Fig 1a

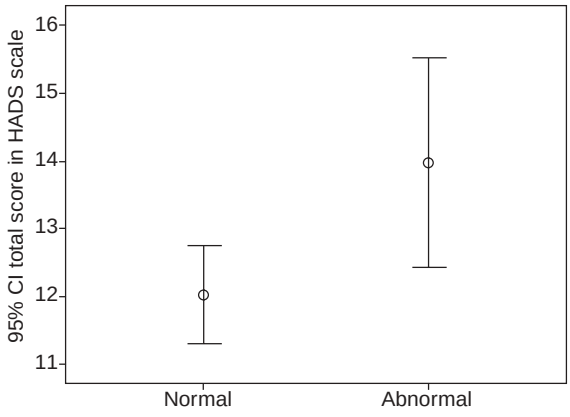

Fig 1b

Fig 1–Total PEAPS-Q and HADS 2 groups.

Table 4
Patient categorization according to the scores in anxiety and depression scales (*n*=390).

	Anxiety		Depression	
	Normal Pap	Abnormal Pap	Normal Pap	Abnormal Pap
Normal cases	205 (65.1)	43 (58.9)	273 (86.3)	60 (82.2)
Mild cases	54 (16.8)	12 (16.4)	27 (8.4)	6 (8.2)
Moderate cases	41 (12.8)	12 (16.4)	12 (3.7)	6 (8.2)
Severe cases	17 (5.3)	6 (8.2)	5 (1.6)	1 (1.4)

Table 4 shows the patients categorized according to the severity of anxiety and depression. The number of anxiety and depression cases (mild to severe) were higher in the abnormal Pap smear group than in the normal Pap smear group (41, 17.8 and 34.9%, 13.7%, respectively). The difference was more prominent with moderate to severe cases for both anxiety and depression.

Factors associated with cytological abnormalities of cervix

On analysis of possible factors associated with occurrence of pre-cervical lesions, two variables predicted severity of cytological changes of the cervix. Women who had their first sexual intercourse at age >20 years (OR=0.46, 95% CI 0.23 - 0.90) showed significantly less vulnerability for abnormalities on Pap smears (p=0.026). A CD4 count >400 cells/μl gave an OR of 0.39 indicating a protective effect with high CD4 counts against pre-cervical cancer lesions compared to lower CD4 counts (p = 0.029).

DISCUSSION

This study was carried out in a province with a high prevalence of pre-cervical cancer lesions among HIV patients. Hluangdansakul *et al* (2006) showed that psychosocial stress in terms of anxiety and routine work loss, measured by HADS and

the WPAI questionnaire, respectively, were significantly greater among women who had abnormal Pap smears. Women with an abnormal Pap smear had an average mean score of 8.16 on the HADS for anxiety which reflects anxiety over the results of the Pap smear. These results are compatible with findings of several other studies which found women with an abnormal Pap smears experience numerous concerns about cancer and fertility (Bennetts *et al*, 1995) and have negative emotions, including embarrassment, fear and anxiety (Deacon *et al*, 2000; Koutsky *et al*, 2002). Women with abnormal high grade lesions (HSIL and above) on Pap smear were more anxious (p=0.014, 95% CI 0.491-4.39) than those with low grade or normal lesions even after adjusting for the factors like age, period of HIV infection and duration since last Pap smear. The sequencel of additional procedures that often accompany an abnormal Pap smear, including colposcopy and biopsy, often cause anxiety among affected women (Koutsky *et al*, 2002) and can have negative effects on self-esteem and body image (Jones *et al*, 1996). In addition, the multiple trips required for diagnosis and/or treatment cause logistical challenges and increase stress in these women (Womack *et al*, 2000).

Women with lower CD4 counts had higher scores on HADS, reflecting higher anxiety and depression. It is difficult to explain the higher anxiety and depression levels among college level educated participants compared to the other three groups (primary, secondary and higher than college education levels), which demands further investigation. Twenty-four point six percent and 9.6% of women with moderate to severe anxiety and depression, respectively, among women with abnormal Pap smears were greater than the 18.1% and 5.3%, respectively, of cases with a normal Pap smear. These anxiety levels were significantly higher than those found by Molassiotis *et al* (2004), in regard to quality of life, coping and psychological status of Thai people living with AIDS, where only 8.1% of participants were diagnosed as having anxiety. Health care professionals need to be aware of the anxiety and depression in these patients to improve their quality of life. Researchers need to evaluate the factors associated with anxiety and depression.

The anxiety (revealed by the PEAPS-Q) which happened 3 months after the diagnosis of an abnormal Pap smear is of concern. These results are in contrast to the findings of a previous study (McCaffery *et al*, 2004) done on the psychosocial impact of HPV infection, where anxiety was observed just after receiving the Pap smear results. Usually, Pap smear results are sent to patients by postcard two weeks after the test. However, in the HIV clinic, patients are reviewed once every 3 months. There is no system arranged to call immediately for those who have abnormal Pap smears either by the HIV or gynecology clinics. This deficit may have influenced the PEAPS-Q scores. A significantly higher psychosocial burden found among participants who were never married ($p < 0.001$) is in contrast to the ever married group (married, widowed or separated), and was another interesting factor which emerged from the PEAPS-Q questionnaire. A feeling of social insecurity among never married women could be a possible explanation for this finding, though the reasons are not clear. However, this instrument failed to show any significant association between grade of abnormality and psychosocial burden.

Another important aspect of psychosocial burden is loss of productivity of the patient due to disease conditions. In 2001

in the USA, the estimated direct cost associated with cervical precancerous lesions was USD 3.6 billion (Herzog and Wright, 2007), which clearly depicts the scale of the problem. This is valid for our study population since >64% in both groups were directly involved in productivity jobs. However, the HIV infected patients in our study had no significant loss of work/occupation in terms of working hours (0.96 and 1.36 hours, respectively in the normal and abnormal groups) due to abnormal Pap smears. However, people in the abnormal Pap smear group had a significantly greater loss of time for daily activities (p= 0.009) than those in the normal Pap smear group with possible adverse effects on their social life, which could contribute to a high psychosocial burden. However, we did not observe a significant difference between the 2 groups with the EUROQol thermometer questionnaire, which may be probably due to failure of the instrument to measure the health status of these groups (The Euro.Qol Group, 1990), which warrants searching for a better instrument to be used with future studies. The stage of work-up and management of the abnormal Pap smears and the presence of concurrent opportunistic infections may be confounding factors affecting the psychosocial burden which were not considered in this study, since it was not feasible to measure these factors in our study.

The results of the prevalence and characteristics of Pap smears in the present study show improvement in the quality of cytological finding after a 5-year period, compared to the results of another study done on similar patients in 2003 (Hluangdansakul *et al*, 2006). In the above study, the incidences of LSIL, HSIL and Squamous Cell Carcinoma (SCC) were 2.2, 8.3 and 2.2%, respectively, whereas in our study the figures were 3.8, 7.4 and 1.7%, indicating a low prevalence of high grade lesions (HSIL and SCC) after a 5 year period. However, the low-grade lesions (LSIL) were on the rise (from 2.2% to 3.8%), probably due to improvement in the quality of Pap smear testing and/or due to improvement in the quality of medical care in HIV patients. These results are in contrast to those of a cohort study done on HIV positive and HIV negative women by Massad *et al* (2008) at the Division of Gynecologic Oncology, Washington University School of Medicine. Very high prevalence rates of low grade lesions were observed in this study, 19% had ASCUS lesions and 3.6% had LSIL; high-grade lesions had remarkably low prevalence rates (HSIL 1% and SCC 0.05%). These differences may be indicators of the quality of medical care (including patient knowledge, quality of screening, diagnosis and management of patients) in a developed country, compared to a developing country like Thailand. Hence, this should be a matter of concern for health care professionals in planning and implementing preventive programs concerned with cervical cancers.

To re-iterate the fact low cell mediated immunity leads to emergence of malignancies, participants in this group had a high incidence of pre-cervical cancer lesions with low CD4 counts (Wright *et al*, 1994). Delmas *et al* (2000) found that HIV infected women with CD4 cell counts $<200x10^6$/l had a two-fold greater prevalence and incidence of SIL compared to women with CD4 cell counts $>500x10^6$/l. The high prevalence of cytological abnormalities in those with early sexual exposure is prominent etiological factor (Arends *et al*, 1998) supported by our study showing a greater number of lesions among those who had first sexual intercourse before age 20 years. However, in our study sample we did not find an association between cytological

abnormalities and factors, such as smoking, period of HIV infection, number of sexual partners, type of contraceptive they used, number of children of the patient or type of antiretroviral regimen received, which are established risk factors for pre-cervical lesions seen in other populations (Arends *et al*,1998). There was no specific age group showing more vulnerability for pre-cervical cancer lesions among this group of HIV infected women in our study.

In summary, an abnormal Pap smear causes significant psychosocial stress with increased anxiety and negative effect on regular daily activities. The effect of high-grade lesions on heightening anxiety in these patients was more prominent than in those with low-grade lesions. A higher prevalence of anxiety cases was detected among those with abnormal Pap smears compared to other HIV patients. Careful disclosure of abnormal Pap smear results to patients and proper education and counseling are needed to improve their quality of life. The high prevalence of high-grade pre-cervical cancer lesions (HSIL and SCC) in this population is also significant. Apart from education and counseling, development of clinical infrastructure facilities for detection, diagnosis, management and follow-up of pre-cervical cancer lesions are recommended for reducing the prevalence rates of cervical cancers and improving the quality of life of HIV infected women.

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