Prevalence of SIL and SCCA in Human Immunodeficiency Virus-Seropositive Women at Anonymous Clinic in Chonburi Hospital

Wiyada Hluangdansakul MD*,
Pitcha Phinchantra MD*, Chureeratana Bowonwatanuwong MD**

** Department of Obstetrics & Gynecology, Chonburi Hospital, Chonburi*
*** Department of Medicine, Chonburi Hospital, Chonburi*

This cross sectional study was established to assess the prevalence of SIL and SCCA in HIV-infected women.

The series of 231 HIV-infected women were recruited in Chonburi Hospital, Thailand. Demographic, gynecologic factors were interviewed. Pap smear was performed and classified based on the Bethasda system (1991) by a cytotechnologist. All abnormal Pap smear slides were reviewed by a cytopathologist. The prevalence of LSIL, HSIL and SCCA were 2.2%, 8.3% and 2.2%, respectively. There was statistically significant association between the duration of HIV infection and occurrence of SIL and SCCA. (p = 0.007) Conclusion, the present study showed a high prevalence of SIL and SCCA in - HIV-infected women at Chonburi Hospital.

Keywords: *Prevalence, Papanicoloau smear, CIN, SIL, SCCA, Human Immunodeficiency Virus, Chonburi Hospital*

J Med Assoc Thai 2006; 89 (3): 289-93
Full text. e-Journal: *http://www.medassocthai.org/journal*

HIV (Human Immunodeficiency Virus) infection is a major public health problem faced by most nations including Thailand. In 2002, 1,033,500 Thai HIV-infected patients were reported and 398,400 HIV-infected patients died. Recent data showed that cervical HPV infection and CIN were clearly increased in HIV-positive women compared with risk-matched HIV-negative women[1] and in America, HIV-infected women were 4-10 times more susceptible for CIN (Cervical intraepithelial neoplasia)[2]. The American CDC (Center of Disease Control and Prevention) suggested that HIV-infected women should have a Pap smear test every six months. If two consecutive test results show no evidence of CIN, the subject should have a Pap smear repeated once a year[3]. However, in Thailand the prevalence of CIN in HIV-infected women has not been reported and a Pap smear guideline for Thai HIV-infected women has not been issued.

Correspondence to : Phinchantra P, Department of Obstetrics and Gynecology, Chonburi Hospital, Muang, Chonburi 20000, Thailand. Phone: 0-3893-1332, Fax: 0-3893-1331, E-mail: ipitcha@yahoo.com

The purpose of the present study was to identify the prevalence of cervical intraepithelial abnormalities in - HIV-infected women.

Material and Method

The present research design was a cross sectional study. The present study was approved by the hospital ethics committee, and informed written consent was obtained from each participant. Two hundred and thirty one HIV-infected women at the anonymous clinic in Chonburi Hospital were recruited between July 1, 2003 and September 30, 2004. The HIV-infected women with a history of total hysterectomy, conization or the Loop Electrosurgical Excision Procedure (LEEP) and history of carcinoma of the cervix treatment were excluded from the present study. A questionnaire was used to collect data by two interviewers and the Papanicolaou smear technique using a single slide fixed immediately with 95% alcohol was used. Cells were collected from the posterior fornix, ectocervix and endocervix using a wooden Arye spatula. All the Papanicolaou smear tests were classified based

on the Bethesda system (1991). All Papanicolaou smears were initially interpreted by a cytotechnologist and all abnormal Papanicolaou smears were interpreted by a medical cytologist. Data was collected and analyzed for the prevalence of SIL and SCCA in HIV-infected women. Risk factors were analyzed using Chi-square test, Fisher's exact test and logistic regression test as appropriately of < 0.05 was considered to be significant.

Results

Demographic characteristics and gynecologic history of patients in the present study are shown in Table 1 and 2. 15.3% of abnormal Papanicolaou smear results showed at least ASCUS and ACUS stage. Low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL) and squamous cell carcinoma (SCCA) were 2.2%, 8.3% and 2.2%, respectively. (Table 3) The correlation between risk factors and abnormal Papanicolaou smears (SIL and SCCA) are shown in Table 4-5. The analysis using Chi-square and Fisher's exact tests indicated no statistically significant association between risk factors and SIL and SCCA. However, the analysis using logistic regression indicated statistically significant association between the duration of infection and occurrence of SIL and SCCA ($p = 0.007$) (Table 6).

Table 1. Dermographic characteristic of HIV-infected women

Characteristics (N = 231)	N (%)
Age (years)	
< 35	143 (61.9)
≥ 35	88 (38.1)
Smoking	
Yes	209 (90.5)
No	22 (9.5)
Route of infection	
Sexual intercourse	219 (94.8)
Other	13 (5.6)
Length of infection	
≤ 10 years	223 (96.5)
> 10 years	8 (3.5)
CD4 (cells/mm^3)	
< 200	87 (37.7)
≥ 200	112 (48.5)
Unknown	32 (13.9)
Symptom	
Asymptomatic	63 (27.3)
Symptomatic	168 (72.7)
Medical treatment	
No	50 (21.6)
Yes	181 (78.4)

Discussion

HIV infection is a major public health problem in Thailand and worldwide. In 2001, 6,297 HIV-infected patients received medical treatment at the outpatient department of Chonburi Hospital. Interestingly, women are an increasing proportion of the HIV-infected population. In addition, compared with their HIV-negative counterparts, HIV-positive women have a greater incidence of both cervical intraepithelial neoplasia (CIN) and invasive cervical cancer which tends to be more progressive and aggressive[4]. The prevalence of CIN in HIV-positive women was 37% more than twice the 17% prevalence of CIN in HIV-negative women[5]. The present study was performed to search for prevalence of squamous cells of uncertain significance (SIL) and squamous cells carcinoma (SCCA) in HIV-infected women at the anonymous clinic, Chonburi Hospital.

Table 2. Gynaecologic history of HIV infected patients

Gynecologic history (N = 231)	N (%)
Age of first sexual intercourse (years)	
≤ 20	149 (64.5)
> 20	82 (35.5)
Years of Marriage	
≤ 10	141 (61.0)
> 10	90 (39.0)
Sexual partner	
1	75 (32.8)
> 1	154 (67.2)
History of STD infection	
No	200 (86.6)
Yes	31 (13.4)
History of pelvic exam and Pap smear	
No	100 (43.3)
Yes	131 (56.7)
Result of previous Pap smear (N = 131)	
Normal	117 (89.3)
Abnormal	9 (6.9)
Unknown	5 (3.8)

Table 3. Pap smear results in HIV infected women

Pap smear results (N = 228)	N (%)
Normal	113 (49.6)
Benign cellular change	80 (35.1)
ASCUS, ACUS	6 (2.6)
LSIL	5 (2.2)
HSIL	19 (8.3)
SCCA	5 (2.2)

Table 4. Risk factors and Pap smear result in HIV infected women

Characteristics	Normal Pap smear (N = 199) (%)	Abnormal Pap smear (N = 29) (%)	p-value
Age (years)			0.817
< 35	122 (61.3)	19 (65.5)	
≥ 35	77 (38.7)	10 (34.5)	
Smoking			1.000
Yes	180 (90.9)	27 (93.1)	
No	18 (9.1)	2 (6.9)	
Route of infection			0.654
Sexual intercourse	189 (95)	27 (93.1)	
Other	10 (5.0)	2 (6.9)	
Duration of infection			0.067
≤ 10 years	194 (97.5)	26 (89.7)	
> 10 years	5 (2.5)	3 (10.3)	
CD4 (cells/mm^3)			0.114
< 200	102 (51.2)	9 (31.0)	
≥ 200	72 (36.2)	14 (48.3)	
Unknown	25 (12.6)	6 (20.7)	
Symptom			0.824
Asymptomatic	54 (27.1)	9 (31.0)	
Symptomatic	145 (72.9)	20 (69.0)	
Medical treatment			0.117
No	39 (19.7)	10 (28.6)	
Yes	159 (80.3)	19 (65.4)	

None of the comparisions were statistically significant

Table 5. Gynecologic history and Pap smear result in HIV infected women

Gynecologic history	Normal Pap smear (N = 199) (%)	Abnormal Pap smear (N = 29) (%)	p-value
Age of first intercourse			0.052
≤ 20	124 (62.3)	24 (82.8)	
> 20	65 (37.7)	5 (17.2)	
Years of Marriage			0.357
≤ 10	124 (62.6)	15 (51.7)	
> 10	74 (37.4)	14 (48.3)	
Sexual partner			0.505
1	66 (33.3)	7 (25.0)	
> 1	132 (66.7)	21 (75.0)	
History of STD infection			0.236
No	175 (87.9)	23 (79.3)	
Yes	24 (12.1)	6 (20.7)	
History of pelvic exam and Pap smear			0.244
No	83 (41.7)	16 (55.2)	
yes	116 (58.3)	13 (44.8)	
Result of previous Pap smear			0.746
Normal	104 (89.7)	11 (84.6)	
Abnormal	8 (6.9)	1 (7.7)	
Unknown	4 (3.4)	1 (7.7)	

None of the comparisions were statistically significant

Table 6. Risk factors and Pap smear result in HIV infected women use Logistic regression analysis

Characteristic	p-value
Age	0.307
Route of infection	0.741
Length of infection	0.007*
CD4 level	0.087
Symptom	0.978
Treatment	0.156
Smoking	0.943
Years of Marriage	0.782
Age of first intercourse	0.121
Sexual partner	0.145
History of STD	0.099
History of pelvic exam and Pap smear	0.371
Result of previous Pap smear	0.489

p = 0.05

Pap smear was chosen for cytology test in the present study because it is a highly sensitive and specific diagnostic tool in the clinic monitoring. Although, a previous study showed 52.9% of false-negative Pap smear result in HIV-infected women and suggested that colposcopy should be added to cytology as a screening procedure for squamous lesions of the lower genital tract[6]. But these results have not been confirmed by other authors[7-10].

From previous studies, the prevalence of cervical intraepithelial neoplasia (CIN) in this high-risk population ranges between 14-30%[6,11-14], with a nearly fivefold increased risk compared to HIV-negative controls[11]. However, the present study showed that the prevalence of SIL and SCCA in HIV-infected women was only 12.7% and the advanced stage (HIL and SCCA) was 10.5%. Probably, sexual behavior, HIV subtype, socioeconomic status, service provided and highly active antiretroviral therapy (HAART) taking might be the causes of different prevalence. A recent study showed that the risk of regression of CIN was twice as high in women receiving HAART compared with women not receiving HAART[15]. In the present study, 78.4% of HIV-infected women received HAART which might cause CIN to regress and decrease the risk of cervical cancer[16].

In the past, many studies for the correlation between factors and prevalence of SIL and SCCA in HIV-infected women were performed. In Massad et al's study, age, CD4 level, history of HPV infection, genital wart and history of previous abnormal Pap smear were associated with CIN occurrence[14]. A study by Wrigth et al demonstrated race, prostitution, number of sexual partners, age of first intercourse, history of HPV infection, genital wart, genital herpes and intravenous drug use were risk factors of SIL and SCCA occurrence[13]. In contrast, the present study showed that there was no correlation between the risk factors and the occurrence of SIL and SCCA. Although logistic regression analysis showed that there was a statistically significant correlation between the duration of HIV infection and occurrence of SIL and SCCA but the sample size of the present study was calculated for prevalence of SIL and SCCA and was not enough for a correlation study.

The present study attempted to decrease the inter-observer error using the interpretation Papanicolaou smear by one cytotechnologist and one cytopathologist. However, the cytology was interpreted with the knowledge of the patient's serostatus. Thus, this information might tend to bias the cytologist toward diagnosing cytologic abnormalities.

In conclusion, the present study showed a high prevalence of SIL and SCCA in HIV-infected women. Thus, the screening programs for cervical carcinoma in this group should be provided for early detection and treatment. In addition, the associated factors of abnormal Papanicolaou smear in HIV-infected women should be further studied.

References

1. Palesky JM. Cervical human papillomavirus infection and cervical intraepithelial neoplasia in women positive for human immunodeficiency virus in the era of highly active antiretroviral therapy. Curr Opin Oncol 2003; 15: 382-8.
2. Schafer A, Friedmann W, Mielke M, Schwartlander B, Koch MA. The increased frequency of cervical dysplasia-neoplasia in women infected with the human immunodeficiency virus is related to the degree of immunosuppression. Am J Obstet Gynecol 1991; 164: 593-9.
3. Centers for Disease Control and Prevention. 1993 Revised classification systems for HIV infection and expanded surveillance definition for AIDS among adolescents and adult. MMWR Recomm Rep 1992; 41(RR-17): 1-19.
4. Wallace SV, Carlin EM. HIV in cervical cancer. Int J STD AIDS 2001; 12: 283-5.
5. Goodman A, Chaudhuri PM, Tobin-Enos NJ, Hutchinson ML. The false negative rate of cervical smears in high risk HIV seropositive and seronegative women. Int J Gynecol Cancer 2000; 10: 27-32.

6. Spinillo A, Capuzzo E, Tenti P, De Santolo A, Piazzi G, Iasci A. Adequacy of screening cervical cytology among human immunodeficiency virus-seropositive women. Gynecol Oncol 1998; 69: 109-13.
7. Maiman M, Tarricone N, Vieira J, Suarez J, Serur E, Boyce JG. Colposcopic evaluation of human immunodeficiency virus-seropositive women. Obstet Gynecol 1991; 78: 84-8.
8. Johnstone FD, McGoogan E, Smart GE, Brettle RP, Prescott RJ. A population-based, controlled study of the relation between HIV infection and cervical neoplasia. Br J Obstet Gynaecol 1994; 101: 986-91.
9. Adachi A, Fleming I, Burk RD, Ho GY, Klein RS. Women with human immunodeficiency virus infection and abnormal Papanicolaou smears: a prospective study of colposcopy and clinical outcome. Obstet Gynecol 1993; 81: 372-7.
10. Korn AP, Autry M, DeRemer PA, Tan W. Sensitivity of Papanicolaou smear in human immunodeficiency virus-infected women. Obstet Gynecol 1994: 83: 401-4.
11. Mandelblatt JS, Fahs M, Garibaldi K, Senie RT, Peterson HB. Association between HIV infection and cervical neoplasia: Implications for clinical care of women at risk for both conditions. AIDS 1992; 6: 173-8.
12. Smith JR, Kitchen VS, Botcherby M, Hepbuen M, Wells C, Gor D, et al. Is HIV infection associated with an increase in the prevalence of cervical neoplasia? Br J Obstet Gynaecol 1993; 100: 149-53.
13. Wrigth TC Jr, Ellerbrock TV, Chiasson MA, Van Devanter N, Sun XW. Cervical intraepithelial neoplasia in women infected with human immunodeficiency virus: prevalence, risk factor, and validity of Papanicolaou smears. New York Cervical Disease Study. Obstet Gynecol 1994; 84: 591-7.
14. Massad LS, Riester KA, Anastos KM, Fruchter RG, Palefsky JM, Burk RD, et al. Prevalence and predictors of squamous cell abnormalities in Papanicolaou smears from women infected with HIV-1. Women's Interagency HIV Study Group. J Acquir Immune Defic Syndr 1999; 21: 33-41.
15. Heard I, Tassie JM, Kazatchkine MD, Orth G. Highly active antiretroviral therapy enhances regression of cervical intraepithelial neoplasia in HIV-seropositive women. AIDS 2002; 16: 1799-802.
16. Sellors J, Lewis K, Kidula N, Muhombe K, Tsu V, Herdman C. Screening and management of precancerous lesions to prevent cervical cancer in low-resource settings. Asian Pac J Cancer Prev 2003; 4: 277-80.

การศึกษาความชุกของ squamous intraepithelial lesion และ squamous cell carcinoma ในสตรีที่ติดเชื้อเอช ไอ วี ณ คลินิกนิรนาม โรงพยาบาลชลบุรี

วิยะดา เหลืองด่านสกุล, พิชชา ปิ่นจันทร์, จุรีรัตน์ บวรวัฒนุวงศ์

การวิจัยเชิงพรรณนาแบบไปข้างหน้านี้ เพื่อศึกษาความชุกของความผิดปกติของเซลล์เยื่อบุผิวปากมดลูกในสตรีผู้ติดเชื้อเอช ไอ วี

สตรีผู้ติดเชื้อเอช ไอ วี จำนวน 231 คนได้เข้าร่วมการศึกษา ณ โรงพยาบาลชลบุรี ข้อมูลได้จากการสัมภาษณ์ สตรีเหล่านี้จะได้รับการตรวจมะเร็งปากมดลูกและผล Pap smear ถูกแบ่งกลุ่มโดยใช้ Bethesda system ปีพ.ศ. 2536 Pap smear อ่านโดยเจ้าพนักงานเซลล์วิทยาและผลPap smear ที่ผิดปกติจะได้รับการตรวจสอบซ้ำโดยพยาธิแพทย์ พบอุบัติการณ์ของ Low-grade squamous intraepithelial lesion (LSIL) ร้อยละ 2.2 High-grade squamous intraepithelial lesion (HSIL) ร้อยละ 8.3 และ squamous cell carcinoma (SCCA) ร้อยละ 2.2 ตามลำดับ พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างระยะเวลาการติดเชื้อเอชไอวีกับการเกิดความผิดปกติของเซลล์เยื่อบุผิวปากมดลูก (p = 0.007) จากการศึกษานี้พบความชุกของความผิดปกติของเซลล์เยื่อบุผิวปากมดลูกสูงในสตรีผู้ติดเชื้อเอชไอวี